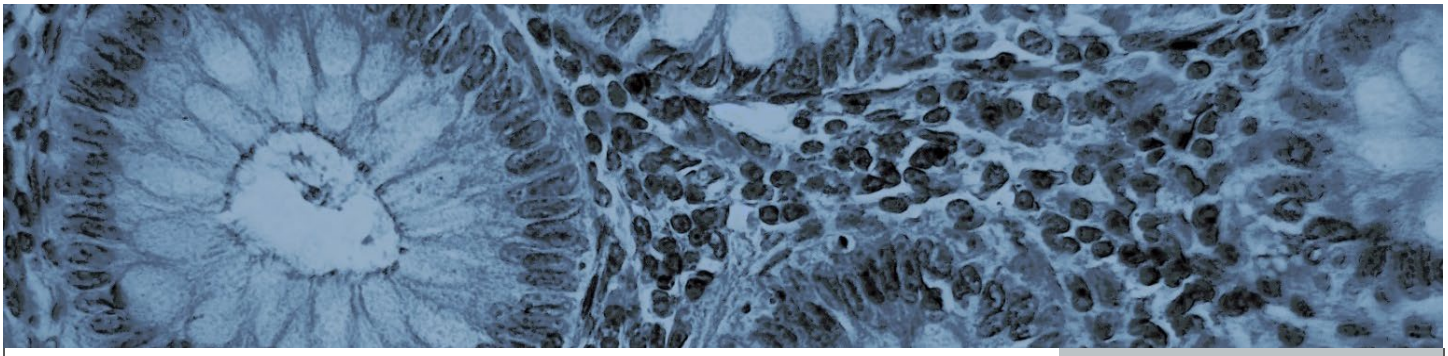

Fasneg Tregs as an “immunometer” in Bone Marrow Failure Syndromes (BMF)

Thursday, November, 11, 2021
11:30 AM to 12:30 PM
https://purdue-edu.zoom.us/j/99822915094

Immune aplastic anaemia (AA) has two key characteristics: an autoimmune response against haematopoietic stem/progenitor cells and a reduction in the number and function of regulatory T cells (Tregs). Using deep phenotyping, we have previously demonstrated a reduction in a specific subpopulation of Treg in AA, which predicts response to immunosuppression. We have identified two mechanisms that lead to skewed Treg composition in AA. Firstly, Fas-L mediated apoptosis on ligand interaction and, secondly, relative IL-2 deprivation. We have shown that IL-2 augmentation can overcome these mechanisms.
Interestingly, when high concentrations of IL-2 were used for in vitro Treg expansion cultures, AA Tregs were able to expand. The expanded populations expressed a high level of p-BCL-2, which makes them resistant to apoptosis. Using a xenograft mouse model, the function and stability of expanded AA Tregs were tested. We have shown that these Tregs could suppress the macroscopic clinical features and tissue manifestations of T cell-mediated graft-versus-host disease. These Tregs maintained their suppressive properties as well as their phenotype in a highly inflammatory environment. Our findings provide an insight into the mechanisms of Treg reduction in AA. We have identified novel targets with potential for therapeutic interventions. This work highlights the importance of systems immunology and “big data” in clinical translational research and how it may lead to novel therapeutic approaches.

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