The Effect of Genistein on Thyroid Hormone-dependent Tail Regression in the *Rana catesbeiana* Tadpole

by

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Abstract

Thyroid hormone (TH) regulated gene expression is mediated by TH binding to thyroid hormone nuclear receptors (TRs). Despite extensive studies in mammalian cells that showed that signaling pathways, such as the mitogen-activated protein kinase, cyclin-dependent-kinase, and tyrosine kinase signaling are involved in the regulation of diverse and important TH functions, little is known about their regulation and functional roles *in vivo* during development. Anuran metamorphosis is a postembryonic process that is absolutely dependent upon the presence of TH. Tadpole tail resorption is one of the last changes during anuran natural metamorphosis and is entirely controlled by TH. This process can be precociously induced by exogenous administration of 3,5,3'-triiodothyronine (T_3). In this study, it is shown that genistein inhibits T_3-induced tail regression in the *Rana catesbeiana* tadpole. This inhibition is *via* inhibition of tyrosine kinase action rather than through genistein's classic estrogenic action. Quantitative polymerase chain reaction analysis demonstrates that genistein significantly attenuates T_3-induced up-regulation of TRβ mRNA but not TRα mRNA. Further evidence shows that genistein affects T_3-induced phosphorylation of TRα, which indicates that phosphorylation is an important factor in establishing T_3-dependent gene expression programs. Partial sequences of two inhibitor of growth (ING)1 variants were cloned from the tail (*rING1*$_{tail}$) and brain (*rING1*$_{brain}$) of *Rana catesbeiana*. rING1$_{brain}$ mRNA is a T_3-responsive gene and is down-regulated by genistein during the T_3-induced tail regression program. cDNA array analysis suggests that gelatinase B may also require tyrosine kinase signaling during T_3-dependent tadpole tail regression. Taken together, these findings demonstrate that genistein affects T_3 signaling in the context of normal cells *in*

vivo and indicate that phosphorylation is important for the establishment of T_3-dependent gene expression programs.

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List of Abbreviations

5'-D	5'-deiodinase
5'-D-I	5'-deiodinase-I
5'-D-II	5'-deiodinase-II
°C	Degree Celsius
aRNA	Amplified RNA
AIB	Amplified in breast cancer-1 protein
ATP	Adenosine triphosphate
bp	Base pair
C/EBP	CCAAT/enhancer core binding protein
CAT	TRE-chloramphenicol acetyltransferase
CBP	CREB-binding protein
Cdk	Cyclin-dependent-kinase
cDNA	Complementary deoxyribonucleic acid
Ci	Curie
CP	Cross points
CREB	cyclic adenosine monophosphate-response element-binding protein
CTD	Carboxy-terminal domain
d	Day
DAD-1	Defender against cell death 1
dATP	Deoxyadenosinetriphosphate
DBD	DNA-binding domain
D-D	Tadpole injected with DMSO and tail tip incubated in DMSO-containing medium

DMBA	7,12-dimethylbenzantracene
DEPC	Diethyl pyrocarbonate
D-G	Tadpole injected with DMSO and tail tip incubated in genistein-containing medium
DIT	Diiodotyrosine
DLL4	Distal-less 4
DMSO	Dimethyl sulfoxide
DNA	Deoxyribonucleic acid
dNTP	Deoxynucleotidetriphosphate
DRIPs	Vitamin D receptor interactin proteins
DRs	Direct repeats
DTT	Dithiothreitol
E_2	17β-estradiol
EGFR	Epidermal growth factor receptor
EMSA	Electrophoretic mobility shift assays
ER	Estrogen receptor
ERE	Estrogen response elements
ERK	Extracellular regulated protein kinase
EtBr	Ethidium bromide
EtOH	Ethanol
G	Genistein
GAPDH	Glyceraldehyde-3-phosphate dehydrogenase
GM	Geometric mean
GPCR	G protein–coupled receptor

GSK-3	Glycogen synthase kinase 3
GTF	General transcription factor
h	hour
HATs	Histone acetyl transferase
HBD	Hormone binding domain
HDAC1	Histone deacetylase 1
HPT	Hypothalamic/pituitary/thyroid axis
HRE	Hormone response elements
HSP	Heat shock protein
IFN-γ	Human interferon- γ
IGFR	Insulin-like growth factor receptor
ING1	Inhibitor of growth 1
IP	Immunoprecipitation
IPs	Inverted palindromes
K_d	Dissociation constant
LB medium	Luria-Bertani medium
LBD	Ligand-binding-domain
Lyz	Lysozyme
m	Milli
μ	Micro
M	Molarity
MAGEX	Multispecies analysis of gene expression
MAPK	Mitogen-activated protein kinase

μCi	microCurie
MEK	MAPK/ERK activating kinase
mg	Milligram
MHC	Major histocompatibility complex
MIT	3-monoiodotyrosine
ml	Millitre
μl	Microlitre
mm	Milmetre
mM	Millimolar
mRNA	messenger RNA
mSin3A	Mammalian Sin3
mtPPAR	Mitochondrial peroxisome proliferator activator receptor
mtRXR	Mitochondrial retinoid X receptor
NCoR	Nuclear receptor co-repressor
NF	Normalization factor
nm	Nanometre
P/CAF	p300/CBP-associated factor
p160/SRCs	Steroid receptor co-activators
p300/CBP	cAMP-response element-binding protein
pal	Palindromes
PCR	Polymerase chain reaction
PDGFR	Platelet-derived growth factor receptor
PHD finger	Plant homeodomian finger

PI3K	Phosphoinositide-3 kinase
PKA	Protein kinase A
PKC	Protein kinase C
PLC	Phospholipase C
PLD	Phospholipase D
pmol	picomole
PTK	Protein tyrosine kinase
QPCR	Quantitative PCR
RARs	Retinoic acid receptors
RNA	Ribonucleic acid
rT_3	Reverse T_3
RT-PCR	Reverse transcription-PCR
RXR	Retinoid X receptor
RXRs	Retinoid X receptors
SD	Standard deviation
SDS	Sodium dodecyl sulfate
SDS-PAGE	SDS-polyacrylamide gel electrophoresis
SMRT	Silencing mediator of retinoid and thyroid hormone receptors
SPARC	Secreted protein acidic and rich in cysteine
SPI+	Soy protein isolate
SRC-1	Steroid receptor coactivator-1
SSC	Sodium chloride and sodium citrate
ST3	Stromelysin 3

STAT	Signal transducers and activators of transcription
T_3	3,5,3'-triiodothyronine
T_4	Thyroxine
TAF	TBP associated factor
Taq	DNA *Thermus aquaticus* DNA polymerase
TBG	Thyroxine binding globulin
TBP	TATA box binding protein
T_3-D	Tadpole injected with T_3 and tail tip incubated in DMSO-containing medium
TF	Transcription factor
Tg	Thyroglobuin
T_3-G	Tadpole injected with T_3 and tail tip incubated in genistein-containing medium
TGF	Transforming growth factor
TH	Thyroid hormone
TH/bZIP	TH-induced basic leucine-zipper containing transcription factor gene
TK stage	Taylor and Kollros stage
TMEM	Tadpole minimal essential medium
TPO	Thyroid peroxidase
TR	Thyroid hormone receptor
TRAPs	Thyroid receptor associated proteins
TRE	Thyroid hormone response element
TRH	Thyrotropin releasing hormone
TSH	Thyroid stimulating hormone or pituitary thyrotropin

Chapter 1. Introduction

I. Thyroid Hormone and Genistein Overview

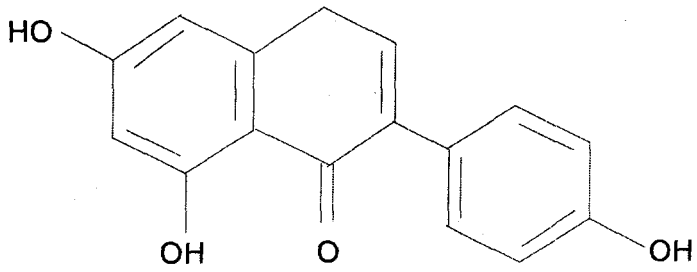
The thyroid hormones (THs), 3,5,3'-triiodothyronine (T_3) and 3,5,3',5'-tetraiodothyronine (T_4, thyroxine), play critical roles in the growth, metabolism, differentiation, and apoptosis of nearly all tissues in a variety of organisms such as fish, amphibia, and higher vertebrates [1]. During the past century, advances in clinical medicine, physiology, biochemistry, and molecular genetics have greatly enhanced our understanding of TH action. In humans, thyroid gland disorders are one of the most common endocrine diseases. For example, endemic cretinism (caused by iodine deficiency and subsequent lack of TH synthesis) is still a huge public health problem in developing countries. In North America, about 7% of the population has thyroid disease making this the most common endocrine disorder. Neonatal hypothyroidism can cause mental retardation and permanent neurological defects because TH is responsible for myelin basic protein synthesis and myelination of axons in the brain [1]. TH is required for the homeostasis of nearly all organs in the human body, including brain, bone, heart, and liver. The study of TH action has great biological and medical implications. Molecular genetics has provided insight into our understanding of the mechanisms of TH action in normal and disease states. Recent studies at the molecular level have demonstrated that TH regulates target gene expression through genomic effects by binding thyroid hormone nuclear receptors (TRs) [1]. However, there is increasing

evidence of signaling transduction and membrane receptors [2] or transporters [3-5] that could affect TH genomic action [6-10].

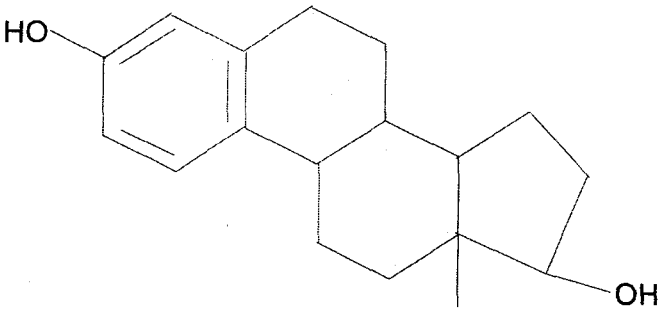
Genistein (4',5,7—trihydroxyisoflavone) is a precursor of phytoalexins in legumes and an important nutraceutical molecule found in soybean seeds [11]. Genistein, a phytoestrogen, has structural similarity to 17β estradiol (**Figure 1.1**) and a wide variety of pharmacological effects on animal cells [11]. In the last 10 years, two important observations have significantly shaped research on genistein. Since 1991, many epidemiological studies have reported that Asian women who consume traditional diets (high in soy products) have low incidences of breast cancer [12]. This finding suggests a possible correlation between soy diet and morbidity of breast cancer. Based on both epidemiological and animal model studies, genistein has been linked with a variety of potential beneficial health effects, which include: chemoprevention of breast [12, 13] and prostate cancers [14], cardiovascular disease [15], osteoporosis [16] and relief of menopausal symptoms [17]. Most of these effects are associated with genistein's estrogenic activity. Moreover, *in vitro* research has demonstrated that genistein can act as a specific inhibitor of tyrosine kinases [18] affecting different growth factor signaling pathways in cells [7, 19, 20]. Further, a series of *in vitro* and *in vivo* studies has demonstrated that genistein can also inhibit thyroid peroxidase (TPO) [7, 19-24] and 5'-deiodinase (5'-D) [25], two important enzymes involved in the synthesis and metabolism of TH. It is not known whether genistein can affect TH signaling at the cellular level leading to a change in biological consequence.

II Thyroid Hormone Background

i. Thyroid hormone synthesis and regulation.



Genistein



Estradiol

Figure 1.1. Structure of genistein in relation to estradiol.

Modified from Dixon *et al.* [11].

Thyroid hormones are synthesized in the follicular cells of the thyroid gland under the regulation of pituitary thyrotropin (TSH) [26, 27]. Initially, thyroglobulin (Tg), a large globular glycoprotein containing tyrosine residues, is synthesized in the follicular cells and transported to the cell surface (**Figure 1.2**). Once at the surface, thyroglobulin is iodinated by thyroid peroxidase (TPO), a membrane-bound heme-protein enzyme located at the apical surface, which activates I^- and couples iodinated tyrosines to form thyronines. The iodinated Tg containing 3-monoiodotyrosine (MIT), 3,5-diiodotyrosine (DIT), T_3, and T_4 (thyroxine) (**Figure 1.3**) is transported to the lumen of thyroid follicles as a component of colloid. With the stimulation of TSH, the iodinated Tg, stored in the lumen of follicles is endocytosed into the follicular cells and hydrolyzed. Tg hydrolysis occurs within the endolysosome and releases MIT, DIT, T_3 and T_4. Only T_3 and T_4 diffuse from the cell into the capillary network surrounding the follicles.

TH synthesis and secretion is accurately regulated by a negative-feedback system that involves the hypothalamus, pituitary, and thyroid gland (hypothalamic/pituitary/thyroid (HPT) axis) (**Figure 1.4**). TH negatively regulates both thyrotropin releasing hormone (TRH) and TSH secretion [26, 27] in mammals. However, in anuran amphibian, instead of TRH, it is corticotrophin releasing factor (CRF) that acts as a stimulator to release TSH from the pituitary gland [28].

ii. Deiodinase enzymes involved in thyroid hormone activation and inactivation.

Most of the circulating thyroid hormones (about 99%) are bound reversibly to plasma carrier proteins, such as thyroxine binding globulin (TBG), albumin, and thyroid binding prealbumin (also called transthyretin). Only the free TH enters target cells to exert biological effects [27]. In most cases, T_4 is the major circulating thyroid hormone

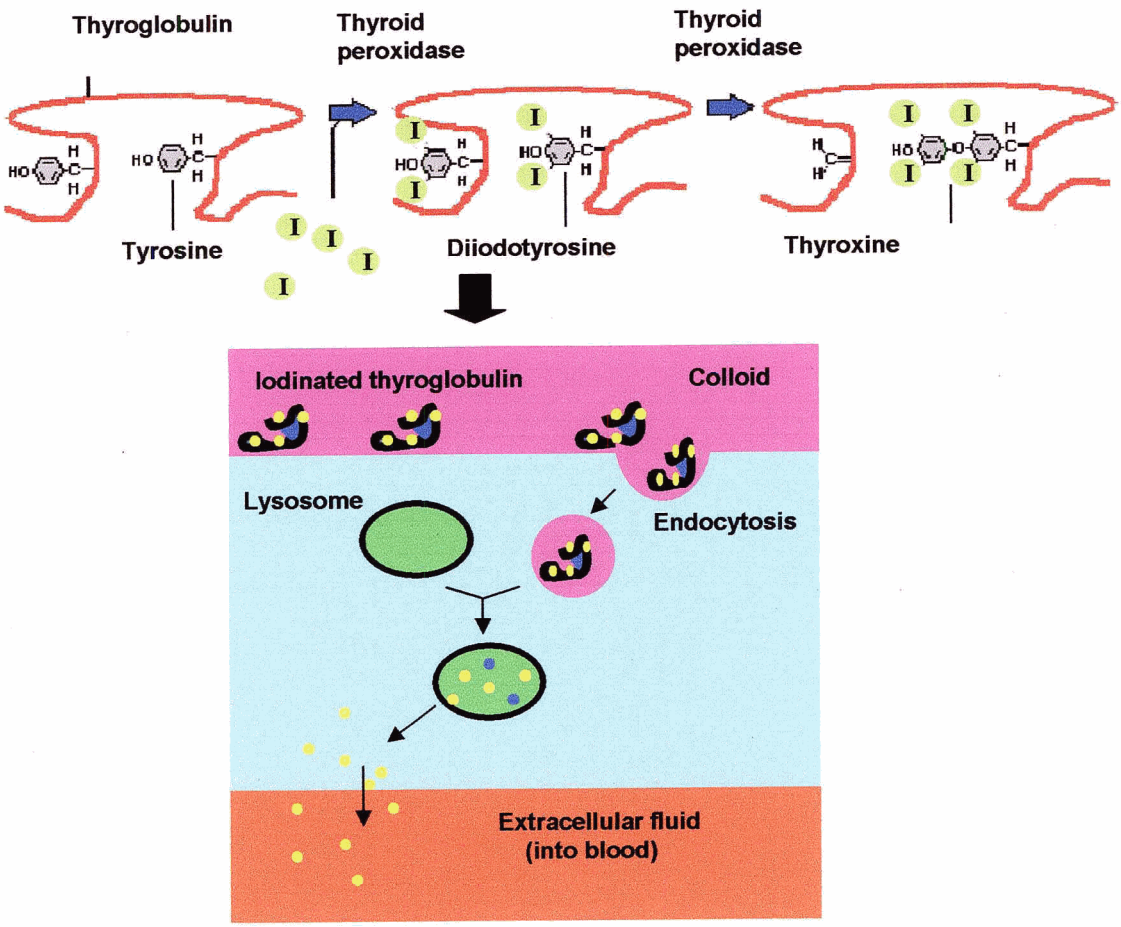


Figure 1.2. The steps of thyroid hormone biosynthesis and release.

The yellow circles represent 3,5,3'-triiodothyronine (T_3) and 3,5,3',5'-tetraiodothyronine (T_4, thyroxine). The blue circles denote 3-monoiodotyrosine (MIT) and 3,5-diiodotyrosine (DIT).

Modified from

http://arbl.cvmbs.colostate.edu/hbooks/pathphys/endocrine/thyroid/physio.html

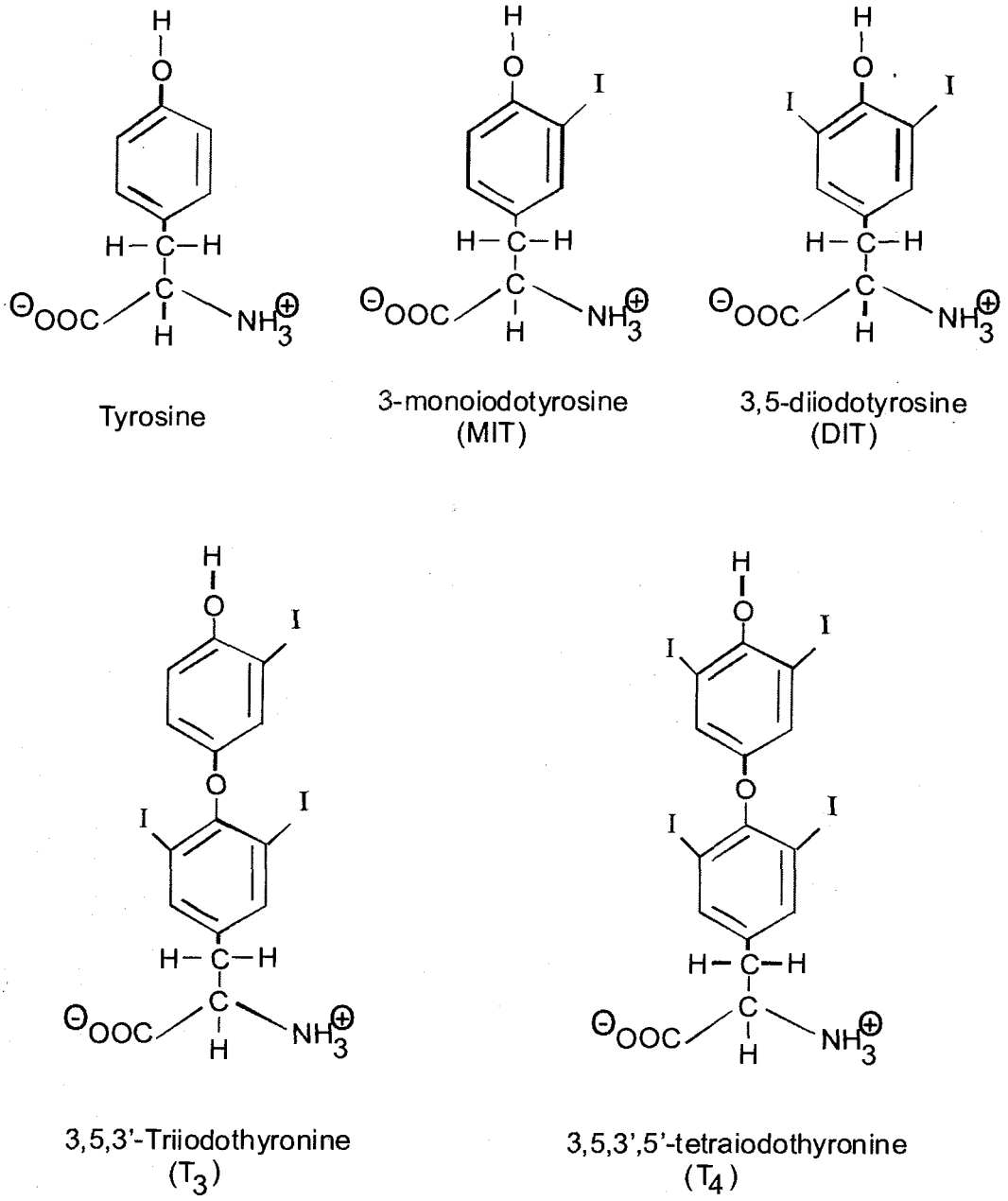


Figure 1.3. Structure of tyrosine, 3-monoiodotyrosine (MIT), 3,5-diiodotyrosine (DIT), 3,5,3'-triiodothyronine (T_3), and 3,5,3',5'-tetraiodothyronine (T_4, thyroxine).

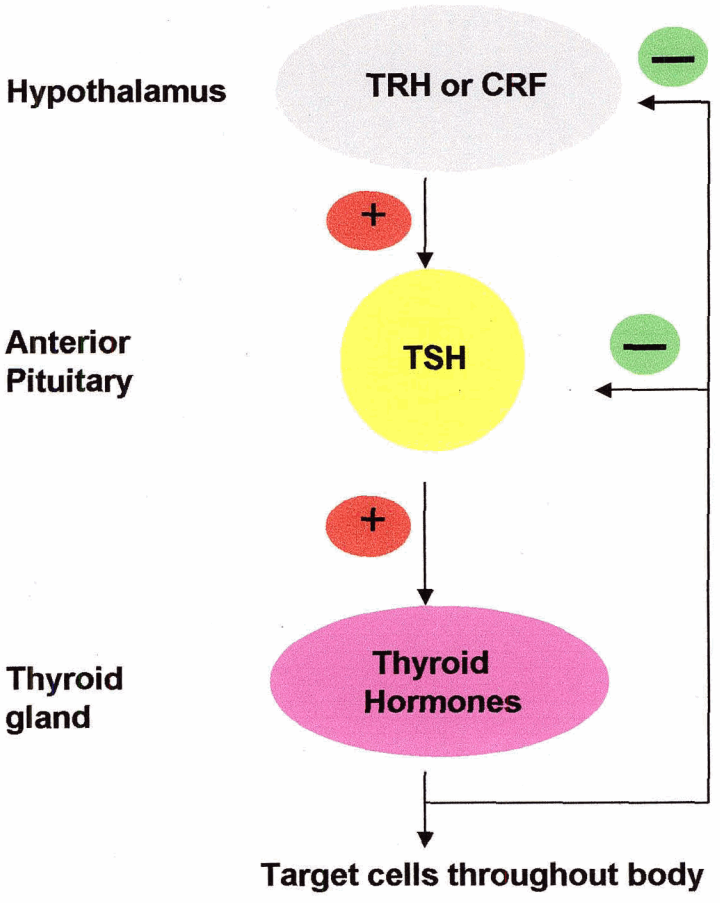


Figure 1.4. Regulation of thyroid hormone synthesis and secretion.

The thyroid gland is part of the hypothalamic-pituitary-thyroid axis, and control of thyroid hormone secretion is exerted by classical negative feedback. Thyroid-releasing hormone (TRH) (in mammals) or corticotrophin releasing factor (CRF) (in anuran amphibian) from the hypothalamus stimulates TSH from the pituitary, which stimulates thyroid hormone release. As blood concentrations of thyroid hormones increase, they inhibit both TSH and TRH or CRF, leading to "shutdown" of thyroid epithelial cells. Later, when blood levels of thyroid hormone have decayed, the negative feedback signal fades, and the system wakes up again. Modified from http://arbl.cvmbs.colostate.edu/hbooks/pathphys/endocrine/thyroid/physio.html

(in mammals, total serum T_4 is 40-fold higher than serum T_3) and is converted to T_3 by 5'-deiodinase (5'-D) at peripheral tissues [1]. There are two types of 5'-deiodinases known in mammals, 5'-deiodinase-I (5'D-I) which is found primarily in the liver, kidney, and thyroid and 5'-deiodinase II (5'D-II) which is found in the brain, pituitary, and placenta (**Table 1.1**). A third deiodinase, 5-deiodinase-III (5 D-III), found in the brain and placenta, can convert T_3 to T_2. Free T_3 is the most biologically active form of the hormone [1].

III. Thyroid Hormone Classical Genomic Effects

T_3 and T_4 are hydrophobic, and their mechanisms of action are similar to those of steroid hormones. TH, like steroid hormones that have a lipophilic nature, is thought to enter target cells by passive diffusion. However, there is some evidence to support the concept that a carrier system is important for both steroid and thyroid hormones to enter cells. For example, Ritchie *et al.* [3] using *Xenopus* oocytes demonstrated that System L serves as a plasma membrane transporter of T_3 to the nucleus and enhances transcriptional activation by TRs. Conversely, specific inhibitors blocking System L activity decreases both T_3 uptake and TR function.

Early studies showed that the effects of TH at the genomic level are mediated by the binding of TH to nuclear TRs. In the nucleus, TH binds to TRs with high affinity and specificity. The K_d (dissociation constant) of T_3 is about 10^{-10} M [29]. TRs, which have 10-fold greater affinity for T_3 than T_4 [29], function as monomers, homodimers, and heterodimers [1]. The heterodimer is commonly formed between TRs and retinoid X receptors (RXRs). RXR heterodimerization with TR enhances the specificity and efficiency of the receptor interaction with the thyroid response elements (TREs) thereby

Table 1.1. Characteristics of the human iodothyronine deiodinases. Adapted from Griffin *et al.* [29].

	Type I	Type II	Type III
Deiodination site	5' and 5	5'	5
Physiologic roles	• Provide T_3 for the circulation • Inactivate T_4 and T_3 • Degrade rT_3	• Provide intracellular T_3 in pituitary, brain, and brown adipose tissue • Provide T_3 for the circulation	• Inactivate T_4 and T_3
Tissue location	Liver, kidney, thyroid, brain	Pituitary, brain, brown adipose tissue, placenta, thyroid, skeletal and cardiac muscle	Brain, placenta, skin

modulating transcriptional activity [1]. TRs regulate gene expression by binding to specific TREs in the promoters of T_3-target genes then activate or repress transcription in response to hormone [30-32]. In unliganded state, TRs associate with co-repressors and then actively repress transcription. In the presence of T_3, TRs dissociate from co-repressors and bind to co-activators and activate transcription (**Figure 1.5**). These nuclear actions (called the classical genomic effects) of T_3 are sensitive to inhibitors of transcription and translation and have a considerable latency with response times in hours to days [1].

i. Thyroid hormone receptor isoforms.

Vennstrom and Evans first cloned TR in 1986 from embryonic chicken (TRα) and human placental (TRβ) cDNA libraries [33, 34], respectively, and showed that TRs are the cellular homologues of v-*erb A*, a known viral oncogene. Presently, TRs belong to a large superfamily of nuclear hormone receptors including steroid, vitamin D, retinoic acid receptors, and "orphan" receptors, which have no known ligand or function [1].

The two different genes *THRA* and *THRB* encode eight nuclear TR isoforms due to alternative splicing or alternative promoter usage (**Figure 1.6b**). TRα and TRβ are encoded on human chromosomes 17 and 3 respectively. All isoforms of TR share a similar domain organization (**Figure 1.6a**): an amino-terminal A/B domain, a central DNA-binding domain (DBD) containing two "zinc fingers" (**Figure 1.7**), a hinge region (lysine-rich sequence that is highly conserved among TRs) containing the nuclear localization signal, and a carboxyl-terminal ligand-binding domain (LBD). The DBD is localized N-terminal to these domains and the two zinc-fingers are responsible for the

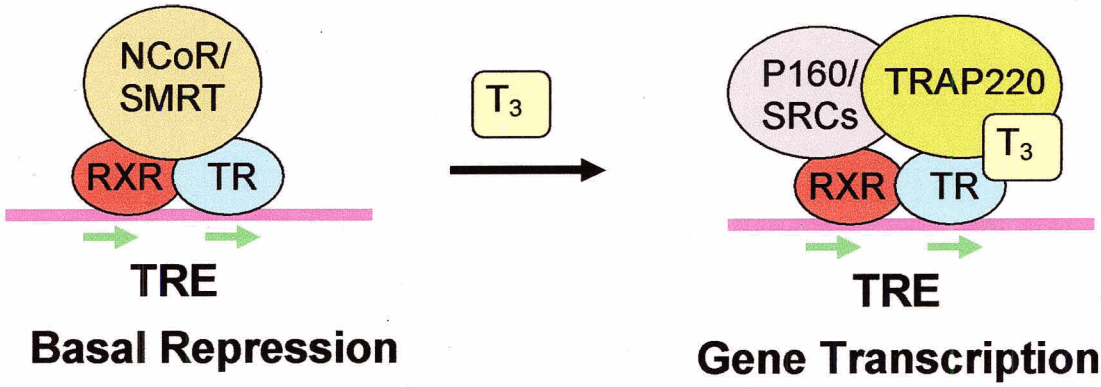


Figure 1.5. General model for thyroid hormone action in the nucleus.

In the nucleus, unliganded TR associates with co-repressors NCoR (nuclear receptor co-repressor) and SMRT (silencing mediator of retinoid and TH receptors) and then actively represses transcription. T_3 binding of the TR leads to dissociation of co-repressors and binding of co-activators p160/ SRCs (steroid receptor co-activators) and TRAPs (thyroid receptor associated proteins). This results in the relief of basal transcriptional repression and induction of transcription. The green arrows denote direct repeats of TRE half-sites. Abbreviations: thyroid hormone receptor (TR), retinoid X receptors (RXR), thyroid hormone responsive element (TRE). Modified from Bassett *et al.* [30].

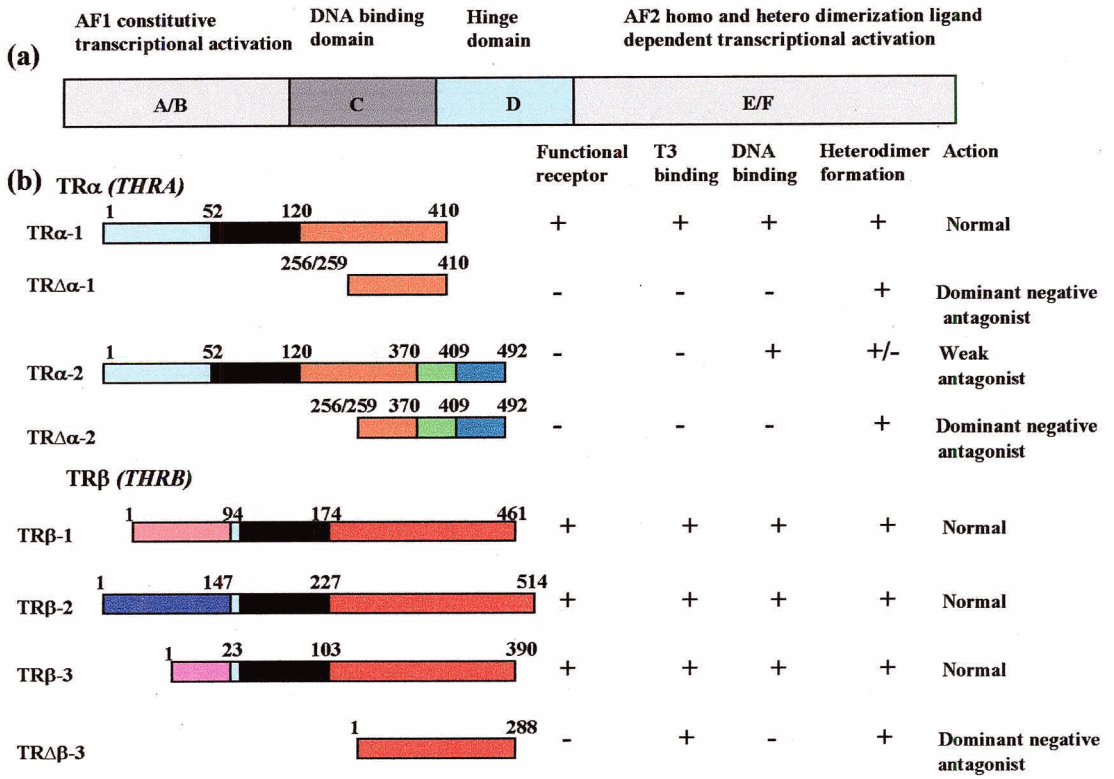


Figure 1.6. A schematic representation of the four functional domains of the thyroid hormone receptor protein is shown in (a). The protein products of the thyroid hormone receptor alpha and beta genes (*THRA* and *THRB*) are shown in (b).

The TR isoforms are generated by alternative splicing or alternative promoter usage of the two TR genes encoding TRα and TRβ. Colours represent identical or divergent regions that result from alternative mRNA splicing. The filled black region represents the DNA binding domain. Modified from Bassett *et al.* [30].

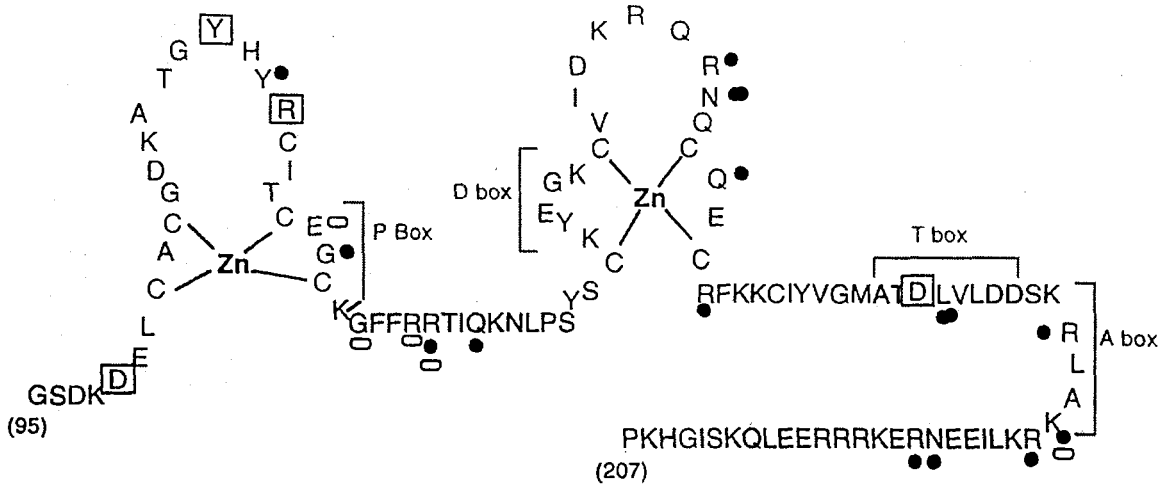


Figure 1.7. The DNA-binding domain of human TRα.

Schematic drawing of the two zinc fingers of human TRα and the various subregions within the DNA-binding domains. Squares, TR/RXR heterodimerization contacts; ovals, direct base contacts; solid circles, direct phosphate contacts. Adapted from Yen *et al.* [1].

binding to TREs and also for dimerization. The LBD is not only critical for TH binding but also necessary for dimerization, transactivation, and basal repression by unliganded TRs [1]. The LBD consists of 12 α-helices that are arranged to create a pocket for ligand binding (**Figure 1.8**). The helix 12 is essential for the switch of the receptor from a silencer to an activator. In the absence of TH, helix 12 protrudes away from the core structure of the LBD and allows corepressor binding. TH binding induces helix 12 to contact to the LBD core, which results in corepressor release and coactivator association [35]. Deletion of helix 12 leads to constitutive silencing even in the presence of ligand [36]. This indicates that helix 12 is involved in the coordination of repression and activation.

Five out of eight TR isoforms (**Figure 1.6b**) TRα1, and TRβ1, TRβ2, TRβ3 and TRΔβ3 can bind T_3. Three isoforms TRα2, TRΔα1, TRΔα2, which are derived from the TRα locus, are not able to bind T_3 and act as TR inhibitors [37]. TRΔα1 and TRΔα2 lack the DBD. TRα2 cannot bind T_3 because its carboxyl-terminal replaces a region (122-amino acids) in TRα1 that is critical for TH binding [1].

TRα1, TRα2, TRβ1 and TRβ3 are expressed ubiquitously in all tissues, whereas TRβ2 is predominantly restricted to the hypothalamic/pituitary axis. TRβ2 acts as a negative regulator of thyroid stimulating hormone (TSH) α- and β- subunit transcription [30]. Selective generation of transgenic and knockout mouse models has shed light on the roles of TRs in the regulation of specific target genes and development. These studies indicated that TRα is responsible for postnatal development, heart rate and temperature regulation. The TRβ seems to be mainly involved in the appropriate maturation of cochelar and retinal cells and the regulation of liver metabolism [38].

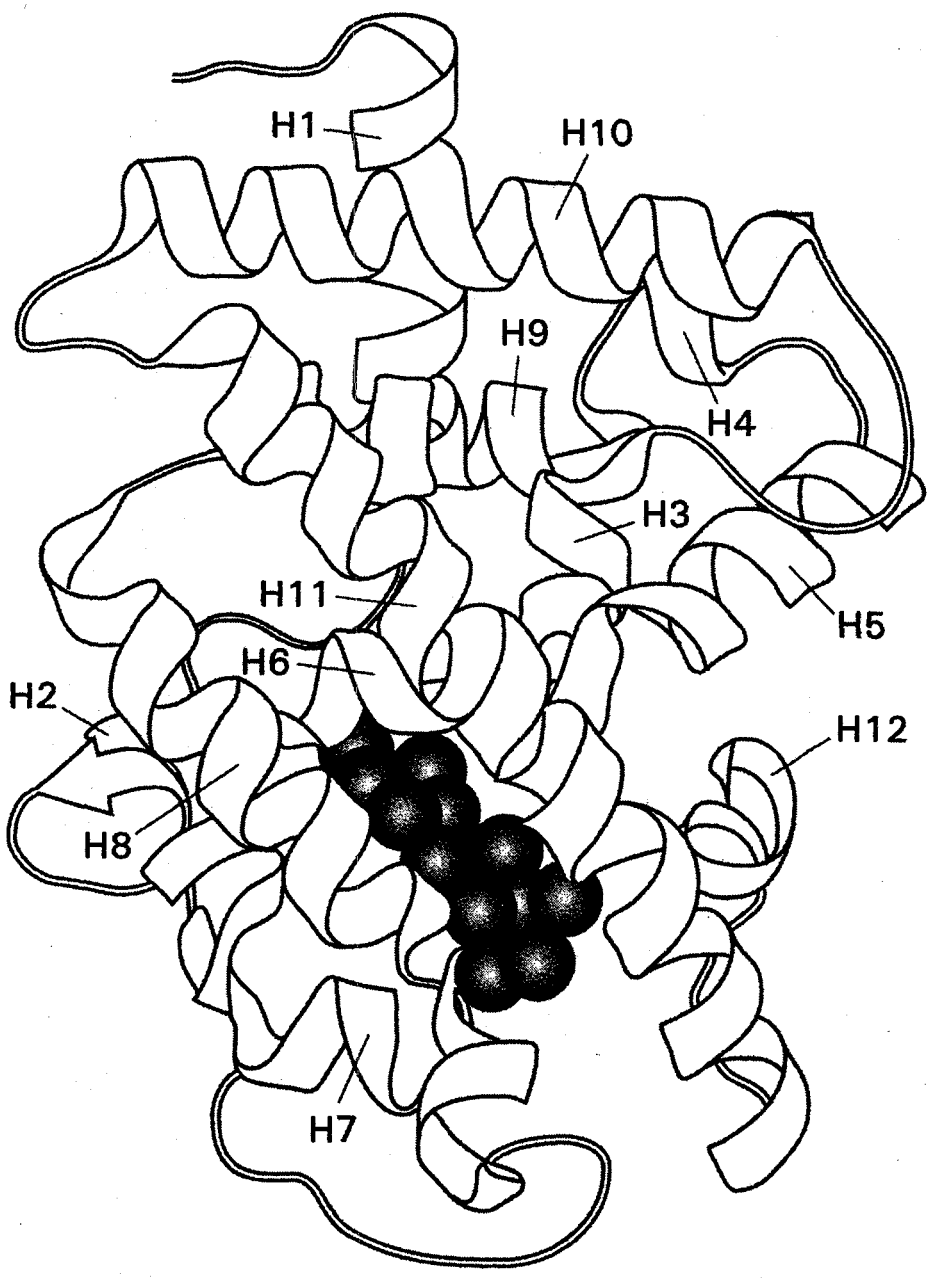


Figure 1.8. TRα-1 ligand-binding domain (LBD) crystal structure.

α-Helices (H) are indicated and the T_3 ligand is represented as a series of dark spheres. Adapted from Yen *et al.* [1]

ii. Thyroid hormone response elements.

TRs bind to the thyroid hormone response elements (TREs), which contain consensus hexamer half-site sequences (G/A)GGT(C/G)A, as monomers, homodimers, and heterodimers. Most TREs are located upstream of the promoter. There is considerable variation in the nucleotide sequences, number, spacing, and orientation of TRE half-sites. Half-sites are arranged as palindromes (TREpal), direct repeats (DRs), and inverted palindromes (IPs). Among 30 known natural TREs, DRs are more common than IPs which are more common than TREpal [1]. The optimal spacing for these half-site arrangements is zero, four, and six nucleotides, respectively (TREpal0, DR4, and IP6) (**Figure 1.9**).

iii. Thyroid hormone receptor co-regulators.

The classical genomic model of steroid hormone action dictates that ligand binding leads to a conformational change in the nuclear receptor, which results an exchange of co-activators/accessory proteins. In the nucleus, the ligand/receptor complex binds DNA at hormone response elements (HREs) in the promoters of target genes leading to chromatin modification and regulation of gene transcription [39]. *In vitro* and *in vivo* studies in *Xenopus laevis* have shown that co-repressor/co-activators recruited to unliganded or liganded TRs bind to TREs regulating target gene transcription [32, 40].

In the absence of TH (**Figure 1.10a**), the corepressor complexes, which contain histone deacetylases (HDACs), bind to helices three and five of the unliganded TR LBD [30]. This TR/RXR/corepressor complexes leads to histone deacetylation and gene repression. There are two well-characterized corepressors: nuclear receptor corepresssor

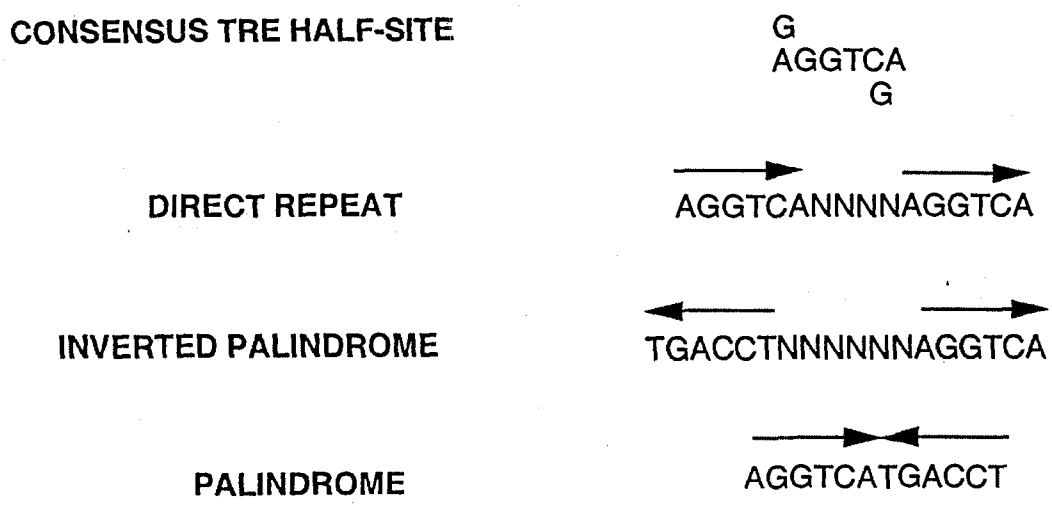


Figure 1.9. Half-site orientation and optimal nucleotide spacing between half-sites of thyroid hormone response element (TRE).

N refers to nucleotides, and arrows show direction of half-sites on the sense strand. Adapted from Yen *et al.* [1].

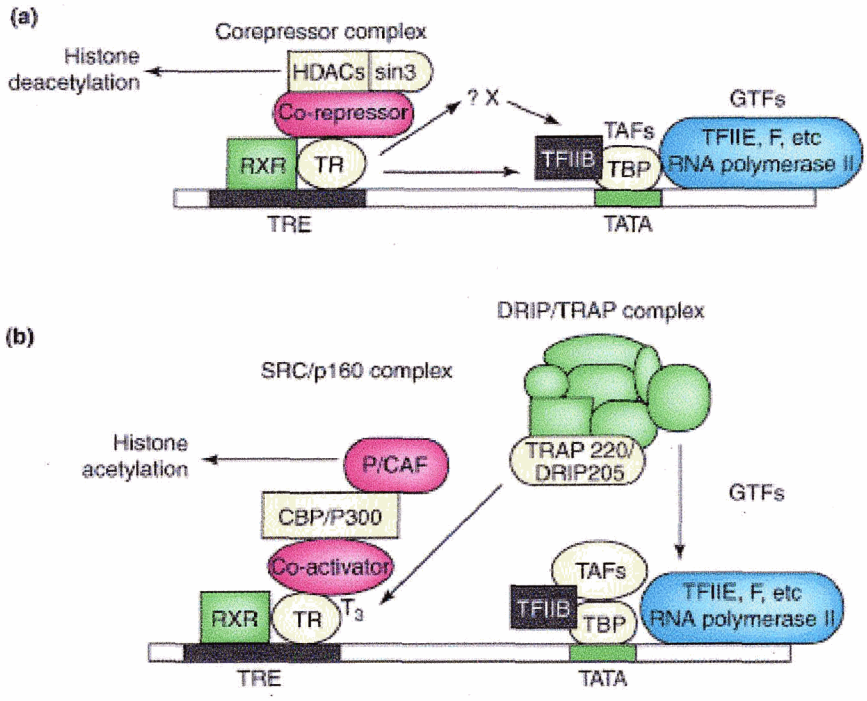


Figure 1.10. A molecular model for (a) basal repression by corepressors in the absence of T_3 and (b) transcriptional activation by coactivators in the presence of T_3.

Abbreviations: cAMP-response element-binding protein (CBP), vitamin D receptor-interacting protein (DRIP), general transcription factor (GTF), histone deacetylase (HDAC), p300/CBP-associated factor (P/CAF), retinoid X receptor (RXR), steroid receptor coactivator (SRC), TATA-binding protein-associated factor (TAF), TATA-binding protein (TBP), transcription factor (TF), thyroid hormone receptor (TR), TR-associated protein (TRAP), thyroid hormone-response element (TRE). Adapted from Yen *et al.* [41].

(NCoR) and silencing mediator of retinoid and TH receptors (SMRT). NCoR, a 270-kDa protein, can interact with both RXRs and retinoic acid receptors (RARs). NCoR also interacts with preinitiation transcriptional complex II members, TFIIB, TAFII32, and TAFII7. Therefore, part of its ability to repress transcription may be due to its ability to interact with the preinitiation transcriptional complex. SMRT, containing sequence homology to NCoR, is able to modulate basal repression of TRs and RARs in cotransfection studies [42, 43]. Moreover, corepressors can complex with other repressors, such as Sin3 and histone deacetylase 1 (HDAC1). Thus histone deacetylation, which helps maintain local chromatin structure in a repressive state, may play a critical role in basal repression by nuclear hormone receptors [1, 40].

When TH is present (**Figure 1.10b**), corepressor complexes dissociate from TR/RXR heterodimers. Coactivator complexes, which often contain histone acetyl transferase (HATs) activity, can then bind to TR/RXR heterodimers, leading to histone acetylation and gene expression. So, it is hypothesized that TH activates gene transcription in part by increasing local acetylation of histone [1]. Steroid receptor co-activator (p160/SRC1) is an example of a co-activator having intrinsic HAT activity. The SRC1-associated protein, cAMP-response element-binding protein (p300/CBP), directly binds RNA polymerase II thus acting as an adaptor protein for liganded TR/RXR and the basal transcriptional machinery [30]. In addition to coactivator complexes having histone acetyltransferase activities, other coactivator complexes have been identified. TR associated proteins (TRAPs) or Vitamin D receptor interacting proteins (DRIPs) are other well characterized co-activators which lack HAT activity. The critical co-activator

TRAP220 anchors a TRAP/DRIP complex of proteins that mediates RNA polymerase II binding [44].

A two-stage process of liganded TR/RXR mediate transcriptional activation has been proposed [30]. First, the p160/SRC proteins initially recruit HAT activity leading to chromatin remodeling. This process may then be followed by recruitment of TRAP220 and the TRAP/DRIP complex of proteins to promote gene transcription in a hormone-dependent fashion.

iv. Thyroid hormone receptor phosphorylation.

Phosphorylation has been reported to modulate TR-mediated regulation of transcription both *in vitro* and *in vivo*. Sugaware *et al.* [45] assessed the effect of phosphorylation on the binding of TRβ1 to a TRE by using an electrophoretic mobility shift assay *in vitro*. They expressed human TRβ1 (hTRβ1) in bacteria and phosphorylated it with ATP (the ratio of phosphoserine to phosphothreonine was 5:1) in HeLa cytosolic extract, which lacks endogenous TRs. They found that phosphorylation of hTRβ1 selectively increases binding of the TR homodimer, but not the TR/RXR heterodimer, to TRE. Addition of alkaline phosphatase to phosphorylated hTRβ1 eliminates this increase in TRE binding. However, Bhat *et al.* [46] demonstrated *in vitro* that phosphorylation of TRβ1 enhances TR/RXR heterodimer binding to three different TREs: i) the chicken lysozyme (lyz) gene TRE, ii) Direct repeats of a half-site separated by four gaps (DR4), and iii) a palindromic (Pal) TRE. Furthermore, they cotransfected hTRβ1, RXRβ and TRE-chloramphenicol acetyltransferase (CAT) expression plasmid into CV-1 cells. Using the CAT reporter gene in the absence or presence of okadaic acid, an inhibitor of phosphatases, they showed that okadaic acid enhances hTRβ1-mediated CAT activity.

Although the mechanism of this enhanced transcriptional activation is unknown, these findings suggest that phosphorylation, in addition to ligand binding, may modulate TR-mediated transcription. It is hypothesized that phosphorylation regulates the transcriptional activity of hTRβ1 at several levels [46]. Phosphorylation affects the DNA-binding of both homodimers and heterodimers. It increases the ability of homodimers to bind DNA. As for heterodimers, unphosphorylated hTRβ1/RXR heterodimers bind weakly in the order of DR4 > lyz > Pal. After phosphorylation, not only the binding ability of the heterodimers were enhanced, but also the order of binding activity changes to lyz > DR4 > Pal. Therefore, the extent of TRE binding enhancement depends on the orientation of the half-site binding motifs, suggesting that this increase is mediated by phosphorylation-induced conformational change. The above studies have focused on TRβ. There are limited studies on TRα phosphorylation. One study showed that phosphorylation of rat TRα enhances its nuclear localization [47], but its functional and biological roles are unclear. Thus phosphorylation may be one of the mechanisms by which TRs achieve their diverse biological functions. However, the biological relevance of this phosphorylation *in vivo* remains to be determined.

IV. Thyroid Hormone Non-classical Effects

Most thyroid hormone effects are thought to be primarily mediated *via* binding of the TRs to the TRE in the nucleus. However, non-classical actions for thyroid hormone (T_3 and T_4) have been recognized recently. It is hypothesized that the mechanism of these non-classical effects involves TH binding to putative specific membrane receptors, thereby exerting biological effects through signal transduction pathways including cAMP, calmodulin, phosphatidylinositol, and protein kinase pathways [1, 48]. The recent

identification of novel seven-transmembrane receptors for progestins and estrogens [49-51] and integrin $\alpha_v\beta_3$ as a cell surface receptor for T_4 [2] has highlighted the potential importance of non-classical actions of TH. The putative non-classical effects of TH are diverse and the biological mechanisms are still under investigation.

The major difference between classical genomic and non-classical effects is the time of action [48]. Genomic effects are characterized by their delayed onset, usually more than 10 min. This longer delay may be due to the time required for *de novo* synthesis and processing of proteins, processes that are sensitive to the effects of transcriptional and translational inhibitors (e.g. actinomycin D and cycloheximide). For example, genomic action resulting from mineralocorticoid stimulation takes about 30-min [48]. On the other hand, there is a short delay for non-classical actions, which are insensitive to the inhibitors of transcription or protein synthesis. For example, estrogens have been shown to influence intracellular signaling and vasoregulation within 1-2 min upon administration [48]. Schmidt *et al.* [9] conducted a clinical experiment with T_3 and showed that T_3 treatments cause a significant increase in cardiac output and a decrease in systemic vascular resistance in healthy male volunteers. The time interval of the action was within 3 min of T_3 administration. This short time clearly excludes a genomic effect. **Table 1.2** compares the classical/genomic with non-classical/non-genomic actions of thyroid hormones.

These non-classical responses are frequently associated with the modulation of Na^+, K^+, Ca^{2+} and glucose transport, activation of protein kinase C (PKC), cyclic AMP dependent kinase (PKA) and extracellular signal-regulated protein kinase

Table 1.2. Comparison of thyroid hormone classical and non-classical actions.

	Classical/ genomic actions, Nuclear transcription	Non-classical/non-genomic actions, Cell surface receptor
Ligand	T_3 (hours to days)	T_4/T_3 (seconds to minutes)
Receptor	TRα and TRβ	Putative GPCR
Dimerization partners	RXR, TRs	
Associated factors or signaling pathways	• NCoR/SMRT • SRC/p160/TRAPs	Raf1/MEK/MAPK
Actions	• Basal trascriptional repression • Transcriptional activation • Transcriptional repression	• TR phosphorylation and altered transcriptional activity • p53 phosphorylation and altered transcriptional activity • Increased STAT mediated transcription

Abbreviations: thyroxine (T_4), triiodothyronine (T_3), retinoid X receptor (RXR), thyroid hormone receptor (TR), G protein coupled receptor (GPCR), nuclear receptor co-repressor (NCoR), silencing mediator of RAR and TR (SMRT), steroid receptor cooactivator (SRC), thyroid receptor associated protein (TRAPs), Raf serine/threonine kinase (Raf1), mitogen activated protein kinase kinase (MEK), MAPK mitogen -activated protein kinase (MAPK), signal transducers and activators of transcription (STAT). Modified from Bassett *et al.* [30].

(ERK)/mitogen-activated protein kinase (MAPK) and regulation of phospholipid metabolism by activation of phospholipase C (PLC) and phospholipase D (PLD).

Bassett *et al.* [30] proposed a non-classical action model of TH in mammalian cells. In this model (**Figure 1.11**), T_4 or T_3 initially bind a putative G protein coupled receptor (GPCR). TH binding results in activation of PLC and PKC, the PKA may also be involved. Then PKC activates PLD sustaining the non-classical response and also activates the Raf serine/threonine kinase (Raf1) leading to MAPK phosphorylation *via* the mitogen activated protein kinase kinase (MEK). Tyrosine phosphorylation of MAPK results in its nuclear translocation and its phosphorylation of TRs, signal transducer and activator of transcription (STAT) and p53 (a tumor suppressor gene). Serine phosphorylation of TRs induces dissociation from the co-repressors NCoR and SMRT and increase transcriptional activity following binding of ligand, RXR and the co-activators p160/SRCs and TRAPs. In the cytoplasm, activated MEK also tyrosine phosphorylates STAT1α and STAT3 resulting in their activation and nuclear translocation, further serine phosphorylation of these STATs by the nuclear MAPK maximizes the STAT transcriptional activity.

More recent studies described below suggest some possible mechanisms for the non-classical effects of TH. Using whole-cell recording methods and fluorescence microscopy, Wang *et al.* [10] demonstrated that when cat atrial myocytes are acutely exposed to T_3, the inward Na^+ current and cardiac contraction strength are significantly increased. However, treatment with either reverse T_3 (rT_3) or T_4 has no effect on Na^+ movement. This suggests that acute T_3 exposure increases Na^+ influx and thereby stimulates reverse-mode, Na^+-Ca^{2+} exchange, to increase intracellular Ca^{2+} concentration

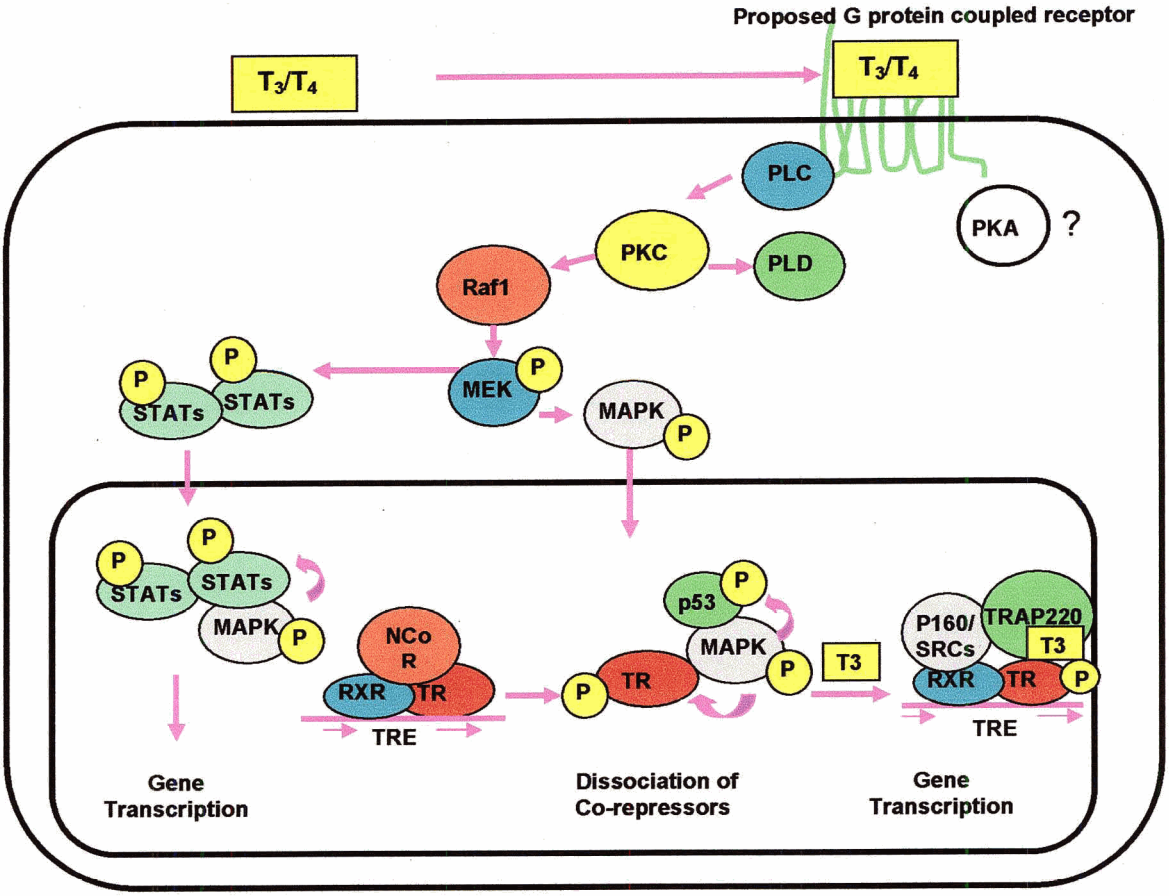


Figure 1.11. Schematic representation of the proposed mechanism by which thyroid hormone activates the MAPK (mitogen activated protein kinase) and STAT (signal transducer and activators of transcription) signaling pathways.

Modified from Bassett *et al.*[30].

resulting in enhancement of cardiac output. There is also evidence that showed that TH can exert its effects independently of nuclear TRs and that this effect can be abrogated by kinase inhibitors. Lin *et al.* [8] observed that the antiviral activity of human interferon-γ (IFN-γ) can be potentiated by T_4 and T_3 in HeLa cells that lack endogenous TRs. These effects are blocked by inhibitors of PKC and PKA, but not by 5'-deiodinase inhibitor. Lin *et al.* [7] also investigated IFN-γ induced human leukocyte antigen (HLA)-DR expression in HeLa and CV-1 cells, which both lack TRs. HLA-DR, the major histocompatibility complex (MHC) class II antigen, is usually expressed on B lymphocytes, monocytes, macrophages, and is induced by IFN-γ in HeLa and CV-1 cells. They found that T_4 potentiates IFN-γ-induced HLA-DR expression, but that effect is blocked by PKC inhibitors and genistein. Furthermore, Lin *et al.* [6] examined T_4 induced tyrosine phosphorylation and STAT3 nuclear translocation. This effect occurs in as little as 10-20 min. They also found that the activation of STAT3 in HeLa and CV-1 cells is similar to that in BG-9 cells (the human skin fibroblasts which do have TRs). This effect is reproduced by T_4–agarose, which prevents T_4 from entering the cell, and is blocked by genistein as well as the inhibitors of PKC and MAPK kinase. This suggests that T_4-induced the activation of STAT3 is mediated *via* non-classical mechanisms that require PKC, protein tyrosine kinase (PTK), and the MAPK pathway. These observations suggest that the rapid non-classical effects of thyroid hormone are widespread and may be involved in multiple physiological processes in many different cell types.

The identification of a progestin membrane receptor and the sub-cellular targeted nuclear receptor isoforms estrogen receptor α (ER) [52], mitochondrial retinoid X receptor α isoform mtRXR (mtRXR), mitochondrial peroxisome proliferator activator

receptor γ^2 associated protein (mtPPAR) [49-51], demonstrate that membrane receptors do exist for hormones previously defined for their genomic action. The recent finding that integrin, $\alpha_v\beta_3$ [2] as a cell surface receptor for T_4 in mammalian cells, lends credence to non-classical actions TH.

V. Thyroid Hormone Classical and Non-classical Effects – A Complex Model of Actions

The data presented so far has made a clear distinction between classical and non-classical effects of TH. However, it is more plausible that the two effects are interconnected to elicit a cellular response. For example, by non-classical mechanisms, TH can facilitate serine or/and threonine phosphorylation, which alters transcriptional activity of TR in the nucleus [45, 46, 53]. Davis and others [53-55] proposed a two-step model. This model (also see **Figure 1.11**) suggests that TH first binds to putative membrane receptors such as G protein couped receptor, which induces second messengers including PKC, Ras, Raf1, MEK and electrolyte movements. These results in tyrosine phosphorylation, activation and nuclear translocation of MAPK, which in turn phosphorylates a serine residue in the second zinc finger of TR. This phosphorylation results in dissociation of TR from the co-repressors SMRT and NCoR, and association with co-activators to induce transcriptional activity. Although these data suggest that phosphorylation may be important in TH-mediated regulation of gene expression, its relative importance is not clear, particularly as it relates to biological outcome.

VI. Thyroid Hormone Receptors and Estrogen Receptors Cross-talk

i. Estrogen action.

Estrogen binds to estrogen receptors (ERs), which bind to estrogen response elements (EREs) as homodimers [52]. ERs have two isoforms ERα and ERβ (**Figure 1.12**) that are encoded on human chromosomes 6 and 14, respectively [56]. Although there is high degree of sequence homology (only three amino acids differ) in the ERα and ERβ DNA-binding domain, the ligand-binding domain shows only 53% homology. ERα is primarily expressed in the mammary gland and in the uterus and is mainly involved in reproductive events. While, ERβ is very important in the central nervous system and the cardiovascular system [56]. For example, using ERα -/- mice, Iafrati *et al.* [57] showed that 17β-estradiol (E_2) can protect against vascular injury to a similar degree in both wide-type and ERα-/- mice. This suggests that this effect of estrogens is mainly mediated *via* ERβ.

Similar to TRs, in the presence of estrogen or tamoxifen, liganded ERs bind to EREs and recruit specific co-regulators with HATs or HDACs activity to remodel chromatin (**Figure 1.13**). The net agonist/antagonist activity of ER and ligands depends on ligand-induced conformational changes of the receptor. The receptor isoform as well as the specific coregulatory and promoter sequences also contribute to the functional specificity of the receptor down to the gene expression level [58]. The remodeling and "opening" up of the chromatin structure leads to gene activation [52]. However, unlike TRs, ERs cannot regulate transcription in the absence of ligand and are cytoplasmic until ligand binding allows for the translocation of the ER to the nucleus [1].

ii. TR cross-talk with ER.

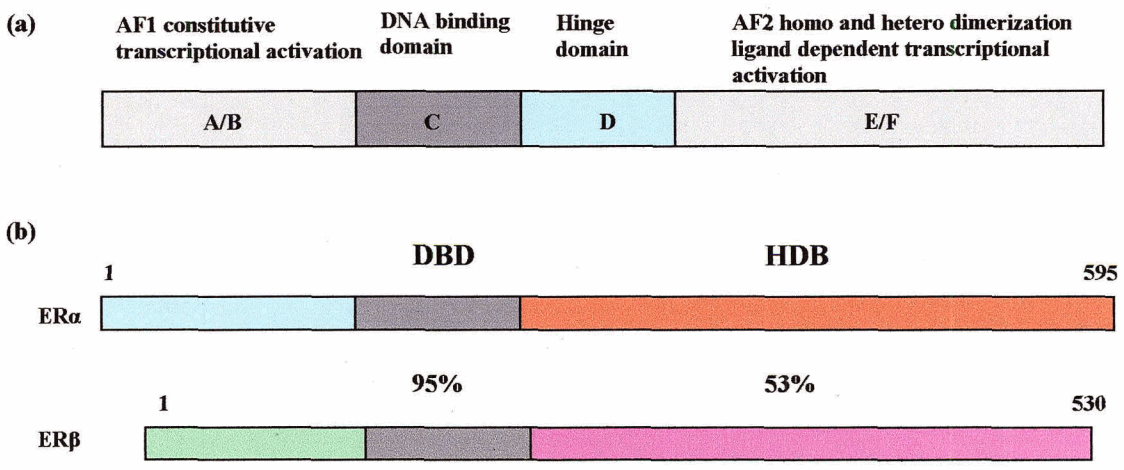


Figure 1.12. A schematic representation of the four functional domains of the estrogen receptor protein is shown in (a). The protein products of the estrogen receptor alpha and beta are shown in (b).

ERα contains 595 amino acids and ERβ is somewhat shorter than ERα, containing 530 amino acids. ERα and ERβ consists with a central DNA-binding domain (DBD), along with a carboxy-terminal hormone-binding domain (HBD). The region of highest homology between ERα and ERβ is in the DBD (95%). Whereas, there is less homology (53%) in the crucial HBD. Their functional domains have been designated AF. Modified from Osborne *et al.* [58].

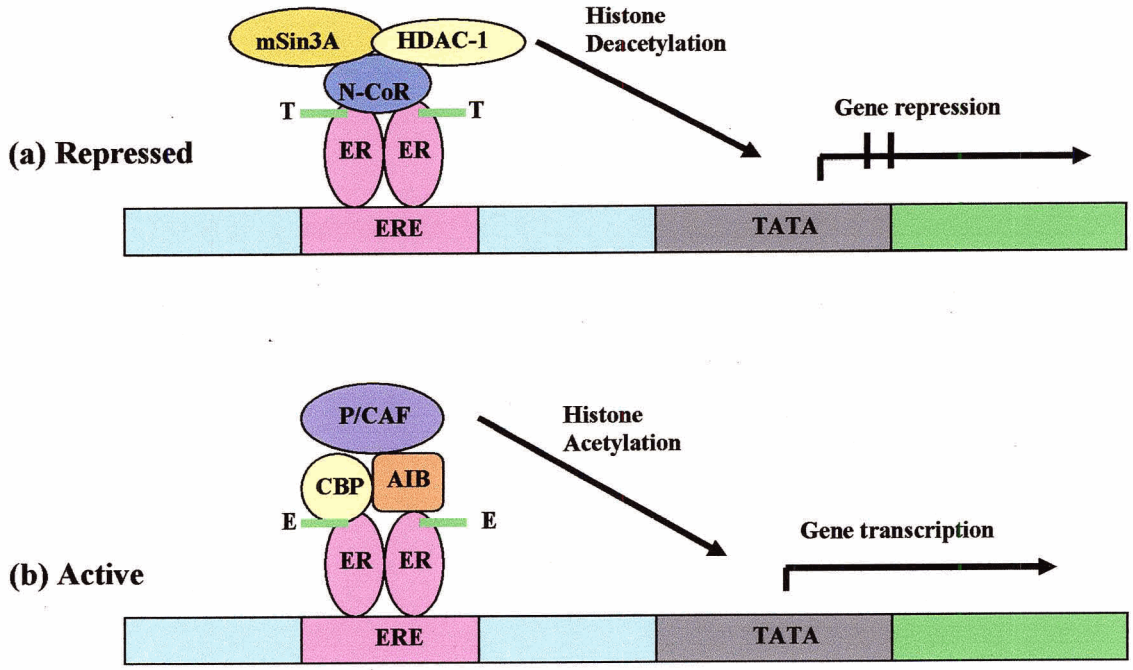


Figure 1.13. The role of ER coregulators in gene transcription regulation.

(a) When tamoxifen (T) binds to ER, it antagonizes the effect of estrogen by the recruitment of corepressors to the receptor complex. The corepressors possess histone deacetylase activity, and this activity silences transcription by allowing DNA to wrap more tightly around the core histone proteins. (b) Ligand estrogen (E) binding then releases the corepressors from the transcription complex, enabling the receptor to recruit coactivators and cointegrators with their associated histone acetylase activity. These acetyl transferases add acetyl groups to histones, thereby loosening their interaction with DNA, which then exposes important residues to the basal transcriptional machinery. Abbreviation: estrogen receptor (ER), estrogen response element (ERE), mammalian Sin3 (mSin3A), histone deacetylase 1 (HDAC-1), nuclear receptor co-repressor (N-CoR), p300/CBP-associated factor (P/CAF), CREB-binding protein (CBP), amplified in breast cancer-1 protein (AIB). Modified from Osborne *et al.* [58].

TRs and ERs can each modulate the transcriptional activity of the other as both TRs and ERs have identical "P boxes" within the first finger of their DBDs (**Figure 1.7**) [59]. This "P box" is important in the recognition of hormone response elements. The "P box" of the TRs and ERs recognizes the same consensus HRE half-site sequence (AGGTCA). ERs bind as homodimers to EREs, which are arranged as palindromes separated by three nucleotides; while, TRs bind to TREs as monomers, homodimers, or heterodimers. Therefore, it is possible that competition between the two receptors may lead to antagonism. This crosstalk can occur by either competition for half-site binding or by squelching of coactivators.

TRs can block ER-mediated transcription. Using electrophoretic mobility shift assays (EMSA), Zhun *et al.* [60] demonstrated that both ERα and TR (α1 and β1) can bind rat preproenkephalin (PPE) gene promoter ERE. Furthermore, Zhun *et al.* [61] transiently cotransfected ERα and TRα1 into CV-1 cells, which have low endogenous ERs and TRs, and assessed the activity of 437 bp of the rat PPE gene promoter fused to the CAT reporter gene. After pretreatment with exogenous 17β-estradiol and/or T_3, they showed that estrogen-induced PPE promoter activity is significantly inhibited by liganded TRα1, suggesting TR antagonism of the ERE. However, when they performed transient cotransfection assays with a P-box mutated TRα1 (TRα1p), which is unable to bind the AGGTCA TRE consensus sequence, treatment with T_3 also significantly inhibits estrogen-induced increase in CAT activity. This suggests that competition for half-site binding is not the only mechanism for crosstalk between TRs and ERs. Furthermore, Vasudevan *et al.* [62] performed the same transient cotransfection assays with the addition of SRC-1, which can bind the LBD of both ER and TR. They demonstrated that

SRC-1 overexpression can rescue P-box mutated TRα1 inhibition. This indicates that squelching of common coactivators is another important mechanism of inhibition by TR isoforms.

