Weill Cornell Medicine

Generation of Glucose-Responsive Stomach Cells for the Treatment of Diabetes

Lead Inventor:

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Background & Unmet Need

- 8.4 million patients worldwide have type 1 diabetes
- Standard of care requires lifelong insulin replacement therapy, during which patients remain vulnerable to hypoglycemic episodes
- Islet-cell replacement has shown success as an alternative therapy for diabetes, but is limited by a short supply of donors and transplant rejection
- Generating insulin-producing islet cells from stem cells is a potential solution to patient demand, and could overcome rejection issues if cells are derived from patients
- However, deriving islet cells from iPSCs for autologous cell therapy is complex, and cells are prone to mutation during iPSC reprogramming
- **Unmet Need:** An abundant and autologous source of insulin-secreting cells as a cell therapy for diabetes

Technology Overview

- **The Technology:** A method of generating gastric insulin-secreting (GINS) cells from human gastric stem cells (hGSCs) as a transplantable therapeutic for diabetes
- **The Discovery:** The inventors have developed a novel differentiation path which induces hGSCs to develop β-cell identity
- **PoC Data:** Cultured hGSCs differentiate into islet-like cells at an efficiency of approximately 70%
- GINS organoids were able to produce insulin upon glucose stimulation 8-10 days after induction
- GINS organoids were stable for the duration of the 6-month period monitored after transplantation
- Transplantation of GINS organoids reversed diabetes in mice and provided glucose homeostasis for over 100 days

Inventors:
Joe Qiao Zhou
Xiaofeng Huang

Patents:
Provisional Filed

Publications:
Huang & Zhou. *Res Sq*. 2023 (preprint)

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Technology Applications

- Manufacture of β-cell transplants from patient biopsies
- Personalized islet-cell replacement therapy for type 1 diabetes and insulin-dependent type 2 diabetes

Technology Advantages

- Gastric stem cells are readily available through biopsy and are easy to propagate
- Applicable to the generation of autologous organoids, reducing risk of rejection
- Transplanted cells did not show proliferation post-transplantation and consequently have low tumorigenic risk

Supporting Data / Figures

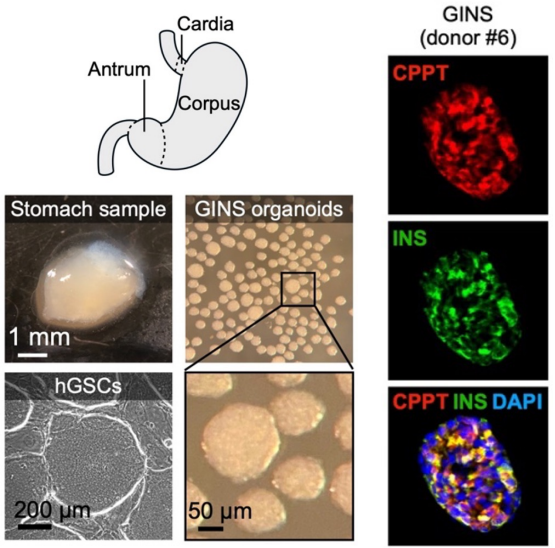

Figure 1: Gastric insulin-secreting (GINS) organoids are derived from human gastric stem cells (hGSCs) cultured and expanded from stomach biopsies.

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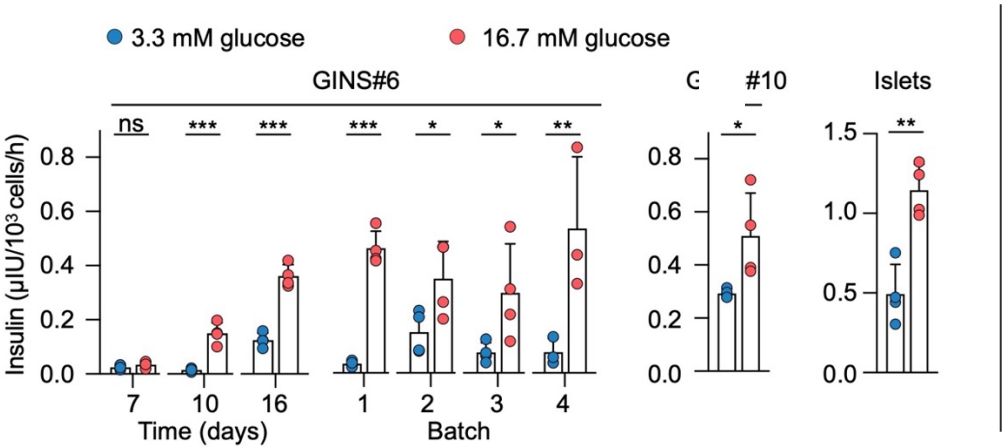

Figure 2: Left: GINS organoids begin producing insulin in response to glucose stimulation starting 8-10 days after differentiation.
Right: GINS organoids respond to multiple glucose challenges.

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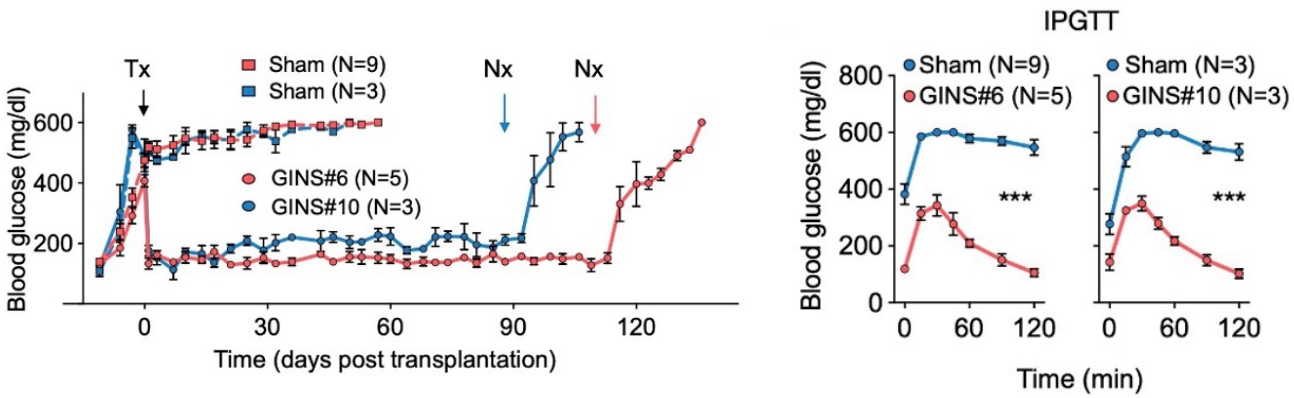

Figure 3: Left: Mice engrafted with GINS cells from two different donors (GINS#6 or GINS#10) showed improved random-fed glucose levels compared to control (Sham) mice. **Right:** Engrafted mice showed normalized responses in glucose tolerance tests.

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