

# Mapping reelin in the gastrointestinal tract: A chemistry-informed approach to colorectal cancer

Hailey Abbott<sup>1</sup>, Sophie Thom<sup>2</sup>, Hector J. Caruncho<sup>2</sup>, Violeta Iosub<sup>1</sup>



1. Department of Chemistry, University of Victoria, Victoria, B.C. Canada  
2. Division of Medical Sciences, University of Victoria, Victoria, B.C. Canada

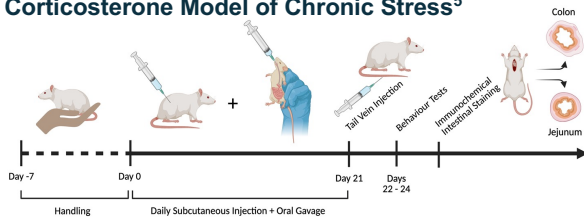
## INTRODUCTION

- Colorectal cancer is the **4<sup>th</sup> most common** cancer worldwide<sup>1</sup>
- Compromised intestinal integrity may be linked to colorectal cancer onset<sup>2</sup>
- Corticosterone (CORT) is a **glucocorticoid stress hormone** used in animal models of chronic stress<sup>3</sup>
- Chronic stress reduces intestinal reelin expression, suggesting a contribution to disrupted gut barrier integrity<sup>3</sup>
- Reelin** is a glycoprotein proposed to be involved in **gut barrier renewal**<sup>3,4</sup>
- Reelin could be a **biomarker** for colon pathology progression, and its repression favours the development of colorectal cancer<sup>4</sup>
- Previous research has explored CORT-induced changes in reelin expression in the small intestine<sup>3</sup>, but not in the large intestine, despite potential implications for colorectal cancer development

**Objective:** To evaluate and compare reelin-immunoreactive (IR) cell density in the small and large intestine in an animal model of chronic stress

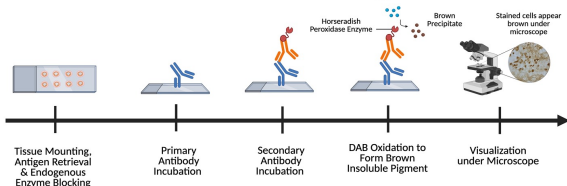
## METHODS

### Corticosterone Model of Chronic Stress<sup>5</sup>



**Figure 1.** Animal care procedure carried out before tissue processing; 12 Long-Evans rats underwent 21 consecutive days of subcutaneous CORT or vehicle injections and daily oral gavage. The rats then received a tail-vein injection and were subjected to behavioural testing as part of a larger study, before being sacrificed for immunohistochemical tissue analysis.

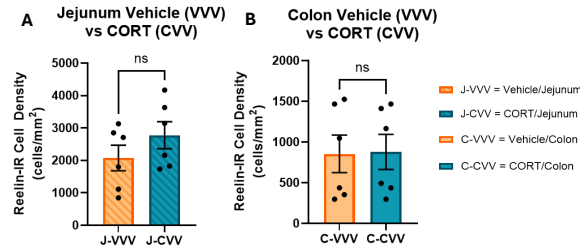
### Immunohistochemical Staining of Jejunum and Colon<sup>5</sup>



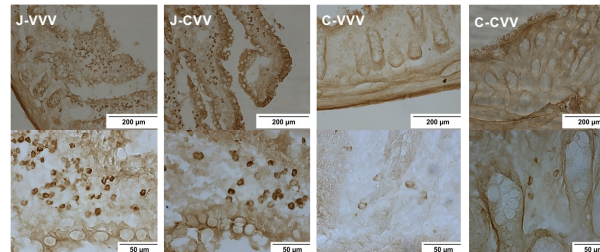
**Figure 2.** Immunohistochemistry staining procedure using the oxidation of 3,3'-diaminobenzidine (DAB) as a chromogen to visualize reelin-IR cells. Detection chemistry shown on top right panel.

## RESULTS

### 1. CORT treatment did not significantly alter reelin-IR cell density

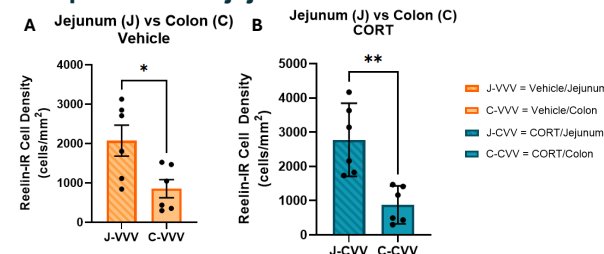


**Figure 3.** CORT treatment did not significantly alter the reelin-IR cell density in the jejunum (A) or the colon (B). Reelin-IR cells were quantified using an unbiased optical fractionator method at 20x magnification. All data are expressed as mean  $\pm$  SEM; ns = no significant difference.



