Spinal cord injury patients who experience an AIS grade conversion have a distinct proteome compared to those who do not.

Proteomic analysis of bloods from SCI patients

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Introduction

- Neurological outcomes following spinal cord injury (SCI) are currently difficult to predict.
- Initial American Spinal Injury Association (ASIA) Impairment Scale (AIS) grade can give an estimate of outcome, but this is unreliable, thus leaving patients with uncertainty and impairing the development of novel therapies due the highly heterogeneous nature of the SCI population.
- This has stoked interest in biomarker discovery.
- This study compared the proteomes from the plasma of AIS grade C patients who experience an AIS grade conversion ("improvers", n=10) and those who did not ("non-improvers", n=7).

Methods

- This study used iTRAQ labelling MALDI TOF/TOF mass spectrometry to investigate potential biomarkers from blood with an unbiased methodology.
- Plasma was collected within 2 weeks ("acute") of injury and at approximately 3 months ("sub-acute") post-injury.
- Data analysis was initially conducted with the ProteinPilot software, but is currently being re-examined via open-source packages in the R programming language, for greater reproducibility.
- The results presented here are produced from the ProteinPilot data output

Results

- Data analysis is ongoing.
- Initial examination indicates several proteins with large fold changes between improvers and non-improvers at both time points (Figures 1 & 2).
- STRING network plots of the proteins identified in the acute and sub-acute groups were produced (Figures 3 & 4)
- Reactome plots to identify the biological pathways associated with the proteins in the acute and sub-acute groups were also produced (Figures 5 & 6)

- The proteins retinol-binding protein (RPB-4), serum amyloid A-1 protein (SAA1), apolipoprotein A-IV precursor (APOA4) and alpha-2-macroglobulin precursor (A2M) were selected for enzyme-linked immunosorbent assay (ELISA) validation based on the fold change and biological relevance.

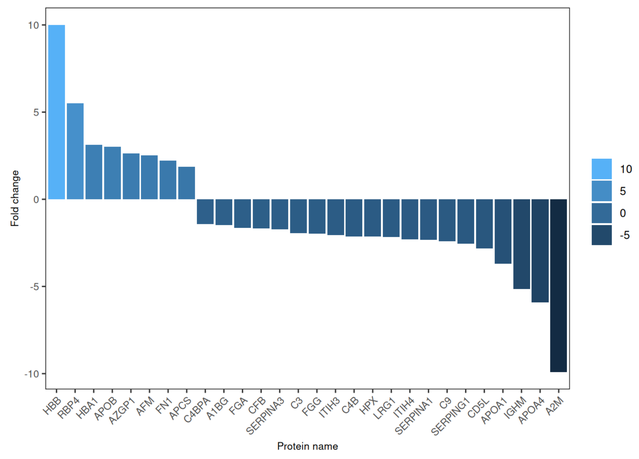

Figure 1: Change in relative plasma protein expresion at less than two weeks post-injury between AIS C grade patients who experienced a grade conversion and those who did not.

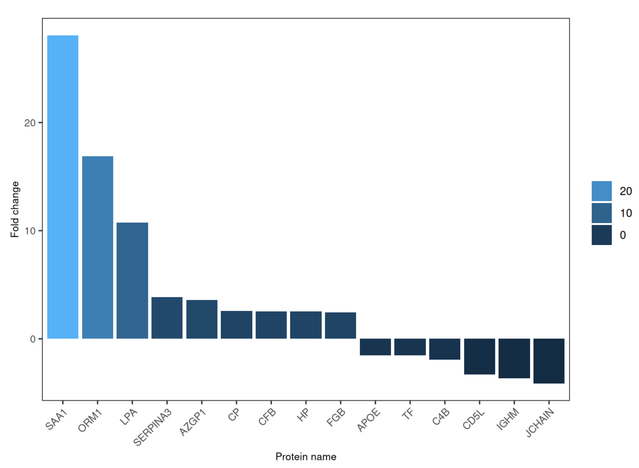

Figure 2: Change in relative plasma protein expresion at 3 months post-injury between AIS C grade patients who experienced a grade conversion and those who did not.

