

## **Regulatory T cell engineered with Chimeric Antigen Receptor (CAR-Treg) for Inflammatory and Autoimmune diseases<**

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The adoptive transfer of autologous Regulatory T cells (Treg cells) with anti-inflammatory and immunomodulatory properties brings the promises of a breakthrough therapeutic strategy for the treatment of patients with severe chronic inflammatory and autoimmune diseases, escaping to conventional treatments. Clinical results obtained with autologous antigen-specific Tregs in Crohn's Disease and with autologous polyclonal Tregs in Type 1 Diabetes showed a good tolerability together with promising signs of efficacy. Not surprisingly, comparative results obtained with Treg cells in animal models of inflammatory diseases suggest that antigen-specific Tregs are more efficient than polyclonal Treg cells for the in vivo inhibition of inflammation. On T lymphocytes, antigen-specificity could be either obtained through the natural T Cell Receptor (TCR) or through gene transduction of a Chimeric Antigen Receptor (CAR). Treg cells engineered with CARs have a stable Treg phenotype and displays immunoregulatory activities upon ligation of the CAR with the target antigen. Several CAR-Treg cell based approaches have been described in the literature showing in vivo and in vitro efficacy and bringing a new dimension to the already known Treg cell therapy approach.

Development of CAR-Treg cell based immunotherapy products brings also challenges, some reminiscent of the CAR-T cell field, including CAR-T for cancer, some other specific to regulatory cell nature, function and target disease areas. However, the unmet need present in inflammatory and autoimmune diseases, the preliminary data of safety and efficacy of Treg cell adoptive therapy in humans and the huge potential of the CAR technology warrant the development of CAR-Treg cell based products for patients that are refractory to available treatments.