Institute for Pancreatic Islet Research
Pancreatic Islet Physiology

Highlight / Publication:
Cohrs CM, Chen C, Jahn SR, Stertmann J, Chmelova H, Weitz J, Bähr A, Klymiuk N, Steffen A, Ludwig B, Kamvissi V, Wolf E, Bornstein SR, **Solimena M, Speier S.**
Vessel network architecture of adult human islets promotes distinct cell-cell interactions in situ and is altered after transplantation.
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Keywords:
Diabetes, human islet of Langerhans, islet architecture, islet transplantation, revascularization

Central statement of the highlight in one sentence:
In human islets of Langerhans the distinct cellular arrangement promotes alpha-beta cell interactions, while beta-endothelial cell connections are limited by the comparably low vascular component which is further reduced in an age-dependent manner after transplantation.

Text of the highlight:
Islet cell hormone release is modulated by signals from endothelial and endocrine cells within the islet. However, models of intra-islet vascularization and paracrine cell signaling are mostly based on rodent pancreas. We here assessed for the first time the architecture and endocrine cell interaction of the vascular network in unperturbed human islets in situ and their potential to re-establish their endogenous vascular network after transplantation in vivo. We prepared pancreas tissue slices of fresh tissue obtained from non-diabetic patients undergoing partial pancreatectomy. In addition, we transplanted human donor islets into the anterior chamber of the mouse eye. Next, we performed three-dimensional in situ and in vivo imaging of islet cell and vessel architecture at cellular resolution and compared our findings to mouse and porcine islets. Our data reveal a significantly different vascular architecture with decreased vessel diameter, reduced vessel branching and shortened total vessel network in human compared to mouse islets. Together with the distinct cellular arrangement in human islets this limits beta-endothelial cell interactions, facilitates connection of alpha and beta cells and promotes the formation of independent beta cell clusters within islets. Furthermore, our results show that the endogenous vascular network of islets is significantly altered after transplantation in a donor-age related mechanism. Thus, our study provides new insight into vascular architecture and cellular arrangement of human islets with apparent consequences for intercellular islet signaling. Moreover, our findings suggest that human islet engraftment after transplantation can be improved by the use of alternative, less mature islet cell sources.

Taking account of the HMGU mission:
This work contributes to our understanding in human islet physiology which is a prerequisite for our understanding in diabetes development. Furthermore, the assessment of human islet engraftment after transplantation enables the optimization of islet cell transplantation for diabetes therapy.