International Graduate School in Molecular Medicine
PhD Project on Basic and Applied Immunology and Oncology

Project Title: **Characterization and targeting of autoreactive memory stem T cells in patients with type 1 diabetes undergoing to islet transplantation**

DoS: Paolo Monti, PhD-Transplant Immunology Unit (Diabetes Research Institute)

Memory autoimmunity is a hallmark of patients who developed type 1 diabetes (1). The memory T cell response can be re-activated after islet transplantation and is difficult to control with standard immunosuppression (2). A novel memory T cell subset with stem-cell like properties has been recently discovered and named memory stem T cells (Tscm) (3). Tscm are responsible for the maintenance of long-term memory and therefore represent an ideal target cell population to eradicate memory autoimmunity. However Tscm have been poorly characterized in the autoimmune clinical setting.

The overall aim of this project is to detect, characterize and find potentially targetable molecules or pathways to selectively inhibit autoreactive Tscm to control the autoimmune mediated destruction of insulin-producing beta cells.

Specific aims are:

1) Aim 1. To determine the role of autoreactive Tscm in islet transplanted patients by flow cytometry in human samples from patients pre and post transplantation.
2) Aim 2. To characterize Tscm gene expression and phenotype in order to identify molecular target of drugs and biological for Tscm modulation
3) Aim 3. To develop innovative strategies for selective inhibition of Tscm for translation in the human disease.

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2. Monti P, Scirpoli M, Maffi P, Ghidoli N, De Taddeo F, Bertuzzi F, Piemonti L, Falcone M, Secchi A, Bonifacio E. Islet transplantation in patients with autoimmune diabetes induces homeostatic cytokines that expand autoreactive memory T cells. J Clin Invest. 2008. 118 (5), pp. 1806-1814

3. Lugli E, Dominguez MH, Gattinoni L, Chattopadhyay PK, Bolton DL, Song K, Klatt NR, Brenchley JM, Vaccari M, Gostick E, Price DA, Waldmann TA, Restifo NP, Franchini G, Roederer M. Superior T memory stem cell persistence supports long-lived T cell memory. J Clin Invest. 2013 Feb;123(2):594-9

http://www.hsr.it/research/organization/institutes/diabetes-research-institute-hsr-dri/transplant-immunology/