Background:
- 1.25 million Americans have Type 1 Diabetes (T1D), a condition where the body is unable to create insulin to regulate glucose.
- Current T1D treatments require stringent and intrusive monitoring of glucoses and administering of insulin.
- Research has been conducted to create pancreatic organoids (group of cells functioning as an “organ-like” structure) to restore patients’ insulin production.

Needs Statement:
- Develop a highly immune-compatible organoid therapy system for patients with impaired insulin production for recapitulation of pancreatic function without rejection.

Proposed Solution:
- Organoid Therapeutics has developed such an organoid therapy.
- Solution is classified as a “biologic”.
- Fibrin not currently used to deliver organoids.
- Similar hydrogel encapsulation methods do not exist.

Design of Solution

Organoid Components
- Beta-Islet cells derived from induced pluripotent stem cells to mimic pancreatic functionality
- Extracellular Matrix (ECM) assists in beta-islet cell aggregation/organoid formation

Fibrin-based Hydrogel Coating
- Fibrin is a natural biopolymer that encourages blood vessel growth.
- Produced when fibrinogen is enzymatically cleaved by thrombin.
- Coating encapsulates and protects organoids during delivery.
- Low immunogenicity: minimal immune response.

Fibrin Properties Ideal for Organoid Protection
- Elastic and viscous properties
- If cross-linked, can withstand large amounts of stress
- Young’s modulus = 14.5 ± 3.5 MPA
- Can stretch up to 3.3 times its original length
- Fracture strain = 332%

Coating Method Effectively Coats Organoids
- Anticipated coating tests on the following:
  1) Fabricated alginate beads
  2) Liver tissue spheroids
  3) Pancreatic organoids
- Results of preliminary alginate bead testing:
  - Fabricated alginate beads (~ 0.5 mm in diameter)
  - Fibrin hydrogel developed evenly around bead.

Organoid Survivability During Injection
- Generalized velocity profiles shown above.
- Calculated wall shear for varying needle gauge and flow conditions shown below.

<table>
<thead>
<tr>
<th>Needle Gauge</th>
<th>Wall Shear (Pa)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Inlet Flow Rate (m/s)</td>
</tr>
<tr>
<td></td>
<td>0.005</td>
</tr>
<tr>
<td>24G</td>
<td>240</td>
</tr>
<tr>
<td>26G</td>
<td>260</td>
</tr>
<tr>
<td>27G</td>
<td>270</td>
</tr>
<tr>
<td>28G</td>
<td>280</td>
</tr>
</tbody>
</table>

- Fibrin elasticity withstands even the largest shear values.

Future Hypothesis:
- Hypothesis: Hydrogel coating will be thinner around organoids.
  - Integrim binding will allow a thin coating of fibrinogen to adhere to the surface.
  - Finish coating tests with liver tissue and organoids.
  - Optimize needle gauge by performing live-dead assay on organoids after injection.
  - In vivo testing in mice over several months monitoring insulin levels to determine number of organoids per dose and frequency of dosages.

Future Testing:
- Hypothesis: Hydrogel coating will be thinner around organoids.
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COSTS & REIMBURSEMENT

Cost Breakdown per Dose:
- Total material cost per dose: $8,638
- Total labor cost per dose: $1,246
- 50% overhead costs: $4,942
- 25% profit margin: $2,471
- Total selling price for one dose: $17,297

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