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251-LB: Tracking Beta-Cell Regeneration in Human Pancreatic Slices using Adenovirus Transduction

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Introduction: The study of pancreatic regeneration would benefit greatly from the design and validation of robust human-based models. Human Pancreatic Slices (HPSs) are thin organotypic sections of live pancreatic tissue. The sectioning method preserves the overall histological structure of the organ, maintaining the integrity of the extracellular matrix and the natural interaction between the endocrine and exocrine compartments, as well as the local neural, vascular and immune milieu. Conditions for the long-term culture of HPSs, recently reported by our team, have enabled the real-time analysis of beta-cell neogenesis using adenoviral (AV) co-transduction of a red-green reporter and an insulin tracer in human pancreatic slices. However, the ability of these cells to respond to glucose was not established at that time.

Methods: To determine whether new INS+ cells respond to glucose, we have designed an AV in which INS-dependent recombination leads to the expression of a blue marker (moxBFP) and a Calcium Imaging Reporter (gcAMP6s, green) whose intensity is proportional to glucose-dependent INS secretion. This allowed us to monitor glucose-stimulated calcium influx in the newly created cells. To track the generation of new beta cells with an even higher degree of resolution we subsequently placed the transduced slices in a custom-made microfluid chip.

Conclusions: This setting further allows for longitudinal functional analyses in precise and highly controlled experimental conditions. Our ability to study regeneration in a clinically meaningful model represents a groundbreaking advance that may fast-track the screening and preclinical development of therapeutic agents.

Disclosure

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