Project Design Specifications—Bioreactor Cassette
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Function:

The bioreactor cassette will provide appropriate conditions to culture multiple samples (from different patients) of iPS cells without exchanging media between samples. The cassette will be translucent with a transparent growth plate and have a footprint less than 400 cm^2. It will facilitate confluent healthy growth and adherence by encouraging appropriate fluid flow coverage. The perfusion interface will allow variable control of flow rate and volume of nutrient media supplied to each cassette, while maintaining physiological growth conditions within them. A trap mechanism will be included before or incorporated within the cassette to remove bubbles that may occlude flow tracks.

The cassette will be designed such that loading and priming of cells can be done in a sterile environment, in a straightforward, user-friendly process. We will monitor the ease of bubble removal as we design an ergonomic cassette housing and cell growth system.

Components will be sterilizable with gamma irradiation or steam. Materials will be disposable and composed of polymers known to not affect stem cell fate. The cassette and interface will be designed such that sterility can be maintained if iPS cells need to be removed from the bioreactor for microscopic analysis.

Client Requirements:

- Steam or gamma sterilizable
- Connects to bioreactor interface and allows variable media perfusion flow
- Gas-impermeable cell growth plate and cassette material
- Optically translucent
- No extractables, or chemical leaching, in contact with media
- Induce and maintain confluent cell growth
- Ergonomic loading/priming procedure
- Mechanism to prevent bubbles from occluding media flow

Design Requirements:

1) Physical and Operational Characteristics

a) *Performance requirements* – Must provide an appropriate cell growth environment with proficient perfusion of media. Cell products must be high viability and comparable or better than static culture.

b) *Safety* – Must not contain any chemicals or substances that will negatively influence the cell, cell growth or initiate differentiation. Cassette must

prevent contamination of sample for similar reasons.

c) *Accuracy and Reliability* – Must provide appropriate culture conditions that allow healthy growth and do not initiate differentiation. Must monitor and maintain these conditions.

d) *Life in Service* – Prototype: sterilizable, withstands repeated use (at least 10) and fluid submersion.

Final product: One-time use, up to 3 months

e*) Shelf Life* – Able to withstand a basic medical storage environment

f) *Operating Environment* – Must work properly at 37° C and in constant exposure to a liquid media.

g) *Ergonomics* – Should not interfere negatively with the user's ability to monitor the cells. Loading and priming should be straightforward when working under sterile conditions, and promote even seeding. Bubble removal at the priming stage should be easy.

h) *Size* – Total volume less than 8000 cm^3, cell growth area depth less than 2mm, less than 60mL volume reservoir when perfusing

i) *Weight* – Under 1 kg/cassette

j) *Materials* – sterilizable, translucent, allow cell growth, not influence differentiation

k) Aesthetics – Transparent cell plate

2) Production Characteristics

a) *Quantity* – One, but should be designed with the intent of mass production in the future.

b) *Target Product Cost* – $1,000 for prototype

3) *Miscellaneous*- Final design should be scalable.

a) *Standards and Specifications* – Uses USP Class VI materials, adheres to Good Manufacturing Practice Guidelines and Good Tissue Practices

b) *Customer* – Medical Research Community

c) *Patient-related concerns* – Must not negatively influence the cells. Must maintain independence of each sample. Each cassette must be easily identifiable.

d) *Competition* – There are currently different culture systems (static culture, CLINIcell Cassettes) but none that allow for several different samples with no exchange in media, or have gas impermeable membranes.