Session 18: New Molecular Targets in Personalized Therapy of Autoimmune Diseases

Lectures

L18.1

Tolerance-induction with autologous tolerogenic dendritic cells treated with VITamin D3 and loaded with myelin peptides in Multiple Sclerosis (Tolervit-MS)

M. J. Mansilla[1,2], S. Presas-Rodríguez[3,4], J. Navarro-Barriuso[1,2], A. Teniente-Serra A[1,2], B. Quirant-Sánchez[1,2], A. L. Lopez-Díaz de Cerio[5], S. Inogés[5], F. Prósper[5], C. Ramo-Tello[3,4], E. M. Martinez-Cáceres[1,2]

[1]Immunology Division, Germans Trias i Pujol University Hospital and Research Institute, Campus Can Ruti, Badalona, Espania; [2]Department of Cellular Biology, Physiology and Immunology, Universitat Autònoma de Barcelona, Espania; [3] Multiple Sclerosis Unit, Department of Neurosciences, Hospital Universitari Germans Trias i Pujol, Badalona, Espania; [4]Department of Medicine, Universitat Autònoma de Barcelona, Espania; [5]Cell Therapy Center, Clínica Universidad de Navarra, Pamplona, Espania

Eva Maria Martinez-Caceres <emmartinez.germanstrias@gencat.cat>

Multiple sclerosis (MS) is an autoimmune disease of the central nervous system. Current treatments reduce disease activity but do not decrease long-term disability and have relevant side effects. Thus, there is an unmet need for safer and effective treatments. Autologous therapy with tolerogenic dendritic cells (tolDC) is a promising strategy for the attenuation of pathogenic T cells in autoimmune diseases. Our group has developed an antigen-specific cell therapy based on autologous vitamin D3 (VitD3)-tolDC loaded with myelin peptides.

In vitro studies have demonstrated a potent immunoregulatory activity of vitD3-tolDC reducing lymphocyte proliferation and IFN-g production and increasing IL-10 levels, in co-culture experiments. Moreover, *in vivo* studies in the animal model of MS revealed a beneficial effect of VitD3-tolDC ameliorating the severity of the disease. Considering these pre-clinical results, as well as reported outcomes from previous clinical trials using DC, a clinical trial has just started recruitment.

Active MS patients will be included in a dose-escalation best-of-five design: Cohort 1 (5x10^6 VitD3-tolDC), Cohort 2 (10x10^6), Cohort 3 (15x10^6). A fourth Cohort of patients under IFN-beta treatment receiving the selected dose of VitD3-tolDC will be included. The trial protocol has been approved by the Spanish regulatory authorities (AEMPS) (Nº EudraCT: 2015-003541-26, available at ClinicalTrials.gov Identifier: NCT02903537, Tolervit-MS). Each cohort will received 6 administrations of tolDC (first 4 every 2 weeks and last 2 every 4 weeks). Clinical, MRI and immunological monitoring of 12 patients will be performed for 24 months. Each patient will be its own pre- and post-intervention control.

L18.2

T regulatory cells to treat autoimmune diseases

Piotr Trzonkowski

Department of Clinical Immunology and Transplantology, Medical University of Gdansk, Gdańsk, Poland

Piotr Gdansk Trzonkowski <ptrzon@gumed.edu.pl>

T regulatory cells (Tregs) are considered a viable option in tolerance induction treatment in the clinic. First promising clinical experiments and trials with clinical-grade Tregs cultured as advanced therapy medicinal product (ATMP) are completed already. We will present long-term results (more than 2 years follow up) of our trial with Tregs in type 1 diabetes discussing metabolic and immune background of the patients, which, in our opinion, influenced the efficacy of this treatment. *In vivo* results will be supported with in vitro and animal models showing activity of Tregs in auto- and allogeneic settings.

References:

Marek-Trzonkowska N (2016) Factors affecting long-term efficacy of T regulatory cell-based therapy in type 1 diabetes. *J Transl Med* **14**: 332.

Marek-Trzonkowska N *et al.* (2012) Administration of CD4+CD25 high-CD127-regulatory T cells preserves β-cell function in type 1 diabetes in children. *Diabetes Care* **35**: 1817-1820.

Marek N *et al.* (2011) Coating human pancreatic islets with CD4(+) CD25(high)CD127(-) regulatory T cells as a novel approach for the local immunoprotection. *Ann Surg* **254**: 512-518.

Trzonkowski P *et al.* (2009) First-in-man clinical results of the treatment of patients with graft versus host disease with human *ex vivo* expanded CD4+CD25+CD127- T regulatory cells. *Clin Immunol* **133**: 22-26.