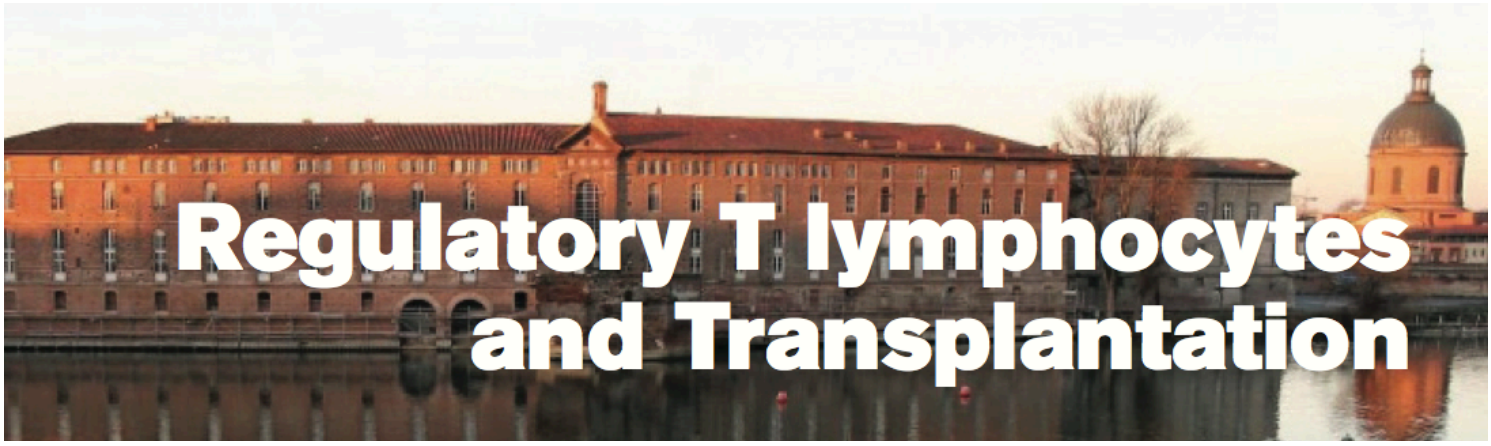

$CD4^+CD25^+$ regulatory T cells

in allogeneic stem cell transplantation

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Graft-versus-host disease (GVHD) is a major complication after allogeneic stem cell transplantation (SCT) and induced by donor T cells recognizing major or minor histocompatibility antigens of the recipient. After their activation and expansion, such alloreactive effector T cells attack typical target organs, such as skin, liver and gut. A main goal of current research in SCT is the separation of beneficial donor T cell effects, such as the graft-versus-leukemia/lymphoma response of donor T cells, from harmful effects, such as severe GVHD. In murine disease models, we and others previously showed that the adoptive transfer of donor $CD4^+CD25^+$ regulatory T cells (Treg) does not induce GVHD after allogeneic SCT, but protects from GVHD otherwise induced by co-transplanted conventional donor T cells. Importantly, donor Treg cells do not completely paralyse donor T cell functions, as their graft-versus leukaemia/lymphoma activity can be maintained in the presence of Treg cells. Thus, the adoptive transfer of $CD4^+CD25^+$ Treg cells seems an attractive strategy for the prevention of GVHD after allogeneic SCT in humans. For the preparation of such clinical trials we described methods for the GMP-compatible isolation and *in vitro* expansion of human Treg cells. Furthermore, we showed that $CD45RA^+$ Treg cells generate homogeneous Treg cell lines after *in vitro* expansion, while even CD127-depleted $CD4^+CD25^+$ T cells partially lose their Treg cell characteristics, as illustrated by the loss of FOXP3 expression, the emergence of cytokine producers and by changes in the methylation pattern within the FOXP3 locus. Based on these various findings, we suggested that the isolation and expansion of naïve Treg cells is the safest strategy for clinical trials in SCT exploring the suppressive activity of *in vitro* expanded Treg cells for GVHD prevention or therapy. Strategies and preliminary results from the efforts to translate these findings into clinical trials will be presented.