Characterizing Stages of Syphilis Infection Using Plasma Proteomics

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INTRODUCTION

- Syphilis is a multistage disease caused by the bacterium *Treponema pallidum* (1)
- 2018-2023: Infectious syphilis cases in Canada nearly doubled, and the rate of congenital syphilis increased 220% (2)
- Available diagnostic tests cannot distinguish between stages (3)
- Differentiating early latent and late latent syphilis would ensure appropriate use of antibiotics and appropriate treatment (3)
- Host processes are disrupted when human brain endothelial cells are exposed to *T. pallidum* (4,5)

Infection with *T. pallidum*

Primary syphilis

Secondary syphilis

Early latent syphilis

Late latent syphilis (>1 year since infection)

Figure 1. Stages of syphilis infection.

Significance

To combat rising syphilis cases and the challenges of diagnosing stages of infection, we need a deeper understanding of the host response to *T. pallidum* across disease stages and the ability to identify host biomarkers during infection

Hypothesis

Plasma from individuals across syphilis disease stages and diagnosis-free controls will display distinct proteomic profiles reflecting differences in host response between stages

Objectives

1. Characterize proteins/pathways differentially expressed across stages of syphilis
2. Identify potential biomarkers for early latent syphilis and late latent syphilis

METHODS

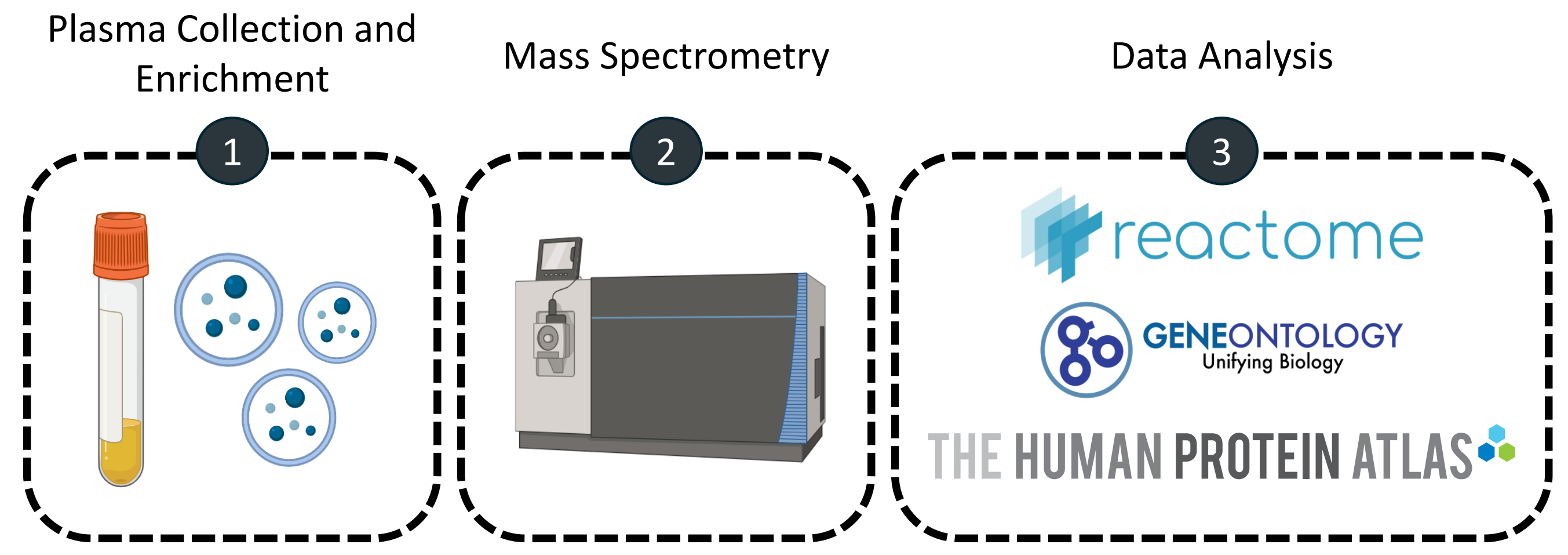

Figure 2. Workflow overview: 1) collected plasma was enriched for extracellular vesicles; 2) samples were analyzed using liquid chromatography tandem mass spectrometry (LC-MS/MS); 3) data was analyzed for pathway enrichment and differences in protein abundance across stages of infection.

RESULTS

Table 1. Number of participants per cohort and clinical staging (P = Primary, S = Secondary, EL = Early Latent, LL = Late Latent, unk = unknown).

