Project Title: Association of Platelet Parameters and Subpopulations Identified by High Dimensional Mass Cytometric Analysis of Platelets with Bleeding Severity in Pediatric patients with Immune Thrombocytopenia

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Summary: Little information on bleeding risk is available to patients with ITP and their physicians to inform decisions about treatment. This study asks whether platelets in patients who have more severe bleeding have different markers on their surfaces compared to platelets of patients with little bleeding. Identification of platelet markers that are strongly associated with bleeding, and creation of a corresponding clinical test, will help avoid unnecessary treatment (with the associated risk of side effects) while helping to correctly identify patients who would benefit from such treatment. This study uses a new method called mass cytometry to identify the levels of 14 different markers on the surface of each platelet, providing a more detailed picture of the platelets than previous studies which used only three markers. Patients with ITP and platelet counts under 50,000/μL are being studied because their risk of bleeding is greater than patients with ITP and higher platelet counts. A small amount of blood (less than a drop) collected at a regular office visit, is reacted with antibodies targeting each of the 14 markers and then analyzed by mass cytometry. The level of each marker on platelets from patients with and without severe bleeding is compared, to see if any single marker is a good predictor of bleeding. Because combinations of the levels of 2, 3, or more markers may provide a stronger predictor of bleeding risk, new high dimensional data analysis tools will be used to see if any combination of the 14 markers together differs in patients with severe bleeding compared to those without. Combinations of platelet surface markers identified in this study that are strongly associated with bleeding could form the basis for a new test to help patients with ITP and their physicians in making decisions regarding treatment options.

The study is still on-going with about 17 of the desired 25 total patients enrolled to date. Preliminary results reveal that this new test works even in ITP patients with very low platelet counts, and that the combination of surface markers identifies subsets of platelets. This is important because platelet subsets may differ between patients with and without severe bleeding. Following analysis of all 25 patients, the bleeding scores for the patients will be unblinded and the association of bleeding score with individual platelet surface markers and platelet subsets will be analyzed. This study is the first analysis of platelets from patients with ITP by mass cytometry, providing the most detailed information currently possible on the phenotypic diversity of ITP platelets, and identification of platelet subpopulations.