Immunotherapy of autoimmune diseases using autologous IL-10 producing Tr1 regulatory cells- A first injection trial in humans.

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IL-10 producing regulatory cells, also called Tr1 cells were discovered in 1997 based on their properties to prevent in vitro bystander T-cell proliferation and to inhibit in vivo chronic colitis in mice. In 2001, TxCell biotech was founded on the idea that such regulatory cell populations could have a strong efficacy also in humans in severe chronic inflammatory conditions.

In order to assess the potency of Tr1 cell therapy in patients displaying severe Crohn's disease, a reproducible manufacturing process for ovalbumin specific human Tr1 cell was set-up in GMP conditions. Characterization of the human cell therapy product shows an in vitro suppressive activity on T-cell proliferation dependent on the production of both IL-10 and TGF-beta. Manufactured Tr1 cells display a regulatory phenotype including Foxp3, GITR and CTLA4 surface expression and express a set of homing molecules crucial for the homing to inflammatory tissues. In vitro toxicity studies of human Tr1 cell products (tumorogenicity, karyotyping, telomerase activity) showed a safety profile compatible with the use of these lymphocytes for cell therapy.

Based on these elements, a phase I/IIa clinical trial was initiated in March 2008 in severe Crohn's disease patients. In this trial, concomitant administration of the control antigen (ovalbumin) and of the autologous ovalbumin specific Tr1 cells is performed in order to induce a massive release of suppressive cytokines in the inflamed gut tissues upon encounter of the cells with the antigen.