

ISCT 2014 - Abstract Submission

A PRODUCTION PLATFORM FOR ANTIGEN-SPECIFIC T-REGULATORY (AG-TREG) IMMUNOCELLULAR THERAPY OF AUTOIMMUNE AND INFLAMMATORY DISEASES.

Belmonte. N, Asnagli H, Brun V, Neveu V, Clerget -Chossat N, Foussat A.
TxCell, Valbonne, Sophia-Antipolis, France.

INTRODUCTION: Antigen-specific Treg (Ag-Treg) cells have shown tolerability and potential efficacy in first in man clinical trials in inflammatory diseases such as Crohn's Disease. A robust production platform is required to exploit their potential.

METHODS: Human PBMCs are activated with a selected antigen (Ag) depending on the condition to treat and the Ag localization in the target tissues. Ag-T cells are cloned and expanded in-vitro. Clones showing Treg identity based on IL-10 secretion are selected, expanded and frozen. Mouse Ag-Treg cells were produced from splenocytes. The Ag Ovalbumin (Ova), Collagen-type II (Col-II), Myelin-Oligodendrocyte-glycoprotein (MOG), Dust-mite antigen Derp1 and Heat-shock Protein-60 (HSP60) have been used in mice and/or in humans for Ag-Tregs production to treat inflammatory-bowel disease, joint/eye inflammatory diseases, central nervous system inflammatory diseases, dust mite allergy and other autoimmune diseases, respectively.

RESULTS: Ag-Tregs for different antigens were successfully produced using the production platform. Adoptive transfer of mouse Ova-Tregs, Col-Tregs and MOG-Tregs leads to inhibition of inflammation in animal models of inflammatory colitis, Rheumatoid Arthritis and Multiple sclerosis, respectively. Ag-Treg cells migrated in inflamed tissues within 24hours. Ova-Treg and Col-Treg were produced from the blood of healthy donors and Crohn's Disease or Rheumatoid arthritis patients, respectively with comparable surface markers expression and cytokine profile. Human Ag-Treg cells were successfully produced with HSP60 and Derp-1 demonstrating Ag-Treg production platform can address other inflammatory diseases.

CONCLUSION: We developed a production platform for Ag-Treg cells allowing treatment of multiple inflammatory conditions according to the Treg specific antigen. This technology triggers Treg cell suppressive activity leading inflammation inhibition by targeting Ags localized in the inflamed tissues.

Contact E-mail Address: nathalie.belmonte@txcell.com

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