ERs can also block T_3-regulated transcription by TRs. Using EMSA, Yarwood *et al.* [63] demonstrated that both TR and ER bind the TRE of the human glycoprotein hormone α subunit gene. T_3 is known to be a major negative regulator of α subunit transcription [63]. They performed cotransfection assays with TRβ in JEG-3 human choriocarcinoma cells, which produce endogenous α subunit and are deficient in TR. They showed that estradiol inhibits T_3-mediated negative regulation of the glycoprotein hormone α-subunit gene transcription, suggesting that competition between ER and TR for TRE binding may block T_3-mediated negative regulation of this target gene. However, Yen *et al.* [64] observed that two ER mutants that cannot bind TREs or EREs also block T_3-mediated transcriptional activation *via* DR4 (four-nucleotide gap) and IP (six-nucleotide gap), suggesting that these ERs may titrate a critical coactivator (unknown) also required for T_3-mediated transcriptional activation.

VII. The Amphibian Model

The importance of TH in vertebrate postembryonic development was first discovered by Gudernatsch (1912) who fed thyroid glands to frog tadpoles and precociously induced metamorphosis [65]. Amphibian metamorphosis is divided into three periods [66]: premetamorphosis, prometamorphosis, and metamorphic climax. The entire process is under the control of TH which increases in amount throughout prometamorphosis reaching a peak concentration at climax [67] (**Figure 1.14**). During anuran metamorphosis, virtually every tissue exhibits profound morphological and

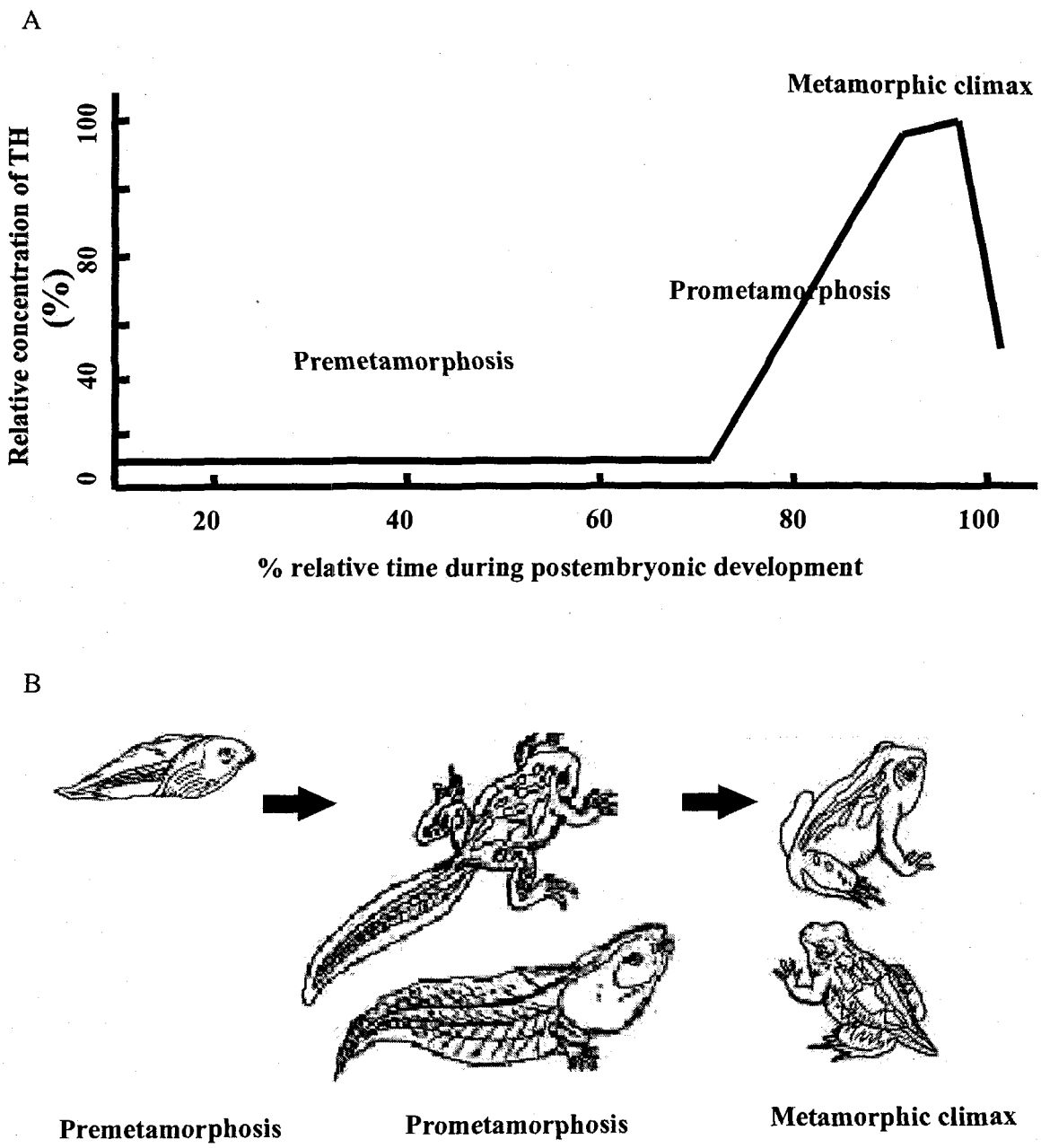


Figure 1.14. Thyroid hormones are the central trigger for tadpole metamorphosis. Concentrations of T_4 and T_3 in blood plasma in tadpoles are usually undetectable in premetamorphosis stage, rise during prometamorphosis, peak dramatically during metamorphic climax, and then decrease to the suprabasal levels of the frog [67].

biochemical changes. For example, the larval liver and skin undergo genetic reprogramming that leads to synthesis of serum albumin and urea cycle enzymes in the liver and collagen deposition and keratinization of the skin. Among the most dramatic morphological and biochemical changes are the emergences of limbs and the total cell loss in the tail. All these changes could be induced precociously by exogenous TH in organ culture experiments [68-71]. Due to the central role of TH during amphibian metamorphosis, it has become a classic model for the study of TH actions.

Numerous studies have utilized cell lines to investigate the action of TH. However, the postembryonic amphibian presents a better study system, because remodeling of the entire organism during metamorphosis is controlled by a single hormonal signal. Amphibian metamorphosis is a simple and highly reproducible experimental model. At the premetamorphosis stage, the tadpole is euthyroid (has normal thyroid gland) but functionally athyroid (cannot secrete TH). These tadpoles readily take up T_3 from the aqueous rearing solution or cultured medium and respond in a dose dependent and highly stereotypic manner which matches the onset and completion of natural metamorphosis [72, 73]. Thus, amphibian metamorphosis represents a unique opportunity to address important questions regarding the biological actions of TH that may be conserved across all vertebrate species.

Ever since the successful cloning of TRs (1986), there has been an explosion of information on the molecular mechanisms of TH actions. TRα and TRβ are the two major isoforms of TRs and are differentially regulated in *Xenopus laevis* [74, 75]. The TRα genes are constitutively expressed after the completion of embryogenesis and are required for the initial response to exogenous TH [72, 76]. The TRβ genes have little

expression prior to metamorphosis and are up-regulated by exogenous T_3 which is critical for the establishment of tissue-specific genetic programs for metamorphosis [72]. Recent studies in *Xenopus laevis* has greatly aided our understanding of the roles of unliganded and liganded TRs in regulating target genes [40]. Further evidence from mammals showed that the nuclear action of TRs is influenced by diverse signaling transduction pathways [6-8, 10, 54]. Therefore, a complex model of TH action has been proposed. The effects of TH are mediated *via* the hormones first binding with nuclear TRs which bind to specific TREs and/or *via* signaling transduction through a putative membrane receptor, which result in the phosphorylation of TRs. These interactions alter the transcription of specific genes, followed by translation to protein, and finally to morphological metamorphic changes.

During amphibian metamorphosis, diverse responses such as tail resorption [72, 73], limb growth and differentiation [77], intestinal remodeling [78], and restructuring and functional differentiation of liver [70, 71, 79] are mediated by TH-regulated gene expression. Each organ or tissue has been programmed to respond to TH in its own specific way. However, how a different gene regulation and signaling cascade occurs in different tissues has yet to be resolved.

Tail resorption is the last change; it occurs rapidly at metamorphic climax. It is easy to manipulate and serves as ideal model system to investigate the mechanisms of action of TH in apoptosis. The TH-induced gene regulation cascade leading to tail resorption has been studied extensively in *Xenopus laevis* [72, 73, 76, 80-82] and *Rana catesbeiana* [83-85]. Given there is increasing evidence showing the potential importance of protein phosphorylation cascades in the action of TH, the question arises as to which

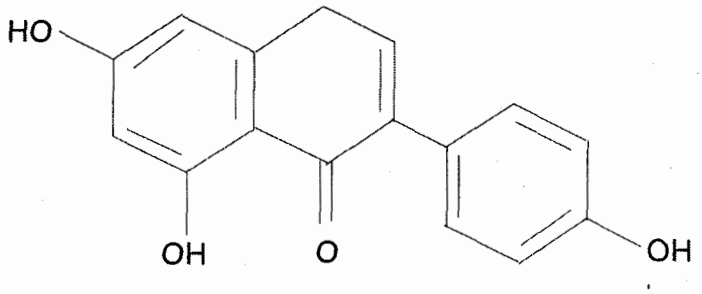
signaling pathway and what precise substrates are involved in TH induced tail regression. The advantage of the tail organ culture system is that it allows one to answer such questions as the involvement of a particular signaling pathway by using specific inhibitors which would otherwise be toxic to the intact tadpoles.

VIII. Genistein

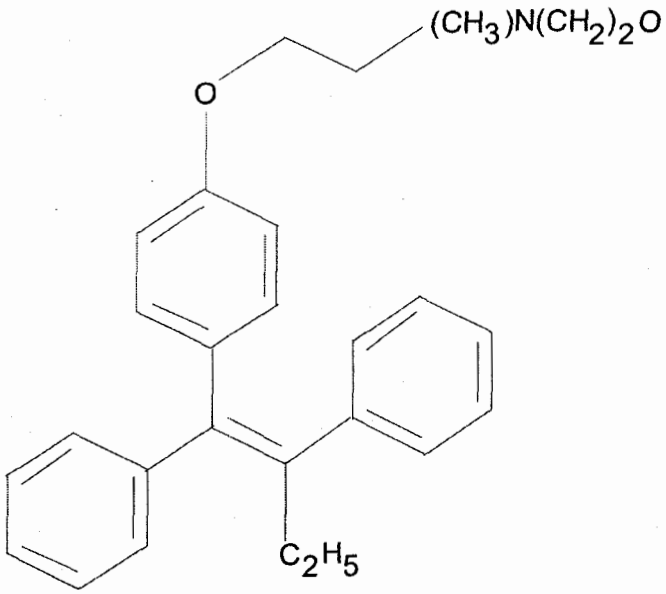
Genistein (4',5,7—trihydroxyisoflavone) is one of major components in soy formula and shares similar structural features with E_2 as well as tamoxifen (**Figure 1.15**), a synthetic anti-estrogen. At low concentrations, genistein can exert either estrogenic or anti-estrogenic effects [86-88]. However, at high concentrations, genistein is a specific inhibitor of tyrosine kinase [18]. Due to its dual function, genistein has been used as a tool to investigate molecular mechanisms in signaling pathways in numerous studies. It has been shown that genistein can disrupt TH action in *in vitro* studies [6-8, 20-25]. Genistein can also regulate transforming growth factor (TGF)β-1 [19], in addition to its estrogenic and tyrosine kinase inhibiting effects.

i. Genistein and soy formula.

In 1929 Hill and Stuart [89] reported the use of soy formula as a replacement for infants with allergies to cow's milk protein. Since then, soy formula has been used for several other related medical indications including postdiarrhea lactose intolerance, galactosemia and primary lactase deficiency [90]. Presently, with the improvement of soy formula quality, the U. S. Food and Drug Administration has established safety and quality standards for infant formulas [91]. Genistein and daidzein are two major components in soy formula [11]. Commercially available baby soy formula marketed in the United States is made with soy protein isolate (SPI+) [91]. Setchell and Cole [92]



Genistein



Tamoxifen

Figure 1.15. Structure of genistein in relation to tamoxifen.

reported that isoflavone levels in SPI+ was 30.2 +/- 5.8 mg/L (Mean +/- SD) and the ratio of genistein to daidzein isoflavone forms was 2.72 +/- 0.24 (Mean +/- SD).

The soyfood habits of Americans differ substantially from those of Asians. Asians are more likely to consume relatively high levels of soyfoods throughout life, except between birth and weaning. Asian infants are fed either cow milk formula or breast milk for the first year of life [91]. In contrast a substantial number of North American infants are exposed to an exclusively soy-based diet. In 1998, marketing data and hospital discharge records of the U. S. showed that ~25% of the nearly 4 million newborns were fed with baby soy formula [90]. The reason for the infant consuming soy formula may be, not only that the American Academy of Pediatrics recommends soy formula as a safe and effective alternative for infants, but also the desire of parents to maintain a vegetarian lifestyle and the increasing belief that soyfoods provide the potential benefits. Before birth and after weaning, most Americans are not exposed to appreciable levels of soyfoods [91].

Genistein is associated with a decreased risk of hormone-dependent cancer initiation later in life (e.g. breast and prostate cancers) and a variety of potential beneficial health effects including chemoprevention of cardiovascular disease, osteoporosis and relief of menopausal symptoms [11]. However, genistein exerts goitrogenic effects at dose of 0.33 mg/kg/day [93] which is three times higher than the amount typically consumed in Japan (0.08 to 0.13 mg/kg/day).

ii. Genistein and the tyrosine kinase signaling pathway.

Tyrosine phosphorylation plays a pivotal role for cell proliferation and cell transformation, because tyrosine-specific protein kinase activity such as Src [94],

epidermal growth factor receptor (EGFR) [95], platelet-derived growth factor receptor (PDGFR) [96], and insulin-like growth factor receptor (IGFR) [97], is strongly correlated with the ability of retroviruses to transform cells. Therefore, a specific inhibitor for tyrosine kinases could be a promising antitumor candidate as well as a tool for elucidating the role of tyrosine phosphorylation in cells. In 1987, Akiyama *et al.* [18] first demonstrated that genistein is a specific inhibitor of tyrosine kinase *in vitro*. It was shown that genistein inhibition of the EGFR kinase activity is competitive with ATP and leads to the formation of nonproductive enzyme-substrate complexes. For the phosphate acceptor, histone H2B, genistein functions as a noncompetitive inhibitor. This finding "unleashed" a great interest in using genistein as a tool to investigate molecular mechanisms of cancer and signaling pathways. For example, genistein, can trigger cancer cell apotosis in B-cell precursor leukemia [98]. As discussed on page 26, using genistein as a specific tyrosine kinase inhibitor, there was some *in vitro* evidence showing that tyrosine kinase signaling plays a critical role in the action of TH.

iii. Estrogenic activity of genistein and breast cancer.

Genistein has been clinically tested as a chemopreventive agent in women with high risk of breast cancer due to its similar structural features with E_2 and tamoxifen. Genistein, an analog of estrogen, at low concentrations can exert either estrogenic or anti-estrogenic effects [86-88]. These effects may be by competing binding to the ERs.

Using a rat model, it is suggested that exposure to genistein during the perinatal or early juvenile period can induce mammary cell differentiation and suppress the development of mammary cancer [99, 100]. Rats were exposed to genistein only in a limited segment of the early life and yet were apparently protected from chemically-

induced cancer initiation later in life. This latter point is extremely important for possible health benefits of soy infant formula, since genistein is a major component in soy formula.

The mechanism of genistein and soy formula exerting chemoprotective effects has been investigated. Cotroneo *et al.* [101] showed that the protective effect of genistein against 7,12-dimethylbenzantracene (DMBA)-induced mammary cancer results from its alteration rat mammary cell development by inducing cell differentiation. This effect is through up-regulated expression of EGFRs both at mRNA and protein levels [102] or *via* mimicking ER actions [101]. With the soy formula (the unpurified form of genistein), it was shown although DMBA-induced mammary cancer is reduced, the gross mammary gland morphology (differentiation stage), epithelial cell apoptotic index, expression of estrogen and progesterone receptors, and mammary density of treated animals are the same as control [103]. DMBA is a procarcinogen that must be metabolized to a carcinogen (activation stage) by cytochrome P450 enzymes, primarly those in gene family 1 (CYP1) [91]. The soy formula is working to reduce the incidence of DMBA-induced mammary gland cancer by down-regulating CYP1 and reducing DMBA-DNA adducts [103]. This represents a significant difference between feeding soy formula and a diet to which purified genistein is added.

The perinatal period is the most sensitive window for reproductive tract development and alterations. The safety of genistein and soy formula on animal reproductive systems is the centre of the debate. There are controversial results on reproductive effects of the consumption soy formula and genistein on the rat model [99, 104, 105] and sheep [106]. There is very little research on the reproductive effects of

consumption soy phytoestrogens by human neonates. Setchell *et al.* [107] reported the plasma isoflavone concentrations of infants fed soy formula is ~7000 nM, which is 280-fold higher than milk formula and breast milk fed infants. Soy isoflavones contain high proportions of genistein and daidzein, two well-known estrogenic endocrine disrupters that may alter reproductive development and function. Although the estrogenic potency of isoflavones is lower than that of E_2 (genistein is ~1000 times less potent than E_2 [87, 91]), the plasma isoflavone concentrations are ~50-100 times higher in infants fed soy formula than the E_2 levels achieved by women during pregnancy and nearly 3000 times higher that the E_2 concentrations achieved during the estrogen surge of the menstrual cycle [91]. Since humans do not normally have high concentrations of estrogens until after puberty, this raises great concerns of short- and long-term effects on reproductive systems of consuming soy formula especially in infants. Given that Asians who do have lower incidence of breast and prostate cancer usually do not consume soy formula in the first year of life, the health benefit of infants consuming soy formula should be carefully evaluated. Since large studies focusing on this issue have not been conducted, the adverse effects of soy formula and purified genistein on reproductive systems need to be further monitered and investigated.

iv. Genistein and thyroid hormone metabolism.

There is considerable interest in the putative health benefits from genistein, such as chemoprevention of breast and prostate cancer, relief of postmenopausal symptoms, and osteoporosis amelioration [11]. However, soybean consumption also has a long-standing association with goiter in animals and humans [23]. This suggests that genistein, a major component of soybean, can affect TH metabolism.

Mori *et al.* [25] investigated the role of genistein in the regulation of 5'-deiodinase, an enzyme that converts T_4 to T_3. They found that the remarkable increase of 5'D-I activity induced by TSH or Bu2cAMP in rat FRTL-5 cell (a thyroid gland cell) is completely inhibited by 100 μM genistein. Similarly, the same concentration of genistein also blocked Bu2cAMP and hydrocortisone increased activity of 5'D-II in rat astrocytes (brain). Since genistein at high concentrations is a specific tyrosine kinase inhibitor, this finding suggests that tyrosine phosphorylation may play an important role in the regulation of thyroid hormone metabolism in the rat thyroid and brain. Given that TH is important in proper brain development of infants and given that TH levels are critical around the neonatal period [108], consuming large amounts of genistein-rich foods may pose a risk for infant brain development.

In addition, genistein is identified as the component in soy that inhibits TPO-catalyzed iodination and coupling. Doerge *et al.* [21-24] examined the TPO activity in rats fed with genistein-fortified diets, it was shown that TPO activity significantly decreased and this reduction was dose-dependent [24]. The mechanism of this effect is not known.

IX. Research Hypothesis and Thesis Outline

Genistein disrupts non-classical TH action by inhibition of tyrosine kinases [6-8], but it may also act through affecting classical pathways. The mechanism remains unclear, particularly in the context of normal cells. Using genistein as a tool and tadpole metamorphosis as a model for TH action, I address the hypothesis that phosphorylation is important in TH-dependent tadpole tail regression.

The effect of genistein on TH-dependent tadpole tail regression was examined and the evidence indicates that genistein inhibits tail regression *via* inhibition of tyrosine kinase action rather than estrogenic action. The molecular mechanism underlying the biological outcomes is further examined by cDNA array, real-time quantitative polymerase chain reaction (QPCR), and protein analyses. This work demonstrates that genistein affects TH signaling in target tissues directly without the requirement of an intact HPT axis and indicates that phosphorylation is an important factor in establishing TH-dependent gene expression programs.

Chapter 2. The Effect of Genistein on Thyroid Hormone-dependent Tadpole Tail Regression in *Rana catesbeiana*

1. Introduction

Thyroid hormones (THs) are required for the homeostasis of nearly all organs in the human body, including brain, bone, heart, and liver. The study of TH action has great biological and medical implications. Early studies showed that the effects of TH at the genomic level are mediated by the binding of TH to the nuclear receptors called thyroid hormone receptors (TRs). TRs belong to a large superfamily of nuclear hormone receptors including steroid, vitamin D, retinoic acid receptors, and "orphan" receptors, which have no known ligand or function. In the nucleus, TH binds to TRs with high affinity and specificity (K_d of T_3 is about 10^{-10} M [29]). TRs, which have 10-fold greater affinity for T_3 than T_4 [29], function as monomers, homodimers, and heterodimers. The heterodimers are commonly formed between TRs and retinoid X receptors (RXRs). TRs regulate gene expression by binding to specific DNA sequences in target genes, the TH response elements (TREs), then activation or repression transcription in response to hormone [30-32].

Most TH effects are thought to be primarily mediated *via* binding of the TRs to the TRE in the nucleus. However, non-classical actions for thyroid hormone (T_3 and T_4) have been recognized recently. It is hypothesized that the mechanism of these non-classical effects involves TH binding to putative specific membrane receptors [2], thereby exerting biological effects through signal transduction pathways including cAMP, calmodulin, phosphatidylinositol, and protein kinase pathways [1, 9, 48]. The putative

non-classical effects of TH are diverse and the biological mechanisms are still under investigation.

Despite accumulating evidence showing that signaling pathways, such as the MAPK [6-8, 54], cyclin dependent kinase (Cdk) [109], and tyrosine kinase signaling [20] are involved in the regulation of diverse and important TR functions, the precise substrate, the location of phosphorylation sites, their regulation, and functional roles remain to be elucidated. Moreover, genistein (4',5,7-trihydroxyisoflavone), one of major components in soy formula, disrupts T_4 action by inhibition of tyrosine kinase signal transduction [6-8, 20, 54] and by inhibiting 5'-deiodinase and thyroid peroxidase (TPO) [25], two important enzymes involved in the conversion of T_4 to T_3 and TH synthesis, respectively. This is consistent with the observation that high soybean consumption, which mainly consists of genistein, increases the incidence of goiter in animals and humans [23].

Another possible mechanism of antagonism to TH action for genistein is its known activity as a phytoestrogen at low concentrations [86-88]. Nuclear TRs and estrogen receptors (ERs) are capable of modulating the transcriptional activity of each other. Despite this, little is known regarding its potential effects on T_3 action (which is considered to be the bioactive form) and whether genistein affects target tissues directly.

Most research on TH uses either rats or mammalian cell lines as the experimental model. In both cases, the requirement for TH for healthy cells makes it difficult to accurately delineate the molecular mechanism of TH action by depletion and subsequent replenishment of TH. The tadpole at a premetamorphic stage serves as a better experimental model to investigate the mechanism of TH by exogenous T_3 administration.

Anuran metamorphosis is a postembryonic process that is absolutely dependent upon the presence of TH. Postembryonic development is divided into three phases: premetamorphosis, prometamorphosis, and metamorphic climax. At the premetamorphosis stage, the tadpole is competent to respond to TH, but is functionally athyroid. At this stage tadpoles readily take up TH from the aqueous rearing solution and respond in a dose-dependent highly stereotypical manner. Each tissue in the tadpole is a target for action and the responses include apoptosis, growth, or differentiation [110]. Thus, amphibian metamorphosis presents a unique opportunity to address important questions regarding TH action that is common to all vertebrates.

The purpose of this study is to address the hypothesis that phosphorylation may be important in TH-dependent tadpole tail regression. Resorption of the tadpole tail is one of the last changes during anuran natural metamorphosis and is entirely controlled by TH. This process can be precociously induced by exogenous administration of T_3 [72, 73, 80].

TRα and TRβ are the two major isoforms of TRs. T_3 binds to TRα and TRβ eliciting a variety of cellular outcomes (apoptosis, proliferation, or differentiation) during anuran metamorphosis [1]. Their genes are TH-responsive and this response has been well characterized [72]. Previous studies showed that heat shock protein (HSP)30 mRNA expression is T_3-dependent in the liver of *Rana catesbeiana* during both natural and T_3-induced precocious metamorphosis [79].

Inhibitor of growth (ING)1 is a negative growth regulator tumor suppressor, which shares many biological functions with p53, such as playing a role in oncogenesis, apoptosis [111, 112], DNA repair [113], and cell cycle regulation [114]. Transcriptional dysregulation of ING1b has been observed in many diverse tumor types and cancer cell

lines [115, 116]. We have previously shown that ING is T_3-responsive and that its expression correlates with induction of tail regression in *Xenopus laevis* [117, 118]. The molecular basis of how ING is involved in the regulation of gene expression has not been fully elucidated.

In this study, different concentration effects of genistein on the T_3-dependent tadpole tail regression were investigated. I show that genistein inhibits T_3-induced tadpole tail regression most likely through its tyrosine kinase inhibitory action. The critical window for this signaling to occur is between 24 and 48 h of T_3 induction, which is coincident with the time required for the establishment genetic program for tail resorption [73]. The molecular mechanisms underlying this biological outcome were further investigated. Given tadpole tail regression requires the modulation of a number of genes [72, 73, 80], I used cDNA array and reverse transcriptase quantitative real-time PCR (RT-QPCR) analysis to identify changes in gene expression. Although many genes were identifies as being T_3-responsive, only one transcript, TRβ was identified whose expression correlates strongly with genistein's inhibition of T_3-induced tail regression. Although TRα transcript levels were not affected, I show that genistein affects T_3-induced phosphorylation of the TRα protein. Since phosphorylation of TRα may be linked to increased transcriptional activity of the TRβ promoter, this provides the first evidence that changes in phosphorylation are important in T_3-dependent biological outcomes.

2. Material and Methods

2.1 Experimental animals.

Taylor and Kollros (TK) [119] stage VI-XV *Rana catesbeiana* tadpoles were locally caught (Victoria, BC) or purchased (Ward's Natural Science Ltd., St, Catharines, ON). The care and treatment of animals used in this study were in accordance with the guidelines of the Animal Care Committee, University of Victoria. Animals were housed in the University of Victoria aquatics facility and maintained in charcoal filtered, aerated tap water at 15°C in a constant flow-through system with exposure to natural daylight. Tadpoles were fed daily with spirulina (Aquatic ELO-Systems, Inc., FL).

2.2 Tail organ culture.

The procedure used for tail culture was adapted from procedures described previously [70]. Tadpoles were euthanized in 0.1% tricaine methanesulfonate (MS-222) (Syndel Laboratories, Vancouver, BC). The animals were then rinsed in 100 ml sterile distilled water for 10 seconds, followed by a 5 second immersion in 100 ml 70% ethanol and two subsequent 10 second immersions in 100 ml sterile distilled water. Then 2 cm tail tips were aseptically removed and placed into Tadpole Minimal Essential Medium (TMEM) at a density of 1 tip per 5ml dish media individually. The TMEM consists of a 55% strength solution of Minimal Essential Medium (MEM) (Invitrogen), 25 mM HEPES (Sigma-Aldrich, St. Louis, MO), 3 mM $NaHCO_3$, 1.2 mM Na_2HPO_4, 1.2 mM NaH_2PO_4, 20 mM NaCl, 2 mM L-glutamine, 50 units/ml penicillin, 50 mg/ml streptomycin, and 50 mg/ml neomycin, and final pH was adjusted to 7.1. Tail tips were incubated for 24 hours at 25°C prior to the addition of treatment reagents except in the *in vivo* T_3 treatment experiments (**section 2.3**) in which chemical treatments were directly applied after the tail was removed. After 24 hours, equal volumes (10 µl DMSO in 5 ml

medium) of dimethyl sulfoxide (DMSO) solution (ACP chemicals Inc., Montreal, QC), 0.1 μM genistein (Sigma-Aldrich, Canada Ltd), 1 μM genistein, 100 μM genistein, 1 nM T_3 (Sigma, St. Louis, MO), 10 nM T_3, 100 nM T_3, or a combination of genistein and T_3 (100 nM T_3 + 100 μM genistein, 100 nM T_3 + 1 μM genistein, 100 nM T_3 + 0.1 μM genistein, 10 nM T_3 + 100 μM genistein, 10 nM T_3 + 1 μM genistein, or 10 nM T_3 + 0.1 μM genistein) were added to the media. Media and chemicals were replenished every 24 h for the duration of the experiment.

2.3 *In vivo* T_3 tadpole treatment.

Prior to T_3 exposure, TK stage [119] VI-XV tadpoles (1 per 2 L water) were collected and maintained at 25°C in dechlorinated water by using an automatic aquarium heater (Warnock Hersey) for 2 days to acclimate to laboratory conditions. After 2 days, the animals were immobilized on ice and injected intraperitoneally through the tail muscle with either DMSO solution or T_3-containing solution at dose of $3x10^{-10}$ moles/body weight which equals 3 μl/g 10^{-4} M T_3 (**Figure 2.1**). Animals were continuously maintained at 25°C in dechlorinated water using an automatic aquarium heater for the duration of the experiment and water was changed daily. During the acclimatization and *in vivo* T_3 exposure periods, animals were not fed. At either 24 h (24 h injection set) or 48 h (48 h injection set), animals were sacrificed in MS-222. Tail tips of the animals were aseptically removed for subsequent tail organ culture as described above. Cultured tail tips were treated for 24 h, 48 h, or 72 h with equal volume (10 μl in 5 ml medium) of DMSO or 100 μM (final concentration) genistein. Media and chemical reagents were replenished every 24 h. At the end of the culture treatment time points, tail

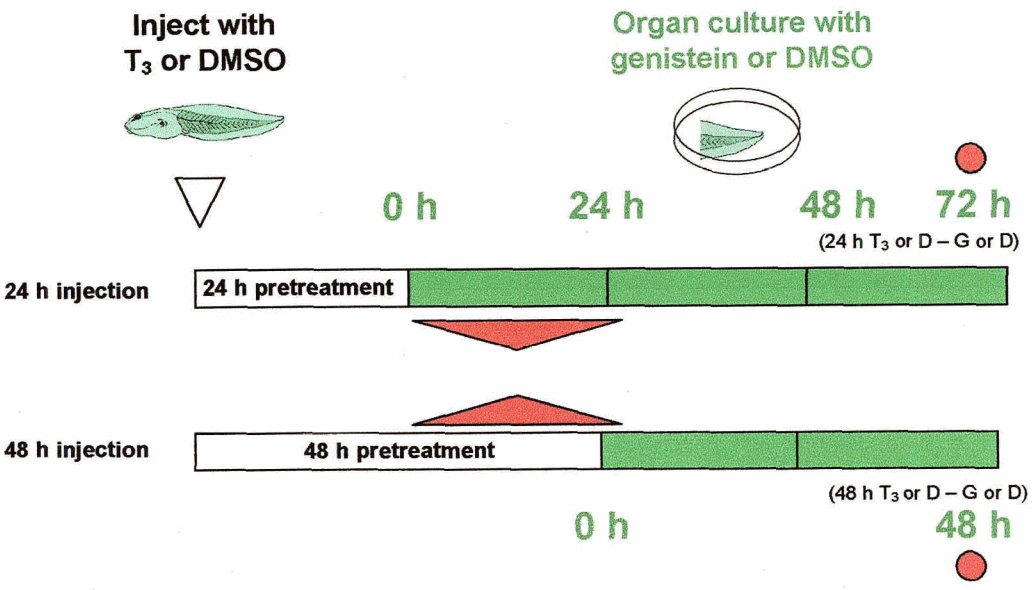


Figure 2.1. Experimental design of effects of genistein on T_3-induced tadpole tail regression.

TK stage VI-X tadpoles were injected intraperitoneally through the tail muscle with either DMSO (vehicle) or T_3. Animals were continuously maintained in 25°C water for 24 h (24 h injection set) or 48 h (48 h injection set). Following the exposure time course (either 24 h or 48 h), animals were sacrificed and tail tips of the animals were aseptically removed for tail organ culture. Cultured tail tips were treated for 24 h, 48 h, or 72 h with an equal volume of DMSO or 100 μM (final concentration) genistein. Media and chemical reagents were replenished every 24 h and pictures were taken at same time. At the end of treatment time points (24 h, 48 h, or 72 h) tail tips were collected for molecular analysis. The red circles are the time points selected for cDNA array analysis. The red triangle represents the "time commitment" points, which is an important transition phase in which inhibitors of transcription and translation can prevent tail regression up until 24h but not after 48 h.

tissue was collected and preserved in RNAlater (Ambion Inc., Austin, TX) at 4°C for later RNA isolation.

2.4 Tail measurement and analysis.

Photographs of cultured tails were taken every 24 hours using a digital camera (DVC Company, Austin, TX). Tail area was measured using Northern Eclipse version 5.0 (Empix Imaging Inc., Mississauga, ON) software. Statistical analysis was conducted using SPSS version 11.0 (Chicago, IL) software.

2.5 Tissue homogenization for protein phosphorylation analysis.

Tail tips were homogenized on ice using a Barnant Mixer in a buffer containing 50 mM HEPES, 150 mM NaCl, 2.5 mM EGTA, 1 mM EDTA, 0.1% Tween 20, 100 μM PMSF, 20 U/ml aprotinin, 10 mM β-glycerophosphate, 0.1 mM Na_3VO_4, 1 mM NaF, 1 mM DTT, 53 U/ml benzonase (Sigma-Aldrich), using a volume of 3 ml buffer per gram tissue [120]. After tissue homogenization, the reactions were sonicated 4 times for 15 sec each on ice and then incubated on ice for 30 min. Homogenates were centrifuged at 12,000 xg for 10 min at 4°C and the collected supernatant was stored at −70°C. The homogenate concentration was determined using the Bio-Rad Protein Assay (Bio-Rad).

2.6 Preparation of RNA.

Total RNA was isolated from RNAlater preserved *Rana catesbeiana* tadpole tail tips using TRIzol reagent as described by the manufacturer (Invitrogen Canada Inc., Burlington, ON). The procedure was adapted from procedures described previously [72, 82, 121]. Individual tail tips were homogenized in 1 ml TRIzol per 100 mg tail tissue using a MM 300 Mixer Mill (Retsch GmbH & Co.KG, Haan, Germany) at 20 Hz for 6 min. After tissue homogenization, chloroform (200 μl chloroform /1 ml TRIzol) was

added for phase separation. RNA was precipitated using isopropyl alcohol and washed with 75% ethanol. The isolated RNA was resuspended in RNase-free water and stored at -70°C until cDNA or amplified RNA (aRNA) was prepared. The concentration of total RNA for each sample was determined by spectrophotometry at 260 nm.

2.7 Preparation of amplified RNA (aRNA).

Amplified RNA (aRNA) was made using a MessageAmp aRNA kit (Ambion Inc., Austin, Texas, USA) according to the manufacturer. Briefly, first-strand cDNA was generated using 1 μg total RNA annealed with 1 μl (100 ng/μl) T7 Oligo $(dT)_{24}$ primer and 200 U of Reverse Transcriptase. The 20 μl reaction was incubated at 42°C for 2 h. Second-strand cDNA was synthesized using 2 μl (5 U/μl) DNA polymerase (supplied by the kit) and incubated at 16°C for 2 h. cDNA purification was performed as described by the manufacturer (reagents supplied by kit). *In vitro* transcription to synthesize aRNA was conducted by using double-stranded cDNA, 7.5 mM dNTPs, and 4 μl (20 U/μl) T7 RNA polymerase mix at 37°C for 14 h. Two microlitres (2U/μl) of DNase I was applied to digest any remaining cDNA following the *in vitro* transcription. aRNA purification was performed as described by the manufacturer (reagents supplied by kit). aRNA was stored at -70°C until cDNA array analysis. The concentration of aRNA for each sample was determined by spectrophotometry at 260 nm. The typical yield is ~20 μg.

2.8 Target preparation and labeling for cDNA array analysis.

Five hundred nanograms tadpole tail aRNA was annealed with 500 ng random hexamer oligonucleotide (Amersham Biosciences Inc., Montreal, QC), and cDNA targets were generated in a 20 μl reaction using 200 U Superscript II RNase H^- reverse

transcriptase (Invitrogen Canada Inc., Burlington, ON) incubated for 2 h at 42°C with 500 μM dGTP, dTTP, and dCTP, and 4 μM dATP, and 50 μCi [α-^{32}P] dATP (PerkinElmer Life Sciences Inc., Boston, MA) as described previously [72, 82, 121]. RNA was removed from the cDNA probe by adding 10 μl of 1 M NaOH and incubated at 70°C for 10 min. The cDNA probes were neutralized by adding 10 μl of 1 M HCl and then purified using QIAquick PCR purification column (Qiagen Inc., Mississauga, ON) with the following modification: wash cDNA with 600 μl PE buffer instead of 700 μl to avoid overflow. The specific activity of the cDNA target was measured by taking 1 μl target in 10 ml scintillation fluid (Fisher Scientific) using Beckman LS8000 series liquid scintillation systems (Beckman Instruments Inc., Irvine, CA). Various amounts of cDNA targets were used for following hybridization to reach a final concentration of 5 x 10^5 counts per minute (cpm)/ml.

2.9 Multi-species analysis of gene expression cDNA hybridization.

The frog MAGEX (multi-species analysis of gene expression) cDNA array membranes (ViagenX Biotech. Inc., Victoria, BC) were used to examine the gene expression profiles in the genistein inhibition study (see **Figure 2.1** for experimental design). This frog MAGEX cDNA array consists of a total of 420 gene sequences spotted in duplicate at adjacent grid positions on a nylon membrane. About 90% of the genes are *Xenopus laevis* and 10% are *Rana catesbeiana* in origin. The abundance of *Xenopus* cDNA compared to *Rana* sequences on the array is proportional to their relative abundance in GenBank (2001) [121]. The cDNA sequences represented on the array mainly consisted of cDNA fragments (~450-550 bp) encoding structurally and functionally important products involved in the regulation of amphibian development

(embryogenesis and metamorphosis) and basal cell metabolism. Two intron controls were also present to assess if there was any genomic DNA contamination. Radiolabeled cDNA from 3 individual animals of each treatment from the genistein inhibition study were independently examined. Before hybridization, the membranes were overlayed on two 3MM filter papers (Rose Scientific Ltd., Edmonton, AB) for 5 min each with the following solutions: 0.5 M NaOH (for denaturation of cDNA on the membrane), 1 M Tris pH 7.5, and 0.5 M Tris pH 7.5/1.25 M NaCl. To block nonspecific hybridization, the membranes were prehybridized with pre-warmed (58°C) hybridization solution at 58°C in a siliconized glass hybridization tube of 35 mm inner diameter x 150 mm length (Amersham Biosciences Inc., Montreal, QC) for 2 h. The 20 ml hybridization solution contained 4 x SSC [0.6M NaCl and 0.06M NaCitrate, pH 7.0, (both chemicals supplied by EMD Chemicals Inc., Gibbstown, NJ)], 1% SDS (Fisher Scientific), 0.5% skim milk powder (Fraser Valley Milk Producers' Cooperative Association, Vancouver, BC) and 10% dextran sulfate (Sigma-Aldrich, Oakville, ON). Before hybridization, the cDNA targets were heat denatured for 5 min at 95°C and then quickly cooled on ice for 5 min to prevent renaturation. To prevent direct exposure of the membrane to concentrated target, I transferred 13 ml of the prehybridization solution to a 15 ml Falcon tube and added the target. The hybridization solution was then reapplied to the membrane at a final concentration of 5 x 10^5 cpm/ml and incubated at 58°C for 18 h.

After hybridization, membranes were rinsed with 50 ml 2 x SSC at room temperature and then washed twice with 50 ml 2 x SSC/0.1% SDS at 58°C for 15 min, once with 50 ml 0.1 x SSC/1.0% SDS at 58°C for 30 min, and finally rinsed with 50 ml 0.1 x SSC at room temperature. The arrays were placed on two 3MM filter papers soaked

with ddH_2O and wrapped with plastic wrap (SC Johnson & Son, Inc., ON). The membranes were exposed to phosphor screens (Molecular Dynamics Inc., Sunnyvale, CA) for 5 days. The hybridization signals were collected using a Storm 840 optical scanner phosphor-imaging system at 50 μm resolution (Molecular Dynamics, Inc. Piscataway, NJ). The resulting image data were converted to a standard 16-bit TIFF file using Photoshop version 7.0 software (Adobe Systems Inc., San Jose, CA). Both nonauto- and auto-level images were prepared for analysis to account for signal saturation.

2.10 Array data analysis.

Array image data collection was performed using ImaGene version 5.6.1 software (BioDiscovery Inc., EI Segundo, CA). Signal intensities for each gene and blank position were determined from the median spot pixel intensities subtracted by the local background by ImaGene. Non-specific hybridization on the arrays was checked manually and excluded for further analysis. Multiple transcripts were used for inter-array normalization. These transcripts were chosen after analysis for stable expression using Bestkeeper [122] (results section **table 2.1**) and Spearman's correlation analysis using SPSS version 11.0 software (Chicago, IL) (results section **table 2.2**) followed by an estimation of inter-array variance analysis (**Appendix 2.1**). Then the variance of individual genes was determined as follows: the mean of duplicate spots per array was determined for each gene. Then the minimum value was subtracted from the maximum and the difference was divided by the median for that gene. If the value was greater than 1.50 on any array for a gene, then that gene was not considered further for gene analysis. Using this method, ribosomal protein L8 (L8), protein S10 (S10), glyceraldehyde-3-

phosphate dehydrogenase (GAPDH), elongation factor-1 α chain (EF-1), NM23/nucleoside diphosphate kinase (NM23), and ubiquitin were chosen as normalization genes. The geometric mean of these six genes were used to calculate the normalization factor (NF) for each array in Excel (Microsoft) (**Appendix 2.2**). The geometric mean was chosen rather than the arithmetic mean in order to equalize the relative contributions of the individual gene median values in the overall mean calculation.

After normalization, the no-signal ("floor") value was determined for each array by using all of the blank positions on the array (**Appendix 2.3**). The floor value for each array was determined by the following formula: Median + (3^{rd} quartile-1^{st} quartile)/2 [as a robust standard deviation (SD)]. The highest value across the all arrays were chosen as the final floor value, and signal intensities for gene positions below this value were adjusted to the floor.

Normalized, floor adjusted and non-blank data were subjected to intraclass correlation coefficient (ICC) analysis to examine the quality of the array replicates using SPSS version 12.0 software (Chicago, IL) (**Appendix 2.4**). One sample was removed from the 48 h T_3-D set (tadpole sacrificed 48 h after T_3 injection and tail subsequently incubated in DMSO for 48 h) for further data analysis due to its high background, some non-specific hybridization spots, and not passing ICC analysis for examining sample integrity. After removing this sample, the intraclass correlation range is 0.51 to 0.94.

For the cDNA probe spots, saturated gene positions identified in auto-leveled data were replaced across all data sets by the corresponding values obtained in the non auto-level data. Both non-auto- and autolevel data for each array were normalized using the

same normalization factors derived from the geometric means of the six genes mentioned above. The relative expression values for each gene were determined from the median intensities across at least 4 replicate spots of array membranes for each treatment. For the normalized and floor adjusted final data applied for the determination relative gene expression see **Appendix 2.5.1** for the 24 h injection sets and **Appendix 2.5.2** for the 48 h injection set.

The overall signal intensities from the tadpole T_3 injection and tail tips incubated in the presence of genistein (T_3-G) for both 24 h and 48 h sets were lower than other 3 treatments which can be observed from NF (**Appendix 2.2**). However, the auto-level procedure (Photoshop) enhanced the overall signal intensities for T_3-G treatment artificially. This was determined to be the case by comparison of QPCR to cDNA array data. Therefore, the median intensities for T_3-G treatment were subjected to correction factors of 13.5 for 24 h injection set or 10 for 48 h injection set respectively (non-autolevel data were not subjected to the adjustment). These two correction factors were derived from QPCR data versus cDNA array data for TRα and TRβ. Because QPCR is a much more accurate method to measure gene expression levels than cDNA array. After correction, the signal intensities for gene positions below floor value were adjusted to the floor value. Fold change for all available genes and correction procedures for T_3-G treatment see **Appendix 2.6.1** for the 24 h injection set and **Appendix 2.6.2** for the 48 h injection set.

Gene transcripts that met an arbitrary 2-fold cut-off were further examined by variance analysis as described above. The variance analysis cut-off was less than or equal to 1.50. If the gene did not pass variance analysis, the gene was removed from 2-fold

change gene list. Cluster analysis were done as follows: the fold change ratios were imported into Cluster [123] and log-transformed before being filtered to values greater than or equal to 1.0 in at least one observation (corresponds to 2.0-fold change). The un-centered data were then subjected to average linkage clustering to produce a hierarchical cluster tree in Treeview [123].

2.11 Statistical analysis.

Statistical analysis was conducted using SPSS version 11.0 software (Chicago, IL). Shapiro-Wilk test and Levene's test was used for examination of normality of data distribution and homogeneity of variances respectively. Parametric One-Way ANOVA test followed by Post Hoc Tukey test were applied for the examination of expression $rING1_{brain}$ transcript during natural and T_3-precocious metamorphosis in the *Rana catesbeiana* tail. The rest of the data analyses used non-parametric Kruskal-Wallis test (for K-independent samples) followed by Mann-Whitney U two-tailed test (for two-independent samples). We consider it statistically significant if P value is less than 0.05 or 0.001.

2.12 Preparation of cDNA.

One microgram total RNA was annealed with 500 ng random hexamer oligonucleotides and cDNA was generated using 200 units (U) Superscript II Rnase H^- reverse transcriptase as described by the manufacturer (Invitrogen Canada Inc., Burlington, ON). The 20-µl reaction was incubated at 42°C for 2 h to generate cDNA and then diluted 20-fold for real-time quantitative polymerase chain reaction (QPCR) examination.

2.13 Real-time quantitative polymerase chain reaction (QPCR).

A MX4000 real-time quantitative polymerase chain reaction system (Stratagene, La Jolla, CA) was used to examine the expression of several gene transcripts. Each 15-μl DNA amplification reaction contained 5 mM Tris HCl, 5 mM Tris Base, 50 mM KCl, 3 mM $MgCl_2$, 0.01% Tween 20, 0.8% glycerol, 40,000-fold dilution of SYBR Green I (Molecular Probes Inc., Eugene, OR), 200 μM dNTPs, 83.3 nM ROX reference dye (Stratagene), 10 pmol of each primer (except 5 pmol for HSP30 and alpha 1 collagen type I primers), 2 μl of 20-fold diluted cDNA, and 1.0 U platinum Taq DNA polymerase (Invitrogen). The primers used were: TRα-forward 5'-GGACCAGAATCTTAGCGG-3', TRα-reverse 5'-CATTGGTGCTTCGGTGAG-3'; TRβ-forward 5'-CAGGGGACAGAGAAAAGGTG-3', TRβ-reverse 5'-TGAGCTTTCTTGCCACAG-3'; L8-forward 5'-AGCAGCATGTCAGGGTAC-3', L8-reverse 5'–TGAAGGCTTCTAAGTCCA-3'; HSP30-forward 5'-GCCTCCACCAGACTTACCA-3', HSP30-reverse 5'-CAGAGGAAGGAAGGCAGGAG-3'. α 1 collagen type I-forward 5'-CCCAGGTGGCGGATTTGA-3', α 1 collagen type I-reverse 5'-AGGCGGAGGAAGGTGAGT-3'; α 2 collagen type I-forward 5'-TGGCAACACTGGACCCTC-3', α 2 collagen type I-reverse 5'-GTGGCATCAACTTCATAATCCT-3'; cytoplasmic β actin-forward 5'-TCACCACCACAGCCGAAAG-3', cytoplasmic β actin-reverse 5'-GGGCCAGACTCATCATACTCCT-3'. For each set of QPCRs, I included two controls which do not have cDNA template or Taq DNA polymerase to determine the specificity of target cDNA amplification. The specificity of the appropriate products were verified by electrophoresis on 2% agarose gels. Standard plots for each target sequence were

generated using known amounts of plasmid containing the amplicon of interest. The thermocycle started at 95°C (9 min) and then 40 cycles of 95°C (15 sec), 55°C (30 sec) annealing (except for HSP30 primers at 61°C, α 1 collagen type I at 63°C, and α 2 collagen type I at 58°C), and 72°C (45 sec) extension (except for HSP30 30 sec). Cycle threshold (*Ct*) values obtained were converted into copy numbers. The copy numbers were determined using standard plots of *Ct* versus log copy number. Quadruplicate data for each target cDNA amplification were averaged and normalized to the invariant ribosomal L8 control to get relative copy numbers.

2.14 Cloning and sequence analysis of *rING1* (Rana inhibitor of growth 1) from *Rana catesbeiana* brain and tail.

$rING1_{tail}$ and $rING1_{brain}$ were cloned using forward primer 5'-TGGTGGAGTTGGTTGAGAAC-3' and reverse primer 5'-CCTGGATCTTTTATTGCTGG-3' provided by Mary Wagner in our lab from *Xenopus laevis ING1* for cross-species cloning. The RT-PCR products were cloned into a pCR II-TOPO vector and TOP10 cells using a TOPO TA Cloning Kit (Invitrogen). The potentially positive clones were confirmed by colony RT-PCR using M13 forward primer and reverse primer provided by TOPO TA Cloning Kit. The confirmed clones were picked for the creation of liquid stocks in LB broth containing 100 μg/ml ampicillin (Sigma-Aldrich, Oakville, ON) overnight at 37°C with shaking. Plasmids were isolated with a Qiaprep Spin Miniprep kit (Qiagen, Mississauga, ON,) and sequenced in the DNA Sequencing Facility, Centre for Biomedical Research, University of Victoria. The DNA and predicted amino acid sequence alignment was conducted using CLUSTALW version 1.8 software (http://clustalw.genome.ad.jp)

2.15 RT-PCR and densitometry analysis for *rING1*$_{brain}$ transcripts expression in *Rana catesbeiana* tail.

To examine the expression level of *rING1*$_{brain}$ and *rING1*$_{tail}$, two primer sets which are specific for these two isoforms were designed manually (the product is only 145 and 150 bp, which are not long enough for using the software to design). The primer sets were: rING1$_{brain}$-forward 5'-TGGTGGAGTTGGTTGAGAACAG-3', rING1$_{brain}$-reverse 5'-TCAGTCTGAGAGATTGTTTCAC-3'; rING1$_{tail}$-forward 5'-TGGTGGAGTTGGTTGAGAACAA-3', rING1$_{tail}$-reverse 5'-TCTTTTCAGTCTGGGCAATGGC-3'. *rING1*$_{brain}$ is expressed in *Rana catesbeiana* brain and tail. To determine the relative expression level of *rING1*$_{brain}$ transcripts in *Rana catesbeiana* tail, RT-PCR followed by densitometry analysis was performed. The reason QPCR is not applied is that the *Ct* value difference between no cDNA template control (NTC) and the target is ~2 cycles, which is not good enough for distinguishing signal between the targets and primer dimers. QPCR is based on the detection and quantitation of the fluorescent dye of SYBR Green [binds to any double strand DNA (dsDNA)] emitted during the reaction as an indicator of amplicon production during each PCR cycle. RT-PCR for each 15-μl DNA amplification reaction contained 5 mM Tris HCl, 5 mM Tris Base, 50 mM KCl, 3 mM $MgCl_2$, 0.01% Tween 20, 0.8% glycerol, 40,000-fold dilution of SYBR Green I (which can be monitored by MX4000 QPCR system for the reaction cycles), 200 μM dNTPs, 83.3 nM ROX reference dye, 2.5 pmol of each primer, 2 μl of 20-fold diluted *Rana catesbeiana* tail cDNA, and 1.0 U platinum Taq DNA polymerase. The PCR reaction conditions were 95°C (9 min); 30 to 32 cycles of 95°C (15 sec), 63°C (30 sec), and 72°C (30 sec). The PCR reaction was stopped at 30 to 32 cycles

in the linear range of amplification, which was monitored by the MX4000 QPCR system. The amplified products were separated on 2% agarose gels and visualized by ethidium bromide staining. Densitometry of the bands was done using Northern Eclipse version 5.0 software. Relative band densitometry was determined by band intensity subtracted by local background, then normalized by the expression of the invariant ribosomal L8 determined by QPCR.

2.16 Immunoprecipitation (IP).

Tissue homogenates (500 μg) were diluted to a 1 ml volume in IP buffer containing 25 mM Tris-HCl (pH 8.0), 400 mM KCl, 10 mM EDTA, 0.1%Triton X-100, 1 mM dithiothreitol, 1 mM β-glycerophosphate, 2.5 mM sodium pyrophosphate, 1 mM Na_3VO_4, 1 μg/ml leupeptin, and 1 mM phenylmethylsulfonyl fluoride. Homogenates were precleared by rotation with 20 μl/ml of protein G-sepharose beads (Amersham) for 20 minutes at 4°C. Following preclearing, the mixture was centrifuged at 3,000 xg for 10 min at 4°C and the supernatant transferred to microfuge tubes containing 20 μl of fresh beads and 5 μl of TRα rabbit polyclonal antibodies (gifts from D. Brown, Carnegie Institute). The antibody-bead-homogenate mixture was mixed by rotation at 4°C for 3 h and the beads were washed 3 times with 1 ml IP buffer. The proteins on the beads were boiled for 3 minutes in 30 μl 3 x sodium dodecyl sulfate (SDS) (187.5 mM Tris-HCl, 6% SDS, 30% glycerol, 150 mM DTT, 0.03% bromophenol blue, pH 6.8) an then resolved by 10% SDS-polyacrylamide gel electrophoresis (SDS-PAGE).

2.17 Immunoblotting.

Equal quantities of tail tissue homogenates [64 μg (30 μl) /lane] or 30 μl IP proteins in SDS sample buffer were electrophoresed through either 8% or 10% SDS-

PAGE respectively. The proteins were transferred to 0.2 μm nitrocellulose membrane (Bio-Rad) [124]. Protein loading and transfer quality were verified by membrane staining with 0.1% Ponceau S (Sigma) in 5% acetic acid. Membranes were blocked with 5% nonfat milk in 140 mM NaCl, 20 mM Tris-base (TBS), pH 7.6, at 4°C overnight and probed with a primary antibody solution diluted in 5% nonfat milk/TBS and 0.1% Tween (TBST) with gentle agitation for 1 h at room temperature. The primary antibodies are mouse monoclonal anti-phospho-tyrosine antibody (1:2000 dilution, Cell Signaling technology, Inc., MA), a rabbit polyclonal anti-phospho-serine antibody (1:125 dilution, Stressgen Bioreagents, BC), or a mouse monoclonal anti-human TRα whose epitope has 60% amino acid sequence identity to *Rana catesbeiana* TRα (1:1000 dilution, LabVision, Corp., CA). The blots were washed with TBST for 1 h. The membranes were incubated with secondary antibody solution diluted (1:2000) in 5% nonfat milk/TBST for 1 h at room temperature. The secondary antibody is a IRDye 800CW conjugated anti-mouse IgM or anti-rabbit IgG antibody depending upon the primary antibody used, which has a emission wavelength at 800 nm (Rockland Inc., Gilbertsville, PA) The blots were washed with TBST for 1 h. The prepared blots were scanned by Odyssey infrared imaging system (LI-COR Biosciences, Lincoln, NE) at 42 μm resolution. The bands intensities were measured using Northern Eclipse version 5.0 software.

3. Results

3.1 Induction of T_3-dependent tadpole tail regression in serum-free organ culture.

Previous studies showed that tadpole tail regression can be induced by administration of exogenous 100 nM T_3 in serum-free organ culture *in vitro* [73, 109]. However, the physiological range of T_3 is ~8 nM [67]. To determine whether T_3 can

induce tadpole tail regression at a more physiological concentration, 2 cm tail tips from premetamorphic (TK stage VI to X) *Rana catesbeiana* tadpoles were removed and cultured *in vitro* over 96 h in the presence of vehicle control (DMSO), 100 nM T_3, 10 nM T_3, or 1 nM T_3 (n=4 for each treatment group). At 100 nM T_3 (**Figure 2.2**), tail tips showed a significant regression at 48 h, 72 h, 96 h time points in comparison to control ($P<0.05$). At 10 nM T_3, tail tips showed a significant regression at 72 h and 96 h in comparison to control ($P<0.05$). However, 1 nM T_3 has no effect on tail regression during the time points tested. T_3 at 10 nM (close to physiological concentration) has very similar effects as 100 nM T_3, except for at 96 h in which 100 nM T_3 showed a statistical difference compared to 10 nM T_3 ($P<0.05$).

3.2 Genistein inhibits T_3-induced tadpole tail regression.

Previous work indicates that genistein affects TH action, but no information exists as to its possible cellular effects on TH signaling. Genistein (G), an analog of estrogen at low concentrations (10 nM-10 μM), can exert either estrogenic or anti-estrogenic effects [11]. This effect of G is through binding to estrogen receptor and sex hormone binding proteins [86]. At higher concentrations (≥30 μM), G is a specific tyrosine kinase inhibitor [18]. To determine whether genistein affects TH-dependent tail regression, 2 cm tail tips from premetamorphic stage tadpoles were removed and cultured in serum-free medium over 96 h and treated with vehicle control (DMSO), 100 nM T_3, 100 μM G, 1 μM G, 0.1 μM G, 100 nM T_3 + 100 μM G, 100 nM T_3 + 1 μM G, or 100 nM T_3 + 0.1 μM G (n=4 for each treatment group). Tails treated with 100 nM T_3 showed a 83% reduction in tail area over 96 h in organ culture media (**Figure 2.3B**). This regression is completely inhibited by the addition of 100 μM G ($P<0.001$). However, tails cultured in the presence

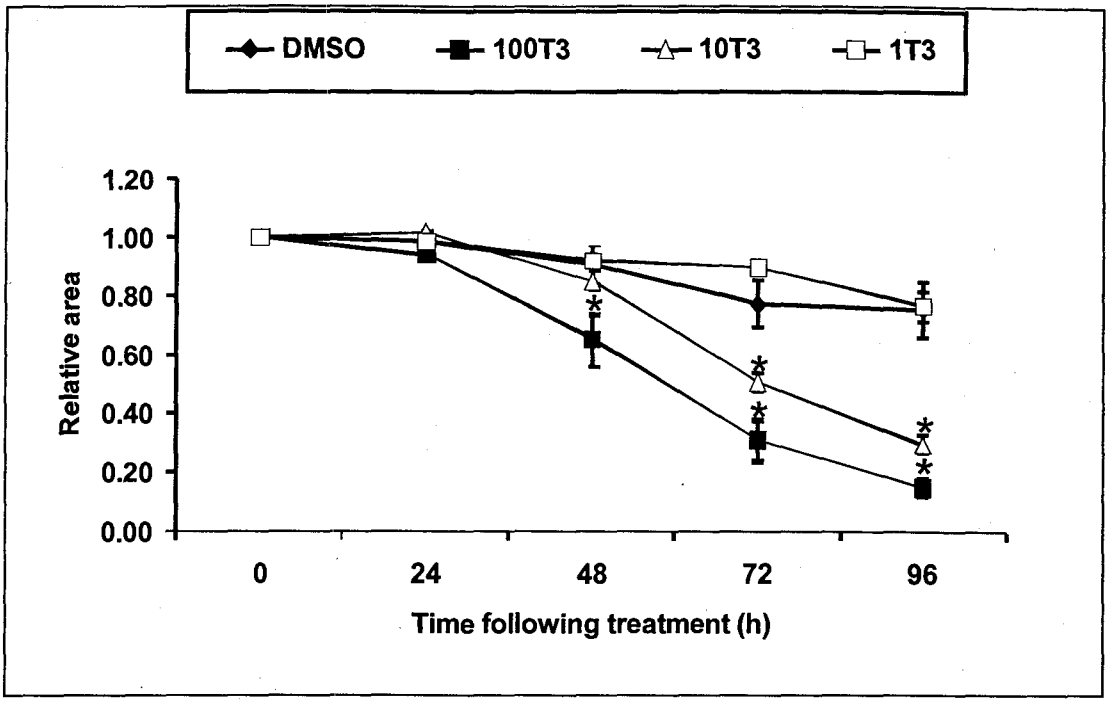


Figure 2.2. 100 nM T_3 and 10 nM T_3 induce T_3-dependent tadpole tail regression in serum-free organ culture.

Two centimetre tail tips were aseptically removed from premetamorphic tadpoles (TK stage VI to X) and cultured in serum-free organ culture medium, TMEM, over 96 h. Tail tips were treated with either vehicle (DMSO), 100 nM T_3, 10 nM T_3, 1 nM T_3. The tail tip area was measured at each time point and plotted relative to the 0 h time point of its treatment. N/treatment = 4. * $P<0.05$ relative to DMSO. The error bars represent standard error of the mean (SEM).

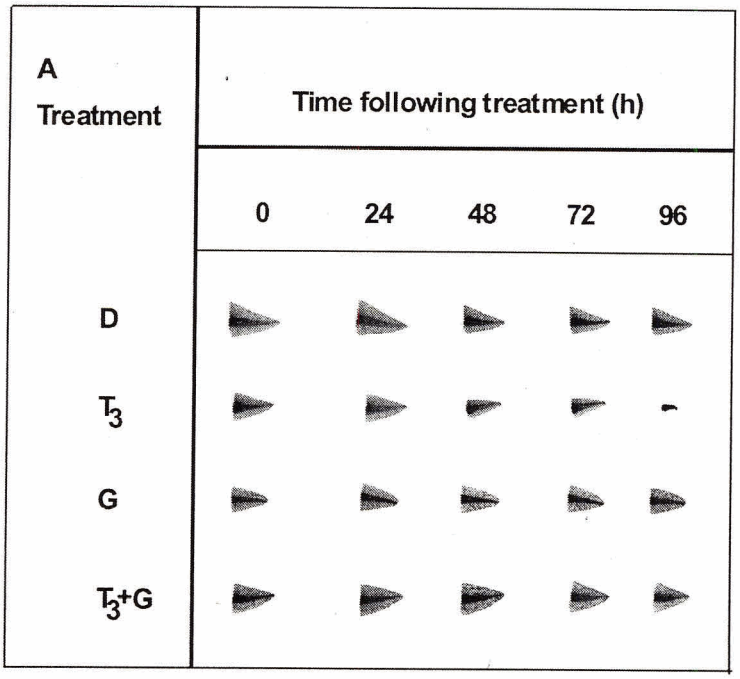


Figure 2.3. 100 μM genistein inhibits T_3-induced tadpole tail regression.

Two centimeter tail tips were aseptically removed from premetamorphic tadpoles and cultured over 96 h. (A) Shown is representative pictures of tail tip regression inhibited by addition 100 μM Genistein. Abbreviation: DMSO, D; 100 nM T_3, T_3; 100 μM genistein, G.

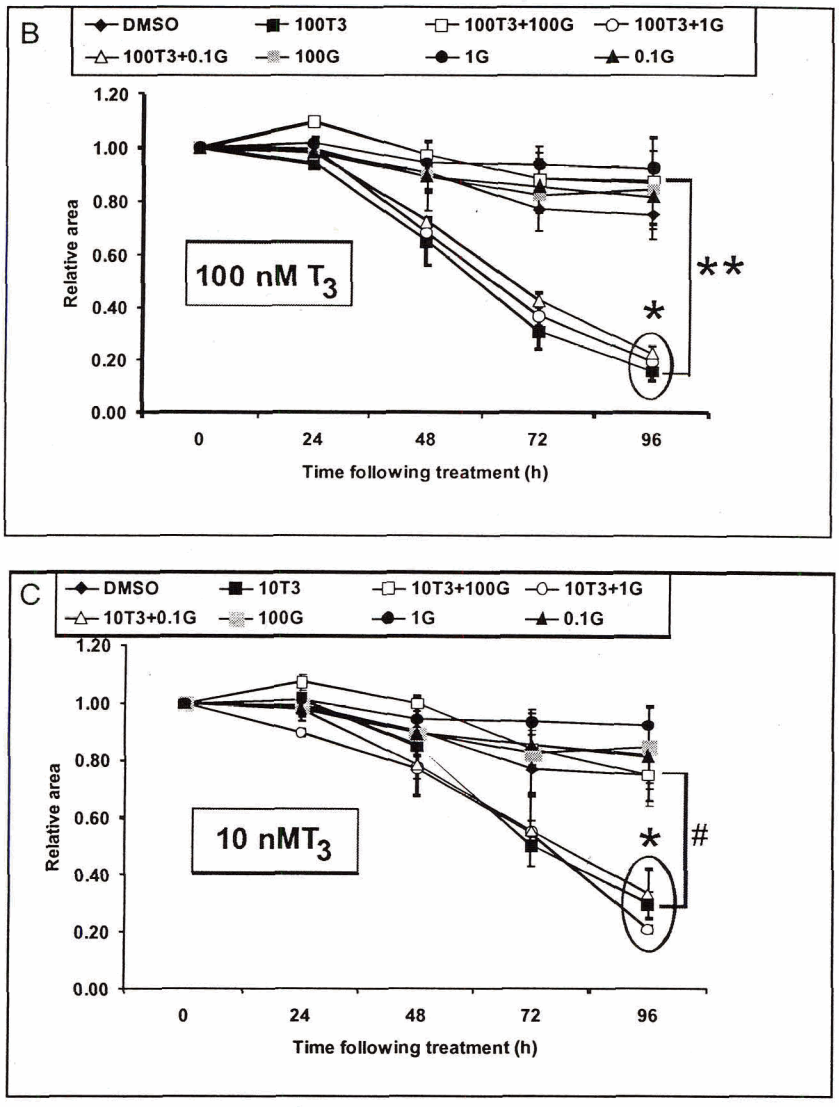


Figure 2.3. 100 μM genistein inhibits 100 nM T_3- (B) or 10 nM T_3-induced (C) tadpole tail regression.

(B) Tail tips were treated with either vehicle (DMSO), 100 nM T_3, 100 μM genistein (G), 1 μM G, 0.1 μM G, or a combination 100 nM T_3 and G. The tail tip area was measured at each time point and plotted relative to the 0 h time point of its treatment. (C) Tail tips were treated with 10 nM T_3 instead of 100 nM T_3. * $P<0.05$ relative to DMSO.

**P<0.001 in comparison 100 nM T_3 with 100 nM T_3 + 100 μM G. # P<0.05 in comparison 10 nM T_3 with 10 nM T_3 + 100 μM G. (n=4 for each group of treatment).

of 100 nM T_3 + 1 μM G or 100 nM T_3 + 0.1 μM G still underwent significant regression over 96 h in comparison to DMSO ($P<0.05$) (the experiment has been repeated four times). There is no statistical difference among 100 nM T_3 + 1μM G, 100 nM T_3 + 0.1μM G, and 100 nM T_3. I also applied 10 nM T_3 and got very similar results as with 100 nM T_3 **(Figure 2.3C)**.

3.3 Genistein reduces steady state levels of a 75 kDa protein phosphorylation during T_3-induced tail regression.

Genistein inhibits the EGF-stimulated increase in phosphotyrosine level in mammalian cells [18]. To further confirm that genistein inhibition of T_3-induced tail regression is *via* inhibition of protein phosphotyrosine levels, TK stage VI to XV tadpoles were injected with T_3 or DMSO vehicle control for 24 h and then the tail tips were removed and incubated in serum-free medium in the presence of 100 μM G or vehicle control for a further 24 h. The tail tip protein homogenates were collected and separated by SDS-PAGE. The protein phosphotyrosine levels were assessed by immunoblot analysis. A 75 kDa protein phosphotyrosine level up-regulated by 60% upon T_3 treatment in comparison to the control **(Figure 2.4)**. In contrast, the 75 kDa protein phosphotyrosine level is attenuated by 20% when tail tips were cultured in the medium inthe presence of 100 μM G after tadpole T_3 injection. This result was reproducible in another independent set of pooled tail tip protein homogenates. This indicates T_3 treatment is associated with an elevation in tyrosine phosphorylation and that genistein inhibits that phosphorylation. This method is limited in that the entire cell homogenate was examined for rare phosphorylation events. It is therefore not very sensitive.

3.4 Genistein blocks tail regression up to hours to days after T_3-treatment.

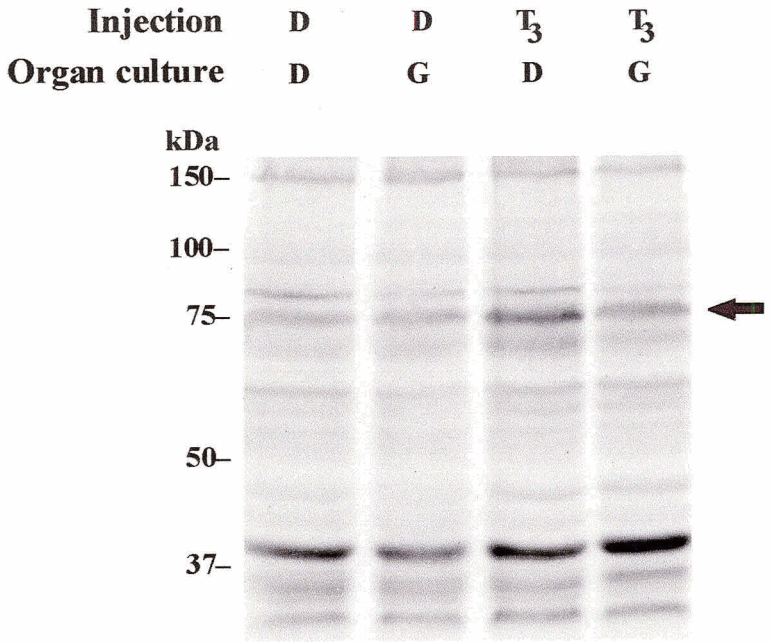


Figure 2.4. Genistein inhibits protein phosphotyrosine level during T_3-induced tail regression.

TK stage VI to XV tadpoles were injected with 3 x 10^{-10} moles/body weight vehicle (DMSO, D) or T_3 and maintained for 24 h. At this time point, tail tips were removed and cultured in serum-free medium in the presence of DMSO or 100 µM genistein (G) for 24 h. Tail tip protein homogenates [64 µg (30 µl)/lane] were separated by 8% SDS-PAGE and immunoblotted with mouse monoclonal anti-phospho-tyrosine antibodies. This blot is representative of two independent experiments.

Previous studies showed that there is a critical time for the establishment of the genetic program for tail regression [73]. Up until about 24 h, inhibition of transcription and translation can prevent tail regression. However, after 48 h, these inhibitors are not effective at inhibiting tail regression. This important transition phase was referred to as the "commitment point" [73]. To determine when genistein inhibits T_3-induced tadpole tail regression, tadpoles (TK stage VI to X) were injected with 3×10^{-10} moles/body weight T_3 or vehicle alone (DMSO) and maintained in 25°C dechlorinated water foreither 24 h or 48 h (see **Figure 2.1** for experimental design). At this time, 2 cm tail tips were aseptically removed and placed in serum-free organ culture medium in the presence of vehicle (DMSO, D) or 100 μM G and incubated at 25°C for 24 h, 48 h, or 72 h. Tail tips from tadpoles injected with T_3 and subsequently cultured in DMSO-containing serum-free medium showed at least 80 % regression by day 2 (**Figure 2.5A**). This is statistically significant compared to animals that were injected with DMSO and their tail tips subsequently cultured in DMSO ($P<0.001$). Tail tips collected from animals injected with T_3 after 24 h and incubated in the presence of 100 μM G showed a complete inhibition of tail regression (**Figure 2.5B**). Tail tips collected from tadpoles sacrificed 48 h after T_3 injection and then cultured in 100 μM G did not show a complete inhibition (68% inhibition). This release from inhibition is statistically significant ($P<0.05$) (**Figure 2.5B**). This suggests that the target(s) for genistein action are available up to 24 h with more limited availability after 48 h.