	Primary and Secondary Syphilis No History of Prior Infection	Latent Syphilis No History of Prior Infection	Latent Syphilis Reinfection	No Diagnosis Control
Number of Participants	4 (P), 2 (S)	2 (EL), 2 (LL)	4 (EL), 1 (unk)	5

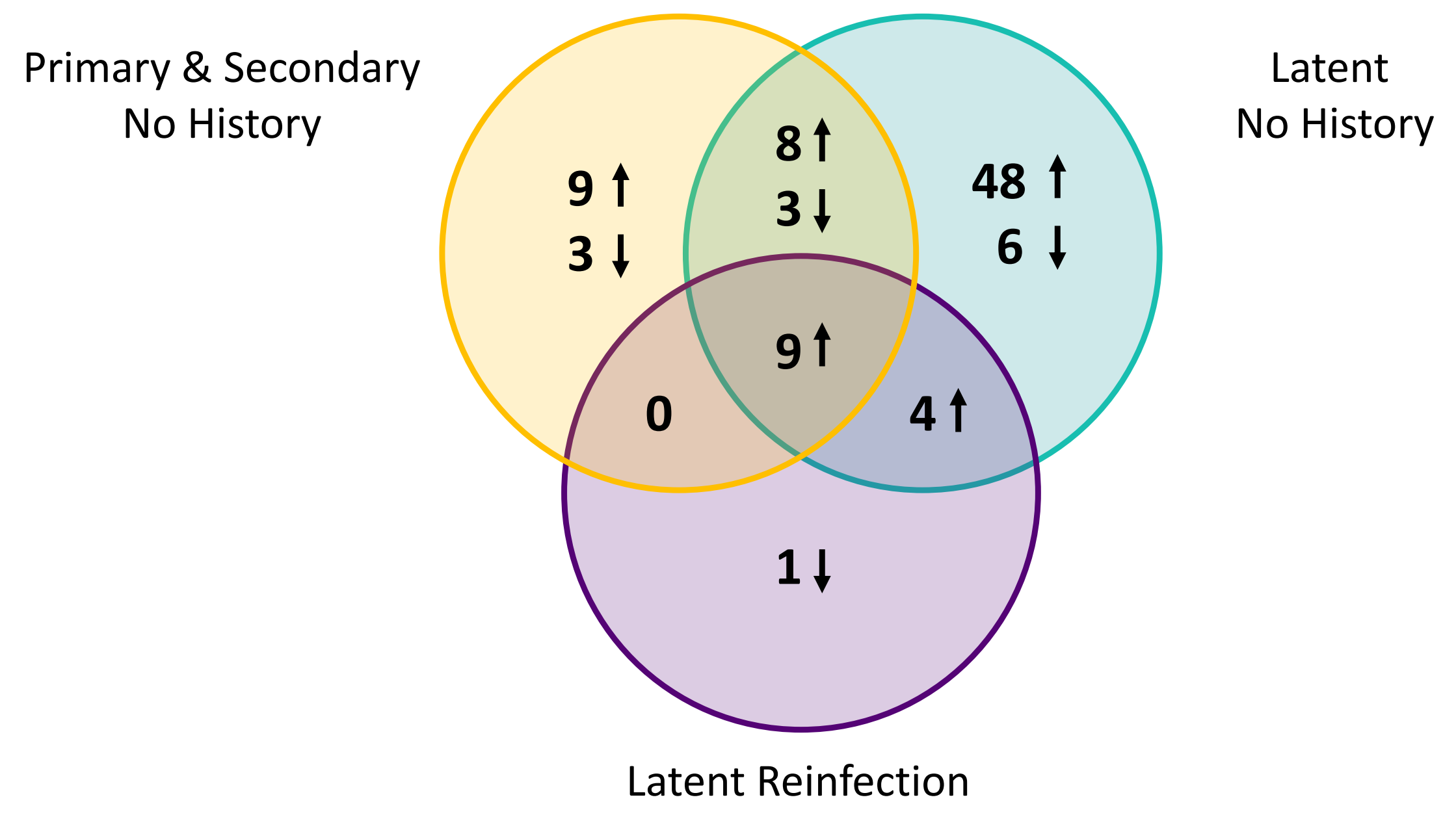

Figure 3. Differentially abundant proteins in primary and secondary syphilis (no history), latent syphilis (no history), and latent reinfection. Proteins showed FC > 2 or FC < 0.5 relative to undiagnosed control.

