Title: Negative vaccination with IGRP-pulsed dendritic cells expressing ectopic IL-35Ig prevents the development of NOD autoimmune diabetes.

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Dendritic cells (DCs) are specialized antigen presenting cells capable of triggering either stimulatory or regulatory T cell immune responses, according to their cell maturation state and microenvironment stimuli. IL-35, a heterodimeric cytokine belonging to the IL-12 family, is produced by regulatory T and B cells, and is known to induce a strong immunosuppressive response. In this study, we explored the possible regulatory and protective effect of IL-35 in a tolerogenic vaccination protocol aimed to prevent autoimmune diabetes in prediabetic NOD mice.

To this purpose we prepared murine splenic DCs transfected with an IL-35Ig single chain gene construct and loaded with IGRP peptide (one of the most relevant type 1 diabetes self-antigens) to be administered in a prophylactic cell therapy. Interestingly, we found that such IL-35Ig-producing and IGRP-presenting DCs—capable to suppress antigen specific, T cell-mediated responses in a skin test assay—induced in prediabetic NOD mice a delayed and less severe form of diabetes, an effect accompanied by the increase of $CD4^{+}CD39^{+}$ suppressive T cells in pancreatic lymph nodes. Protective immunosuppression achieved in this model suggests that DCs overexpressing ectopic IL-35Ig might represent a powerful tool in negative vaccination strategies.

Biography

Maria Laura Belladonna is Professor of Molecular Pharmacology at the University of Perugia and Researcher of the Department of Experimental Medicine (Pharmacology Section) of the University of Perugia since 1999. She received her degree in 'Pharmaceutical Chemistry and Technology' and PhD in 'Experimental Medicine' from the University of Perugia. She performed postdoctoral studies at the Ludwig Institute for Cancer Research in Brussels.

Dr. Belladonna's research field is the study of dendritic cell functions, cytokines linked to immunological mechanisms driven by these cells, and the tolerogenic activity of tryptophan

catabolizing enzyme indoleamine 2,3-dioxygenase (IDO). She has published over 60 research articles and reviews (>7000 citations, H-index 37).