3.5 cDNA array analysis to examine the effects of genistein on T_3-induced gene expression profiles.

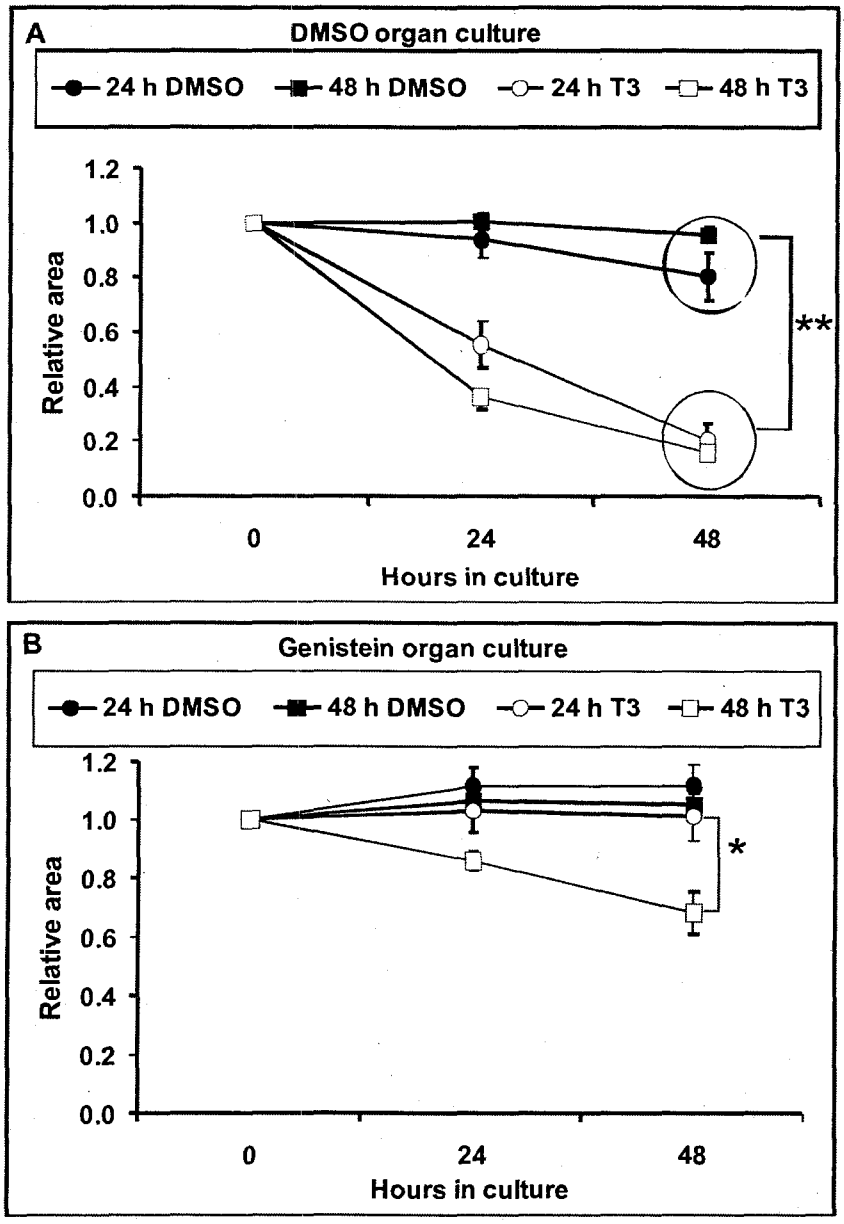


Figure 2.5. Genistein inhibits T_3-induced tail regression in serum-free organ culture within 24h.

Premetamorphic stage tadpoles (TK stage VI to X) were injected with 3×10^{-10} moles/body weight vehicle (DMSO) or T_3 and maintained for 24 h or 48 h, then tail tips were removed and cultured in the presence of DMSO or 100 μM genistein (G) for a further 48 h. The tail tip area was measured at each time point and plotted relative to the

0 h time point of its treatment. (A) Tail tips that were collected from tadpoles that were DMSO or T_3 injected and cultured in DMSO containing medium. ** $P<0.001$ in comparison to animals that were injected with DMSO and their tail tips subsequently cultured in DMSO. (B) After tadpole injection, tail tips removed and cultured in 100 μM G. * $P<0.05$ in comparison to 24 h T_3-injected then cultured in 100 μM G. (n=4 for 24 h group, n=8 for 48 h group).

24 h/48 h denotes: tail tips collected from animals were injected with DMSO or T_3 after 24 h/48 h.

A primary factor controlling tail regression is through the modulation of gene expression [73, 80]. Evidence from my organ culture experiments suggests that the critical tyrosine signaling is coincident with the establishment of the genetic program. To begin to identify genes that may be targets for tyrosine kinase signaling in T_3-induced tail regression in *Rana catesbeiana*, I employed the frog multispecies analysis of gene expression (MAGEX) cDNA array [72] as a "gene expression screen" tool. This array is comprised of 420 genes with a variety of origins (90% of *Xenopus* and 10% of *Rana*) and is a powerful tool for simultaneously examining hundreds of coordinated gene expression profiles. Tail tips from tadpoles injected with T_3 or DMSO only and subsequently cultured with G or DMSO alone were used for array hybridization analysis (see **Figure 2.1** for experimental design). Three individual animals were subject to array analysis separately for each treatment condition.

3.5.1 Determining stable normalizer genes for array data analysis.

Although I attempted to ensure that equal amount of input target was used for each array hybridization (such as equal amounts of total RNA to make aRNA, equal amount of aRNA to make radiolabeled cDNA, and equal amount of radiolabeled cDNA for hybridization), experimental errors during hybridization itself are not easy to control. These errors include different hybridization efficiency between individual samples, different background from exposure within or between experiments. Therefore, determination of stable normalization genes for accounting for differences only due to hybridization efficiency and exposure is necessary. A number of normalizer genes, such as tubulins, actins, GAPDH, 18S or 28S rRNA, and ubiquitin, have been described in the literature [125, 126]. To determine stable normalizer genes in my experimental system, I

applied the BestKeeper method [122] and Spearman correlation analysis. First, 12 potential normalizer genes were selected. Descriptive statistics of the derived crossing points (CP) for each potential normalizer gene are shown in **Table 2.1**. Based on the calculation of variation [coefficient of variance (CV)], the first estimation of the stability of the potential normalizer genes was done. The lower the coefficient of variation (CV) of the gene is, the more stably the gene is expressed across all arrays. Therefore, α skeletal actin, C/EBP-2, and HSP30, whose CV value was greater than 1.00, were excluded for further pair-wise correlation analysis. To determine inter-gene relations of those 9 potential normalizer genes, pair-wise correlation analyses were performed. Within each such correlations the Spearman correlation coefficient (r) and the probability p value are calculated. All those highly correlated genes (**Table 2.2**), L8, S10, GAPDH, elongation EF-1, NM23, and ubiquitin were considered as normalizer genes in my experimental system for further normalization factor (NF) calculation. An estimation of inter-array variance analysis were further performed (**Appendix 2.1**) to examine expressional stability of those 12 potential normalizer genes. All those 6 genes chosen as normalizer genes described above passed the 1.50 cut-off variance analysis.

The NF value for each array was determined using the highest geometric mean (GM) derived from those six normalizer genes for each array among all 24 arrays as a divisor for each individual GM (**Appendix 2.2**). **Figure 2.6** shows the expression profiles of the six normalizer genes (median pixel values for each gene in each array) and GM for each array across all 24 arrays. These six housekeeping genes showed tight correlation with their GM.

Table 2.1. Descriptive statistics of twelve candidate normalizer genes based on their crossing point (CP) values.

Factors	Number (N)	Mean (CP)	Min (CP)	Max (CP)	GM (CP)	SD of CP	CV (SD/Mean)
-Ribosomal protein L8	24	415	97	891	341	332	0.80
-Ribosomal protein S 10	24	535	101	1251	427	485	0.91
-GAPDH	24	348	85	757	295	281	0.81
-Elongation factor-1 α chain	24	663	89	1388	554	537	0.81
-Cytoplasmic β actin	24	1365	507	2709	1280	915	0.67
-Repressor brain factor 2	24	421	153	825	384	279	0.66
-Brain factor 2	24	332	130	693	302	237	0.71
-NM23/nucleoside diphosphate kinase	24	833	298	1672	744	573	0.69
-α skeletal actin	24	513	67	1388	388	565	1.10
-Ubiquitin	24	493	136	1095	410	404	0.82
-C/EBP-2	24	296	11	752	240	311	1.05
-HSP30	24	155	1	854	57	396	2.56

- Non-auto-leveled data from "Median Intensity" of each gene across all 24 arrays were collected, then their Mean, Minimum, Maximum, and Geometric Mean were calculated.
- Standard deviation (SD) of the CP is based on Mean, Minimum, Maximum, and Geometric Mean (GM).
- Coefficient of variance (CV) is SD divided by mean.
- The smaller the CV of the genes is, the more stably the gene is expressed. Therefore, α skeletal actin, C/EBP-2, and HSP30 were excluded for further pair-wise correlation analysis.

Table 2.2. Pair-wise correlation analysis of candidate normalizer genes. Target genes are pair-wise correlated among each other. Non-parametric Spearman correlation coefficient (*r*) and the value of probability *p* are shown.

vs.	L8	S10	GAPDH	EF-1	β-actin	RBF-2	BF2	NM23
S10	0.884							
p-value	0.000							
GAPDH	0.831	0.617						
p-value	0.000	0.001						
EF-1	0.915	0.747	0.823					
p-value	0.000	0.000	0.000					
***β-actin**	0.573	0.337	0.787	0.657				
p-value	0.003	0.107	0.000	0.000				
***RBF-2**	0.472	0.446	0.293	0.293	0.324			
p-value	0.020	0.029	0.157	0.165	0.122			
***BF2**	0.612	0.640	0.395	0.439	0.308	0.900		
p-value	0.001	0.001	0.056	0.032	0.143	0.000		
NM23	0.931	0.773	0.726	0.888	0.536	0.434	0.563	
p-value	0.000	0.000	0.000	0.000	0.007	0.034	0.004	
Ubiquitin	0.925	0.862	0.749	0.835	0.456	0.414	0.610	0.890
p-value	0.000	0.000	0.000	0.000	0.025	0.044	0.002	0.000

• Gray highlighted is the *p*-value greater than 0.05 and does not show significant correlation.

• Abbreviations: β-actin (cytoplasmic β actin), RBF-2 (repressor brain factor 2), BF-2 (brain factor 2).

* Gene is excluded as normalizer gene for array data analysis.

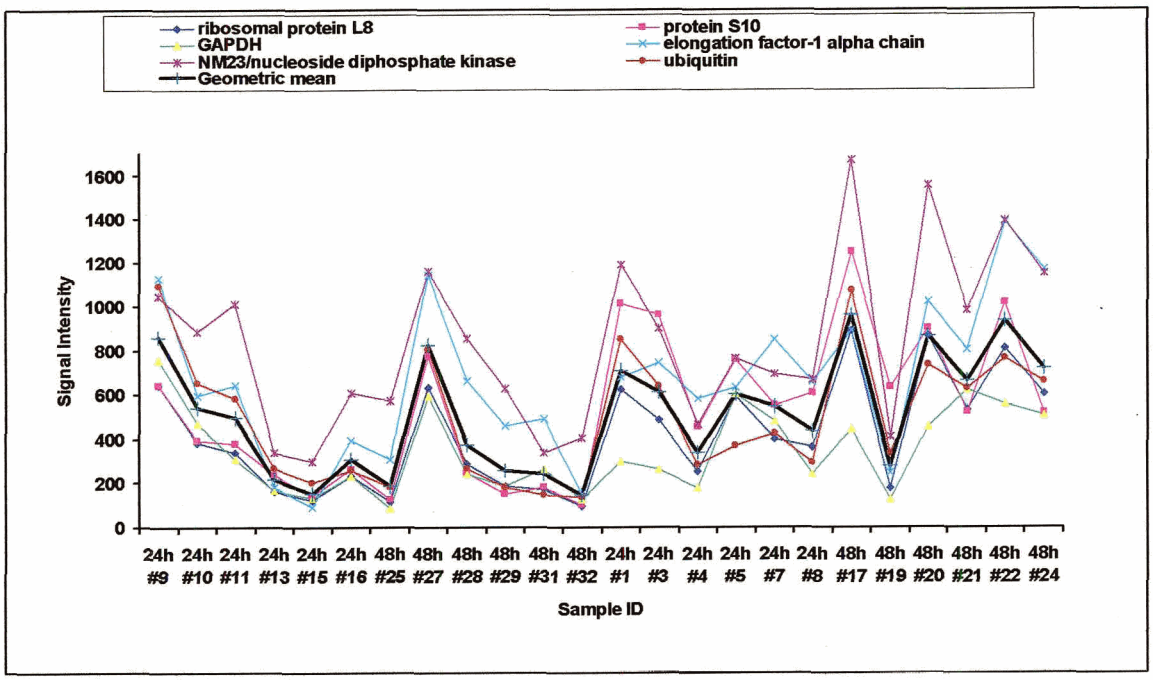


Figure 2.6. Expression of six normalizer genes and their geometric mean across all 24 arrays.

Signal intensities for each gene are represented median intensities. The signal intensities of Geometric Mean (GM) is derived from median intensities of these six normalizer genes for each array.

3.5.2 Identification of T_3-responsive genes.

TH is responsible for a change in the expression of many target genes during tadpole tail regression [72, 73, 80, 121]. To identify T_3-responsive genes, normalized and floor adjusted densitometric values obtained from MAGEX array analysis of the T_3-D tail samples (T_3 injection and tail subsequently incubated in DMSO in culture) were expressed as fold change relative to the D-D tails (DMSO injection and DMSO in culture). In the 24 h injection set, six genes were up-regulated and five genes were down-regulated (**Table 2.3**). Nine genes were previously identified as T_3-responsive, or up-regulated or down-regulated in anuran natural metamorphosis or mammals (81.82%). The relative expression levels of α 1 collagen type I and α 2 collagen type I were confirmed by QPCR respectively (**Table 2.3**). Five genes (myosin heavy chain 3, mitochondrial cytochrome c oxidase subunit 1, arginase, proteasome subunit Y, and hsp30) did not pass variance analysis (**Appendix 2.7**) and are therefore not presented in **Table 2.3**.

In the 48 h injection set, twenty genes were up- regulated and one gene was down-regulated (**Table 2.4**). Seventeen of these genes were previously identified as T_3-responsive, or up-regulated or down-regulated in anuran natural metamorphosis or mammals (80.95%). The relative expression levels of cytoplasmic β actin and α 2 collagen type I were confirmed by QPCR (**Table 2.4**). Nine of these genes (mitochondrial cytochrome c oxidase subunit 1, hsp30, proteasome subunit XC3, C/EBP, brain factor 1, NK-2 homolog, POU2, zic2, and frizzled 7) did not pass variance analysis (**Appendix 2.8**) and do not appear in the final **Table 2.4**.

A total of twenty-six genes displayed a 2 fold-change in relative gene expression in at least one time point. Five genes were up-regulated at both time points. These include

Table 2.3. T_3-induced gene expression profiles in the tail of *Rana catesbeiana* tadpoles in the 24 h injection set.

Gene Name	GenBank Accession No.	Functional Code[a]	Fold Change[b] T_3-D vs. D-D	
			Array	QPCR
•• cyclin D2[d]	X89476	1	-3.33	
activated protein kinase C	AF105259	3	-2.20	
• MAP kinase phosphatase	X83742	3	-2.13	
•• lactate dehydrogenase B	U07176	6	-2.12	
•• proteasome subunit XC3	S51111	8	-2.15	
•• GSK-3 binding protein	AF062738	3	2.12	
Δ •• α 1 collagen type I[c]	AB015440	9	2.17	1.98
α skeletal actin[c]	X03470	9	2.27	
Δ •• α 2 collagen type I[c]	D88764	9	2.45	2.62
•• SPARC[c]	X62483	1	3.10	
•• gelatinase B (MMP-9)[c]	AF072455	8	3.52	

•• Genes previously identified as T_3-responsive in *Xenopus laevis*, *Rana catesbeiana* or mammals.

• Genes previously identified up- or down-regulated during natural metamorphosis in *Xenopus laevis* or *Rana catesbeiana*.

Δ Gene relative expression level was confirmed by QPCR.

[a] Functional codes: 1, cell growth control; 2, chromatin structure; 3, signal transduction; 4, transcription; 5, hormonal regulation; 6, metabolism/biosynthesis; 7, transport/binding; 8, apoptosis/protein processing; 9, structural; 10, unknown function.

[b] Fold change T_3-D vs. D-D is that tadpoles were injected with T_3 and at 24 h time point tail tips were removed and subsequently incubated in serm-free medium containing DMSO versus DMSO injection follwed by incubation in medium containing DMSO. The positive ratio denotes up-regulation, the negative ratio is down-regulation.

[c] Gene that was up-regulated at both time points.

[d] Gene that was down-regulated at both time points.

Table 2.4. T_3-induced gene expression profiles in the tail of *Rana catesbeiana* tadpoles in the 48 h injection set.

Gene Name	GenBank Accession No.	Functional Code[a]	Fold Change[b] T_3-D vs. D-D	
			Array	QPCR
•• cyclin D2[d]	X89476	1	-2.78	
Δ • cytoplasmic β actin	AF079161	9	2.24	3.71
Δ •• α 2 collagen type I[c]	D88764	9	2.27	3.75
retinoic acid converting enzyme	AF057566	5	2.55	
aldolase B	AB030822	6	2.56	
DLL4	L09728	4	2.57	
•• DAD-1	D15059	8	2.59	
•• α 1 collagen type I[c]	AB015440	9	2.64	
•• RNA pol I transcription factor UBF	X57561	4	2.64	
•• arginase	D38303	6	2.64	
•• nuclear factor I-C1	L43149	4	2.65	
•• mitotic phosphoprotein 90	U95102	2	2.67	
• caspase-6	AB038169	8	3.10	
α skeletal actin[c]	X03470	9	3.68	
•• thyroid hormone binding protein	U03878	5	3.73	
•• raf ser/thr kinase	X12948	3	3.75	
•• SERCa1 fast skeletal muscle	X63009	3	4.01	
•• SPARC[c]	X62483	1	4.47	
•• gelatinase B (MMP-9)[c]	AF072455	8	5.13	
• iodothyronine deiodinase type II	L42815	5	5.49	
•• myosin heavy chain 3	AF097906	9	10.77	

•• Genes previously identified as T_3-responsive in *Xenopus laevis*, *Rana catesbeiana* or mammals.

• Genes previously identified up- or down-regulated during natural metamorphosis in *Xenopus laevis* or *Rana catesbeiana*.

Δ Gene relative expression level was confirmed by QPCR.

[a] Functional codes: 1, cell growth control; 2, chromatin structure; 3, signal transduction; 4, transcription; 5, hormonal regulation; 6, metabolism/biosynthesis; 7, transport/binding; 8, apoptosis/protein processing; 9, structural; 10, unknown function.

[b] Fold change T_3-D vs. D-D is that tadpoles were injected with T_3 and at 48 h time point tail tips were removed and subsequently incubated in serm-free medium containing DMSO versus DMSO injection follwed by incubation in medium containing DMSO. The positive ratio denotes up-regulation, the negative ratio is down-regulation.

[c] Gene that was up-regulated at both time points.

[d] Gene that was down-regulated at both time points.

α 2 collagen type I, α 1 collagen type I, gelatinase B, SPARC, α skeletal actin. Cyclin D2 was down-regulated at both time-points. Thirteen out of those twenty-six genes (50.00%) encode protein products important in transcription, signal transduction and cell structure. Activated protein kinase C, α skeletal actin, retinoic acid converting enzyme, aldolase B, and DLL4 are newly identified as T_3-response genes.

To identify the expression pattern of T_3-response genes at both time points, a hierarchical tree cluster was generated for those 18 genes having a 2 fold-change in at least one time point and with values that passed all of the quality control measures for both time points (**Figure 2.7**) (Among those 26 genes, 8 genes had data for only one time point due to replicate spots being less than 4 or not passing variance analysis). Three clusters were indentified with correlation coefficients ranging 0.97 to 0.99. Gene cluster 1 is characterized by down-regulation in only the 24 h injection set. These include activated protein kinase C and lactate dehydrogenase B. Cluster 2 is characterized by up-regulation in both injection sets. These include α 2 collagen type I, α 1 collagen type I, gelatinase B (MMP-9), SPARC, and α skeletal actin. Cluster 3 is characterized by up-regulation in only the 48 h injection set. These include cytoplasmic β actin, nuclear factor I-C1, iodothyronine deiodinase type II, raf ser/thr kinase, aldolase B, caspase-6, mitotic phosphoprotein 90, retinoic acid converting enzyme, thyroid hormone binding protein, and SERCa1 fast skeletal muscle. Cyclin D2 did not fall into the three clusters. Cyclin D2 was down-regulated in both injection sets.

3.5.3 T_3-responsive transcripts modulated by genistein during T_3-induced tail regression.

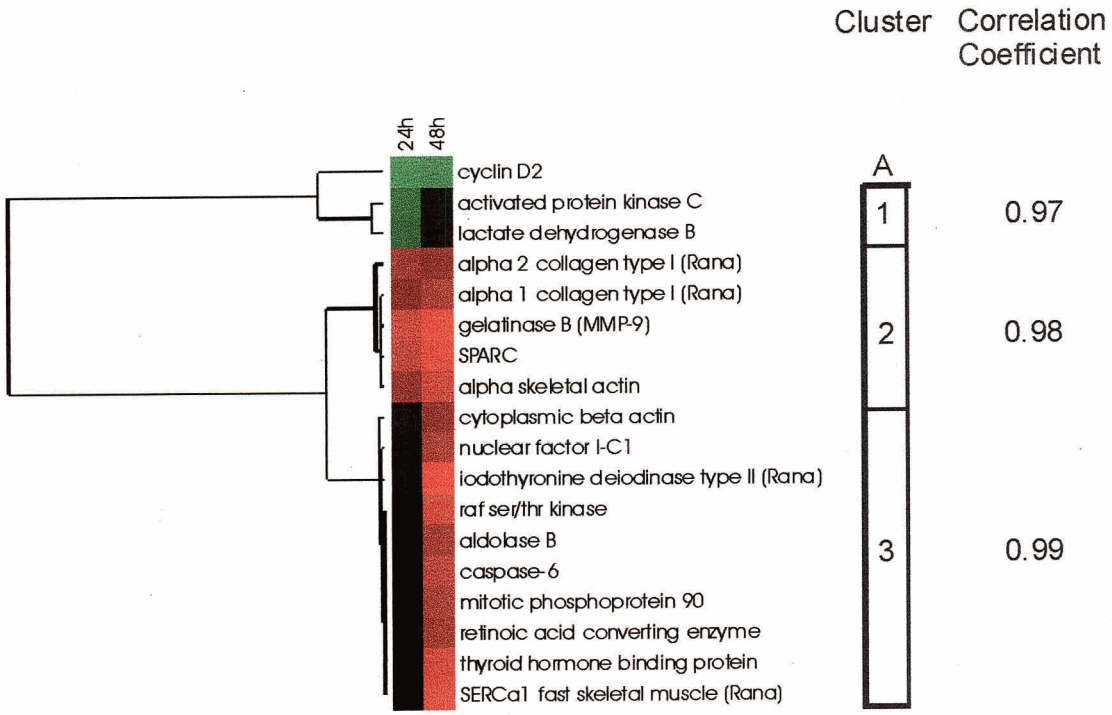


Figure 2.7. Cluster analysis of transcripts responsive to T_3 in the tadpole tail tissue of *Rana catesbeiana*.

Gene transcripts that met an arbitrary 2-fold change in at least one observation and with values for both time points (in the 24 h injection set and in the 48 h injection set), were subjected to agglomerative hierarchical clustering analysis. Shown is a hierarchical tree. All gene expression data were normalized to NF before clustering. An increase of gene expression is red, a decrease is green, and no change is black. The right of the diagram shows three gene clusters and their correlation coefficient. A is an unclustered gene.

Since the change in the gene expression program appears to be affected by genistein, possible gene targets should be uncovered by identifying genes that are T_3-responsive that are affected by genistein treatment after T_3 exposure, but not DMSO injection after 24 h injection, but not after the 48 h injection.

To identify transcripts potentially affected by genistein during T_3-induced tail regression program, I examined the fold changes of genes that were affected by T_3 identified above and compared their T_3-induced levels with those from T_3-injected animals whose tails were incubated in genistein. If the values differed by less than a factor of two, the gene was removed from the list. I then compared the remaining genes to DMSO injected and genistein organ cultured (D-G) tails. If the gene was affected by genistein regardless of whether the animals were injected with DMSO or T_3, this gene was removed from the list since unlikely that a change in its expression contributed to the biological outcome.

For the 24 h injection set, genistein treatment with T_3 injection results in arrays with a high intraclass correlation coefficient similar to the T_3-D tails (**Appendix 2.4**). This correlation coefficient decreases substantially in the 48 h injection set suggesting that the tail tissue responses are becoming more divergent. Only three gene transcripts are substantially affected by genistein after T_3 injection in the 24 h injection set. Of these, two that are down-regulated by T_3 are further depressed (**Table 2.5**). The remaining gene, gelatinase B, shows that its T_3-induced up-regulation is strongly attenuated. This is maintained in the 48 h injection set (**Table 2.6**) suggesting that its T_3-induced up-regulation may require a constant input of a tyrosine kinase mediated signal. In 48 h injection set, four other genes showed marked down-regulation by genistein in the

Table 2.5. Transcripts modulated by genistein during T_3-induced tail regression in *Rana catesbeiana* in the 24 h injection set.

Gene Name	GenBank Accession No.	Functional Code[a]	Fold Change[b]	
			T_3-D vs. D-D	T_3-G vs. D-D
activated protein kinase C	AF105259	3	-2.20	-9.64
•• lactate dehydrogenase B	U07176	6	-2.12	-6.30
•• gelatinase B (MMP-9)[d]	AF072455	8	3.52	1.00

•• Genes previously identified as T_3-responsive in *Xenopus laevis* or *Rana catesbeiana*.

[a] Functional codes: 1, cell growth control; 2, chromatin structure; 3, signal transduction; 4, transcription; 5, hormonal regulation; 6, metabolism/biosynthesis; 7, transport/binding; 8, apoptosis/protein processing; 9, structural; 10, unknown function.

[b] Fold change: *T_3-D/T_3-G vs. D-D*, is that tadpoles were injected with T_3 and at 24 h time point and whose tail tips were removed and subsequently incubated in serm-free medium containing DMSO/100 μM genistein (G) versus animals injected with DMSO and tail tips incubated in medium containing DMSO.
The positive ratio denotes up-regulation, the negative ratio is down-regulation.

[d]Gene that was down-regulated by genistein at both time points.

Table 2.6. Transcripts modulated by genistein during T_3-induced tail regression in *Rana catesbeiana* in the 48 h injection set.

Gene Name	GenBank Accession No.	Functional Code[a]	Fold Change[b]	
			T_3-D vs. D-D	T_3-G vs. D-D
•• raf ser/thr kinase	X12948	3	3.75	1.00
• caspase-6	AB038169	8	3.10	1.00
••gelatinase B (MMP-9)[d]	AF072455	8	5.13	1.00
iodothyronine deiodinase type II	L42815	5	5.49	0.99
aldolase B	AB030822	6	2.56	1.00

•• Genes previously identified as TH-responsive in *Xenopus laevis* or *Rana catesbeiana*.

• Genes previously identified up- or down-regulated during natural metamorphosis in *Xenopus laevis* or *Rana catesbeiana*.

[a] Functional codes: 1, cell growth control; 2, chromatin structure; 3, signal transduction; 4, transcription; 5, hormonal regulation; 6, metabolism/biosynthesis; 7, transport/binding; 8, apoptosis/protein processing; 9, structural; 10, unknown function.

[b] Fold change: *T_3-D/T_3-G vs. D-D*, is that tadpoles were injected with T_3 and at 48 h time point and whose tail tips were removed and subsequently incubated in serm-free medium containing DMSO/100 μM genistein (G) versus animals injected with DMSO and tail tips incubated in medium containing DMSO.
The positive ratio denotes up-regulation, the negative ratio is down-regulation.

[d]Gene that was down-regulated by genistein at both time points.

presence of T_3 treatment but not DMSO injected animals (**Table 2.6**). None of the other genes that were identified to be affected by T_3 showed any alteration in the T_3-induced response by genistein in either injection set.

The arrays were able to identify strongly expressed genes, but due to their limit of sensitivity, key regulators of the T_3-induced program such as transcription factors, were not detected. This includes TRα and TRβ transcripts.

3.6 Using reverse transcriptase quantitative real-time PCR (RT-QPCR) to examine effects of genistein on T_3-induced TRα, TRβ, and HSP30 gene expression profiles.

Total RNA was isolated from the tail tips of tadpoles that were cultured in the presence or absence of genistein for 24 h, 48 h or 72 h after the tadpoles were injected with T_3 or vehicle control (see **Figure 2.1** for experimental design). Ribosomal L8 protein mRNA, which remains relatively constant throughout different treatments, was used as an internal control [127] (see **Appendix 2.2**)

3.6.1 T_3-induced TRα transcript levels are not affected by genistein.

Tail tips from animals sacrificed 24 h after T_3 injection and subsequently incubated in serum-free medium (T_3-D) showed a significant increase in TRα mRNA levels at 24–72 h in organ culture compared to tail tips from DMSO only injected tadpoles (D-D) ($P<0.05$) (**Figure 2.8A**). However, when T_3-induced tail regression was completely blocked by 100 μM G (**Figure 2.5B**), TRα transcript levels were still significantly up-regulated in comparison to DMSO injected followed by DMSO cultured (D-D) ($P<0.05$). Furthermore, there was no statistical difference between T_3 injection followed by DMSO culture (T_3-D) and T_3 injection followed by 100 μM G culture (T_3-

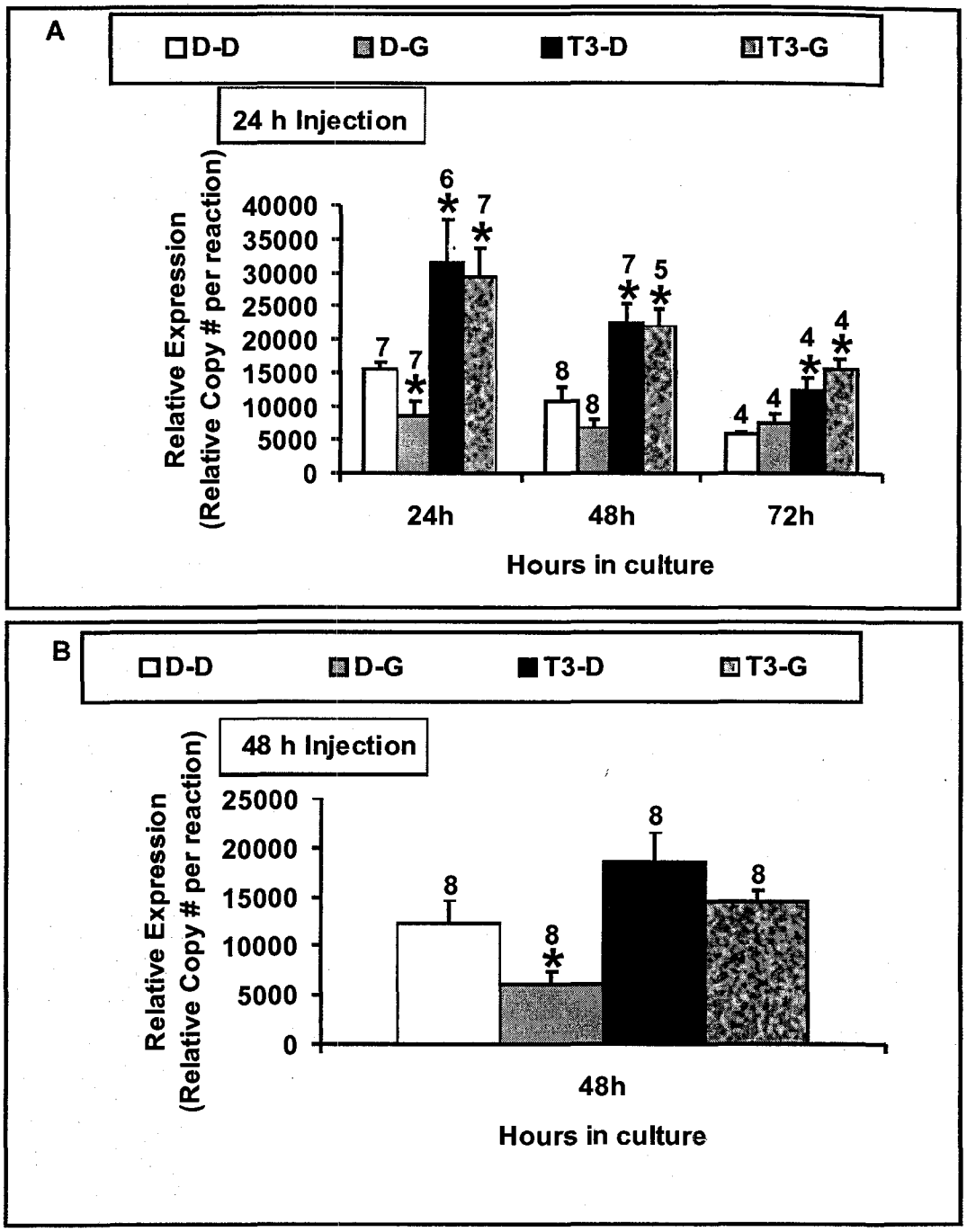


Figure 2.8. T_3-dependent TRα expression is not affected by genistein.

Relative expression levels of TRα (A) After 24 h DMSO (D) or T_3 injection *in vivo*, tadpole tail tips were removed and cultured in medium in the presence of D or 100 μM G

for 24 h, 48 h, or 72 h. (B) After 48 h D or T_3 injection *in vivo,* tadpole tail tips were removed and cultured in medium in the presence of D or 100 μM G for 48 h. * $P<0.05$ relative to D injection followed by D culture (D-D). N number for each treatment group is shown above the error bar.

G). This suggests that TRα up-regulation is not affected by genstein. Tail tips from animals sacrificed 48 h after T_3 injection and subsequently incubated in serum-free medium for 48 h (T_3-D) showed that TRα expression was not significantly up-regulated (**Figure 2.8B**). This may be due to the examining time after 96 h T_3 administration, which is consistent with the observation from Zhang *et al.* (Helbing lab unpublished data) that TRα goes down at 96 h. However, genistein culture alone [24 h after DMSO injection of tadpoles and tail tips culturing for 24 h (**Figure 2.8A**) and 48 h after DMSO injection of tadpoles and tail tips culturing for 48 h (**Figure 2.8B**)] did show a significant decrease in TRα levels in comparison to control.

3.6.2 Genistein affects T_3-induced up-regulation of TRβ.

Tail tips from animals sacrificed 24 h after T_3 injection and subsequently incubated in serum-free medium (T_3-D) showed a significant increase in TRβ mRNA levels at 24-72 h in organ culture compared to tail tips from DMSO only injected tadpoles (D-D) ($P<0.05$) (**Figure 2.9A**). This increase was significantly attenuated ($P<0.05$) (T_3-D vs. T_3-G) (**Figure 2.9A**) when tail regression was completely blocked by 100 μM G (**Figure 2.5B**). Tail tips from animals sacrificed 48 h after T_3 injection and subsequently incubated in DMSO containing medium for 48 h showed a significant increase in TRβ mRNA levels compared to DMSO only injected tadpoles (T_3-D vs. D-D) (**Figure 2.9B**). This T_3-induced increase in TRβ transcript levels was significantly attenuated in the presence of G (T_3-D vs. T_3-G) ($P<0.05$). This effect was to a lesser extent than that observed in the tail tips taken from after 24 h tadpoles injected with T_3 and incubated in G containing culture (**Figure 2.9A**) and is in keeping with the partial inhibition of G on tail regression (**Figure 2.5B**).

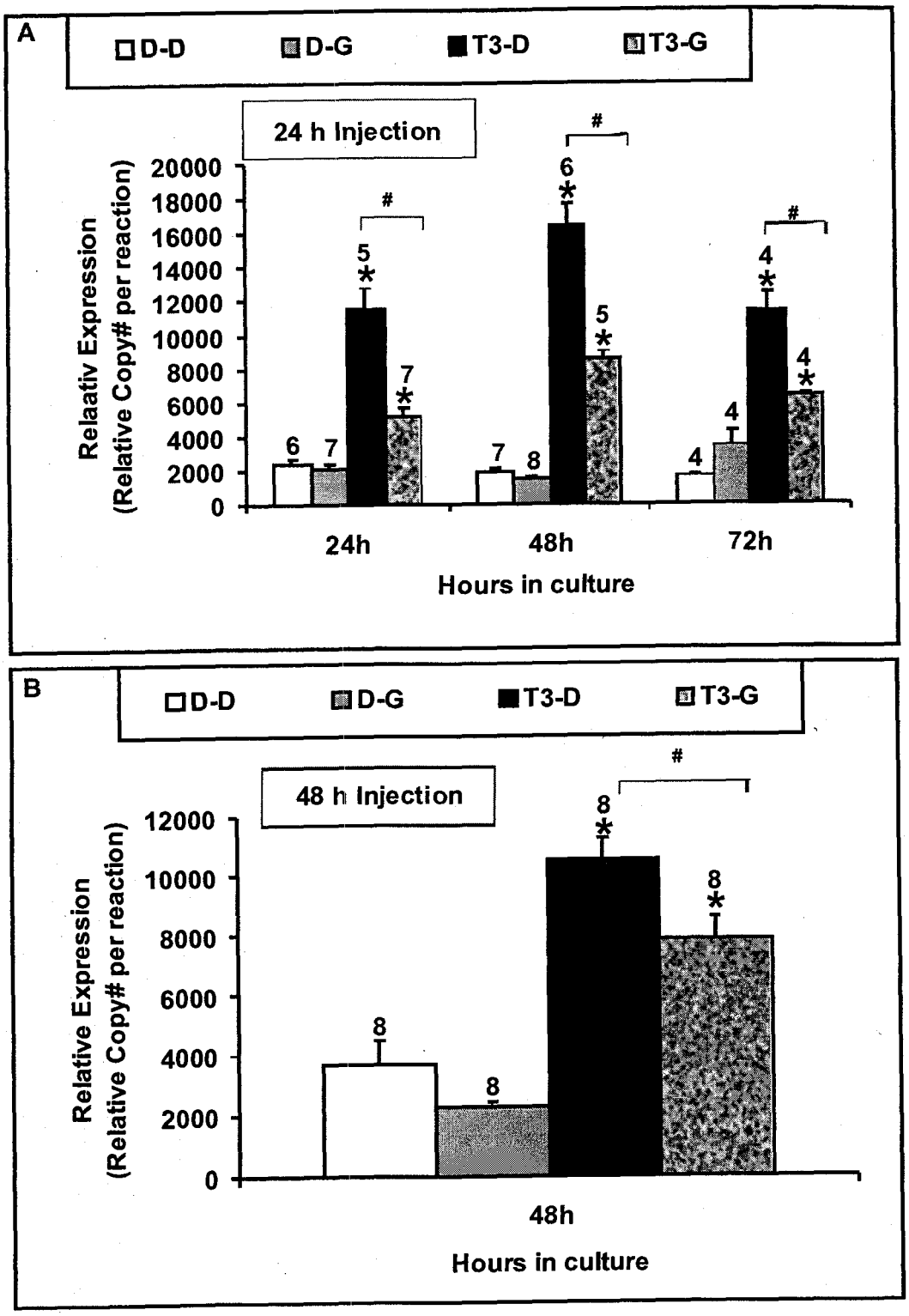


Figure 2.9. Genistein affects T_3-induced up-regulation of TRβ.

A) After 24 h DMSO (D) or T_3 injection *in vivo,* tadpole tail tips were removed and cultured in medium in the presence of D or 100 μM G for 24 h to 72 h. (B) After 48 h D or T_3 injection *in vivo,* tadpole tail tips were removed and cultured in medium in the presence of D or 100 μM G for 48 h. * $P<0.05$ relative to D injection followed by D culture (D-D). # $P<0.05$ in comparison to T_3 injection followed by D culture (T_3-D). N number for each treatment group is shown above the error bar.

To determine whether there is any correlation between TRα, TRβ expression levels and tail regression, I applied non-parametric Spearman correlation analysis. After 24 h tadpole injection with DMSO or T_3 followed by culturing of the tail tip in serum-free medium in the presence of DMSO or 100 μM G, TRβ relative expression levels correlate with tail regression (r=0.368, P<0.01). In contrast, no correlation was found between TRα relative expression levels and tail regression (r=0.086, P=0.487). These data suggest that TRβ up-regulation is crucial for tail regression and that this up-regulation may, in part, require tyrosine kinase signaling.

3.6.3 T_3 up-regulated HSP30 expression is not affected by genistein.

It is possible that more T_3-responsive genes may be affected by genistein in the same way as TRβ. HSP30 has been previously shown to be T_3-responsvie [79] and is also an indicator of cellular stess [128]. To determine whether HSP30 expression is affected when tail regression is blocked by 100 μM G, RT-QPCR was performed to examine HSP30 expression levels. Tail tips from animals sacrificed 24 h after T_3 injection and subsequently incubated in serum-free medium showed that HSP30 was significantly up-regulated at 24-72 h in comparison to D-D control (P<0.05) (**Figure 2.10A**). This is consistent with previous work that HSP30 is a T_3-responsive gene [79]. This response was not affected when tail regression was completely inhibited by 100 μM G (**Figure 2.10A**). Tail tips from animals sacrificed 48 h after T_3 injection and subsequently incubated in serum-free organ culture for 48 h also showed a significant increase of HSP30 mRNA levels compared to controls (**Figure 2.10B**). Like the response for the 24 h T_3 injected animals, G had no effect on this response. However, genistein alone (DMSO injected tadpoles) did show a significant increase in HSP30 levels which

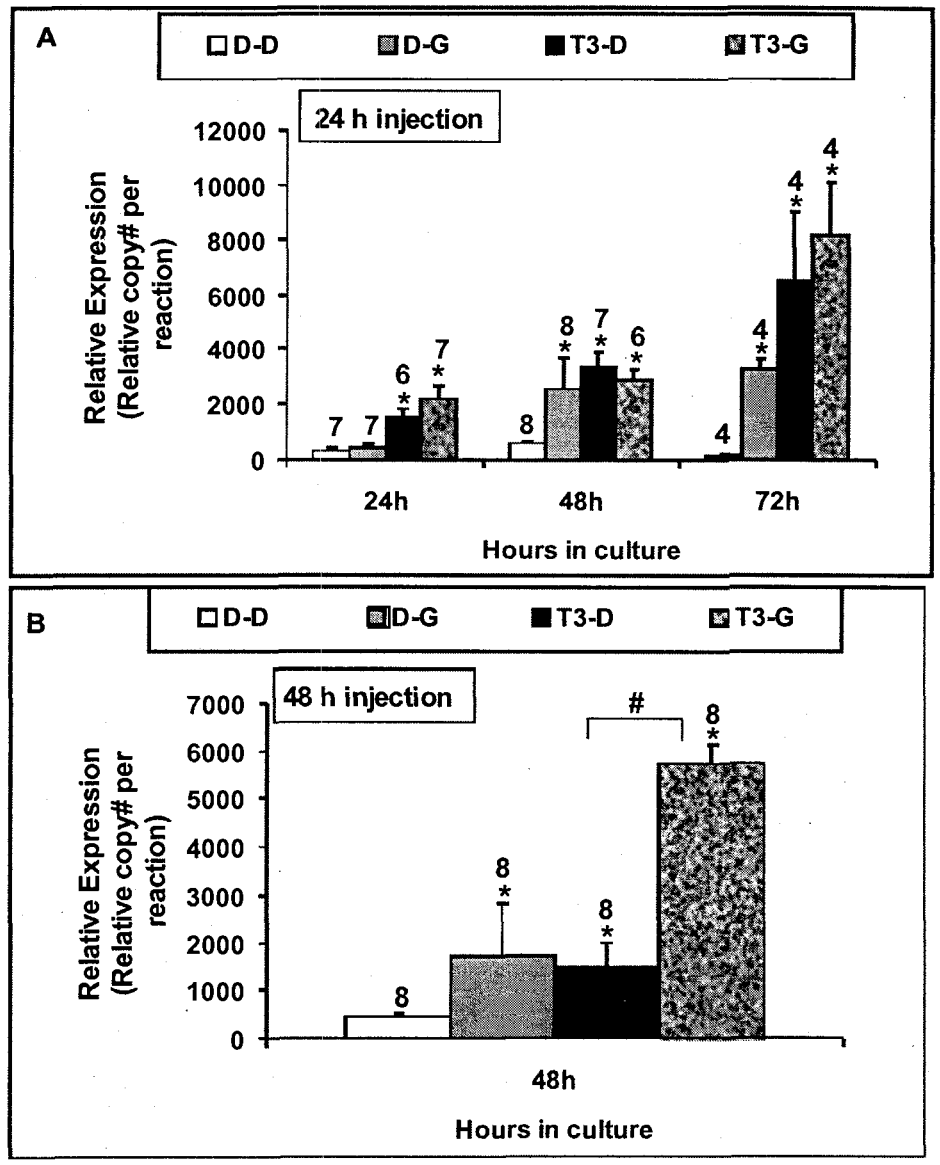


Figure 2.10. T_3-dependent increase in HSP30 expression is not affected by genistein. Relative expression levels of HSP30 after 24 h (A) and 48 h (B) DMSO (D) or T_3 injection *in vivo*, then tail tips were removed and incubated in the presence of D or 100 μM G. * $P<0.05$ relative to D injection followed by D culture (D-D). # $P<0.05$ in comparison to T_3 injection followed by D (T_3-D) culture. N number for each treatment group is shown above the error bar.

indicates that prolonged G treatment may be perceived as a stress in the tail tips. Overall, these data show that T_3-induced HSP30 expression is not affected by genistein.

3.7 Isolation and determination of T_3- and genistein sensitivity of two *Rana catesbeiana* ING1 (inhibitor of growth) genes.

To determine ING1 cellular function, we use amphibian metamorphosis as an experimental model in which TH acts to orchestrate tissue-specific proliferation, differentiation and apoptosis. I isolated the partial sequences of two *ING1* variants from the tail (*rING1*$_{tail}$) and brain (*rING1*$_{brain}$) tissue of the North American bullfrog, *Rana catesbeiana*. Multiple CLUSTALW alignments comparison *rING1*$_{brain}$ and *rING1*$_{tail}$ with isoforms of *Xenopus laevis ING1* (*xING1*) [118] show that they are most identical to *xING1b* exon 2 and share 85% DNA sequence identity to *xING1b*. CLUSTALW alignment shows that *rING1*$_{tail}$ and *rING1*$_{brain}$ share 85% sequence identity **(Figure 2.11A)**. The predicted polypeptide is translated from the third reading frame for *rING1*$_{tail}$ and *rING1*$_{brain}$. The putative rING1$_{tail}$ and rING1$_{brain}$ share 78% amino acid sequence identity to the putative xING1b protein [118] **(Figure 2.11B)**; and they are located after the conserved exon 1 and 2 boundary and before the highly conserved C terminus of the ING proteins containing a PHD finger domain, which is common to a family of proteins known to be associated with chromatin remodeling [129] **(Figure 2.11C)**.

The *rING1*$_{tail}$ transcripts is only expressed in the *Rana catesbeiana* tail but not the brain. The *rING1*$_{brain}$ is expressed in the *Rana catesbeiana* brain and tail **(Figure 2.12A)**. However, *rING1*$_{tail}$ mRNA expression levels are too low making it impossible to

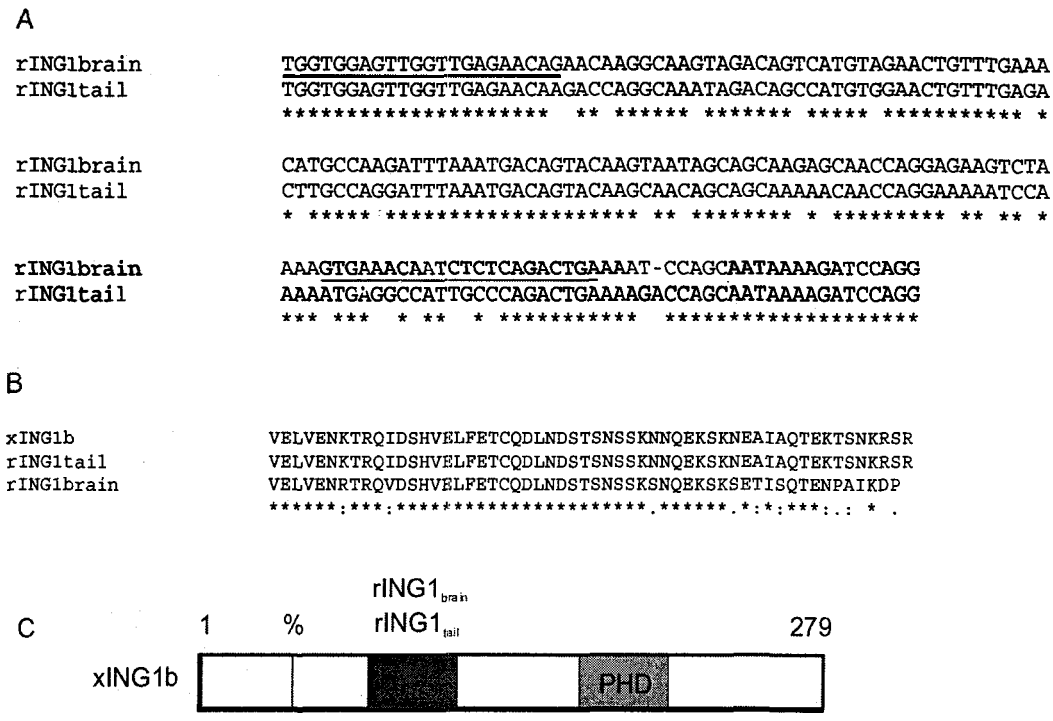


Figure 2.11. Sequence alignments of transcript variants for *rING1*$_{brain}$ and *rING1*$_{tail}$ and their putative encoded proteins.

(A) CLUSTALW alignment shows that *rING1*$_{brain}$ and *rING1*$_{tail}$ share 85% sequence identity. The locations of forward and reverse primer pair used for *rING1*$_{brain}$ RT-PCR analyses are underlined. (B) CLUSTALW Multiple alignments of putative rING1$_{brain}$ and rING1$_{tail}$ amino acid sequences with putative xING1b protein. The predicted proteins, rING1$_{tail}$ and rING1$_{brain}$, share 78% amino acid identity to the putative xING1b protein. (C) Schematic diagram shows the location of rING1$_{brain}$ and rING1$_{tail}$ in putative xING1b. The % symbol indicates the boundary between exon 1 and exon 2 as determined from the *Xenopus laevis* [117, 118].

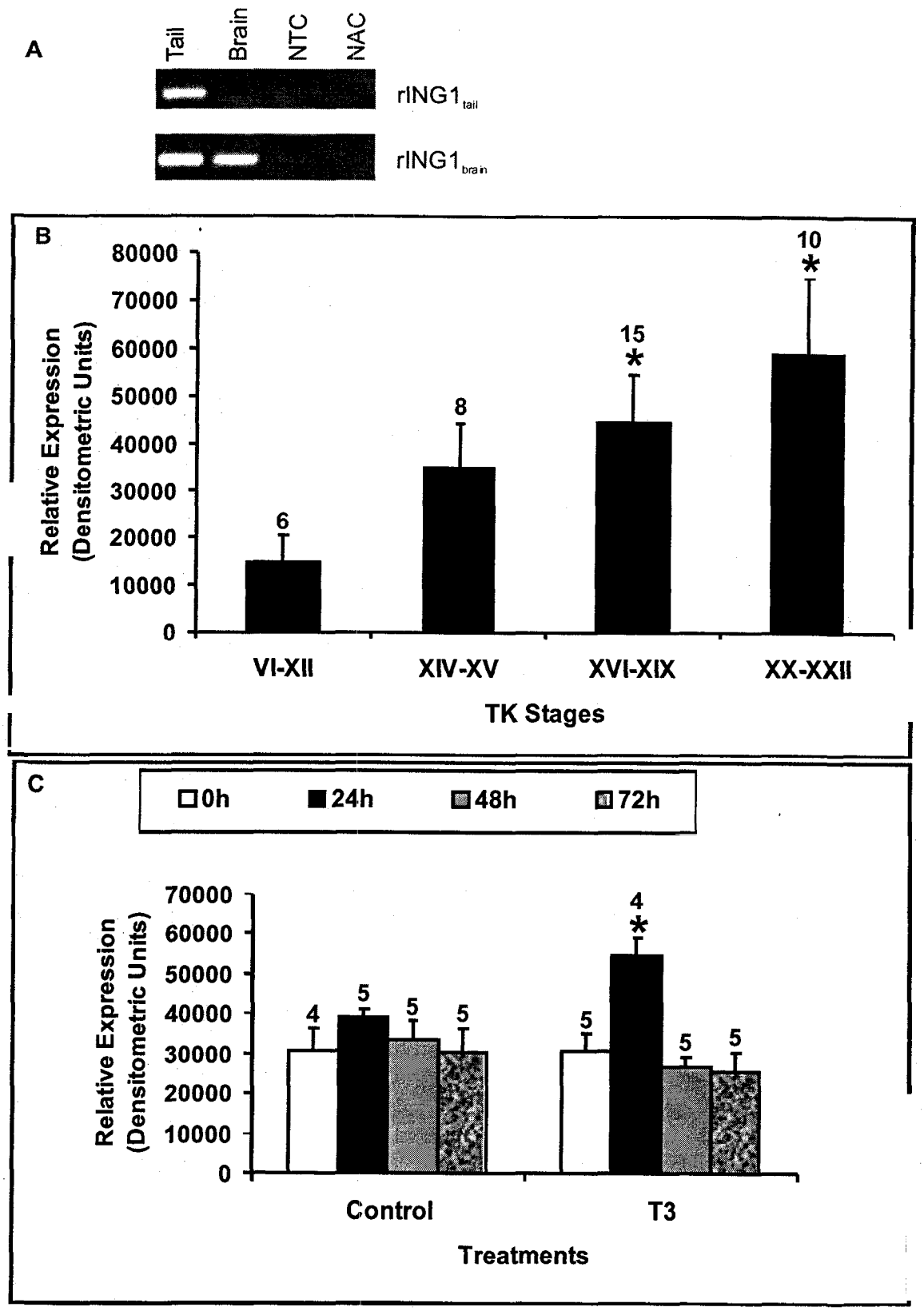


Figure 2.12. Expression of the *rING1brain* transcript during natural and T_3-

precocious metamorphosis in the *Rana catesbeiana* tail.

(A) Shown here are the representative 2% agarose gels of RT-PCR products of $rING1_{tail}$ and $rING1_{brain}$. NTC denotes no template control; NAC denotes no enzyme control. (B) $rING1_{brain}$ expression during natural metamorphosis in tail tips. * $P<0.05$ comparison to TK stages VI to XII. (C) $rING1_{brain}$ expression during T_3-precocious metamorphosis in tail. Tail biopsy was taken at each time point for each animal. * $P<0.05$ comparison to 0 h. N number for each treatment time points is shown above the error bar. Parametric One-Way ANOVA test followed by Post Hoc Tukey test were applied.

determine its expression level within all samples. I therefore focused on *rING1*$_{brain}$ for expression analysis. To determine *rING1*$_{brain}$ expression at the mRNA level in the tail during natural and T_3-induced precocious metamorphosis (both natural and T_3-precocious metamorphosis tail cDNA were kindly provided by Dr. Nik Veldhoen), I performed a modified RT-QPCR in which PCR reaction was stopped at 30 to 32 cycles in the linear range of amplification, followed by densitometry analysis. The *rING1*$_{brain}$ transcript is significantly up-regulated during tadpole natural metamorphosis in comparison to TK stages VI to XII ($P<0.05$) **(Figure 2.12B)**. During T_3-induced metamorphasis **(Figure 2.12C)**, *rING1*$_{brain}$ transcript is transiently up-regulated at 24 h in comparison to 0 h control ($P<0.05$). This indicates that *rING1*$_{brain}$ expression is T_3-responsive.

To address whether *rING1*$_{brain}$ expression is affected by genistein, I examined the effect of G on T_3-induced *rING1*$_{brain}$ expression. Tail tips from animals sacrificed 24 h after T_3 injection and cultured in serum–free medium showed that *rING1*$_{brain}$ maintained a significant up-regulation throughout tail tip culture compared to the D-D control ($P<0.05$) **(Figure 2.13A)**. When tail regression was completely suppressed by addition of 100 μM G, the increase of *rING1*$_{brain}$ levels remained high until 72 h in culture where the increase was no longer evident. Tail tips from animals sacrificed 48 h after T_3 injection and cultured in serum-free medium for 48 h showed a significant increase of *rING1*$_{brain}$ in comparison to the D-D control **(Figure 2.13B)** ($P<0.05$). However, when tail regression was partially blocked by 100 μM G **(Figure 2.5B)**, the T_3-induced increase of *rING1*$_{brain}$ was not evident. This suggests that *rING1*$_{brain}$ may be a later contributor for T_3-induced tail regression program and its expression is dependent, in part, on tyrosine kinase signaling.

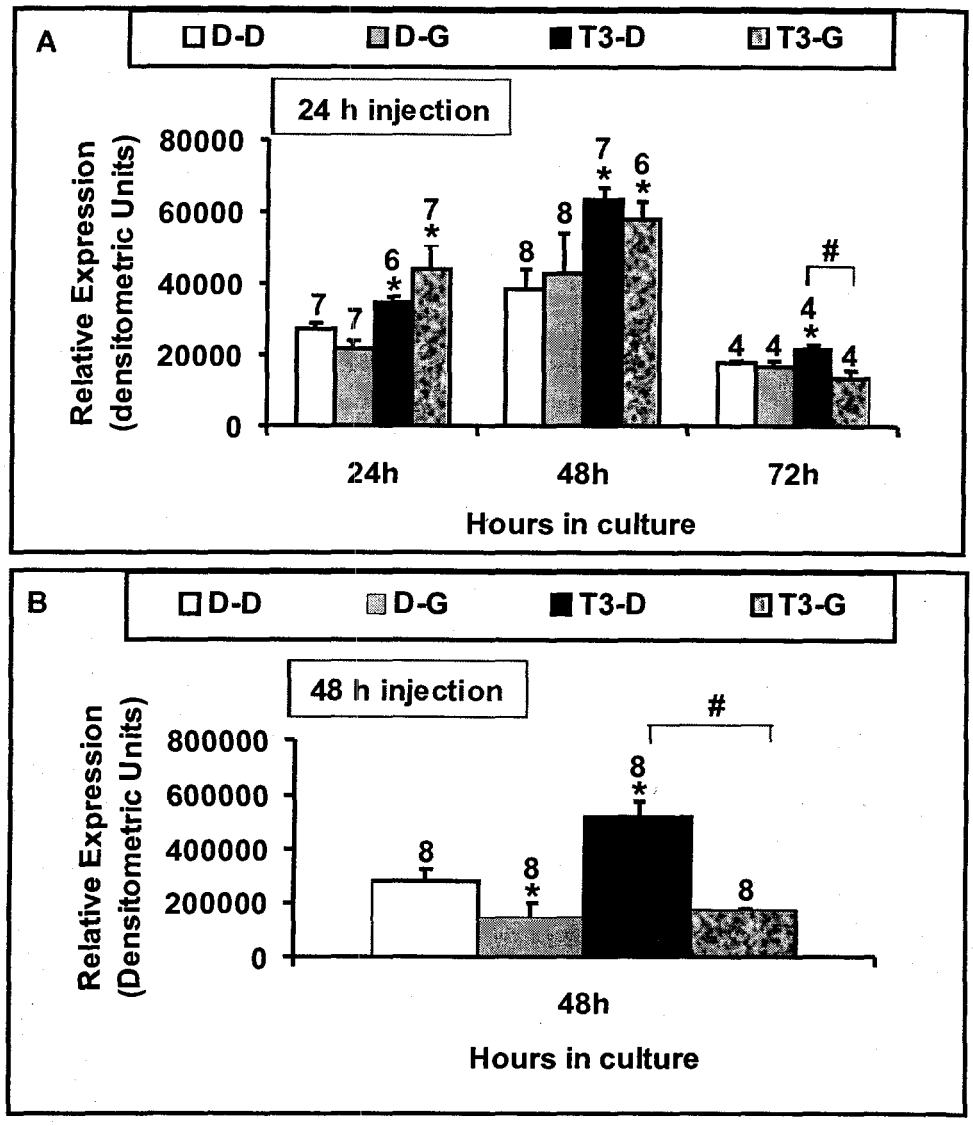


Figure 2.13. Relative expression levels of *rING1*$_{brain}$ in the tadpole injection followed by genistein inhibition study.

RT-QPCR followed by densitometry analysis was used to determine the relative expression level of *rING1*$_{brain}$ at (A) 24 h injection (B) 48 h injection. * $P<0.05$ comparison to DMSO (D) injection followed by D culture (D-D). # $P<0.05$ comparison to T_3 injection followed by D (T_3-D) culture. N number for each treatment time point is shown above the error bar.

3.8 TRα steady state level of phosphorylation is reduced by genistein during T_3-induced tail regression.

My data showed that TRβ mRNA (**Figure 2.9**), but not TRα mRNA (**Figure 2.8**), is significantly attenuated by genistein. My data also showed that genistein inhibition of T_3-induced tail regression is through alteration of protein phosphorylation level (**Figure 2.4**). *In vitro* and mammalian cell studies showed that phosphorylation of TRs modulates TR-mediated regulation of target gene expression [45, 46]. But there is no information about the functional role of TR phosphorylation *in vivo*.

To further understand the molecular mechanism underlying TRα transcriptional regulation of TRβ and determine whether this regulation is *via* alteration of TRα steady state level of phosphorylation, tadpoles (TK stage VI to XV) were injected with T_3 or vehicle control (DMSO) for 24 h and then the tail tips were removed and incubated in serum-free medium in the presence of 100 μM G or DMSO for a further 24 h. The tail tip protein homogenates were subjected to IP with anti-TRα and immunoblotted with anti-human TRα (hTRα) or anti-phospho-serine antibodies (**Figure 2.14**). T_3 induces TRα phosphorylation, this T_3-induced phosphorylation is attenuated by genistein by 24.23%. This result is re-reproducible in another pooled tail tip protein homogenate. This suggests that genistein inhibition of T_3-induced tail regression is *via* inhibition TRα phosphorylation, which regulates TRβ mRNA expression.

4. Discussion

Recent studies at the molecular level have demonstrated that TH regulates target gene expression through genomic effects by binding TRs [1]. Although there is increasing evidence of TH-induced signaling transduction affecting TH genomic action

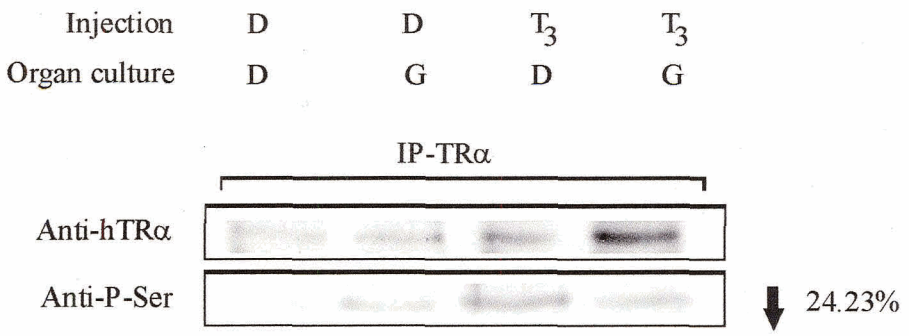


Figure 2.14. Genistein inhibition T_3-induced TRα phosphorylation.

TK stage VI to XV tadpoles were injected with 3 x 10^{-10} moles/body weight vehicle (DMSO, D) or T_3 and maintained for 24 h then the tail tips were removed and incubated in serum-free medium in the presence of 100 μM G or D for a further 24 h. The tail tip protein homogenates were subjected to immunoprecipitation (IP) with anti-TRα. The IP-proteins were resolved on 10% SDS-PAGE and immunoblotted with anti-human TRα (hTRα) or anti-phospho-serine antibodies.

[6-10] *in vitro*, few studies have addressed their relevance at cellular level *in vivo*. In this study, by using a tadpole tail organ culture system as an experiment model, I demonstrate the possible involvement of TH-induced tyrosine kinase signaling regulating TR classical/genomic action both at mRNA and protein phosphorylation levels.

Anuran metamorphosis is a complex process, which is absolutely dependent upon the TH controlling of gene expression as its basis. Tadpole tail regression is one of the most conspicuous events at the climax of metamorphosis. It requires a series of very complex changes of biochemical and gene expression [67, 72, 73, 80, 81]. We chose this system because it has distinct advantages for study. The tail can be cultured in a serum free medium for many days, and it responds to exogenously administrated T_3 in a fashion similar to the normal process of tail resorption that occurs at the climax of metamorphosis when endogenous TH is at its highest level. More importantly, it allows us to use specific inhibitors which would otherwise be toxic to the intact tadpoles and determining the involvement of a particular signaling pathway.

In tadpole tail organ culture experiment, it is shown that 100 μM genistein inhibits T_3-induced tail resorption (**Figure 2.3**). Although genistein shares structural similarity with E_2 and Sone *et al.* [130] showed that 10 μM E_2 alters *Xenopus laevis* embryonic development, genistein is ~1000 times less potent than E_2 [87, 91]. Genistein at high concentrations (30 μM to 100 μM) acts as a tyrosine kinase inhibitor, this suggests that the inhibition of T_3-induced tail regression most likely is through alteration of tyrosine kinase signaling rather than through TR/estrogen pathway crosstalk. Protein analysis show that this effect is *via* genistein inhibition of protein phosphotyrosine level of a 75 kDa protein (**Figure 2.4**).

In the tadpole injection experiment, it is shown that 24 h to 48 h is a critical window for this signaling to occur (**Figure 2.5**). This is coincident with the time required for the establishment genetic program for tail resorption [73]. The timing of these effects suggests that tyrosine kinase signaling may be important in the genetic program transition. This would be consistent with genistein's action as a tyrosine kinase inhibitor. This may also suggest that tyrosine kinase activity is required within 24 h during T_3-induced tail regression, while after 48 h its activity is not so crucial (G partially inhibited tail regression). Furthermore, it was shown that the inhibitor of Cdks, roscovitine, also completely inhibited tail regression in organ culture after 24 h exogenous T_3 administration [109]. This suggests that non-classical effects persist at least 24 h after TH treatment and stands in contrast to the concept that non-classical effects act within minutes up to 30 min [48]. Therefore, non-classical effects can be important not only minutes but also hours to days after TH treatment.

Induction of metamorphosis is dependent upon the TH-responsive nuclear receptors, TRα and TRβ. Previous studies showed that the steady-state levels of TRα mRNA and protein remained relatively constant during both natural and T_3-precocious metamorphosis, whereas the expression of TRβ was increased [72, 76, 82]. TRα levels were present in the prematmorphic tadpole whereas TRβ levels were extremely low until TH induction [76, 82] suggesting that TRα is critical for competence to respond to TH, TRβ is required for establishment the genetic programs during metamorphosis. Using QPCR analysis, an induction of mRNA TRα and TRβ was observed upon T_3 treatment (**Figure 2.15**, **Figure 2.8**, and **Figure 2.9**) as was expected from previous studies. T_3-induced up-regulation of TRβ transcripts levels, but not TRα, and the TRβ response was

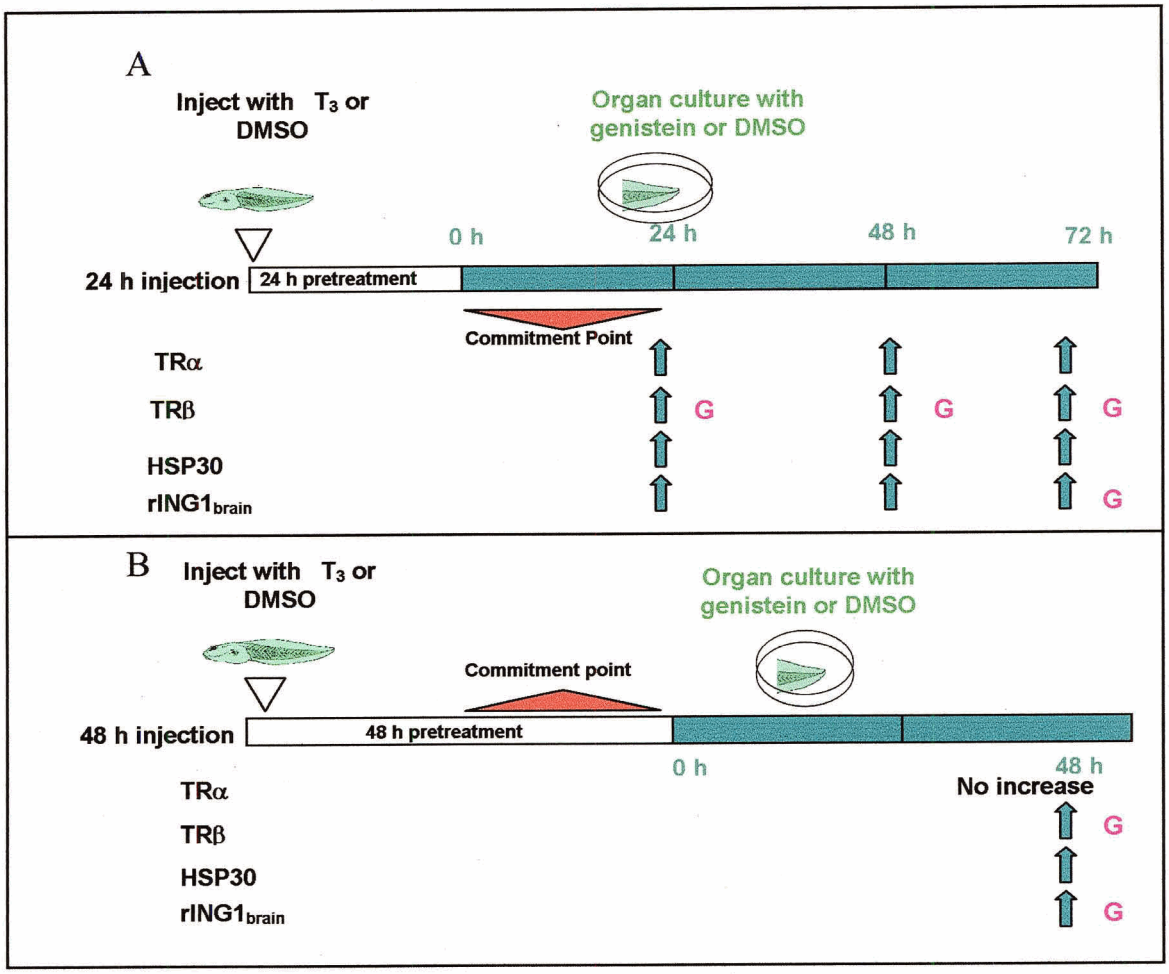


Figure 2.15. Summary of effects of genistein on T_3-induced TRα, TRβ, HSP30, and $rING1_{brain}$ mRNA expression levels in the 24 h injection set (A) and in the 48 h injection set (B).

The green arrows show the measured effect of T_3 treatment at the indicated time points. In those instances where genistein affects the T_3 induction, these effects are indicated by the pink "G".

attenuated by genistein in a time course that strongly correlated with the biological effects of this chemical on the inhibition T_3-induced tail regression (**Figure 2.3** and **Figure 2.5**). Moreover, genistein inhibition of TRβ mRNA in the tail tips taken from tadpoles injected with T_3 and incubated in culture 48 h after injection showed a lesser inhibition than that observed at 24 h (**Figure 2.9**), and this coincided with the partial inhibition by genistein on tail regression (**Figure 2.5**). These data are consistent with the previous studies that THs regulate the target gene expression at the transcriptional level and also suggest that tyrosine kinase signaling may play a role in the regulation of this process.

