



POSTER PRESENTATION

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Inducible Treg cell populations as cell based-therapy for rheumatoid arthritis

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From 7th European Workshop on Immune-Mediated Inflammatory Diseases Noordwijk aan Zee, the Netherlands. 28-30 November 2012

Background

Adoptive cell transfer of Treg cells is a promising approach to restore tolerance in autoimmune disease.

However the various type of Tregs, their doses of injection and their *in vivo*-suppressive mechanism need to be precisely define to clearly establish which Tregs will be able to dampen efficiently the immune response in the various settings.

In our study, we compared the therapeutic potential of induced CD25⁺FoxP3⁺ and two IL10-secreting Tregs: Tr1 and CD49b-induced Tregs.

Materials and methods

CD49b Treg cells were generated in naive mice following repetitive injections of iDC. The purification was based on the negative selection of CD4 T cells isolated from the spleen and liver of the iDC-vaccinated mice.

Cell sorting experiments were realized to obtain 98% pure CD49b⁺ T or CD25⁺ cells. Collagen type II (bCII) specific Tr1 clones were obtained from TCR transgenic mice and expanded *in vitro*. Selected clones showed *in vitro* antigen specificity, Tr1 cytokine profile and IL10- and TGF -dependent suppressive activity.

Results

Several doses of CD49b or Tr1 cells were injected i.v. at day 28 in established collagen-induced arthritis. Clinical signs of arthritis were scored, as well as biological parameters such as the level of anti-bCII antibodies in sera and the cytokine profile of bCII specific T cells.

We defined for both Treg cell populations the dose effect in curative settings experiments. One single dose of 3x10⁶ or 1x10⁶ of Tr1 cell administration could reduce

the incidence and severity of CIA. Interestingly, higher dose of 10M of Tr1 cells did not improve the disease. In the same manner, the dose of 10⁵ CD4CD49b⁺ or CD25⁺ cells reverse clinical symptom with a lack of efficacy of higher doses. The cytokinic profile of the Tr1 cells was also investigated in inflammatory settings as well as the impact of the various Treg cells on the proliferation of effector cells *in vivo*.

Conclusions

Our results suggest that even if the Treg cells present some similarities, we need to precisely define the dose and type of Treg that will be efficient in each experimental setting.

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Published: 28 November 2012

doi:10.1186/1479-5876-10-S3-P55

Cite this article as: Martire et al.: Inducible Treg cell populations as cell based-therapy for rheumatoid arthritis. *Journal of Translational Medicine* 2012 **10**(Suppl 3):P55.

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