Changes in biological processes are unique across stages of disease

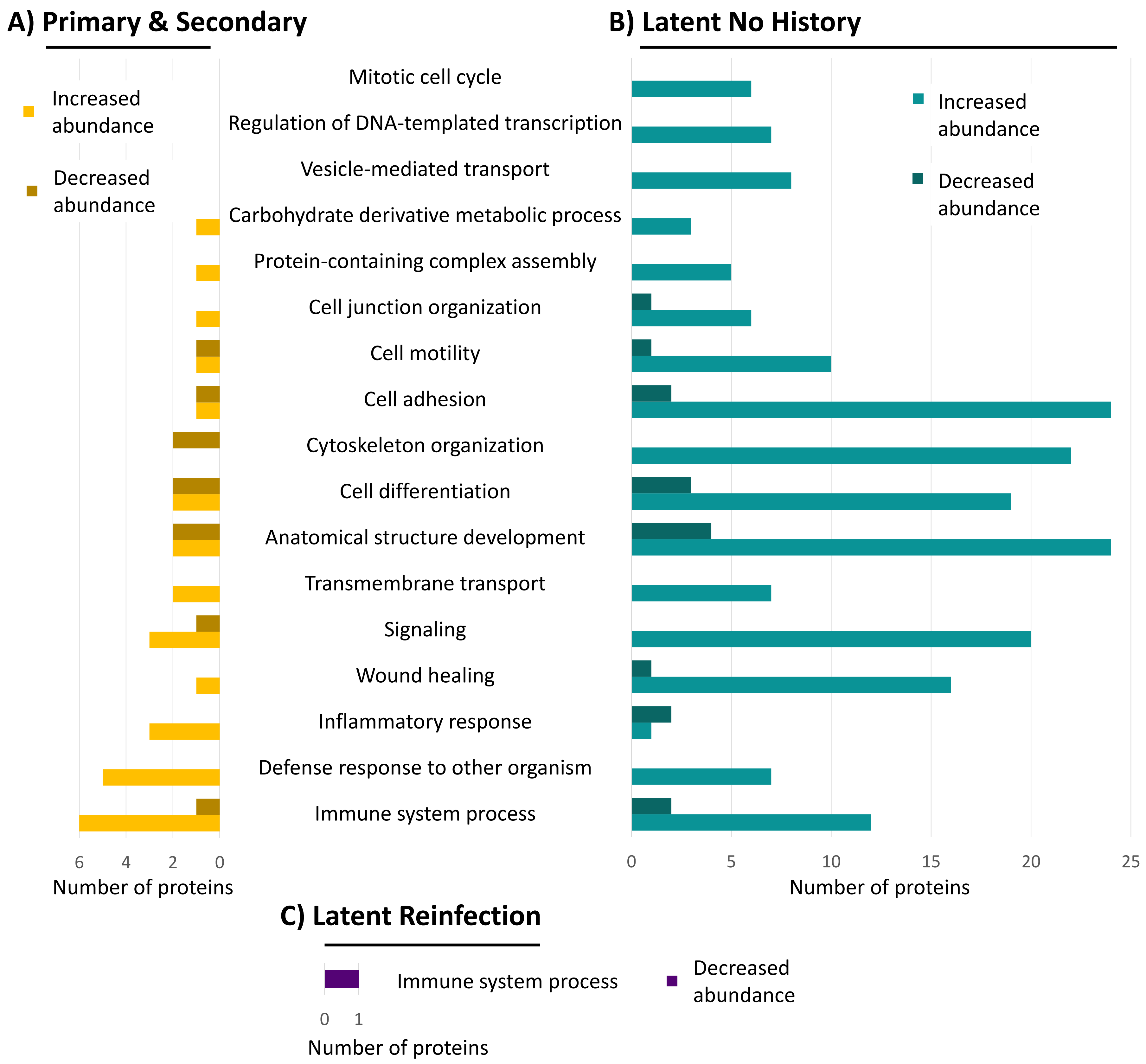

Figure 4. Biological processes identified from differentially abundant proteins unique to a) primary and secondary syphilis (no history), b) latent syphilis (no history) or c) latent reinfection.

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CONCLUSIONS

Mapping the impact of each stage of syphilis on biological processes improves our understanding of disease progression

Future Directions

- Compare results with publicly available datasets to identify host responses unique to syphilis and thereby aid development of biomedical interventions
- Integrate results with whole blood RNAseq data from the same study to obtain a more complete biological picture
- Further investigate results in a larger cohort study

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CIHR IRSC Canadian Institutes of Health Research Instituts de recherche en santé du Canada
OS4 – 190784 HIV – 194095

NIH National Institute of Allergy and Infectious Diseases
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Ethics Statement: This study was reviewed and received approval through the BC Harmonized Research Ethics Process (H23-01642), Board of Record: University of Victoria (BC23-0590).