Although the TRs are ligand-activated receptors, they are also phosphoproteins and their functions can be regulated by phosphorylation [45, 46]. The phosphorylation and dephosphorylation reactions are accomplished by multiple enzymes, indicating cell alteration of protein activity in response to different signaling pathways. In eukaryotes, protein phosphorylation is the most important regulatory event. Since most signaling pathways contain tyrosine phosphorylation steps early on in the pathway that are amplified by subsequent serine/threonine phosphorylation events and since TRs have many more serine/threonine phosphorylation sites with regulatory consequences [131, 132], I examined the steady state level of TRα phosphorylation to investigate a possible molecular mechanism of genistein down-regulation of the TRβ gene. I showed that T_3-induced phosphorylation of TRα is reduced by genistein (**Figure 2.14**). This suggests that T_3 induces TRα phosphorylation, which regulates T_3-response gene, TRβ mRNA. This observation agrees with a previous study [32] that showed using dominant-negative TRα not only blocks transgenic tadpole metamorphosis, but also inhibits the expression of

known T_3 reponse genes, such as TRβ, TH/bZIP, and ST3 at transcripitional level in tail. More importantly, it provides the first direct biologically relevant *in vivo* evidence suggesting TR phosphorylation may be one of the mechanisms by which TRs achieve their diverse biological functions. Previous work from D. Brown's laboratory suggested that TR phosphorylation is not important during metamorphosis [76]. However, they only examined stage 59 tadpoles (*Xenopus laevis*) in which most TRs have already been phosphorylated and will not be able to further phosphorylated by [^{32}P]orthophosphate. Protein phosphorylation targets the protein for degradation by the ubiquitin-proteosome pathway [133]. I also observed that the increase of steady state levels TRα upon genistein treatment (**Figure 2.14**). This suggests that genistein inhibits TRα phosphorylation, which make this protein less likely to be degraded. It is also important to note that the T_3-dependent induction of TRβ transcripts, although greatly attenuated, is not completely blocked even when tail regression is (**Figure 2.9**). This suggests that part of the induction of the TRβ gene does not require phosporylation with further enhancement requiring it. How this translates to the production TRβ protein is currently being investigated.

ING protein acts as a class II tumor suppressor [111]. ING proteins contain a plant homeodomain (PHD) finger, a motif common to many chromatin-regulatory proteins. Recent studies suggested that the ING family of protein contribute to chromatin remodeling, and bind to and affect the activity of HATs, HDACs, and factor acetyltransferase protein complexes [134-137]. It is also shown that ING2 PHD finger interacts with phosphoinositides *in vivo*, which play a critical role in cytoplasmic signal transduction pathways [138]. Despite reports linking ING to chromatin remodeling and signal transduction, the molecular basis of how ING is involved in regulation of gene

expression has not been fully elucidated. There is evidence showing that down-regulation or mislocalization of ING1 protein, particularly the $p33^{ING1b}$ isoforms are common events in gliomas, glioblastomas [115], and human brain tumors [116]. Little is known how ING1 affects the phenotype by expression changes. To address the functional significance of ING1, we used anuran metamorphosis as an experimental model. In this study, *rING1*$_{brain}$ was cloned from *Rana catesbeiana* brain. rING1$_{brain}$ expression at transcript level is significantly up-regulated in natural and T_3-precocious tail resorption respectively (**Figure 2.12**), a finding that is consistent with previous studies in *Xenopus laevis* [117, 118]. Evidence also shows when tail regression is blocked by genistein, rING1$_{brain}$ expression is significantly down-regulated (**Figure 2.13**). This suggests that rING1$_{brain}$ may be a later contributor during TH-dependent tail regression. The mechanism of how ING1$_{brain}$ is involved in tyrosine kinase signaling during this process remains to be elucidated.

cDNA array hybridization experiments were designed to identify the potential genes affected by genistein during T_3-induced tail resorption. Across species cDNA hybridization and stringent step by step analysis were performed. The Excel (Microsoft) and SPSS based normalizer genes selection, SPSS based ICC analysis examining the quality of replicates, and Excel (Microsoft) based variance analysis of expressional stability of target genes serve as a good example for how to analyze complicated cDNA array data.

By comparison of fold change of transcript expression levels of T_3-G to T_3-D tail data, I showed that very few gene transcripts were affected by G in the presence of T_3. This suggests that tyrosine kinase signaling may be important in the regulation of only a

specific subset of T_3-responsive genes. It is important to note that the cNDA arrays may have missed important factors due to sensitivity and/or absence of the probes on the array. More work needs to done to look at more candidates. Nevertheless, gelatinase B, a matrixmetalloproteinase, is down-regulated by genistein at 24 h (**Table 2.5**) and 48 h (**Table 2.6**) sets, which supports a role for gelatinase B in T_3-induced tail regression. However, the relationship of this down-regulation of gelatinase B transcript by genistein and the inhibition of tail regression do not coincide, it is unlikely that the modulation of this gene is a key factor in this process. The observation of gelatinase B in cDNA arrays needs to be further confirmed by QPCR. The mechanism of how gelatinase B is linked to tyrosine kinase signaling transduction during T_3-dependent tail regression remain to be investigated. Recently, MAPK [139-142] and PI3K [141] pathways involving transcriptional regulation of gelatinase B has been demonstrated in mammals. It may be possible that PI3K and/or MAPK pathways are involved in the regulation of the gelatinase B in tadpole tail regression.

In summary, this study demonstrates phosphorylation is an important factor in establishing TH-dependent gene expression programs and suggests that TH classical/genomic and non-classical actions are interwoven to elicit a cellular response important in development. These data strongly implicate TRα as a target for phosphorylation which may selectively change the induction of specific target genes. However, it is possible that the major mechanism involving tyrosine kinase signaling may target additional cellular components that are improtant in the induction of tail regression. They may not be directly involved with gene expression changes such as caspases for example. Nevertheless, the findings presented in this thesis help decipher

non-classical and classica mechanisms behind T_3-dependent tail regression in the *Rana catesbeiana* tadpole. This work also contributes insight into our understanding the mechanism of TH-induced apoptosis.

5. Conclusions and Future Directions

The objective of this study was to determine whether tyrosine kinase signaling transduction affects TH classical/genomic action at cellular level *in vivo*. Genistein (one of major components in soy formula), which acts as tyrosine kinase inhibitor *in vitro* as well as shares similar structural features with E_2, was applied as a tool to investigate this hypothesis. Results show that genistein inhibits T_3-dependent tadpole tail regression and this effect is most likely through its tyrosine kinase inhibition action. QPCR data suggest a possible involvement of TRβ as a tyrosine signaling target during T_3-dependent tadpole tail resorption, which could reflect a novel mechanism interweaving of TH classical/genomic and non-classical actions. It is also shown that genistein affects T_3-induced phosphorylation of TRα, which indicates that phosphorylation is an important factor in establishing aspects of the T_3-dependent gene expression program.

TRs regulate target gene expression by recruiting TR-interacting cofactors [143-146], which are tissue dependent. Future work needs to investigate whether genistein affects TRβ phosphorylation level as well the interaction of TRs with their cofactors in the context of T_3-induced tail regression program. The steady state level of phosphorylation of TR cofactors will be investigated as it is well known that their activities can modulated by changes in phosphorylation. The well-characterized co-factors are SMRT, NCoR, and SRC. Of particular interest are the cofactors that inhibit TR-mediated gene activation [31, 147-149]. IP and immunoblotting using specific

antibodies can be performed. Both cell homogenates and fractionate protein homogenates into nuclear and cytoplasmic proteins can be examined. Fractionating cells into cellular compartments can enrich low abundance proteins and give us information about the function of the proteins whose expression profile can differ between cell compartments. SMRT for example has been shown to be a target for phosphorylation which results in the translocation of the protein from nucleus (active) to the cytoplasm (inactive) [149, 150]. Future work will focus on identifying possible targets for tyrosine kinase to begin to identify which signaling pathways are important for TH-dependent tail regression. Pro-Q Diamond stain (stains only phosphoproteins) for 1D and 2D gels can be performed to examine the change of overall phosphoproteins affected by genistein. The potential spots identified on 2D gel can be isolated for MS analysis to characterize the proteins.

My cDNA array data suggest that gelatinase B requires ongoing tyrosine kinase signaling during TH-dependent tadpole tail regression and might be important early on in tail regression. To further confirm the involvement of gelatinase B, QPCR analysis at its transcript level and gelatin zymography analysis [151] at the protein level can be performed. Cloning the gelatinase B gene is being conducted in our lab. Once the gene has been cloned, specific primers will be designed for QPCR analysis. Genes identified as affected by genistein in the **Table 2.5** and **Table 2.6** can be confirmed by QPCR when those genes have been cloned. The known T_3-response genes, such as TH/bZIP and ST3 which are undetectable on cDNA array, will also be examined by QPCR.

This work has and will contribute to the understanding of the connection between TH classical and non-classical effects, which helps to establish a new model for TH-induced apoptosis.

Literature cited

1. Yen, P.M., *Physiological and molecular basis of thyroid hormone action.* Physiol Rev, 2001. **81**(3): p. 1097-142.

2. Bergh, J.J., et al., *Integrin alphaVbeta3 contains a cell surface receptor site for thyroid hormone that is linked to activation of mitogen-activated protein kinase and induction of angiogenesis.* Endocrinology, 2005. **146**(7): p. 2864-71.

3. Ritchie, J.W., et al., *A role for thyroid hormone transporters in transcriptional regulation by thyroid hormone receptors.* Mol Endocrinol, 2003. **17**(4): p. 653-61.

4. Friesema, E.C., et al., *Identification of monocarboxylate transporter 8 as a specific thyroid hormone transporter.* J Biol Chem, 2003. **278**(41): p. 40128-35.

5. Dumitrescu, A.M., et al., *A novel syndrome combining thyroid and neurological abnormalities is associated with mutations in a monocarboxylate transporter gene.* Am J Hum Genet, 2004. **74**(1): p. 168-75.

6. Lin, H.Y., et al., *Thyroid hormone promotes the phosphorylation of STAT3 and potentiates the action of epidermal growth factor in cultured cells.* Biochem J, 1999. **338 (Pt 2)**: p. 427-32.

7. Lin, H.Y., et al., *Potentiation by thyroid hormone of human IFN-gamma-induced HLA-DR expression.* J Immunol, 1998. **161**(2): p. 843-9.

8. Lin, H.Y., et al., *Protein synthesis-dependent potentiation by thyroxine of antiviral activity of interferon-gamma.* Am J Physiol, 1997. **273**(4 Pt 1): p. C1225-32.

9. Schmidt, B.M., et al., *Nongenomic cardiovascular effects of triiodothyronine in euthyroid male volunteers.* J Clin Endocrinol Metab, 2002. **87**(4): p. 1681-6.

10. Wang, Y.G., et al., *Acute exposure to thyroid hormone increases Na+ current and intracellular Ca2+ in cat atrial myocytes.* J Physiol, 2003. **546**(Pt 2): p. 491-9.

11. Dixon, R.A. and D. Ferreira, *Genistein.* Phytochemistry, 2002. **60**(3): p. 205-11.

12. Lee, H.P., et al., *Dietary effects on breast-cancer risk in Singapore.* Lancet, 1991. **337**(8751): p. 1197-200.

13. Lamartiniere, C.A., *Protection against breast cancer with genistein: a component of soy.* Am J Clin Nutr, 2000. **71**(6 Suppl): p. 1705S-7S; discussion 1708S-9S.

14. Marks, L.S., et al., *Prostate cancer in native Japanese and Japanese-American men: effects of dietary differences on prostatic tissue.* Urology, 2004. **64**(4): p. 765-71.

15. Hwang, J., H.N. Hodis, and A. Sevanian, *Soy and alfalfa phytoestrogen extracts become potent low-density lipoprotein antioxidants in the presence of acerola cherry extract.* J Agric Food Chem, 2001. **49**(1): p. 308-14.

16. Alekel, D.L., et al., *Isoflavone-rich soy protein isolate attenuates bone loss in the lumbar spine of perimenopausal women.* Am J Clin Nutr, 2000. **72**(3): p. 844-52.

17. File, S.E., et al., *Eating soya improves human memory.* Psychopharmacology (Berl), 2001. **157**(4): p. 430-6.

18. Akiyama, T., et al., *Genistein, a specific inhibitor of tyrosine-specific protein kinases.* J Biol Chem, 1987. **262**(12): p. 5592-5.

19. Kim, H., T.G. Peterson, and S. Barnes, *Mechanisms of action of the soy isoflavone genistein: emerging role for its effects via transforming growth factor beta signaling pathways.* Am J Clin Nutr, 1998. **68**(6 Suppl): p. 1418S-1425S.

20. Utoh, R., et al., *Platelet-derived growth factor signaling as a cue of the epithelial-mesenchymal interaction required for anuran skin metamorphosis.* Dev Dyn, 2003. **227**(2): p. 157-69.

21. Doerge, D.R. and D.M. Sheehan, *Goitrogenic and estrogenic activity of soy isoflavones.* Environ Health Perspect, 2002. **110 Suppl 3**: p. 349-53.

22. Divi, R.L., H.C. Chang, and D.R. Doerge, *Anti-thyroid isoflavones from soybean: isolation, characterization, and mechanisms of action.* Biochem Pharmacol, 1997. **54**(10): p. 1087-96.

23. Doerge, D.R. and H.C. Chang, *Inactivation of thyroid peroxidase by soy isoflavones, in vitro and in vivo.* J Chromatogr B Analyt Technol Biomed Life Sci, 2002. **777**(1-2): p. 269-79.

24. Chang, H.C. and D.R. Doerge, *Dietary genistein inactivates rat thyroid peroxidase in vivo without an apparent hypothyroid effect.* Toxicol Appl Pharmacol, 2000. **168**(3): p. 244-52.

25. Mori, K., et al., *Involvement of tyrosine phosphorylation in the regulation of 5'-deiodinases in FRTL-5 rat thyroid cells and rat astrocytes.* Endocrinology, 1996. **137**(4): p. 1313-8.

26. Gorbman, A., W. W. W. Dickhoff, S. R. Vigna, N. B. Clark, and C. L. Ralph, *Comparative Endocrinology.* 1983: A Wiley-interscience Publication.

27. Norris, D., O., *Vertebrate Endocrinology.* Third edition ed. 1996: Academic Press.

28. Denver, R.J., *Acceleration of anuran amphibian metamorphosis by corticotropin-releasing hormone-like peptides.* Gen Comp Endocrinol, 1993. **91**(1): p. 38-51.

29. Griffin, J., E., and S. R. Ojeda, *Textbook of endocrine physiology.* Fourth edition ed. 2000: Oxford University Press.

30. Bassett, J.H., C.B. Harvey, and G.R. Williams, *Mechanisms of thyroid hormone receptor-specific nuclear and extra nuclear actions.* Mol Cell Endocrinol, 2003. **213**(1): p. 1-11.

31. Tomita, A., D.R. Buchholz, and Y.B. Shi, *Recruitment of N-CoR/SMRT-TBLR1 corepressor complex by unliganded thyroid hormone receptor for gene repression during frog development.* Mol Cell Biol, 2004. **24**(8): p. 3337-46.

32. Buchholz, D.R., et al., *Transgenic analysis reveals that thyroid hormone receptor is sufficient to mediate the thyroid hormone signal in frog metamorphosis.* Mol Cell Biol, 2004. **24**(20): p. 9026-37.

33. Sap, J., et al., *The c-erb-A protein is a high-affinity receptor for thyroid hormone.* Nature, 1986. **324**(6098): p. 635-40.

34. Weinberger, C., et al., *The c-erb-A gene encodes a thyroid hormone receptor.* Nature, 1986. **324**(6098): p. 641-6.

35. Eckey, M., U. Moehren, and A. Baniahmad, *Gene silencing by the thyroid hormone receptor.* Mol Cell Endocrinol, 2003. **213**(1): p. 13-22.

36. Apriletti, J.W., et al., *Molecular and structural biology of thyroid hormone receptors.* Clin Exp Pharmacol Physiol Suppl, 1998. **25**: p. S2-11.

37. O'Shea, P.J. and G.R. Williams, *Insight into the physiological actions of thyroid hormone receptors from genetically modified mice.* J Endocrinol, 2002. **175**(3): p. 553-70.

38. Brent, G.A., *Tissue-specific actions of thyroid hormone: insights from animal models.* Rev Endocr Metab Disord, 2000. **1**(1-2): p. 27-33.

39. Aranda, A. and A. Pascual, *Nuclear hormone receptors and gene expression.* Physiol Rev, 2001. **81**(3): p. 1269-304.

40. Sachs, L.M., et al., *Nuclear receptor corepressor recruitment by unliganded thyroid hormone receptor in gene repression during Xenopus laevis development.* Mol Cell Biol, 2002. **22**(24): p. 8527-38.

41. Yen, P.M., *Molecular basis of resistance to thyroid hormone.* Trends Endocrinol Metab, 2003. **14**(7): p. 327-33.

42. Chen, J.D. and R.M. Evans, *A transcriptional co-repressor that interacts with nuclear hormone receptors.* Nature, 1995. **377**(6548): p. 454-7.

43. Lee, J.W., et al., *Two classes of proteins dependent on either the presence or absence of thyroid hormone for interaction with the thyroid hormone receptor.* Mol Endocrinol, 1995. **9**(2): p. 243-54.

44. Rosenfeld, M.G. and C.K. Glass, *Coregulator codes of transcriptional regulation by nuclear receptors.* J Biol Chem, 2001. **276**(40): p. 36865-8.

45. Sugawara, A., et al., *Phosphorylation selectively increases triiodothyronine receptor homodimer binding to DNA.* J Biol Chem, 1994. **269**(1): p. 433-7.

46. Bhat, M.K., K. Ashizawa, and S.Y. Cheng, *Phosphorylation enhances the target gene sequence-dependent dimerization of thyroid hormone receptor with retinoid X receptor.* Proc Natl Acad Sci U S A, 1994. **91**(17): p. 7927-31.

47. Nicoll, J.B., et al., *Compartment-specific phosphorylation of rat thyroid hormone receptor alpha1 regulates nuclear localization and retention.* Mol Cell Endocrinol, 2003. **205**(1-2): p. 65-77.

48. Schmidt, B.M., et al., *Rapid, nongenomic steroid actions: A new age?* Front Neuroendocrinol, 2000. **21**(1): p. 57-94.

49. Li, L., M.P. Haynes, and J.R. Bender, *Plasma membrane localization and function of the estrogen receptor alpha variant (ER46) in human endothelial cells.* Proc Natl Acad Sci U S A, 2003. **100**(8): p. 4807-12.

50. Zhu, Y., et al., *Cloning, expression, and characterization of a membrane progestin receptor and evidence it is an intermediary in meiotic maturation of fish oocytes.* Proc Natl Acad Sci U S A, 2003. **100**(5): p. 2231-6.

51. Zhu, Y., J. Bond, and P. Thomas, *Identification, classification, and partial characterization of genes in humans and other vertebrates homologous to a fish membrane progestin receptor.* Proc Natl Acad Sci U S A, 2003. **100**(5): p. 2237-42.

52. Moggs, J.G. and G. Orphanides, *Estrogen receptors: orchestrators of pleiotropic cellular responses.* EMBO Rep, 2001. **2**(9): p. 775-81.

53. Davis, P.J., et al., *Thyroxine promotes association of mitogen-activated protein kinase and nuclear thyroid hormone receptor (TR) and causes serine phosphorylation of TR.* J Biol Chem, 2000. **275**(48): p. 38032-9.

54. Lin, H.Y., et al., *Thyroid hormone induces activation of mitogen-activated protein kinase in cultured cells.* Am J Physiol, 1999. **276**(5 Pt 1): p. C1014-24.

55. Shih, A., et al., *Thyroid hormone promotes serine phosphorylation of p53 by mitogen-activated protein kinase.* Biochemistry, 2001. **40**(9): p. 2870-8.

56. Gustafsson, J.A., *Estrogen receptor beta--a new dimension in estrogen mechanism of action.* J Endocrinol, 1999. **163**(3): p. 379-83.

57. Iafrati, M.D., et al., *Estrogen inhibits the vascular injury response in estrogen receptor alpha-deficient mice.* Nat Med, 1997. **3**(5): p. 545-8.

58. Osborne, C.K., H. Zhao, and S.A. Fuqua, *Selective estrogen receptor modulators: structure, function, and clinical use.* J Clin Oncol, 2000. **18**(17): p. 3172-86.

59. Vasudevan, N., S. Ogawa, and D. Pfaff, *Estrogen and thyroid hormone receptor interactions: physiological flexibility by molecular specificity.* Physiol Rev, 2002. **82**(4): p. 923-44.

60. Zhu, Y.S., et al., *Estrogen and thyroid hormone interaction on regulation of gene expression.* Proc Natl Acad Sci U S A, 1996. **93**(22): p. 12587-92.

61. Zhu, Y.S., et al., *Molecular analysis of estrogen induction of preproenkephalin gene expression and its modulation by thyroid hormones.* Brain Res Mol Brain Res, 2001. **91**(1-2): p. 23-33.

62. Vasudevan, N., et al., *Crosstalk between oestrogen receptors and thyroid hormone receptor isoforms results in differential regulation of the preproenkephalin gene.* J Neuroendocrinol, 2001. **13**(9): p. 779-90.

63. Yarwood, N.J., et al., *Estradiol modulates thyroid hormone regulation of the human glycoprotein hormone alpha subunit gene.* J Biol Chem, 1993. **268**(29): p. 21984-9.

64. Yen, P.M., E.C. Wilcox, and W.W. Chin, *Steroid hormone receptors selectively affect transcriptional activation but not basal repression by thyroid hormone receptors.* Endocrinology, 1995. **136**(2): p. 440-5.

65. Gudernatsch, J.F., *Feed experiments on tadpoles. I. The influence of specific organs givens a food on frowth and differentiation. A contribution to the knowledge of organs with internal secretion.* Wilhelm Roux Arch. Entwicklungsmech. Org., 1912. **35**: p. 457-483.

66. Dodd, M.H., Dodd, J. M., *in physiology of the Amphibia*, ed. B. Lofts. 1976, New York: Academic Press.

67. Shi, Y.B., *Amphibian metamorphosis from morphology to molecular biology.* 2000, New York: A John Wiley & Sons, Inc., Publication.

68. Ishizuya-Oka, A. and A. Shimozawa, *Induction of metamorphosis by thyroid hormone in anuran small intestine cultured organotypically in vitro.* In Vitro Cell Dev Biol, 1991. **27A**(11): p. 853-7.

69. Shi, Y.B. and D.D. Brown, *The earliest changes in gene expression in tadpole intestine induced by thyroid hormone.* J Biol Chem, 1993. **268**(27): p. 20312-7.

70. Helbing, C., G. Gergely, and B.G. Atkinson, *Sequential up-regulation of thyroid hormone beta receptor, ornithine transcarbamylase, and carbamyl phosphate synthetase mRNAs in the liver of Rana catesbeiana tadpoles during spontaneous and thyroid hormone-induced metamorphosis.* Dev Genet, 1992. **13**(4): p. 289-301.

71. Helbing, C.C. and B.G. Atkinson, *3,5,3'-Triiodothyronine-induced carbamyl-phosphate synthetase gene expression is stabilized in the liver of Rana catesbeiana tadpoles during heat shock.* J Biol Chem, 1994. **269**(16): p. 11743-50.

72. Helbing, C.C., et al., *Expression profiles of novel thyroid hormone-responsive genes and proteins in the tail of Xenopus laevis tadpoles undergoing precocious metamorphosis.* Mol Endocrinol, 2003. **17**(7): p. 1395-409.

73. Wang, Z. and D.D. Brown, *Thyroid hormone-induced gene expression program for amphibian tail resorption.* J Biol Chem, 1993. **268**(22): p. 16270-8.

74. Kawahara, A., B.S. Baker, and J.R. Tata, *Developmental and regional expression of thyroid hormone receptor genes during Xenopus metamorphosis.* Development, 1991. **112**(4): p. 933-43.

75. Yaoita, Y. and D.D. Brown, *A correlation of thyroid hormone receptor gene expression with amphibian metamorphosis.* Genes Dev, 1990. **4**(11): p. 1917-24.

76. Eliceiri, B.P. and D.D. Brown, *Quantitation of endogenous thyroid hormone receptors alpha and beta during embryogenesis and metamorphosis in Xenopus laevis.* J Biol Chem, 1994. **269**(39): p. 24459-65.

77. Buckbinder, L. and D.D. Brown, *Thyroid hormone-induced gene expression changes in the developing frog limb.* J Biol Chem, 1992. **267**(36): p. 25786-91.

78. Shi, Y.B., et al., *Thyroid hormone regulation of apoptotic tissue remodeling during anuran metamorphosis.* Cell Res, 2001. **11**(4): p. 245-52.

79. Helbing, C., C. Gallimore, and B.G. Atkinson, *Characterization of a Rana catesbeiana hsp30 gene and its expression in the liver of this amphibian during both spontaneous and thyroid hormone-induced metamorphosis.* Dev Genet, 1996. **18**(3): p. 223-33.

80. Brown, D.D., et al., *The thyroid hormone-induced tail resorption program during Xenopus laevis metamorphosis.* Proc Natl Acad Sci U S A, 1996. **93**(5): p. 1924-9.

81. Brown, D.D., et al., *Amphibian metamorphosis: a complex program of gene expression changes controlled by the thyroid hormone.* Recent Prog Horm Res, 1995. **50**: p. 309-15.

82. Veldhoen, N., et al., *Distinctive gene profiles occur at key points during natural metamorphosis in the Xenopus laevis tadpole tail.* Dev Dyn, 2002. **225**(4): p. 457-68.

83. Gauthier, F.V., et al., *Postembryonic expression of the myosin heavy chain genes in the limb, tail, and heart muscles of metamorphosing amphibian tadpoles.* Microsc Res Tech, 2000. **50**(6): p. 458-72.

84. Suzuki, K., et al., *Novel Rana keratin genes and their expression during larval to adult epidermal conversion in bullfrog tadpoles.* Differentiation, 2001. **68**(1): p. 44-54.

85. Yamauchi, K., et al., *Structural characteristics of bullfrog (Rana catesbeiana) transthyretin and its cDNA--comparison of its pattern of expression during metamorphosis with that of lipocalin.* Eur J Biochem, 1998. **256**(2): p. 287-96.

86. Wang, T.T., N. Sathyamoorthy, and J.M. Phang, *Molecular effects of genistein on estrogen receptor mediated pathways.* Carcinogenesis, 1996. **17**(2): p. 271-5.

87. Zava, D.T. and G. Duwe, *Estrogenic and antiproliferative properties of genistein and other flavonoids in human breast cancer cells in vitro.* Nutr Cancer, 1997. **27**(1): p. 31-40.

88. Kuiper, G.G., et al., *Interaction of estrogenic chemicals and phytoestrogens with estrogen receptor beta.* Endocrinology, 1998. **139**(10): p. 4252-63.

89. Hill, L., W., and Stuart, H., C.,, *A soy bean food preparation for feeding infants with milk idiosyncrasy.* J. Am. Med. Assoc., 1929. **93**: p. 985-987.

90. *American Academy of Pediatrics. Committee on Nutrition. Soy protein-based formulas: recommendations for use in infant feeding.* Pediatrics, 1998. **101**(1 Pt 1): p. 148-53.

91. Badger, T.M., et al., *The health consequences of early soy consumption.* J Nutr, 2002. **132**(3): p. 559S-565S.

92. Setchell, K.D. and S.J. Cole, *Variations in isoflavone levels in soy foods and soy protein isolates and issues related to isoflavone databases and food labeling.* J Agric Food Chem, 2003. **51**(14): p. 4146-55.

93. Ishizuki, Y., et al., *[The effects on the thyroid gland of soybeans administered experimentally in healthy subjects].* Nippon Naibunpi Gakkai Zasshi, 1991. **67**(5): p. 622-9.

94. Hunter, T. and J.A. Cooper, *Protein-tyrosine kinases.* Annu Rev Biochem, 1985. **54**: p. 897-930.

95. Ushiro, H. and S. Cohen, *Identification of phosphotyrosine as a product of epidermal growth factor-activated protein kinase in A-431 cell membranes.* J Biol Chem, 1980. **255**(18): p. 8363-5.

96. Ek, B., et al., *Stimulation of tyrosine-specific phosphorylation by platelet-derived growth factor.* Nature, 1982. **295**(5848): p. 419-20.

97. Jacobs, S., et al., *Somatomedin-C stimulates the phosphorylation of the beta-subunit of its own receptor.* J Biol Chem, 1983. **258**(16): p. 9581-4.

98. Uckun, F.M., et al., *Biotherapy of B-cell precursor leukemia by targeting genistein to CD19-associated tyrosine kinases.* Science, 1995. **267**(5199): p. 886-91.

99. Fritz, W.A., et al., *Dietary genistein: perinatal mammary cancer prevention, bioavailability and toxicity testing in the rat.* Carcinogenesis, 1998. **19**(12): p. 2151-8.

100. Hakkak, R., et al., *Diets containing whey proteins or soy protein isolate protect against 7,12-dimethylbenz(a)anthracene-induced mammary tumors in female rats.* Cancer Epidemiol Biomarkers Prev, 2000. **9**(1): p. 113-7.

101. Cotroneo, M.S., et al., *Genistein action in the prepubertal mammary gland in a chemoprevention model.* Carcinogenesis, 2002. **23**(9): p. 1467-74.

102. Brown, N.M., et al., *Prepubertal genistein treatment modulates TGF-alpha, EGF and EGF-receptor mRNAs and proteins in the rat mammary gland.* Mol Cell Endocrinol, 1998. **144**(1-2): p. 149-65.

103. Rowlands, J.C., et al., *Soy and whey proteins downregulate DMBA-induced liver and mammary gland CYP1 expression in female rats.* J Nutr, 2001. **131**(12): p. 3281-7.

104. Badger, T.M., M.J. Ronis, and R. Hakkak, *Developmental effects and health aspects of soy protein isolate, casein, and whey in male and female rats.* Int J Toxicol, 2001. **20**(3): p. 165-74.

105. Stroheker, T., et al., *Influence of dietary soy isoflavones on the accessory sex organs of the Wistar rat.* Food Chem Toxicol, 2003. **41**(8): p. 1175-83.

106. Adams, N.R., *Permanent infertility in ewes exposed to plant oestrogens.* Aust Vet J, 1990. **67**(6): p. 197-201.

107. Setchell, K.D., et al., *Exposure of infants to phyto-oestrogens from soy-based infant formula.* Lancet, 1997. **350**(9070): p. 23-7.

108. Zoeller, R.T. and J. Rovet, *Timing of thyroid hormone action in the developing brain: clinical observations and experimental findings.* J Neuroendocrinol, 2004. **16**(10): p. 809-18.

109. Skirrow, R.C., *Cyclin dependent kinase activity is necessary for thyroid hormone induced tail regression in the Rana catesbeiana tadpole (M.Sc. thesis).* 2003, University of Victoria.

110. Lim, W., et al., *A thyroid hormone antagonist that inhibits thyroid hormone action in vivo.* J Biol Chem, 2002. **277**(38): p. 35664-70.

111. Sager, R., *Expression genetics in cancer: shifting the focus from DNA to RNA.* Proc Natl Acad Sci U S A, 1997. **94**(3): p. 952-5.

112. Helbing, C.C., et al., *A novel candidate tumor suppressor, ING1, is involved in the regulation of apoptosis.* Cancer Res, 1997. **57**(7): p. 1255-8.

113. Campos, E.I., et al., *Mutations of the ING1 tumor suppressor gene detected in human melanoma abrogate nucleotide excision repair.* Int J Oncol, 2004. **25**(1): p. 73-80.

114. Zhu, J.J., et al., *[p33(ING1b) enhances chemosensitivity of osteosarcoma cell U2OS to etoposide].* Ai Zheng, 2004. **23**(6): p. 640-4.

115. Vieyra, D., et al., *Altered subcellular localization and low frequency of mutations of ING1 in human brain tumors.* Clin Cancer Res, 2003. **9**(16 Pt 1): p. 5952-61.

116. Tallen, G., et al., *No ING1 mutations in human brain tumours but reduced expression in high malignancy grades of astrocytoma.* Int J Cancer, 2004. **109**(3): p. 476-9.

117. Wagner, M.J., et al., *Expression of novel ING variants is regulated by thyroid hormone in the Xenopus laevis tadpole.* J Biol Chem, 2001. **276**(50): p. 47013-20.

118. Wagner, M.J., Helbing, C. C., *Multiple variants of the ING1 and ING2 tumor suppressors are differentially expresed and thryroid hormone-responsive in Xenpus laevis. (in press).* General and Comparative Endocrinology, 2005.

119. Taylor, A.C., J.J. Kollros, *Stages in the normal development of Rana pipiens larvae.* Anatomical Reacord, 1946. **94**: p. 7-24.

120. Minshull, J., et al., *A MAP kinase-dependent spindle assembly checkpoint in Xenopus egg extracts.* Cell, 1994. **79**(3): p. 475-86.

121. Crump, D., et al., *Exposure to the herbicide acetochlor alters thyroid hormone-dependent gene expression and metamorphosis in Xenopus Laevis.* Environ Health Perspect, 2002. **110**(12): p. 1199-205.

122. Pfaffl, M.W., et al., *Determination of stable housekeeping genes, differentially regulated target genes and sample integrity: BestKeeper--Excel-based tool using pair-wise correlations.* Biotechnol Lett, 2004. **26**(6): p. 509-15.

123. Eisen, M.B., et al., *Cluster analysis and display of genome-wide expression patterns.* Proc Natl Acad Sci U S A, 1998. **95**(25): p. 14863-8.

124. Helbing, C.C., et al., *Quiescence versus apoptosis: Myc abundance determines pathway of exit from the cell cycle.* Oncogene, 1998. **17**(12): p. 1491-501.

125. Foss, D.L., M.J. Baarsch, and M.P. Murtaugh, *Regulation of hypoxanthine phosphoribosyltransferase, glyceraldehyde-3-phosphate dehydrogenase and beta-actin mRNA expression in porcine immune cells and tissues.* Anim Biotechnol, 1998. **9**(1): p. 67-78.

126. Schmittgen, T.D. and B.A. Zakrajsek, *Effect of experimental treatment on housekeeping gene expression: validation by real-time, quantitative RT-PCR.* J Biochem Biophys Methods, 2000. **46**(1-2): p. 69-81.

127. Shi, Y.B. and V.C. Liang, *Cloning and characterization of the ribosomal protein L8 gene from Xenopus laevis.* Biochim Biophys Acta, 1994. **1217**(2): p. 227-8.

128. Piper, P.W., *The heat shock and ethanol stress responses of yeast exhibit extensive similarity and functional overlap.* FEMS Microbiol Lett, 1995. **134**(2-3): p. 121-7.

129. Aasland, R., T.J. Gibson, and A.F. Stewart, *The PHD finger: implications for chromatin-mediated transcriptional regulation.* Trends Biochem Sci, 1995. **20**(2): p. 56-9.

130. Sone, K., et al., *Effects of 17beta-estradiol, nonylphenol, and bisphenol-A on developing Xenopus laevis embryos.* Gen Comp Endocrinol, 2004. **138**(3): p. 228-36.

131. Goldberg, Y., et al., *Activation of protein kinase C or cAMP-dependent protein kinase increases phosphorylation of the c-erbA-encoded thyroid hormone receptor and of the v-erbA-encoded protein.* Embo J, 1988. **7**(8): p. 2425-33.

132. Glineur, C., M. Bailly, and J. Ghysdael, *The c-erbA alpha-encoded thyroid hormone receptor is phosphorylated in its amino terminal domain by casein kinase II.* Oncogene, 1989. **4**(10): p. 1247-54.

133. Poizat, C., et al., *Phosphorylation-dependent degradation of p300 by doxorubicin-activated p38 mitogen-activated protein kinase in cardiac cells.* Mol Cell Biol, 2005. **25**(7): p. 2673-87.

134. Loewith, R., et al., *Three yeast proteins related to the human candidate tumor suppressor p33(ING1) are associated with histone acetyltransferase activities.* Mol Cell Biol, 2000. **20**(11): p. 3807-16.

135. Skowyra, D., et al., *Differential association of products of alternative transcripts of the candidate tumor suppressor ING1 with the mSin3/HDAC1 transcriptional corepressor complex.* J Biol Chem, 2001. **276**(12): p. 8734-9.

136. Kuzmichev, A., et al., *Role of the Sin3-histone deacetylase complex in growth regulation by the candidate tumor suppressor p33(ING1).* Mol Cell Biol, 2002. **22**(3): p. 835-48.

137. Vieyra, D., et al., *Human ING1 proteins differentially regulate histone acetylation.* J Biol Chem, 2002. **277**(33): p. 29832-9.

138. Gozani, O., et al., *The PHD finger of the chromatin-associated protein ING2 functions as a nuclear phosphoinositide receptor.* Cell, 2003. **114**(1): p. 99-111.

139. Cooper, K.L., et al., *Roles of mitogen activated protein kinases and EGF receptor in arsenite-stimulated matrix metalloproteinase-9 production.* Toxicol Appl Pharmacol, 2004. **200**(3): p. 177-85.

140. Ringshausen, I., et al., *Constitutive activation of the MAPkinase p38 is critical for MMP-9 production and survival of B-CLL cells on bone marrow stromal cells.* Leukemia, 2004. **18**(12): p. 1964-70.

141. Qiu, Q., et al., *EGF-induced trophoblast secretion of MMP-9 and TIMP-1 involves activation of both PI3K and MAPK signalling pathways.* Reproduction, 2004. **128**(3): p. 355-63.

142. Kang, J.L., et al., *Genistein prevents nuclear factor-kappa B activation and acute lung injury induced by lipopolysaccharide.* Am J Respir Crit Care Med, 2001. **164**(12): p. 2206-12.

143. Burke, L.J. and A. Baniahmad, *Co-repressors 2000.* Faseb J, 2000. **14**(13): p. 1876-88.

144. Chen, J.D. and H. Li, *Coactivation and corepression in transcriptional regulation by steroid/nuclear hormone receptors.* Crit Rev Eukaryot Gene Expr, 1998. **8**(2): p. 169-90.

145. Ito, M. and R.G. Roeder, *The TRAP/SMCC/Mediator complex and thyroid hormone receptor function.* Trends Endocrinol Metab, 2001. **12**(3): p. 127-34.

146. McKenna, N.J., R.B. Lanz, and B.W. O'Malley, *Nuclear receptor coregulators: cellular and molecular biology.* Endocr Rev, 1999. **20**(3): p. 321-44.

147. Jones, P.L., et al., *Multiple N-CoR complexes contain distinct histone deacetylases.* J Biol Chem, 2001. **276**(12): p. 8807-11.

148. Hong, S.H., C.W. Wong, and M.L. Privalsky, *Signaling by tyrosine kinases negatively regulates the interaction between transcription factors and SMRT (silencing mediator of retinoic acid and thyroid hormone receptor) corepressor.* Mol Endocrinol, 1998. **12**(8): p. 1161-71.

149. Hong, S.H. and M.L. Privalsky, *The SMRT corepressor is regulated by a MEK-1 kinase pathway: inhibition of corepressor function is associated with SMRT phosphorylation and nuclear export.* Mol Cell Biol, 2000. **20**(17): p. 6612-25.

150. Zhou, Y., et al., *The SMRT corepressor is a target of phosphorylation by protein kinase CK2 (casein kinase II).* Mol Cell Biochem, 2001. **220**(1-2): p. 1-13.

151. Jung, J.C., et al., *Matrix metalloproteinases mediate the dismantling of mesenchymal structures in the tadpole tail during thyroid hormone-induced tail resorption.* Dev Dyn, 2002. **223**(3): p. 402-13.

Appendices cDNA Array Data Process

Appendix 2.1. Variance analysis of twelve candidate normalizer genes.

24h			estimated SD	estimated SD	estimated SD	estimated SD	D/D				D/ G				T/D				T3/G			
Gene Name	GenBank	Functional	D/D	D/G	T3/D	T3/G	24h #1	24h #3	24h #4		24h #5	24h #7	24h #8		24h #9	24h #10	24h #11		24h #13	24h #15	24h #16	
	Accession #	Code	24h	24h	24h	24h	Mean	Mean	Mean	Median	Mean	Mean	Mean	Median	Mean	Mean	Mean	Median	Mean	Mean	Mean	Median
ribosomal protein L8	U00920	11	0.90	0.64	0.37	0.44	498	319	210	319	495	373	257	373	405	295	299	299	151	131	197	151
ribosomal protein L8	U00920	11	0.87	0.27	0.81	0.77	667	478	253	478	533	546	403	533	695	428	347	428	161	136	260	161
ribosomal protein L8	U00920	11	0.64	1.21	0.62	0.57	523	473	220	473	726	301	352	352	515	342	302	342	169	122	219	169
ribosomal protein L8	U00920	11	0.80	0.32	0.83	0.73	679	528	258	528	534	517	367	517	660	375	348	375	167	109	231	167
ribosomal protein L8	U00920	11	0.59	1.16	0.61	0.84	658	532	342	532	768	323	382	302	683	474	393	474	166	127	267	166
protein S10	S57432	11	0.58	0.34	0.66	0.47	1011	963	453	963	760	553	606	606	687	440	399	440	295	180	320	295
GAPDH	U41753	6	0.41	0.67	1.06	0.52	299	302	180	299	598	521	247	521	865	524	308	524	178	143	235	178
GAPDH	U41753	6	0.67	0.83	1.10	1.02	307	218	161	218	645	477	251	477	744	449	248	449	173	107	284	173
GAPDH	U41753	6	0.40	0.85	0.81	0.57	254	258	157	254	516	376	198	376	717	443	356	443	147	118	201	147
elongation factor-1 alpha chain	M25504	11	0.23	0.33	0.82	1.66	676	742	584	676	630	848	656	656	1126	596	645	645	184	89	395	184
NM23/nucleoside diphosphate kinase	X97899	2	0.81	0.14	0.16	0.92	1191	903	464	903	763	694	668	694	1050	885	1013	1013	339	298	608	339
ubiquitin	M11512	8	0.89	0.36	0.78	0.26	852	637	284	637	370	425	293	370	1095	654	584	654	260	201	258	258
cytoplasmic beta actin	AF079161	9	0.86	0.51	0.56	0.52	952	1613	796	952	1804	1417	1082	1417	2001	1381	1232	1381	1155	1008	1608	1155
cytoplasmic beta actin	AF079161	9	0.72	0.33	0.25	0.41	844	1337	732	844	1557	1483	1065	1483	1799	1717	1367	1717	951	988	1353	988
cytoplasmic beta actin	AF079161	9	1.12	0.61	0.53	0.54	874	1671	690	874	1872	1334	1054	1334	1876	1442	1108	1442	1026	1012	1570	1026
repressor brain factor 2	AF072889	4	0.76	1.19	0.61	0.69	461	407	153	407	526	302	167	302	454	276	291	291	689	354	489	489
brain factor 2	AJ011652	4	0.98	1.11	1.01	0.38	416	286	136	286	393	236	130	236	413	216	194	216	392	276	303	383
alpha skeletal actin	X03470	9	1.56	0.69	1.02	1.08	202	515	201	202	670	804	340	670	1223	806	399	806	152	226	396	226
C/EBP-2	U08605	4	1.25	0.76	0.37	0.67	203	155	11	155	182	255	117	182	280	227	197	227	752	393	538	538
hsp 30	U44894	7	1.00	1.26	1.09	0.22	4	11	15	11	98	61	21	61	781	529	204	529	111	95	119	111

No #25

48h			estimated SD	estimated SD	estimated SD	estimated SD	D/D				D/G				T3/D				T3/G			
Gene Name	GenBank	Functional	D/D	D/G	T3/D	T3/G	48h #17	48h #19	48h #20		48h #21	48h #22	48h #24		48h #25	48h #27	48h #28		48h #29	48h #31	48h #32	
	Accession #	Code	48h	48h	48h	48h	Mean	Mean	Mean	Median	Mean	Mean	Mean	Median	Mean	Mean	Mean	Median	Mean	Mean	Mean	Median
ribosomal protein L8	U00920	11	0.87	0.40	0.69	0.90	705	175	786	705	476	681	510	510		403	195	299	174	168	23	168
ribosomal protein L8	U00920	11	0.98	0.48	0.72	1.11	932	202	1118	932	546	897	733	733		621	291	456	196	294	76	196
ribosomal protein L8	U00920	11	0.96	0.61	0.67	0.73	853	157	728	728	442	734	479	479		632	316	474	190	123	100	123
ribosomal protein L8	U00920	11	0.83	0.53	0.80	0.46	892	184	926	892	536	860	612	612		647	277	462	170	184	106	170
ribosomal protein L8	U00920	11	0.97	0.31	0.69	1.04	1086	175	938	938	608	813	672	672		706	343	524	218	115	99	115
protein S10	S57432	11	0.69	0.95	1.08	0.45	1251	631	902	902	520	1015	518	520		853	255	554	135	169	108	135
GAPDH	U41753	6	0.85	0.20	0.81	0.55	424	122	483	424	636	581	522	581		648	273	461	210	276	160	210
GAPDH	U41753	6	0.77	0.18	0.86	0.95	522	142	495	495	621	581	516	581		613	245	429	189	276	97	189
GAPDH	U41753	6	0.76	0.22	0.77	0.57	419	113	404	404	489	509	403	489		518	231	374	175	193	94	175
elongation factor-1 alpha chain	M25504	11	0.87	0.50	0.53	0.74	889	247	1022	889	807	1388	1169	1169		1143	663	903	461	492	153	461
NM23/nucleoside diphosphate kinase	X97899	2	0.81	0.35	0.30	0.72	1672	411	1554	1554	984	1391	1151	1151		1157	854	1005	630	339	404	404
ubiquitin	M11512	8	1.00	0.21	1.00	0.33	1073	336	734	734	629	767	656	656		806	268	537	184	145	136	145
cytoplasmic beta actin	AF079161	9	0.68	0.27	0.73	0.60	1426	541	1305	1305	2054	2466	1904	2054		2880	1342	2111	1568	1102	910	1102
cytoplasmic beta actin	AF079161	9	0.62	0.12	0.86	0.40	1171	450	1176	1171	1932	1924	1701	1924		2725	1082	1903	1355	1010	947	1010
cytoplasmic beta actin	AF079161	9	0.61	0.17	0.66	0.48	975	504	1098	975	1841	2123	1817	1841		2516	1265	1890	1418	979	952	979
repressor brain factor 2	AF072889	4	0.64	0.60	0.59	0.62	825	422	625	625	423	687	438	438		533	290	412	439	186	458	439
brain factor 2	AJ011652	4	0.50	0.70	0.60	0.52	693	425	540	540	372	619	360	372		441	238	339	285	145	294	285
alpha skeletal actin	X03470	9	0.66	0.17	1.11	0.90	287	125	315	287	1024	1015	847	1015		1388	398	893	436	360	113	360
C/EBP-2	U08605	4	1.40	0.41	0.39	0.70	226	136	452	226	257	238	343	257		374	252	313	551	168	549	549
hsp 30	U44894	7	3.77	1.19	1.15	1.15	24	15	104	24	74	109	21	74		229	854	541	99	12	126	99

Appendix 2.2. Calculation of geometric mean (GM) and normalization factor (NF) based on the six normalizer genes.

Gene Name	GenBank Accession #	Functional Code	24h D/D 24h #1	24h #3	24h #4	D/G 24h #5	24h #7	24h #8	T3/D 24h #9	24h #10	24h #11	T3/G 24h #13	24h #15	24h #16
ribosomal protein L8	U00920	11	538	423	213	480	436	234	483	365	338	148	118	216
ribosomal protein L8	U00920	11	458	214	207	510	310	280	326	224	260	154	144	178
ribosomal protein L8	U00920	11	682	552	264	550	582	366	758	450	354	161	122	260
ribosomal protein L8	U00920	11	652	404	242	516	509	440	632	406	340	160	150	260
ribosomal protein L8	U00920	11	487	527	266	634	328	364	538	345	336	162	122	212
ribosomal protein L8	U00920	11	558	418	174	817	273	340	492	338	268	176	122	226
ribosomal protein L8	U00920	11	654	549	294	410	494	362	656	410	392	166	122	259
ribosomal protein L8	U00920	11	704	506	222	658	539	372	710	538	394	166	132	274
ribosomal protein L8	U00920	11	590	596	326	682	280	380	662	344	358	158	106	232
ribosomal protein L8	U00920	11	726	467	358	854	366	384	658	406	338	176	112	229
protein S10	S57432	11	1018	920	452	660	498	582	628	384	423	304	174	302
protein S10	S57432	11	1003	1006	454	860	608	630	746	496	374	286	186	338
GAPDH	U41753	6	288	286	182	540	466	240	924	494	302	162	140	220
GAPDH	U41753	6	309	318	178	656	576	253	805	554	314	194	146	250
GAPDH	U41753	6	306	239	176	606	492	250	700	452	272	172	82	294
GAPDH	U41753	6	307	197	146	684	462	252	788	446	224	174	132	274
GAPDH	U41753	6	233	232	138	438	255	204	707	385	358	146	102	202
GAPDH	U41753	6	274	284	176	594	497	192	726	501	354	147	133	200
elongation factor-1 alpha chain	M25504	11	635	616	611	606	806	555	1172	574	750	172	98	376
elongation factor-1 alpha chain	M25504	11	716	868	556	654	889	756	1080	618	540	196	80	413
NM23/nucleoside diphosphate kinase	X97899	2	1049	802	507	721	660	662	1001	868	990	361	300	563
NM23/nucleoside diphosphate kinase	X97899	2	1333	1003	420	804	728	674	1098	902	1036	316	295	652
ubiquitin	M11512	8	818	618	288	366	408	256	1034	643	629	252	198	266
ubiquitin	M11512	8	886	656	280	373	441	330	1156	664	538	283	204	250
		Median												
ribosomal protein L8			621	487	253	592	401	365	644	386	339	162	122	231
protein S10			1011	963	453	760	553	606	687	440	399	295	180	320
GAPDH			297	262	176	600	479	245	757	473	308	167	133	235
elongation factor-1 alpha chain			676	742	584	630	848	656	1126	596	645	184	89	395
NM23/nucleoside diphosphate kinase			1191	903	464	763	694	668	1050	885	1013	339	298	608
ubiquitin			852	637	284	370	425	293	1095	654	584	268	201	258

Final NF	24h D/D 24h #1	24h #3	24h #4	D/G 24h #5	24h #7	24h #8	T3/D 24h #9	24h #10	24h #11	T3/G 24h #13	24h #15	24h #16
GM	710	611	340	603	546	437	870	550	501	226	158	320
NF	**1.4**	**1.6**	**2.8**	**1.6**	**1.8**	**2.2**	**1.1**	**1.8**	**1.9**	**4.4**	**6.3**	**3.1**

Gene Name	GenBank Accession #	Functional Code	48h D/D 48h #17	48h #19	48h #20	D/G 48h #21	48h #22	48h #24	T3/D 48h #25	48h #27	48h #28	T3/G 48h #29	48h #31	48h #32
ribosomal protein L8	U00920	11	750	182	798	456	617	478	124	391	178	158	166	24
ribosomal protein L8	U00920	11	660	168	774	496	744	542	102	414	212	190	169	22
ribosomal protein L8	U00920	11	921	222	1094	552	903	796	128	654	282	184	337	50
ribosomal protein L8	U00920	11	942	182	1141	540	890	669	116	587	299	208	250	102
ribosomal protein L8	U00920	11	861	166	842	404	700	542	52	638	298	188	98	114
ribosomal protein L8	U00920	11	845	148	614	480	768	416	62	626	334	192	148	86
ribosomal protein L8	U00920	11	858	210	1006	549	848	612	138	682	334	202	59	96
ribosomal protein L8	U00920	11	926	158	846	523	871	611	122	729	352	234	170	102
ribosomal protein L8	U00920	11	1047	162	888	614	754	592	63	566	278	180	176	114
ribosomal protein L8	U00920	11	1124	188	988	602	872	752	120	727	276	159	192	98
protein S10	S57432	11	1146	580	885	441	939	525	138	823	222	140	174	104
protein S10	S57432	11	1356	682	919	599	1090	511	160	882	288	130	164	112
GAPDH	U41753	6	398	82	439	638	554	512	80	612	268	214	264	176
GAPDH	U41753	6	450	162	527	634	608	532	90	684	278	206	288	144
GAPDH	U41753	6	494	136	515	630	558	535	110	666	234	182	264	68
GAPDH	U41753	6	550	148	474	612	603	496	14	560	255	196	288	126
GAPDH	U41753	6	394	118	394	458	484	344	26	460	231	176	152	60
GAPDH	U41753	6	444	108	414	520	534	461	108	576	230	174	234	127
elongation factor-1 alpha chain	M25504	11	955	246	981	911	1342	1202	326	1082	692	506	486	176
elongation factor-1 alpha chain	M25504	11	823	248	1062	702	1434	1136	294	1204	634	416	498	130
NM23/nucleoside diphosphate kinase	X97899	2	1538	372	1412	890	1230	1062	528	1112	752	652	330	374
NM23/nucleoside diphosphate kinase	X97899	2	1805	449	1696	1078	1552	1240	620	1202	955	607	348	434
ubiquitin	M11512	8	942	344	686	670	762	634	173	716	264	186	140	144
ubiquitin	M11512	8	1204	328	781	588	771	678	196	896	272	181	150	128
		Median												
ribosomal protein L8			891	175	867	532	808	602	118	632	290	189	170	97
protein S10			1251	631	902	520	1015	518	149	853	255	135	169	108
GAPDH			447	127	457	621	556	504	85	594	245	189	264	127
elongation factor-1 alpha chain			889	247	1022	807	1388	1169	310	1143	663	461	492	153
NM23/nucleoside diphosphate kinase			1672	411	1554	984	1391	1151	574	1157	854	630	339	404
ubiquitin			1073	336	734	629	767	656	185	806	268	184	145	136

Final NF	48h D/D 48h #17	48h #19	48h #20	D/G 48h #21	48h #22	48h #24	T3/D 48h #25	48h #27	48h #28	T3/G 48h #29	48h #31	48h #32
GM	962	280	864	664	936	719	191	836	374	252	238	149
NF	**1.0**	**3.4**	**1.1**	**1.4**	**1.0**	**1.3**	**5.2**	**1.2**	**2.6**	**3.8**	**4.0**	**6.5**

- **Median intensity of each gene in each array were calculated using non-auto-leveled data**
- **Geometric mean of each array were calculated based on median intensity of these six genes.**
- **Normalization factors were determined by the highest geometric mean (GM) across all array divided by GM from a array.**

Appendix 2.3. Floor determination.

	24h set											
GM	**4.4**	**6.3**	**3.1**	**1.4**	**1.6**	**2.8**	**1.6**	**1.8**	**2.2**	**1.1**	**1.8**	**1.9**
Sample ID	#13	#15	#16	#1	#3	#4	#5	#7	#8	#9	#10	#11
Median	0	-684	0	0	0	-421	-38	-99	0	0	0	0
Quartile SD	2247	2894	1338	694	716	1065	477	447	1231	121	353	711
Floor	2247	2210	1338	694	716	644	439	348	1231	121	353	711
Max	8210	9928	6446	9216	2624	5438	6363	1825	6703	2708	4300	6738
Min	-8713	-9231	-7123	-2816	-4576	-6629	-3311	-3311	-5712	-1948	-2105	-3330
Blank value used	346	405	407	461	480	342	431	458	423	457	475	407
	48h set											
GM	**1.0**	**3.4**	**1.1**	**1.4**	**1.0**	**1.3**	**5.2**	**1.2**	**2.6**	**3.8**	**4.0**	**6.5**
Sample ID	#17	#19	#20	#21	#22	#24	#25	#27	#28	#29	#31	#32
Median	0	0	0	0	0	0	0	-84	-186	0	0	417
Quartile SD	169	705	445	374	369	419	1821	337	833	1136	1980	2129
Floor	169	705	445	374	369	419	1821	253	647	1136	1980	2545
Max	3215	7136	6615	3721	3848	5245	9033	3812	9831	8756	9922	9647
Min	-1184	-3544	-3049	-1898	-2603	-2273	-7632	-2799	-6939	-6340	-9850	-9784
Blank value used	499	501	477	455	409	409	437	405	433	398	359	464

- **The highest value across the all arrays "2545" were chosen as the final no-signal background (floor).**

Appendix 2.4. Intraclass correlation coefficient analysis sample integrity.

Treatments	24 h				48 h			
	D-D	D-G	T_3-D	T_3-G	D-D	D-G	T_3-D	T_3-G
Intraclass Correlation (α)*								
1) Consistency	0.82	0.51	0.9	0.87	0.76	0.94	0.79**	0.66
2) Absolute agreement	0.82	0.51	0.9	0.85	0.75	0.94	0.77**	0.62

* Denotes average measures.

** After removing sample #25, if include #25, the α value will be 0.33 and 0.32 for consistency and absolute agreement.

24 h/48 h is the period of time after the tadpoles were injected with DMSO or T_3.

Appendix 2.5.1 The normalized and floor adjusted final data applied for determination relative gene expression for 24 h injection set.

highlighted is spots number (N) <4.

NF from GM correction factors			1.36	1.57	2.83		1.60	1.76	2.20		1.12	1.78	1.93		4.41	6.33	3.10	
[redacted]			D/D				D/ G				T3/D				T3/G			
Gene Name	GenBank Accession #	Functional Code	#1	#3	#4	Median	#5	#7	#8	Median	#9	24h #10	#11	Median	#13	#15	#16	Median
c-mos	M25366	4	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545		2545	2545
c-mos	M25366	4	2545	2545	2545		2545	2545	2545			2545	2545		2545	2545	4225	
N-ras	M97960	3	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	7584	2545	2545	2545
N-ras	M97960	3	2545	2545			2545	2545	11323		2545	2545	7106			2545	2545	
K-ras	AF085280	3	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	59429	53565	35216	39505
K-ras	AF085280	3	2545	2545	2545		2545	2545	2545		2545	2545	2545		37912	41098	36575	
yes	X14377	3	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545		2545	2545	4636	2545	2545
yes	X14377	3	2545	2545	2545		2545	2545	2545		2545	2545			3713	2545	2545	
c-fos	AJ224511	4	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545		2545	2545	2545
c-fos	AJ224511	4	6593	2545	2545		2545	2545	2545		2545	2545	2545			2545	2545	
raf ser/thr kinase	X12948	3	6248	2545	2545	2545	2645	2545	2627	2545	2545	2545	2545	2545		8902		8902
raf ser/thr kinase	X12948	3	2545	2545	2545		2545		2545		2545	2545	2545					
c-ets-1a	X52692	4	2545	2545	2607	2545	2545	2545	6808	2545	2545	2545	2545	2545	26544	8484	2545	4103
c-ets-1a	X52692	4	2545	2545	2545		2545	2545	2545		2545	2545	2545		5662	2545	2545	
c-ets-1b	X52691	4		2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	32659	12752	22569	26740
c-ets-1b	X52691	4	2545	2545	2545		2545	2545	2545		2545	2545	2545		43106	9459	30911	
ets-2a	M81683	4	7201	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	4418	2545		4418
ets-2a	M81683	4	2545	2545	2545		2545	2545	2545		2545	2545	2545		7699	2545	4984	
c-myc I	X14806	4	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	28211	11903	17838	14871
c-myc I	X14806	4	6073	2545	2545		2545	2545	2545		2545	2545	2545		8360	4812	22051	
L-myc	L11363	4	2545	2545		2545	2545	2545	2545	2545	2545	2545	2545	2545	5582	2545	6111	5847
L-myc	L11363	4	2545	2545			2545	2545	2545		2545	2545	2545		6614	8548	3648	
pp60c-src	M24704	3	2545	2545	2545	2545	2545	2545	8095	2545	2545	2545	2545	2545	20257	6775	28050	26614
pp60c-src	M24704	3	2545	2545	2545		2545	2545	2545		2545	2545	2545		32694	44030	25178	
mdm2	PubMed ID: 9136986	1	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545		2545	2545	2545
mdm2	PubMed ID: 9136986	1	2545	2545	2545		2545	2545	2545		2545	2545	2545		2545	3926	2545	
ING2	AY014017	4	2545	2545	2984	2545	2545	2545	2545	2545	2545	2545	2545	2545	7946	5116	7017	6067
ING2	AY014017	4	2545	2545	2545		2545	2545	3501		2545	2545	2545		2545	11150	2718	
colorectal cancer tumor suppressor	U10986	3	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	31968	2545	26716	26097
colorectal cancer tumor suppressor	U10986	3	2545	2545	2545		2545	2545	2545		2545	2545	2545		25477	5610	28205	
protein/lipid phosphatase Pten	AF144732	3	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	29596	4014	2545	3689
protein/lipid phosphatase Pten	AF144732	3	2545	2545	2545		2545	2545	2545		2545	2545	2545		25874	2545	3363	
Wt1	D82051	4	2545	2545		2545	2545	2545	2545	2545	2545	2545	2545	2545	75232	43371	34453	44084
Wt1	D82051	4	2545	2545	2545		2545	2545	2545		2545	2545	2545		66034	44796	31835	
retinoblastoma 1	PubMed ID: 1516743	4	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545		2545	2545	2545	2545	2545
retinoblastoma 1	PubMed ID: 1516743	4	2545	2545	2545		2545	2545	2545		2545	2545			2545	2545	2545	
C/EBP-1	U08604	4	10564	3575	2545	2574	2545	7371	7386	5090	2545	2545	2545	2545	238039	151527	87746	147760
C/EBP-1	U08604	4	2603	2545	2545		2545	7568	2810		2545	2545	2545		229785	143992	103474	
C/EBP-2	U08605	4	260	245	71	243	278	462	286	295	300	395	333	364	3536	2621	1756	2488
C/EBP-2	U08605	4	290	241	-11		303	437	229		326	413	429		3095	2355	1579	
C/EBP	S44193	4	4164	2545	2545	2661	2545	2545	3508	2545	2545	3601	2545	3589	103620	49589	2545	47398
C/EBP	S44193	4	2776	2545	3962		2545	5838	2545		3576	4567	5106		81600	45207	2545	
transcription co-repressor Sin3	AF154112	2	6940	2545	2545	2545	2545	2545	2545	2545	2607	2545	2545	2545	2545	2545	2545	2545
transcription co-repressor Sin3	AF154112	2	6940	2545	2545		2545	2545	2545			2545	2545		2545	2545	2545	
circadian CLOCK	AF203107	4	5726	2545		2545	2545	2545	2545	2545	2545	2545	2545	2545	31774	19071		25422
circadian CLOCK	AF203107	4	2545	2545	2545		2545	2545	2545		2545	2545	2545		41501	7678		
c-Jun	6650725	4	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	61577		2545	5179
c-Jun	6650725	4	2545	2545	2545		2545	2545	2545		2545	2545	2545		71749	5179	2545	
c-Myb	L22741	4	2545	2545		2545	2545	4450	2545	2545	2545	2545	2545	2545	26890	4343	2545	6173
c-Myb	L22741	4	2545	2545			2545	2545	2545		2545	2545	2545		22020	8003	2545	
nuclear factor I-B1	L43146	4	2545	2545	3258	2545	2545	2545	2545	2545	2545	2545	2545	2545	30310	8003	2545	13182
nuclear factor I-B1	L43146	4	2545	2545	2545		2545	2545	2545		2545	2545	2545		35892	18362	2545	
nuclear factor I-C1	L43149	4	2545	7517	2545	2545	2545	6839	5263	3904	2545	2545	10270	2640	186390	110752	2545	120996
nuclear factor I-C1	L43149	4	2545	2545			2545	6122	2545		2545	4314	2735		229370	131241	4691	
TFIIA	K02938	4	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	3051	3356	5286	3449
TFIIA	K02938	4	2545	2545	2545		2545	2545	2545		2545	2545	2545		2545	6142	3543	
Oct-1	X17190	4	2545	2545	2545	2545	2545		2545	2545	2545	2545	3307	2545	46497	10320	4852	17282
Oct-1	X17190	4	2545	2545	2545		2545	2545	2545		2545	2545	2545		53547	24244	2545	
AP-2	M59455	4	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545		2545	10177	4850	2600	6825
AP-2	M59455	4	2545	2545	2545		2545	2545	2545		2545	2545			12858	8801	4715	
TBP-binding repressor Dr1	AB003582	4		2545	2545	2545	2545	2545	2545	2545	2545	2545		2545	2545	2545	5026	2545
TBP-binding repressor Dr1	AB003582	4		2545	2545		2545	2545	2545		2545	2545	2545		2545	2545	2545	
TFIID subunit	D50054	4		2870	2545	2545	2545	6610	2545	2545	4334	4488	2545	3360	159270	72965	33504	87835
TFIID subunit	D50054	4		2545	2545		2545	6550			4174	2545	2545		210357	57408	62305	
transcription factor A	U36728	4	2603	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	29022		8593	7273
transcription factor A	U36728	4	2545	2545			2545	2545	3514		2545	2545	2545		5953		2545	
RNA pol I transcription factor UBF	X57561	4	2545	8062	2545	2582	2545	2545	2545	2545	2545	2545	2545	2545	27179	2545	2545	2545
RNA pol I transcription factor UBF	X57561	4	2545	8052	2619		2545	5401	2545		3647	2545	3106		2545	2678		
elongation factor-1 alpha chain	M25504	11	861	969	1726	1168	987	1420	1222	1321	1310	1022	1450	1154	758	620	1166	811
elongation factor-1 alpha chain	M25504	11	971	1366	1572		1044	1566	1665		1208	1101	1044		864	507	1281	
neuroD	U28067	4	2545	2545	2545	2545	2545	2545	2545	2545	3041	2545	2545	2545	39058	7788	4821	3683
neuroD	U28067	4	2545	2545	2545		2545	2545	2545		2545	2545	2545		2545	2545	2545	
Tcf-3 co-repressor CtBP	AF152006	4	4685	2545	2545	2545	2545	2545	4558	2545	2545	2545	2545	2545	26430	9409	2545	4672
Tcf-3 co-repressor CtBP	AF152006	4	2545	2545	2545		2545	2545	2545		2545	2545	2545		6799	2545	2545	
repressor brain factor 2	AF072889	4	584	607	390	596	795	518	374	531	505	463	671	515	3034	2077	1448	2238
repressor brain factor 2	AF072889	4	666	673	475		884	544	361		510	520	553		3038	2400	1588	
co-repressor MITR	Z97214	4	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	3723	2545	2545
co-repressor MITR	Z97214	4	2545	2545	2545		2545	2545	2545		2545	2545	2545		2545	2545	2545	
negative regulator Id2	AB019520	4	2545	9289	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	12756	10827	10337	11792
negative regulator Id2	AB019520	4	2545	2545	2545		2545	2545	2545		2545	2545	2913		28484	7800	28367	
XCOE2	AF041138	4	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545
XCOE2	AF041138	4	2545	2545	2545		2545	2545	2545		2545	2545	2545		2545	8054	2916	
MRF4	S34392	4	5986	2545		2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545
MRF4	S34392	4	2545	2545			2545	2545	2545		2545	2545	2545		3139	2545	2545	
Pax-2	AF179300	4	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545		7224	4560	3713
Pax-2	AF179300	4	2545	2545	2545		2545	2545	2545		2545	2545	2545			2545	2866	
Pax-8	AF179301	4	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	61351	60074	36457	59235
Pax-8	AF179301	4	2545	2545	2545		2545	2545	2545		2545	2545	2545		67710	58396	22907	
LFB1/HNF1	64688	4	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	58900	47702	9611	47151
LFB1/HNF1	64688	4	6940	2545	2545		2545	2545	2545		2545	2545	2545		50708	46600	20679	
LFB3/HNF1 beta	X76052	4	6940	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	37559	47259	25500	40702
LFB3/HNF1 beta	X76052	4	2545	2545	2545		2545	2545	2545		2545	2545	2545		61748	43846	27641	
Gli2	AF109923	4	5699	2545	2545	2545	2545	2545	2801	2545	2675	2545	2545	2545	27946	7332	2545	5281
Gli2	AF109923	4	2545	2545	2545		2545	2545	2545		2545	2545	2545		22408	3229	2545	
brain factor 1	AF101387	4	2545	2545	2545	2545	2545	5105	2545	2545	2545	4446	8602	2545	198981	107649	130284	143451
brain factor 1	AF101387	4	2545	2545	2545		2545	2545	2545		2545	2545	2545		224194	166616	92933	
brain factor 2	AJ011652	4	582	450	419	450	600	451	286	416	449	370	441	420	2072	1735	958	1360
brain factor 2	AJ011652	4	545	450	351		654	381	286		474	399	309		1385	1760	912	
GATA-5a	L13701	4		2545	2545	2545	2545	6236	6421	5010	2545	2545	2572	2545	136932	57225	50634	64970
GATA-5a	L13701	4		2545	2545		2545	5535	4598		2545	2545	9312		113501	70217	59724	
CCCH zinc finger protein C3H-3	AF061982	4	5205	2545		3875	2545	2545	2545	2545	2545	4011	2545	2545	106975	59821	66226	67960
CCCH zinc finger protein C3H-3	AF061982	4	8502	2545			2545	2545			2545	3840	2545		106041	69546	66375	
NK-2 homolog	S65507	4	2545	2545	2545	2545	2545	2545		2545		2545	2545	2545	45566	6496	7061	6778
NK-2 homolog	S65507	4	6676	2545	2545		2545	5792			2545	3801	2545		36545	2545	4089	
Iriquois 3	AF027175	4	2545	2545		2545	2545	2545	3906	2545	2545	2545	2545	2545	51422		23074	22494
Iriquois 3	AF027175	4	2545	2545			2545	2545	2545		2545	2545	2545		19848		21914	
myb-related protein 1 (myb 1)	M75870	4	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	39622	4381	2545	5035
myb-related protein 1 (myb 1)	M75870	4	2545	2545	2545		2545	2545	2545		2545	2545	2545		14039	2545	5689	
Pitx-1	AF155206	4	2545	2545		2545	2545	6789	3168	2545	2545	2545	2545	2545	141121	68913	42711	55812
Pitx-1	AF155206	4	2545		2545		2545	2545	2545		2545	2545	2545		139375	12549	35080	
MOX2	L20432	4	2545	2545		2545	2545	2545	2545	2545	2545	2545	2545	2545	4824	7864	2545	6296
MOX2	L20432	4	2545	2545			2545	2545	5285		2545	2545	2545		35292	6053	6539	
HoxD1	L25857	4	2545	2545		2545	2545	2545	2545	2545	2545	2545	2545	2545	28665	2545	2545	2545
HoxD1	L25857	4	2545	4113	2545		2545	2545	2545		2545	2545	2545		3942	2545	2545	
goosecoid homebox protein isoform	M81481	4	2545	2545	2545	2545	2545	6672	3550	2545	2545	2545	2739	2545	45945	59909	25215	40535
goosecoid homebox protein isoform	M81481	4	2545	2545	2545		2545	2545	2545		2545	2545	2545		35125	47943	31836	
Xhox.lab2	X62053	4	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	3730	2545	2545	2545
Xhox.lab2	X62053	4	2545	2545	2545		2545	2545	2545		2545	2545	2545		6543	2545	2545	
DLL4	L09728	4	4164	2545	15158	3355	2545	2545	3162	2545	2545	2545	2545	2545	123096	63493	38698	59871
DLL4	L09728	4	2545	2545	4423		2545	2545	2545		2545	2545	2545		125045	56250	40968	
DLL3	L09729	4	3470	2545		2545	2545	5391	2545	2545	2545	2545	2545	2545	236460	108916	95818	102367
DLL3	L09729	4	2545	2545			2545	2545	2545		2545	3673	2545		238039	88148	75288	
DLL2	L09730	4	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	41183	6136	9710	7923
DLL2	L09730	4	2545	2545	2545		2545	2545	2545		2545	2545	2545		36936	4495	5762	
Fez	AF195021	4	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	69932	43751	28441	50659
Fez	AF195021	4	2545	2545	2545		2545	2545	3862		2545	2545	2545		73892	57567	2545	
eroA	AJ224125	4	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	32171		4660	17735
eroA	AJ224125	4	2545	2545	2545		2545	2545	2545		2545	2545	2545		30910		2545	
achaete-scute protein homolog (ASH	M98272	4	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	58054	47906	21585	37770
achaete-scute protein homolog (ASH	M98272	4	2545	2545			2545	2545	2545		2545	2545	2545		51610	18665	27635	
DNA binding protein E12	X86959	4	2545	2545	2545	2545		2545	2545	2545	2545	2545	2545	2545	33943	2545	4821	5063
DNA binding protein E12	X86959	4	2545				2545	2545	2545		2545	2545	2545		29005	5306	3612	
sonic hedgehog	L39213	4	2545	2678	2545	2545	2545	2545	2545	2545	2545	2545	3288	2545	40063	7623	24689	25407
sonic hedgehog	L39213	4		2545	2545		2545	2545	2619		2545	2545	2545		49394	6862	26145	

