Washington University in St. Louis
Office of Technology Management

GENERATING PANCREATIC BETA CELLS FROM PLURIPOTENT STEM CELLS FOR DIABETES CELL THERAPY OR DRUG DEVELOPMENT

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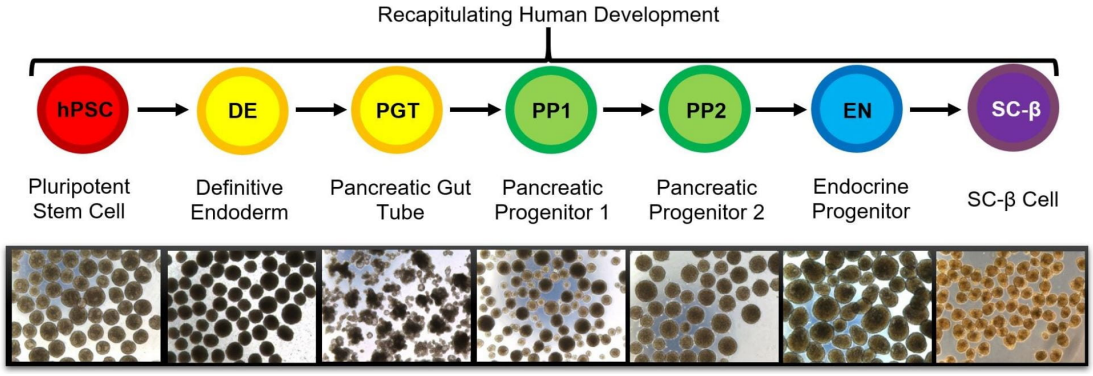
Technology Description:

Researchers in Prof. Jeffrey Millman's laboratory have developed multiple techniques for enhancing the differentiation, maturation and function of glucose-responsive, insulin-producing SC-beta cells (pancreatic beta cells made from human pluripotent stem cells). Downstream, these SC-beta cells could potentially be used for cell therapy to treat diabetes or as a disease model system for research and high throughput drug screening.

These methods leverage both developmental biology and bioengineering techniques to discover and recapitulate conditions during normal human development. For example, certain culture techniques and reagents can be used to scale production, freeze cells (for shipping and quality control) or promote function or maturation at specific stages of cell development. Furthermore, tools for functional studies of SC-beta cells have revealed microenvironmental cues and stress responses that can influence cell fate or improve cell function. Collectively, these protocols and discoveries represent the most advanced system for affordable, scalable and reproducible generation SC-beta cells. The cells provide a unique window to study Type 1, Type 2 or monogenic forms of diabetes. The cells also offer a potential therapy to help the millions of people who currently require insulin injections to control their diabetes.



The state-of-the-art protocol generates glucose-responsive SC-beta cells from embryonic and induced human pluripotent stem cells.

Stage of Research:

The Millman lab has successfully used their protocols to convert human stem cells into insulin-producing cells with secretion dynamics approaching that of primary islets; transplanted those SC-beta cells into diabetic model mice; and demonstrated that they can control blood sugar and functionally cure diabetes for 9 months (Nature Biotechnology). They continue to employ a variety of techniques to identify novel signaling pathways regulating beta cell differentiation and

functional maturation with a goal to refine and improve the process for better scalability and cell function.

Applications:

- **Diabetes cell therapy** – pancreatic islet beta cell replacement therapy
- **Drug discovery and research**:
  - reporter cells for quantification and **high throughput screening** of compounds that affect insulin expression
  - in vitro **disease modeling system** for basic research and evaluation of drug candidates

Key Advantages:

- **Efficient conversion** of human stem cells into functional, insulin producing cells with fewer off-target cells
- **Effective control of blood sugar**:
  - physiologically responsive SC-beta cells rapidly and effectively controlled blood sugar in diabetic mice for 9 months
  - various techniques to improve differentiation, maturation and function of cells in vivo and in vitro
- **Scalable production techniques** for producing and preserving large batches of cells to facilitate quality control and shipping

Publications:

- Hogrebe, N. J., Augsornworawat, P., Maxwell, K. G., Velazco-Cruz, L., & Millman, J. R. (2020). Targeting the cytoskeleton to direct pancreatic differentiation of human pluripotent stem cells. *Nature Biotechnology*, 38(4), 460-470.
- Diabetes in mice cured rapidly using human stem cell strategy, *the Source* Feb. 24, 2020.

Patents: Application filed

Related Web Links: Millman Profile; Millman Lab