Antigen-specific TCR-Treg Therapy

THERAPEUTIC: Autoimmune Disease

Product Type	Engineered Regulatory T cells (Tregs) expressing autoantigen-specific T cell receptors (TCRs)
Indication / ROA	Autoimmune disease
Target / MoA	Autoantigen-specific $CD4^+$ Tregs interact with antigen presenting cells, resulting in both antigen specific and non-specific immune suppression towards autoimmunity.
Development Stage	Lead series
Brief Description & Differentiation	Potential "first-in-class" undisclosed autoantigen specific TCRs were identified from Tregs in healthy donors. Advantages of using TCR-Treg therapy to treat autoimmune disease include: • Ability to target intracellular antigen that cannot be targeted by CAR-Treg therapy. • Our TCR series cover two HLA types that are enriched in patients. • Potent autoantigen-directed immunosuppression, limited inhibition on protective immunity. • Establishing immune tolerance through interaction with APCs, compared with traditional treatments targeting T cells, B cells or cytokines. • Lower dose of cell infusion expected, compared with polyclonal Treg therapy.
Research Team	Dr. Joshua Ooi, Prof. Eric Morand
Intellectual Property	Provisional patent application filed claiming compositions of TCR and autoantigen peptide and method of treatment in Autoimmune disease.
Future	• Testing efficacy of TCR-Treg therapy in humanized mouse disease models. • Testing TCR cross-reactivity with other antigens (e.g. antigens derived from pathogen and cancer).

➢ Key Data

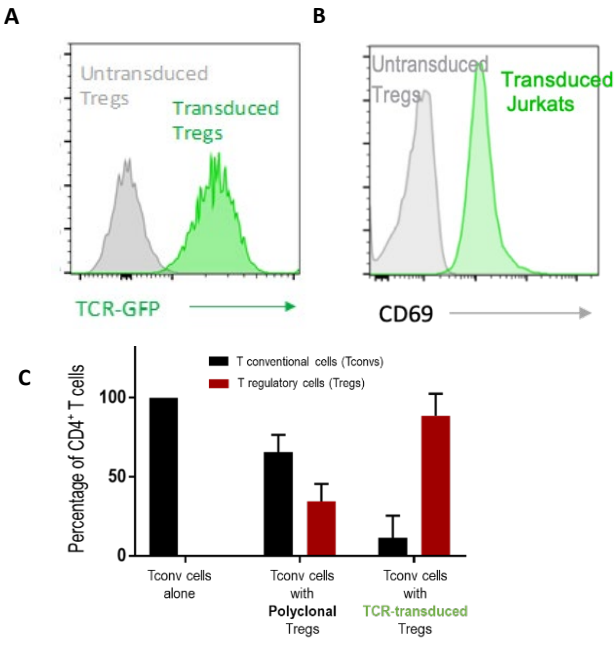

Figure: Tregs transduced with antigen-specific TCR efficiently suppress T cell response.

A: TCR expression 18 days after lentiviral transduction in human primary Tregs.

B: Jurkat T cells, either transduced or not transduced with TCR, were stimulated with B-LCL pulsed with cognate autoantigen peptide. Jurkat T cells transduced with TCR upregulated CD69 expression following stimulation.

C: PBMCs from patients (n=2) were stimulated with autoantigen peptide then co-cultured with either polyclonal Tregs or TCR-transduced Tregs at a Tconv:Treg ratio of 1:1. At the end of culture, TCR-transduced Tregs markedly out-competed Tconvs, Tconv:Treg ratio ~1:9, while polyclonal Tregs had inferior reactivity, Tconv:Treg ~6:4.