

# ISCT 2014 - Abstract Submission

## Development of Col-Treg, an Antigen specific Treg based immune-cellular therapy for joint and eye inflammatory disease

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**INTRODUCTION:** Treg cells are ideal tools for antigen-specific suppressive treatment of inflammation. The objectives of these studies were to evaluate the therapeutic potential of Collagen-II specific type 1 Treg (Col-Treg) in experimental model of Arthritis and, based on this technology, to generate and characterize Col-Treg from the peripheral blood of refractory Rheumatoid Arthritis (RA) patients.

**METHODS:** Col-Treg were isolated, cloned, selected and expanded cells from (i) Collagen II-specific TCR transgenic mice and (ii) from Rheumatoid Arthritis patients' PBMCs exposed to collagen type II. The therapeutic potential of Col-Treg was evaluated after adoptive transfer in collagen-antibodies and collagen induced arthritis mice models or through analysis of their suppressive function *in vitro*.

**RESULTS:** A single Col-Treg cell-infusion led to a significant decrease of incidence and clinical severity in both acute and chronic mice models of arthritis. Col-Treg migrated specifically to the inflamed joints suggesting that the suppressive activity of Col-Treg is triggered locally by local collagen-II. Long-term tracking of Col-Treg cells in mice did not show any tumourigenicity or unlimited proliferation. Production of Col-Treg was successful in 10/11 RA patients whatever the disease history and immunosuppressive or anti-inflammatory treatment. Col-Treg from RA patients showed surface molecule expression and cytokine secretion consistent with Type 1 Treg identity. Consistent *in vitro* suppressive activity of Col-Treg isolated from RA patients on CD4+ T-cell proliferation was observed.

**CONCLUSION:** We demonstrated the efficacy and safety of Col-Treg administration in two mice models of arthritis. Feasibility of translation of this model to the human settings was also documented by the successful production of functional suppressive Col-Treg from RA patients. Collagen-II, the specific antigen for Col-Treg cells is naturally present in joints and eyes. These results suggest that triggering autologous Col-Treg activation is feasible and has a potential for treatment in articular and ophthalmic inflammatory diseases.

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