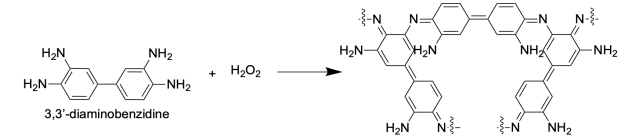
**Figure 4.** Representative photomicrographs (20X and 63X magnification) of Reelin-IR cell populations in cross-sections of rat jejunum and colon, stained via DAB immunohistochemistry. J-VVV = vehicle/jejunum, J-CVV = CORT/jejunum, C-VVV = vehicle/colon, C-CVV = CORT/colon

### 2. Expression of reelin is reduced in the colon, compared to the jejunum



**Figure 5.** Density of reelin-IR cells is lower in colon compared to jejunum in both vehicle (A) and CORT (B) groups. Reelin-IR cells were quantified using an unbiased optical fractionator method at 20x magnification. All data are expressed as mean  $\pm$  SEM; \* =  $p < 0.05$ , \*\* =  $p < 0.01$

## CHEMISTRY OF DAB STAINING



**Figure 6.** Horseradish peroxidase catalyzed oxidation of 3,3'-diaminobenzidine (DAB) by H<sub>2</sub>O<sub>2</sub> to a brown, insoluble polymer used to visualize and identify reelin-IR cells for counting

## DISCUSSION

Reelin-IR cell density is lower in the colon than in the jejunum, suggesting regional differences in gut barrier renewal capacity along the intestinal tract. Reduced reelin-induced repair of damaged or nonfunctional cells in the colon could contribute to the high prevalence of colorectal cancers.

CORT treatment was not associated with a decrease in reelin-IR cell density. Treatment via oral gavage or a small sample size may explain the differing findings from previous studies.

### Future Directions

Quantify changes in reelin expression independent of reelin-IR cell density using Western blot techniques

Measure markers of cell proliferation and inflammation in the colon to determine the functional effects of decreased reelin on gut barrier integrity

Measure reelin-IR cell density in colorectal cancer tissue to explore links between tumour development and reelin levels

Assess the impacts of exogenous reelin administration on reelin-IR cell density in the colon in chronic stress (CORT) conditions

## REFERENCES

- Ravita, P.; Surikara, T.; Barsouk, A. Epidemiology of Colorectal Cancer: Incidence, Mortality, Survival, and Risk Factors. *Gastroenterology Rev* 2019, 14 (2), 89–103. <https://doi.org/10.4137/GTR.41079>
- Gandhi, H.; Sood, P.; Li, Y.; Wang, F.; Hui, P.; Daniel, N.; Doherty, G.; Hughes, D. J. Association of Circulating Protein Biomarkers of Gut Barrier Integrity and Inflammation with Colorectal Adenomas and Colorectal Cancers. *Dig Dis Sci* 2025. <https://doi.org/10.1007/s12029-025-03603-y>
- Halvorsen, C. S.; Sánchez-Lafuente, C. L.; Reive, B. S.; Solomons, L. S.; Allen, J.; Kalynchuk, L. E.; Caruncho, H. J. An Intravenous Injection of Reelin Rescues Endogenous Reelin Expression and Epithelial Cell Apoptosis in the Small Intestine Following Chronic Stress. *Chronic Stress (Thousand Oaks)* 2025, 9, 24705470251381456. <https://doi.org/10.1177/17474253251381456>
- Serrano-Morales, J. M.; Vázquez-Camero, M. D.; García-Miranda, P.; Carvajal, A. E.; Calonge, M. L.; Iundani, A. A.; Peral, M. J. Reelin Protects against Colon Pathology via PCS and May Be a Biomarker for Colon Cancer Progression. *Biology* 2022, 11 (10), 1436. <https://doi.org/10.3390/biology11101436>
- Figures 1 and 2 were created in <https://BioRender.com>

## ACKNOWLEDGEMENTS

This research was supported by the Jamie Cassels Undergraduate Research Awards, University of Victoria, and supervised by Dr. Violeta Iosub and Dr. Hector Caruncho. Poster Date: February 18, 2026.