XLMO1	U94991	4		2545	2545	2545	2545	4615	2545	2545	2645	2545	2545	2545	62401	36698	38492	47991
XLMO1	U94991	4		16117	2545		2545	2645	2545		2646	2545	2545		86670	57491	33330	
POU2	U17654	4	5899	3776		3883	2545	6969	4615	4611	4365	2545	2545	3141	40469		20344	33664
POU2	U17654	4	3891	2545			2545	6455	4607		3737	4289	2545		42938		26859	
X-MyT1	U67078	4	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	3025	2545	2545	2767
X-MyT1	U67078	4	2545	2545			2545	2545	2545		2545	2545	2545		2990	2545	3834	
Xsal-1	L46583	4	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	5398	2545
Xsal-1	L46583	4	2545	2545	2545		2545	2545	4686		2545	2545	2545		5838	2545	2545	
zic2	U57463	4	9370	2545		5957	2545	8183	2545	2545	2545	2545	4580	3421	160514	76511	85457	80984
zic2	U57463	4	10758	2545			2545	2545	2836		2545	4296	10084		179778	62784	73250	
TFIIIA	X58369	4	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545
TFIIIA	X58369	4	2545	2545	2653		2545	2545	2545		2545	2545	2545		2545	2545	2545	
TH/bZip	U37375	4	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	80664		7210	45657
TH/bZip	U37375	4	2545	2545	2545		2545	2545	2545		2545	2545	2545		74236		30650	
glucocorticoid receptor	X72211	5	2545	2545	3295	2545	2545	2545	2545	2545	2545	2545	2545	2545	8537		2545	5532
glucocorticoid receptor	X72211	5	2545	2545	2545		2545	2545	2545		2545	2545	2545		8519		2545	
estrogen receptor	L20736	5	2545	2545	46979	2545	2545	2545	2545	2545	2545	2545	2545	2545	3774		2545	2545
estrogen receptor	L20736	5	2545	2545	48260		2545	2545	2545		2545	2545	2545		2545		2546	
vitamin D receptor	U91846	5	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545
vitamin D receptor	U91846	5	2545	2545	2545		2545	2545	2545		2545	2545	2545		2545	2545	2545	
tif2	AJ243119	4	2950	3779		3364	2545	7748	2545	2865	2545	5033	2754	4416	241108	174086	98724	167289
tif2	AJ243119	4	8155	2545			2545	8269	3184		3799	5263	9446		239591	160492	101682	
TRIP4	AW199631	5	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	7223	2545	2545	5116
TRIP4	AW199631	5	2545	2545	4242		2545	2545	2545		2545	2545	2545		6323	5116		
TRIP7	AW200492	5		2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	4065	12309		7557
TRIP7	AW200492	5		2545	2545		2545	2545	2545		2545	2545	2545		7478	7636		
thyroid hormone receptor alpha A	M35343	5		2545	3716	2545	2545	2545	2545	2545	2545	2545		2545	3501	2545	2546	2545
thyroid hormone receptor alpha A	M35343	5		2545	2545		2545	2545	2545		2545	2545				14056	2545	
thyroid hormone receptor beta A1	M35359	5	2545	2545	2545	2545	2545	2545	2545	2545	3869	2545	2545	2545	2545	9257	2545	2741
thyroid hormone receptor beta A1	M35359	5	2545	2545	2545		2545	2545	2545		2545	2545	2545		2937	3444	2545	
androgen receptor alpha	U67129	5	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	3114	2545	178336	142169	72970	139231
androgen receptor alpha	U67129	5	2545	2545	2545		2545	2545	3523		3922	2545	2545		198725	136293	60853	
mineralocorticoid receptor	U15134	5	2545	2545	2546	2545	2545	2545	2545	2545	2545	2545	2545	2545	4683	2545	2545	2545
mineralocorticoid receptor	U15134	5	2545	2545	2545		2545	2545	2545		2545		2545		2545	2545	2545	
RXR xSRC-3	AF044080	5	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	5080	2545	2545	3610
RXR xSRC-3	AF044080	5	2545	2545	2545			2545	2805		2545	2545	2545		4674	5888	2545	
RAR beta	X87366	5		2545	2771	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	8130	3710	3471
RAR beta	X87366	5		2545	2545		2545	2545	2545		2545	2545	2545		2545	6382	3233	
RAR gamma B	X59396	5		2545		2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	8700	2780	2662
RAR gamma B	X59396	5		2545			2545	2545	2545		2545		2545		3316	2545	2545	
PPAR alpha	M84161	5	2545	2545		2545	2545	2545	2545	2545	2545	2545	2545	2545	14498		2545	19940
PPAR alpha	M84161	5	2545	2545			2545	2545	4607		2545	2545	2545		29728		25382	
PPAR beta	M84162	5		2545	2545	2545		2545	2545	2545	2545	2545	2545	2545	5256	2545	3164	2855
PPAR beta	M84162	5		2545			2545	2545	2545		2545	2545	2545		3907	2545	2545	
PPAR gamma	M84163	5	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545
PPAR gamma	M84163	5	2545	2545	4123		2545	2545	3541		2545	2545	2545		2545	2545	2545	
NGFI-B	X70700	4	2545	2545		2545	2545	2545	2545	2545	2545	2545	2545	2545	7708	6888	2546	3646
NGFI-B	X70700	4	2545	2545			2545	2545	2545		2545	2545	2545		2619	2545	4672	
orphan nuclear receptor	X75163	4	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	40257		27911	27911
orphan nuclear receptor	X75163	4	2545	2545	3784		2545	2545	2545		2545	2545	2545		48968	2545	26121	
COUP transcription factor 1	AF157558	4	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	14361		5677	22192
COUP transcription factor 1	AF157558	4	2545	2545	2545		2545	2545	2545		2545	2545	2545		41809		30023	
thyroid hormone receptor alpha	L06064	5	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	76670		35986	56138
thyroid hormone receptor alpha	L06064	5	2545	2545			2545	2545	2545		2545	2545	2545		76291		25215	
thyroid hormone receptor beta	L27344	5	2545	2545		2545	2545	2545	2545	2545	2545	2545	2545	2545	35645		6502	13892
thyroid hormone receptor beta	L27344	5	2545	2545			2545	2545	2545		2545	2545	2545		3580		21261	
metastasis associated 1-like protein	AF170344	2	2545	2545	2545	2545	2545	2545	2545	2545	2645	2545	2545	2545	7461	6420	23372	6420
metastasis associated 1-like protein	AF170344	2	2545	2545	2645		2545	2545	2545		2545	2545	2545		4753		6229	
recombination activation (RAG-2)	L19325	2	2545	2545	2885	2545	2545	2545	2545	2545	2545	2545	2545	2545		5749	16293	11622
recombination activation (RAG-2)	L19325	2	2545	2545	2545		2545	2545	2545		2545	2545	2545			6962	21784	
methyl-CpG binding protein	AF170347	2	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	10000	10726		6431
methyl-CpG binding protein	AF170347	2	2545	2545	2545		2545	2545	2545		2545	2545	2545		2734	2862		
replication protein A	X67240	2		2545	2545	2545		2545	2545	2545	2545	2545	2545	2545	2545	2545		2545
replication protein A	X67240	2		2545	2545			2545	2545		2545	2545	2545		2545	2545		
Mi-2 histone deacetylase	AF171099	2		2545	2545	2545	2545	2545	2545	2545	2545	2545		2545	65867	16158		16158
Mi-2 histone deacetylase	AF171099	2		2545	2545		2545	2545	2545		2545	2545			57233	8852	2545	
mitochondrial RNA polymerase	AF200705	2	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	11298	8900	7040
mitochondrial RNA polymerase	AF200705	2	2545	2545	2545		2545	2545	2545		2545	2545	2545		36474	8180	2545	
mitotic phosphoprotein 43	U95097	2	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	42832	64899	31339	37066
mitotic phosphoprotein 43	U95097	2	2545	2545	2545		2545	2545	2545		2645	2645	2545		65867	13993	26871	
mitotic phosphoprotein 90	U95102	2	2545	2545	2545	2545	2545	4675	2545	2545	2545	2545	2545	2545	72322	87325	40651	69035
mitotic phosphoprotein 90	U95102	2	2545	2545	2545		2545	2545	2545		2545		2545		93434	65747	44256	
meskin	AF200212	11	2545	2545	2545	2545	2545	2545	2545	2545	2545		2545	2545	3863	2545	3195	2870
meskin	AF200212	11	2545	2545	2545		2545	2545	2545		2545	2545	2545		2545	5369	2545	
plexin	D38175	9	2545	2545		2545	2545	2545	2545	2545	2545	2545	2545	2545	41263	20540	31148	25843
plexin	D38175	9	2545	2545	2545		2545	2645	2545		2545	2545	2545		51043	16931	14270	
contactin/F3/F11	D86505	9		2545	2545	2545	2545	2545	3871	2545	2545	2545	2545	2545	2545	4457	2545	2545
contactin/F3/F11	D86505	9		2545	2545		2545	2545	2545		2545	2545	2545		2545	4242	2545	
non-muscle tropomyosin (TM-4)	L35238	9	7808	12838		9656	2545	2545	2545	2545	6809	7673	12807	8246	33829	11587	36812	35220
non-muscle tropomyosin (TM-4)	L35238	9	8155	11158			2545	5908	2875		8274	8218	12169		17435	64489	53135	
coronin	AB025246	9	2545	2545		2545	2545	2545	2545	2545	2545	2545	2545	2545	4065	12676		4065
coronin	AB025246	9	2545	2545			2545	2545	2545		2545	2545	2545		7584	2545	3648	
kinesin central motor 1 XKCM	U36485	9	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545		3634	2546	2814
kinesin central motor 1 XKCM	U36485	9	2545	2545	2545		2545	2545	2545		2545	2545	2545			2545	3084	
katanin p60	AF177942	9	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	42250	8662	40924	35145
katanin p60	AF177942	9	2545	2545	2545		2545	2545	2545		2545	2545	2545		42568	3026	29366	
calponin H3	AF081576	9	2545	2545		2545	2545	2545	2545	2545	2645	2545	2545	2545	2545	2545	2545	2545
calponin H3	AF081576	9	2545	2545			2545	2545	2545		2545	2545	2545		2545	2545	2545	
myelin proteolipid protein	Z19522	9	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	4868	2545	5720	3610
myelin proteolipid protein	Z19522	9	2545	2545	2545		2545	2645	2545		2546	2546	2545		4498	2723	2637	
myelin basic protein	AB000736	9	2545	2545	2545	2545	2545	2545	3514	2545	2545	2545	2545	2545	11235	9713	17205	9713
myelin basic protein	AB000736	9	2545	2545	2545		2545	2645	2545		2545	2545	2545			3723	9394	
class II beta-tubulin	X15798	9	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2546	2545	2545
class II beta-tubulin	X15798	9	2545	2545			2545	2545	2545		2546	2545	2545		2545	2545	2545	
beta tubulin	L06232	9	2545	2545	4284	2545	2545	2545	3519	2545	2545	2545	2546	2545	34402		5795	28887
beta tubulin	L06232	9	2545	2545	2545		2545	2545	4598		2545	2545	2546		33379		24396	
fibronectin	M77820	9	2545	2545	2545	2545	2545	2545	4071	2545	2545	2545	2545	2545			6397	6397
fibronectin	M77820	9	2545	2545			2545	2545	2545		2545	2546	2645		4008		19675	
Xefiltin	U63711	9	2545	2545	2545	2545	2545	2645		2545	2545	2545	2545	2545	67697		7011	9664
Xefiltin	U63711	9	2545	2545	2545		2545	2645			2545	2545	2545		12717		2545	
myosin heavy chain 3	AF097906	9	2545	11249	2545	2545	2545	18634	21809	16260	8902	6323	9194	7249	14723	13271	82603	18464
myosin heavy chain 3	AF097906	9	2545	10475	2545		2545	17172	15348		8176	4859	4046		22206	5167	61641	
alpha skeletal actin	X03470	9	252	809	611	567	1015	1441	722	1069	1474	1553	894	1290	635	1418	1269	1227
alpha skeletal actin	X03470	9	296	812	523		1124	1392	775		1261	1318	650		705	1444	1165	
cytoplasmic beta actin	AF079161	9	1370	2741	2432	2023	2765	2216	2453	2437	2407	2923	2623	2295	5221	6800	4691	4995
cytoplasmic beta actin	AF079161	9	1209	2336	2067		2993	2776	2310		2067	1997	2143		4965	5964	5286	
cytoplasmic beta actin	AF079161	9	1063	1979	1807		2006	2260	2233		1892	2080	2431		3942	5205	3543	
cytoplasmic beta actin	AF079161	9	1224	2226	2333		2963	2965	2455		2131	4034	2855		4445	7307	4852	
cytoplasmic beta actin	AF079161	9	1121	2557	2223		2806	2280	2330		2256	2803	2615		4559	5781	4716	
cytoplasmic beta actin	AF079161	9	1247	2701	1680		3170	2420	2310		1939	2333	1669		4484	7028	5026	
ribosomal protein L8	U00920	11	729	666	602	2545	766	768	515	2545	540	650	654	2545	653	747	670	3899
ribosomal protein L8	U00920	11	621	337	585		814	546	617		365	399	503		679	912	552	
ribosomal protein L8	U00920	11	924	868	747		878	1025	806		848	801	685		710	772	807	
ribosomal protein L8	U00920	11	884	636	684		824	897	969		707	723	658		705	950	807	
ribosomal protein L8	U00920	11	660	829	752		1012	578	802		602	614	650		714	772	658	
ribosomal protein L8	U00920	11	756	658	492		1304	461	749		560	602	518		776	772	701	
ribosomal protein L8	U00920	11	887	864	631		654	870	797		740	613	692		697	871	720	
ribosomal protein L8	U00920	11	954	796	626		1050	950	819		736	723	654		776	709	710	
ribosomal protein L8	U00920	11	800	938	922		1089	493	837		733	730	758		732	772	803	
ribosomal protein L8	U00920	11	984	735	1012		1363	645	846		794	958	762		732	836	850	
protein S10	S57432	11	1380	1447	1276	1370	1054	877	1282	1176	702	684	818	771	1340	1102	937	1140
protein S10	S57432	11	1360	1563	1264		1373	1071	1387		634	883	723		1261	1178	1049	
mitochondrial 16s ribosomal RNA	U66113	11	1273	1219	1482	1365	1983	1811	1651	1897	1221	1485	1168	1226	2688	7307	2438	2662
mitochondrial 16s ribosomal RNA	U66113	11	1412	1400	1329		2238	2079	1352		1199	1523	1230		2635	3064	2600	
HMG-1	U21933	4	2545	2545	2545	2545	2545	2545	2645	2545	2545	2545	2545	2545	61598	7990	25941	25277
HMG-1	U21933	4	2545	2545	2805		2545	2545	2545		2545	2545			47480	5432	24813	
histone H1	J00968	2	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	41439		34038	37738
histone H1	J00968	2	2545	2545	2545		2545	2545	2545		2546	2545	2545		46968		29955	
51 KDa cytokeratin type I	Y00968	9	2545	2545	2545	2545	2545	6428	5765	6096	5190	2545	2924	3199	2545	2546	7737	3178
51 KDa cytokeratin type I	Y00968	9	2545	2545	2545		2545	6472	7201		4644	2545	3473		2545	3812	18731	
epidermal type 1 keratin b1	65242	9	11278	2545	27788	13913	2545	7332	7868	5986	19274	9386	12207	15417	6508	2545	24836	4527
epidermal type 1 keratin b1	65242	9	14748	2545	31374		2545	7008	4963		18627	8264	20199		2546	2546	22677	
alpha 1 collagen type I	AB015440	9	2545	2545		2545	2545	5419	4624	4614	5298	4444	11384	5530	68662	50950	38523	54233
alpha 1 collagen type I	AB015440	9	2545	2545			2545	6139	5003		5763	4709	10212		71943	57516	2643	
alpha 2 collagen type I	D88764	9	2545	2545		2545	2545	7614		5013	7198	5058	9701	6247	64721	11080	45975	45975
alpha 2 collagen type I	D88764	9	3470	2545			2545	7480			5295	5058	10544		73768		40335	
alpha-1 collagen type II	M63595	9	2545	2545		2545	2545	2545	2545	2545		2545		2545	28396	11298	6788	19420
alpha-1 collagen type II	M63595	9	2545	2545	2545		2545	2646	2545		2545	2545	2545		39014	13309	25531	
ribosomal protein L32	X55030	11	936	944	1233	1142	745	877	1246	911	625	793	1097	871	820	1165	1080	1091
ribosomal protein L32	X55030	11	1114	1171	1437		792	944	1253		687	949	1257		962	1102	1235	
serum retinol binding protein	J02718	5	2545	2545	2546	2545	2545	2545	2545	2545	2545	2545	2545	2545	2546	2545	2545	2545
serum retinol binding protein	J02718	5	2545	2545	2545		2545	2545	2545		2545	2545	2545		2545	2546	2545	
cellular retinoic acid binding protein	S74933	5	2545	2545	2546	2545	2546	2546	2545	2545	2545	2545	2545	2545	2545	2546	2548	2545
cellular retinoic acid binding protein	S74933	5	2545	2546	2545		2545	2546	2545		2545	2545	2546		6335	4635	2545	
thyroid hormone binding protein	U03878	5	2546	2546		2545	2546	2545	2545	2545		2546	2545	2545	2545	4166	2546	2836
thyroid hormone binding protein	U03878	5	2546	2545			2545	6799	2814			2546	3292		2546	3381	3127	
IFABP	L19946	7	2546	2546	2646	2545	2546	2646	2545	2545	2545	2546	2645	2545	2546	2546	2545	2545
IFABP	L19946	7	2546	2545	2545		2545	2545	2645		2545	2546	2645		2645	6394	2646	
L-amino acid transporter-1	Y12716	7	2546	2545	2545	2545	2545	4749	2545	2545	2546	2545	2646	2545	69059	8852	32437	21382

L-amino acid transporter-1	Y12716	7	2545	2545	2545		2545	2545	2545		2545	2545	2546		62472	7446	10727	
chloride channel ClC-3	Y09941	7	2545	2645	2545	2545	2545	2545	2545	2545	2545	2545	2646	2545	36583	37166	29310	26183
chloride channel ClC-3	Y09941	7	2545	2545	2545		2545	2545	2545		2545	2645	2545		18709	14259	23066	
chloride channel ClC-5	AF063904	7	2545	2645	2545	2545	2545	2545	2545	2545	2546	2545	2545	2545	27726		7284	28102
chloride channel ClC-5	AF063904	7	2545	2545	2545		2545	2645	2545		2546	2546	2545		37047		28478	
multidrug resistance gene	U17608	7		2645	2545	2545	2545	2545		2545	2545	2545	2545	2545	48468		24557	34839
multidrug resistance gene	U17608	7		2545	2545		2545	2545			2545	2545	2545		44543		26134	
importin alpha 1a	L36339	7				#NUM!				#NUM!		6330		6289	3139			3260
importin alpha 1a	L36339	7										6248			3466	3343	3177	
Ca2+-binding protein frequenin	U27274	7				#NUM!				#NUM!				#NUM!	46104	6914		24648
Ca2+-binding protein frequenin	U27274	7													39583	9713		
calbindin D28K	U76636	7	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2645	2545	8869	2545	2545	2545
calbindin D28K	U76636	7	2545	2545	2545		2545	2545	2546		2545	2545	2545		2645	2545	2545	
adult beta-globin	J00978	7	2545	2545	3043	2545	2545	2545	2810	2545	2545	2545	2545	2545	5547	2545		3236
adult beta-globin	J00978	7	2545	2545	2545		2545	2545	2545		2545	2545	2545		3236	2545	5627	
larval beta I globin	X03143	7	2545	2545	2545	2545	2546	8586	54616	9092	2545	2545	2545	2545	106601	23161	60543	66197
larval beta I globin	X03143	7		2545	2545		2545	9597	48506		2545	2545	2545		91036	71851	53985	
sodium phosphate cotransporter	L78835	7	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	7699	8130	4225	6357
sodium phosphate cotransporter	L78835	7	2545	2545	2545		2545	2545	2545		2545	2545	2545		9030	5016	2643	
Na+/dicarboxylate cotransporter	U87318	7	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545		2545	7176	2545	2545	3081
Na+/dicarboxylate cotransporter	U87318	7	2545	2545	2545		2545	2545	2545		2545	2545			3076	6446	3064	
Na+-glucose cotransporter type I	AB006225	7	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	28775			28775
Na+-glucose cotransporter type I	AB006225	7	2545	2545	2545		2545	2545	4954		2545	2545	2545		31465		3493	
epithelial Na+ channel alpha subunit	U23535	7	2545	2545		2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	3508	2545	2545
epithelial Na+ channel alpha subunit	U23535	7	2545	2545			2545	2545	2545		2545	2546	2545		2545	2545	2546	
poly A-binding protein ABP-EF	M27072	4	2545	2545	2545	2545	2545	2545	2545	2545	2548	2545	2545	2545	2545	2545	2904	2545
poly A-binding protein ABP-EF	M27072	4	2545	2545			2545	2545	2545		2545	2545	2545		2545	2545	2545	
nervous system-specific RNA bindin	M34894	4		2545	2545	2545	2545	2545		2545	2545	2545	2545	2545	56069	2545		21600
nervous system-specific RNA bindin	M34894	4		2545	2545		2545	2545			2545	2545	2545		40654	2545		
Xfin	X06021	4	2545	2545	2545	2545	2545	2545	5716	2545	2545	2545	2545	2545	63415	2545	32052	32248
Xfin	X06021	4	2545	2545	2545		2545	2545	2545		2545	2545	2545		63424	5698	32443	
p54 mRNA binding protein	M80257	4	2545	2545	2545	2545	2545		2545	2545	2706	2545	2545	2545	108558	29290	43115	66501
p54 mRNA binding protein	M80257	4	2545	2545	2545		2545	5140	2545		2545	2545	2545		126581	84894	48109	
74 kDa/68 kDa serum albumin	M21442	7	2545	2545	2545	2545	2545	2545	2545	2545		2545	2545	2545	3076	2545	2545	2545
74 kDa/68 kDa serum albumin	M21442	7	2545	2545	3726		2545	2545	2545		2545	2546	2545		2545	2545	4151	
aldehyde dehydrogenase class 1	AB016718	6	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545		7370	3692	5397
aldehyde dehydrogenase class 1	AB016718	6	2545	2545	2545		2545	2545	2545		2545	2545	2545			4875	5919	
Wnt inhibitory factor-1	AF122924	3	2545		2545	2545	2545	2545	3334	2545	2545	2545	2545	2545	20433	4571	3890	5292
Wnt inhibitory factor-1	AF122924	3	2545	2545	2545		2545	2545	2545		2545	2545	2545		22276	2900	6012	
transferrin	X54530	7	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	11341	2545	6298	5730
transferrin	X54530	7	2545	2545	2545		2545	2545	2545		2545	2545	2545		6085	5375	2545	
hnRNP I-related RNA transport prote	AF091370	4	2545		2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	10726		6635
hnRNP I-related RNA transport prote	AF091370	4	2545		2545		2545	2545	2545		2545	2545	2545			14056	2545	
urea transporter	Y12784	7	2545	2545	2545	2545	2545	2545	4932	2545	2545	2545	2545	2545	37127	9814		15626
urea transporter	Y12784	7	2545	2545	2545		2545	2545	2545		2545	2545	2545		27611	15626	3549	
SPARC	X62483	1	2545	2545	2545	2545	2545	2545	2545	2545	10873	4880		7889	37294	2545	6839	7612
SPARC	X62483	1	2545	2545	2545		2545	2545	2545		10644	5133			14710	7598	7626	
L-epinephrine transporter	U72677	7	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545		2545	4921	2545	4114	3045
L-epinephrine transporter	U72677	7	2545	2545			2545	2545	2810		2545	2545			2545	3546	2545	
TIMP-2	AY037944	8	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545		2545	49499	10105	31339	28742
TIMP-2	AY037944	8	2545	2545	2545		2545	2545	2545		2545	2545			40672	13917	26145	
transthyretin	AB006134	5	2545	2545	2766	2545	2545	2545	2545	2545	2545	2645	2545	2545		2621	9344	2621
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interleukin 1 beta	AJ010497	3	2545	2545		2545	2545	2545	2545	2545	2545	2545	2545	2545	16844	8104	5689	6200
interleukin 1 beta	AJ010497	3	2545	2545			2545	2545	2545		2545	2545	2545		6200	4685		
NEDD 8	Not Submitted	8	2545		2545	2545	2545	2545	2545	2545	2545	2545		2545	77578	4204	33355	32486
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osteogenic protein-1 homolog precu	U40034	1		2545	2545	2545	2545	2545	2545	2545	2545	2546	2545	2545	5741	8586	5156	5156
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connective tissue growth factor XCT	U43524	1	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	53230	8206		30718
connective tissue growth factor XCT	U43524	1	2545	2545	2545		2545	2545	2545		2545	2545	2546		67816	7554		
nerve growth factor	X55716	1	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545		2545	17912	2545
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prepronuropeptide Y	S55577	3	2545	2545	2545	2545	2645	2545	2545	2545	2545	2545	2545	2545	2545	2545	2645	2545
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neuromedin	L01530	3	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	6914		6819	6866
neuromedin	L01530	3	2545	2545	2545		2545	2545	2545		2545	2545	2545		7399		5596	
thyroid-stimulating hormone a	L07619	5	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2645	2545		5129	2545	2634
thyroid-stimulating hormone a	L07619	6	3036	2545	2545		2545	2545	2545		2646	2545	2545			2723	2545	
thyrotropin-releasing hormone precu	X64056	5	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	22638	12840		8731
thyrotropin-releasing hormone precu	X64056	5	2545	2545	2545		2545	2545	2545		2645	2546	2545			4622	2545	
corticotropin-releasing factor	S50096	5		9638	2545	2545		2545	2545	2545	2645	2545	2545	2545	75614	79094	60392	65654
corticotropin-releasing factor	S50096	5	2545	2545	2545		2545	4605	2810		2545	2545	3091		74933	56376	44089	
prolactin	L07620	5	2545	2545		2545	2545	2545	2545	2545	2546	2545	2545	2545		2545	4269	3937
prolactin	L07620	5	2545	2545	3037		2545	2545	2545		2545	2645	7473			5369	3605	
ubiquitin	M11512	8	1109	972	614	1002	584	719	584	657	1156	1145	1216	1169	1111	1254	825	1180
ubiquitin	M11512	8	1201	1032	792		595	777	727		1293	1183	1040		1248	1292	776	
X Wnt-2b	U66288	3	2545	2545	2545	2545	2545	2545	2545	2545	2545	2645	2545	2545	14524	3126		6873
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A5-protein	D10467	3	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	20442		4906	17598
A5-protein	D10467	3	2545	2545	2545		2545	2545	2545		2545	2545	2545		14754		22187	
geminin H	AF067856	2	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2621	3064	2563
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fibroblast growth factor receptor ligar	U40457	1	2545	2545	2545	2545	2545	2545	2545	2545	2545	2546	2545	2545			2545	2562
fibroblast growth factor receptor ligar	U40457	1	2545	2545	2545		2545	2545	2545		2645	2545	2545		6967		2562	
FGF-3	Z25539	1	2545	2546	2545	2545	2545	2545	2545	2545	2546	2545	2545	2545	61669	60336	35562	51355
FGF-3	Z25539	1	2545	2545	2545		2545	2545	2545		2545	2545	2545		59967	52375	24247	
FGF-20	AB012615	1	2545	2545	2545	2545	2545	2545	2545	2545	2545	2546	2545	2545	29966	7028	3146	6794
FGF-20	AB012615	1	2603	2545	2545		2645	2545	2545		2646	2545	2545		31916	6559	2545	
TGF-beta 2	X51817	1	2545	2545	2545	2545	2545	2545	2545	2545	2646	2545		2545	2545	2545	2545	2545
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c-type natriuretic peptide 1	D17413	5	2545	2545		2545	2545	2545	2545	2545	2645	2545	2545	2545	2619	2545	4405	2822
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thyroid-stimulating hormone beta	L07618	5	2545	2545		2545	2545	2545	3541	2545	2545	2545		2545	2545	2545	2545	2545
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growth hormone A	AF193797	5	2545	2546	2545	2545	2546	2545	2545	2545	2545	2545	2545	2545		2545		2545
growth hormone A	AF193797	5	2545	2545	2545		2545	2545	2545		2545	2545	2545			2545		
RSK2	AF165162	3	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545		2545	2624	2585
RSK2	AF165162	3	2545	2545	2545		2545	2545	2545		2645	2545	2545			29011	2645	
PCNA	M34080	2	10064	2545	2545	2545	2546	7571	2545	2708	2545	2545	2545	2545	3898	2546	8494	4007
PCNA	M34080	2	2545	2645	2545		2545	8449	2871		2545	2545	2545		2545	6952	4117	
RING finger subunit MAT	U29667	1	2545	2545	2545	2545	2546	2545	2827	2545	2545	2545	2545	2545	2725	2545	2545	2545
RING finger subunit MAT	U29667	1	2545	3222	2545		2545	2546	2545		2545	2545	2545		3713	2545	2545	
Chk1 checkpoint kinase	AF117816	1	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545			2545
Chk1 checkpoint kinase	AF117816	1	2545	2545	2545		2545	2545	2545		2546	3452	2545		2545			
fyn	X52188	3	2545	2545		2545	2545	2545	2545	2545	2545	2545	2545	2545		7750	2545	2566
fyn	X52188	3	2545	2545	2545		2545	2545	2545		2545	3167	2546		2566	4318	2546	
XDRP1	AB030502	1	2545	2545	2545	2545	2546		2545	2545	2545	2545	2545	2545	2545	5306	10275	3926
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wee 1A kinase	U13962	1	2545	8206	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	23572	8370	23527	8684
wee 1A kinase	U13962	1	2545	2545	2645		2545	2545	2546		2646	2545	2913			5369	8664	
Max2/Max4	L09738	4	2545	2545	2545	2545	2545	2545	2545	2545	2545	2546	8571	2545	2545	6154	3822	3320
Max2/Max4	L09738	4	2545	2545	2545		2645	2545	2546		2545	2546	2646		2848	2545	3791	
Mad1	L77888	1	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	8685			8219
Mad1	L77888	1	2545	2545	2545		2545	2645	2546		2545	2545	2545		8219	4837		
Mad2	L77885	1	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	4921	5711	2546	2545
Mad2	L77885	1	2545	2545	2545		2545	2545	2545		2545	2545	2545		2646	2545		
MAP kinase 1 (MPK1)	X59813	3	8569	2546	2545	2545	2545	4802	2545	2545	2545		2545	2545	2545	6749	2545	2545
MAP kinase 1 (MPK1)	X59813	3	2545	2545	2545		2645	2545	2545		2545	2545	2545		2545	2545	2545	
MAP kinase 2 (MPK2)	X80751	3	2545	2545	2545	2545	2545	2545	2545	2545	2645	2545	2545	2545	2645	2545	3934	2545
MAP kinase 2 (MPK2)	X80751	3	2545	2545	2545		2545	2545	2545		2546	5272	2545		2545	5268	2545	
MAP kinase activator 2 (XMEK2)	Z22736	3	2545	2546	2545	2545	2645	2545	2545	2545	2545	2546	8599	2545	69368	57744	36339	43667
MAP kinase activator 2 (XMEK2)	Z22736	3	2545	2546	2545		2545	2645	2545		2545	2645	2546		34640	50994	29117	
MAP kinase activator (XMEK3)	AF172848	3	2776	2545	2545	2545	2545	2546	18261	2545	2545	2545	2546	2545	9639	3128	4508	5445
MAP kinase activator (XMEK3)	AF172848	3	2545	8946	2545		2545	2645	2545		2545	2545	2545		6455	6382	2545	
MAP kinase phosphatase	X83742	3	18132	3414	34491	16787	2545	14268	4417	3575	9962	7678	14397	7878	99343	35671	45131	45736
MAP kinase phosphatase	X83742	3	18442	19461	6920		2545	15862	2733		7476	6916			98880	30050	46341	
MAP kinase interacting kinase	AB023807	3	2545		2545	2545	2545	2546	2545	2545	2645	2545		2545	85841	63518	46806	63560
MAP kinase interacting kinase	AB023807	3	2545	2545	2545		2545	2545	2545		2545	2545	2545		83169	62569	63602	
MAPKK	D13700	3	2545	2545	2545	2545	2545	2545	2545	2545	2646	2545	2645	2545	75105	16018	46564	41371
MAPKK	D13700	3	2545	2546	2545		2646	2545	2545		2545	2545	2545		74765	24351	36178	
phosphoinositide 3 kinase catalytic s	AF204924	3	2545	2545		2545	2646	2545	2545	2545	2545	2545	2545	2545		2545	2804	3289
phosphoinositide 3 kinase catalytic s	AF204924	3	2545	2545			2545	2545	2545		2545	2545	2545			3774	4014	
casein kinase 1-alpha	Y08817	3	2545	2545		2545	2545	2546	2545	2545	2545	2545		2545	2545	2545	2545	2545
casein kinase 1-alpha	Y08817	3	2545	2545			2545	2546	2545		2545	2545			2645	2545	2545	
casein kinase 1-epsilon	AF183394	3	2545	2546	2545	2545	2545	2545	2546	2545	2545	2545	2546	2545	32550	2545		17548
casein kinase 1-epsilon	AF183394	3	2545	2546	2545		2545	2546	2545		2545	2545	2545		71599	2545		
calmodulin-dependent protein kinas	U06636	3	2545	2545	2545	2545	2545	2546	2545	2545	2645	2546	2545	2545	2545	2545		2545
calmodulin-dependent protein kinas	U06636	3	2546	2545	2545		2545	2546	2545		2646	2545	2545		2545	2546		
protein kinase PKN	D43890	3	2545	2684	2545	2545	2545	2546	2545	2545	2546	2545	2545	2545		9979	2545	2545
protein kinase PKN	D43890	3	2545	2545	2545		2545	2545	2645		2545	2545	2645		2545	9231	2545	
PKC-related kinase 2	AF027183	3	2545	2545	2545	2545	2546	2545	2545	2545	2546	2546	2545	2545	2693	9789	3116	3493
PKC-related kinase 2	AF027183	3	2546	2546	2545		2546	2545	2814		2646	2548	2545		3871	5952	3098	
DNA-PK	AF001413	2	2545	2546	2545	2545	2545	2545	2545	2545	2645	2545	2546	2545	2545	2545	2545	2545
DNA-PK	AF001413	2	2545	2546	2545		2545	2545	2545		2546	2545	2545			2545	2546	

ATM	AF174488	2	2545	2545	2545	2545	2545	2545	2827	2545	2545	2545	2545	2545	37334	7155	22001	15346
ATM	AF174488	2	2545	2545	2545		2545	2545	2545		2545	2545	2545		10503	2545	20189	
protein phosphatase 5	AF018263	3	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	4727	2545		5119
protein phosphatase 5	AF018263	3	2545	2545	2545		2545	2545	2545		2545	2545			5612	7699		
guanylyl cyclase 1	AB025111	3	2545	2545	2545	2545		2545	3514	2545	2545	2545	2545	2545	4727	5838	2545	4228
guanylyl cyclase 1	AB025111	3	2545	2545	2545		2545	2545	2545		2545	2545	2545		3536	5268	3729	
guanylyl cyclase 2	AB025112	3	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	4418	3026	4984	3185
guanylyl cyclase 2	AB025112	3	2545	2545	2545		2545	2545	2545		2545	2545	2545		2545	2545	3344	
cyclin A1	X53746	1	2545	2545	2545	2545	2545	2545	4937	2545	2641	2545	2545	2545	2545	8358	2545	2545
cyclin A1	X53746	1	2545	2545	2545			2545	2545		2545	2545	2545		2545	2545	18799	
cyclin A2	X85746	1	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	8297	6661	2545	6479
cyclin A2	X85746	1	2545	2545	2545		2545	2545	2545		2545	2545	2545		7866	7155	2545	
cyclin B1	J03166	1	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	8545	2545	2545	2545
cyclin B1	J03166	1	2545	2545	2545		2545	2545	2545		2545	2545	2545		2545	2545	2545	
cyclin B2	J03167	1	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	5609	11296	5119	5364
cyclin B2	J03167	1	2545	2545			2545	2545	2545		2545	2545	2545		2545	7091	3214	
cyclin D1	X89475	1	2545	2545	2545	2545	2545	2545	2814	2545	2545	2545	2545	2545	2545	7466	6434	6769
cyclin D1	X89475	1	2545	2545	2545		2545	2545	2545		2545	2545	2545		2545	12739	7104	
cyclin D2	X89476	1	14401	2545		8473	2545	2545	2545	2545	2545	2545	2545	2545		2545		2545
cyclin D2	X89476	1	14401	2545			2545	2545	2545		2545	2545	2545			6370	2545	
cyclin E	L23857	1	2545	2545		2545	2545	2545	2545	2545	2545	2545		2545	2545	11840	2545	2545
cyclin E	L23857	1	2545				2545	2545	2545		2545	2545	2545		2545	2545	2545	
cyclin H	U20506	1	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2824		2666
cyclin H	U20506	1	2545	2545	2545		2545	2545	3514		2545	2545	2545		2787	2545		
cyclin B2	AB005253	1	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545		2545	6473	2545	2545	2545
cyclin B2	AB005253	1	2545	2545	2545		2545	2545	2545		2545	2545				2545	3493	
cdc2	AB005254	1	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545		2545	2545	2545
cdc2	AB005254	1	2545	2545	2545		2545	2545	2545		2545	2545	2545		6156	2545	3915	
Eg1 Ser/Thr kinase (cdc2 homolog)	X14227	1	2545	8219	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	3466	2748	2545	3107
Eg1 Ser/Thr kinase (cdc2 homolog)	X14227	1	2545	2545	2545		2545	2545	2545		2545	2545	2545		2545	5597	3915	
cdc2-related MO15	X53962	1	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	3495	2545	3020
cdc2-related MO15	X53962	1	2545	2545	2545		2545	2545	2545		2545	2545	2545			5787		
cdc2 kinase homologous protein	M60680	1	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545		4014	2545	2545
cdc2 kinase homologous protein	M60680	1	2545	2545	2545		2545	2545	2545		2545	2545	2545		17677	2545	2545	
MYT1	U28931	1	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	8571	2545	25839	2545	6204	2653
MYT1	U28931	1	2545	2545	2545		2545	2545	2545		2545	2545	2545		2545	2545	2761	
cdc7-related kinase	AF060068	1	2545	2545		2545	2545	2545	2545	2545	2545	2545	2545	2545	3413	2545	4722	3584
cdc7-related kinase	AF060068	1	2545	2545	2545		2545	2545	2545		2545	2545	2545			3584	4622	
cdc21	U44049	1	2545	2545	2545	2545	2545	2545	3514	2545	2545	2545	2545	2545		2545	4226	3385
cdc21	U44049	1	2545	2545	2545		2545	2545	4210		2545	2545	2545			4419	2545	
tyrosine phosphatase cdc25A	AF090829	1	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545		2545	3236	2545	2545	2545
tyrosine phosphatase cdc25A	AF090829	1	2545	2545	2545		2545	2545	2545		2545	2545			5335	2545	2545	
tyrosine phosphatase cdcC1	M96857	1	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545		2545	3360	8776	2545	2545
tyrosine phosphatase cdcC1	M96857	1	2603	2545	2545		2545	2545	2545		2545	2545			2545	2545	2545	
MCM5/CDC46	U44048	1	2603	2545	2545	2545	2545	2545	2545	2545	2545	2545	7500	2545	57666	40079	34683	43447
MCM5/CDC46	U44048	1	2545	2545	2545		2545	2545	2545		2545	2545	2545		109630	46816	32133	
cdk 4	X89477	1	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	3495	3196	2710
cdk 4	X89477	1	2545	2545	2545		2545	2545	2545		2545	2545	2545		2545	2875	2545	
activator of cdk5	AF000951	1	2545	2545	2545	2545	2545	2545	4941	2545	2545	2545	2545	2545	6702	2900	4672	5687
activator of cdk5	AF000951	1	2545	2545	2545		2545	2545	2545		2545	2545	2545		8969	35849	2545	
cdk inhibitor p28	U38844	1	2950	2545	2545	2545	2545	2545	2545	2545	2545	2545	9214	2545	145919	91478	105274	105619
cdk inhibitor p28	U38844	1	8849	2545	2545			2545	2545		2545	2545	2545		152731	105965	74124	
cdk inhibitor	U24434	1	2545	2545	2545	2545	2545	2545	3519	2545	2545	2545	2545	2545	38017	3900	23516	23434
cdk inhibitor	U24434	1	2545	2545	2545		2545	2545	2545		2545	2545	2545		35134	11296	23353	
p33 ringo (ls26)	AJ133499	1	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	66061	19362	29366	29018
p33 ringo (ls26)	AJ133499	1	2545	2545			2545	4735	2545		2545	2545	2545		83923	25542	28671	
calcium/calmodulin-dependent prote	AF233633	3	2545	2545		2545	2545	2545	2545	2545	2545	2545		2545		4875	2545	2545
calcium/calmodulin-dependent prote	AF233633	3	2545	2545			2545	2545	3536		2545	2545			2545	2545	2545	
protein phosphatase-2A B'epsilon	AF298157	3	2545	2545		2545	2545	2545	2545	2545	2545	2545		2545	4621	2545	3934	2970
protein phosphatase-2A B'epsilon	AF298157	3	2545	2545			2545	2545	2642		2545	2545			3395	2545	2545	
serotonin receptor	U10161	5	2545	8210	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	8208	4533	4908	5558
serotonin receptor	U10161	5	2545	2545	2545		2545	2545	2545		2545	2545	8390		12840	7307	2545	
muscle nicotinic acetylcholine recep	U04618	3	2545	2545		2545	2545	4735	2545	2545	2545	2545	2545	2545	8722	2545	6626	7674
muscle nicotinic acetylcholine recep	U04618	3	2545	2545	2545		2545	2545	2545		2545	2545			34023	14006	4877	
prolactin receptor A	AF193800	5	2545	2545	2545	2545	2545	2545	5637	2545	2545	2545		2545	2545	2545	5565	2545
prolactin receptor A	AF193800	5	2545	2545	2545		2545	2545	2545		2545	2545			2545	2545	2545	
neurotrophic factor BDNF receptor	S69713	3	2545	2545	2545	2545	2545	2545	2545	2545		2545	2545	2545		8605	2545	3261
neurotrophic factor BDNF receptor	S69713	3	2545	2545	2545		2545	2545	2545			2545	2545			3976	2545	
lysophosphatidic acid receptor	AJ249844	3	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545
lysophosphatidic acid receptor	AJ249844	3	2545	2545			2545	2545	2545		2545	2545	2545		2545	2545	2545	
pituitary adenylate cyclase-activating	AF187878	3	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	3856	2545	4806	2545	5305	4806
pituitary adenylate cyclase-activating	AF187878	3	2545	2545	2545		2545	2545	2545		2545	2545	2553		30910		2545	
luteinizing hormone receptor	AJ249845	5	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545		2545
luteinizing hormone receptor	AJ249845	5	2545	2545	2545		2545	2545	2545		2545	2545	2545		5335			
inositol 1,4,5-trisphosphate receptor	D14400	3	2545	2545	14149	2545	2545	2545	2545	2545	2545	2545		2545	34719	2545	24340	24790
inositol 1,4,5-trisphosphate receptor	D14400	3	2545	2545	2545		2545	2545	2545		2545	2545			33088	2545	25240	
BMP receptor	D32066	3	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545		2545	2545	2545
BMP receptor	D32066	3	2545	2545	2545		2545	2545	2545		2545	2545	2545		2545	2545	9834	
frizzled 2	AF139165	3	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2723	3549	2545
frizzled 2	AF139165	3	2545	2545	2545		2545	2545	2545		2545	2545	2545			2545	2545	
cadherin precursor	AF002983	9	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	4293	2662
cadherin precursor	AF002983	9	2545	2545	2545		2545	2545	2545		2545	2545	2545			6851	2662	
NPY/PYY Receptor Y1	L25416	3	2545	2545	2907	2545	2545	2545	2545	2545	2545	2545	2545	2545		2545	2545	2545
NPY/PYY Receptor Y1	L25416	3	2545	2545	2545		2545	2545	2545		2545	2545	2545		2545	2545	2545	
muscle acetylcholine receptor a	X07067	3	2545	2545	3558	2545	2545	2545	2545	2545	2545	2545	2545	2545	5080	12182	4213	3379
muscle acetylcholine receptor a	X07067	3	2545	2545	2545		2545	2545	4629		2545	2545	2545		2545	2545	2545	
acetylcholine receptor alpha subunit	X17244	3	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	4761	2545	2545
acetylcholine receptor alpha subunit	X17244	3	2545	2545	2545		2545	2545	2545		2545	2545	2545			2545	2545	
activin receptor	S70930	1	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545		2545	2545	2545
activin receptor	S70930	1	2545	2545	2545		2545	2545	2545		2545	2545	2545			2988	2545	
Ftz-F1-related orphan receptor A	U05001	4		2545	2545	2545	2545	2545	2545	2545	2545	2545		2545	10627		2545	8282
Ftz-F1-related orphan receptor A	U05001	4		2545	2545		2545	2545	2545		2545	2545			35733		5938	
fibroblast growth factor receptor 1	M55163	1	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545		2545	3880	6547	2545	4099
fibroblast growth factor receptor 1	M55163	1	2545	2545	2545		2545	2545	2545		2545	2545			5124	4316	3326	
Pagliaccio receptor tyrosine kinase	L28099	3	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2924	2545	66281	12663	28796	30185
Pagliaccio receptor tyrosine kinase	L28099	3	2545	2545	2545		2545	2545	2545		2545	2545	2545		46263	14942	31574	
angiotensin II receptor	S73388	3	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545		8687	2545	2545
angiotensin II receptor	S73388	3	2545	2545	2545		2545	2545	2545		2545	2545	2545		2545	3432	2545	
angiotensin receptor related protein	U72029	3	2545	2675	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	24886	5445	4746	5724
angiotensin receptor related protein	U72029	3	2545	2545	2545		2545	2545	4250		2545	2545	2545		8016	6002	2545	
activated protein kinase C	AF105259	3	30017	27517	36541	30494	2545	21231	66503	21359	17041	10982	14215	13834	43838	40991	43729	42707
activated protein kinase C	AF105259	3	30972	28645	37333		2545	21486	50298		19068	11713	13453		41686	38534	46204	
5-HT1A receptor	Y07901	3	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	34710	6775	7061	7061
5-HT1A receptor	Y07901	3	2545	2545	2545		2545	2545	2545		2545	2545	2545		7866	2545		
14-3-3 protein	M86928	3	2545	2545		2545	2545	2545	3554	2545	2545	2545		2545	2545	2545	2545	2545
14-3-3 protein	M86928	3	2545	2545	2545		2545	2545	2545		2545	2545			3810	3204	2545	
ALK-2 receptor	AF012245	3	2545	2545	2545	2545	2545	2545	2545	2545	2545	3918	2545	2545	2545	2545		2545
ALK-2 receptor	AF012245	3	2545	2545	2545		2545	6067	2545		3576	2545	2545		2545	2545		
adenosine A1 receptor (a1R gene)	AJ249842	3	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545		2545	2545	2545
adenosine A1 receptor (a1R gene)	AJ249842	3	2545	2545	2545		2545	2545	2545		2545	2545	2545			3229	2545	
CRF receptor type1	Y14036	5	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	33493	2545	6974	13702
CRF receptor type1	Y14036	5	2545	2545	2545		2545	2545	2545		2545	2545	2545		30204	2545	20431	
VIP/pituitary cAMP receptor	AF100644	3	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	15071		2545	6964
VIP/pituitary cAMP receptor	AF100644	3	2545	2545	2545		2545	2545	2545		2545	2545	2545		7073		6856	
dihydropyrimidine receptor	AF037625	3	2545		2545	2545	2545	2545	2545	2545	2545	2545	2545	2545			7123	6552
dihydropyrimidine receptor	AF037625	3	2545	2545	2545		2545	2545	2545		2545	4235	2564				5961	
follicle stimulating hormone receptor	AJ249846	5	2545	2545		2545	2545	2545	2545	2545	2545	2545	2545	2545		3609	4337	3609
follicle stimulating hormone receptor	AJ249846	5	2545	2545			2545	2545	2545		2545	2545	2545		5582	2545	2545	
CRF receptor type 2	Y14037		2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	9533	9200	23257	8717
CRF receptor type 2	Y14037		2545	2545	2545		2545	2545	2545		2545	2545	2545		4692	2545	8233	
insulin receptor substrate protein xIR	AF297960		2545	2545	3207	2545	2545	2545	2545	2545	2545	2545		2545	26809	6836	2545	2545
insulin receptor substrate protein xIR	AF297960		2545	2545	2545		2545	2545	2545		2545	2545				2545	2545	
natriuretic peptide receptor type C	AF231035		2545	2545	2545	2545	2545	2545	3541	2545	2545	2545	2545	2545		9763	2545	2545
natriuretic peptide receptor type C	AF231035		2545	2545	2545		2545	2545	3898		2545	2545	2545			2545	2545	
XICE-a	D69783		2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	5503	2545	2545	2545
XICE-a	D69783		2545	2545	2545		2545	2545	4844		2545	2545	2545			2545	3686	
CPP32	D69784		2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545
CPP32	D69784		2545	2545	2545		2545	2545	3184		2545	2545	2545		2545	5698	2545	
calpastatin 1	AJ243713		2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	3197	2545	21094	12663	5628	16879
calpastatin 1	AJ243713		2545	2545	2545		2545	2545	2545		2545	2545	2545		44967	37521	5187	
caspase7-precursor	AW199521		2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	13766	5800	8637	9163
caspase7-precursor	AW199521		2545	2545	2545		2545	2545	2545		2545	2545	2545		32400	9789	4611	
bcl-2-like R11	X82461		2545	3219	2545	2545	2545	2545	5003	2545	2545	2545	2545	2545	84166	15411	41247	49003
bcl-2-like R11	X82461		2545	3219	2545		2545	2545	3645		2545	2545	2545		72988	33089	56758	
scythe	AF098511		2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545		42675	27557	32296
scythe	AF098511		2545	2545	2545		2545	2545	2545		2545	2545				11929	37034	
survivin	AW198821		3297	2545	2545	2545	2545	3932	2545	2545	2545	2545		2545	7399	2545	2545	2988
survivin	AW198821		2545	2545			2545	2545	2545		2545	2545			3430	7156	2545	
requiem	AB021737		2950	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	41615	2545	13191	34317
requiem	AB021737		2545	2545			2545	2545	2545		2545	2545	2545		46610		34317	
p21-activated kinase (PAK1)	AF000239		2545	2545	2545	2545	2545	2545	2545	2545	2545	3986	2545	2545	20592	6737		13664
p21-activated kinase (PAK1)	AF000239		2545	2545	2545		2545	2545	2545		2545	2545	2545		43300	3306		
DAD-1	D15059		9283	2863	2545	2704	2545	5211	2864	2545	5235	2545	2545	2545	2545	2545	2545	2545
DAD-1	D15059		12493	2545	2545		2545	2545	2545		5074	2545	2545		2813	2545	2545	
caspase-2	AB038168		2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	30477	2545	2545	2906
caspase-2	AB038168		2545	2545	3620		2545	2545	2545		2545	2545	2545		25804	2545	3267	
caspase-6	AB038169		2545	9131	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	7469	2621	5156	4055
caspase-6	AB038169		2776	2545	2545		2545	2545	2545		3949	2545	2545		3792	4318	2545	
caspase-7	AB038170		2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545		2545	8864	7992

caspase-7	AB038170	8	2545	2545	2545		2545	2545	2545		2545	2545	2545		7129	11329		
caspase-8	AB038171	8	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	3508	2545	2545	
caspase-8	AB038171	8	2545	2545	2545		2545	2545	4241		2545	2545	2545		2545	2545	2545	
caspase-8	AB038172	8	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545		2545	31580		28102	27821
caspase-9	AB038172	8	2545	2545	4615		2545	2545	2545		2545	2545	2545		31403	2545	27821	
caspase-10	AB038173	8	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545
caspase-10	AB038173	8	2545	2545	2545		2545	2545	2545		2545	2545	2545			2545	2545	
metalloprotease-disintegrin (MDC11	AF032384	8	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	33218	7914	23726	17351
metalloprotease-disintegrin (MDC11	AF032384	8	2545	2545	2545		2545	2545	2545		2545	2545	2545		39834	6154	10976	
metalloproteinase (XMMP)	U62541	8	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	13140	19583	12533	14351
metalloproteinase (XMMP)	U62541	8	2545	2545	2545		2545	2545	3168		2545	2545	2545		7899	36153	23808	
membrane anchored metalloprotease	U78185	8	2545	2545	3303	2545	2545	2545	2819	2545	2545	2545	2545	2545	2545	2545	2545	2545
membrane anchored metalloprotease	U78185	8	2545	2545	2545		2545	2545	2545		2545	2545	2545		2545	8208	2545	
metalloprotease-disintegrin (MDC11	AF032383	8	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545		2545	6729	3872	21107	7752
metalloprotease-disintegrin (MDC11	AF032383	8	2545	2545	2545		2545	2545	2545		2545	2545			3466	8776	20078	
pancreatic trypsin	X53468	6	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545		2545	37003	7307	8004	8282
pancreatic trypsin	X53458	6	2545	2545	2545		2545	2545	3867		2545	2545	2564		67190	8580	4182	
trypsinogen	U72330	6	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	51413	60984	33740	40107
trypsinogen	U72330	8	2545	2545	2545		2545	2545	4223		2545	2545	2545		46475	13398	26065	
serine protease (Csp1)	AF029404	6	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545
serine protease (Csp1)	AF029404	8	2589	2545	2545		2545	2545	2545		2545	2545	2545		2545	8345	5100	
stromelysin-3	Z27093	8	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545		2545	2545	7307	2545	2690
stromelysin-3	Z27093	8	2545	2545	2545		2545	2545	2545		2545	2545			3708	2545	2835	
alpha-aspartyl dipeptidase	U37377	8	2545	2545	2545	2545	2545	2545	2545	2545		2545	2545	2545	3501	145	2545	2545
alpha-aspartyl dipeptidase	U37377	8	2545	2545	2692		2545	2545	2545			2545	2545		4550	2545	2545	
xepsin	AB018694	3	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	23281	2545	23279	23280
xepsin	AB018694	3	2545	2545			2545	2545	2545		2545	2545	2545		27003	7231	24129	
alpha-1 antiproteinase	AB014091	8	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545
alpha-1 antiproteinase	AB014091	8	2545	2545			2545	2545	2545		2545	2545	2545		5194	8358	2545	
carbamyl phosphate synthetase	U05193	6	2545	2545	2545	2545	2545	2545		2545	2545	2545	2545	2545		2788	2545	2545
carbamyl phosphate synthetase	U05193	6	2545	2545	2545		2545	2545			2545	2545	2545			2545	2545	
ornithine transcarbamylase	D38304	6	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	5353	6421	2545	5353
ornithine transcarbamylase	D38304	6	2545	2545	2545		2545	2545	2545		2545	2545	2545		9171		2545	
ornithine decarboxylase	X56316	6	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	41095		26500	33298
ornithine decarboxylase	X56316	6	2545	2545	2545		2545	2545	2545		2545	2545	2545		47983		23062	
lactate dehydrogenase B	U07178	6	28195	26771	45396	27935	2545	15233	36964	14344	13909	11164	15750	13176	70938	120971	42918	59846
lactate dehydrogenase B	U07178	6	27675	27473	40350		2545	13455	41111		12442	11306	16157		35284	78196	46756	
GAPDH	U41753	6	390	450	515	415	862	821	528	817	1033	880	584	792	714	886	682	763
GAPDH	U41753	6	419	500	503		1047	1015	557		900	967	607		855	924	776	
GAPDH	U41753	6	415	376	498		967	867	550		783	805	526		758	519	912	
GAPDH	U41753	6	416	310	413		1092	814	556		881	794	433		767	838	850	
GAPDH	U41753	6	316	365	390		699	449	449		791	846	592		644	645	627	
GAPDH	U41753	6	371	447	498		948	876	423		812	892	686		648	842	620	
gelatinase B (MMP-9)	AF072456	8	2545	2545		2545	2545	2545	2545	2545	8598	8610	16424	8971	2545	7218		5131
gelatinase B (MMP-9)	AF072456	8	2545	2545	2545		2545	2545	2545		7248	9333	15147		21668	2545	5131	
NM23/nucleoside diphosphate kinase	X97899	2	1422	1262	1434	1428	1151	1183	1458	1283	1119	1548	1915	1576	1592	1899	1747	1807
NM23/nucleoside diphosphate kinase	X97899	2	1807	1578	1188		1263	1282	1484		1228	1907	2004		1388	1868	2023	
Nit1	D86491	6	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545		2545		3375
Nit1	D86491	6	2545	2545	2545		2545	2545	2545		2545	2545	2545		2545	4204	2545	
Na+/K+ transporting ATPase beta su	M37788	7	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2549	5835	2545	2547
Na+/K+ transporting ATPase beta su	M37788	7	2545	2545	2545		2545	2545	2545		2545	2545	2545		3139	2545	2545	
SERCa1 fast skeletal muscle	X53009	3	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	36351	4571	5001	6643
SERCa1 fast skeletal muscle	X53009	3	2545	3027	2545		2545	2545	2545		2545	2545	2545		36767	6889	6397	
E2 ubiquitin conjugating enzyme (Ub	U86551	8	3904	2545	2545	2545	2545	2545	2545	2545	2545		2545	2545	7857	2545	2545	2599
E2 ubiquitin conjugating enzyme (Ub	U86551	8	10237	2545	2545		2545	2545	2545		2545		2545		3827	2653	2545	
metallothionein	M86729	7	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	37606	8915	4580	7845
metallothionein	M86729	7	2545	2545	2545		2545	2545	2545		2545	2545	2545		32286	6775	6173	
iodothyronine deiodinase type II	L42815	5	2545	2545	2545	2545	2545	2545	2545	2545	2545		9156	2644	16853		20810	18405
iodothyronine deiodinase type II	L42815	5	2545	2857	2545		2545	2545	2545		2545		2742		18405	13879	26760	
iodothyronine 5'-deiodinase III	L28111	5	3991	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	103601	68203	48187	70281
iodothyronine 5'-deiodinase III	L28111	5	2776	2545	2545		2545	2545	4298		2545	4029			91618	74320	31500	
retinoic acid converting enzyme	AF057565	5	2776	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	45743	10143	8711	16598
retinoic acid converting enzyme	AF057565	6	2545	2545	2545		2545	2545	2545		2545	2545	2545		50214	7914	23056	
FCP1 serine phosphatase	AJ132385	4	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	9507		4089	8029
FCP1 serine phosphatase	AJ132385	4	2545	2545	2545		2545	2545	2545		2545	2545	2545		9718		6662	
protein phosphatase 1-gamma 1	L17039	1	2545	2545		2545	2545	2545	2545	2545	2545	2545	2545	2545	11456	2545	2545	2545
protein phosphatase 1-gamma 1	L17039	1	2545	2545	2545		2545	2545	2545		2545	2545	2545		3898	2545	2545	
convertase PC2	X95493	5	2545	2545	2545	2545	2545	2545		2545		5272	2545	3909	35682	7497	7011	13538
convertase PC2	X95493	5	2545	2545	2545		2545	2545				8713	2545		28992	7155	19575	
aconitase	AF186471	6	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	5616		12707	12707
aconitase	AF186471	6	2545	2545	2545		2545	2545	2545		2545	2545	2545		2545	13271	23989	
phospholipase C-gamma-1a	AF090111	3	2545	2545	2545	2545	2545	2545		2545	2545	2545	2545	2545	41095	2545	12146	24462
phospholipase C-gamma-1a	AF090111	3	2545	2545	2545		2545	2545			2545	2545	2545		32812	16791	32133	
Cu/Zn SOD	X16585	6	11712		2598	3401	2545	2545	2545	2545	5378	2545	2789	3499	8898	2900		5039
Cu/Zn SOD	X16585	6	15095	3401	2545		2545	2545	2545		6598	2545	4228		7178	2545		
collagenase-4 precursor	L76275	8	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	3648	2545	2545	2545	2545	2545
collagenase-4 precursor	L76275	8	2545	2545	2545		2545	2545	2545		2545	2545	2545		2545	2545	2545	
cytochrome P-450 (11beta, aldo)	D10984	6	2545	2545	2545	2545	2545	3858	2545	2545	2545	2545	2545	2545	67813		22783	36142
cytochrome P-450 (11beta, aldo)	D10984	6	2545	2545	2645		2545	2545	2545		2545	2545	2545		45747		26536	
mitochondrial cytochrome c oxidase	M10217	6	10064	2545		2545	2545	5851	6377	4246	7308	5347	13163	7235	2545	2545	25389	2545
mitochondrial cytochrome c oxidase	M10217	6	11365	2545	2545		2545	7848	2545		7163	5732	11855		2545	2545	24869	
alcohol dehydrogenase class 1 (ADH	AF056255	6	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545			2545	2545
alcohol dehydrogenase class 1 (ADH	AF056255	6	2545	2545	2545		2545	2545	2545		2545	2545	2545				2545	
alcohol dehydrogenase class 4 (ADH	AF056256	6	2546	10028		2545	2545	2545	3180	2545	2545	2545	2545	2545		6597	5398	5398
alcohol dehydrogenase class 4 (ADH	AF056255	6	2545	2545	2545		2545	2545	2545		2545	2545	2545		2618	8002	2705	
adenyl cyclase	Z46958	3	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	6341	3077	2545	2545
adenyl cyclase	Z46958	3	2545	2545	2545		2545	2545	2545		2545	2545	2545		2545	2545	2545	
fibroblast activation factor alpha	U41856	1		2545	2545	2545	2545	2545	2545	2545	2545	2545		2545	2760	2545		2760
fibroblast activation factor alpha	U41856	1		2545	2545		2545	2545	2545		2545	2545				5091		
aldolase C	3926510	6		2545	2545	2545	2545	2545	2664	2545	2545	2545		2545		14259	2545	6344
aldolase C	3926510	6		2545	2545		2545	2545	13644		2545	2545				6775	5813	
2',3'-cyclic-nucleotide 3'-phosphodie	AB002145	9	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2734	2545	2545	2582
2',3'-cyclic-nucleotide 3'-phosphodie	AB002145	9	2545	2545	2545		2545	2545	2545		2545	2545	2545		5335	2545	2616	
arginase	D38303	6	2545	14125	5057	6779	2545	2545	2545	2545	13270	7673	23734	14447		9497	27256	9497
arginase	D38303	6	8502	12977	3148		2545	5670	2545		15025	6051	21680			9497	8192	
arginase 1	U06408	6	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	70797	2545	10914	30678
arginase 1	U06408	6	2545	2545	2545		2545	2545	2545		2545	2545	2545		47983	36520	24836	
argininosuccinate lyase	D38302	6	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545
argininosuccinate lyase	D38302	6	2863	2545	2545		2545	2545	2545		2545	2545	2545		2545		2545	
ATPase Na+/K+ pump alpha 1 subu	U49238	8	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	6071	5015	2545	2545
ATPase Na+/K+ pump alpha 1 subu	U49238	6	2545	2545	2545		2545	2545	2545		2545	2545	2545		2545	2545	2545	
ADP-ribosylation factor (ARF1)	U31350	6	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2546	2545	2545	2545
ADP-ribosylation factor (ARF1)	U31350	6	2545	2545	2545		2545	2545	2545		2545	2545	2545		2545	6154	2545	
allantoicase	AF153230	6	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2546	9071	3038
allantoicase	AF153230	8	2545	2545	2805		2545	2545	2814		2545	2545	2545		2545	4571	3630	
exonuclease Exo1	AF134570	2	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545		2545	2545	2545
exonuclease Exo1	AF134570	2	2545	2545	2545		2545	2545	2545		2545	2545	2545			2545	2545	
deoxyribonuclease gamma	AF059812	2	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	3439	2545	2545	2545
deoxyribonuclease gamma	AF059812	2	2545	2545	2545		2545	2545	2545		2545	2545	2545		3867	2545	2545	
DNA polymerase beta	Y15732	2	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545		9814	2545	2589
DNA polymerase beta	Y15732	2	2545	2545	2545		2545	2545	2545		2545	2545	2545				2589	
ligase I	L43496	2	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2840	4850	2545	3781
ligase I	L43496	2	2545	2545	2545		2545	2545	2545		2545	2545	2545		4883	9459	2545	
ATP-dependent RNA helicase	X57328	4	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	13131	2545		4474
ATP-dependent RNA helicase	X57328	4	2545	2545	2545		2545	2545	2545		2545	2545	2545		5794	3153		
cytosine-5-methyltransferase	D78638	2	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	38899	9459	24508	15805
cytosine-5-methyltransferase	D78638	2	2545	2545	2545		2545	2545	2545		2545	2545	2545		8261	2545	22150	
flap endonuclease 1 (FEN1)	U64563	2	2545	8581	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	49685	12119	24869	22795
flap endonuclease 1 (FEN1)	U64563	2	2545	2545	2545		2545	2545	2545		2545	2545	2545		52621	6382	20921	
terminal deoxynucleotidyl transferase	U07803	2	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545		3166	6397	4781
terminal deoxynucleotidyl transferase	U07803	2	2545	2545	2545		2545	2545	2545		2545	2545	2545			6587	2972	
gelatinase A	AY037943	8	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	4224	2545	2984	3604
gelatinase A	AY037943	8	2545	2545	2545		2545	2545	2545		2545	2545	2545		8713	2545	4827	
liver helicase	AF302423	4	2545	2545	2545	2545	2545	2829	15524	4138	2545	3348	2913	3131	5670	8142	3912	5778
liver helicase	AF302423	4	2545	2545	2545		2545	6109	5448		4184	2545	8227		7223	2545	6888	
aldolase B	AB030822	6	2545	2545	2545	2545	2545	2545	2678	2545	2545	2545	2545	2545	70179	26707	22237	28365
aldolase B	AB030822	6	2545	2545	2545		2545	2645	2545		2545	2545	2545		63415	19577	30023	
cytochrome b	M10217	6	2545	2545	2545	2545	2545	2545		2545	2545	2545	2545	2545	4718	6164	3116	4793
cytochrome b	M10217	8	2545	2545	2545		2545	2545			2545	2545	2545		3636	9871	4867	
aromatase p450	AB031278	5	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2953	2545	2545
aromatase p450	AB031278	6	2545	2545	2546		2545	2545	3671		2545	2545	2545		2545	2545	2545	
NEDD 4	AJ000085	8	2545	2545	2670	2515	2545	2545	2545	2545	2545	2545	2545	2545	44005		13712	14436
NEDD 4	AJ000085	8	2545	2545	2545		2545	2545	2545		2545	2545	2545		14436	9852	26515	
ring finger protein	U63817	1	2545	2545	2545	2515	2545	2545	2545	2545	2545	2545	2545	2545		2545		3484
ring finger protein	U63817	1	2545	2545	2545		2545	2545	2545		2545	2545	2545			4343		
REST	AF068301	4	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	3761	2545	2545
REST	AF068301	4	2545	2545	2545		2545	2545	3671		2545	2545	2545		2576	2545	2545	
MCM2	U44047	1	2603	2545	2545	2545	2545	2545	2545	2545	2545	4859	2545	2545	40531	8161	27481	27048
MCM2	U44047	1	2545	2545	2545		2545	2545	2545		2545	2545	2545		46386	10536	29836	
proteasome subunit Y	D87689	8	188	49	-6	22	195	204	163	196	127	210	266	167	1332	1013	670	1038
proteasome subunit Y	D87689	8	166	-6	-23		198	257	31		145	189	39		1252	1084	589	
transmembrane protein containing a	X83962	10	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	5221	2545	2545	3529
transmembrane protein containing a	X83962	10	2545	2545	2545		2545	2545	2545		3578	2545	2545		8080	4495	2545	
OTX5b	AJ251846	4	2545	2545	2545	2545	2545	2545	2545	2545	2545	3787	2545	2545	29587	2545	22616	28101
OTX5b	AJ251846	4	2545	2545	2545		2545	2545	2545		2545	2545	2545		41642	3356	30712	
13S condensin XCAP-D2	AF067969	2	2545	2545	2545	2545	2545	2545	3842	2545	2545	2545	2545	2545	18544	3457	6131	5153
13S condensin XCAP-D2	AF067969	2	2545	2545	2545		2545	2545	2545		2545	2545	2545		47304	2545	5175	
chaperonin subunit OCT gamma	U57052	7	2545	2545	2545	2545	2545	2545	2545	2545	2546	2545	2545	2545	6432		7758	6566
chaperonin subunit OCT gamma	U57052	7	2545	2545	4214		2545	2545	2545		2546	2545	2545		7699		3527	

HMG-X	D30765	2	2545	2545	2545	2545	2545		2545	2545	2545	2545	2545	2545	34199	8700	4188	9149
HMG-X	D30765	2	2545	2545	2545		2545		2545		2545	2545	2545		34297	9599	2545	
GSK-3 binding protein	AF062738	3	2545	2545	2545	2545	2545	6302	3999	3717	2646		8254	5400	63336		16752	40899
GSK-3 binding protein	AF062738	3	2545	2545	2545		2545	2545	2889		2545		8597		54870		26927	
cartilage homeoprotein 1	U15278	4	2545	2545	2545	2545	2545	2545	5671	2545	2545	2545	2646	2545	62093		28913	43286
cartilage homeoprotein 1	U15278	4	2545	2545	2545		2545	2545	9240		2545	2545	2545		60443		36126	
beta-amyloid precursor protein	S62417	9	2545	2545	2545	2545	2545	2545	2545	2545	2545	5400	2646	2545	33486	4343	25047	22680
beta-amyloid precursor protein	S62417	9	2545	2545	2545		2646	2545	2545		2545	4367	2645		28817	2545	20313	
frizzled 7	AF159106	3	8676	9481		8676	2545	6803	3955	3250	4258	4602	4939	4430	63768	34798	43791	54293
frizzled 7	AF159106	3	9196	2645	3122		2545	6994	2545		4068	2545	8487		51739	56857	63006	
calcineurin A	AF019569	3				#NUM!				#NUM!				#NUM!		11308		9611
calcineurin A	AF019569	3														7914		
BMP1	L12249	8	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545		3723	3906	3814
BMP1	L12249	8	2545	2545	2545		2545	2545	2545		2545	2545	2545			2545	5249	
BMP1b	Y09660	8	2545	2545	2545	2545	2545	2545	2545	2545	4155	2545	2545	2545		2545	3679	2545
BMP1b	Y09660	8	2545	2545	2545		2545	2545	2545		2545	2545	2545			2545	2545	
BMP4	AF058764	3	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	3986	2545	3326	4183
BMP4	AF058764	3	2545	2545	2545		2545	2545	2646		2545	2545	2545		8200	5952	4380	
18S ribosomal	X04025	11	333	214	277	281	405	229	273	294	143	175	251	183	879	810	509	789
18S ribosomal	X04025	11	366	245	236		457	250	315		145	192	282		1067	709	527	
18S ribosomal	X04025	11	2545	2545	2545	2545		2545		2545				2545				30037
18S ribosomal	X04025	11	2545	2545	2545			2545				2545						
18S ribosomal	X04025	11	2545	2545			2545	2545	2545			2545	3187	2545		53730		
MCM3	U28067	1	2545	2645	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	46385		
MCM3	U28067	1	2545	2545	2545		2545	2545	2645		2545	2545	2545		2545	2786	5689	2545
MAM domain protein	U37376	10	19607	15824	4559	17715	2545	9971	22073	9938	12123	10428	21680	13127	8729	2545	2545	
MAM domain protein	U37376	10	20301	12863	20090		2545	10045	9905		14131	9319	20914			55870	25558	25556
XPACx1	D31894	2		2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	51868	21287	
XPACx1	D31894	2		2545	2545		2545	2545	2545		2545	2545	2545		2545	2640	2545	2545
nuclear factor 7	S64515	4		2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2584	2545	2545	
nuclear factor 7	S64515	4		2545			2545	2545	2545			2545	2545		11685	6955	3098	5109
vitellogenin	65210	6	4251	2545	2545	3244	2545	2545		2545	2545	2545	2545	2545	3264	8586	2545	
vitellogenin	65210	6	10411	3943	2545		2545	6391			2545	2545	2545		101631	54261	39342	46862
hsp30B	X02512	7	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	118008	20932	31438	
hsp30B	X02512	7	2545	2545	2545		2545	2545	2545		2545	2545	2545		33714	2545	7836	4964
hsp 30	U44894	7	5	22	34	17	144	18	53	98	910	894	418	865	450	848	391	489
hsp 30	U44894	7	5	13	51		169	197	40		836	980	371		629	557	347	
integrin alpha-1	U44025	9	2545	2545	2545	2545	2545	2545		2545	2545	2545	2545	2545	2681	2545	3754	2545
integrin alpha-1	U44025	9	2545	2545	2545		2545	2545			2545	2545	2545		2545	2545	2545	
gene 5	U37373	10	2545	2545	2545	2545		2545	2545	2545	2545	2545	2545	2545	5900	10118		4222
gene 5	U37373	10	2545	2545	3006			2545	2545		2545	2545	2545		2545	2545		
fos-related antigen-2	U37374	4	2545	2545	2545	2545		2545	2545	2545	2545	2545	2545	2545	46788	3280	5454	5300
fos-related antigen-2	U37374	4	2545	2545	2545			2545	2545		2545	2545	2545		84059	2545	5147	
gene 12	U41854	10	2545	2545	2545	2545		2545	2545	2545	2545	2545	2545	2545	7478			2545
gene 12	U41854	10	2545	2545	2545				2545		2545	2545	2545		2545	2545		
gene 18	U41857	10	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	10888	2545	67401	8206	23304	28810
gene 18	U41857	10	2545	2545	2545		2545	2545	2545		2545	2545	2545		60690	9231	34317	
gene 17	U41860	10	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545		2545		2545
gene 17	U41860	10	2545	2545	2545		2545	2545	2545		2545	2545	2545			3381		
gene 18	U41839	10	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	7800		5173
gene 18	U41839	10	2545	2545	2545			2545	2545		2545	2545	2545		2545	7927		
gene 19	U41861	10	2545	2545	2620	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2621	2545	2545
gene 19	U41861	10	2545	2545	2545		2545	2545	2545		2545	2545	2545		2545	2545	2545	
gene 20	U46575	10	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	27576	2545		15061
gene 20	U46575	10	2545	2545	2645		2545	2545	2545		2545	2545	2545		33793	2545		
regulator for chromosome condensa	D00679	2	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	129607	78868	43288	72218
regulator for chromosome condensa	D00679	2	2545	2545			2545	2545	2545		2545	2545	2545		137303	64569	48550	
proteasome subunit XC3	S61111	8	9717		3071	9717	2545	5140	21247	3843	3936	4727	4580	4527	9277	10023	22714	9277
proteasome subunit XC3	S61111	8	10064	2545	16537		2545	2545	8337		4475	3943	9759			2545	5689	
B-50/GAP 43	X87562	1	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	78822	7990	25029	25342
B-50/GAP 43	X87562	1	2545	2545	2545		2545	2545	2545		2545	2545	2545		75638	2545	25855	
fragile mental retardation protein 1	U25164	4	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	4013	3128	2545	2545
fragile mental retardation protein 1	U25164	4	2645	2545	2882		2545	2545	4673		2545	2545	2545		2545	2545	2545	
forkhead protein lens1	AF186464	4	2545	2545	2545	2545	2545	2545	2546	2545	2545	2545	2545	2545	48300	3606		20648
forkhead protein lens1	AF186464	4	2545	2545	2545		2545	2545	2545		2545	2545	2545		34746	6547		
ER1	AF015454	4	2645	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	8702	5129	6012	3370
ER1	AF015454	4	2545	2545	2545		2545	2545	2545		2545	2545	2545		8537	4822	2545	
B-cell translocation protein 1 (btg1)	AB028243	4	2545	2545	2545	2545	2545	2545	2545	2545	3272	2545	2545	2545	4660	2545	2545	2545
B-cell translocation protein 1 (btg1)	AB028243	4	2545	2545	2545		2545	2545	3206		2545	2545	2545		2545	2988	2545	
SP 1	AF027151	4		2545	2545	2545	2545	2545	2949	2545	2545	2545	2545	2545	67083	7690	33504	30425
SP 1	AF027151	4		2545	2545			2545	4607		2545	2545	2545		62842	28755	27346	
beta-A1-1 crystallin	X87759	9	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545		2545
beta-A1-1 crystallin	X87759	9	2545	2545	2545		2545	2545	2545		2545	2545	2545		2546	5876	2545	
gamma-M1-1 crystallin	X96072	9	2545	2545	2545	2545		2545	3602	2545	2545	3676	2545	2545	2545	2545		2545
gamma-M1-1 crystallin	X96072	9	2545	2545	2545			2646	2545		2545	2545	2645		2545	2545		
SF-1/Ad4BP	AB017352	4	2545	2545	2545	2545		2545	2545	2545	2545	2545	2545	2545	100242	56580	49617	63069
SF-1/Ad4BP	AB017352	4	2545	2545	2545			2545	2545		2545	2545	2545		135107	71559	41604	
fibronectin intron 1	AF061058	control	2545	2545	2545	2545	2645	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545
fibronectin intron 1	AF061058	control	2545	2545	2545		2545	2545	2545		2545	2545	2545		2545	6648	2980	
alpha tubulin intron 1	65164	control	2545	2545	2545	2545	2545	2545	3550	2545	2645	2545	2545	2545		8776	6875	8778
alpha tubulin intron 1	65164	control	2545	2545	2545		2545	2545	2545		2545	2545	2545		31192	2545	18105	
alpha tubulin	X07046	9	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545		2545	2545	2545
alpha tubulin	X07046	9	2950	2545	2545		2545	2545	2545		2545	2545	2545			2545	2545	
delta tubulin	AF430839	9	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545		4329	2545	2545
delta tubulin	AF430839	9	2546	2545	2545		2546	2545	3937		2545	2545	2545			2545	2545	
desmin	X16842	9	2545	2545	2545	2545	2545		2645	2545	2545	2545	2545	2545	2545	2545	5323	2545
gamma fibrinogen precursor	J02894	9	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2940	2545	2545	2545	2545	
gamma fibrinogen precursor	J02894	9	2545	2545	2545		2545	2545	2545		2545	2545	2545	2545	2545	2545	2545	2545
ribonucleotide reductase submit M1	AF168794	9	2545	2545	2545	2545	2545	2545	2545	2545	2645	2545	2545	2545	7170	2545	9056	4708
ribonucleotide reductase submit M1	AF168794	9	2645	2545	2545		2545	2545	2545		2545	2545	2545		7162	3356	2645	

Appendix 2.5.2. The normalized and floor adjusted final data applied for determination relative gene expression for 48 h injection set.

