Project Design Specifications

Team:

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Problem Statement:

A method of treatment for various endocrine diseases incorporates the encapsulation of cells and tissues and the time-released delivery of chemical mediators. Presently, this method encounters a slew of problems, including a lack of biocompatibility, limited immunoprotective properties, and hypoxia. The client desires the development of microcapsules that would permit the successful release of hormones (namely, testosterone and inhibin) by encapsulated cells into animals, while avoiding the aforementioned problems.

Function:

The resulting microcapsules should allow transplantation of hormone-releasing tissue without the use of immunosuppressant drugs by providing a mechanical barrier to immune system attack.

Client requirements:

- Microencapsulation of Murine Leydig Tumor Cells Type 1 (MLTC-1)
- Must release hormones of interest (testosterone and inhibin) over time, while keeping harmful molecules (antibodies, etc.) out
- Biocompatible, immunoprotective, minimize mechanical and chemical degradation

Design requirements:

Physical and operational characteristics

a) *Viability*: the encapsulation process may have adverse effects on initial cell viability in microcapsules. The proposed design should retain at least 75% cell viability measured 1d post-encapsulation using a Cell Titer Blue® assay.

b) *Hormone release*: normal values of testosterone in human males ranges from 2 to 12 ng/mL.

c) *Degradation*: the biomaterial (Polyethylene glycol [PEG]) should remain intact long enough to sustain a critical cell mass, such to provide adequate hormone release for at least six months.

d) *Capsule size*: various thickness of the PEG will be tested experimentally to determine the optimal range of capsule diameter.

e) *Molecular weight cutoff* (MWCO): MWCO should be 75kDa in order to allow diffusion of relevant molecules, specifically testosterone (300 Da), inhibin (32 kDa), activin, LH (30 kDa), FSH (36 kDa), but block out human antibodies (IgG; 150 kDa).

f) *Immune response*: microcapsules must not allow the diffusion of antibodies or immune system cells by providing a sufficiently small mesh size.

g) *Biocompatibility*: biomaterial (PEG) and its degradation products must be nontoxic and not cause inflammation within the body. Injected microcapsules must resist protein adsorption and fibroblast overgrowth.

h) *Life in service*: therapy should sustain patient at minimum serum testosterone concentration (2 ng/mL) for at least 6 months.

i) *Production timeframe*: microencapsulated cell therapy, at present will be prepared from start to finish as needed by patient demand. Microencapsulated cells will be implanted soon after production. The microencapsulated cells should be sustainable *in vitro* for at least several days.

j) *Operating environment*: *in vitro*, site of implantation to be determined. Subcutaneous and intraperitoneal injections are both possible (Machluf *et al.*, 2003).

Product characteristics:

a) *Quantity*: thousands to hundreds of thousands of microcapsules will be required per injection. The cell mass required to provide adequate hormone release is currently unknown, but likely on the order of 10^6 cells.

b) *Sterility*: final product must be sterile prior to implanatation.

c) *Target product cost*: not specified.

d) *Research costs*: unknown.

Miscellaneous:

a) *Standard and specifications*: FDA approval is required. University approval required prior to animal or human subject testing.

b) *Competition*: Several patents regarding cell encapsulation exist and define specific production protocols. These are US Patent 5,762,959, US Patent 5,100,673, and US Patent 5,164,126. This study is not expected to infringe upon past technology as a novel capsule design is desired.