Title: *Heparan Sulphate Loss and ECM Remodelling in Persistent CVB-1 Infection: Linking Proteomics to Tissue Vulnerability*

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Abstract
Persistent viral infections, such as those caused by coxsackievirus B1 (CVB-1), are increasingly recognized for their role in driving chronic tissue dysfunction without overt cytolysis. One underappreciated mechanism is remodelling of the extracellular matrix (ECM), which undermines structural integrity, cell survival, and immune modulation. In type 1 diabetes (T1D), similar ECM changes, particularly the loss of heparan sulphate (HS) and its carrier proteoglycans like perlecan; precede β-cell destruction, suggesting that ECM collapse may be a shared mechanism linking viral persistence to autoimmune pathology.

This project aims to investigate ECM remodelling in CVB-1–persistent PANC-1 models and validate proteomic signatures through antibody-based spatial analysis, thereby supporting the development of predictive and preventive strategies grounded in the principles of P4 medicine.

Our label-free proteomic analysis of a persistent CVB-1 model revealed significant downregulation of basement membrane components including perlecan (HSPG2) and laminin α-5, alongside upregulation of LOXL4, an ECM crosslinking enzyme associated with matrix stiffening and fibrotic disease. These findings suggest basement membrane destabilization and HS loss as measurable features of persistence.

To validate and extend these findings, we will use immunohistochemistry and immunofluorescence with antibodies targeting intact HS (10E4), cleaved HS stubs (3G10, post-hepari(tin)ase digestion), perlecan (E-6), and LOXL4 (B-6). This approach enables personalized profiling of ECM damage and may support future participatory research through biomarker-guided monitoring.

Overall, this study integrates molecular pathology with P4 medicine by identifying predictive ECM markers of viral persistence and opening preventive therapeutic avenues targeting matrix resilience.