* Highlighted is spots number (N) < 4 for the gene.

NF from GM correction factors

[redacted]

Gene Name	GenBank Accession #	Functional Code	1.00 D/D #17	3.44 #19	1.11 #20	Median	1.45 D/G #21	1.03 #22	1.34 #24	Median	1.17 T3/D #27	2.58 #28	Median	3.75 T3/G #29	3.98 #31	6.51 #32	Median
c-mos	M25366	4	2545	2545		**2545**	2545	2545	2545	**2545**	2545	2545	**2545**	2545	2545	2545	**2545**
c-mos	M25366	4	2545	2545	2545		2545	2545	2545		2545	2545		2545		8241	
N-ras	M97960	3	2545	2545	2545	**2545**	2545	2545		**2545**	2545	2545	**2545**	2545	21333	3229	**2887**
N-ras	M97960	3	2545	2545	2545		2545	2545			2545			2545	3395	2545	
K-ras	AF085280	3	2545	2545	2545	**2545**	2545	2545	2545	**2545**	2545	2545	**2545**	14447	10248	79584	**24401**
K-ras	AF085280	3	2545	2545	2545		2545	2545	2545		2545	2693		34355	7379	70536	
yes	X14377	3	2545	2545	2545	**2545**	2545	2545	2545	**2545**	2545	2545	**2545**	2545		2545	**2545**
yes	X14377	3	2545	2545	2545		2545	2545	2545		2545	2545		2545	3395	2545	
c-fos	AJ224511	4	2545	3613	2545	**2545**	2545	2545	2545	**2545**	2545	2545	**2545**	2545	3961	2545	**2545**
c-fos	AJ224511	4	2545	2545	5911		2545	2545	2545		2545	2545		2545	2545	2786	
raf ser thr kinase	X12948	3	2545	2545		**2545**	6080	2545		**4602**	5949	13135	**9556**		2545		**4699**
raf ser thr kinase	X12948	3	2545	2545			6062	4602	2545		5976	13195			6853		
c-ets-1a	X52692	4	2545	2545	2545	**2545**	2545	2545	2545	**2545**	2545	2545	**2545**	2545	2545	5455 *	**2974**
c-ets-1a	X52692	4	2545	2545	2545		2545	2545	2545		2545	2545		2545	3403	5090	
c-ets-1b	X52691	4	2545	2545	4029	**2545**	2545	3199	2545	**2545**	2545	2545	**3419**	20295	7403	37768	**13849**
c-ets-1b	X52691	4	2545	2545	2545		2545	2545	2545		4294	9480		5192	2545	35711	
ets-2a	M81683	4	2545	2545	2545	**2545**	2545	2545	3648	**2545**	2545	2545	**2545**	3241	17763	2545	**2893**
ets-2a	M81683	4	2545	2545	2545		2545	3941	2545		2545	2545		2545	17181	2545	
c-myc I	X14806	4	2545	2545	2545	**2545**	2545	2545	2545	**2545**	2545	2545	**2545**	4487	2545	8124	**5316**
c-myc I	X14806	4	2545	2545	2545		2545	2545	2545		2545	2545		6145	2545	8736	
L-myc	L11363	4	2545	2545	2545	**2545**	2545	3162	2545	**2545**	2545	2545	**2545**	2545	2545	3372	**2959**
L-myc	L11363	4	2545	2545	2545		2545	3143	2545		2545	2545		2545	13093	8189	
pp60c-src	M24704	3	2545	2545	2545	**2545**	2545	2545	2545	**2545**	2545	2545	**2545**	5995	2545	15623	**5878** *
pp60c-src	M24704	3	2545	2545	2545		3608	2545	2545		2545	2545		5762	3403	17745	
mdm2	PubMed ID: 9136986	1	2545	2545	2545	**2545**	2545	2545	2545	**2545**	2545	2545	**2545**	2545	2545	4960	**2545**
mdm2	PubMed ID: 9136986	1	2545	2545	2545		2545	2545	2545		2545	2545		2545	3395	2545	
ING2	AY014017	4	2545	2545	2545	**2545**	2545	2545	2545	**2545**	2545	2545	**2545**	2545	2545	4153	**3161**
ING2	AY014017	4	2545	2545	2545		2545	2545	2894		2545	2545		2904	3419	3502	
colorectal cancer tumor suppressor	U10986	3	2545	2545	2545	**2545**	2545	2545	2545	**2545**	2545	2545	**2545**	19935	2545	43704	**11828**
colorectal cancer tumor suppressor	U10986	3	2545	2545	2545		2545	2545	2545		2545	2545		3721	2545	40163	
protein lipid phosphatase Pten	AF144732	3	2545	2545	2545	**2545**	2545	2545	2545	**2545**	2545	2545	**2545**	2545	2545	2552	**2548**
protein lipid phosphatase Pten	AF144732	3	2545	2545	2545		2545	2545	2545		2545	2545		3091	2545	5767	
Wt1	D82051	4	2545	2545	2545	**2545**	2545	2545	2545	**2545**	2545	2545	**2545**	29418	6298	61254	**26579**
Wt1	D82051	4	2545	2545	2545		2545	2545	2545		2545	2545		23739	21931	56580	
retinoblastoma 1	PubMed ID: 1516743	4	2545	2545	2545	**2545**	2545	2545	2545	**2545**	2545	2545	**2545**	3414	5379	4505	**2979**
retinoblastoma 1	PubMed ID: 1516743	4	2545	2545	2545		2545	2545	2545		2545	2545		2545	2545	2545	
C/EBP-1	U08604	4	3505	2545	10414	**3505**	7075	5658	8879	**7490**	2545	2545	**2545**	117302	39033	196617	**115141**
C/EBP-1	U08604	4	3315		11421		8830	5520	7906		2545	2545		112921	43041	195341	
C/EBP-2	U08605	4	214	468	479	**468**	377	179	425	**372**	451	599	**525**	2138	638	3339	**2067**
C/EBP-2	U08605	4	238	468	528		368	310	492		422	702		1996	701	3788	
C/EBP	S44193	4	2545	3048	6657	**2797**	4735	2545	6654	**5217**	3887	8581	**7161**	2545	2545	128613	**2545**
C/EBP	S44193	4	2545	2545	7468		4842	5592	6480		5741	12676		2545	2545	118159	
transcription co-repressor Sin3	AF154112	2	2545	2545	2545	**2545**	4219	2545	2545	**2545**	2545	2545	**2545**	2545	2545	2545	**2545**
transcription co-repressor Sin3	AF154112	2	2545	2545	2545		2545	2545	2545		2545	2545		2545	2545	2545	
circadian CLOCK	AF203107	4	2545	2545	2545	**2545**	2545	2545	2545	**2545**	2545	2545	**2545**	2545	2545	12967	**2545**
circadian CLOCK	AF203107	4	2545	2545	2545		2545	4499	2545		2545	2545		2545	2545	12902	
c-Jun	S650725	4	2545	2545	5641	**2545**	2545	2545	2545	**2545**	2545	2974	**2545**	2545	2545	60538	**2545**
c-Jun	S650725	4	2545	2545	4744		4639	3098	2545		2545	2545		2545	2545	33979	
c-Myb	L22741	4	2545	2545	2545	**2545**	2545	2545	2545	**2545**	2545	2545	**2545**	2545	2545	16195	**2545**
c-Myb	L22741	4	2545	2545	2545		3225	2545	2545		2545	2545		2545	2545	52336	
nuclear factor I-B1	L43146	4	2545	2545	2545	**2545**	2545	2545	2545	**2545**	2545	2545	**2545**	2545	2545	8423	**2545**
nuclear factor I-B1	L43146	4	2545	2545	2545		3205	2545	2545		2545	2545		2545	2545	2552	
nuclear factor I-C1	L43149	4	2545	4411	5632	**2921**	4581	3762	2629	**3762**	4558	10063	**7735**	2545	2545	105296	**5170**
nuclear factor I-C1	L43149	4	2545	3296	2545		4410	2545			5407	11937		5957	4383	85221	
TFIIIA	K02938	4	2545	2545	2545	**2545**	2545	2545	2545	**2545**	2545	2545	**2545**	5807	4399	2545	**3957**
TFIIIA	K02938	4	2545	2545	2545		2545	2545	2545		2545	2545		4952	3514	2545	
Oct-1	X17190	4	2545	2545	5180	**2545**	4124	2545	2545	**2545**	2545	3717	**3131**	5214	4534	78517	**4874**
Oct-1	X17190	4	2545	2545	5361		4254	2545	2545		2545	3903		2545	2545	59392	
AP-2	M59455	4	2545	2545	2545	**2545**	2545	2545	2545	**2545**	2545	2545	**2545**	2545	2606	11665	**4519**
AP-2	M59455	4	2545	2545	2545		2545	2545	2545		2545	2545		5755	3530	5507	
TBP-binding repressor Dr1	AB003582	4	2545	2545	2545	**2545**	2545	2545	2545	**2545**	2545	2545	**2545**	4884	4271	2545	**2545**
TBP-binding repressor Dr1	AB003582	4	2545	2545	2545		2545	2545	2545		2545	2545		2545	2545	2545	
TFIID subunit	D50054	4	2545	2545	9710	**5443**	5506	5679	6895	**5592**	2545	3547	**2727**	59640	29422	168913	**71644**
TFIID subunit	D50054	4	2545	10989	8341		5004	5163	5873		2545	2909		83648	28203	159735	
transcription factor A	U35728	4	2545	2545	2545	**2545**	2545	2545	2545	**2545**	2545	2545	**2545**		2545	10975	**3544**
transcription factor A	U35728	4	2545	2545	2545		2545	2545	2545		2545	2545			2545	4544	
RNA pol I transcription factor UBF	X57561	4	2559	2545	5701	**2573**	2689	2545	2545	**2617**	3848	8496	**6783**	2994	6794	6926	**6860**
RNA pol I transcription factor UBF	X57561	4	2587	2545	6287		4689	3914	2545		5070	11194		4704	8686	11691	
elongation factor-1 alpha chain	M25504	11	955	846	1092	**904**	1320	1379	1607	**1426**	1265	1786	**1522**	1898	1937	1146	**1729**
elongation factor-1 alpha chain	M25504	11	823	853	1183		1017	1473	1519		1408	1637		1561	1984	846	
neuroD	U28067	4	2545	2545	2545	**2545**	2545	2545	2545	**2545**	2545	2545	**2545**	2545	2545	6926	**2545**
neuroD	U28067	4	2545	2545	2545		2545	2545	2545		2545	2545		2545	2545	6588	
Tcf-3 co-repressor CtBP	AF152006	4	2545	2545	2545	**2545**	2545	2545	2545	**2545**	2545	2545	**2545**	6182	3427	8332	**6182**
Tcf-3 co-repressor CtBP	AF152006	4	2545	2545	2545		2545	2545	2545		2545	2545			2545	6744	
repressor brain factor 2	AF072889	4	812	1356	661	**824**	582	703	540	**637**	550	759	**718**	1741	693	2708	**1647**
repressor brain factor 2	AF072889	4	837	1548	729		643	709	631		697	738		1553	789	3255	
co-repressor MITR	Z97214	4	2545	2545	2545	**2545**	2545	2545	2545	**2545**	2545	2545	**2545**		2545	2545	**2545**
co-repressor MITR	Z97214	4	2545	2545	2545		2545	2545	2545		2545	2545		2545	21333	2545	
negative regulator Id2	AB019520	4	2545	3114		**2545**	8580		2545	**2545**	2545	2545	**2545**	17114	5164	38171	**23993**
negative regulator Id2	AB019520	4	2545	2746	2545		2545		2545		2545	4094		9949	30872	47675	
XCOE2	AF041138	4	2545	2545	2545	**2545**	2545	2545	2545	**2545**	2545	2545	**2545**	2545	23748	7486	**2545**
XCOE2	AF041138	4	2545	2545	2545		2545	2545	2545		2545	2545		2545	2545	2545	
MRF4	S34392	4	2545	2545	2545	**2545**	2545	3971	2545	**2545**	2545	2545	**2545**	2545	2545	2545	**2545**
MRF4	S34392	4	2545	2545	2545		2545	2545	2545		2545	2545		2545	2545	2545	
Pax-2	AF179300	4	2545	2545	2545	**2545**	2545	2545	2545	**2545**	2545	2545	**2545**	2545	2545	4010	**2545**
Pax-2	AF179300	4	2545	2545	2545		2545	2545	2545		2545	2545		2545	2545	3372	
Pax-8	AF179301	4	2545	2545	5572	**2545**	4735	2545	2545	**2545**	2545		**3418**	19785	33271	53273	**30099**
Pax-8	AF179301	4	2545	2545	5292		4581	2545	2545		4291			26927	2545	70061	
LFB1/HNF1	64688	4	2545	2545	2545	**2545**	3987	2545	2545	**2545**	2545	2545	**2545**	15171	2545	61254	**22295**
LFB1/HNF1	64688	4	2545	2374	2545		2545	2545	2545		2545	2545		29418	2545	51008	
LFB3/HNF1 beta	X76052	4	2545	2545	2545	**2545**	2545	2545	2545	**2545**	2545		**2545**	24069	2545	52752	**24069**
LFB3/HNF1 beta	X76052	4	2545	2545	2545			2545	2545		2545			2545		40970	
Gli2	AF109923	4	2545	2545	2545	**2545**	2545	2545	2545	**2545**	3995	8821	**3270**	3541	2545	11665	**5494**
Gli2	AF109923	4	2545	2545	2545		3845	2545	2545		2545	2545		17151	2545	7447	
brain factor 1	AF101387	4	2545	2839	6748	**2702**	6952	3994	5945	**5750**	5243	11576	**7963**	81098	8304	178977	**85288**
brain factor 1	AF101387	4	2545	2545	6775		6992	4249	5555		4839	10683		89478	30522	161967	
brain factor 2	AJ011652	4	664	1362	640	**693**	524	682	480	**539**	433	550	**574**	1133	630	1927	**1069**
brain factor 2	AJ011652	4	722	1339	561		553	590	481		599	676		1005	526	1901	
GATA-5a	L13701	4	2545	2545	7009	**2545**	2545	2545	6082	**5494**	2545	3733	**2545**	56646	7921	140109	**59366**
GATA-5a	L13701	4	2545	2545	7681		6914	5307	6705		2545	2545		62085	31128	140460	
CCCH zinc finger protein C3H-3	AF061982	4	2545	4301	7338	**4012**	4526	4823	5884	**4824**	3742	8261	**6298**	35908	33192	52023	**36542**
CCCH zinc finger protein C3H-3	AF061982	4	2545	3723	7603		2796	4824	5009		4336	9573		37176	12759	76186	
NK-2 homolog	S65507	4	2545	2545	3463	**2611**	2545	3661	5197	**4336**	4018	8870	**6953**	8403	2545	10975	**9689**
NK-2 homolog	S65507	4	2677	2545	8176		4292	4381	4926		5035	11116		16574	5244	15440	
iriquois 3	AF027175	4	2545	2545	2545	**2545**	2545	2545	2545	**2545**	2545	2545	**2545**	30221	2545	41608	**13370**
iriquois 3	AF027175	4	2545	2545	2545		2545	2545	2545		2545	2545		13370		2545	
myb-related protein 1 (myb 1)	M75870	4	2545	2545		**2545**	3350	2545	2545	**2545**	2545	2545	**2545**	4794	2545	5090	**4942**
myb-related protein 1 (myb 1)	M75870	4	2545	2545	2545		3416	2545			2545	2545		7600	2545	12785	
Pitx-1	AF155206	4		2545	2545	**2545**	4862	2545	2545	**2819**	2545	2545	**2545**	55521	7491	129733	**56443**
Pitx-1	AF155206	4	2545	2545	2545		5372	3092	2545		2545	2545		57366	2545	109515	
MOX2	L20432	4	2545	2545	2545	**2545**	2545	2545	2545	**2545**	2545	2545	**2545**	3361	2545	4361	**2953**
MOX2	L20432	4	2545	2545	2545		2545	2545	2545		2545	2545		2545	2545	8996	
HoxD1	L25857	4	2545	2545	2545	**2545**	2545	2545	2545	**2545**	2545	3341	**2545**	4179	4566	2545	**3342**
HoxD1	L25857	4	2545	2545	2545		2545	2545	2545		2545	2545		2545	8599	2545	
goosecoid homebox protein isoform B	M81481	4	2545	2545	2545	**2545**		2545	2545	**2545**	2545	2545	**2545**	29118	2545	69729	**26000**
goosecoid homebox protein isoform B	M81481	4	2545	2545	2545		2545	2801	2545		2545	2545		27802	2933	24358	
Xhox.lab2	X62053	4	2545	9276	2545	**2545**	2545	2545	2545	**2545**	2545	2545	**2545**	2545		4120	**2760**
Xhox.lab2	X62053	4	2545	2545	2545		2545	2545	2545		2545	2545		5192	2545	2760	
DLL4	L09728	4	2545	2545	2545	**2545**	3703	2545	4793	**3000**	3966	8757	**6530**	42983	11743	67307	**40005**
DLL4	L09728	4	2545	2545	2545		3454	2545	2545		4303	9500		37026	9698	74689	
DLL3	L09729	4	2545	2545	5842	**4193**	4735	5064	5202	**5133**	5164	11400	**7249**	77376	9089	165346	**72784**
DLL3	L09729	4	2545	8911	6641		5995	4146	5386		4228	9335		68193	6909	126439	
DLL2	L09730	4	2545	2545	2545	**2545**	2545	2545	2545	**2545**	4055	8953	**3300**	3331	2545	7720	**4614**
DLL2	L09730	4	2545	2545	2545		2545	2545	2545		2545	2545		5897	2545	34917	
Fez	AF195021	4		2545	2545	**2545**	3532	2545	2545	**2545**	3796	8380	**3170**	32412	2845	60642	**32213**
Fez	AF195021	4	2545	3372	2545		2545	2545	2545		2545	2545		32014	2545	52726	
ergA	AJ224125	4	2545	2545	2545	**2545**	2545	2545	2545	**2545**	2545		**2545**	18839	2893	27235	**14751**
ergA	AJ224125	4	2545	2545	2545		2545	2545	2545		2545			22441	2545	10662	
achaete-scute protein homolog (ASH1)	M98272	4	2545	2545	5698	**2545**	2545	4253	5138	**4046**	2545		**3254**	2545	6359	34318	**7782**
achaete-scute protein homolog (ASH1)	M98272	4	2545	2545	5118		4219	3873	2545		3966			2663	9204	35209	
DNA binding protein E12	X66959	4	2545	2545	2545	**2545**	2545	2545	5213	**2545**	2545	2545	**2545**	4434	2545	33966	**4374**
DNA binding protein E12	X66959	4	2545	2545	2545		2545	2545			2545	2545		4314	2545	33810	
sonic hedgehog	L39213	4	2545	2545	6000	**2545**	2545	2545	2545	**2545**	4390	9691	**3467**	9183	2545	44824	**18179**

sonic hedgehog	L39213	4	2545	2545	6022		3648	2545	2545		2545	2545		27175	7395	46920	
XLMO1	U94991	4	2545	2545	2545	2545	4045	3244	2545	3401	2545	2545	2545	29351	6447	77267	29711
XLMO1	U94991	4	2545	3269	2545		4558	3558	2545		2545	2545		30071	2545	80469	
POU2	U17654	4	4256	2545	10221	4196	5940	5805	7307	6177	5713	12614	9638	27235	10436	43275	20999
POU2	U17654	4	4136	2918	9790		5401	6414	7502		6663	14710		14743	2545	48547	
X-MyT1	U67078	4	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	3346	2545	2545	2545
X-MyT1	U67078	4	2545	2545	2545		2545	2545	2545		2545	2545		2545	2545	2545	
Xsal-1	L46583	4	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	3294	2545	2545	2545
Xsal-1	L46583	4	2545	2545	2545		2545	2545	2545		2545	2545		2545	2945	2545	
zic2	U57453	4	2791	2545	8944	4172	5604	4619		5168	6193	13672	9561	88158	7021	123568	78400
zic2	U57453	4	4172		10666		6558	4732			5856	12929		68643	2545	126022	
TFIIIA	X58369	4	2545	2545	2545	2545	2545	2545		2545		2545	2545	2545	2545	2545	2545
TFIIIA	X58369	4	2545	2545	2545		2545	2545				2545		2545	2545	2545	
TH bZip	U37375	4	2545	2545	2545	2545	2545		2545	2545	2545	2545	2545	32776	2545	72235	31198
TH bZip	U37375	4	2545	2545	2545		2545		2545		2545	2545		29621	2545	65042	
glucocorticoid receptor	X72211	5	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	3624	2545	9504	3085
glucocorticoid receptor	X72211	5	2545	2545	2545		2545	2545	2545		2545	2545		2545	24362	2545	
estrogen receptor	L20736	5	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	4550	2545	2545
estrogen receptor	L20736	5	2545	2545	2545		2545	2545	2545		2545	2545		2545	2545	4609	
vitamin D receptor	U91846	5	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545
vitamin D receptor	U91846	5	2545	2545	2545		2545	2545	2545		2545	2545		2545	2545	2545	
tif2	AJ243119	4	3157	3172	10784	6935	8406	6184	9569	8667	7108	15693	11414	97337	32434	229021	104626
tif2	AJ243119	4	3585	13885	10285		14686	7542	8927		7135	15753		111915	45711	181242	
TRIP4	AW199631	5	2545	2545	2545	2545	2545	2545	[illegible]	2545	2545	2545	2545	2545		2545	2545
TRIP4	AW199631	5	2545	2545	2545		2545	2545	2545		2545	2545		2545		6796	
TRIP7	AW200492	5	2545	2545	2545	2545		3554	2545	2545	2545	2545	2545	2545	7045	3164	2854
TRIP7	AW200492	5	2545	2545	2545		2545	2545	2545		2545	2545		2545	2545	6601	
thyroid hormone receptor alpha A	M35343	5	2545	2545	4488	2545	2545	2545	2545	2545	2545	2545	2545	2545	2861	33589	2703
thyroid hormone receptor alpha A	M35343	5	2545	2545	2545		2545	2545	2545		2545	2545		2545	2545	24866	
thyroid hormone receptor beta A1	M35359	5	2545	2545	2545	2545	3527	2545	2545	2545	2545	2545	2545	2545	7419	2545	2545
thyroid hormone receptor beta A1	M35359	5	2545	2545	2545		2545	2545	2545		2545	2545		2545	2545	6835	
androgen receptor alpha	U67129	5	2545	3797	7220	4665	5627	4610	2545	4782	2545	4853	4963	40935	8734	87161	44870
androgen receptor alpha	U67129	5	2545	3544	5786		5769	4828	4735		5072	11199		48806	13787	88476	
mineralocorticoid receptor	U15134	5	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	4817	2545	7199	2683
mineralocorticoid receptor	U15134	5	2545		2545		2545	2545	2545		2545	2545		2821	2545	2545	
RXR xSRC-3	AF044080	5	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	7199	4153
RXR xSRC-3	AF044080	5	2545	2545	2545		2545	2545	2545		2545	2545		2545	5762	6744	
RAR beta	X87366	5	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545
RAR beta	X87366	5	2545	2545	2545		2545	2545	2545		2545	2545		2545	2545	4439	
RAR gamma B	X59396	5	2545	2545	2545	2545	2545	2545	2545	2545	2545		2545	2545	3168	2545	2856
RAR gamma B	X59396	5	2545	2545	2545		2545	2545	2545		2545			5822	2545	4192	
PPAR alpha	M84161	5	2545	2545	2545	2545	2545	2545	2545	2545	4050	8943	3298	3781	37670	43275	9839
PPAR alpha	M84161	5	2545	2545	2545		2545	3371	2545		2545	2545		4329	2545	15349	
PPAR beta	M84162	5	2545	2545	2545	2545	2545	2545	2545	2545	2545		2545	2545	2545	2545	2545
PPAR beta	M84162	5	2545	2545	2545		2545	2545	2545		2545			5204	2545	2545	
PPAR gamma	M84163	5	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2837	2545	2545
PPAR gamma	M84163	5	2545	2545	2545		2545	2545	2545		2545	2545		3054	2545	2545	
NGFI-B	X70700	4	2657	2545	2545	2545	2545	2545		2545	2545	2545	2545	2545	2885	3710	2545
NGFI-B	X70700	4	2545	2545	2545		2545	2545			2545	2545			2545	2545	
orphan nuclear receptor	X75163	4	2545	2545	2545	2545	2545	2545		2545		12732	7639	9183	2545	58337	8582
orphan nuclear receptor	X75163	4	2545	2545	2545		2545	2545				2545		30994	2545	7981	
COUP transcription factor 1	AF157558	4	2545	2545	5111	2545	2545		4156	2545	2545	2793	3377	25780	5180	90350	22615
COUP transcription factor 1	AF157558	4	2545	2545	6454		2545		2545		3962	8746		26815	5148	19450	
thyroid hormone receptor alpha	L06064	5	2545	2545	2545	2545	2545	2545	2545	2545	2545		2545	40860	4630	64079	39517
thyroid hormone receptor alpha	L06064	5	2545	2545	2545		3503	2545	2545		2545			38174	5881	86653	
thyroid hormone receptor beta	L27344	5	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	4697	2545	9946	2608
thyroid hormone receptor beta	L27344	5	2545	2545	2545		2545	2545	2545		2545	2545		2671	2545	2545	
metastasis associated 1-like protein	AF170344	2	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	7225	2545	9543	5896
metastasis associated 1-like protein	AF170344	2	2545	2545	2545		2545	2545	2545		2545	2545		4044	4566	8046	
recombination activation (RAG-2)	L19325	2	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545
recombination activation (RAG-2)	L19325	2	2545	2545	2545		2545	2545	2545		2545	2545		2545	6272	2545	
methyl-CpG binding protein	AF170347	2	2545	2545	2545	2545	2545	3357	2545	2545	2545	2545	2545	3136		6809	4973
methyl-CpG binding protein	AF170347	2	2545	2545	2545		2545	2545			2545	2545		2545		7447	
replication protein A	X67240	2	2545	2545	2545	2545		2545		2545	2545	2545	2545	2545		2545	2545
replication protein A	X67240	2	2545	2545	2545			2545			2545	2545		2545		2545	
Mi-2 histone deacetylase	AF171099	2	2545	2545	2545	2545	2545	2545		2545	2545	2545	2545	4697	2545	16534	16534
Mi-2 histone deacetylase	AF171099	2	2545	2545	2545		2545	2545			2545	2545		19552		49224	
mitochondrial RNA polymerase	AF200705	2	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545
mitochondrial RNA polymerase	AF200705	2	2545	2545	2545		2545	2545	2545		2545	2545		6505	2545	2545	
mitotic phosphoprotein 43	U95097	2	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	4179	2845	13527	6853
mitotic phosphoprotein 43	U95097	2	2545	2545	2545			2545	2545		2545	2545		24324	3411	21143	
mitotic phosphoprotein 90	U95102	2	2545	2545	5027	2545		4058	2545	2545	4019	5873	6803	35792	4016	72515	34211
mitotic phosphoprotein 90	U95102	2	2545	2545	6381			2545	2545		4733	10450		32630	5786	56925	
maskin	AF200212	11	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	3459	2545	2545
maskin	AF200212	11	2545	2545	2545		2545	2545	2545		2545	2545		2545	7180	2545	
plexin	D38175	9	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	16919	2545	31906	13485
plexin	D38175	9	2545	2545	2545		2545	2545	2545		2545	2545		10451	2545	34396	
contactin F3 F11	D86505	9	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	3211	2545	4322	2878
contactin F3 F11	D86505	9	2545	2545	2545		2545	2545	2545		2545	2545		2545	2545	6796	
non-muscle tropomyosin (TM-4)	L35238	9	2593	2545	7705	2874	3979	4506		3842	7158		8277	16697	2545	57478	19128
non-muscle tropomyosin (TM-4)	L35238	9	3156	2545	5882		2545	3706			9396			25142	5682	21559	
coronin	AB025246	9	2545	2545	2545	2545	2545	2545	2545	2545	2545	3342	2574	2952	2545	5950	3551
coronin	AB025246	9	2545	2545	2545		2545	2545	2545		2545	2602		4149	2545	8176	
kinesin central motor 1 XKCM	U36485	9	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545
kinesin central motor 1 XKCM	U36485	9	2545	2545	2545		2545	2545	2545		2545	2545		2545	2837	2545	
katanin p60	AF177942	9	2545	2545	2545	2545	2545	2545		2545	2545	2974	2545	5117	5116	60075	13212
katanin p60	AF177942	9	2545	2545	2545		2545	2545			2545	2545		21308	2545	56059	
calponin H3	AF081576	9	2545	2545	4848	2545	2545	2545		2545	2545	3351	2545	3594	2545	2929	2737
calponin H3	AF081576	9	2545	2545	4207		2545	3462	2545		2545	2545		2545	2545	5338	
myelin proteolipid protein	Z19522	9	2545	2545	2545	2545	2545	2545	2545	2545	2545		2545	2545	2545	14802	3569
myelin proteolipid protein	Z19522	9	2545	2545	2545		2545	2545	2545		2545	2545		2596	4542	5780	
myelin basic protein	AB000736	9	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2845	2545	2695
myelin basic protein	AB000736	9	2545	2545	2545		2545	2545	2545		2545	2545		3684	2545	39343	
class II beta-tubulin	X15798	9	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	7707	2818
class II beta-tubulin	X15798	9	2545	2545	2545		2545	2545	2545		2545	2545		3091	2545	7095	
beta tubulin	L06232	9	2545	2545	2702	2545	2545	2545	2545	2545	2545	3547	3046	16574	2545	17862	13058
beta tubulin	L06232	9	2545	2545	4575		3631	2545	2545		2545	4748		2545		13058	
fibronectin	M77820	9	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	4804	2545
fibronectin	M77820	9	2545	2545	2545		2545	2545	2545		2545	2545		2545	2545	2545	
Xefiltin	U63711	9	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	8216	2545	53260	15625
Xefiltin	U63711	9	2545	2545	2545			2545			2545	2545		23034	2545	58741	
myosin heavy chain 3	AF047906	9	2545	3300	2545	2545	24747	12795	17593	17545	17687	39049	27415	2545	40268	10090	9504
myosin heavy chain 3	AF047906	9	2545	2545	2545		27146	33969	17496		16924	37144		2545	17245	8918	
alpha skeletal actin	X03470	9	268	420	350	351	1436	1011	1062	1139	1695	1022	1292	1666	1442	723	1434
alpha skeletal actin	X03470	9	306	437	352		1530	1073	1204		1550	1033		1606	1426	742	
cytoplasmic beta actin	AF079161	9	1351	1837	1528	1491	3019	2438	2599	2494	3152	3119	3135	5957	4393	5689	5374
cytoplasmic beta actin	AF079161	9	1469	1888	1777		2933	2628	2584		3583	3810		5807	4399	6158	
cytoplasmic beta actin	AF079161	9	1066	1424	1118		2615	1757	2069		2689	2504		4952	3514	5546	
cytoplasmic beta actin	AF079161	9	1775	1672	1590		2082	2196	2479		3682	3082		5214	4534	6783	
cytoplasmic beta actin	AF079161	9	1622	1517	1258		2644	2056	2388		2701	2889		5755	3530	5533	
cytoplasmic beta actin	AF079161	9	928	1652	1297		2991	2305	2471		3183	3640		4894	4271	6861	
ribosomal protein L8	U00920	11	750	626	889	859	661	634	639	790	457	460	739	593	661	156	674
ribosomal protein L8	U00920	11	660	578	862		719	764	725		484	547		713	673	143	
ribosomal protein L8	U00920	11	921	764	1218		800	928	1064		765	728		690	1343	325	
ribosomal protein L8	U00920	11	942	626	1271		782	914	895		686	772		780	996	664	
ribosomal protein L8	U00920	11	861	571	938		585	719	725		746	769		705	390	742	
ribosomal protein L8	U00920	11	845	509	684		695	789	556		732	862		720	590	560	
ribosomal protein L8	U00920	11	858	723	1120		795	871	818		662	718		675	701	742	
ribosomal protein L8	U00920	11	926	544	942		758	895	817		850	713		596	765	638	
ribosomal protein L8	U00920	11	1047	557	989		890	775	792		797	862		758	235	625	
ribosomal protein L8	U00920	11	1124	647	1100		872	896	1006		852	909		878	677	664	
protein S10	S57432	11	1146	1996	986	1251	639	965	792	785	962	573	853	525	693	677	665
protein S10	S57432	11	1355	2347	1023		868	1120	683		1031	743		488	653	729	
mitochondrial 16s ribosomal RNA	U66113	11	1096	1693	1105	1186	1452	1078	1534	1309	959	1327	1233	2198	2184	2838	2402
mitochondrial 16s ribosomal RNA	U66113	11	1166	1700	1207		1185	1183	1432		1139	1353		2195	2606	3216	
HMG-I	U21933	4	2545	2545	5517	2596		2545		2545	2545	2545	2545	6212	6726	45214	6469
HMG-I	U21933	4	2647	2545	5657		2545	2545	2545		2545	2545		4524	2545	48808	
histone H1	J00968	2	2545	2545	3102	2545	2545	2545	2545	2545	2545	2545	2545	5364	2545	49517	9472
histone H1	J00968	2	2545		2545		2545	2545	2545		2545	2545		22966	2545	13579	
51 KDa cytokeratin type I	Y00968	9	2545	2545	6232	2545	8531	6845	5999	6868	2545		2545	2545	2545		2545
51 KDa cytokeratin type I	Y00968	9	2545	2545	6000		8798	6827	6892		2545			2731	2545		
epidermal type I keratin kI	65242	9	2933	5450	15434	10143	18830	10445	9042	10316	5750	12650	9261	3459	2545	6379	3754
epidermal type I keratin kI	65242	9	3605	14836	15238		19314	10186	8615		5872	12965		2545	4048	4791	
alpha 1 collagen type I	AB015440	9	2545	2545	4742	2807	12565	7883	6301	7255	4177	9221	7400	31046	6511	64144	30217
alpha 1 collagen type I	AB015440	9	2545	3069	5203		13089	6519	6627		5579	12317		29388	7252	82409	
alpha 2 collagen type I	D88764	9	2545	9723	5764	3982	13484	9502	9944	9723	5526	12201	9049	28593	31036	56723	31131
alpha 2 collagen type I	D88764	9	2545	2545	5419		11055	7723	8192		5898	13022		30899	31207	67281	
alpha-1 collagen type II	M63595	9	2545	2545	2545	2545	4074	2545	2545	2545	2545		2545	2545	44699	14256	29477
alpha-1 collagen type II	M63595	9	2545	2545	4122		2545	3100	2545		2545			8906	68439	45254	
ribosomal protein L32	X55030	11	904	1266	1140	1115	664	703	710	696	630	1456	1052	1411	1387	1608	1585
ribosomal protein L32	X55030	11	954	1260	1059		690	822	590		689	1415		1711	1562	1836	
serum retinol binding protein	J02718	5	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545
serum retinol binding protein	J02718	5	2545	2545	2545		2545	2545	2545		2545	2545		2545	2545	2545	
cellular retinoic acid binding protein	S74933	5	2545	2545	4203	2545	2545	2545		2545	2545	2545	2545	2545	2545	7629	3387
cellular retinoic acid binding protein	S74933	5	2545	2545	2545		2545	2545			2545	2545		6632	3435	3339	
thyroid hormone binding protein	U03878	5	2545	2545	2545	2545	7682	4238		6123	6221	13734	9500	5612	5148	10845	5446
thyroid hormone binding protein	U03878	5	2545	2545	2545		7511	4736			5788	12779		5680	3969	11769	
IFABP	L19946	7	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	22537	2545	2545
IFABP	L19946	7	2545	2545	2545		2545	2545	2545		2545	2545		2545	19540	2545	

L-amino acid transporter-1	Y12716	"	2545	2545	2545	2545	2545	2545	2545	2545		2545	2545	28742	17181	33073	21462
L-amino acid transporter-1	Y12716	"	2545	2545	2545		2545	2545	2545			2545		9251	7539	51803	
chloride channel ClC-3	Y09941	"	2545	2545	2545	2545	2545	2545	2545	2545	2545	2878	2545	10076	2545	66919	10594
chloride channel ClC-3	Y09941	"	2545	2545	2545		2545	2545	2545		2545	2545		11112	5140	53703	
chloride channel ClC-5	AF063904	"	2545	2545	2545	2545	2545	2545	4720	2545	4296	9485	3421	7653	3969	17536	9412
chloride channel ClC-5	AF063904	"	2545	2545	2545		2545	2545	2545		2545	2545		11172	3427	19915	
multidrug resistance gene	U17608	"	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	9469	2545	62399	8474
multidrug resistance gene	U17608	"	2545	2545	2545		2545	3182	2545		2545	2545		7490	2545	23864	
importin alpha 1a	L26329	"		4198		3571				#NUM!			#NUM!	8126		6861	5641
importin alpha 1a	L26329	"		2545										4021		2545	
Ca2+-binding protein frequenin	U27274	"				#NUM!				#NUM!			#NUM!	3961		30266	7923
Ca2+-binding protein frequenin	U27274	"												2545		11986	
calbindin D28K	U76036	"	2545	2545	2545	2545		2545	2545	2545	2545	2545	2545		2543	2545	2545
calbindin D28K	U76036	"	2545	2545	2545		2545	2545	2545		2545	2545		2545	2543	2721	
adult beta-globin	J00078	"	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	3549		3489	3519
adult beta-globin	J00078	"	2545	2545	2545		2545	2545	2545		2545	2545		2545		6015	
larval beta 1 globin	X03143	"	2929	2545	4385	2888	11522	9130	9449	9667	2545	2545	2545	81784	2545	98761	90273
larval beta 1 globin	X03143	"	2847	2545	4655		14335	10203	8679		2545	2545		105778	33869	109918	
sodium phosphate cotransporter	L78833	"	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	5930	2545
sodium phosphate cotransporter	L78833	"	2545	2545	2545		2545	2545	2545		2545	2545		2545	2545	10949	
Na+ dicarboxylate cotransporter	U87318	"	2545	2545	6422	2548		2545	2545	2545	3866	9535	3295	2545	4948	9387	3297
Na+ dicarboxylate cotransporter	U87318	"	2545	2545	2545			2545	2545		2545	2545		2545	2545	6783	
Na+-glucose cotransporter type I	AB008225	"	2545	2545	2545	2545		2545	4846	2548	2545	3717	2545	2545	2545		2545
Na+-glucose cotransporter type I	AB008225	"	2545	2545	2545			2545	2545		2545	2545		2545	2545		
epithelial Na+ channel alpha subunit	U23535	"	2545	2545	2545	2545	2545	2545	7152	2545	2545	2545	2545	3459	2980		2763
epithelial Na+ channel alpha subunit	U23535	"	2545	2545	2545		2545	2545			2545	2545		2545	2545		
poly A-binding protein ABP-EF	M27072	4	2545	2545	2545	2545		2545	3949	3416	2545		4135	2545	2545	5767	2545
poly A-binding protein ABP-EF	M27072	4	2545	2545	2545			3782	4643		4135	9128		2545		5247	
nervous system-specific RNA binding protein	M34894	4	2545	2545	2545	2545	2545	2545		2545		10512	6529	3620	2545	58698	5620
nervous system-specific RNA binding protein	M34894	4	2545	2545	4298		2545	2545				2545			2895	71826	
Xlin	X04021	4	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	30071	2545	2545	11006
Xlin	X04021	4	2545	2545	2545		4402	2545	2545		2545	2793		30716	5817	16195	
p54 mRNA binding protein	M80257	4	2545	2545	5081	2545	4982	2545	2545	3766	2617	5778	3481	47290	4016	88431	47253
p54 mRNA binding protein	M80257	4	2545	2545	4746		4184	3347	4896		2545	4285		47305	2545	101690	
"4 kDa 68 kDa serum albumin	M21442	"	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2552	2545
"4 kDa 68 kDa serum albumin	M21442	"	2545	2545	2545		2545	2545	2545		2545	2545		2545	3395	2545	
aldehyde dehydrogenase class 1	AB016718	6	2545	2545	2545	2545	2545	2545	2545	2545		2545	2545	2545	2545	2545	2545
aldehyde dehydrogenase class 1	AB016718	6	2545	2545	2545		2545	2545	2545			2545		2545	2545	8645	
Wnt inhibitory factor-1	AF122924	3	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	6457	3129
Wnt inhibitory factor-1	AF122924	3	2545	2545	2545		2545	2545	2545		2545	2545		2545	3714	3932	
transferrin	X54330	"	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	1686	2545	2545
transferrin	X54330	"	2545	2545	2545		2545	2545	2545		2545	2545		2545	2545	3906	
hnRNP I-related RNA transport protein	AF091370	4	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2626	2545	5767	2586
hnRNP I-related RNA transport protein	AF091370	4	2545	2545	2545		2545	2545	2545		2545	2545		17654	2545	2545	
urea transporter	Y12784	"	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	9834		5950	7876
urea transporter	Y12784	"	2545	2545	4835		2545	2545	2545		2545	2545		7218		44917	
SPARC	X62483	1	2545	2545	4029	2545	7076	6938		8005	6438	14214	11380	2545	2545	9022	4870
SPARC	X62483	1	2545	2545	4844		9108	8933			8545	18866		7195	11842	2545	
L-epinephrine transporter	U72877	"	2545	2545	2545	2545	2545	2545		2545	2545	2545	2545	2545	2545	4439	2545
L-epinephrine transporter	U72877	"	2545	2545	2545		2545	2545			2545	2545		2545	2545	2545	
TIMP-2	AY037944	8	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	3694	2545	16378	10736
TIMP-2	AY037944	8	2545	2545	2545		2545	2545	2545		2545	2545		17894	2545	17862	
transthyretin	AB006134	5	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	6287	2545	7291	4986
transthyretin	AB006134	5	2545	2545	2545		2545	2545	2545		2545	2545		3684	2545	8241	
interleukin 1 beta	AJ010497	3	2545	2545	2545	2545	2545	2545	2545	2545	2545	2964	2757	2545	2545	4088	2545
interleukin 1 beta	AJ010497	3	2545	2545	2545		2545	2545	2545		2545	3717		20122	2545	2545	
XEDD 8	Not Submitted	8	2545	2545	2545	2545	2545	2545	2545	2545	2545		2545	43861	2545	64248	36951
XEDD 8	Not Submitted	8	2545	2545	2545		2545	2545	2545		2545			30641	3674	56547	
osteogenic protein-1 homolog precursor	U49934	1	2545	2545	2545	2545		2545	2545	2545	2545	2545	2545	3174		7408	7408
osteogenic protein-1 homolog precursor	U49934	1	2545	2545	2545		2545	2545	2545		2545			19230	6343	15453	
connective tissue growth factor XCTGF	U43524	1	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	12237	5315	36502	11933
connective tissue growth factor XCTGF	U43524	1	2545	2545	2545		2545	2545	2545		2545	2545		11929	8973	63565	
nerve growth factor	X55716	1	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	5418	2545	50110	2981
nerve growth factor	X55716	1	2545	2545	2545		2545	2545	2545		2545	2545		2545	2545	5038	
prepronociceptin/pre Y	S55577	3	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	4088	2545
prepronociceptin/pre Y	S55577	3	2545	2545	2545		2545	2545	2545		2545	2545		2545	2545	7186	
neuromedin	L01530	3	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	3249	2545	9133	2922
neuromedin	L01530	3	2545	2545	2545		3527	2545	2545		2545	2545		2596	2545	17536	
thyroid-stimulating hormone a	L07619	5	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	3112	2828
thyroid-stimulating hormone a	L07619	5	2545	2545	2545		2545	2545	2545		2545	2545		2545	3395	7727	
thyrotropin-releasing hormone precursor	X64056	5	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	17198	2545
thyrotropin-releasing hormone precursor	X64056	5	2545	2545	2545		2545	2545	2548		2545	2845		2545	2545	6561	
corticotropin-releasing factor	S50096	5	2545	2545	2591	2545	4903	2545	2545	3816	2545	2974	2974	48145	6961	119630	44248
corticotropin-releasing factor	S50096	5	2545	2545	5361		5280	3291	4341		4043			40550	6925	190180	
prolactin	L07620	5	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	10845	2545
prolactin	L07620	5	2545	2545	2545		2545	2545	2545		2545	2545		2545	2545	51854	
ubiquitin	M11512	8	942	1184	764	1035	951	783	848	850	837	682	776	698	558	937	688
ubiquitin	M11512	8	1294	1129	870		852	792	907		1048	792		679	598	853	
X Wnt-2b	U66288	3	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	3931	2545	2545	3120
X Wnt-2b	U66288	3	2545	2545	2545		2545	2545	2545		2545	2545		2724	3395	12173	
A5-protein	D10447	3	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	4224	2545	45169	12102
A5-protein	D10447	3	2545	2545	2545		2545	2545	2545		2545	2964		19980	2545	44485	
geminin H	AF067856	2	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545
geminin H	AF067856	2	2545	2545	2545		2545	2545	2545		2545	2545		2545	2545	2545	
fibroblast growth factor receptor ligand	U40457	1	2545	2545	2545	2545	3834	2545	2545	2545	2545	2545	2545	4599		4674	4659
fibroblast growth factor receptor ligand	U40457	1	2545	2545	4477		2545	2545	2545		2545	2545		2545	2545	7655	
FGF-5	Z25539	1	2545	2545	2545	2545	2545	3092	2545	2545	2545	2545	2545	25292		63063	25367
FGF-5	Z25539	1	2545	2545	2545		3616	2545	2545		2545	2545		2586	2545	31922	
FGF-20	AB012615	1	2545	2545	2545	2545	2545	2545		2545	2545		2545	3211	2545	5455	2757
FGF-20	AB012615	1	2545	2545	2545		2545	2545			2545	2545		2545	2545	2968	
TGF-beta 2	X51817	1	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545
TGF-beta 2	X51817	1	2545	2545	2545		2545	2545			2545	2545		4044	2545	2545	
TGF-beta 5	AJ005497	1	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2861	2545	2545
TGF-beta 5	AJ005497	1	2545	2545	2545		2545	2545			2545	2545		2821	2545	2545	
Myf-5	X56738	4	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	3684	2545	10558	5115
Myf-5	X56738	4	2545	2545	2545		2545	2545	2545		2545	2545		2545	2545	8631	
c-type natriuretic peptide 1	D17413	5	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	7788	2545	9204	7788
c-type natriuretic peptide 1	D17413	5	2545	2545	2545		2545	2545	2545		2545	2545			2545	39057	
thyroid-stimulating hormone beta	L07618	5	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	45377	7770	2545	2545
thyroid-stimulating hormone beta	L07618	5	2545	2545	2545		2545	2545	2545		2545	2545		2545	2545	2545	
growth hormone A	AF193797	5	2545	2545	2545	2545	2545	2545	2545	2545	2545	2613	2545	3586	2545	3411	2965
growth hormone A	AF193797	5	2545	2545	2545		2545	2545	2545			2545		2545	2545	5385	
RSK2	AF165162	3	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545
RSK2	AF165162	3	2545	2545	2545		2545	2545	2545		2545	2545		2545	2545	2545	
PCNA	M34089	2	3699	2545	6887	3480	5978	5217	5619	5788	2545	2545	2545	5229	2545	2545	4038
PCNA	M34089	2	3261	2545	7423		5958	5603	6355		2545	2545		3541	4534	9295	
RING finger subunit MAT	U29667	1	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545
RING finger subunit MAT	U29667	1	2545	2545	2545		2545	2545	2545		2545	2545		2545	2545	2545	
Chk1 checkpoint kinase	AF117816	1	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545
Chk1 checkpoint kinase	AF117816	1	2545	2545	2545		2545	2545	2545		2545	2545		2545	2545	2545	
fyn	X52188	3	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545		2545	2545
fyn	X52188	3	2545	2545	2545		2545	2545	2545		2545	2545		2545	4044	2545	
XORP1	AB030502	1	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	5837		7994	6004
XORP1	AB030502	1	2545	2545	4024		2545	3565	2545		2545	2545		2545		6171	
wee 1A kinase	U13962	1	2545	2545	2545	2545	2545	2545		2545	2545	2592	2545	3459		2734	4678
wee 1A kinase	U13962	1	2545	2545	4420		2545	2545			2545	2545		5897		6470	
Max2:Max4	L09738	4	2545	2545	2545	2545	2545	2545		2545	2545	2545	2545	2545	2545	6379	2545
Max2:Max4	L09738	4	2545	2545	2545		2545	2545	2545		2545	2545		2545	2545	2545	
Mad1	L77885	1	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	3549	2681	8931	5299
Mad1	L77885	1	2545	2545	2545		2545	2545	2545		2545	2545		4284	2545	6314	
Mad2	L77885	1	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	4593	3253
Mad2	L77885	1	2545	2545	2545		2545	2545	2545		2545	2545		2545	3961	6236	
MAP kinase 1 (MPK1)	X59813	3	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545
MAP kinase 1 (MPK1)	X59813	3	2545	2545	2545		2545	2545	2545		2545	2545		2545	5164	2545	
MAP kinase 2 (MPK2)	X80531	3	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545
MAP kinase 2 (MPK2)	X80531	3	2545	2545	2545		2545	2545	2545		2545	2545		2545	2545	2545	
MAP kinase activator 2 (XMEK2)	Z22736	3	2545	2545	2545	2545	4663	2545	2545	2545	2545	2545	2545	3095		30514	33267
MAP kinase activator 2 (XMEK2)	Z22736	3	2545	2545	2545		4587	2545	2545		2545	2545		33440		76564	
MAP kinase activator (XMEK3)	AF172848	3	2545	2545	2545	2545	2545	2545		2545	2545	2545	2545		4566	31779	4646
MAP kinase activator (XMEK3)	AF172848	3	2545	2545	2545		2545	2545			2545	2545			2545	4726	
MAP kinase phosphatase	X83742	3	4798	6035	11969	6052	8070	6587	10067	8582	6426		7994	38962	6999	73960	45621
MAP kinase phosphatase	X83742	3	6052		12434		7326	9093	11500		7762			32279	13680	83482	
MAP kinase interacting kinase	AB023807	3	2545	2545	2545	2545	2545	2545		2545	2545	3542	2669	29418	5817	87812	31410
MAP kinase interacting kinase	AB023807	3	2545	2545	4583			2545	2545		2545	2793		33402	2545	99122	
MAPKK	D13709	3	2545	2545	2545	2545	3379	3178	2545	2862	2545	2545	2545	28473	2545	67418	30435
MAPKK	D13709	3	2545	2545	2545		2545	3280	2545		2545			32397	2545	80183	
phosphoinositide 3 kinase catalytic subunit	AF204924	3	2545	2545	2545	2545		2545	2545	2545	2545	2545	2545	2545		2545	2545
phosphoinositide 3 kinase catalytic subunit	AF204924	3	2545	2545	2545		2545	2545	2545		2545	2545		2545	3872	3138	
casein kinase 1-alpha	Y08817	3	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545
casein kinase 1-alpha	Y08817	3	2545	2545	2545		2545	2545	2545		2545	2545		2545	3867	2545	
casein kinase 1-epsilon	AF130394	3	2545	2545		2545	2545	2545	2545	2545	2545	2545	2545	30986		66709	15909
casein kinase 1-epsilon	AF130394	3	2545	2545	2545		2545	2545	2545			2545		11952	2545	15909	
calmodulin-dependent protein kinase beta subunit	U96636	3	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	3079	3321		4609	3286
calmodulin-dependent protein kinase beta subunit	U96636	3	2545	2545	2545		2545	2545	2545		3613	7977		3286	2545	2545	
protein kinase PKN	D43890	3	2545	2545	2545	2545		2545	2545	2545	2545	2545	2545	2545	2545	2545	2545
protein kinase PKN	D43890	3	2545	2545	2545		2545	2545	2545		2545	2545		2545	4120	3606	
PKC-related kinase 2	AF027183	3	2545	2545	2545	2545	2545		3047	2545	2545	2545	2545			13003	3736
PKC-related kinase 2	AF027183	3	2545	2545	2545		2545		2545		2545	2545		3091		3736	
DNA-PK	AF001413	2	2545	2545	2545	2548	2545	2545		2545	2545	2545	2545	2545	2545	4752	2545

DNA-PK	AF001413	2	2545	2545	2545		2545	2545			2545	2545		2545	2545	2721	
ATM	AF174488	2	2545	2545	2545	**2545**	2545	2545	2545	**2545**	2545	2545	**2545**	5094	2545	14256	**6632**
ATM	AF174488	2	2545	2545	2545		3214	3534	2545		2545	2545		8171	2545	49407	
protein phosphatase 5	AF018263	3	2545	2545	2545	**2545**	2545	2545	2545	**2545**	2545	2545	**2545**	2545	2545	2545	**2545**
protein phosphatase 5	AF018263	3	2545	2545	2545		2545	2545	2545		2545	2545		2545	5132	2545	
guanylyl cyclase 1	AB025111	3	2545	2545	2545	**2545**	2545	2545	2545	**2545**	2545	2545	**2545**	2545	3698	4283	**3342**
guanylyl cyclase 1	AB025111	3	2545	2545	2545		2545	2545	2545		2545	2545		2986	2545	8189	
guanylyl cyclase 2	AB025112	3	2545	2545	2545	**2545**	2545	2545	2545	**2545**	2545	2545	**2545**	2545	7969	2545	**2545**
guanylyl cyclase 2	AB025112	3	2545	2545	2545		2545	2545	2545		2545	2545		2545	2545	6106	
cyclin A1	X53745	1	2545	2545	2545	**2545**	3776	2545	2545	**2545**	2545	2545	**2545**	2545	2545	2545	**2545**
cyclin A1	X53745	1	2545	2545	2545		2545	2545	2545		2545	2545		2558	2545	5221	
cyclin A2	X85746	1	2545	2545	2545	**2545**	2545	2545	2545	**2545**	2545	2545	**2545**	2545		2545	**2545**
cyclin A2	X85746	1	2545	2545	2545		2545	2545	2545		2545	2545		2545		2545	
cyclin B1	J03166	1	2545	2545	2545	**2545**	2545	2545		**2545**	2545	2545	**2545**	2545	2545	2545	**2545**
cyclin B1	J03166	1	2545	2545	2545		2545	2545			2545	2545		2545	6893	2545	
cyclin B2	J03167	1	2545	2545	2545	**2545**	2545	3806		**2545**	2545	2545	**2545**	2806	2545		**2806**
cyclin B2	J03167	1	2545	2545	2545		2545	2545	2545		2545	2545		15508	2545	5090	
cyclin D1	X89475	1	2545	2545	2545	**2545**	2545	2545	2545	**2545**	2545	2545	**2545**	2545	2545	12134	**9289**
cyclin D1	X89475	1	2545	2545	2545		2545	2545	2545		2545	2545		16424	43384	6444	
cyclin D2	X89476	1	3139	12806	6949	**7165**	2545	2545	2545	**2545**	2545	2545	**2545**	2545	2545	6763	**2545**
cyclin D2	X89476	1	3045	12373	7382		2545	2545	2545		2545	2545		2545	2545	11274	
cyclin E	L23857	1	2545	2545		**2545**	2545	2545	2545	**2545**	2545	2545	**2545**	2545	2545	2977	**2545**
cyclin E	L23857	1	2545	2545			2545	2545	2545		2545	2545		2545	33056	2545	
cyclin H	U20505	1	2545	2545	2545	**2545**	2545	2545	2545	**2545**	2545	2545	**2545**	2545	4120	2545	**2702**
cyclin H	U20505	1	2545	2545	2545		2545	2545	2545		2545	2545		2859	5802	2545	
cyclin B2	AB005253	1	2545	2545	2545	**2545**	2545	2545	2545	**2545**	2545	2545	**2545**	2545	2545	2545	**2545**
cyclin B2	AB005253	1	2545	2545	2545		2545	2545	2545		2545	2545		2545	2980	8827	
cdc2	AB005254	1	2545	2545	2545	**2545**	2545	2545	2545	**2545**	2545	2545	**2545**	2545	2545	2545	**2545**
cdc2	AB005254	1	2545	11987	2545		4315	3930	2545		2545	2545		2545	2545	2545	
Egl Ser Thr kinase (cdc2 homolog)	X14227	1	2545	2545	2545	**2545**	2545	2545	2545	**2545**	2545	2545	**2545**	2545	3427	8306	**3427**
Egl Ser Thr kinase (cdc2 homolog)	X14227	1	2545	2545	2545		2545	2545	2545		2545	2545		2545		8475	
cdc2-related MO15	X53962	1	2545	2545	2545	**2545**	2545	2545	2545	**2545**	2545	2545	**2545**	2545	2545	2545	**2545**
cdc2-related MO15	X53962	1	2545	2545	2545		2545	2545	2545		2545	2545		2545	2545	5767	
cdc2 kinase homologous protein	M60680	1	2545	2545	2545	**2545**	2545	2545	2545	**2545**	2545	2545	**2545**	2545	2545	2545	**2545**
cdc2 kinase homologous protein	M60680	1	2545	2545	2545		2545	2545	2545		2545	2545		2806	2545	2545	
MYT1	U28931	1	2545	2545	2545	**2545**	2545	2545	2545	**2545**	2545	2545	**2545**	2545		2545	**2545**
MYT1	U28931	1	2545	2545	2545		2545	2545	2545		2545	2545		2545	2545	2545	
cdc7-related kinase	AF080068	1	2545	2545	2545	**2545**	2545	2545	2545	**2545**	2545	2545	**2545**	2545		2545	**2545**
cdc7-related kinase	AF080068	1	2545	2545	2545		2545	2545	2545		2545	2545		3286	2545	2545	
cdc21	U44049	1	2545	2545	2545	**2545**	2545	2545	2545	**2545**	2545	2545	**2545**	2545	2545	3346	**2545**
cdc21	U44049	1	2545	2545	2545			2545	2545		2545	2545		2545	2545	4726	
tyrosine phosphatase cdc25A	AF090829	1	2545	2545	2545	**2545**		2545	2545	**2545**	2545	2545	**2545**	2545	4534	2545	**3043**
tyrosine phosphatase cdc25A	AF090829	1	2545	2545	2545		2545	2545	2545		2545	2545		2545	18951	3541	
tyrosine phosphatase cdcC1	M96857	1	2545	2545	2545	**2545**	2545	2545	2545	**2545**	2545	2545	**2545**	2545	3395	2545	**2545**
tyrosine phosphatase cdcC1	M96857	1	2545	2545	2545		2545	2545	2545		2545	2545		5747	2545	2545	
MCM5 CDC46	U44048	1	2545	2545	2545	**2545**	3677		2545	**2545**	4544	10032	**3545**	29749	2545	32716	**29265**
MCM5 CDC46	U44048	1	2545	2545	2545		2545	2545	2545		2545	2545		28781	2545	56964	
cdk 4	X89477	1	2545	2545	2545	**2545**	2545	2545	2545	**2545**	2545	2545	**2545**	2545	2545	2545	**2545**
cdk 4	X89477	1	2545	2545	2545		2545	2545	2545		2545			2545	2545	4049	
activator of cdk5	AF000951	1	2545	2545	2545	**2545**	2545	2545	2545	**2545**	2545	2545	**2545**			2545	**2545**
activator of cdk5	AF000951	1	2545	2986	2545		2545	2545	2545		2545	2545		2545		2545	
cdk inhibitor p28	U38844	1	2545	2545	5759	**2545**	7007	2545	2545	**3976**	2545	2545	**2545**	53570	2986	155646	**57415**
cdk inhibitor p28	U38844	1	2545	2545	6857		7160	2545	5408		2545	2545		61260	6973	117417	
cdk inhibitor	U24434	1	2545	2545	3951	**2545**	4063	2907	4453	**3774**	2545		**2545**	4817	2545	6744	**5780**
cdk inhibitor	U24434	1	2545	2545	4410		3599	3949	2545		2545			3549	7867	43548	
p33 ringo (ls26)	AJ133499	1	2545	2545	2545	**2545**	2545	6607	2545	**2545**	2545		**2545**	21503	2646	46881	**20539**
p33 ringo (ls26)	AJ133499	1	2545	2545	2545		3837		2545		2545	2545		19575	3379	49576	
calcium calmodulin-dependent protein kinase	AF233633	3	2545	2545	2545	**2545**	2545	2545	2545	**2545**	2545	2545	**2545**	2545	2545	2545	**2823**
calcium calmodulin-dependent protein kinase	AF233633	3	2545	2545	2545		2545	2545	2545		2545	2783		7278	3100	5637	
protein phosphatase-2A B'epsilon	AF298157	3	2545	2545	2545	**2545**	2545	2545	2545	**2545**	2545	2545	**2545**	2545	2545	2545	**2545**
protein phosphatase-2A B'epsilon	AF298157	3	2545	2545	2545		2545	2545	2545		2545	2545		2545	2545	2545	
serotonin receptor	U10161	5	2545	2545	2545	**2545**	2545	2545	2545	**2545**	2545	2545	**2545**	2545	2545	7707	**2986**
serotonin receptor	U10161	5	2545	2545	2545		2545	2545	2545		2545			2545	3427	6366	
muscle nicotinic acetylcholine receptor beta subun	U04618	3	2545	2545	2545	**2545**	2545	2545	2545	**2545**	2545	2545	**2545**	2545	2545	10064	**4286**
muscle nicotinic acetylcholine receptor beta subun	U04618	3	2545	2545	2545		2545	5808	2545		2545	2545		2545	11141	6028	
prolactin receptor A	AF193800	5	2545	2545	2545	**2545**	2545	2545	2545	**2545**	2545	2545	**2545**	2545	2545	3619	**2545**
prolactin receptor A	AF193800	5	2545	2545	2545		2545	2545	2545		2545	2545		2545	2545	5689	
neurotrophic factor BDNF receptor	S69713	3	2545	2545	2545	**2545**		2545	4901	**2545**	2545	2545	**2545**	3939	34220	11235	**7811**
neurotrophic factor BDNF receptor	S69713	3	2545	2545	2545		2545	2545	2545		2545	2545		16821	2545	4387	
lysophosphatidic acid receptor	AJ249844	3	2545	2545	2545	**2545**	2545	2545	2545	**2545**	2545	2545	**2545**	2545	2545	3470	**3007**
lysophosphatidic acid receptor	AJ249844	3	2545	2545	2545		2545	2545	2545		2545	2545		2545	14408	5624	
pituitary adenylate cyclase-activating receptor type	AF157878	3	2545	2545	4383	**2545**	2545	2545	2545	**2545**	2545	2545	**2545**	2545	2545	8579	**2545**
pituitary adenylate cyclase-activating receptor type	AF157878	3	2545	7948	2545		2545	2545	2545		2545	2788		2545	2545	4700	
luteinizing hormone receptor	AJ249845	5	2545	2545	2545	**2545**	2545	2545	2545	**2545**	2545	2545	**2545**	2545	2545	2545	**2545**
luteinizing hormone receptor	AJ249845	5	2545	2622	2545		2545	2545	2545		2545	2545		2545	4088	2545	
inositol 1,4,5-triphosphate receptor (IP-3)	D14400	3	2545	2545	2545	**2545**	2545	2545	2545	**2545**	2545	2545	**2545**	2545	2545	2545	**2545**
inositol 1,4,5-triphosphate receptor (IP-3)	D14400	3	2545	2545	2545		2545	2545	2545		2545	2545		2545	2545	5950	
BMP receptor	D32066	3	2545	2545	2545	**2545**	2545	2545	2545	**2545**	2545	2545	**2545**	2545	2545	2545	**2545**
BMP receptor	D32066	3	2545	2545	2545		2545	2545	2545		2545	2545		2545	2545	2545	
frizzled 2	AF139165	3	2545	8737	2545	**2545**	2545	2545	2545	**2545**	2545	2545	**2545**	2545	2545	2545	**2545**
frizzled 2	AF139165	3	2545	2545	2545		2545	2545	2545		2545	2545		2545	3459	2545	
cadherin precursor	AF002983	9	2545	2545	2545	**2545**	2545	2545	2545	**2545**	3995	8821	**3270**	2545	31598	2545	**5077**
cadherin precursor	AF002983	9	2545	2545	2545		2545	2545	2545		2545	2545		15838		5077	
NPY PYY Receptor Y1	L25416	3	2545	2545	2545	**2545**	2545	2545	2545	**2545**	2545	2545	**2545**	2545		2545	**2545**
NPY PYY Receptor Y1	L25416	3	2545	2545	2545		2545	2545	2545		2545	2545		3054	2545	2545	
muscle acetylcholine receptor a	X07067	3	2545	2545	2545	**2545**	2545	2545	2545	**2545**	2545	2545	**2545**		2545	2545	**2545**
muscle acetylcholine receptor a	X07067	3	2545	2545	2545		2545	2545			2545	2545				9842	
acetylcholine receptor alpha subunit 1A	X17244	3	2545	2545	2545	**2545**	2545	2545	2545	**2545**	2545	2545	**2545**	2545	2545	5051	**2545**
acetylcholine receptor alpha subunit 1A	X17244	3	2545	2545	2545		2545	2545	2545		2545	2545		2545	2545	2545	
activin receptor	S70930	1	2545	2545	2545	**2545**	2545	2545	5223	**2545**	2545	2545	**2545**	2545	2545	2545	**2545**
activin receptor	S70930	1	2545	2545	2545			2545	2545		2545	2545		2545	2545	5155	
Ftz-F1-related orphan receptor A	U05001	4	2545	2545	2545	**2545**	2545	2545	2545	**2545**	2545	2545	**2545**	7758	12727	2545	**2545**
Ftz-F1-related orphan receptor A	U05001	4	2545	2545	2545		2545	2545	2545		2545	2545		2545	2545	2545	
fibroblast growth factor receptor 1	M55163	1	2545	2545	2545	**2545**	2545	2545	2545	**2545**	2545	2545	**2545**	2545	2545	9308	**2545**
fibroblast growth factor receptor 1	M55163	1	2545	2545	2545		2545	2545	2545		2545	2545		2545		5494	
Pagliaccio receptor tyrosine kinase	L26099	3	2545	2545	3926	**2545**	2545	4064	2545	**2545**	2545	2545	**2545**	27993	2545	60538	**29358**
Pagliaccio receptor tyrosine kinase	L26099	3	2545	2545	2545		2545	2545	2545		2545	2545		30724	5116	66149	
angiotensin II receptor	S73388	3	2545	2545	2545	**2545**	2545	2545	2545	**2545**	2545	2545	**2545**	2545	2545	2545	**2545**
angiotensin II receptor	S73388	3	2545	2545	2545		2545	2545	2545		2545	2545		2545	2545	2545	
angiotensin receptor related protein	U72029	3	2545	2545	2545	**2545**	2545	2545	2545	**2545**	2545	2545	**2545**			10324	**2545**
angiotensin receptor related protein	U72029	3	2545	7404	2545		2545	2545	2545		2545	2545		2545		2545	
activated protein kinase C	AF105259	3	20049	31998	27800	**28332**	25602	23884	21719	**23500**	15306	33793	**25847**	35601	8965	14568	**18977**
activated protein kinase C	AF105259	3	20038	29280	25864		27703	21616	23116		17301	38197		23386	4622	36596	
5-HT1A receptor	Y07901	3	2545	2545	2545	**2545**	2545	2545	2545	**2545**	2545	2545	**2545**	2545	5164		**5702**
5-HT1A receptor	Y07901	3	2545	2545	2545		2545	2545	2545		2545	2545		3702	7491	11730	
14-3-3 protein	M86928	3	2545	2545	2545	**2545**	2545	2545	2545	**2545**	2545	2545	**2545**	2545	5929	2545	**2545**
14-3-3 protein	M86928	3	2545	2545	2545		2545	2545	2545		2545	2545		2545	8328	2545	
ALK-2 receptor	AF012245	3	2545	2545	2545	**2545**	4077	2545		**2545**	2545	2545	**2545**	2545	104758	2545	**2545**
ALK-2 receptor	AF012245	3	2545	2545	2545		2545	2545			2545	2793		2545	61522	2545	
adenosine A1 receptor (a1R gene)	AJ249842	3	2545	2545	2545	**2545**	2545	2545	2545	**2545**	2545	2545	**2545**	2545		2545	**2545**
adenosine A1 receptor (a1R gene)	AJ249842	3	2545	2545	2545		2545	2545	2545		2545	2545		2545		5038	
CRF receptor type1	Y14036	5	2545	2545	2545	**2545**	2545	2545		**2545**	2545	2545	**2545**	2545	2545	40821	**4191**
CRF receptor type1	Y14036	5	2545	2545	2545		2545	2545				9299		5807	2545	49120	
VIP pituitary cAMP receptor	AF100644	3	2545	2545	2545	**2545**	2545	2545	2545	**2545**	2545	2545	**2545**	3796	2545	13227	**4667**
VIP pituitary cAMP receptor	AF100644	3	2545	2545	2545		2545	2545	2545		2545	2545		5537	2545	12355	
dihydropyrimidine receptor	AF037625	3	2545	2545	2545	**2545**	5691	2545	2545	**4268**	2545	2545	**3591**	6512	2545	7564	**7229**
dihydropyrimidine receptor	AF037625	3	2545	2545	2545		6410	3865	4672		4637	10239		18839	6893	13748	
follicle stimulating hormone receptor	AJ249846	5	2545	2545	2545	**2545**	2545	2545	2545	**2545**	2545	2545	**2545**	2545	2545	5247	**2743**
follicle stimulating hormone receptor	AJ249846	5	2545	2545	2545		2545	2545	2545		2545	2545		2941	2545	9881	
CRF receptor type 2	Y14037	5	2545	2545	2545	**2545**	2545	2545	2545	**2545**	2545	2545	**2545**		2545	13800	**8173**
CRF receptor type 2	Y14037	5	2545	2545	2545		2545	2545	2545		2545	2545			2545	43418	
insulin receptor substrate protein xIRS-u	AF297960	5	2545	2545	2545	**2545**	2545	2545	2545	**2545**	2545	2545	**2545**	2545	2545	3736	**2545**
insulin receptor substrate protein xIRS-u	AF297960	5	2545	2545	2545		2545	2545	2545		2545	2545		2545	2545	4635	
natriuretic peptide receptor type C	AF231035	5	2545	2545	2545	**2545**	2545	2545	2545	**2545**	2545	2545	**2545**	2545		2545	**2545**
natriuretic peptide receptor type C	AF231035	5	2545	2545	2545		2545	2545	2545		2545	2545		2545		6666	
XICE-a	D89783	8	2545	2545	2545	**2545**	2545	2545	2545	**2545**	2545	2545	**2545**	2545		8631	**3160**
XICE-a	D89783	8	2545	2545	2545		2545	2545	2545		2545	2545		3774		2545	
CPP32	D89784	8	2545	2545	2545	**2545**	2545	2545	2545	**2545**	2545	2545	**2545**	2545	2545	2545	**2545**
CPP32	D89784	8	2545	2545	2545		2545	2545	2545		2545	2545		2545	2545	2545	
calpastatin I	AJ243713	8	2545	2545	2545	**2545**	2545	2545	2545	**2545**	2545	2545	**2545**		2546	12472	**7509**
calpastatin I	AJ243713	8	2545	2545	2545		2545	2545	2545		2545	2545			2545	36943	
caspase7-precursor	AW199521	8	2545	2545	2545	**2545**	2545	2545	2545	**2545**	2545		**2545**		12528	9022	**10477**
caspase7-precursor	AW199521	8	2545	2545	5107		2545	2545	2545		2545				9850	11105	
bcl-2-like R11	X82461	8	2545	2545	2545	**2545**	2545	2545	2545	**2545**	4464		**3505**	67135	5116	63649	**57739**
bcl-2-like R11	X82461	8	2545	9524	2545		4497	2545	2545		2545				2545	57739	
scythe	AF098511	8	2545	2545	2545	**2545**	2545	2545	2545	**2545**	2545	2602	**2545**	6227	5156	17758	**5492**
scythe	AF098511	8	2545	2545	2545		2545	2545	2545		2545	2545		2545	5156	39252	
survivin	AW198821	8	2545	2545	2545	**2545**	2545	2545	2545	**2545**	2545	2545	**2545**	2545	2545	2545	**2545**
survivin	AW198821	8	2545	2545	2545			2545	2545		2545	3351		2545	2545	4791	
requiem	AB021737	8	2545	2545	2545	**2545**	2545	2545	2545	**2545**	2545	2969	**2669**	19417	2545	54887	**28336**
requiem	AB021737	8	2545	2773	2545			2545	2545		2545	2793		21255	2545	50604	
p21-activated kinase (PAK1)	AF000239	3	2545	2545	2545	**2545**	2545	4448		**2545**	2545	2545	**2545**	10328	3929	64027	**17104**
p21-activated kinase (PAK1)	AF000239	3	2545	2545	2545		2545	2545			2545	2545		23981	2893	63792	
DAD-1	D15059	8	2831	2545	3860	**2869**		3982	5431	**4716**	4317	9531	**7429**	2545	2545	2545	**2545**
DAD-1	D15059	8	2907	2545	6844			6448	2545		5327	11762		2545	2545	2545	
caspase-2	AB038168	8	2545	2545	2545	**2545**		2545		**2545**	2545	2545	**2545**	2545		2545	**2545**
caspase-2	AB038168	8	2545	2545	2545			2545			2545	2545		3909	15325	2545	
caspase-6	AB038169	8	2545	2545	4122	**2545**		2545	2545	**2545**	5514	12175	**7887**		2545	2545	**4495**
caspase-6	AB038169	8	2545	2545	4924			2545	2545		4637	10239			7619	6444	

