

Principal Investigator: Morten Andersen
Grant Title: Glycan markers against septic shock

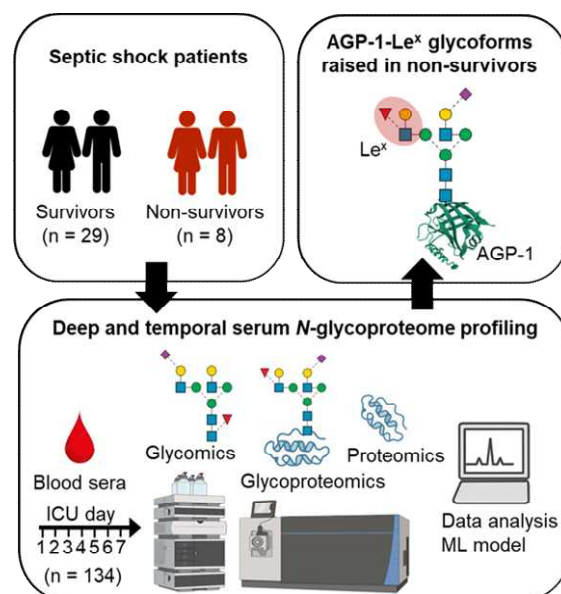
(a) Abstract

Septic shock, the excessive immune response to pathogen infection, accounts globally for ~20% of all deaths. Current methods to establish disease severity are unacceptably slow, unspecific and insensitive, hindering timely and effective treatment.

1. Objectives: This study sets out to establish easy-to-measure glyco-signatures that identify septic shock patients with high mortality risk.

2. Methods used: Comparative glycomics and glycoproteomics were applied to sera longitudinally collected from septic shock survivors (n = 29) and non-survivors (n = 8).

3. Results: Glycomics of all 134 serum samples (sampled daily in the ICU until recovery/death) revealed significant N-glycome dynamics across both patient groups. Unsupervised clustering of the serum N-glycome upon ICU admission indicated survivorship-specific glyco-signatures. Machine learning was employed to train a random forest model using the serum N-glycome data. The model accurately classified survivorship outcomes of 35 of 37 patients (accuracy 94.6%) and correctly predicted 29 of 29 survivors (specificity 100%) and 6 of 8 non-survivors (sensitivity 75%). Further interrogation of the serum N-glycome data revealed that Lewis x (Le^x)-type N-glycans are elevated in non-survivors relative to survivors at ICU admission, a finding recapitulated by glycoproteomics. Amongst the 58 other Le^x-containing serum glycoproteins that were strongly associated with acute phase response and stress pathways, alpha-1-acid-glycoprotein (AGP-1) was identified as a principal carrier of Le^x glycoepitopes with a potential to stratify septic shock survivors from non-survivors (AUC 0.90).



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This study lays a foundation for risk stratification of septic shock patients by uncovering easy-to-assay AGP-1-Le^x glycoforms that identify individuals experiencing poor survival outcomes already upon ICU admission, with the potential to translate to early individualised clinical care at the bedside.

Reference: Chau TH, Chatterjee S, Caulfield L, Chernykh A, Traini M, Fehring J, Hwang H, Kawahara R, Meyer EJ, Torpy DJ, Thaysen-Andersen M. Serum AGP-1-Lex Glycoforms Report on Survivorship of Patients with Septic Shock Upon Admission to Intensive Care Unit. *Mol Cell Proteomics*. 2026 Jan;25(1):101470. doi: 10.1016/j.mcpro.2025.101470.