

Discovery of a new tracer targeting pancreatic beta cells for non-invasive imaging of human pancreatic endocrine cells, with support from JDRF, the leading global organization funding type 1 diabetes (T1D) research, and the IMI project INNODIA (published on line in Science Reports on 09.11.2017; www.nature.com/articles/s41598-017-15417-2)

There are presently no reliable ways to quantify endocrine cell mass (ECM) *in vivo*, which prevents an accurate understanding of the progressive beta cell loss in diabetes or following islet transplantation. Furthermore, the lack of beta cell imaging hampers evaluation of the impact of new drugs aiming to prevent beta cell loss in diabetes.

To address this unmet need, the group of Prof. Decio L. Eizirik (ULB Center for Diabetes Research, Brussels, Belgium), in collaboration with several other partners of the IMI project INNODIA, used advanced functional genomic tools to identify new biomarkers of the endocrine pancreas. Dipeptidyl-Peptidase 6 (DPP6) was identified as a novel target whose expression is at least 25-fold higher in human pancreatic islets as compared to surrounding tissues. Importantly, DPP6 expression is not changed by pro-inflammatory cytokines, to which beta cells are exposed in type 1 diabetes. At the protein level, DPP6 localizes only in beta and alpha cells within the pancreas. Next, Prof. Eizirik, in collaboration with Prof. Devoogdt and colleagues (VUB, Brussels) generated a high-affinity camel single-domain antibody (nanobody) targeting human DPP6. These camel or llama antibodies are very small (around 10% of an human antibody), and provide a very good tool for imaging, since they bind to their target and leave the circulation fast. Nanobodies are already been used to image and target cancers, but they have not been previously used to image beta cells.

The nanobody was radiolabelled and *in vivo* SPECT/CT imaging and biodistribution studies were performed in immunodeficient mice that were transplanted with insulin-producing human EndoC- β H1 cells. The human DPP6-expressing cells were well visualized, providing a clear image of the graft. In conclusion, researchers from the INNODIA consortium have identified a novel beta and alpha cell biomarker and developed a tracer for *in vivo* imaging of human insulin secreting cells. This may provide a useful tool to non-invasively follow up of these cells, and is an important step in the direction of future individualized therapies for type 1 diabetes, one of the key goals of INNODIA.

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