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

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<th>Background &amp; Unmet Need</th>
<th>Technology Overview</th>
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<td>• 8.4 million patients worldwide have type 1 diabetes</td>
<td>• <strong>The Technology</strong>: A method of generating gastric insulin-secreting (GINS) cells from human gastric stem cells (hGSCs) as a transplantable therapeutic for diabetes</td>
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<td>• Standard of care requires lifelong insulin replacement therapy, during which patients remain vulnerable to hypoglycemic episodes</td>
<td>• <strong>The Discovery</strong>: The inventors have developed a novel differentiation path which induces hGSCs to develop β-cell identity</td>
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<td>• Islet-cell replacement has shown success as an alternative therapy for diabetes, but is limited by a short supply of donors and transplant rejection</td>
<td>• <strong>PoC Data</strong>: Cultured hGSCs differentiate into islet-like cells at an efficiency of approximately 70%</td>
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<td>• 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</td>
<td>• GINS organoids were able to produce insulin upon glucose stimulation 8-10 days after induction</td>
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<td>• However, deriving islet cells from iPSCs for autologous cell therapy is complex, and cells are prone to mutation during iPSC reprogramming</td>
<td>• GINS organoids were stable for the duration of the 6-month period monitored after transplantation</td>
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<td>• <strong>Unmet Need</strong>: An abundant and autologous source of insulin-secreting cells as a cell therapy for diabetes</td>
<td>• Transplantation of GINS organoids reversed diabetes in mice and provided glucose homeostasis for over 100 days</td>
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</table>

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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.](image)

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Supporting Data / Figures

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.