Professor, Center Director Decio Eizirik, MD, PhD
Place of enrolment: Université Libre de Bruxelles, Belgium

Principal investigator: Professor, DMSc Flemming Pociot, Steno Diabetes Center Copenhagen, Faculty of Health and Medical Sciences, University of Copenhagen, Copenhagen, Denmark.

Title of the project: Targeting key hubs for beta cell preservation in type 1 diabetes

ABSTRACT

Type 1 diabetes (T1D) results from the interaction between predisposing genes and environmental factors, triggering an autoimmune attack against pancreatic beta cells that provokes islet inflammation and progressive beta cell loss. Islet inflammation takes place in the context of a dialogue between invading immune cells and the targeted beta cells, which is modulated by T1D candidate genes, acting on both immune and pancreatic beta cells, and by inflammatory cytokines and chemokines. Most research in the field have focused on the immune system, with the beta cells seen as passive victims of the autoimmune attack. However, studies from the Eizirik group, in collaboration with Prof. Flemming Pociot, Copenhagen, suggested that stress pathways triggered within beta cells early in T1D may trigger a dialog with the immune system that initiates and/or accelerates autoimmune beta cell destruction. Furthermore, they showed that T1D candidate genes regulate beta cell responses to “danger signals” (such as viral infections), innate immunity, activation of cell death and the loss of beta cell ability to produce insulin. The molecular mechanisms linking genetic variation and environmental triggers with T1D, and the signalling events promoting beta cell dysfunction and loss, remain poorly understood. The present project proposes an integrative and multidisciplinary approach, to be developed in collaboration with the Pociot’s group, that combines genomics, epigenomics, transcriptomics and proteomics to unravel the complex multi-layered regulation of inflammation-induced gene networks in human beta cells. Integration of these multiple omics datasets will unveil critical molecular hubs for beta cell survival and pinpoint novel therapeutic targets to protect beta cells in T1D. Based on this innovative approach, the Eizirik group has already identified two potential targets that are now undergoing pre-clinical evaluation. Importantly, drugs modulating one of these targets are already under clinical investigation for other autoimmune diseases, and can be tested in early T1D.