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## **Functional and metabolic characterization of beta cells during type 1 diabetes progression**

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Type 1 diabetes (T1D) is an autoimmune disorder that is characterized by a progressive loss of insulin-producing beta cells. The decline in beta cells is accompanied by the infiltration of immune cells within pancreatic islets and an increase in ER stress. To date the mechanism behind the decline in beta cell function is poorly characterized. As part of the BioTechMed consortium “MIDAS - Inflammatory Mechanism involved in Diabetes Uncovered by Tissue Imaging and Machine Learning”, we want to link systemic immune cell response during T1D progression to functional and metabolic alterations within beta cells. To resemble the pathogenesis of human T1D we use non-obese diabetic (NOD) mice. Recent data from our consortium indicate that the decline in beta cell function occurs before any symptomatic manifestation of diabetes. Hence, we characterized the systemic and beta cell-specific immune- and molecular phenotype of NOD mice at defined non-diabetic blood glucose levels. Multiparameter flow cytometry analyses revealed only minor changes in immune cell populations in the blood of NOD mice before the onset of T1D. In contrast, pancreatic islets isolated from non-diabetic NOD mice exhibit already a decline in insulin secretion and storage ability associated with an upregulation in ER stress. Notably, plasma from these NOD mice induced ER stress and impaired cell viability of murine beta cells and pancreatic islets obtained from healthy mice. Thus, plasma from NOD mice comprises metabolic factors that modulate functional and metabolic pathways in pancreatic islet before the onset of T1D. However, whether these factors are coming from immune cells needs further investigations.