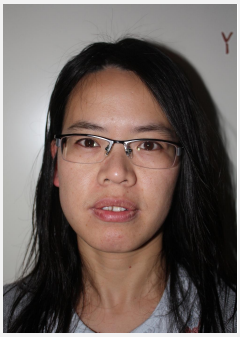
ImmunoTools IT-Box-139 Award 2012



Xuehui He

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Immunosuppressive compounds and human regulatory T cells

Regulatory T-cells (Treg) are an integral part of the immune system and are crucial for the maintenance of immune homeostasis and the prevention of immune pathology. Treg are found in the peripheral blood, as well as in peripheral and lymphoid tissues. The Treg pool is heterogeneous in nature and comprises both thymic derived (naturally occurring) as well as peripherally induced Treg. These subsets differ in function and phenotype. Following identification of Treg, the regulation role of these cells was demonstrated in a variety of preclinical autoimmunity and transplantation models and their clinical relevance was proven by demonstrating that regulating function of Treg was hampered in autoimmunity and allergy. This knowledge is currently exploited for the development of new therapeutic designs in the prevention of human chronic-inflammatory diseases and transplant rejection. In preclinical (stem cell and solid organ) transplant and autoimmunity mouse models, Treg-based immunotherapy has already proven successful. Currently, phase I clinical trials have been initiated in stem cell transplant an diabetes patients using ex vivo generated or freshly isolated human Treg populations. So far no serious adverse effects have been described. However, recent insights point to the notion that human peripheral blood derived Treg may lose the expression of the Treg-master transcription factor Foxp3 and convert into less suppressive and even inflammatory phenotypes under pro-inflammatory environmental stumuli. To harness clinical Treg based cell therapy, the question of how to maintain human Treg stability under both ex vivo expansion conditions as well as under in vivo inflammatory conditions awaits immediate resolution, and the search for pharmaceutical agents that may realize such a feat has only just started. Stable Foxp3 expression is under tight epigenetic control and already there are indications that pharmaceutical agents such as DNA methyl transferase (DNMT) inhibitors and Histon Deacetylase (HDAC) inhibitors can support Foxp3 stability in human Treg. Also, Rapamycin, an mTOR inhibitor, is now successfully used in Treg expansion protocols to maintain Treg stability. My PhD project mainly focuses on the effect of distinct immunosuppressive compounds (ISDs) on the stability of human Treg.

$CD4^+CD25highCD45RA^+$ naive and $CD4^+CD25highCD45RO^+$ memory Treg are treated with several ISDs of interest, targeting different routes of activation. The expression of activation, differentiation, homing markers plus related transcription factors and Annexin V will be analyzed.by flowcytometry. The ideal ISD should preserve Treg regulatory phenotype and suppressor function.

ImmunoTools IT-Box-139 for Xuehui He includes 100 antibodies

FITC - conjugated anti-human CD1a, CD3, CD4, CD5, CD6, CD7, CD8, CD14, CD15, CD16, CD19, CD21, CD25, CD29, CD35, CD36, CD41a, CD42b, CD45, CD45RA, CD45RB, CD45RO, CD49d, CD53, CD57, CD61, CD63, CD80, CD86, HLA-DR, IL-6, Control-IgG1, Control-IgG2a, Control-IgG2b, Annexin V

PE - conjugated anti-human CD3, CD4, CD8, CD11b, CD15, CD14, CD18, CD19, CD20, CD21, CD22, CD31, CD33, CD38, CD40, CD45, CD45RB, CD50, CD52, CD56, CD58, CD62p, CD72, CD95, CD105, CD147, CD177, CD235a, HLA-ABC, IL-6, Control-IgG1, Control-IgG2a, Control-IgG2b, Annexin V

PE/Dy647 -tandem conjugated anti-human CD3, CD4, CD8, CD14, CD19, CD20, CD25, CD54

APC -conjugated anti-human CD2, CD3, CD4, CD8, CD10, CD11a, CD11c, CD14, CD16, CD27, CD37, CD42b, CD44, CD45, CD59, CD62L, CD69, CD71, IL-6, Control-IgG1, Control-IgG2a, Control-IgG2b, Annexin V

DETAILS