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Extended Abstract
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# Allergy 2018: Immune Thrombocytopenia (ITP) Pathogenesis and Treatment; More Than Meets The Eyes - Anwar A. Sayed - UK 2 Taibah University Sumita A Jain

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## Abstract

Immune thrombocytopenia (ITP) is an autoimmune disorder characterized by isolated low platelet count. It was thought to be primarily due to autoantibody against platelets. However, the absence of detectable autoantibodies in over 30% of patients and their unresponsiveness to B-cell-targeting therapy suggested an active role for T cells. Studies have confirmed the proinflammatory nature of ITP characterized as Th1/Th17 profile. However, little is known about the involvement of CD8+ cytotoxic T cells (CTL) in ITP pathophysiology and whether they are

regulared by regulatory T cells (Treg). Immunosuppressive therapy has been the mainstay treatment in ITP. More recently, Thrombopoietin receptor agonists (TPO-RA); Romiplostim (Romi) and Eltrombopag (EPAG), have been increasingly used to stimulate megakaryocytopoiesis to produce more platelets. TPO-RAs are reported to induce complete remission in up to 30% of cases, with limited understanding of their impact on the immune system. Here we describe changes in T cell subsets, particularly CTL and Tregs, in patients with ITP: how these changes are affected by disease activity and how TPO-RA may induce remission through modulating the immune system.

Multi-color flow cytometric panels were designed to characterize peripheral blood T cell subsets phenotypically as well as functionally through intracellular cytokine expression. Forty patients with ITP were studied and compared with 26 age and gender-matched healthy controls (HC).

Terminally-differentiated effector CTLs were significantly higher in patients compared to HC. This effector population is polyfunctional, expressing high levels of proinflammatory cytokines compared to HC.

Although Treg functionality was preserved in these patients, they corresponded to disease activity and in relation to CTLs.

Romi and EPAG demonstrate differential T-cell changes which also impacted the disease activity.

While Th1/Th2-cell ratio is considered as driving ITP, these results highlight the role of cytokine-secreting CTLs in the disease pathogenesis, as well as suggesting an immunomodulatory mechanism of these TPO-

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RAs. Immune Thrombocytopenia (ITP) is a type of autoimmune disorder indicated by isolated low platelet count. It was thought to be primarily due to autoantibody against platelets. However, the absence of detectable autoantibodies in over 30% of patients and their unresponsiveness to B-cell-targeting therapy suggested an active role for T cells. Studies have confirmed the proinflammatory nature of ITP characterized as Th1/Th17 profile. However, little is known about the involvement of CD8+ Cytotoxic T cells (CTL) in ITP pathophysiology and whether they are regulated by regulatory T cells (Treg). Immunosuppressive therapy has been the mainstay treatment in ITP. Most recently, Thrombopoietin Receptor Agonists romiplostim changes are affected by various disease activity and how these TPO-RA may induce effect remission through regulating the immune system. Multi-color flow cytometric panels were designed to characterize peripheral blood T cell subsets phenotypically as well as functionally through intracellular cytokine expression. Forty (40) patients with ITP were studied and compared with 26 age and gender matched Healthy Controls (HC). Terminally-differentiated effector CTLs were significantly higher in patients compared to HC. This effector population is polyfunctional, expressing high levels of proinflammatory cytokines compared to HC. Although Treg functionality was preserved in these patients, they corresponded to disease activity and in relation to CTLs. The acronym ITP stands for ‘immune thrombocytopenia’ and has, by international agreement, replaced the term ‘idiopathic thrombocytopenic purpura’. This is because ITP is no longer idiopathic. The Greek term ‘ídios pathos’ designates a disease without a tangible cause, but today we know that ITP is caused by a dysregulation of the immune system [4]. The term ‘purpura’ is also misleading since almost one-third of the newly diagnosed ITP patients have no bleeding but only low platelet counts.

## Image

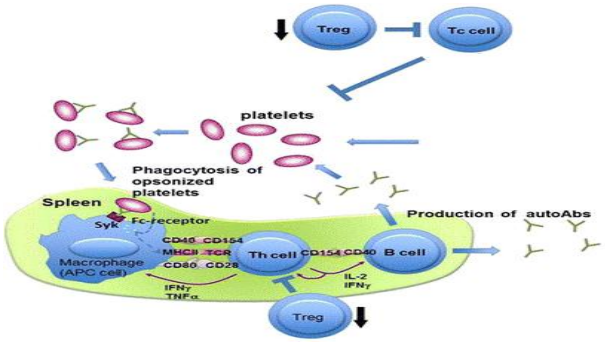


**Figure 1. Overview of the current understanding of ITP pathogenesis.**

Platelets are opsonized by autoantibodies to be phagocytosed by macrophages in the spleen. These macrophages stimulate T cells leading to a subsequent CTL-mediated destruction of platelets.

## Recent Publications

1. Sayed, A *et al*. 2017. 'CD8 T cells are involved in the pathogenesis of immune thrombocytopenia (ITP) and may be differentially modulated by the two thrombopoietin receptor agonists (TPO-RAs)', British Society for Haematology (BSH) Annual scientific meeting 2017, *Br J Haematol*. 2017;176:39. doi:10.1111/bjh.14613
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2. Rong W, Yan-xiang Z, Shan-shan X, Ju-mei S. Lymphocyte subsets in primary immune thrombocytopenia. Blood Coagul Fibrinolysis. 2014;25:816–9.
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