**Harnessing the plasma proteome to predict cardiac remodeling after myocardial infarction**

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**Background:** Myocardial infarction (MI) induces cardiac remodeling represented by infarct wall thinning and dilation. For this study, we used plasma proteomics to identify proteins that predict MI cardiac remodeling across the time span of wound healing.

**Methods:** Retrospectively, we interrogated the plasma proteome of day 0 control (n=16) and day 3 MI (n=15) from C57/BL6 mice (age 3-6 months) using 3 targeted proteomic platforms that combined measured 165 unique proteins and correlated proteins with 6 cardiac physiology variables (dimensions, volumes, and wall thickness in systole and diastole) measured by echocardiography. Prospectively, we tested the hypothesis that the plasma candidates identified reflect cardiac physiology at an extended timepoint of MI (day 7) in a second cohort of mice (n=20). To evaluate clinical relevance, we examined plasma from healthy controls (n=18) and patients 48h after presentation for MI (n=41) using the RayBio® Human Glycosylation Antibody Array 1000 to determine protein-protein interactions, which were used to identify enriched pathways and transcription factors.

**Results:** Using a cut-off of r≥0.60 and p<0.05, 5 markers were identified: Apolipoprotein A1 (ApoA1), Haptoglobin, Immunoglobulin A (IgA), Interleukin (IL)-17E, and Tissue Inhibitor of Metalloproteinase-1 (TIMP-1). Prospectively, ApoA1, IgA, and IL-17E mirrored current and predicted future adverse cardiac remodeling, indicating a linear response over MI time. ApoA1, IL-17E, Haptoglobin, and TIMP-1 protein all associated with cytokine-cytokine receptor signaling as the most enriched Kotyo encyclopedia genes and genomes pathway and were most linked to foxm1, stat3, stat1, and usf1 transcription factor induction, respectively.

**Conclusion:** We identified plasma proteins involved in MI wound repair that mirror current and predict future continuation of cardiac remodeling.