The novel proteomic signature for the detection of cardiac allograft vasculopathy

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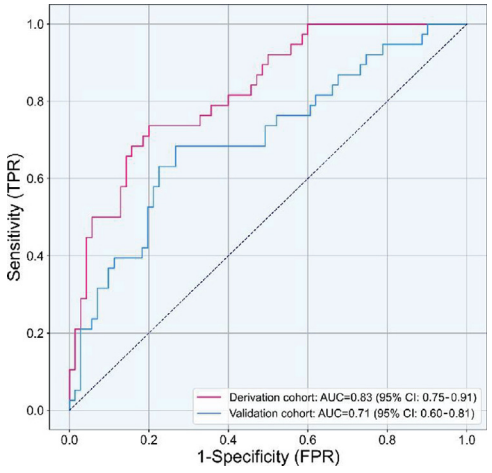
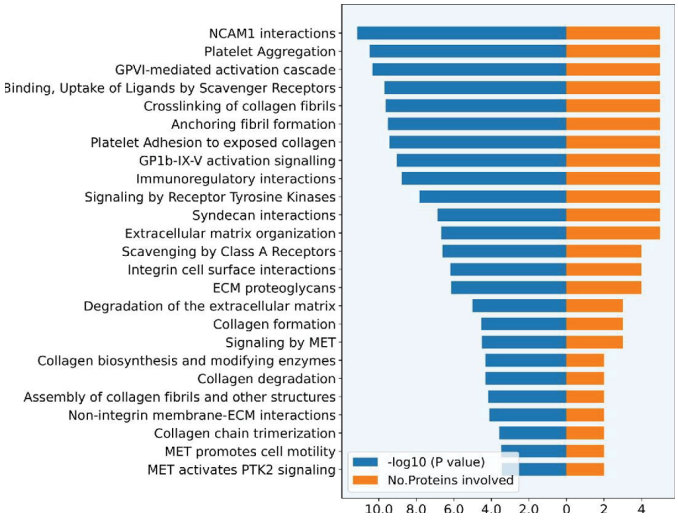
Funding Acknowledgement: Type of funding sources: Public grant(s) – EU funding. Main funding source(s): European Research Council Advanced Researcher Grant and Proof-of-Concept Grant

Background: Cardiac allograft vasculopathy (CAV) is the major long-term complications after heart transplantation, leading to mortality and re-transplantation. As available noninvasive biomarkers are scarce for CAV screening, we aimed to identify a proteomic signature for CAV detection.
Methods: Urinary proteome was measured by capillary electrophoresis coupled to mass spectrometry in 217 heart transplantation recipients. Participants were further randomly and evenly divided into the derivation cohort and validation cohort. The proteomic signature for CAV was identified by decision tree-based machine learning in the derivation cohort and further tested in the validation cohort. The pathway analysis was investigated with Reactome Pathway Database.
Results: We identified a proteomic signature with 27 urinary peptides, which yielded areas under the curve (AUC) of 0.83 and 0.71 in the derivation and validation cohort, respectively. In the validation cohort, it had a sensitivity of 68.4%, specificity of 73.2%, accuracy of 71.6%, negative predictive value of 81.3%. Including the proteomic signature into the basic model further improved the diagnostic accuracy with an relative integrated discrimination improvement of 25.9% and the continuous net reclassification improvement of 83.3% ($p \leq 0.023$). The pathways analysis on revealed that collagen turnover, platelet aggregation and coagulation, cell adhesion and motility might involve in the pathogenesis of CAV.
Conclusions: The proteomic signature might be valuable for the surveillance of CAV thereby reduce the frequency of invasive procedures after HTx. Moreover, the highlighted pathways might provide insights in the potential novel treatment targets for CAV.



ROC curves of the urinary proteomic



The 25 highlighted enrichment pathways