A Longitudinal Study of Plasma Proteomic Expression in Stroke Survivors

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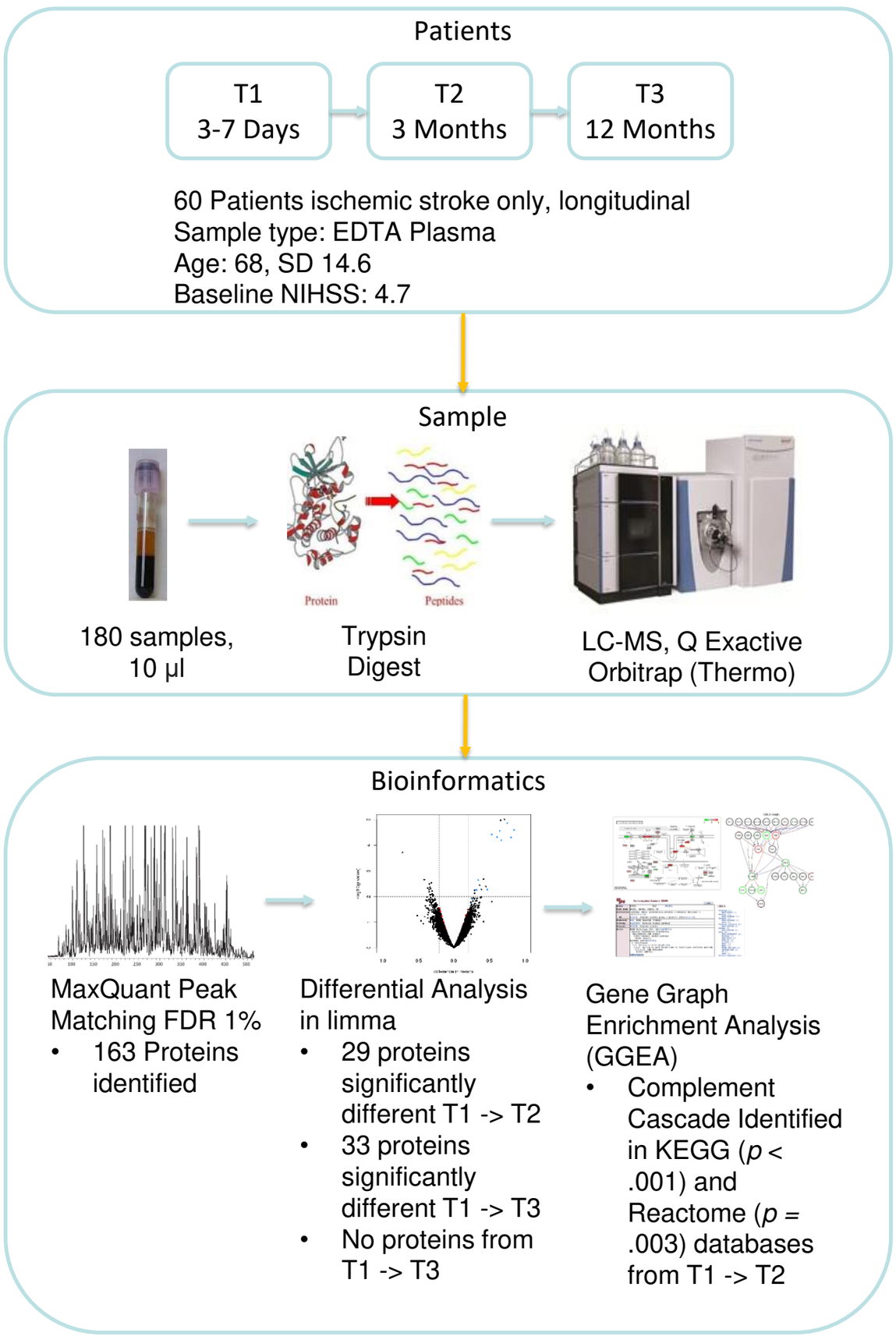
Background and Rationale

Post-stroke recovery is an ongoing process where biological cascades following biological perturbations, affecting immunity and inflammatory processes in the periphery as well as the cerebral parenchyma. Current studies primarily examine single or biomarker panels. Thus this study aimed to use an untargeted mass spectrometry workflow with topology based bioinformatics analysis based on differential expression to elucidate the pathways involved the longitudinal stroke trajectory. We have previously shown that the complement system is suppressed in association with 3 month depression scores.

Methods



- Overall the complement system is upregulated from 3-7 days to 3 months post-stroke. Similarly, proteins that regulate this system such as complement factor I (CFI) and vitronectin (VTN) are significantly upregulated.

