Bioengineering the Pancreas

Developing Novel Regenerative Therapies to Address Type 1 Diabetes

by

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Part I – A New Therapy for Type 1 Diabetes

Bio-Art is the leader in artificial engineering strategies to cure complex diseases. Therapies developed by the company thus far have been completely artificial, incorporating no living tissues, instead solely relying on innovative materials to replicate tissue function. However, using only artificial materials limits the available approaches for curing complex diseases.

You are a bioengineer at Bio-Art recently promoted to head their Regenerative Strategies Department. The company would like to expand their operations to incorporate more regenerative and tissue engineering approaches, harnessing biology to solve complex problems. You have been tasked with developing a new therapy for type 1 diabetes, which is the next disease that Bio-Art would like to conquer.

You must prepare for your first meeting with company executives to present your new regenerative therapy. In order to come up with a viable starting place, you must first understand how type 1 diabetes works and how normal pancreatic tissue functions.

Questions

1. How does the pancreas regulate glucose in a healthy person?

2. What is type-I diabetes? What goes wrong that results in a loss of glucose regulation?

3. What cell types are involved/need to be repaired in type 1 diabetes?

4. What are common treatments? How do they work?

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Part II – Beta Cell Transplantation

After conducting preliminary research, you've learned that the most common treatment for type 1 diabetes is blood glucose monitoring and regular insulin injections. However, some success has been made transplanting beta cells (the cells of the pancreas responsible for insulin production). Your plan is to research this strategy further to identify possible therapies for type 1 diabetes.

Questions

1. How many beta cells are required to reestablish normal glucose monitoring?

2. What are some cons to implanting beta cells from another person?

3. Another caveat: many of the transplanted beta cells will not survive the initial implantation. Why?

4. Bio-Art has access to porcine beta cell islets. They can be used for transplantation into patients. What are some advantages of using porcine (pig) beta cells?

5. What are some cons to using porcine (pig) beta cell islets?

6. Look at Table 1. Are there any patterns that you notice about the molecules involved in the disease?

Table 1. Sizes for notable molecules involved in type 1 diabetes.

Molecule	Size (hydrodynamic radius, nm)
Glucose	0.4
Insulin	1.3
Cytokines	3
Antibodies	5

7. How could you use the size of these molecules to design an effective therapy?

8. Based on what we've discussed so far today, list factors that would need to be included in a design to create a successful treatment.

9. Research a biomaterials/tissue engineering strategy that could be used to improve the longevity (lifespan) of transplanted porcine islets. Select two therapies based on scientific articles that fulfill a majority of the criteria developed in Question 8 above.

Part III – A Novel Encapsulation Strategy

Bio-Art executives will have their first meeting with you this afternoon to discuss your basic strategy for the new type 1 diabetes therapy. While they don't require specifics yet, you will need to convince them that your approach is a viable method to treat type 1 diabetes using porcine islets.

After presenting your findings to the CEO, he has chosen cell encapsulation as the best strategy.

Questions

1. What pore size should you choose for your device?

2. What complication would arise if the pore size was too small? Too big?

Macro and Microencapsulation

There are two main types of cell encapsulations strategies: macro encapsulation and micro encapsulation. A macro encapsulation device encloses all transplanted beta cells into a single capsule. Micro encapsulation therapies rely on isolating cell clusters or even single cells. Table 2 displays data on micro and macroencapsulation techniques assuming 1,000,000 cells are being transplanted inside a 5 μm thick membrane. Insulin production is reported relative to that of a single beta cell.

Table 2. Micro and macroencapsulation techniques.

Strategy	Cells per capsule	Number of capsules	Total Insulin Production (rel. units)	Radius of each capsule (μm)	Total Surface Area (mm²)	Total Volume (mm³)
Micro (single cell)	1	1,000,000	1	15	2830	14
Micro (cluster)	1,000	1,000	4	105	140	5
Macro	1,000,000	1	10	1005	13	4

Questions

3. What are the pros and cons of microencapsulation?

4. What are the pros and cons of macroencapsulation?

Design

In groups, develop your own strategy for encapsulation. You will present your design to the class by drawing diagrams of your device on the board. Prepare to explain the following:

- Whether your group chose to use micro or macro encapsulation (and why).
- How your design overcomes the shortcomings of your chosen strategy (e.g., a new geometry that will increase the effective surface area of a macroencapsulation device).