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New protocol for generation of insulin-specific T regulatory cells

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Immunotherapy of autoimmune diseases with CD4⁺CD25^{high}FoxP3⁺ T regulatory cells (Tregs) is currently in the stage of clinical trials. Tregs used for human therapy are polyclonal, but studies in animals showed that autoantigen-specific Tregs are more effective in preventing or ameliorating the pathogenesis of autoimmune diseases compared to polyclonal Tregs. Since Tregs are usually defective in individuals with an autoimmune process, the basic idea of our research was to convert insulin-specific T effector cells into insulin-specific Tregs using various *in vitro* manipulations. In NOD mice that develop T1D spontaneously, the occurrence of insulin-specific CD4⁺ T cells was 0,1%. In order to increase the number of insulin-specific T cells, CD4⁺ T cells were co-cultivated *in vitro* with autologous mature dendritic cells in the presence of insulin peptide (B9:23). The proportion of insulin-specific CD4⁺ cells after 48 h increased up to 3,4±0,1% and this level remained stable for 2 days. Insulin-specific CD4⁺ cells were then stained by fluorescent insulin-loaded MHC class II tetramer and sorted using flow cytometer. Obtained cells were cultured in RPMI-1640 medium supplemented with TCR stimulators (anti-CD3 and anti-CD28 antibody), recombinant IL-2 and TGF-β proteins. After 5 days, the number of CD4⁺CD25^{high}FoxP3⁺ Tregs reached 48%. However, further cultivation (with medium replacement every second day) did not lead to an increase in the number of Tregs, on the contrary, the Treg proportion was reduced to 14%. These results imply that it is feasible to generate antigen-specific Tregs from antigen-specific effector cells, but the protocol still requires a few modifications in order to produce sufficient number of Tregs for *in vivo* use

Biography

Ivana Stojanovic is a Research Professor and the Principal Investigator of the project funded by the Iacocca Family Foundation (Boston, MA, USA), that aims at developing new protocol for generation of insulin-specific T regulatory cells for the therapy of individuals with type 1 diabetes. The focus of her research has been on the modulation of type 1 diabetes in the animal models, as well as investigation of the pathologic processes involved in the progression of this disease. She was a Principal Investigator of the project funded by European Foundation for the Study of Diabetes between 2007 and 2009 and involved in numerous projects funded by the Ministry of Science, Republic of Serbia. She is an expert in flow cytometry. She was a Supervisor for 2 PhD theses and several master and diploma theses. She has published 51 research articles in peer-reviewed journals, with 950 citations and *h*-index 19

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