Novel Biomarkers for Platelet Reactivity and Cardiovascular Risk: “PRESS” and “PROSPER”

Reliable, scalable, and non-invasive diagnostic tools for the (early) detection of platelet hyperreactivity and associated cardiovascular risk.

Technology

The NYU investigators have developed a suite of novel diagnostic tools, which can discriminate individuals with platelet hyperreactivity and those at increased cardiovascular risk: Platelet Reactivity ExpreSsion Score (PRESS) and PROtein Signature of PlateletET Reactivity (PROSPER).

Platelet Reactivity ExpreSsion Score (PRESS) is derived from the weighted expression values of 76 genes, identified through platelet RNA sequencing of samples collected from 129 patients with symptomatic peripheral artery disease (PAD) before receiving lower extremity revascularization (LER) in the well-phenotyped PACE-PAD clinical study. This gene signature is significantly correlated with the current gold standard measure of platelet reactivity; platelet aggregation in response to submaximal epinephrine. PRESS demonstrated high accuracy, sensitivity, and specificity in discriminating platelet hyperreactivity across disease states, was associated with acute myocardial infarction, and those at increased risk for cardiovascular events.

PROtein Signature of PlateletET Reactivity (PROSPER) is a plasma protein signature derived from the weighted values of 40 proteins, quantified using a Proximity Extension Assay (PEA). PROSPER was derived by integrating standardized platelet aggregation measurements with proteomic data from plasma samples in 2 cohorts of healthy patients. PROSPER was then validated for association with cardiovascular risk across 3 additional cohorts comprising >50,000 patient samples (PACE-PAD, ISCHEMIA, UK Biobank). In these cohorts, the highest values of PROSPER correlated with a significant risk of cardiovascular events like myocardial infarction, amputation stroke or death. These innovative tools overcome current technical barriers that limit routine clinical assessment of platelet aggregation responses and open the possibility for a personalized approach to antithrombotic therapy for cardiovascular risk reduction in both patients at risk and with established cardiovascular disease.

Background

Platelets play a crucial role in the pathogenesis of atherogenesis and thrombosis, and individuals with platelet hyperreactivity are at increased risk for platelet-mediated events (e.g., myocardial infarction, stroke, acute limb ischemia). Current cardiovascular risk assessment (e.g., measuring blood pressure, cholesterol, and metabolic function) includes measurement of biomarkers that are BOTH prognostic and modifiable. While platelet activity and aggregation can be measured, current methods (i.e., light transmission aggregometry, flow cytometry) are labor-intensive, costly, and subject to significant pre-analytical variation, making them unsuitable for large-scale use. The development of PRESS and PROSPER address this highly unmet need by providing a reliable and reproducible transcriptomic and/or proteomic signature that can accurately discriminate platelet hyperreactivity and predict cardiovascular risk. This

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approach could revolutionize the management of diseases associated with platelet hyperreactivity, such as cardiovascular disease, by enabling early detection and precision-based intervention.

Development Stage

PRESS and PROSPER have been validated in multiple retrospective clinical cohorts representing diverse patient populations. NYU now seeks a commercial partner to develop these tools into a suite of in vitro diagnostics for measuring platelet hyperactivity and predicting cardiovascular risk.

Applications

- Early detection and risk stratification in diseases associated with platelet hyperreactivity, such as atherosclerosis, PAD, ischemia, and coronary artery disease.
- Guiding personalized therapeutic interventions in patients at increased cardiovascular risk.
- Potential application in other conditions associated with platelet hyperreactivity, such as systemic lupus erythematosus (SLE) and infectious diseases.

Advantages

- **Exploits recognized biomarker:** PRESS and PROSPER indirectly measure platelet aggregation and hyperreactivity, a recognized biomarker of cardiovascular risk.
- **Broad applicability:** PRESS and PROSPER consistently detect platelet hyperreactivity across diverse patient subgroups, including by age, sex, race/ethnicity, and antiplatelet therapy.
- **Care-changing predictive value:** PRESS and PROSPER provide additional predictive value beyond traditional cardiovascular risk assessments. Test results are able to guide clinical intervention.
- **High accuracy:** PRESS and PROSPER accurately and objectively discriminate platelet hyperreactivity in healthy individuals and across disease states.
- **Ease of implementation:** PROSPER can be measured directly from small plasma samples, enabling point-of-care testing.

Intellectual Property

NYU has filed a US non-provisional patent application for PRESS and a US provisional patent application for PROSPER. Applications cover the method of calculating each score to determine patient platelet hyperactivity and predict cardiovascular risk.

References

1. Berger, J.S., Cornwell, M.G., Xia, Y. et al. , https://www.nature.com/articles/s41467-024-50994-7