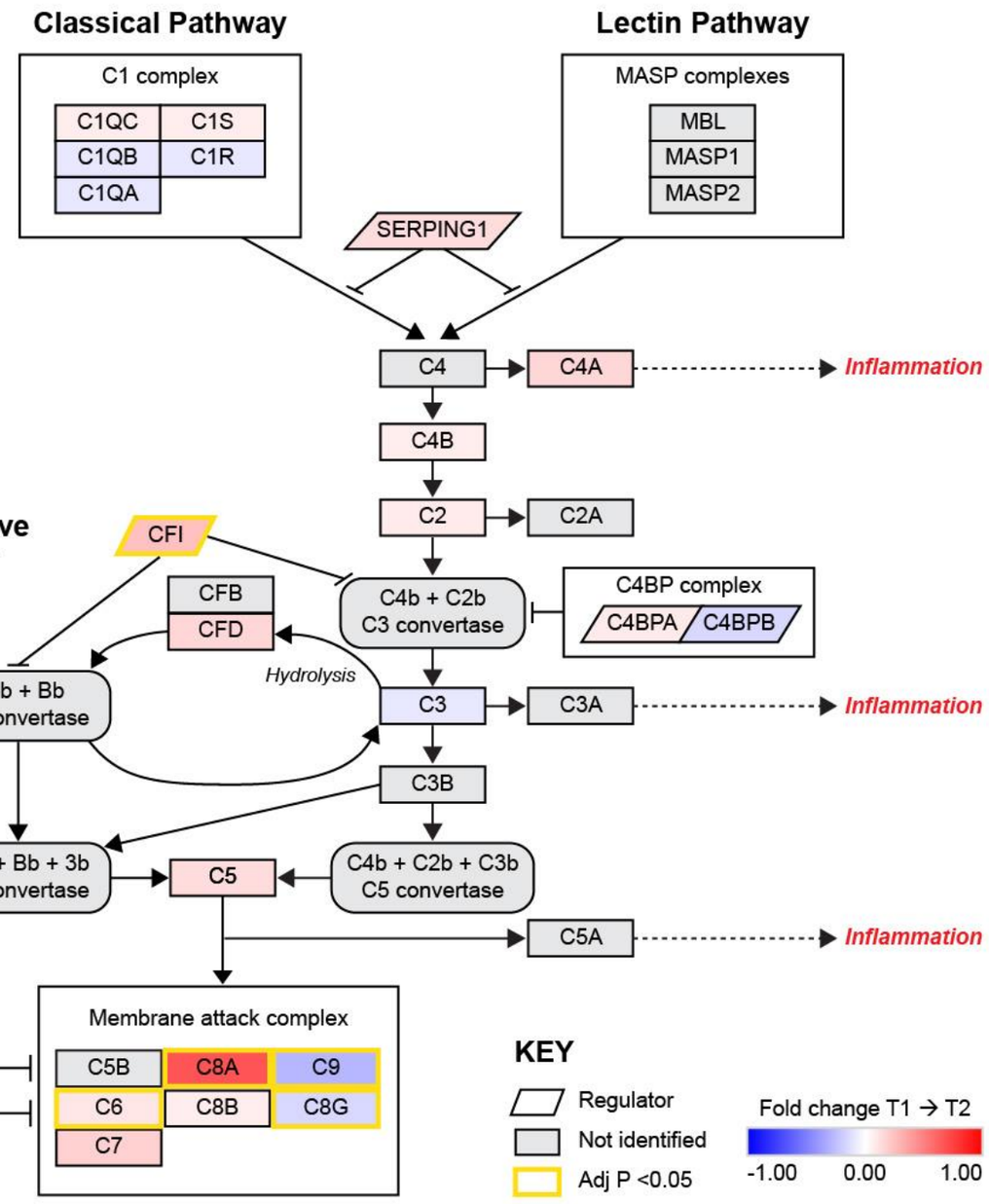


Figure 1. The pathway diagram amalgamating information from GGEA analysis and differential expression analysis, representing the complement pathway from T1 to T2.

Interpretation

- Activation of the complement cascade in plasma -→: chemotactic phagocytosis (recruitment of immune cells) via C3a and C5a and local cytolysis by forming destructive cellular membrane pore formations via the membrane attack complex (MAC).
- System provides an interface between mechanisms that target unwanted cellular material and destructive immune processes.
- The alternative pathway maintains this cascade at a baseline level of activation via overturn of C3 i.e provides surveillance for immune threats.
- The overexpression of alternative pathway complement factors suggests an increased state of **sterile immune activation, possibly** leading to increased expression of circulating anaphylactic proteins, C3a and C5a.
- Significant overexpression of regulating factors such as CFI and VTN suggests that the system is functionally regulated to prevent autoimmune insult.
- This may explain the mechanism for post-stroke immune suppression, whereby MAC protein expression is heavily regulated and therefore unable to effectively respond to pathogens such as viral pneumonia.