caspase-7	AB038170	8	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	4092	20423		65042	11127	
caspase-7	AB038170	8	2545	2545	2545		2545	2545	2545		5638	12448		11127	2545	7981		
caspase-8	AB038171	8	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	
caspase-8	AB038171	8	2545	2545	2545		2545	2545	2545		2545	2545		2545	2545	2545		
caspase-9	AB038172	8	2545	2545	2545	2545	2545	2545		2545	2545	2545	2545	31182	2545	59249	29055	
caspase-9	AB038172	8	2545	2545	2545		2545	2545			2545	2545		26927	2545	62113		
caspase-10	AB038173	8	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2869	2877	2873	
caspase-10	AB038173	8	2545	2545	2545		2545	2545	2545		2545	2545		2545	5228	3372		
metalloproteinase-disintegrin (MDC11a)	AF032384	8	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	3991	2545	4934	3775	
metalloproteinase-disintegrin (MDC11a)	AF032384	8	2545	2545	2545		2545	2545	2545		2545	2545		3991		3775		
metalloproteinase (XMMP)	U82541	8	2545	2545	2545	2545		2545	4341	2545	2545	2545	2545	17884	2545	9452	5153	
metalloproteinase (XMMP)	U82541	8	2545	2545	2545		2545	2545	2545			2545		2821	2545	7486		
membrane anchored metalloprotease	U78188	8	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545		2545	2545	
membrane anchored metalloprotease	U78188	8	2545	2545	2545		2545	2545	2545		2545	2545		2545		2545		
metalloprotease-disintegrin (MDC11b)	AB032383	8	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545		2545	7968	2545	
metalloprotease-disintegrin (MDC11b)	AB032383	8	2545	2545	2545		2545	2545	2545		2545	2545		2545	2545	27235		
pancreatic trypsin	X53458	6	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	6970		40697	7135	
pancreatic trypsin	X53458	6	2545	2545	2545		2545	2545	2545		2545	2545		7135	4072	45078		
trypsinogen	U72330	6	2545	2545	2545	2545	2545	2061	2545	2545	2545	3341	2545	23611	5730	53599	24349	
trypsinogen	U72330	6	2545	8712	2545		2545	2545	5049		2545	2545		31849	2545	25087		
serine protease (Cap1)	AF026494	6	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545		2861	2545	2861	
serine protease (Cap1)	AF026494	6	2545	2545	2545		2545	2545	2545		2545	2545		2545	20736	61696		
stromelysin-3	Z27093	8	2545	2545		2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	
stromelysin-3	x 27093	8	2545	2545			2545	2545	2545		2545	2545		2545	2545	4609		
alpha-aspartyl dipeptidase	U83777	8	2545	2545	2545	2545	2545	2545	2545	2545	2545	3361	3747	2545	2893	2545	2719	
alpha-aspartyl dipeptidase	U83777	8	2545	2545	3926		2545	2545	2545		4132	9123		2545	5865	3997		
serpin	AB015694	3	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	3376		39141	5027	
serpin	AB015694	3	2545	2545	2545		2545	2545	2545		2545	2545		5027	2545	10246		
alpha-1 antiproteinase	AB014091	8	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	6588	2545	
alpha-1 antiproteinase	AB014091	8	2545	2545	2545		2545	2545	2545		2545	2545		2545	2545	2545		
carbamyl phosphate synthetase	U05193	6	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	
carbamyl phosphate synthetase	U05193	6	2545	2545	2545		2545	2545	2545		2545	2545		2545	2545	2545		
ornithine transcarbamylase	D38304	6	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	
ornithine transcarbamylase	D38304	6	2545	2545	2545		2545	2545	2545		2545	2545		2545	3120	2545		
ornithine decarboxylase	X56316	6	2545	2545	2545	2545	2545	3086	2545	2545	2545	2545	2545	4719	8662	54600	13383	
ornithine decarboxylase	X56316	6	2545	2574	2545		2545	2545	2545		2545	2545		18104	2545	54938		
lactate dehydrogenase B	U97176	6	19710	5560	28206	19692	31797	14248	17747	17686	13398	29559	21524	49728	12926	2545	26862	
lactate dehydrogenase B	U97176	6	17561	19874	23369		34856	13566	17628		13489	29781		46733	35901	17823		
GAPDH	U41753	6	398	292	489	464	924	569	685	663	716	692	666	893	1052	1146	811	
GAPDH	U41753	6	450	557	587		919	625	711		809	718		773	1148	937		
GAPDH	U41753	6	494	468	573		913	573	715		779	604		683	1052	443		
GAPDH	U41753	6	550	509	528		887	619	663		655	658		735	1148	820		
GAPDH	U41753	6	394	406	439		664	497	460		538	596		660	606	391		
GAPDH	U41753	6	444	372	561		783	549	616		674	594		653	932	527		
gelatinase B (MMP-9)	AF072455	8	2545	2545	2545	2545	2545	2545		2545	8279	18278	13069	2545	2545	2545	2545	
gelatinase B (MMP-9)	AF072455	8	2545	2545	2545		2545	2545			8089	17859		3286	2545	2545		
NM23 nucleoside diphosphate kinase	X95369	2	1537	1290	1572	1559	1290	1264	1420	1491	1300	1941	1673	2446	1315	2435	2356	
NM23 nucleoside diphosphate kinase	X95369	2	1804	1545	1889		1562	1594	1658		1405	2465		2277	1387	2825		
Nit1	D86491	6	2545	2545	2545	2545			2545	2545	2545		2545		2545	2545	2545	
Nit1	D86491	6	2545	2545	2545		2545	2545	2545		2545	2545		2545		2545		
Na+ K+ transporting ATPase beta subunit	M37788	7	2545	2545	2545	2545	2545	2545	2545	2545	3286	7234	3915	2545	2545	2545	2545	
Na+ K+ transporting ATPase beta subunit	M37788	7	2545	2545	2545		2545	2545	2545		2545	2545		2545	2545	3815		
SERCA1 fast skeletal muscle	X63099	3	2545	2545	2545	2545	5825	2545	5472	5648	6099	13466	10214		8041	26998	8681	
SERCA1 fast skeletal muscle	X63099	3	2545	2545	2545		6098	2545	6995		6962	15371			4590	9321		
E2 ubiquitin conjugating enzyme (Ubc9)	U88561	8	2545	2545	5209	2545	2545	2545	2545	2545	2545	2545	3253	4202	2545	2545	2545	
E2 ubiquitin conjugating enzyme (Ubc9)	U88561	8	2545	2545	5670		3532	2545	2545		3962	8746		2545	2545	2545		
metallothionein	M96729	7	2545	2545	2545	2545	2545	2545	2545	2545	4046	8932	3295	5282		2545	4357	
metallothionein	M96729	7	2545	2545	2545		2545	2545	2543		2545	2545		4367		4348		
iodothyronine deiodinase type II	L42815	5	3081	2545	4559	2566	2545		2545	2545	7804	17230	14078		2545	9543	8744	
iodothyronine deiodinase type II	L42815	5	2586	2545	2545		2545		4999		10927	24125			2545	10492		
iodothyronine 5'-deiodinase III	L29111	5	4277	2545	8877	4254	6152	4442	5542	5687	4876	10765	7988	19312	6861	70454	28351	
iodothyronine 5'-deiodinase III	L29111	5	4230	2545	10278		10000	4684	5833		5210	11504		37390	2545	75015		
retinoic acid converting enzyme	AF057566	5	2545	2545	2545	2545	2545	2545	2545	2545	3949	8715	6502	5747	3443	9918	6010	
retinoic acid converting enzyme	AF057566	5	2545	2545	2545		2545	2545	2545		4289	9469		6272	2545	13071		
FCP1 serine phosphatase	AJ132585	4	2545	2545	2545	2545	2545	3376	2545	2545	2545	2545	2545		3395	35001	6205	
FCP1 serine phosphatase	AJ132585	4	2545	2545	2545		2545	2545	2545		2545	2545			3666	6744		
protein phosphatase 1-gamma 1	L17039	1	2545	2545	2545	2545	2545	2545		2545	2545	2545	2545	2545	4534	2545	2545	
protein phosphatase 1-gamma 1	L17039	1	2545	2545	2545		2545	2545			2545	2545		2545	2545	5221		
convertase PC2	X66493	5	2545	2545	4468	2545	2545	2545		2545	2545	2545	3507	18809	2545	5904	5631	
convertase PC2	X66493	5	2545	2545	4383		2545	2545			4469	9867		5357	2545	9738		
aconitase	AF186471	6	2545	2545	2545	2545	2545	2545		2545	2545	2545	2545	2626	2545	14047	9068	
aconitase	AF186471	6	2545	2545	2545		3043	2545			2545	2545		14165	4088	39421		
phospholipase C-gamma-1a	AF090111	3	2545	2545	2545	2545	2545	2545	2545	2545	3870	8545	3241	22388	2901	27444	12645	
phospholipase C-gamma-1a	AF090111	3	2545	2545	2545		2545	2545	2545		2545	2613		2750	2545	39447		
Cu Zn SOD	X16585	6	4248	2545	7278	4688	6737	3882		6430		2545	6802	4847	6830	2545	4495	
Cu Zn SOD	X16585	6	5128	2545	8427		6981	6122				11060		18329	4144	2545		
collagenase-1 precursor	L76275	8	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2566	2545	2545	2545	
collagenase-1 precursor	L76275	8	2545	2545	2545		2545	2545	2545		2545	2545		2545	23445	2545		
cytochrome P-450 (11beta, aldo)	D10984	6	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	27531	2545	57745	18069	
cytochrome P-450 (11beta, aldo)	D10984	6	2545	2545	2545		2545	2545	2545		2545	2545		8606	6335	31844		
mitochondrial cytochrome c oxidase subunit I	M10217	6	3517	2545	14905	3767	11942	12687	20618	12883	10942	24159	17806	22913	32594	2545	15868	
mitochondrial cytochrome c oxidase subunit I	M10217	6	4916	2545	12229		13079	11442	19959		11454	25289		39823	37041	2545		
alcohol dehydrogenase class I (ADH1)	AF059255	6	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	
alcohol dehydrogenase class I (ADH1)	AF059255	6	2545	2545	2545		2545	2545	2545		2545	2545		2545	2545	9894		
alcohol dehydrogenase class 4 (ADH4)	AF059256	6	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	8944	2646	
alcohol dehydrogenase class 4 (ADH4)	AF059256	6	2545	2545	2545		2545	2545	2545		2545	2545		2746	2545	2825		
adenyl cyclase	Z46958	3	2545	2545	2545	2545		2545	2545	2545	2545	2545	2545	3069	3419	2545	3069	
adenyl cyclase	Z46958	3	2545	2545	2545			2545	2545		2545				20138	2545		
fibroblast activation factor alpha	U41856	1	2545	2545		2545				[illegible]			[illegible]		2545	2545	3990	
fibroblast activation factor alpha	U41856	1	2545	2545											3435	4270		
aldolase C	3928510	6	2545	2545	2545	2545	2545	2545	2545	2545	2545		2716		6256	2545	3346	
aldolase C	3928510	6	2545	2545	2545		3078	2545				2886		2545	4550	3346		
2,3'-cyclic-nucleoside 3'-ribonucleodiesterase (CNP1	AB002345	9	2545	2567	2545	2545	2545	2545		2545	2545	2545	2545	2545	2545	2545	2545	
2,3'-cyclic-nucleoside 3'-ribonucleodiesterase (CNP1	AB002345	9	2545	2545	2545		2545	2545			2545	2545		2545	2545	2545		
arginase	D38303	6	2545	2545	5385	2545	2545	4220		3215	4139	9139	6719	6889	115469	11522	15098	
arginase	D38303	6	2545	2545	5909		2545	3885			4298	9490		18674	35953	4283		
arginase 1	U08696	6	2545	2693	2545	2545	2545	3573	2545	2545	2545	2545	2545	9979		46725	36087	
arginase 1	U08696	6	2545	2545	2545		2545	2545	2545		2545	2545		25439		68063		
argininosuccinate lyase	D38302	6	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545		2545	2545	
argininosuccinate lyase	D38302	6	2545	2545	2545		3396	2545	2545		2545	2545		2545		2545		
ATPase Na+ K+ pump alpha 1 subunit	U49238	6	2545	2545	2545	2545		2545	2545	2545	2545	2545	2545	2545	2545	4387	3422	
ATPase Na+ K+ pump alpha 1 subunit	U49238	6	2545	2545	2545			2545	2545		2545	2545		4299	2545	4892		
ADP-ribosylation factor (ARF1)	U31330	6	2545	2711	4288	2545	2545	2545	2545	2545	2545	2545	2545		2545	2545	2545	
ADP-ribosylation factor (ARF1)	U31330	6	2545	2545	2545		2545	2545	2545		2545	2545			3999	2545		
allantoicase	AF153230	6	2545	2545	2545	2545	2545	2545	5560	2545	3697	8163	3121			4439	4439	
allantoicase	AF153230	6	2545	2545	2545		2545	3285	2545		2545	2545			6798	2545		
exonuclease Exo1	AF134570	2	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545		5416	2545	
exonuclease Exo1	AF134570	2	2545	2545	2545			2545	2545		2545	2545		2545	2545	3815		
deoxyribonuclease gamma	AF059612	2	2545	2545	2545	2545	7482	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	
deoxyribonuclease gamma	AF059612	2	2545	2545	2545		2545	2545	2545		2545	2545		2545	2545	2545		
DNA polymerase beta	Y15732	2	2545	2545	2545	2545	2545	2545	2545	2545	4057	8958	3361	2545	4032	2920	3757	
DNA polymerase beta	Y15732	2	2545	2545	2545		2545	2545			2545	2545		2545	6838	2545		
ligase I	L43496	2	2545	2545	2545	2545	2545	2545	2545	2545		2545	3431	2545	2545	2545	2545	
ligase I	L43496	2	2545	2545	2545		2545	2545	2545			4316		2545	3403	8527		
ATP-dependent RNA helicase	X57328	4	2545	2545	5160	2545	2545	2545	2545	2545	2545	2545	2545	4187	2545	2545	2550	
ATP-dependent RNA helicase	X57328	4	2545	2545	2545		2545	2545	2545		2545	2545		2545	2545	11769		
cytosine-5-methyltransferase	D78638	2	2545	2545	2545	2545	2545	2545	2545	2545	2545	3155	2545		2545	20166	5552	
cytosine-5-methyltransferase	D78638	2	2545	2545	4599			2545	2545		2545	2545		5552	2545	54276		
flap endonuclease 1 (FEN1)	U64563	2	2545	2545	2545	2545	2545		2545	2545	2545	2545	2545	6092	5666	45911	11791	
flap endonuclease 1 (FEN1)	U64563	2	2545	2622	2545		2545	2545	2545		2545	2545		17579	2545	49328		
terminal deoxynucleotidyl transferase	U07803	2	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2812	2679	
terminal deoxynucleotidyl transferase	U07803	2	2545	2545	2545		2545	4228	2545		2545	2545		5980	2545	4283		
gelatinase A	AY037943	8	2545	2545	6570	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	
gelatinase A	AY037943	8	2545	2545	6176		2545	2545	2545		2545	2545		2545	2545	2545		
liver helicase	AF302423	4	2545	2545	2545	2545	9957	3958	10080	9013	2545	4487	4610	2545	2545	7265	2545	
liver helicase	AF302423	4	2545	2545	2545		9856	6963	9821		4733	10490		21632	2545	2545		
aldolase B	AB030822	6	2545	2545	2545	2545	2545	2545	2545	2545	3882	8571	6521	24407	6236	21859	22789	
aldolase B	AB030822	6	2545	2545	2545		3321	2545	2545		4471	9872		23739	18951	56450		
cytochrome b	M10217	6	2545	2545	5189	2545	2545	2545	2545	2899	2545	2545	2545		2545	2545	2545	
cytochrome b	M10217	6	2545	2545	2545		3909	3074	4868		2545	2545			2545	3424		
aromatase p450	AB031278	5	2545	2545	2545	2545	2545		2545	2545	2545	2545	2545	2545	2545	2545	2545	
aromatase p450	AB031278	5	2545	2545	2545		2545		2545		2545	2545		2545	2545	2545		
NEDD 4	AB000985	8	2545	2545	3385	2545	2545	2545	2545	2545	2545	2545	2545	6145	3961	15675	9629	
NEDD 4	AB000985	8	2543	2545	2545			2545	2545		2545	2545		20258	9077	10181		
ring finger protein	U63817	1	2545	2545	2545	2545	2545	3556	2545	2545	2545	2602	2545	3414	2545	39148	4629	
ring finger protein	U63817	1	2545	2545	2545			2545	2545		2545	2545		5845	2545	41556		
REST	AF096301	4	2545	2545	2545	2545	2545	2545		2545	2545	2545	2545	2545	2545	2545	2545	
REST	AF096301	4	2545	2545	2545		2545	2545			2545	2545		2545	2545	7512		
MCM2	U44047	1	2545	3503	4298	3024	3321	2545	2545	2545	2545	2545	2545	3556	8910	9009	8959	
MCM2	U44047	1	2545	2545	4846		2545	3526	2545		2545	2545		15932	3578	9621		
proteasome subunit Y	D87680	8	166	145	223	161	142	177	187	169	143	330	245	645	494	1289	623	
proteasome subunit Y	D87680	8	156	76	205		148	162	179		175	313		600	414	1315		
transmembrane protein containing an EGF domain	X80962	10	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545		2545	
transmembrane protein containing an EGF domain	X80962	10	2545	2545	5479		2545	2545	2545		2545	2545		2545	2545	6978		
OTX2b	AJ251846	4	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	12702	2545	66826	21218	
OTX2b	AJ251846	4	2545	2545	2545		2545	2545	2545		2545	2545		20734	2545	64482		
138 condensin XCAP-D2	AF067969	2	2545	2545		2545	2545	2545	2545	2545	2545	2545	2545	2558	2545	9126	2552	
138 condensin XCAP-D2	AF067969	2	2545	2545	2545		2545	2545	2545		2545	2545		2545	2545	10845		
chaperonin subunit CCT gamma	U37062	7	2545	2545	2545	2545	3051	2545	2545	2545	2545	2545	2545	3286	2545	7265	3352	

chaperonin subunit CCT gamma	U37062	7	2545	2545	2545		2545	2545	2545		2545	2545		2545	3419	4928	
HMG-X	D30765	2	2545	2545	2545	2545	2545	2545	2545	2545	2545	5029	2948	2545	2545	3164	2854
HMG-X	D30765	2	2545	2545	3857		2545	2545	2545		2545	3351		6197	2545	5234	
GSK-3 binding protein	AF062738	3	2545	2545	7296	2603	4476	3511	2545	3828		2989	7502	2515?	4048	72085	29261
GSK-3 binding protein	AF062738	3	2661	2545	7846		4613	4140	2545			12015		33363	10290	67952	
cartilage homoprotein 1	U15276	4	2545	2545	6231	2545	2545	3232	2545	2545			#NUM!	9634	6248	10490	7941
cartilage homoprotein 1	U15276	4	2845	2545	8303			3649	2545					5357	2545	46126	
beta-amyloid precursor protein	S52417	9	2545	2545	2545	2545	2545	2545		2545		11411	8323	9333	2545	46998	9333
beta-amyloid precursor protein	S52417	9	2545	2545	2545		2845	2545				5235		3988		57986	
frizzled 7	AF159106	3	2753	2545	8946	2799	6227	4351	5219	4853	5075	11204	7868	49278		94777	64802
frizzled 7	AF159106	3	2845	2545	9537		4489	3688	5378		4829	10662		46360		80326	
calcineurin A	AF019569	3				#NUM!				#NUM!			#NUM!		2545		2545
calcineurin A	AF019569	3													2545		
BMP1	U12249	8	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545			3007	2839
BMP1	U12249	8	2545	2545	2545		2545	2545	2545		2545	2545		2671	2545	5832	
BMP1b	Y09660	8	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	5221	2545
BMP1b	Y09660	8	2545	2545	2545		2545	2545	2545		2545	2545		2545	2545	2545	
BMP4	AF058764	3	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	5090	2545
BMP4	AF058764	3	2545	2545	2545		2545	2545	2545		2545	2545		3294	2545	2545	
18S ribosomal	X04025	11	233	1658	293	256	206	189	222	218	239	395	317	649	693	1002	673
18S ribosomal	X04025	11	249	1896	194		214	228	255		236	439		630	653	1120	
18S ribosomal	X04025	11	2545	38274	4285	2545	2545		2545	2545		2545	2545		2545	7994	7363
18S ribosomal	X04025	11	2545	44308	2545		2545		2545			16991			2545	2545	
18S ribosomal	X04025	11	2545		2545		2545		2545		2545	2545		14856		6431	
18S ribosomal	X04025	11	2545		2545		2545		2545		2545	2545		11794	7363	22444	
MCM3	U29057	1	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	3619	2545
MCM3	U29057	1	2545	2545	2545		2545	2545	2545		2545	2545		2545	2829	2545	
MAM domain protein	U37376	10	9346	14430	13456	12658	14132	14512	9446	13262	13218	29182	21910	8943		30581	6051
MAM domain protein	U37376	10	10632	16157	11981		19250	11707	12991		14457	32316			6830	5273	
XPACx1	D31894	2	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	3020	2739
XPACx1	D31894	2	2545	2545	2545		2545	2545	2545		2545	2545		2934	2545	6106	
nuclear factor 7	S64515	4	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	4352		5318	4352
nuclear factor 7	S64515	4	2545	2545	2545		2545	2545	2545		2545	2545		4847	2829	2545	
Vitellogenin	65210	6	2747	2670	4666	2825	4263	4721	5774	4941	2619	5782	5428	39360	8041	65537	65537
Vitellogenin	65210	6	2545	2904	7211		5161	2545	5975		5072	11199		70519		73960	
hsp30B	X02512	7	2545	2545	2545	2545	2545	2545	2545	2545	5234	11555	3889	2545	2545	38464	2961
hsp30B	X02512	7	2545	2545	2545		2545	2545	2545		2545	2545		3376	2545	3618	
hsp 30	U44894	7	36	41	111	52	105	117	35	107	264	1941	1106	495	72	781	371
hsp 30	U44894	7	31	62	119		105	107	21		271	2468		248	24	859	
integrin alpha-1	U44025	9	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545
integrin alpha-1	U44025	9	2545	2545	2545		2545	2545	2545		2545	2545		2545	5802	2545	
gene 5	U37373	10	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545
gene 5	U37373	10	2545	2545	2545		2545	2545	2545		2545	2545		2545		5793	
fos-related antigen-2	U37374	4	2545	2545	2545	2545	2545	2545		2545	2545	2545	2545	2545		5142	2952
fos-related antigen-2	U37374	4	2545	2545	2545		2545	2545			2545	2545		2545		3359	
gene 12	U41854	10	3015	2545		2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	11309	2859
gene 12	U41854	10	2545	2545	2545		2545	2545	2545		2545	2545		2859		6783	
gene 16	U41857	10	2545	2545	4655	2545	4564	2545	4410	3233		8240	9407	33042	2545	64639	32209
gene 16	U41857	10	2545	2545	2545		3921	2545	2545			10574		31377	6965	57786	
gene 17	U41860	10	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	4558	2545	2545
gene 17	U41860	10	2545	2545	2545		2545	2545	5774		2545	2545		2545	2545	10064	
gene 18	U41839	10	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545
gene 18	U41839	10	2545	2545	2545		2545	2545	2545		2545	2545		2545	2545	5539	
gene 19	U41861	10	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	3658	2545
gene 19	U41861	10	2545	2545	2545		2545	2545	2545		2545	2545		2545	2545	2545	
gene 20	U46575	10	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	18967	10951	11925	10057
gene 20	U46575	10	2545	2545	2545		2545	2961	2545		2545	2545		4881	2545	8189	
regulator for chromosome condensation (RCC1)	D00679	2	2587	2545		2545	2545	2545	4884	3856	2545	2545	2545	53435	10878	96222	53551
regulator for chromosome condensation (RCC1)	D00679	2	2545	2545	4281		3909	3893	5959		2545	2545		53667	9977	92356	
proteasome subunit XC3	S51111	8	3209	2545	13218	3337	4415		5116	4781	5334	11777	8605	2596		5624	5560
proteasome subunit XC3	S51111	8	3475	2615	12968		4402		5984		5434	11907		5569	22537	2545	
B-50 GAP-43	X87582	1	2545	2545	2545	2545	3938	3232	5160	3581	4408	9733	3477	55423	6224	50318	40131
B-50 GAP-43	X87582	1	2545	2545	2545		3929	3230	2545		2545	2545		29944	2829	66787	
fragile mental retardation protein 1	U23164	4	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	20736	2545	2545
fragile mental retardation protein 1	U23164	4	2545	2545	2545		2545	2545	2545		2545	2545		2545	2545	2545	
forkhead protein lewd	AF186454	4	2545	2545	2545	2545	2545	2545		2545	2545	2545	2545	3991	5100	6132	6132
forkhead protein lewd	AF186454	4	2545	2545	2545		2545	2545			2545	2545		6617	22748		
ER1	AF015454	4	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	5092	12788	2724
ER1	AF015454	4	2545	2545	2545		2545	2545	2545		2545	2545		2545	2545	2903	
B-cell translocation protein 1 (btg1)	AB028243	4	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	4299	6893	9059	3673
B-cell translocation protein 1 (btg1)	AB028243	4	2545	2545	2545		2545	2545	2545		2545	2545		2545	2545	3046	
SIP 1	AF027151	4	2545	2545	4655	2545	2545	2545		2907	4577	10974	3561	22201	2545	10376	21585
SIP 1	AF027151	4	2545	2545	5442		3909	2907	4934		2545	2545		21585	51580		
beta-A1-1 crystallin	X87759	9	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545
beta-A1-1 crystallin	X87759	9	2545	2545	2545		2545	2545	2545		2545	2545		2545	2545	2545	
gamma-M1-1 crystallin	X86072	9	2545	2545	2545	2548	2545	2545	2545	2548	2545	2545	2545	4877	2545	2545	2545
gamma-M1-1 crystallin	X86072	9	2545	2545	2545		2545	2545			2545	2545		2545		2545	
SF-1 AdrBP	AB017352	4	2545	2545	2545	2545	2545	2545		2545	2545	2545	2545	18307		102888	66650
SF-1 AdrBP	AB017352	4	2545	2545	2545		5561	2545			2545	2545		18412		104696	
fibronectin intron 1	AF061058	control	2545	2545	2545	2545	2545	2545	2545	2545		2545	9245	2545	2545	3450	2545
fibronectin intron 1	AF061058	control	2545	2545	2545		2545	2545	2545			15944		2545	2545	5572	
alpha tubulin intron 1	65164	control	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545
alpha tubulin intron 1	65164	control	2545	2545	2545		2545	2545	2545		2545	2545			2545	2545	
alpha tubulin	X07046	9	2545	2545	3227	2545	2545	2545	2545	2545		2545	2765	2545	2545	21333	4843	2545
alpha tubulin	X07046	9	2545	2545	2545		2545	2545	2545			2984		2545	2545	2545	
delta tubulin	AF430839	9	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545
delta tubulin	AF430839	9	2545	2545	2545		2545	2545	2545		2545	2545		2545	2545	2545	
desmin	X16842	9	2545	2545	2545	2545	6030	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545
desmin	X16842	9	2545	2545	2545		4613	2545	2545		2545	2545		2545	2545	2545	
gamma fibrinogen precursor	J02804	9	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2545	2543	2545	2545	2545
gamma fibrinogen precursor	J02804	9	2545	2545	2545		2545	2545	2545			2545		2545		2545	
ribonucleotide reductase submit M1	AF168794	9	2545	2545	2545	2545	2545	2545	2545	2545		2545	2545			5885	2545
ribonucleotide reductase submit M1	AF168794	9	2545	2545	2545		2545	2545	2545			2545		2543		2545	

Appendix 2.6.1 Fold change for all good data in the 24 h injection set.

A) Rationale of adjustment T3-G treatment

	Fold Change T_3-G vs. T_3-D cDNA array	QPCR	Ratio of array vs. QPCR
TRa	22.06	1.24	17.82
TRb	5.46	0.56	9.74
Average of TRa and TRb			13.5

B)

* Highlighted is spots<4, then delete the value.

Gene Name	GenBank Accession #	Functional Code	D/D Median	D/G Median	T3/D Median	T3/G Median	Adjust with 13.5 T3/G	Floor adjustment T3/G	D-G vs. D-D	T3-D vs. D-D	T3-G vs D-D	T3-G vs T3-D
c-mos	M25366	4	2545	2545	2545	2545	189	2545	1.00	1.00	1.00	1.00
N-ras	M97960	3	2545	2545	2545	2545	189	2545	1.00	1.00	1.00	1.00
K-ras	AF085280	3	2545	2545	2545	39505	2926	2926	1.00	1.00	1.15	1.15
ves	X14377	3	2545	2545	2545	2545	189	2545	1.00	1.00	1.00	1.00
c-fos	AJ224511	4	2545	2545	2545	2545	189	2545	1.00	1.00	1.00	1.00
raf ser/thr kinase	X12948	3	2545	2545	2545	8902			1.00	1.00		
c-ets-1a	X52692	4	2545	2545	2545	4103	304	2545	1.00	1.00	1.00	1.00
c-ets-1b	X52691	4	2545	2545	2545	26740	1981	2545	1.00	1.00	1.00	1.00
ets-2a	M81683	4	2545	2545	2545	4418	327	2545	1.00	1.00	1.00	1.00
c-myc I	X14806	4	2545	2545	2545	14871	1102	2545	1.00	1.00	1.00	1.00
L-myc	L11363	4	2545	2545	2545	5847	433	2545	1.00	1.00	1.00	1.00
pp60c-src	M24704	3	2545	2545	2545	26614	1971	2545	1.00	1.00	1.00	1.00
mdm2	PubMed ID: 9136986	1	2545	2545	2545	2545	189	2545	1.00	1.00	1.00	1.00
ING2	AY014017	4	2545	2545	2545	6067	449	2545	1.00	1.00	1.00	1.00
colorectal cancer tumor suppressor	U10986	3	2545	2545	2545	26097	1933	2545	1.00	1.00	1.00	1.00
protein/lipid phosphatase Pten	AF144732	3	2545	2545	2545	3689	273	2545	1.00	1.00	1.00	1.00
Wt1	D82051	4	2545	2545	2545	44084	3265	3265	1.00	1.00	1.28	1.28
retinoblastoma 1	PubMed ID: 1516743	4	2545	2545	2545	2545	189	2545	1.00	1.00	1.00	1.00
C/EBP-1	U08604	4	2574	5090	2545	147760	10945	10945	1.98	0.99	4.25	4.30
C/EBP-2	U08605	4	243	295	364	2488	2488	2488	1.21	1.50	10.24	6.84
C/EBP	S44193	4	2661	2545	3589	47398	3511	3511	0.96	1.35	1.32	0.98
transcription co-repressor Sin3	AF154112	2	2545	2545	2545	2545	189	2545	1.00	1.00	1.00	1.00
circadian CLOCK	AF203107	4	2545	2545	2545	25422	1883	2545	1.00	1.00	1.00	1.00
c-Jun	5650725	4	2545	2545	2545	5179	384	2545	1.00	1.00	1.00	1.00
c-Myb	L22741	4	2545	2545	2545	6173	457	2545	1.00	1.00	1.00	1.00
nuclear factor I-B1	L43146	4	2545	2545	2545	13182	976	2545	1.00	1.00	1.00	1.00
nuclear factor I-C1	L43149	4	2545	3904	2640	120996	8963	8963	1.53	1.04	3.52	3.40
TFIIIA	K02938	4	2545	2545	2545	3449	255	2545	1.00	1.00	1.00	1.00
Oct-1	X17190	4	2545	2545	2545	17282	1280	2545	1.00	1.00	1.00	1.00
AP-2	M59455	4	2545	2545	2545	6825	506	2545	1.00	1.00	1.00	1.00
TBP-binding repressor Dr1	AB003582	4	2545	2545	2545	2545	189	2545	1.00	1.00	1.00	1.00
TFIID subunit	D50054	4	2545	2545	3360	67635	5010	5010	1.00	1.32	1.97	1.49
transcription factor A	U35728	4	2545	2545	2545	7273	539	2545	1.00	1.00	1.00	1.00
RNA pol I transcription factor UBF	X57561	4	2582	2545	2545	2545	189	2545	0.99	0.99	0.99	1.00
elongation factor-1 alpha chain	M25504	11	1168	1321	1154	811	811	811	1.13	0.99	0.69	0.70
neuroD	U28067	4	2545	2545	2545	3683	273	2545	1.00	1.00	1.00	1.00
Tcf-3 co-repressor CtBP	AF152006	4	2545	2545	2545	4672	346	2545	1.00	1.00	1.00	1.00
repressor brain factor 2	AF072889	4	596	531	515	2238	2238	2238	0.89	0.86	3.76	4.35
co-repressor MITR	Z97214	4	2545	2545	2545	2545	189	2545	1.00	1.00	1.00	1.00
negative regulator Id2	AB019520	4	2545	2545	2545	11792	873	2545	1.00	1.00	1.00	1.00
XCOE2	AF041138	4	2545	2545	2545	2545	189	2545	1.00	1.00	1.00	1.00
MRF4	S34392	4	2545	2545	2545	2545	189	2545	1.00	1.00	1.00	1.00
Pax-2	AF179300	4	2545	2545	2545	3713	275	2545	1.00	1.00	1.00	1.00
Pax-8	AF179301	4	2545	2545	2545	59235	4388	4388	1.00	1.00	1.72	1.72
LFB1/HNF1	64688	4	2545	2545	2545	47151	3493	3493	1.00	1.00	1.37	1.37
LFB3/HNF1 beta	X78052	4	2545	2545	2545	40702	3015	3015	1.00	1.00	1.18	1.18
Gli2	AF109923	4	2545	2545	2545	5281	391	2545	1.00	1.00	1.00	1.00
brain factor 1	AF101387	4	2545	2545	2545	143451	10626	10626	1.00	1.00	4.17	4.17
brain factor 2	AJ011652	4	450	416	420	1560	1560	1560	0.92	0.93	3.47	3.71
GATA-5a	L13701	4	2545	5010	2545	64970	4813	4813	1.97	1.00	1.89	1.89
CCCH zinc finger protein C3H-3	AF061982	4	3875	2545	2545	67960	5034	5034	0.66	0.66	1.30	1.98
NK-2 homolog	S65507	4	2545	2545	2545	6778	502	2545	1.00	1.00	1.00	1.00
iriquois 3	AF027175	4	2545	2545	2545	22494	1666	2545	1.00	1.00	1.00	1.00
myb-related protein 1 (myb 1)	M75870	4	2545	2545	2545	5035	373	2545	1.00	1.00	1.00	1.00
Pitx-1	AF155206	4	2545	2545	2545	55812	4134	4134	1.00	1.00	1.62	1.62
MOX2	L20432	4	2545	2545	2545	6296	466	2545	1.00	1.00	1.00	1.00
HoxD1	L25857	4	2545	2545	2545	2545	189	2545	1.00	1.00	1.00	1.00
goosecoid homebox protein isoform B	M81481	4	2545	2545	2545	40535	3003	3003	1.00	1.00	1.18	1.18
Xhox lab2	X62053	4	2545	2545	2545	2545	189	2545	1.00	1.00	1.00	1.00
DLL4	L09728	4	3355	2545	2545	59871	4435	4435	0.76	0.76	1.32	1.74
DLL3	L09729	4	2545	2545	2545	102367	7583	7583	1.00	1.00	2.98	2.98
DLL2	L09730	4	2545	2545	2545	7923	587	2545	1.00	1.00	1.00	1.00
Fez	AF195021	4	2545	2545	2545	50659	3753	3753	1.00	1.00	1.47	1.47
ergA	AJ224125	4	2545	2545	2545	17735	1314	2545	1.00	1.00	1.00	1.00
achaete-scute protein homolog (ASH1)	M98272	4	2545	2545	2545	37770	2798	2798	1.00	1.00	1.10	1.10
DNA binding protein E12	X86959	4	2545	2545	2545	5063	375	2545	1.00	1.00	1.00	1.00
sonic hedgehog	L39213	4	2545	2545	2545	25407	1882	2545	1.00	1.00	1.00	1.00
XLMO1	U94991	4	2545	2545	2545	47991	3555	3555	1.00	1.00	1.40	1.40
POU2	U17654	4	3883	4611	3141	33664	2494	2545	1.19	0.81	0.66	0.81
X-MyT1	U67078	4	2545	2545	2545	2767	205	2545	1.00	1.00	1.00	1.00
Xsal-1	L46583	4	2545	2545	2545	2545	189	2545	1.00	1.00	1.00	1.00
zic2	U57453	4	5857	2545	3421	80984	5999	5999	0.43	0.57	1.01	1.75
TFIIIA	X58369	4	2545	2545	2545	2545	189	2545	1.00	1.00	1.00	1.00
TH/bZip	U37375	4	2545	2545	2545	45657	3382	3382	1.00	1.00	1.33	1.33
glucocorticoid receptor	X72211	5	2545	2545	2545	5532	410	2545	1.00	1.00	1.00	1.00
estrogen receptor	L20736	5	2545	2545	2545	2545	189	2545	1.00	1.00	1.00	1.00
vitamin D receptor	U91846	5	2545	2545	2545	2545	189	2545	1.00	1.00	1.00	1.00
tif2	AJ243119	4	3384	2885	4416	167289	12392	12392	0.85	1.31	3.68	2.81
TRIP4	AW199631	5	2545	2545	2545	5116	379	2545	1.00	1.00	1.00	1.00
TRIP7	AW200492	5	2545	2545	2545	7557	560	2545	1.00	1.00	1.00	1.00
thyroid hormone receptor alpha A	M35343	5	2545	2545	2545	2545	189	2545	1.00	1.00	1.00	1.00
thyroid hormone receptor beta A1	M35359	5	2545	2545	2545	2741	203	2545	1.00	1.00	1.00	1.00
androgen receptor alpha	U67129	5	2545	2545	2545	139231	10313	10313	1.00	1.00	4.05	4.05
mineralocorticoid receptor	U15134	5	2545	2545	2545	2545	189	2545	1.00	1.00	1.00	1.00
RXR xSRC-3	AF044080	5	2545	2545	2545	3610	267	2545	1.00	1.00	1.00	1.00
RAR beta	X87366	5	2545	2545	2545	3471	257	2545	1.00	1.00	1.00	1.00
RAR gamma B	X59396	5	2545	2545	2545	2662	197	2545				1.00
PPAR alpha	M84161	5	2545	2545	2545	19940	1477	2545	1.00	1.00	1.00	1.00
PPAR beta	M84162	5	2545	2545	2545	2855	211	2545				1.00
PPAR gamma	M84163	5	2545	2545	2545	2545	189	2545	1.00	1.00	1.00	1.00
NGFI-B	X70700	4	2545	2545	2545	3646	270	2545	1.00	1.00	1.00	1.00
orphan nuclear receptor	X75163	4	2545	2545	2545	27911	2067	2545	1.00	1.00	1.00	1.00
COUP transcription factor 1	AF157556	4	2545	2545	2545	22192	1644	2545	1.00	1.00	1.00	1.00
thyroid hormone receptor alpha	L06064	5	2545	2545	2545	56138	4158	4158	1.00	1.00	1.63	1.63
thyroid hormone receptor beta	L27344	5	2545	2545	2545	13892	1029	2545	1.00	1.00	1.00	1.00
metastasis associated 1-like protein	AF170344	2	2545	2545	2545	6420	476	2545	1.00	1.00	1.00	1.00
recombination activation (RAG-2)	L19325	2	2545	2545	2545	11622	861	2545	1.00	1.00	1.00	1.00
methyl-CpG binding protein	AF170347	2	2545	2545	2545	6431	476	2545	1.00	1.00	1.00	1.00
replication protein A	X67240	2	2545	2545	2545	2545	189	2545	1.00	1.00	1.00	1.00
Mi-2 histone deacetylase	AF171099	2	2545	2545	2545	16156	1197	2545	1.00	1.00	1.00	1.00
mitochondrial RNA polymerase	AF200705	2	2545	2545	2545	7940	622	2545	1.00	1.00	1.00	1.00
mitotic phosphoprotein 43	U95097	2	2545	2545	2545	37086	2747	2747	1.00	1.00	1.08	1.08
mitotic phosphoprotein 90	U95102	2	2545	2545	2545	69035	5114	5114	1.00	1.00	2.01	2.01
maskin	AF200212	11	2545	2545	2545	2870	213	2545	1.00	1.00	1.00	1.00
plexin	D38175	9	2545	2545	2545	25843	1914	2545	1.00	1.00	1.00	1.00
contactin/F3/F11	D86506	9	2545	2545	2545	2545	189	2545	1.00	1.00	1.00	1.00
non-muscle tropomyosin (TM-4)	L35238	9	9656	2545	8246	35220	2609	2609	0.26	0.85	0.27	0.32
coronin	AB025246	9	2545	2545	2545	4065	301	2545	1.00	1.00	1.00	1.00
kinesin central motor 1 XKCM	U36485	9	2545	2545	2545	2814	208	2545	1.00	1.00	1.00	1.00
katanin p60	AF177942	9	2545	2545	2545	35145	2603	2603	1.00	1.00	1.02	1.02
calponin H3	AF081676	9	2545	2545	2545	2545	189	2545	1.00	1.00	1.00	1.00
myelin proteolipid protein	Z19522	9	2545	2545	2545	3610	267	2545	1.00	1.00	1.00	1.00
myelin basic protein	AB000736	9	2545	2545	2545	9713	719	2545	1.00	1.00	1.00	1.00
class II beta-tubulin	X15798	9	2545	2545	2545	2545	189	2545	1.00	1.00	1.00	1.00
beta tubulin	L06232	9	2545	2545	2545	28887	2140	2545	1.00	1.00	1.00	1.00
fibronectin	M77820	9	2545	2545	2545	6387			1.00	1.00		
Xefiltin	U63711	9	2545	2545	2545	9864	731	2545	1.00	1.00	1.00	1.00
myosin heavy chain 3	AF097906	9	2545	16260	7249	18464	1368	2545	6.39	2.85	1.00	0.35
alpha skeletal actin	X03470	9	567	1069	1290	1227	1227	1227	1.89	2.27	2.16	0.95
cytoplasmic beta actin	AF079161	9	2023	2437	2295	4995	4995	4995	1.20	1.13	2.47	2.18
ribosomal protein L8	U00920	11	2545	2545	2545	3899	3899	3899	1.00	1.00	1.53	1.53
protein S10	S67432	11	1370	1176	771	1140	1140	1140	0.86	0.56	0.83	1.48
mitochondrial 16s ribosomal RNA	U66113	11	1365	1897	1226	2862	2862	2862	1.39	0.90	2.10	2.34
HMG-1	U21933	4	2545	2545	2545	25277	1872	2545	1.00	1.00	1.00	1.00
histone H1	J00968	2	2545	2545	2545	37738	2795	2795	1.00	1.00	1.10	1.10
51 KDa cytokeratin type I	Y00968	9	2545	6096	3199	3178	235	2545	2.40	1.26	1.00	0.80
epidermal type 1 keratin b1	65242	9	13013	5996	15417	4527	335	2545	0.46	1.18	0.20	0.17
alpha 1 collagen type I	AB015440	9	2545	4814	5530	54233	4017	4017	1.89	2.17	1.56	0.73
alpha 2 collagen type I	D88764	9	2545	5013	6247	45975	3406	3406	1.97	2.45	1.34	0.55
alpha-1 collagen type II	M63595	9	2545	2545	2545	19420	1439	2545	1.00	1.00	1.00	1.00

ribosomal protein L32	X55030	11	1142	911	871	1091	1091	1091	0.80	0.76	0.95	1.25
serum retinol binding protein	J02718	5	2545	2545	2545	2545	189	2545	1.00	1.00	1.00	1.00
cellular retinoic acid binding protein	S74933	6	2545	2545	2545	2545	189	2545	1.00	1.00	1.00	1.00
thyroid hormone binding protein	U03878	5	2545	2545	2545	2838	210	2545	1.00	1.00	1.00	1.00
IFABP	L19946	7	2545	2545	2545	2545	189	2545	1.00	1.00	1.00	1.00
L-amino acid transporter-1	Y12716	7	2545	2545	2545	21582	1599	2545	1.00	1.00	1.00	1.00
chloride channel ClC-3	Y09941	7	2545	2545	2545	26183	1939	2545	1.00	1.00	1.00	1.00
chloride channel ClC-5	AF063904	7	2545	2545	2545	28102	2062	2545	1.00	1.00	1.00	1.00
multidrug resistance gene	U17608	7	2545	2545	2545	34839	2581	2581	1.00	1.00	1.01	1.01
importin alpha 1a	L36339	7	#NUM!	#NUM!	6289	3260	241	2545				
Ca2+-binding protein frequenin	U27274	7	#NUM!	#NUM!	#NUM!	24648	1826	2545				
calbindin D28K	U78636	7	2545	2545	2545	2545	189	2545	1.00	1.00	1.00	1.00
adult beta-globin	J00978	7	2545	2545	2545	3236	240	2545	1.00	1.00	1.00	1.00
larval beta I globin	X03143	7	2545	9092	2545	66197	4903	4903	3.57	1.00	1.93	1.93
sodium phosphate cotransporter	L78835	7	2545	2545	2545	6357	471	2545	1.00	1.00	1.00	1.00
Na+/dicarboxylate cotransporter	U87318	7	2545	2545	2545	3081	228	2545	1.00	1.00	1.00	1.00
Na+-glucose cotransporter type I	AB008225	7	2545	2545	2545	28775	2132	2545	1.00	1.00	1.00	1.00
epithelial Na+ channel alpha subunit	U23535	7	2545	2545	2545	2545	189	2545	1.00	1.00	1.00	1.00
poly A-binding protein ABP-EF	M27072	4	2545	2545	2545	2545	189	2545	1.00	1.00	1.00	1.00
nervous system-specific RNA binding prot	M34894	4	2545	2545	2545	21600	1600	2545	1.00	1.00	1.00	1.00
Xfin	X06021	4	2545	2545	2545	32248	2389	2545	1.00	1.00	1.00	1.00
p54 mRNA binding protein	M80257	4	2545	2545	2545	66501	4926	4926	1.00	1.00	1.94	1.94
74 kDa/68 kDa serum albumin	M21442	7	2545	2545	2545	2545	189	2545	1.00	1.00	1.00	1.00
aldehyde dehydrogenase class 1	AB016718	6	2545	2545	2545	5397	400	2545	1.00	1.00	1.00	1.00
Wnt inhibitory factor-1	AF122924	3	2545	2545	2545	5292	392	2545	1.00	1.00	1.00	1.00
transferrin	X54530	7	2545	2545	2545	5730	424	2545	1.00	1.00	1.00	1.00
hnRNP I-related RNA transport protein	AF091370	4	2545	2545	2545	6635	492	2545	1.00	1.00	1.00	1.00
urea transporter	Y12764	7	2545	2545	2545	15626	1158	2545	1.00	1.00	1.00	1.00
SPARC	X62483	1	2545	2545	7889	7612	564	2545	1.00	3.10	1.00	0.32
L-epinephrine transporter	U72877	7	2545	2545	2545	3045	226	2545	1.00	1.00	1.00	1.00
TIMP-2	AY037944	8	2545	2545	2545	28742	2129	2545	1.00	1.00	1.00	1.00
transthyretin	AB006134	5	2545	2545	2545	2621	194	2545	1.00	1.00	1.00	1.00
interleukin 1 beta	AJ010497	3	2545	2545	2545	6200	459	2545	1.00	1.00	1.00	1.00
NEDD 8	Not Submitted	8	2545	2545	2545	32486	2406	2545	1.00	1.00	1.00	1.00
osteogenic protein-1 homolog precursor	U40034	1	2545	2545	2545	5156	382	2545	1.00	1.00	1.00	1.00
connective tissue growth factor XCTGF	U43524	1	2545	2545	2545	30718	2275	2545	1.00	1.00	1.00	1.00
nerve growth factor	X55716	1	2545	2545	2545	2545	189	2545	1.00	1.00	1.00	1.00
preproneuropeptide Y	S65577	3	2545	2545	2545	2545	189	2545	1.00	1.00	1.00	1.00
neuromedin	L01530	3	2545	2545	2545	6886	509	2545	1.00	1.00	1.00	1.00
thyroid-stimulating hormone a	L07619	5	2545	2545	2545	2634	195	2545	1.00	1.00	1.00	1.00
thyrotropin-releasing hormone precursor	X84056	5	2545	2545	2545	8731	647	2545	1.00	1.00	1.00	1.00
corticotropin-releasing factor	S50096	5	2545	2545	2545	65654	4863	4863	1.00	1.00	1.91	1.91
prolactin	L07620	6	2545	2545	2545	3937	292	2545	1.00	1.00	1.00	1.00
ubiquitin	M11512	8	1002	657	1169	1180	1180	1180	0.66	1.17	1.16	1.01
X Wnt-2b	U66288	3	2545	2545	2545	6873	509	2545	1.00	1.00	1.00	1.00
A5-protein	D10467	3	2545	2545	2545	17596	1304	2545	1.00	1.00	1.00	1.00
geminin H	AF067656	2	2545	2545	2545	2583	191	2545	1.00	1.00	1.00	1.00
fibroblast growth factor receptor ligand	U40457	1	2545	2545	2545	2582			1.00	1.00		
FGF-3	Z25539	1	2545	2545	2545	51355	3804	3804	1.00	1.00	1.49	1.49
FGF-20	AB012615	1	2545	2545	2545	6794	503	2545	1.00	1.00	1.00	1.00
TGF-beta 2	X51817	1	2545	2545	2545	2545	189	2545	1.00	1.00	1.00	1.00
TGF-beta 5	AH005497	1	2545	2545	2545	2545	189	2545	1.00	1.00	1.00	1.00
Mvl-5	X56738	4	2545	2545	2545	2545			1.00	1.00		
c-type natriuretic peptide 1	D17413	5	2545	2545	2545	2822	209	2545	1.00	1.00	1.00	1.00
thyroid-stimulating hormone beta	L07618	5	2545	2545	2545	2545	189	2545	1.00	1.00	1.00	1.00
growth hormone A	AF193797	5	2545	2545	2545	2545			1.00	1.00		
RSK2	AF165162	3	2545	2545	2545	2585	191	2545	1.00	1.00	1.00	1.00
PCNA	M34080	2	2545	2708	2545	4007	297	2545	1.06	1.00	1.00	1.00
RING finger subunit MAT	U29667	1	2545	2545	2545	2545	189	2545	1.00	1.00	1.00	1.00
Chk1 checkpoint kinase	AF117816	1	2545	2545	2545	2545			1.00	1.00		
fyn	X52188	3	2545	2545	2545	2586	190	2545	1.00	1.00	1.00	1.00
XDRP1	AB030502	1	2545	2545	2545	3926	291	2545	1.00	1.00	1.00	1.00
wee 1A kinase	U13962	1	2545	2545	2545	8664	642	2545	1.00	1.00	1.00	1.00
Max2/Max4	L09738	4	2545	2545	2545	3320	246	2545	1.00	1.00	1.00	1.00
Mad1	L77886	1	2545	2545	2545	8219			1.00	1.00		
Mad2	L77885	1	2545	2545	2545	2545	189	2545	1.00	1.00	1.00	1.00
MAP kinase 1 (MPK1)	X59813	3	2545	2545	2545	2545	189	2545	1.00	1.00	1.00	1.00
MAP kinase 2 (MPK2)	X80751	3	2545	2545	2545	2545	189	2545	1.00	1.00	1.00	1.00
MAP kinase activator 2 (XMEK2)	Z22736	3	2545	2545	2545	43667	3235	3235	1.00	1.00	1.27	1.27
MAP kinase activator (XMEK3)	AF172848	3	2545	2545	2545	5445	403	2545	1.00	1.00	1.00	1.00
MAP kinase phosphatase	X83742	3	16787	3575	7878	45736	3388	3388	0.21	0.47	0.20	0.43
MAP kinase interacting kinase	AB023807	3	2545	2545	2545	63560	4708	4708	1.00	1.00	1.85	1.85
MAPKK	D13700	3	2545	2545	2545	41371	3065	3065	1.00	1.00	1.20	1.20
phosphoinositide 3 kinase catalytic subun	AF204924	3	2545	2545	2545	3289	244	2545	1.00	1.00	1.00	1.00
casein kinase 1-alpha	Y08817	3	2545	2545	2545	2545	189	2545	1.00	1.00	1.00	1.00
casein kinase 1-epsilon	AF183394	3	2545	2545	2545	17548	1300	2545	1.00	1.00	1.00	1.00
calmodulin-dependent protein kinase beta	U06636	3	2545	2545	2545	2545	189	2545	1.00	1.00	1.00	1.00
protein kinase PKN	D43890	3	2545	2545	2545	2545	189	2545	1.00	1.00	1.00	1.00
PKC-related kinase 2	AF027183	3	2545	2545	2545	3493	259	2545	1.00	1.00	1.00	1.00
DNA-PK	AF001413	2	2545	2545	2545	2545	189	2545	1.00	1.00	1.00	1.00
ATM	AF174486	2	2545	2545	2545	15346	1137	2545	1.00	1.00	1.00	1.00
protein phosphatase 5	AF018263	3	2545	2545	2545	5119	379	2545	1.00	1.00	1.00	1.00
guanylyl cyclase 1	AB025111	3	2545	2545	2545	4228	313	2545	1.00	1.00	1.00	1.00
guanylyl cyclase 2	AB025112	3	2545	2545	2545	3185	236	2545	1.00	1.00	1.00	1.00
cyclin A1	X53745	1	2545	2545	2545	2545	189	2545	1.00	1.00	1.00	1.00
cyclin A2	X85746	1	2545	2545	2545	6479	480	2545	1.00	1.00	1.00	1.00
cyclin B1	J03166	1	2545	2545	2545	2545	189	2545	1.00	1.00	1.00	1.00
cyclin B2	J03167	1	2545	2545	2545	5364	397	2545	1.00	1.00	1.00	1.00
cyclin D1	X89475	1	2545	2545	2545	6769	501	2545	1.00	1.00	1.00	1.00
cyclin D2	X89476	1	8473	2545	2545	2545			0.30	0.30		
cyclin E	L23857	1	2545	2545	2545	2545	189	2545				1.00
cyclin H	U20505	1	2545	2545	2545	2666	197	2545	1.00	1.00	1.00	1.00
cyclin B2	AB005253	1	2545	2545	2545	2545	189	2545	1.00	1.00	1.00	1.00
cdc2	AB005254	1	2545	2545	2545	2545	189	2545	1.00	1.00	1.00	1.00
Eg1 Ser/Thr kinase (cdc2 homolog)	X14227	1	2545	2545	2545	3107	230	2545	1.00	1.00	1.00	1.00
cdc2-related MO15	X53962	1	2545	2545	2545	3020	224	2545	1.00	1.00	1.00	1.00
cdc2 kinase homologous protein	M60680	1	2545	2545	2545	2545	189	2545	1.00	1.00	1.00	1.00
MYT1	U28931	1	2545	2545	2545	2653	197	2545	1.00	1.00	1.00	1.00
cdc7-related kinase	AF080068	1	2545	2545	2545	3584	265	2545	1.00	1.00	1.00	1.00
cdc21	U44049	1	2545	2545	2545	3385	251	2545	1.00	1.00	1.00	1.00
tyrosine phosphatase cdc25A	AF090829	1	2545	2545	2545	2545	189	2545	1.00	1.00	1.00	1.00
tyrosine phosphatase cdcC1	M96857	1	2545	2545	2545	2545	189	2545	1.00	1.00	1.00	1.00
MCM5/CDC46	U44048	1	2545	2545	2545	43447	3218	3218	1.00	1.00	1.26	1.26
cdk 4	X89477	1	2545	2545	2545	2710	201	2545	1.00	1.00	1.00	1.00
activator of cdk5	AF000951	1	2545	2545	2545	5687	421	2545	1.00	1.00	1.00	1.00
cdk inhibitor p28	U38844	1	2545	2545	2545	105619	7824	7824	1.00	1.00	3.07	3.07
cdk inhibitor	U24434	1	2545	2545	2545	23434	1736	2545	1.00	1.00	1.00	1.00
p33 ringo (ls26)	AJ133499	1	2545	2545	2545	29018	2149	2545	1.00	1.00	1.00	1.00
calcium/calmodulin-dependent protein kin	AF233633	3	2545	2545	2545	2545	189	2545	1.00	1.00	1.00	1.00
protein phosphatase-2A B'epsilon	AF296157	3	2545	2545	2545	2970	220	2545	1.00	1.00	1.00	1.00
serotonin receptor	U10161	5	2545	2545	2545	5558	412	2545	1.00	1.00	1.00	1.00
muscle nicotinic acetylcholine receptor be	U04618	3	2545	2545	2545	7674	568	2545	1.00	1.00	1.00	1.00
prolactin receptor A	AF193800	5	2545	2545	2545	2545	189	2545	1.00	1.00	1.00	1.00
neurotrophic factor BDNF receptor	S69713	3	2545	2545	2545	3261	242	2545	1.00	1.00	1.00	1.00
lysophosphatidic acid receptor	AJ249844	3	2545	2545	2545	2545	189	2545	1.00	1.00	1.00	1.00
pituitary adenylate cyclase-activating rece	AF187878	3	2545	2545	2545	4806	356	2545	1.00	1.00	1.00	1.00
luteinizing hormone receptor	AJ249845	5	2545	2545	2545	2545	189	2545	1.00	1.00	1.00	1.00
inositol 1,4,5-trisphosphate receptor (IP-3	D14400	3	2545	2545	2545	24790	1836	2545	1.00	1.00	1.00	1.00
BMP receptor	D32066	3	2545	2545	2545	2545	189	2545	1.00	1.00	1.00	1.00
frizzled 2	AF139165	3	2545	2545	2545	2545	189	2545	1.00	1.00	1.00	1.00
cadherin precursor	AF002983	9	2545	2545	2545	2662	197	2545	1.00	1.00	1.00	1.00
NPY/PYY Receptor Y1	L25416	3	2545	2545	2545	2545	189	2545	1.00	1.00	1.00	1.00
muscle acetylcholine receptor a	X07067	3	2545	2545	2545	3379	250	2545	1.00	1.00	1.00	1.00
acetylcholine receptor alpha subunit 1A	X17244	3	2545	2545	2545	2545	189	2545	1.00	1.00	1.00	1.00
activin receptor	S70930	1	2545	2545	2545	2545	189	2545	1.00	1.00	1.00	1.00
Ftz-F1-related orphan receptor A	U06001	4	2545	2545	2545	8282	613	2545	1.00	1.00	1.00	1.00
fibroblast growth factor receptor 1	M55163	1	2545	2545	2545	4099	304	2545	1.00	1.00	1.00	1.00
Pagliaccio receptor tyrosine kinase	L26099	3	2545	2545	2545	30185	2236	2545	1.00	1.00	1.00	1.00
angiotensin II receptor	S73388	3	2545	2545	2545	2545	189	2545	1.00	1.00	1.00	1.00
angiotensin receptor related protein	U72029	3	2545	2545	2545	5724	424	2545	1.00	1.00	1.00	1.00
activated protein kinase C	AF105259	3	30494	21339	13834	42707	3164	3164	0.70	0.45	0.10	0.23
5-HT1A receptor	Y07901	3	2545	2545	2545	7061	523	2545	1.00	1.00	1.00	1.00
14-3-3 protein	M86928	3	2545	2545	2545	2545	189	2545	1.00	1.00	1.00	1.00
ALK-2 receptor	AF012245	3	2545	2545	2545	2545	189	2545	1.00	1.00	1.00	1.00
adenosine A1 receptor (a1R gene)	AJ249842	3	2545	2545	2545	2545	189	2545	1.00	1.00	1.00	1.00
CRF receptor type1	Y14036	5	2545	2545	2545	13702	1015	2545	1.00	1.00	1.00	1.00
VIP/pituitary cAMP receptor	AF100644	3	2545	2545	2545	6964	516	2545	1.00	1.00	1.00	1.00
dihydropyrimidine receptor	AF037625	3	2545	2545	2545	6952			1.00	1.00		
follicle stimulating hormone receptor	AJ249846	5	2545	2545	2545	3609	267	2545	1.00	1.00	1.00	1.00
CRF receptor type 2	Y14037	5	2545	2545	2545	8717	646	2545	1.00	1.00	1.00	1.00
insulin receptor substrate protein xIRS-u	AF297960	5	2545	2545	2545	2545	189	2545	1.00	1.00	1.00	1.00
natriuretic peptide receptor type C	AF231035	5	2545	2545	2545	2545	189	2545	1.00	1.00	1.00	1.00
XICE-a	D89783	8	2545	2545	2545	2545	189	2545	1.00	1.00	1.00	1.00
CPP32	D89784	8	2545	2545	2545	2545	189	2545	1.00	1.00	1.00	1.00
calpastatin 1	AJ243713	8	2545	2545	2545	16879	1250	2545	1.00	1.00	1.00	1.00
caspase7-precursor	AW199521	8	2545	2545	2545	9163	679	2545	1.00	1.00	1.00	1.00
bcl-2-like R11	X82461	8	2545	2545	2545	49963	3630	3630	1.00	1.00	1.43	1.43
scythe	AF096511	8	2545	2545	2545	32296	2392	2545	1.00	1.00	1.00	1.00
survivin	AW198621	8	2545	2545	2545	2988	221	2545	1.00	1.00	1.00	1.00

