Current therapies for HI are largely ineffective, poorly tolerated and associated with several adverse reactions. Existing drugs target beta cells, which are found in the islets of Langerhans of the pancreas. These existing therapies for HI suppress insulin release and alleviate hypoglycemia. This project will study several different cell types found within the islets, not only beta cells. These different cell types are all associated with the control of normoglycemia and carry HI-causing gene defects. We know little or nothing of the functional role(s) of these other cell types in the pathology of HI.

To develop new approaches for treatment, we will study these other pancreatic cells and beta cells by sequencing mRNA using the latest technologies. We will compare HI and normal islet cells and the differences between individual HI islet cell types. We will also define how gene changes occur because of HI-causing mutations in the beta cells and other islet cell types. This will provide a greater understanding of disease-associated mutations, (b) who will benefit from surgery and who from drug therapy, and (c) the identification of alternative approaches to managing HI with existing drugs, drug combinations, and novel therapies. From this pilot study, we expect to develop new therapeutic strategies towards precision medicine in HI patients.