

## DPP6 is a new pancreatic islet biomarker suitable for human islet *in vivo* imaging

Demine S, Balhuizen A, Massa S, Ribeiro R, Mathijs I, Turatsinze JV, De Vos J, Xavier C, Villate O, Millard I, Egrise D, Capito C, Scharfmann R, In't Veld P, Marchetti P, Muylderman S, Goldman S, Lahoutte T, Bouwens L, Kerr-Conte J, Patou F, Devoogdt N, Eizirik DL

### Facts & Figures

Start date:	01/11/2015
End date:	31/10/2022
Contributions	
IMI funding:	17 630 000 €
EFPIA in kind:	14 357 739 €
Assoc Partners:	4 044 698 €
Total Cost:	36 665 443 €
Project website:	www.ulbcdiabres.com
Social media:	@ULBCDiabRes

### Challenge

Type I diabetes is characterized by an autoimmune attack resulting in a progressive destruction of the pancreatic beta cells. However, the disease's natural history is not yet fully understood. This is mostly due to a lack of tools allowing non-invasive *in vivo* beta cell mass quantification.

### Approach & Methodology

To address this issue, we used RNAseq data obtained from human islets and 16 other human tissues. We selected genes specifically expressed in human beta cells and unaffected by incubation in presence of proinflammatory cytokines (IL1 $\beta$  and IFN $\gamma$ ). A nanobody targeting one of the biomarker identified (DPP6) was produced and used to quantify, *in vivo*, primary human islets subcutaneously transplanted in NOD-SCID mice.

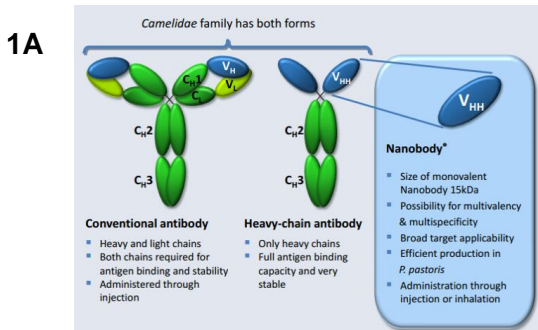


Fig 1A. Advantages of nanobodies vs conventional antibodies

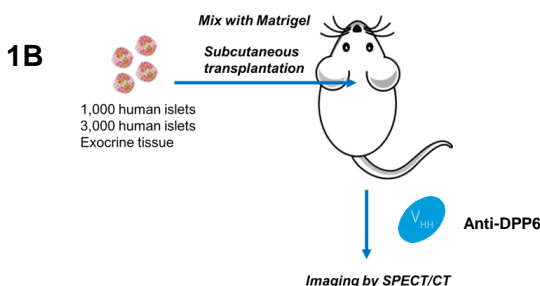


Fig 1B. Experimental approach

### Results

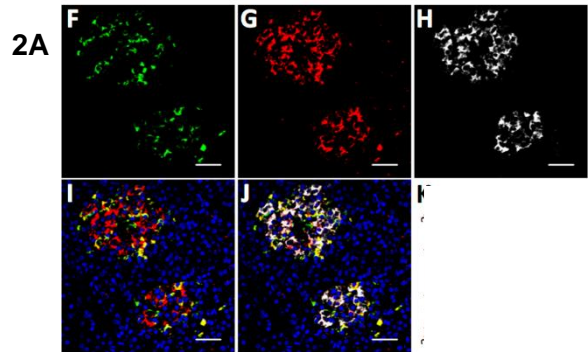


Fig 2A. Validation of the specificity of DPP6 expression in healthy human pancreas tissue. DPP6, insulin and glucagon expression were assessed by immunohistochemistry in a healthy human pancreas. No DPP6 expression was found in other organs but brain (not shown).

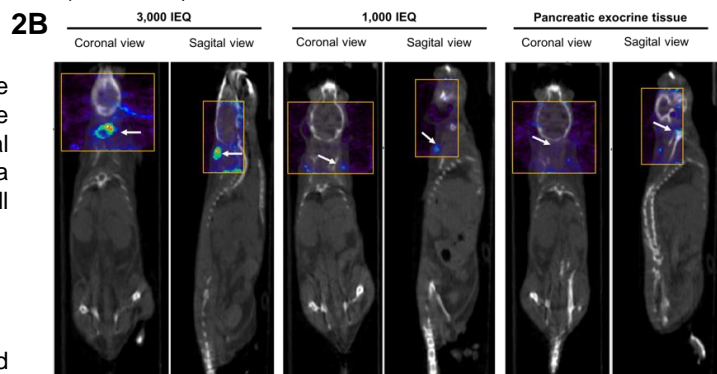
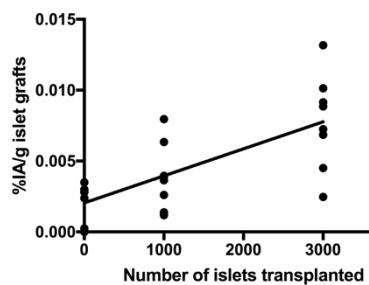


Fig 2B. *In vivo* quantification of human islets in mice. 1000, 3000 human islets or a comparable volume of pancreatic exocrine tissues were transplanted in NOD-SCID mice (n=8 per group). Arrows indicate the graft localization. The SPECT signal was quantified and plotted against the number of islets transplanted.



R<sup>2</sup> = 0.94

### Value of IMI collaboration

The IMI collaboration allowed us to obtain the required human islets and experimental models to validate the anti-DPP6 nanobody. It will also allow an eventual translation to patients, once we have GMP nanobodies for clinical use.

### Impact & take home message

- DPP6 is a biomarker specific to pancreatic beta and alpha cells.
- Our anti-DPP6 can be used to detect and quantify primary human islets grafted in mice and may be a useful tool to follow islet cell mass *in vivo*.