Deepening into the physiopathology and stratification of Immune Thrombocytopenia (ITP) for more rigorous diagnosis, prognosis, and personalized treatment strategies

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Our study sought to better understand ITP and to obtain unique biomarkers (a clue or signpost) that may be used to guide more personalized treatment for ITP patients. We developed insight into the characterization and analysis of the megakaryocytic-platelet lineage (how platelets are produced; megakaryocytes are specialized cells that make platelets). We integrated multiple ways to study how to make megakaryocytes that produce platelets, and to determine the quality of the produced platelets, and how they perform.

Looking with a magnifying glass into platelets and how they are produced and function in ITP may provide us with additional clues to understand the disease which could lead to better treatments. Identifying variables, or biomarkers, that could be used for a more personalized ITP treatment approach is needed and is important to the international research community. A few things we learned along the way:

Platelet production is different in ITP
Studies in animals with ITP show that megakaryocytes are different in mice with ITP compared to healthy mice without ITP, on a genetic level. Our findings suggest that megakaryocytes in ITP are attempting to boost platelet production while also responding to unusual immune activity. This delicate balance between generating more platelets and managing the immune response reflects an ongoing, complex adaptation in the body's effort to handle the disease.

ITP triggers 'stressed' hemato- and megakaryopoiesis (which refers to the production of blood cells and platelets) and disturbs the life-cycle of platelets
To respond to a low platelet count, more megakaryocytes are produced to make platelets. This impacts the overall blood count balance and has an impact on the bone marrow long term. For this reason, ITP patients may experience mild anemia that may become more severe as the disorder progresses or in non-responders to treatment. Restoration of a platelet's normal life-cycle (normal development) is important and could be used to characterize whether an ITP patient responds to treatment. If the platelet life-cycle is not restored, it may signal a poor treatment response despite an improved platelet count, suggesting a need for combined treatments targeting both platelet destruction and production.

Analysis of megakaryocytes in peripheral blood shed light on treatment response
It is possible to distinguish treatment responders from non-responders because they have a higher proportion of mature circulating megakaryocytes in the bloodstream. Biomarkers such as mean platelet volume, immature platelet fraction, and the expression of CD34, GPA, and Annexin V on platelets can also help determine treatment response, as all these parameters reflect on the platelet life cycle and platelet production dynamics. Furthermore, our results also suggest that the longer the patient suffers with ITP, and the more treatment they use, the less capacity they have to respond to treatment.

PDSA has designed our research program to specifically focus on patient priorities and funds studies that will make a significant impact on ITP diagnosis, therapies, and quality of life. If you'd like to donate to our research fund, please visit pdsa.org/pdsa-donation.