A novel serological biomarker targeting a collagen type-I-derived matricryptin predicts all-cause mortality at admission with ST-elevated myocardial infarction.

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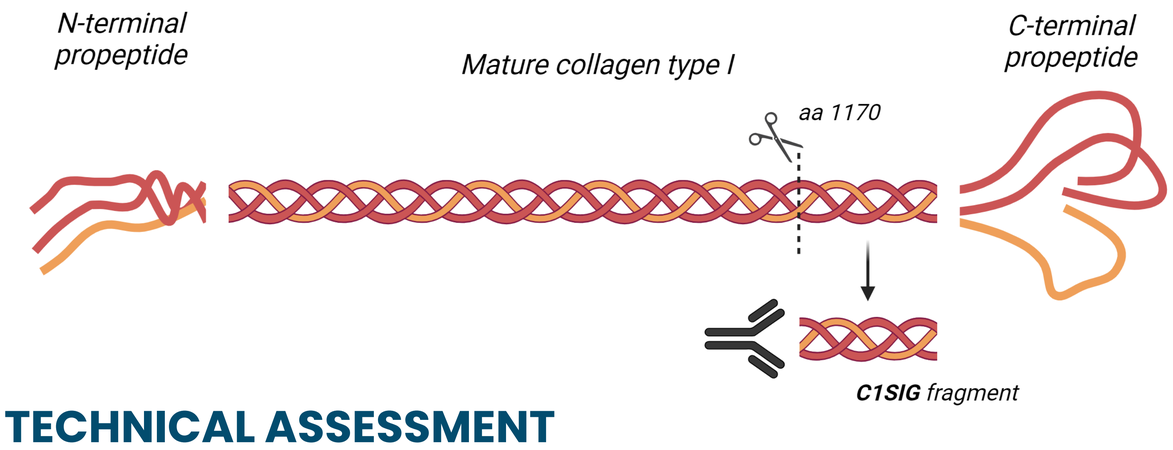
PURPOSE

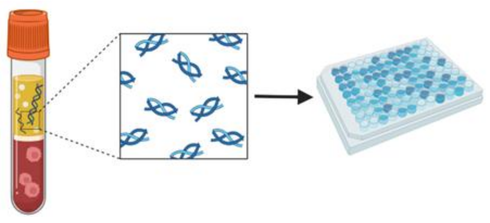
ST-elevated myocardial infarction (STEMI) damages local cardiac tissue and leads to acute inflammation-driven tissue remodelling immediately after injury. A **collagen type I (COL1) matricryptin** cleaved by MMP-2 and MMP-9 was previously identified as being involved in left ventricular remodelling after a MI.

We aimed to **develop, technically evaluate, and quantify** this COL1-derived matricryptin, named **C1SIG**, as a serological biomarker in a clinical cohort of STEMI patients.



TECHNICAL ASSESSMENT

C1SIG was targeted using a highly specific monoclonal antibody in **competitive enzyme-linked immunosorbent assay** format. The conditions of the assay were determined, and technical evaluation established a **measurement range** of 4.69 – 300 ng/ml and IC50 of 37.06 ng/ml. The **intra- and inter-assay variation** (CV%) were deemed low at 7.6% and 11.3%, respectively. The **accuracy** of measured analyte, **stability** of the assay and the analyte, and potential **interference** with haemoglobin, lipids and biotin were successfully evaluated.



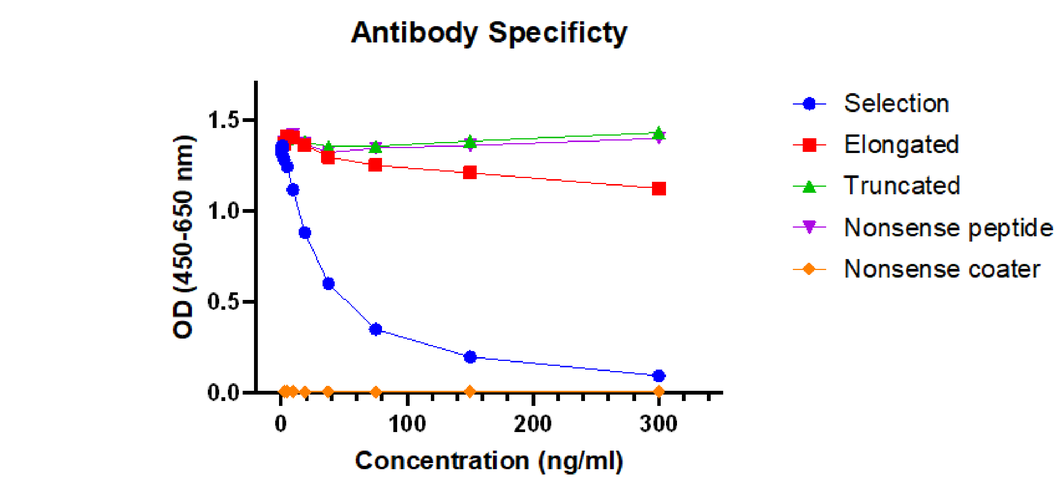


Figure 1: Specificity of the mAb produced for implementation into the C1SIG assay. The mAb is specific to the selection peptide (synthetically produced target sequence (RTGDAGPVGP)), shown by the high affinity of the mAb to this peptide and no affinity to the range of deselection peptides tested (elongated (GRTGDAGPVGP), truncated (TGDAGPVGP)).

CLINICAL COHORT

C1SIG was measured using ELISA in the **PREDICT-CS cohort of verified STEMI patients**. Plasma samples were taken on admission to hospital with STEMI.