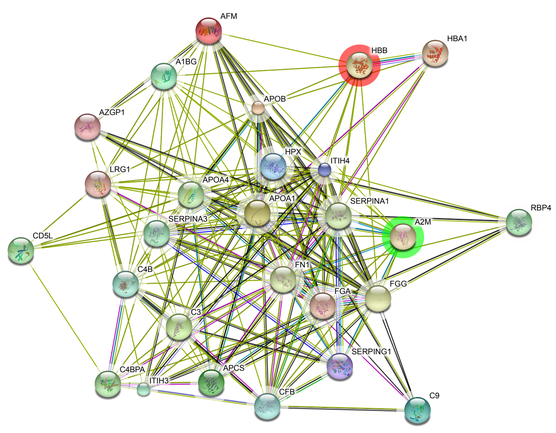

Figure 3: STRING network plot of proteins identified in acute group

Figure 4: STRING network plot of proteins identified in sub-acute group

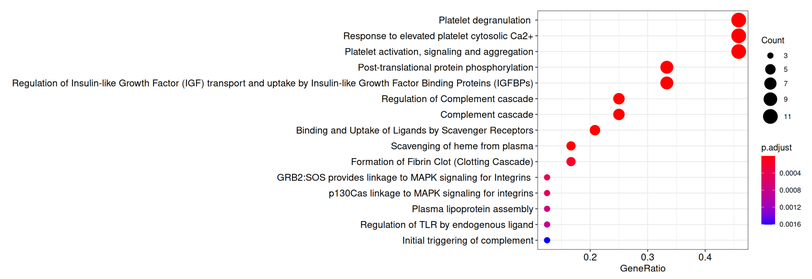

Figure 5: Reactome plot of biological pathways in acute group

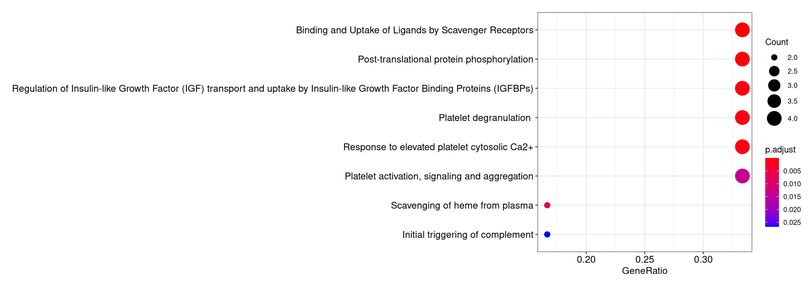

Figure 6: Reactome plot of biological pathways in sub-acute group

Discussion

- The data observed thus far demonstrates a clear and substantial difference in the proteomes of SCI patients who experience a positive AIS grade conversion and those who do not.
- Whilst data analysis is ongoing, preliminary examination suggests that some of the proteins may be implicated with liver function, which corroborates the results found in our previous studies.(Brown et al. 2019)
- With respect to biological pathways, several proteins are associated with the complement cascade, platelet interactions and scavenging heme from plasma.
- Initial network analysis has not identified multiple discrete clusters of proteins, suggesting they are all relatively closely related functionally or that they have many interaction with one another.
- More research is needed to establish whether or not the relationship between SCI recovery and liver function is causal or a proxy measure for another phenomena such as systemic inflammation.

References

Brown, Sharon, Gabriel Mateus Bernardo Harrington, Charlotte Hulme, Rachel Morris, Anna Bennett, Wai-Hung Tsang, Aheed Osman, Joy Chowdhury, Naveen Kumar, and Karina Wright. 2019. "A Preliminary Cohort Study Assessing Routine Blood Analyte Levels and Neurological Outcome Following Spinal Cord Injury." *Journal of Neurotrauma*, July. https://doi.org/10.1089/neu.2019.6495.

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