Single-cell mass cytometry analysis unveils prothrombotic expression and heterogeneity in essential thrombocythemia

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Background/Introduction: Essential thrombocythemia (ET) is recognized for its hallmark elevated platelet count and a consequent increased risk of thromboembolic events including coronary events. Despite its clinical significance, the pathophysiological mechanisms predisposing ET patients to thrombosis remain largely undefined.

Purpose: The aim of this pioneering study was to shed light on the increased thrombotic risk in ET by conducting a detailed phenotypical characterization of platelet expression using single-cell mass cytometry, comparing ET patients to age- and sex-matched healthy controls.

Methods: Platelet samples from six patients diagnosed with ET and six healthy individuals were analyzed. This analysis utilized an extensive panel of 18 transmembrane regulators pivotal for platelet function and activation. Measurements were taken both at baseline and after ex-vivo stimulation with thrombin receptor-activating peptide (TRAP). Advanced clustering analysis via the FlowSOM algorithm helped identify specific subclusters of platelets with a prothrombotic expression profile.

Results: Our investigation revealed a significant overexpression of the activation marker CD62P (P-Selectin, p=0.049) and of the collagen receptor GPVI (p=0.044) in non-stimulated ET platelets (Figure 1A-C). Conversely, a notable decrease in expression was observed for the fibrinogen receptor GPIIb/IIIa units CD41 (p=0.036) and CD61 (p=0.044), as well as for the von Willebrand factor receptor CD42b (p=0.044). The FlowSOM analysis distinguished two prothrombotic subclusters of ET platelets, particularly highlighting one cluster, which was significantly overrepresented in ET (22.13% of total ET platelets versus 2.94% in controls, p=0.035, Figure 1D-E).

Conclusion: This study presents compelling evidence of a distinct prothrombotic phenotype in ET, marked by significant alterations in platelet expression profiles. The overexpression of CD62P and GPVI, alongside the underexpression of CD41, CD61, and CD42b, underscores the complex pathophysiological landscape of ET. Importantly, we identified a specific subcluster, particularly overrepresented in ET, with a specific prothrombic signature. Our findings, while only hypothesis generating, propose GPVI as a potential therapeutic target to mitigate thrombosis in ET patients, paving the way for targeted interventions in this high-risk population.