Multi-omics validation of serum glycoform marker to predict septic shock severity

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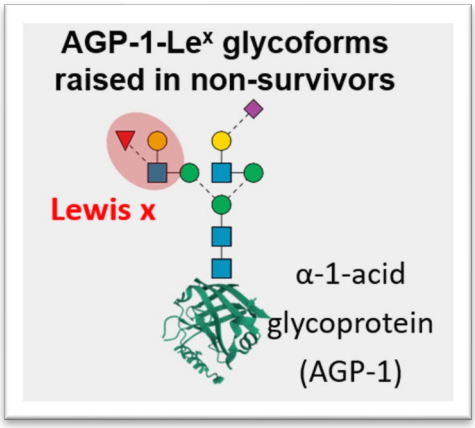

Septic shock, an excessive immune response to infection, accounts for ~20% of global deaths. Current methods for assessing disease severity are slow, non-specific, and insufficiently sensitive, limiting timely clinical intervention. To identify easily measurable glyco-signatures associated with poor outcomes, we recently applied comparative glycomics and glycoproteomics to serum samples longitudinally collected from septic shock survivors (n=29) and non-survivors (n=8) Glycomic profiling of 134 serum samples collected daily until recovery or death revealed that a specific *N*-glycan feature (Lewis x, Le^x) was elevated in non-survivors relative to survivors at ICU admission, a finding corroborated by glycoproteomics. Alpha-1-acid glycoprotein (AGP-1) was identified as a principal carrier of Le^x and demonstrated strong potential to stratify septic shock survivors from non-survivors (AUC=0.90).

Building on these exciting discoveries and to prepare for clinical implementation, ***this multi-omics proposal aims to validate the biomarker potential of serum AGP-1 Le^x to report on septic shock severity in an independent Japanese cohort.***

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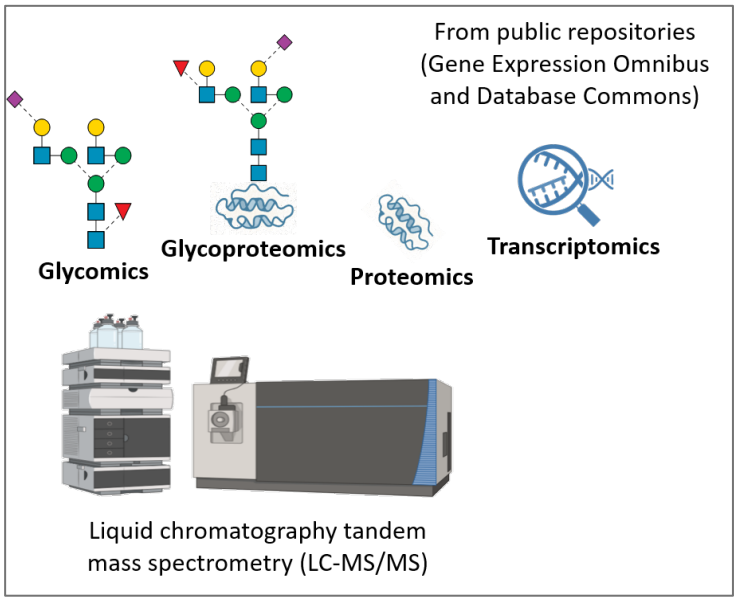
Integrated **glycomics** and **glycoproteomics** analyses of sera from an independent cohort of septic shock survivors (n=32), non-survivors (n=11), and healthy controls (n=10) sourced from Nagoya University Hospital (Japan) is currently on-going. To strengthen biological interpretation, publicly available whole-blood **transcriptomic** datasets will be integrated to assess concordance between transcriptional changes and protein/glycan-level alterations observed in septic shock. Multi-Omics Factor Analysis (MOFA), will be used to identify shared and modality-specific sources of variance across transcriptomic, proteomic, and glycomic datasets, and to uncover additional molecular signatures associated with disease severity.



Together, this study aims to validate AGP-1–Le^x glycoforms as prognostic biomarkers for septic shock outcome, enabling early risk stratification at ICU admission and supporting the development of rapid, personalised clinical decision-making tools.