Thromboinflammation Platelet Signatures (TIPS): A Novel Biomarker for Cardiovascular Disease

Reliable, scalable, and non-invasive diagnostic tool measuring thromboinflammation for the early detection and diagnosis of cardiovascular disease.

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Technology

NYU investigators Dr. Jeffrey Berger and Dr. Tessa Barrett have developed Thromboinflammation Platelet Signature (TIPS), a 42-gene platelet transcriptomic signature that identifies patients at heightened risk for thromboinflammation, a driver of cardiovascular disease. TIPS was derived by profiling platelet activity and sequencing the platelet transcriptome in patients with consistently high versus low monocyte-platelet aggregates (MPA). MPAs are a key interface between thrombosis and inflammation and are associated with increased risk of cardiovascular events. The researchers demonstrated that platelet transcriptomic patterns can distinguish a thromboinflammatory phenotype that in multiple cohorts, was associated with high MPA. In an initial cohort of 149 participants and multiple independent validation cohorts, TIPS signature correlated strongly with MPA levels across studies and was consistent over time, and was elevated in known thromboinflammatory contexts such as COVID-19 and in acute myocardial infarction. Higher TIPS levels in patients with stable peripheral artery disease (PAD) were also associated with increased risk of major adverse cardiovascular and limb events. Additionally, the investigators found that pharmacologic intervention with the antiplatelet agent ticagrelor can lower TIPS scores. This innovative biomarker technology represents a significant improvement upon current methods for measuring MPA (e.g., flow cytometry) and has the potential to enable point-of-care testing towards personalized treatment plans for improved outcomes for patients with and at risk for cardiovascular disease.

Background

Platelets are key players in vascular inflammation culminating in atherosclerosis and thrombosis. Through direct and indirect interactions with other cell types, they can initiate and sustain inflammatory cascades in vascular dysfunction and during cardiovascular events such as atherothrombosis, the rapid formation of a clot on a disrupted atherosclerotic plaque. Platelets adhere to monocytes forming monocyte-platelet aggregates (MPAs) that serve as a sensitive *in vivo* marker of thromboinflammation because platelet activation simultaneously drives both thrombotic (thromboxane generation, coagulation factor assembly) and inflammatory (monocyte tissue factor expression, NF-κB–mediated cytokine release, enhanced monocyte transmigration) cascades, making MPA levels a more durable circulating readout of platelet activation than surface P-selectin alone (which is rapidly shed) and a functional indicator of the pathological crosstalk between hemostasis, innate immunity, and inflammation. Previous work has established that elevated MPA levels are linked to cardiovascular diseases, such as coronary artery disease and peripheral artery disease (PAD), and to worse outcomes in both acute myocardial infarction and stable cardiovascular disease. However, broader clinical use of MPA

levels has been limited by measurement and reproducibility challenges related to blood collection and processing. The Thromboinflammation Platelet Signature (TIPS) addresses this gap by providing a robust platelet gene-expression signature that reliably detects elevated MPA and identifies individuals prone to thromboinflammation, with the potential to enable point-of-care risk stratification and guide personalized therapeutic strategies for thromboinflammation-related cardiovascular conditions.

Development Stage

TIPS has been validated in multiple clinical cohorts representing diverse patient populations. NYU now seeks a commercial partner to develop this tool into an *in vitro* diagnostic for cardiovascular disease.

Applications

- Early detection and risk stratification in diseases associated with thromboinflammation, like myocardial infarction, peripheral artery disease (PAD), and COVID-19.
- Personalized therapeutic interventions for patients with or at risk of thromboinflammation and/or cardiovascular disease.
- Evaluate the efficacy of anti-platelet therapies in patients with thromboinflammation. Diagnostic tool for other inflammatory conditions or autoimmune diseases (e.g., viral infection, sepsis, autoimmune condition).

Advantages

- **Established precedent:** Indirectly measures platelet-myocyte aggregation, a recognized biomarker for platelet activity, thromboinflammation, and cardiovascular risk.
- **Reliable MPA measurements:** Improves upon available tools for measuring MPA, which have high variability.
- **Broad applicability:** Consistently detects thromboinflammation across diverse patient subgroups, including by age, sex, race/ethnicity, and treatment history.
- **Treatment monitoring:** Indirectly measure the effectiveness of anti-platelet therapies like Ticagrelor.
- **Integrated stratification:** Can be combined with analogous measurements of platelet activity (i.e., NYU's PRESS technology) for more detailed patient stratification.

Intellectual Property

NYU has filed a U.S. provisional patent application covering the method of calculating TIPS to determine patient risk of thromboinflammation and susceptibility to cardiovascular disease.

References

1. Beitzen-Heineke A, Muller MA, Xia Y, et al. , https://pubmed.ncbi.nlm.nih.gov/41424389/