requiem	AB021737	8	2545	2545	2545	34317	2542	2545	1.00	1.00	1.00	1.00
p21-activated kinase (PAK1)	AF000239	3	2545	2545	2545	13664	1012	2545	1.00	1.00	1.00	1.00
DAD-1	D15059	8	2704	2545	2545	2545	189	2545	0.94	0.94	0.94	1.00
caspase-2	AB038168	8	2545	2545	2545	2906	215	2545	1.00	1.00	1.00	1.00
caspase-6	AB038169	8	2545	2545	2545	4055	300	2545	1.00	1.00	1.00	1.00
caspase-7	AB038170	8	2545	2545	2545	7992	592	2545	1.00	1.00	1.00	1.00
caspase-8	AB038171	8	2545	2545	2545	2545	189	2545	1.00	1.00	1.00	1.00
caspase-9	AB038172	8	2545	2545	2545	27821	2061	2545	1.00	1.00	1.00	1.00
caspase-10	AB038173	8	2545	2545	2545	2545	189	2545	1.00	1.00	1.00	1.00
metalloprotease-disintegrin (MDC11a)	AF032384	8	2545	2545	2545	17351	1285	2545	1.00	1.00	1.00	1.00
metalloproteinase (XMMP)	U82541	8	2545	2545	2545	14331	1063	2545	1.00	1.00	1.00	1.00
membrane anchored metalloprotease	U78185	8	2545	2545	2545	2545	189	2545	1.00	1.00	1.00	1.00
metalloprotease-disintegrin (MDC11b)	AF032383	8	2545	2545	2545	7752	574	2545	1.00	1.00	1.00	1.00
pancreatic trypsin	X53458	6	2545	2545	2545	8282	613	2545	1.00	1.00	1.00	1.00
trypsinogen	U72330	6	2545	2545	2545	40107	2971	2971	1.00	1.00	1.17	1.17
serine protease (Cap1)	AF029404	6	2545	2545	2545	2545	189	2545	1.00	1.00	1.00	1.00
stromelysin-3	Z27093	8	2545	2545	2545	2690	199	2545	1.00	1.00	1.00	1.00
alpha-aspartyl dipeptidase	U37377	8	2545	2545	2545	2545	189	2545	1.00	1.00	1.00	1.00
xepsin	AB018694	3	2545	2545	2545	23280	1724	2545	1.00	1.00	1.00	1.00
alpha-1 antiproteinase	AB014091	8	2545	2545	2545	2545	189	2545	1.00	1.00	1.00	1.00
carbamyl phosphate synthetase	U05193	6	2545	2545	2545	2545	189	2545	1.00	1.00	1.00	1.00
ornithine transcarbamylase	D38304	6	2545	2545	2545	5353	397	2545	1.00	1.00	1.00	1.00
ornithine decarboxylase	X56316	6	2545	2545	2545	33298	2466	2545	1.00	1.00	1.00	1.00
lactate dehydrogenase B	U07176	6	27935	14344	13176	59846	4433	4433	0.51	0.47	0.16	0.34
GAPDH	U41753	6	415	817	792	763	763	763	1.97	1.91	1.84	0.96
gelatinase B (MMP-9)	AF072455	8	2545	2545	8971	5131	380	2545	1.00	3.52	1.00	0.28
NM23/nucleoside diphosphate kinase	X97899	2	1428	1283	1576	1807	1807	1807	0.90	1.10	1.27	1.15
Nir1	D86491	8	2545	2545	2545	3375	250	2545	1.00	1.00	1.00	1.00
Na+/K+ transporting ATPase beta subunit	M37786	7	2545	2545	2545	2547	189	2545	1.00	1.00	1.00	1.00
SERCa1 fast skeletal muscle	X63009	3	2545	2545	2545	6643	492	2545	1.00	1.00	1.00	1.00
E2 ubiquitin conjugating enzyme (Ubc9)	U66561	8	2545	2545	2545	2599	193	2545	1.00	1.00	1.00	1.00
metallothionein	M96729	7	2545	2545	2545	7845	581	2545	1.00	1.00	1.00	1.00
iodothyronine deiodinase type II	L42816	5	2545	2545	2644	18405	1363	2545	1.00	1.04	1.00	0.96
iodothyronine 5'-deiodinase III	L28111	6	2545	2545	2545	70261	5205	5205	1.00	1.00	2.04	2.04
retinoic acid converting enzyme	AF057566	5	2545	2545	2545	16599	1230	2545	1.00	1.00	1.00	1.00
FCP1 serine phosphatase	AJ132385	4	2545	2545	2545	8029	595	2545	1.00	1.00	1.00	1.00
protein phosphatase 1-gamma 1	L17039	1	2545	2545	2545	2545	189	2545	1.00	1.00	1.00	1.00
convertase PC2	X66493	6	2545	2545	3909	13536	1003	2545	1.00	1.54	1.00	0.65
aconitase	AF186471	6	2545	2545	2545	12707	941	2545	1.00	1.00	1.00	1.00
phospholipase C-gamma-1a	AF090111	3	2545	2545	2545	24482	1812	2545	1.00	1.00	1.00	1.00
Cu/Zn SOD	X16585	6	3401	2545	3499	5039	373	2545	0.75	1.03	0.76	0.73
collagenase-4 precursor	L76275	6	2545	2545	2545	2545	189	2545	1.00	1.00	1.00	1.00
cytochrome P-450 (11beta, aldo)	D10984	6	2545	2545	2545	36142	2677	2677	1.00	1.00	1.05	1.05
mitochondrial cytochrome c oxidase subu	M10217	6	2545	4248	7235	2545	189	2545	1.67	2.84	1.00	0.35
alcohol dehydrogenase class 1 (ADH1)	AF059255	6	2545	2545	2545	2545			1.00	1.00		
alcohol dehydrogenase class 4 (ADH4)	AF059256	6	2545	2545	2545	5398	400	2545	1.00	1.00	1.00	1.00
adenyl cyclase	Z46958	3	2545	2545	2545	2545	189	2545	1.00	1.00	1.00	1.00
fibroblast activation factor alpha	U41856	1	2545	2545	2545	2780			1.00	1.00		
aldolase C	3928510	6	2545	2545	2545	6344	470	2545	1.00	1.00	1.00	1.00
2',3'-cyclic-nucleotide 3'-phosphodiesterase	AB002145	9	2545	2545	2545	2582	191	2545	1.00	1.00	1.00	1.00
arginase	D38303	6	6779	2545	14447	8497	704	2545	0.38	2.13	0.38	0.16
arginase 1	U08406	6	2545	2545	2545	30678	2272	2545	1.00	1.00	1.00	1.00
argininosuccinate lyase	D38302	8	2545	2545	2545	2545	189	2545	1.00	1.00	1.00	1.00
ATPase Na+/K+ pump alpha 1 subunit	U49238	6	2545	2545	2545	2545	189	2545	1.00	1.00	1.00	1.00
ADP-ribosylation factor (ARF1)	U31350	6	2545	2545	2545	2545	189	2545	1.00	1.00	1.00	1.00
allantoicase	AF153230	6	2545	2545	2545	3038	225	2545	1.00	1.00	1.00	1.00
exonuclease Exo1	AF134570	2	2545	2545	2545	2545	189	2545	1.00	1.00	1.00	1.00
deoxyribonuclease gamma	AF059612	2	2545	2545	2545	2545	189	2545	1.00	1.00	1.00	1.00
DNA polymerase beta	Y15732	2	2545	2545	2545	2569			1.00	1.00		
ligase I	L43496	2	2545	2545	2545	3761	279	2545	1.00	1.00	1.00	1.00
ATP-dependent RNA helicase	X57328	4	2545	2545	2545	4474	331	2545	1.00	1.00	1.00	1.00
cytosine-5-methyltransferase	D78638	2	2545	2545	2545	15805	1171	2545	1.00	1.00	1.00	1.00
flap endonuclease 1 (FEN1)	U64563	2	2545	2545	2545	22795	1689	2545	1.00	1.00	1.00	1.00
terminal deoxynucleotidyl transferase	U07803	2	2545	2545	2545	4781	354	2545	1.00	1.00	1.00	1.00
gelatinase A	AY037943	8	2545	2545	2545	3604	267	2545	1.00	1.00	1.00	1.00
liver helicase	AF302423	4	2545	4138	3131	5779	428	2545	1.63	1.23	1.00	0.81
aldolase B	AB030822	6	2545	2545	2545	28365	2101	2545	1.00	1.00	1.00	1.00
cytochrome b	M10217	8	2545	2545	2545	4793	365	2545	1.00	1.00	1.00	1.00
aromatase p450	AB031278	5	2545	2545	2545	2545	189	2545	1.00	1.00	1.00	1.00
NEDD 4	AJ000085	8	2545	2545	2545	14436	1069	2545	1.00	1.00	1.00	1.00
ring finger protein	U63817	1	2545	2545	2545	3444			1.00	1.00		
REST	AF096301	4	2545	2545	2545	2545	189	2545	1.00	1.00	1.00	1.00
MCM2	U44047	1	2545	2545	2545	27048	2004	2545	1.00	1.00	1.00	1.00
proteasome subunit Y	D87689	8	22	196	167	1038	1038	1038	9.11	7.75	48.17	6.21
transmembrane protein containing an EGF	X83962	10	2545	2545	2545	3520	261	2545	1.00	1.00	1.00	1.00
OTX5b	AJ251646	4	2545	2545	2545	26101	1933	2545	1.00	1.00	1.00	1.00
13S condensin XCAP-D2	AF067969	2	2545	2545	2545	5153	382	2545	1.00	1.00	1.00	1.00
chaperonin subunit CCT gamma	U37062	7	2545	2545	2545	6566	486	2545	1.00	1.00	1.00	1.00
HMG-X	D30765	2	2545	2545	2545	9149	678	2545	1.00	1.00	1.00	1.00
GSK-3 binding protein	AF062738	3	2545	2717	5400	40899	3030	3030	1.07	2.12	1.19	0.56
cartilage homeoprotein 1	U15276	4	2545	2545	2545	43286	3206	3206	1.00	1.00	1.26	1.26
beta-amyloid precursor protein	S52417	9	2545	2545	2545	22680	1680	2545	1.00	1.00	1.00	1.00
frizzled 7	AF159106	3	8676	3250	4430	54203	4015	4015	0.37	0.51	0.46	0.91
calcineurin A	AF019569	3	#NUM!	#NUM!	#NUM!	9611						
BMP1	L12249	8	2545	2545	2545	3814	263	2545	1.00	1.00	1.00	1.00
BMP1b	Y09660	8	2545	2545	2545	2545	189	2545	1.00	1.00	1.00	1.00
BMP4	AF058764	3	2545	2545	2545	4183	310	2545	1.00	1.00	1.00	1.00
18S ribosomal	X04025	11	261	294	183	780	760	760	1.13	0.70	2.91	4.14
18S ribosomal	X04025	11	2545	2545	2545	30057			1.00	1.00		
MCM3	U26057	1	2545	2545	2545	2545	189	2545	1.00	1.00	1.00	1.00
MAM domain protein	U37376	10	17715	9938	13127	25556	1893	2545	0.56	0.74	0.14	0.19
XPACx1	D31894	2	2545	2545	2545	2545	189	2545	1.00	1.00	1.00	1.00
nuclear factor 7	S64515	4	2545	2545	2545	5109	378	2545	1.00	1.00	1.00	1.00
vitellogenin	65210	6	3244	2545	2545	46802	3467	3467	0.78	0.78	1.07	1.36
hsp30B	X02512	7	2545	2545	2545	4964	368	2545	1.00	1.00	1.00	1.00
hsp 30	U44894	7	17	98	865	489	489	489	5.68	50.00	28.28	0.57
integrin alpha-1	U44025	9	2545	2545	2545	2545	189	2545	1.00	1.00	1.00	1.00
gene 5	U37373	10	2545	2545	2545	4222	313	2545	1.00	1.00	1.00	1.00
fos-related antigen-2	U37374	4	2545	2545	2545	5300	393	2545	1.00	1.00	1.00	1.00
gene 12	U41854	10	2545	2545	2545	2545				1.00		
gene 16	U41857	10	2545	2545	2545	28810	2134	2545	1.00	1.00	1.00	1.00
gene 17	U41860	10	2545	2545	2545	2545			1.00	1.00		
gene 18	U41839	10	2545	2545	2545	5173	383	2545	1.00	1.00	1.00	1.00
gene 19	U41861	10	2545	2545	2545	2545	189	2545	1.00	1.00	1.00	1.00
gene 20	U46575	10	2545	2545	2545	15061	1116	2545	1.00	1.00	1.00	1.00
regulator for chromosome condensation (I	D00679	2	2545	2545	2545	72218	5349	5349	1.00	1.00	2.10	2.10
proteasome subunit XC3	S61111	6	9717	3143	4527	9277	687	2545	0.40	0.47	0.26	0.56
B-50/GAP 43	X87582	1	2545	2545	2545	25342	1877	2545	1.00	1.00	1.00	1.00
fragile mental retardation protein 1	U25164	4	2545	2545	2545	2545	189	2545	1.00	1.00	1.00	1.00
forkhead protein lens1	AF186464	4	2545	2545	2545	20646	1529	2545	1.00	1.00	1.00	1.00
ER1	AF016454	4	2545	2545	2545	5570	413	2545	1.00	1.00	1.00	1.00
B-cell translocation protein 1 (btg1)	AB028243	4	2545	2545	2545	2545	189	2545	1.00	1.00	1.00	1.00
SIP 1	AF027151	4	2545	2545	2545	30425	2254	2545	1.00	1.00	1.00	1.00
beta-A1-1 crystallin	X87759	9	2545	2545	2545	2545	189	2545	1.00	1.00	1.00	1.00
gamma-M1-1 crystallin	X86072	9	2545	2545	2545	2545	189	2545	1.00	1.00	1.00	1.00
SF-1/Ad4BP	AB017352	4	2545	2545	2545	65069	4820	4820	1.00	1.00	1.89	1.89
fibronectin intron 1	AF061058	control	2545	2545	2545	2545	189	2545	1.00	1.00	1.00	1.00
alpha tubulin intron 1	65164	control	2545	2545	2545	8776	650	2545	1.00	1.00	1.00	1.00
alpha tubulin	X07046	9	2545	2545	2545	2545	189	2545	1.00	1.00	1.00	1.00
delta tubulin	AF430839	9	2545	2545	2545	2545	189	2545	1.00	1.00	1.00	1.00
desmin	X16842	9	2545	2545	2545	2545	189	2545	1.00	1.00	1.00	1.00
gamma fibrinogen precursor	J02894	9	2545	2545	2545	2545	189	2545	1.00	1.00	1.00	1.00
ribonucleotide reductase submit M1	AF168794	9	2545	2545	2545	4706	349	2545	1.00	1.00	1.00	1.00

Appendix 2.6.2 Fold change for all good data in the 48 h injection set.

A) Rationale of adjustment T3-G treatment

	Fold Change T_3-G vs. T_3-D cDNA array	QPCR	Ratio of array vs. QPCR
TRa	15.53	0.77	20.15
TRb	1.02	0.77	1.38
Average of TRa and TRb			10.00

B)

* Yellow highlighted is assumed, then delete the value.

Gene Name	GenBank Accession #	Functional Code	D/D Median	D/G Median	T3/D Median	T3/G Median	Adjust with 10 T3/G	Four adjustment T3/G	D-G vs. D-D	T3-D vs. D-D	T3-G vs D-D	T3-G vs. T3-D
c-mos	M25366	4	2545	2545	2545	2545	255	2545	1.00	1.00	1.00	1.00
N-ras	M97960	3	2545	2545	2545	2887	289	2545	1.00	1.00	1.00	1.00
K-ras	AF085280	3	2545	2545	2545	24401	2440	2545	1.00	1.00	1.00	1.00
ves	X14377	3	2545	2545	2545	2545	255	2545	1.00	1.00	1.00	1.00
c-fos	AJ224511	4	2545	2545	2545	2545	255	2545	1.00	1.00	1.00	1.00
raf ser/thr kinase	X12948	3	2545	4602	9556	4699	470	2545	1.81	3.75	1.00	0.27
c-ets-1a	X52692	4	2545	2545	2545	2974	297	2545	1.00	1.00	1.00	1.00
c-ets-1b	X52691	4	2545	2545	3419	13849	1385	2545	1.00	1.34	1.00	0.74
ets-2a	M81683	4	2545	2545	2545	2893	289	2545	1.00	1.00	1.00	1.00
c-myc I	X14806	4	2545	2545	2545	5316	532	2545	1.00	1.00	1.00	1.00
L-myc	L11363	4	2545	2545	2545	2959	296	2545	1.00	1.00	1.00	1.00
pp60c-src	M24704	3	2545	2545	2545	5878	588	2545	1.00	1.00	1.00	1.00
mdm2	PubMed ID 9136986	1	2545	2545	2545	2545	255	2545	1.00	1.00	1.00	1.00
ING2	AY014017	4	2545	2545	2545	3161	316	2545	1.00	1.00	1.00	1.00
colorectal cancer tumor suppressor	U10986	3	2545	2545	2545	11828	1183	2545	1.00	1.00	1.00	1.00
protein/lipid phosphatase Pten	AF144732	3	2545	2545	2545	2548	255	2545	1.00	1.00	1.00	1.00
Wt1	D82051	4	2545	2545	2545	26579	2658	2658	1.00	1.00	1.04	1.04
retinoblastoma 1	PubMed ID 1516743	4	2545	2545	2545	2979	298	2545	1.00	1.00	1.00	1.00
C/EBP-1	U08604	4	3505	7490	2545	115111	11511	11511	2.14	0.73	3.28	4.52
C/EBP-2	U08605	4	468	372	525	2067	2067	2067	0.80	1.12	4.42	3.94
C/EBP	S44193	4	2797	5217	7161	2545	255	2545	1.87	2.56	0.91	0.36
transcription co-repressor Sin3	AF154112	2	2545	2545	2545	2545	255	2545	1.00	1.00	1.00	1.00
circadian CLOCK	AF203107	4	2545	2545	2545	2545	255	2545	1.00	1.00	1.00	1.00
c-Jun	5650725	4	2545	2545	2545	2545	255	2545	1.00	1.00	1.00	1.00
c-Myb	L22741	4	2545	2545	2545	2545	255	2545	1.00	1.00	1.00	1.00
nuclear factor I-B1	L43146	4	2545	2545	2545	2545	255	2545	1.00	1.00	1.00	1.00
nuclear factor I-C1	L43149	4	2921	3762	7735	5170	517	2545	1.29	2.65	0.87	0.33
TFIIIA	K02938	4	2545	2545	2545	3957	396	2545	1.00	1.00	1.00	1.00
Oct-1	X17190	4	2545	2545	3131	4874	487	2545	1.00	1.23	1.00	0.81
AP-2	M50455	4	2545	2545	2545	4519	452	2545	1.00	1.00	1.00	1.00
TBP-binding repressor Dr1	AB003582	4	2545	2545	2545	2545	255	2545	1.00	1.00	1.00	1.00
TFIID subunit	D50054	4	5443	5592	2727	71644	7164	7164	1.03	0.50	1.32	2.63
transcription factor A	U35728	4	2545	2545	2545	3544	354	2545	1.00	1.00	1.00	1.00
RNA pol I transcription factor UBF	X57561	4	2573	2617	6783	6860	686	2545	1.02	2.64	0.99	0.38
elongation factor-1 alpha chain	M25504	11	904	1426	1522	1729	1729	1729	1.58	1.68	1.91	1.14
neuroD	U28067	4	2545	2545	2545	2545	255	2545	1.00	1.00	1.00	1.00
Tcf-3 co-repressor CtBP	AF152006	4	2545	2545	2545	6182	618	2545	1.00	1.00	1.00	1.00
repressor brain factor 2	AF072889	4	824	637	718	1647	1647	1647	0.77	0.87	2.00	2.29
co-repressor MITR	Z97214	4	2545	2545	2545	2545	255	2545	1.00	1.00	1.00	1.00
negative regulator Id2	AB019520	4	2545	2545	2545	23993	2399	2545	1.00	1.00	1.00	1.00
XCOE2	AF041138	4	2545	2545	2545	2545	255	2545	1.00	1.00	1.00	1.00
MRF4	S34392	4	2545	2545	2545	2545	255	2545	1.00	1.00	1.00	1.00
Pax-2	AF179300	4	2545	2545	2545	2545	255	2545	1.00	1.00	1.00	1.00
Pax-8	AF179301	4	2545	2545	3418	30099	3010	3010	1.00	1.34	1.18	0.88
LFB1/HNF1	64688	4	2545	2545	2545	22295	2229	2545	1.00	1.00	1.00	1.00
LFB3/HNF1 beta	X76052	4	2545	2545	2545	24069	2407	2545	1.00	1.00	1.00	1.00
Gli2	AF109923	4	2545	2545	3270	5494	549	2545	1.00	1.28	1.00	0.78
brain factor 1	AF101387	4	2702	5750	7963	85288	8529	8529	2.13	2.95	3.16	1.07
brain factor 2	AJ011652	4	693	539	574	1069	1069	1069	0.78	0.83	1.54	1.86
GATA-5a	L13701	4	2545	5694	2545	59366	5937	5937	2.24	1.00	2.33	2.33
CCCH zinc finger protein C3H-3	AF061982	4	4012	4824	6298	36542	3654	3654	1.20	1.57	0.91	0.58
NK-2 homolog	S85507	4	2611	4336	6953	9689	969	2545	1.66	2.66	0.97	0.37
iroquois 3	AF027175	4	2545	2545	2545	13370	1337	2545	1.00	1.00	1.00	1.00
myb-related protein 1 (myb 1)	M75870	4	2545	2545	2545	4942	494	2545	1.00	1.00	1.00	1.00
Pitx-1	AF155206	4	2545	2819	2545	56443	5644	5644	1.11	1.00	2.22	2.22
MOX2	L20432	4	2545	2545	2545	2953	295	2545	1.00	1.00	1.00	1.00
HoxD1	L25857	4	2545	2545	2545	3362	336	2545	1.00	1.00	1.00	1.00
goosecoid homebox protein isoform I	M81481	4	2545	2545	2545	26080	2608	2608	1.00	1.00	1.02	1.02
Xhox lab2	X82053	4	2545	2545	2545	2760	276	2545	1.00	1.00	1.00	1.00
DLL4	L09728	4	2545	3000	6530	40005	4000	4000	1.18	2.57	1.57	0.61
DLL3	L09728	4	4193	5133	7249	72784	7278	7278	1.22	1.73	1.74	1.00
DLL2	L09730	4	2545	2545	3300	4614	461	2545	1.00	1.30	1.00	0.77
Fes	AF195021	4	2545	2545	3170	32213	3221	3221	1.00	1.25	1.27	1.02
ardA	AJ224125	4	2545	2545	2545	14751	1475	2545	1.00	1.00	1.00	1.00
achaete-scute protein homolog (ASH	M98272	4	2545	4046	3256	7782	778	2545	1.59	1.28	1.00	0.78
DNA binding protein E12	X86959	4	2545	2545	2545	4374	437	2545	1.00	1.00	1.00	1.00
sonic hedgehog	L39213	4	2545	2545	3467	18179	1818	2545	1.00	1.36	1.00	0.73
XLMO1	U84991	4	2545	3401	2545	29711	2971	2971	1.34	1.00	1.17	1.17
POU2	U17654	4	4196	6177	9638	20989	2099	2545	1.47	2.30	0.61	0.26
X-MyT1	U67078	4	2545	2545	2545	2545	255	2545	1.00	1.00	1.00	1.00
Xsal-1	L46583	4	2545	2545	2545	2545	255	2545	1.00	1.00	1.00	1.00
zic2	U57453	4	4172	5168	9561	78400	7840	7840	1.24	2.29	1.88	0.82
TFIIA	X58369	4	2545	2545	2545	2545	255	2545	1.00	1.00	1.00	1.00
TH/bZip	U37375	4	2545	2545	2545	31198	3120	3120	1.00	1.00	1.23	1.23
glucocorticoid receptor	X72211	5	2545	2545	2545	3085	308	2545	1.00	1.00	1.00	1.00
estrogen receptor	L20736	5	2545	2545	2545	2545	255	2545	1.00	1.00	1.00	1.00
vitamin D receptor	U91846	5	2545	2545	2545	2545	255	2545	1.00	1.00	1.00	1.00
tif2	AJ243119	4	6935	8667	11414	104626	10463	10463	1.25	1.65	1.51	0.92
TRIP4	AW199631	5	2545	2545	2545	2545	255	2545	1.00	1.00	1.00	1.00
TRIP7	AW200492	5	2545	2545	2545	2854	285	2545	1.00	1.00	1.00	1.00
thyroid hormone receptor alpha A	M35343	5	2545	2545	2545	2703	270	2545	1.00	1.00	1.00	1.00
thyroid hormone receptor beta A1	M35359	5	2545	2545	2545	2545	255	2545	1.00	1.00	1.00	1.00
androgen receptor alpha	U67129	5	4665	4782	4963	44870	4487	4487	1.03	1.06	0.96	0.90
mineralocorticoid receptor	U15134	5	2545	2545	2545	2683	268	2545	1.00	1.00	1.00	1.00
RXR xSRC-3	AF044080	5	2545	2545	2545	4153	415	2545	1.00	1.00	1.00	1.00
RAR beta	X87366	5	2545	2545	2545	2545	255	2545	1.00	1.00	1.00	1.00
RAR gamma B	X59396	5	2545	2545	2545	2856	286	2545	1.00	1.00	1.00	1.00
PPAR alpha	M84161	5	2545	2545	3298	9839	984	2545	1.00	1.30	1.00	0.77
PPAR beta	M84162	5	2545	2545	2545	2545	255	2545	1.00	1.00	1.00	1.00
PPAR gamma	M84163	5	2545	2545	2545	2545	255	2545	1.00	1.00	1.00	1.00
NGFI-B	X70700	4	2545	2545	2545	2545	255	2545	1.00	1.00	1.00	1.00
orphan nuclear receptor	X75163	4	2545	2545	7639	8582	858	2545	1.00	3.00	1.00	0.33
COUP transcription factor 1	AF157558	4	2545	2545	3377	22615	2261	2545	1.00	1.33	1.00	0.75
thyroid hormone receptor alpha	L06064	5	2545	2545	2545	39517	3952	3952	1.00	1.00	1.55	1.55
thyroid hormone receptor beta	L27344	5	2545	2545	2545	2608	261	2545	1.00	1.00	1.00	1.00
metastasis associated 1-like protein	AF170344	2	2545	2545	2545	5896	590	2545	1.00	1.00	1.00	1.00
recombination activation (RAG-2)	L19325	2	2545	2545	2545	2545	255	2545	1.00	1.00	1.00	1.00
methyl-CpG binding protein	AF170347	2	2545	2545	2545	4973	497	2545	1.00	1.00	1.00	1.00
replication protein A	X87240	2	2545	2545	2545	2545	255	2545	1.00	1.00	1.00	1.00
Mi-2 histone deacetylase	AF171099	2	2545	2545	2545	16534	1653	2545	1.00	1.00	1.00	1.00
mitochondrial RNA polymerase	AF200705	2	2545	2545	2545	2545	255	2545	1.00	1.00	1.00	1.00
mitotic phosphoprotein 43	U95097	2	2545	2545	2545	8853	885	2545	1.00	1.00	1.00	1.00
mitotic phosphoprotein 90	U95102	2	2545	2545	6803	34211	3421	3421	1.00	2.67	1.34	0.50
maskin	AF200212	11	2545	2545	2545	2545	255	2545	1.00	1.00	1.00	1.00
plexin	D38175	9	2545	2545	2545	13685	1369	2545	1.00	1.00	1.00	1.00
contactin/F3/F11	D86505	9	2545	2545	2545	2878	288	2545	1.00	1.00	1.00	1.00
non-muscle tropomyosin (TM-4)	L35238	9	2874	3842	8277	19128	1913	2545	1.34	2.88	0.89	0.31
coronin	AB025246	9	2545	2545	2574	3551	355	2545	1.00	1.01	1.00	0.99
kinesin central motor 1 XKCM	U36485	9	2545	2545	2545	2545	255	2545	1.00	1.00	1.00	1.00
katanin p80	AF177942	9	2545	2545	2545	13212	1321	2545	1.00	1.00	1.00	1.00
calponin H3	AF081576	9	2545	2545	2545	2737	274	2545	1.00	1.00	1.00	1.00
myelin proteolipid protein	Z19522	9	2545	2545	2545	3569	357	2545	1.00	1.00	1.00	1.00
myelin basic protein	AB000736	9	2545	2545	2545	2695	270	2545	1.00	1.00	1.00	1.00
class II beta-tubulin	X15798	9	2545	2545	2545	2818	282	2545	1.00	1.00	1.00	1.00
beta tubulin	L06232	9	2545	2545	3046	13058	1306	2545	1.00	1.20	1.00	0.84
fibronectin	M77820	9	2545	2545	2545	2545	255	2545	1.00	1.00	1.00	1.00
Xefiltin	U83711	9	2545	2545	2545	15625	1562	2545	1.00	1.00	1.00	1.00
myosin heavy chain 3	AF097906	9	2545	17545	27415	8504	850	2545	6.89	10.77	1.00	0.09
alpha skeletal actin	X03470	9	351	1139	1292	1434	1434	1434	3.25	3.68	4.09	1.11
cytoplasmic beta actin	AF079161	9	1401	2494	3135	5374	5374	5374	1.78	2.24	3.84	1.71
ribosomal protein L8	U00920	11	859	790	739	674	674	674	0.92	0.86	0.78	0.91
protein S10	S57432	11	1251	785	853	665	665	665	0.63	0.68	0.53	0.78
mitochondrial 16s ribosomal RNA	U66113	11	1186	1309	1233	2402	2402	2402	1.10	1.04	2.02	1.95
HMG-1	U21933	4	2596	2545	2545	6469	647	2545	0.98	0.98	0.98	1.00
histone H1	J00968	2	2545	2545	2545	9472	947	2545	1.00	1.00	1.00	1.00
51 KDa cytokeratin type I	Y00968	9	2545	6868	2545	2545	255	2545	2.70	1.00	1.00	1.00
epidermal type 1 keratin b1	65242	9	10143	10316	9261	3754	375	2545	1.02	0.91	0.25	0.27
alpha 1 collagen type I	AB015440	9	2807	7255	7400	30217	3022	3022	2.58	2.64	1.08	0.41
alpha 2 collagen type I	D86764	9	3982	9723	9049	31131	3113	3113	2.44	2.27	0.78	0.34
alpha-1 collagen type II	M63595	9	2545	2545	2545	29477	2948	2948	1.00	1.00	1.16	1.16
ribosomal protein L32	X55030	11	1115	696	1052	1585	2402	2402	0.62	0.94	2.15	2.28
serum retinol binding protein	J02718	5	2545	2545	2545	2545	255	2545	1.00	1.00	1.00	1.00
cellular retinoic acid binding protein	S74933	5	2545	2545	2545	3387	339	2545	1.00	1.00	1.00	1.00
thyroid hormone binding protein	U03878	5	2545	6123	9500	5646	565	2545	2.41	3.73	1.00	0.27
IFABP	L19046	7	2545	2545	2545	2545	255	2545	1.00	1.00	1.00	1.00

L-amino acid transporter-1	Y12716	7	2545	2545	2545	21462	2146	2545	1.00	1.00	1.00	1.00
chloride channel ClC-3	Y09941	7	2545	2545	2545	10594	1059	2545	1.00	1.00	1.00	1.00
chloride channel ClC-5	AF063904	7	2545	2545	3421	9412	941	2545	1.00	1.34	1.00	0.74
multidrug resistance gene	U17608	7	2545	2545	2545	8474	847	2545	1.00	1.00	1.00	1.00
importin alpha 1a	L36339	7	3371	#NUM!	#NUM!	8441						
Ca2+-binding protein frequenin	U27274	7	#NUM!	#NUM!	#NUM!	7824						
calbindin D28K	U76630	7	2545	2545	2545	2545	255	2545	1.00	1.00	1.00	1.00
adult beta-globin	J00978	7	2545	2545	2545	3519	352	2545	1.00	1.00	1.00	1.00
larval beta I globin	X03143	7	2688	9667	2545	90273	9027	9027	3.35	0.88	3.13	3.55
sodium phosphate cotransporter	L78835	7	2545	2545	2545	2545	255	2545	1.00	1.00	1.00	1.00
Na+/dicarboxylate cotransporter	U87318	7	2545	2545	3205	3297	330	2545	1.00	1.26	1.00	0.79
Na+-glucose cotransporter type I	AB008225	7	2545	2545	2545	2545	255	2545	1.00	1.00	1.00	1.00
epithelial Na+ channel alpha subunit	U23535	7	2545	2545	2545	2763	276	2545	1.00	1.00	1.00	1.00
poly A-binding protein ABP-EF	M27072	4	2545	3416	4135	2545	255	2545	1.34	1.62	1.00	0.82
nervous system-specific RNA binding	M34894	4	2545	2545	6529	5620	562	2545	1.00	2.57	1.00	0.39
Xfin	X06021	4	2545	2545	2545	11006	1101	2545	1.00	1.00	1.00	1.00
p54 mRNA binding protein	M80257	4	2545	3766	3451	47253	4725	4725	1.48	1.36	1.86	1.37
74 kDa/68 kDa serum albumin	M21442	7	2545	2545	2545	2545	255	2545	1.00	1.00	1.00	1.00
aldehyde dehydrogenase class 1	AB016718	6	2545	2545	2545	2545	255	2545	1.00	1.00	1.00	1.00
Wnt inhibitory factor-1	AF122924	3	2545	2545	2545	3129	313	2545	1.00	1.00	1.00	1.00
transferrin	X54530	7	2545	2545	2545	2545	255	2545	1.00	1.00	1.00	1.00
hnRNP I-related RNA transport prote	AF091370	4	2545	2545	2545	2586	259	2545	1.00	1.00	1.00	1.00
urea transporter	Y12784	7	2545	2545	2545	7876	788	2545	1.00	1.00	1.00	1.00
SPARC	X82483	1	2545	8005	11380	4870	487	2545	3.15	4.47	1.00	0.22
L-epinephrine transporter	U72877	7	2545	2545	2545	2545	255	2545	1.00	1.00	1.00	1.00
TIMP-2	AY037944	8	2545	2545	2545	10736	1074	2545	1.00	1.00	1.00	1.00
transthyretin	AB006134	5	2545	2545	2545	4986	499	2545	1.00	1.00	1.00	1.00
interleukin 1 beta	AJ010497	3	2545	2545	2757	2545	255	2545	1.00	1.08	1.00	0.92
NEDD 8	Not Submitted	8	2545	2545	2545	36951	3695	3695	1.00	1.00	1.45	1.45
osteogenic protein-1 homolog precu	U40034	1	2545	2545	2545	7408	741	2545	1.00	1.00	1.00	1.00
connective tissue growth factor XCT(	U43524	1	2545	2545	2545	11933	1193	2545	1.00	1.00	1.00	1.00
nerve growth factor	X55716	1	2545	2545	2545	2981	298	2545	1.00	1.00	1.00	1.00
preproneuropeptide Y	S55577	3	2545	2545	2545	2545	255	2545	1.00	1.00	1.00	1.00
neuromedin	L01530	3	2545	2545	2545	2922	292	2545	1.00	1.00	1.00	1.00
thyroid-stimulating hormone a	L07619	5	2545	2545	2545	2828	283	2545	1.00	1.00	1.00	1.00
thyrotropin-releasing hormone precu	X84056	5	2545	2545	2545	2545	255	2545	1.00	1.00	1.00	1.00
corticotropin-releasing factor	S50096	5	2545	3816	2974	44248	4425	4425	1.50	1.17	1.74	1.49
prolactin	L07620	5	2545	2545	2545	2545	255	2545	1.00	1.00	1.00	1.00
ubiquitin	M11512	8	1035	850	770	888	888	888	0.82	0.74	0.87	0.89
X Wnt-2b	U66288	3	2545	2545	2545	3120	312	2545	1.00	1.00	1.00	1.00
A5-protein	D10467	3	2545	2545	2545	12102	1210	2545	1.00	1.00	1.00	1.00
geminin H	AF067856	2	2545	2545	2545	2545	255	2545	1.00	1.00	1.00	1.00
fibroblast growth factor receptor-like	U40457	1	2545	2545	2545	4659	466	2545	1.00	1.00	1.00	1.00
FGF-3	Z25539	1	2545	2545	2545	25367	2537	2545	1.00	1.00	1.00	1.00
FGF-20	AB012615	1	2545	2545	2545	2757	276	2545	1.00	1.00	1.00	1.00
TGF-beta 2	X51817	1	2545	2545	2545	2545	255	2545	1.00	1.00	1.00	1.00
TGF-beta 5	AH005497	1	2545	2545	2545	2545	255	2545	1.00	1.00	1.00	1.00
Myf-5	X56738	4	2545	2545	2545	3115	311	2545	1.00	1.00	1.00	1.00
c-type natriuretic peptide 1	D17413	5	2545	2545	2545	7788	779	2545	1.00	1.00	1.00	1.00
thyroid-stimulating hormone beta	L07618	5	2545	2545	2545	2545	255	2545	1.00	1.00	1.00	1.00
growth hormone A	AF193797	5	2545	2545	2545	2965	297	2545	1.00	1.00	1.00	1.00
RSK2	AF165162	3	2545	2545	2545	2545	255	2545	1.00	1.00	1.00	1.00
PCNA	M34080	2	3480	5786	2545	4036	404	2545	1.66	0.73	0.73	1.00
RING finger subunit MAT	U29667	1	2545	2545	2545	2545	255	2545	1.00	1.00	1.00	1.00
Chk1 checkpoint kinase	AF117816	1	2545	2545	2545	2545	255	2545	1.00	1.00	1.00	1.00
fyn	X52188	3	2545	2545	2545	2545	255	2545	1.00	1.00	1.00	1.00
XDRP1	AB030502	1	2545	2545	2545	8004	800	2545	1.00	1.00	1.00	1.00
wee 1A kinase	U13962	1	2545	2545	2545	4678	468	2545	1.00	1.00	1.00	1.00
Mad2/Mad	L09736	4	2545	2545	2545	2545	255	2545	1.00	1.00	1.00	1.00
Mad1	L77888	1	2545	2545	2545	5299	530	2545	1.00	1.00	1.00	1.00
Mad2	L77885	1	2545	2545	2545	3253	325	2545	1.00	1.00	1.00	1.00
MAP kinase 1 (MPK1)	X59813	3	2545	2545	2545	2545	255	2545	1.00	1.00	1.00	1.00
MAP kinase 2 (MPK2)	X80751	3	2545	2545	2545	2545	255	2545	1.00	1.00	1.00	1.00
MAP kinase activator 2 (XMEK2)	Z22736	3	2545	2545	2545	33267	3327	3327	1.00	1.00	1.31	1.31
MAP kinase activator (XMEK3)	AF172848	3	2545	2545	2545	4646	465	2545	1.00	1.00	1.00	1.00
MAP kinase phosphatase	X83742	3	6052	8582	7094	45621	4562	4562	1.42	1.17	0.75	0.64
MAP kinase interacting kinase	AB023807	3	2545	2545	2669	31410	3141	3141	1.00	1.05	1.23	1.18
MAPKK	D13700	3	2545	2862	2545	30435	3044	3044	1.12	1.00	1.20	1.20
phosphoinositide 3 kinase catalytic s	AF204924	3	2545	2545	2545	2545	255	2545	1.00	1.00	1.00	1.00
casein kinase 1-alpha	Y08817	3	2545	2545	2545	2545	255	2545	1.00	1.00	1.00	1.00
casein kinase 1-epsilon	AF183394	3	2545	2545	2545	15909	1591	2545	1.00	1.00	1.00	1.00
calmodulin-dependent protein kinase	U06636	3	2545	2545	3079	3286	329	2545	1.00	1.21	1.00	0.83
protein kinase PKN	D43890	3	2545	2545	2545	2545	255	2545	1.00	1.00	1.00	1.00
PKC-related kinase 2	AF027183	3	2545	2545	2545	3736	374	2545	1.00	1.00	1.00	1.00
DNA-PK	AF001413	2	2545	2545	2545	2545	255	2545	1.00	1.00	1.00	1.00
ATM	AF174486	2	2545	2545	2545	6632	663	2545	1.00	1.00	1.00	1.00
protein phosphatase 5	AF018263	3	2545	2545	2545	2545	255	2545	1.00	1.00	1.00	1.00
guanylyl cyclase 1	AB025111	3	2545	2545	2545	3342	334	2545	1.00	1.00	1.00	1.00
guanylyl cyclase 2	AB025112	3	2545	2545	2545	2545	255	2545	1.00	1.00	1.00	1.00
cyclin A1	X53745	1	2545	2545	2545	2545	255	2545	1.00	1.00	1.00	1.00
cyclin A2	X85746	1	2545	2545	2545	2545	255	2545	1.00	1.00	1.00	1.00
cyclin B1	J03166	1	2545	2545	2545	2545	255	2545	1.00	1.00	1.00	1.00
cyclin B2	J03167	1	2545	2545	2545	2806	281	2545	1.00	1.00	1.00	1.00
cyclin D1	X89475	1	2545	2545	2545	9289	929	2545	1.00	1.00	1.00	1.00
cyclin D2	X89476	1	7165	2545	2545	2545	255	2545	0.36	0.36	0.36	1.00
cyclin E	L23857	1	2545	2545	2545	2545	255	2545	1.00	1.00	1.00	1.00
cyclin H	U20505	1	2545	2545	2545	2702	270	2545	1.00	1.00	1.00	1.00
cyclin B2	AB005253	1	2545	2545	2545	2545	255	2545	1.00	1.00	1.00	1.00
cdc2	AB005254	1	2545	2545	2545	2545	255	2545	1.00	1.00	1.00	1.00
Eg1 Ser/Thr kinase (cdc2 homolog)	X14227	1	2545	2545	2545	3427	343	2545	1.00	1.00	1.00	1.00
cdc2-related MO15	X53962	1	2545	2545	2545	2545	255	2545	1.00	1.00	1.00	1.00
cdc2 kinase homologous protein	M60680	1	2545	2545	2545	2545	255	2545	1.00	1.00	1.00	1.00
MYT1	U28931	1	2545	2545	2545	2545	255	2545	1.00	1.00	1.00	1.00
cdc7-related kinase	AF080068	1	2545	2545	2545	2545	255	2545	1.00	1.00	1.00	1.00
cdc21	U44049	1	2545	2545	2545	2545	255	2545	1.00	1.00	1.00	1.00
tyrosine phosphatase cdc25A	AF090829	1	2545	2545	2545	3043	304	2545	1.00	1.00	1.00	1.00
tyrosine phosphatase cdcC1	M96857	1	2545	2545	2545	2545	255	2545	1.00	1.00	1.00	1.00
MCM5/CDC46	U44048	1	2545	2545	3545	29265	2926	2926	1.00	1.39	1.15	0.83
cdk 4	X89477	1	2545	2545	2545	2545	255	2545	1.00	1.00	1.00	1.00
activator of cdk5	AF000951	1	2545	2545	2545	2545	255	2545	1.00	1.00	1.00	1.00
cdk inhibitor p28	U38844	1	2545	3976	2545	57415	5742	5742	1.56	1.00	2.26	2.26
cdk inhibitor	U24434	1	2545	3774	2545	5780	578	2545	1.48	1.00	1.00	1.00
p33 ringo (fis26)	AJ133499	1	2545	2545	2545	20539	2054	2545	1.00	1.00	1.00	1.00
calcium/calmodulin-dependent protei	AF233633	3	2545	2545	2545	2823	282	2545	1.00	1.00	1.00	1.00
protein phosphatase-2A B'epsilon	AF298157	3	2545	2545	2545	2545	255	2545	1.00	1.00	1.00	1.00
serotonin receptor	U10161	5	2545	2545	2545	2986	299	2545	1.00	1.00	1.00	1.00
muscle nicotinic acetylcholine recept	U04618	3	2545	2545	2545	4286	429	2545	1.00	1.00	1.00	1.00
prolactin receptor A	AF193800	5	2545	2545	2545	2545	255	2545	1.00	1.00	1.00	1.00
neurotrophic factor BDNF receptor	S69713	3	2545	2545	2545	7811	781	2545	1.00	1.00	1.00	1.00
lysophosphatidic acid receptor	AJ240844	3	2545	2545	2545	3007	301	2545	1.00	1.00	1.00	1.00
pituitary adenylate cyclase-activating	AF187878	3	2545	2545	2545	2545	255	2545	1.00	1.00	1.00	1.00
luteinizing hormone receptor	AJ249845	5	2545	2545	2545	2545	255	2545	1.00	1.00	1.00	1.00
inositol 1,4,5-trisphosphate receptor	D14400	3	2545	2545	2545	2545	255	2545	1.00	1.00	1.00	1.00
BMP receptor	D32066	3	2545	2545	2545	2545	255	2545	1.00	1.00	1.00	1.00
frizzled 2	AF139165	3	2545	2545	2545	2545	255	2545	1.00	1.00	1.00	1.00
cadherin precursor	AF002983	9	2545	2545	3270	5077	508	2545	1.00	1.28	1.00	0.78
NPY/PYY Receptor Y1	L25416	3	2545	2545	2545	2545	255	2545	1.00	1.00	1.00	1.00
muscle acetylcholine receptor a	X07067	3	2545	2545	2545	2545	255	2545	1.00	1.00	1.00	1.00
acetylcholine receptor alpha subunit	X17244	3	2545	2545	2545	2545	255	2545	1.00	1.00	1.00	1.00
activin receptor	S70930	1	2545	2545	2545	2545	255	2545	1.00	1.00	1.00	1.00
Ftz-F1-related orphan receptor A	U05001	4	2545	2545	2545	2545	255	2545	1.00	1.00	1.00	1.00
fibroblast growth factor receptor 1	M55163	1	2545	2545	2545	2545	255	2545	1.00	1.00	1.00	1.00
Pagliaccio receptor tyrosine kinase	L26099	3	2545	2545	2545	29358	2936	2936	1.00	1.00	1.15	1.15
angiotensin II receptor	S73368	3	2545	2545	2545	2545	255	2545	1.00	1.00	1.00	1.00
angiotensin receptor related protein	U72029	3	2545	2545	2545	2545	255	2545	1.00	1.00	1.00	1.00
activated protein kinase C	AF105259	3	28332	23500	25547	18977	1898	2545	0.83	0.90	0.09	0.10
5-HT1A receptor	Y07901	3	2545	2545	2545	5702	570	2545	1.00	1.00	1.00	1.00
14-3-3 protein	M86928	3	2545	2545	2545	2545	255	2545	1.00	1.00	1.00	1.00
ALK-2 receptor	AF012245	3	2545	2545	2545	2545	255	2545	1.00	1.00	1.00	1.00
adenosine A1 receptor (a1R gene)	AJ249842	3	2545	2545	2545	2545	255	2545	1.00	1.00	1.00	1.00
CRF receptor type1	Y14036	5	2545	2545	2545	4191	419	2545	1.00	1.00	1.00	1.00
VIP/pituitary cAMP receptor	AF100644	3	2545	2545	2545	4667	467	2545	1.00	1.00	1.00	1.00
dihydropyrimidine receptor	AF037625	3	2545	4268	3591	7229	723	2545	1.68	1.41	1.00	0.71
follicle stimulating hormone receptor	AJ249846	5	2545	2545	2545	2743	274	2545	1.00	1.00	1.00	1.00
CRF receptor type 2	Y14037	5	2545	2545	2545	8173	817	2545	1.00	1.00	1.00	1.00
insulin receptor substrate protein xIR	AF297960	5	2545	2545	2545	2545	255	2545	1.00	1.00	1.00	1.00
natriuretic peptide receptor type C	AF231035	5	2545	2545	2545	2545	255	2545	1.00	1.00	1.00	1.00
XICE-a	D89783	8	2545	2545	2545	3160	316	2545	1.00	1.00	1.00	1.00
CPP32	D89784	8	2545	2545	2545	2545	255	2545	1.00	1.00	1.00	1.00
calpastatin 1	AJ243713	8	2545	2545	2545	7509	751	2545	1.00	1.00	1.00	1.00
caspase7-precursor	AW199521	8	2545	2545	2545	10477	1048	2545	1.00	1.00	1.00	1.00
bcl-2-like R11	X82461	8	2545	2545	3505	57739	5774	5774	1.00	1.38	2.27	1.65
scythe	AF098511	8	2545	2545	2545	5692	569	2545	1.00	1.00	1.00	1.00
survivin	AW198821	8	2545	2545	2545	2545	255	2545	1.00	1.00	1.00	1.00
requiem	AB021737	8	2545	2545	2669	20336	2034	2545	1.00	1.05	1.00	0.95
p21-activated kinase (PAK1)	AF000239	3	2545	2545	2545	17104	1710	2545	1.00	1.00	1.00	1.00
DAD-1	D15059	8	2869	4716	7429	2545	255	2545	1.64	2.59	0.89	0.34
caspase-2	AB038168	8	2545	2545	2545	2545	255	2545	1.00	1.00	1.00	1.00
caspase-6	AB038169	8	2545	2545	7887	4495	449	2545	1.00	3.10	1.00	0.32
caspase-7	AB038170	8	2545	2545	4092	11127	1113	2545	1.00	1.61	1.00	0.62
caspase-8	AB038171	8	2545	2545	2545	2545	255	2545	1.00	1.00	1.00	1.00
caspase-9	AB038172	8	2545	2545	2545	29055	2905	2905	1.00	1.00	1.14	1.14
caspase-10	AB038173	8	2545	2545	2545	2873	287	2545	1.00	1.00	1.00	1.00
metalloprotease-disintegrin (MDC11a	AF032384	8	2545	2545	2545	3775	378	2545	1.00	1.00	1.00	1.00
metalloproteinase (XMMP)	U82541	8	2545	2545	2545	5153	515	2545	1.00	1.00	1.00	1.00
membrane anchored metalloprotease	U78185	8	2545	2545	2545	2545	255	2545	1.00	1.00	1.00	1.00
metalloprotease-disintegrin (MDC11b	AF032383	8	2545	2545	2545	2545	255	2545	1.00	1.00	1.00	1.00
pancreatic trypsin	X53458	8	2545	2545	2545	7135	714	2545	1.00	1.00	1.00	1.00

trypsinogen	U72330	6	2545	2545	2545	24349	2435	2545	1.00	1.00	1.00	1.00
serine protease (Csp1)	AF029404	6	2545	2545	2545	2861	286	2545	1.00	1.00	1.00	1.00
stromelysin-3	Z27093	8	2545	2545	2545	2545	255	2545	1.00	1.00	1.00	1.00
alpha-aspartyl dipeptidase	U37377	8	2545	2545	3747	2719	272	2545	1.00	1.47	1.00	0.68
xepsin	AB018694	3	2545	2545	2545	5027	503	2545	1.00	1.00	1.00	1.00
alpha-1 antiproteinase	AB014091	8	2545	2545	2545	2545	255	2545	1.00	1.00	1.00	1.00
carbamyl phosphate synthetase	U05193	6	2545	2545	2545	2545	255	2545	1.00	1.00	1.00	1.00
ornithine transcarbamylase	D38304	6	2545	2545	2545	2545	256	2545	1.00	1.00	1.00	1.00
ornithine decarboxylase	X56316	6	2545	2545	2545	13383	1338	2545	1.00	1.00	1.00	1.00
lactate dehydrogenase B	U07176	6	19692	17696	21524	26862	2686	2686	0.90	1.09	0.14	0.12
GAPDH	U41753	6	464	663	666	811	811	811	1.43	1.43	1.75	1.22
gelatinase B (MMP-9)	AF072455	8	2545	2545	13069	2545	255	2545	1.00	5.13	1.00	0.19
NM23/nucleoside diphosphate kinase	X97899	2	1559	1491	1673	2356	2356	2356	0.96	1.07	1.51	1.41
Nr1	D86491	6	2545	2545	2545	2545	255	2545	1.00	1.00	1.00	1.00
Na+/K+ transporting ATPase beta su	M37788	7	2545	2545	2915	2545	255	2545	1.00	1.15	1.00	0.87
SERCa1 fast skeletal muscle	X63009	3	2545	5648	10214	8681	868	2545	2.22	4.01	1.00	0.25
E2 ubiquitin conjugating enzyme (Ub	U88561	8	2545	2545	3253	2545	255	2545	1.00	1.28	1.00	0.78
metallothionein	M96720	7	2545	2545	3295	4357	436	2545	1.00	1.29	1.00	0.77
iodothyronine deiodinase type II	L42815	5	2566	2545	14078	8744	874	2545	0.99	5.49	0.99	0.18
iodothyronine 5'-deiodinase III	L28111	5	4254	5687	7988	28351	2835	2835	1.34	1.88	0.67	0.35
retinoic acid converting enzyme	AF057566	5	2545	2545	6502	6010	601	2545	1.00	2.55	1.00	0.39
FCP1 serine phosphatase	AJ132385	4	2545	2545	2545	6205	620	2545	1.00	1.00	1.00	1.00
protein phosphatase 1-gamma 1	L17039	1	2545	2545	2545	2545	255	2545	1.00	1.00	1.00	1.00
convertase PC2	X86493	5	2545	2545	3507	5631	563	2545	1.00	1.38	1.00	0.73
aconitase	AF186471	6	2545	2545	2545	9068	907	2545	1.00	1.00	1.00	1.00
phospholipase C-gamma-1a	AF090111	3	2545	2545	3241	12645	1264	2545	1.00	1.27	1.00	0.79
Cu/Zn SOD	X16585	6	4686	6430	6802	4495	450	2545	1.37	1.45	0.54	0.37
collagenase-4 precursor	L76275	8	2545	2545	2545	2545	255	2545	1.00	1.00	1.00	1.00
cytochrome P-450 (11beta, aldo)	D10984	6	2545	2545	2545	18069	1807	2545	1.00	1.00	1.00	1.00
mitochondrial cytochrome c oxidase	M10217	8	3767	12883	17806	15868	1587	2545	3.42	4.73	0.68	0.14
alcohol dehydrogenase class 1 (ADH	AF059255	6	2545	2545	2545	2545	255	2545	1.00	1.00	1.00	1.00
alcohol dehydrogenase class 4 (ADH	AF059256	6	2545	2545	2545	2646	265	2545	1.00	1.00	1.00	1.00
adenyl cyclase	Z46958	3	2545	2545	2545	3069	307	2545	1.00	1.00	1.00	1.00
fibroblast activation factor alpha	U41856	1	2545	#NUM!	#NUM!	2990	299	2545			1.00	
aldolase C	3028510	6	2545	2545	2716	3348	335	2545	1.00	1.07	1.00	0.94
2',3'-cyclic-nucleotide 3'-phosphodie	AB002145	9	2545	2545	2545	2545	255	2545	1.00	1.00	1.00	1.00
arginase	D38303	6	2545	3215	6718	15098	1510	2545	1.26	2.64	1.00	0.38
arginase 1	U08406	6	2545	2545	2545	36087	3609	3609	1.00	1.00	1.42	1.42
argininosuccinate lyase	D38302	6	2545	2545	2545	2545	255	2545	1.00	1.00	1.00	1.00
ATPase Na+/K+ pump alpha 1 subur	U49236	8	2545	2545	2545	3422	342	2545	1.00	1.00	1.00	1.00
ADP-ribosylation factor (ARF1)	U31350	6	2545	2545	2545	2545	255	2545	1.00	1.00	1.00	1.00
allantoicase	AF153230	6	2545	2545	3121	4439	444	2545	1.00	1.23	1.00	0.82
exonuclease Exo1	AF134570	2	2545	2545	2545	2545	255	2545	1.00	1.00	1.00	1.00
deoxyribonuclease gamma	AF059612	2	2545	2545	2545	2545	255	2545	1.00	1.00	1.00	1.00
DNA polymerase beta	Y15732	2	2545	2545	3301	2737	274	2545	1.00	1.30	1.00	0.77
ligase I	L43496	2	2545	2545	3431	2545	255	2545	1.00	1.35	1.00	0.74
ATP-dependent RNA helicase	X57328	4	2545	2545	2545	2550	255	2545	1.00	1.00	1.00	1.00
cytosine-5-methyltransferase	D78638	2	2545	2545	2545	5552	555	2545	1.00	1.00	1.00	1.00
flap endonuclease 1 (FEN1)	U64563	2	2545	2545	2545	11791	1179	2545	1.00	1.00	1.00	1.00
terminal deoxynucleotidyl transferas	U07803	2	2545	2545	2545	2679	268	2545	1.00	1.00	1.00	1.00
gelatinase A	AY037943	8	2545	2545	2545	2545	255	2545	1.00	1.00	1.00	1.00
liver helicase	AF302423	4	2545	9813	4610	2545	255	2545	3.86	1.81	1.00	0.55
aldolase B	AB030822	6	2545	2545	6521	22799	2280	2545	1.00	2.56	1.00	0.39
cytochrome b	M10217	8	2545	2809	2545	2545	255	2545	1.10	1.00	1.00	1.00
aromatase p450	AB031278	5	2545	2545	2545	2545	255	2545	1.00	1.00	1.00	1.00
NEDD 4	AJ000085	8	2545	2545	2545	9629	963	2545	1.00	1.00	1.00	1.00
ring finger protein	U63817	1	2545	2545	2545	4629	463	2545	1.00	1.00	1.00	1.00
REST	AF096301	4	2545	2545	2545	2545	255	2545	1.00	1.00	1.00	1.00
MCM2	U44047	1	3024	2545	2545	8959	896	2545	0.84	0.84	0.84	1.00
proteasome subunit Y	D87689	6	161	169	245	623	623	623	1.05	1.52	3.87	2.54
transmembrane protein containing a	X83962	10	2545	2545	2545	2545	255	2545	1.00	1.00	1.00	1.00
OTX5b	AJ251846	4	2545	2545	2545	21218	2122	2545	1.00	1.00	1.00	1.00
13S condensin XCAP-D2	AF067969	2	2545	2545	2545	2552	255	2545	1.00	1.00	1.00	1.00
chaperonin subunit CCT gamma	U37062	7	2545	2545	2545	3352	335	2545	1.00	1.00	1.00	1.00
HMG-X	D30765	2	2545	2545	2948	2854	285	2545	1.00	1.16	1.00	0.86
GSK-3 binding protein	AF062738	3	2603	3826	7502	29261	2926	2926	1.47	2.88	1.12	0.39
cartilage homeoprotein 1	U15276	4	2545	2545	#NUM!	7941	794	2545	1.00		1.00	
beta-amyloid precursor protein	S52417	9	2545	2545	8323	9333	933	2545	1.00	3.27	1.00	0.31
frizzled 7	AF159106	3	2789	4853	7868	64802	6480	6480	1.73	2.81	2.32	0.82
calcineurin A	AF019569	3	#NUM!	#NUM!	#NUM!	2545						
BMP1	L12249	6	2545	2545	2545	2839	284	2545	1.00	1.00	1.00	1.00
BMP1b	Y09880	6	2545	2545	2545	2545	255	2545	1.00	1.00	1.00	1.00
BMP4	AF058764	3	2545	2545	2545	2545	255	2545	1.00	1.00	1.00	1.00
18S ribosomal	X04025	11	238	218	317	673	673	673	0.92	1.34	2.85	2.13
18S ribosomal	X04025	11	2545	2545	2545	7363	736	2545	1.00	1.00	1.00	1.00
MCM3	U26057	1	2545	2545	2545	2545	255	2545	1.00	1.00	1.00	1.00
MAM domain protein	U37376	10	12658	13262	21910	8051	805	2545	1.05	1.73	0.20	0.12
XPACx1	D31894	2	2545	2545	2545	2739	274	2545	1.00	1.00	1.00	1.00
nuclear factor 7	S84515	4	2545	2545	2545	4352	435	2545	1.00	1.00	1.00	1.00
vitellogenin	85210	6	2825	4941	5428	65537	6554	6554	1.75	1.92	2.32	1.21
hsp30B	X02512	7	2545	2545	3889	2961	296	2545	1.00	1.53	1.00	0.65
hsp 30	U44894	7	52	107	1106	371	371	371	2.07	21.44	7.20	0.34
integrin alpha-1	U44025	9	2545	2545	2545	2545	255	2545	1.00	1.00	1.00	1.00
gene 5	U37373	10	2545	2545	2545	2545	255	2545	1.00	1.00	1.00	1.00
fos-related antigen-2	U37374	4	2545	2545	2545	2952	295	2545	1.00	1.00	1.00	1.00
gene 12	U41854	10	2545	2545	2545	2859	286	2545	1.00	1.00	1.00	1.00
gene 16	U41857	10	2545	3233	9407	32209	3221	3221	1.27	3.70	1.27	0.34
gene 17	U41860	10	2545	2545	2545	2545	255	2545	1.00	1.00	1.00	1.00
gene 18	U41839	10	2545	2545	2545	2545	255	2545	1.00	1.00	1.00	1.00
gene 19	U41861	10	2545	2545	2545	2545	255	2545	1.00	1.00	1.00	1.00
gene 20	U46575	10	2545	2545	2545	10057	1006	2545	1.00	1.00	1.00	1.00
regulator for chromosome condensa	D00679	2	2545	3856	2545	53551	5355	5355	1.52	1.00	2.10	2.10
proteasome subunit XC3	S51111	8	3337	4781	8605	5560	556	2545	1.43	2.58	0.76	0.30
B-50/GAP 43	X87582	1	2545	3581	3477	40131	4013	4013	1.41	1.37	1.58	1.15
fragile mental retardation protein 1	U25164	4	2545	2545	2545	2545	255	2545	1.00	1.00	1.00	1.00
forkhead protein lens1	AF188464	4	2545	2545	2545	6132	613	2545	1.00	1.00	1.00	1.00
ER1	AF015454	4	2545	2545	2545	2724	272	2545	1.00	1.00	1.00	1.00
B-cell translocation protein 1 (btg1)	AB028243	4	2545	2545	2545	3673	367	2545	1.00	1.00	1.00	1.00
SIP 1	AF027151	4	2545	2907	3561	21585	2159	2545	1.14	1.40	1.00	0.71
beta-A1-1 crystallin	X87759	9	2545	2545	2545	2545	255	2545	1.00	1.00	1.00	1.00
gamma-M1-1 crystallin	X86072	9	2545	2545	2545	2545	255	2545	1.00	1.00	1.00	1.00
SF-1/Ad4BP	AB017352	4	2545	2545	2545	80650	8065	8065	1.00	1.00	2.38	2.38
fibronectin intron 1	AF061058	control	2545	2545	8245	2545	255	2545	1.00	3.63	1.00	0.28
alpha tubulin intron 1	65164	control	2545	2545	2545	2545	255	2545	1.00	1.00	1.00	1.00
alpha tubulin	X07046	9	2545	2545	2765	2545	255	2545	1.00	1.09	1.00	0.92
delta tubulin	AF430839	9	2545	2545	2545	2545	255	2545	1.00	1.00	1.00	1.00
desmin	X16842	9	2545	2545	2545	2545	255	2545	1.00	1.00	1.00	1.00
gamma fibrinogen precursor	J02894	9	2545	2545	2545	2545	255	2545	1.00	1.00	1.00	1.00
ribonucleotide reductase submit M1	AF168794	9	2545	2545	2545	2545	255	2545	1.00	1.00	1.00	1.00

Appendix 2.7. 24 h set T_3-responsive genes variance analysis (VA).

Gene Name	GenBank Accession #	Functional Code	estimated SD D/D 24h	estimated SD D/G 24h	D/D #1 Mean	#3 Mean	#4 Mean	#4 Median	D/G #5 Mean	#7 Mean	#8 Mean	#8 Median
myosin heavy chain 3	AF097906	9	3.27	0.90	2545	10862	2545	2545	2545	17903	18578	17903
alpha skeletal actin	X03470	9	0.95	0.62	274	810	567	567	1069	1416	749	1069
alpha 1 collagen type I	AB015440	9	0.00	0.67	2545	2545		2545	2545	5779	4814	4814
alpha 2 collagen type I	D88764	9	0.17	0.99	3008	2545		2776	2545	7547		5046
SPARC	X62483	1	0.00	0.00	2545	2545	2545	2545	2545	2545	2545	2545
MAP kinase phosphatase	X83742	3	0.55	3.50	16787	11447	20705	16787	2545	15064	3575	3575
cyclin D2	X89476	1	1.40	0.00	14401	2545		8473	2545	2545	2545	2545
activated protein kinase C	AF105259	3	0.29	2.62	30494	28081	36937	30494	2545	21359	58400	21359
lactate dehydrogenase B	U07176	6	0.56	2.54	27935	27122	42873	27935	2545	14344	39033	14344
gelatinase B (MMP-9)	AF072455	8	0.00	0.00	2545	2545	2545	2545	2545	2545	2545	2545
mitochondrial cytochrome c oxidase subunit I	M10217	6	3.21	0.98	10714	2545	2545	2545	2545	6898	4461	4461
arginase	D38303	6	1.71	0.59	5524	13551	4102	5524	2545	4058	2545	2545
proteasome subunit Y	D87689	8	8.26	0.68	161	21	-14	21	196	231	97	196
GSK-3 binding protein	AF062738	3	0.00	0.40	2545	2545	2545	2545	2545	3924	3444	3444
hsp 30	U44894	7	2.14	1.03	5	17	42	17	156	107	46	107
proteasome subunit XC3	S51111	8	0.75	3.19	9890	2545	9854	9854	2545	3843	14792	3843

Gene Name	GenBank Accession #	Functional Code	estimated SD T3/D 24h	estimated SD T3/G 24h	T3/D #9 Mean	#10 Mean	#11 Mean	#11 Median	T3/G #13 Mean	#15 Mean	#16 Mean	#16 Median
myosin heavy chain 3	AF097906	9	0.45	3.41	8539	5591	6620	6620	18464	9219	72122	18464
alpha skeletal actin	X03470	9	0.49	0.62	1367	1436	772	1367	670	1431	1227	1227
alpha 1 collagen type I	AB015440	9	1.12	0.92	5530	4577	10798	5530	70303	54233	20583	54233
alpha 2 collagen type I	D88764	9	0.81	1.35	6247	5058	10123	6247	69244	11080	43155	43155
SPARC	X62483	1	0.73	2.93	10759	5007		7883	26002	5072	7132	7132
MAP kinase phosphatase	X83742	3	0.80	1.45	8719	7398	14397	8719	99111	32810	45736	45736
cyclin D2	X89476	1	0.00	0.55	2545	2545	2545	2545		4457	2545	3501
activated protein kinase C	AF105259	3	0.48	0.12	18055	11347	13834	13834	42762	39762	44967	42762
lactate dehydrogenase B	U07176	6	0.36	1.01	13176	11235	15954	13176	53111	99583	45837	53111
gelatinase B (MMP-9)	AF072455	8	0.88	1.41	7923	8971	15785	8971	12106	4882	5131	5131
mitochondrial cytochrome c oxidase subunit I	M10217	6	0.96	8.83	7235	5539	12509	7235	2545	2545	25029	2545
arginase	D38303	6	1.03	0.55	14447	7862	22707	14447		9497	16724	13111
proteasome subunit Y	D87689	8	0.43	0.64	136	199	147	147	1292	1038	630	1038
GSK-3 binding protein	AF062738	3	1.07	0.92	2545		8421	5483	59103		21840	40471
hsp 30	U44894	7	0.63	0.47	873	942	395	873	489	601	369	489
proteasome subunit XC3	S51111	8	0.68	0.85	4205	4335	7169	4335	9277	6284	14202	9277

Appendix 2.8. 48 h set T_3-responsive genes variance analysis.

Gene Name	GenBank Accession #	Functional Code	estimated SD D/D 48h	estimated SD D/G 48h	D/D 48h #17 Mean	48h #19 Mean	48h #20 Median	D/G 48h #21 Mean	48h #22 Mean	48h #24 Median
raf serl/thr kinase	X12948	3	0.00	0.99	2545	2545	2545	6071	3574	3574
C/EBP -	S44193	4	1.62	0.52	2545	2797	7062	4789	4069	6567
nuclear factor I-C1	L43149	4	0.40	0.59	2545	3854	4089	4496	3154	2629
RNA pol I transcription factor UBF	X57561	4	1.34	0.35	2573	2545	5994	3689	3230	3154
brain factor 1	AF010387	4	1.56	0.50	2545	2702	6762	2702	4121	3230
NK-2 homolog	S65507	4	0.41	0.31	2545	2702	6762	2702	4121	5750
DLL4	L09728	4	1.64	0.00	2611	2545	6821	2611	3418	4021
POU2	U17654	4	1.73	0.28	2545	2545	2545	3579	3669	5061
zic2	U57453	4	2.09	0.26	4196	2731	10006	4196	5671	6110
mitotic phosphoprotein 90	U95102	2	1.24	0.26	3482	2545	9805	3482	6081	7404
myosin heavy chain 3	AF097906	9	0.15	0.72	2545	2545	5701	2545	4675	5378
alpha skeletal actin	X03470	9	0.40	0.39	2545	2922	2545	2545	3301	2545
cytoplasmic beta actin	AF079161	9	0.39	0.24	287	428	351	25947	13382	17545
alpha 1 collagen type I	AB015440	9	0.86	0.88	2545	1190	1715	1483	1042	1133
alpha 2 collagen type I	D88764	9	0.64	0.29	2545	2807	4972	2807	12827	7201
thyroid hormone binding protein	U03878	5	0.00	0.51	2545	2545	2545	2814	2230	2417
SPARC	X62483	1	0.74	0.02	2545	2545	2545	11269	8613	6464
cyclin D2	X89476	1	1.33	0.00	3092	12589	7165	7596	4487	7201
DAD-1	D15059	8	1.33	0.00	2869	2545	6352	2545	8092	9068
caspase-6	AB038169	8	0.78	0.26	2545	2545	4523	2869	5215	6042
gelsolinase B (MMP-9)	AF072455	8	0.00	0.00	2545	2545	2545	2545	5215	3998
SERCa1 fast skeletal muscle	X63069	3	0.00	0.67	2545	2545	2545	2545	2545	4606
iodothyronine deiodinase type II	L42815	5	0.36	0.39	2833	2545	3552	2545	2545	2545
retinoic acid converting enzyme	AF057566	5	0.00	0.00	2545	2545	2545	2545	2545	2545
mitochondrial cytochrome c oxidase subunit I	M10217	6	3.07	0.66	3767	2545	14112	3767	12510	12064
arginase	D78303	6	1.22	0.46	2545	2545	5647	2545	4053	20263
aldolase B	AB030822	6	0.00	0.15	2545	2545	2545	2933	2545	2545
frizzled 7	AF159106	3	2.37	0.25	2799	2545	9191	2799	4020	5298
hsp 30	U44894	7	1.78	0.78	23	52	115	52	107	112
proteasome subunit XC3	S51111	8	3.11	0.23	3337	2580	12943	3337	4423	5555

Gene Name	GenBank Accession #	Functional Code	estimated SD T3/D 48h	estimated SD T3/G 48h	T3/D 48h #27 Mean	48h #28 Median	T3/G 48h #29 Mean	48h #31 Mean	48h #32 Median
raf ser/thr kinase	X12948	3	1.21	0.00	5963	13165	5963	4699	4699
C/EBP	S44193	4	1.21	47.48	4814	10628	4814	2545	123386	2545
nuclear factor I-C1	L43149	4	1.21	21.59	4982	11000	4982	4251	3464	95259	4251
RNA pol I transcription factor UBF	X57561	4	1.21	0.71	4459	9845	4459	3849	7740	9308	7740
brain factor 1	AF010387	4	1.06	1.77	5041	11129	5750	85288	19413	170472	85288
NK-2 homolog	S65507	4	1.21	0.75	9993	4526	12488	3894	15208	12488
DLL4	L09728	4	1.21	1.51	4135	9128	4135	40005	10721	70998	40005
POU2	U17654	4	1.21	1.88	13662	6188	13300	6024	78400	6490	20989	20989
zic2	U57453	4	1.21	1.53	6024	13300	6024	78400	4783	124795	78400
mitotic phosphoprotein 90	U95102	2	1.21	1.75	4376	9662	4376	34211	4901	64720	34211
myosin heavy chain 3	AF097906	9	1.19	2.76	17255	38097	17545	2545	28757	9504	9504
alpha skeletal actin	X03470	9	0.53	0.63	1623	1027	1133	1636	1434	732	1434
cytoplasmic beta actin	AF079161	9	0.00	0.37	3165	3174	3165	4428	4105	6095	5428
alpha 1 collagen type I	AB015440	9	0.82	2.20	4878	10769	7201	30217	6881	73277	30217
alpha 2 collagen type I	D88764	9	0.76	1.04	5712	12611	9068	29741	31131	62062	31131
thyroid hormone binding protein	U03878	5	1.20	1.20	6004	13256	6042	5646	4558	11307	5646
SPARC	X62483	1	1.13	0.40	7492	16540	8016	4870	7194	5784	5784
cyclin D2	X89476	1	0.00	2.54	2545	2545	2545	2545	2545	9019	2545
DAD-1	D15059	8	1.21	0.00	4822	10646	4822	2545	2545	2545	2545
caspase-6	AB038169	8	1.21	0.12	5081	11217	5081	8184	2916	2545	5082	4495	4788
gelsolinase B (MMP-9)	AF072455	8	1.21	0.15	8184	18069	8184	6530	2545	2545	2545
SERCa1 fast skeletal muscle	X63069	3	1.21	0.97	6530	14418	6530	6316	18155	12235
iodothyronine deiodinase type II	L42815	5	1.21	0.62	9365	20677	9365	5245	9972	7609
retinoic acid converting enzyme	AF057566	5	1.21	1.33	4118	9092	4118	6010	2994	10994	6010
mitochondrial cytochrome c oxidase subunit I	M10217	6	1.08	2.03	11198	24724	12510	15868	34817	2545	15868
arginase	D78303	6	1.21	5.31	4219	9314	4177	12781	75711	7902	12781
aldolase B	AB030822	6	1.21	1.10	4177	9221	4177	24103	12603	39154	24103
frizzled 7	AF159106	3	1.13	0.59	4952	10933	5298	47819		87552	67685
hsp 30	U44894	7	7.23	2.08	268	2203	268	371	48	820	371
proteasome subunit XC3	S51111	8	1.21	4.52	5384	11887	5384	4078	22537	4085