The pancreatic islet: a micro-organ in control

M. H. Abdulreda1,2,3, P. O. Berggren1,4

1Department of Surgery, Diabetes Research Institute, University of Miami Miller School of Medicine, Miami, FL, USA
2Department of Microbiology and Immunology, University of Miami Miller School of Medicine, Miami, FL, USA
3Department of Ophthalmology, University of Miami Miller School of Medicine, Miami, FL, USA
4The Rolf Luft Research Center for Diabetes and Endocrinology, Karolinska Institutet, Karolinska University Hospital L1, SE-17176 Stockholm, Sweden

Corresponding Authors: Midhat H. Abdulreda, MS, PhD; e-mail: mabdulreda@miami.edu
Per-Olof Berggren, PhD; e-mail: per-olof.berggren@ki.se

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Abstract

The islets of Langerhans constitute the endocrine pancreas which regulates blood glucose homeostasis and their dysfunction results in diabetes. Each of the pancreatic islets constitutes an entire micro-organ with intricate cell to cell interactions and that is well vascularized and innervated. An important therapeutic advantage in islet transplant is that pancreatic islets maintain their organ integrity when isolated and transplanted to patients with severe diabetes. Once transplanted, the islet micro-organs actively contribute to their own vascularization and start to function immediately. Hence, in terms of organ transplantation, the application of pancreatic islets will be a decisive clinical tool for future diabetes care (credit: Tilo Moede).

The endocrine part of the pancreas, the islets of Langerhans, constitutes 2% of the pancreatic volume. Although we have more than one million islets in the human pancreas, each one of them constitutes an entire organ that is well vascularized and innervated1-4. This micro-organ is 50-500 micrometers in diameter and contains 2,000-5,000 cells that are mainly the insulin-secreting beta cells, the glucagon-secreting alpha cells, and the somatostatin-secreting delta cells (Figure 1). Not only are these cells regulated by a sophisticated interplay between nutrients in the blood and neurotransmitters released from nerves, but also by intrinsic paracrine signals5,6. Therefore, for islet cells to have their proper physiological function in regulating blood glucose homeostasis, they need to be within the structure of the micro-organ. If islet cells are dissociated, their function is impaired. Hence, the ultimate importance of these micro-organs is well accepted, and their failure will undoubtedly lead to diabetes development. In this context, a big emphasis is put on defects in the insulin-secreting beta cells, but also dysfunctional alpha and delta cells are likely to play a role in diabetes development. An illustration of the fundamental importance of the pancreatic islet micro-organ in regulating glucose homeostasis is the observation that it serves as the systemic “glucostat” and that determines the glycemic set point7.

The fact that the islets of Langerhans constitute entire micro-organs has been taken advantage of not only in basic research but also in the clinic with regard to islet transplantation. In basic research, it is important to understand endocrine cell to cell interactions as well as endocrine cell interactions with blood vessel endothelial cells and nerves. These interactions form the basis for activation of distinct signaling networks that will then lead to the activation of respective cells. Information obtained from such micro-organ studies in the living organism is fundamental to our abilities to identify novel druggable targets and drugs that interact with these targets for treatment of diabetes. In transplantation of pancreatic islets to patients with type 1 diabetes, the relative ease by which the islets can be isolated

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Hence, there is no reason that islet transplantation should be governed by rules and regulations other than organ transplantation in general.

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**ORCID:**
Midhat H. Abdulreda: https://orcid.org/0000-0002-0146-5876
Per-Olof Berggren: https://orcid.org/0000-0001-8991-413X

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