	Overall (n=1,452)
Sex (male)	72.7%
Age (years)	63.5 (12.8) Mean (SD)
C1SIG (ng/ml)	32.0 (12.1) Mean (SD)
Death (n)	82 / 123 (30 / 365 days)

C1SIG IN STEMI

High C1SIG, defined as above the median, are **associated with all-cause mortality** in STEMI patients **30-days** and **1-year** post-admission.

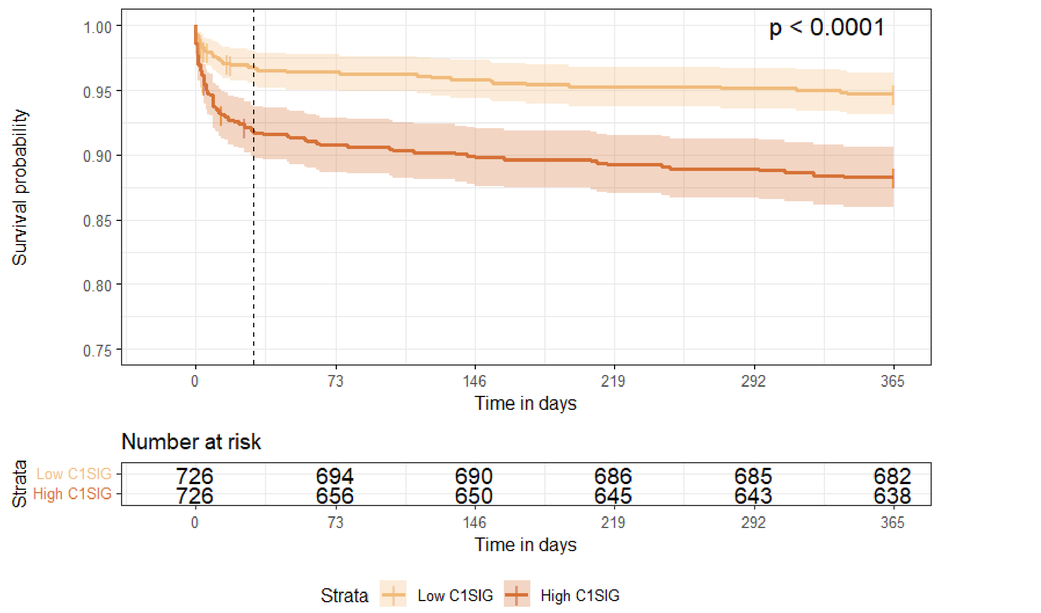


Figure 2: High C1SIG levels are associated with increased probability of all-cause mortality within 30-days and 1-year after an MI. Dashed vertical line indicates 30-day outcome. Log-rank tests show significant difference of high and low C1SIG levels when associated to all-cause mortality (30 days: $p < 0.0001$, 1 year: $p < 0.0001$).

C1SIG is a **risk predictor for all-cause mortality** at 30-days and 1-year post-STEMI in univariable and multivariable cox regression analysis, when adjusted for the Framingham Score (age, sex, systolic and diastolic blood pressure, hypercholesterolemia, diabetes and smoking), a well-used risk prediction model for MI.

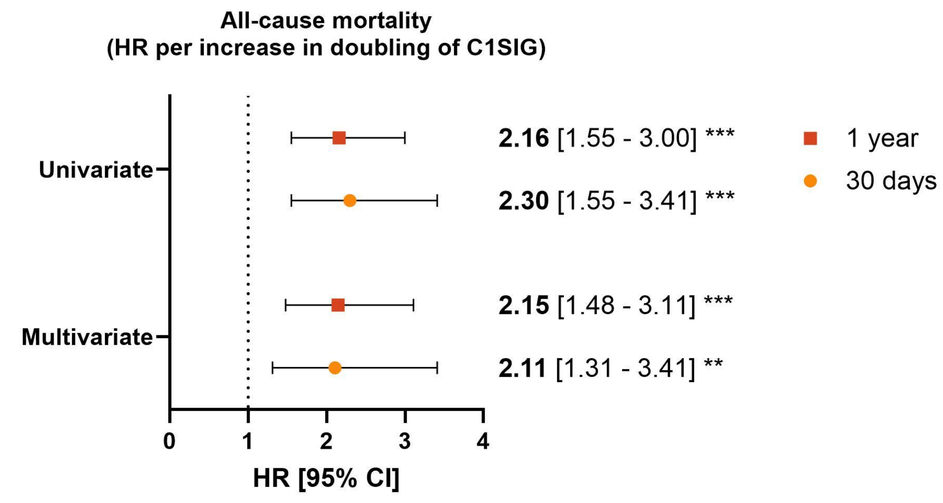


Figure 3: C1SIG is predictive of all-cause mortality risk in univariable and multivariable analysis at 30 days and 1-year post-MI. The multivariate model is based on the Framingham Score (includes age, sex, diastolic blood pressure (BP), systolic BP, hypercholesterolemia status, diabetes status, and smoking status). Hazard ratios (HR) are presented with 95% confidence intervals (CI) and calculated as per biomarker doubling.

CONCLUSION

C1SIG was developed as a technically robust biomarker and demonstrated as an independent predictor of mortality at 30 days and 1-year after STEMI, even when adjusted for multiple clinically-relevant variables. This COL1 biomarker could be helpful in assessing acute extracellular matrix processing in individuals after suffering a STEMI and could identify a subset of patients at increased risk of long-term outcome.

Disclosures: EM is employed as a PhD student, and FG is an employee and shareholder, at Nordic Bioscience.
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