The pancreas consists of the exocrine and endocrine compartment. Exocrine compartment made of acinar cells (the most common cells in the pancreas) and ducts secrete and transport pancreatic juice to the intestine to aid digestion. The endocrine compartment is made up from islets of Langerhans-relatively rare (only 5% of the pancreas) clusters of 5 different endocrine cell types that secrete into blood hormones. One of the endocrine cells is beta-cell that secretes hormone insulin and regulates glucose levels in the blood. Any abnormalities in the proper cellular composition and the functional capacity of pancreatic cells lead to different disease, with diabetes being the most common one. Last year more than 415 million people worldwide were affected by diabetes, and the number of new cases is increasing every year. Therefore diabetes is a significant health and socio-economical burden and brings urgency to a better understanding of how pancreas forms and functions to develop regenerative medicine-based therapies and preventive strategies for diabetes and other pancreatic diseases. We recently showed that nuclear- factor IA, a transcription factor that has not been described previously for pancreas, regulates the balance between endocrine and exocrine compartment. Mice without this gene in the pancreas have very few islets but way more ducts and acinar cells. We also uncovered that this transcription factor regulates cellular composition in the pancreas through its influence of intracellular transport. Intracellular transport is involved in almost every aspect of cell life, and thus changes in this transport can have long-lasting and powerful effects. Here supported by initial data, we propose that NFIA controls also trafficking of insulin vesicles in beta cells, and thus, it regulates how much insulin is secreted when beta-cells are exposed to high glucose. We will study the role of NFIA in insulin secretion using mice, but also human stem cell-derived pancreatic cells. Insulin secretion has to be precisely regulated to prevent too low or too high blood glucose levels. Therefore insulin secretion is a multistep process with many regulatory mechanisms. We aim to understand which step of insulin secretion process is mediated by NFIA and what are the downstream effectors of NFIA. Further, we want to use this knowledge to improve the generation of human beta-cells from stem cells in vitro. Lastly, as NFIA is broadly present in the pancreas and so intracellular trafficking, we want to understand how NFIA effects different pancreatic cell type development and organization to achieve pancreatic cellular and functional homeostasis. In long-term, we aim these efforts will facilitate making fully functional human beta cells for patients with severe diabetes.