**Neural Bioreactor**

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**Function:** Reprogramming adult cells into induced pluripotent stem cells (iPSCs), as well as their subsequent expansion and differentiation, is normally completed in adherent cell cultures. Recently, it has been proven that iPSCs can be derived and expanded in suspension cultures using a stirred suspension bioreactor. These reactors establish stable cell culture conditions by controlling the temperature as well as the level of nutrients (media), $CO_2$ (pH), $O_2$, and other soluble factors. The suspension components are uniformly distributed within the reactor fluid through various mixing techniques, most commonly an impeller. The process of adult cell reprogramming and iPSC expansion and differentiation can be scaled up and automated using bioreactor stirred suspension cultures.

Dr. Saha has asked our team to design a bioreactor that maximizes the production of neural progenitor cells from mouse embryonic fibroblasts in stirred suspension cultures. The project involves designing culture processes and optimizing culture conditions to reprogram adult cells to induced pluripotent stem cells (iPSCs) and differentiate those iPSCs to neural progenitors.

**Client Requirements**

- Stirred suspension culture
- Use mouse embryonic fibroblasts (MEFs)
- Reprogram MEFs into iPSCs
- Culture Environment: 37° C , 5% $CO_2$

**Design Requirements**

1) **Physical and Operational Characteristics**
    a. ***Performance Requirements:*** The bioreactor must be able maintain 37° C and 5% $CO_2$ for multiple weeks at a time. Most components of the bioreactor will be reusable. The bioreactor must provide an environment conducive to cell culturing and reprogramming.
    b. ***Safety:*** The bioreactor will incorporate a heating element that will heat the culture to 37° C, but a malfunction in the heating regulation system could lead to much higher temperatures that could damage the cells, microscope, or even the lab technician.
    c. ***Accuracy and Reliability:*** The bioreactor must maintain an internal temperature of 37±1°C and a $CO_2$ concentration of 5±.5%. The bioreactor must allow for accurate and reproducible conditions.
    d. ***Life in Service:*** The bioreactor will be autoclavable. It would be autoclaved after one use or iteration of reprogramming secondary MEFs into iPSCs, and culturing them to their desired states.

e. ***Operating Environment:*** The device will be used in a cell culture hood by a skilled lab researcher or technician. The device will only be exposed to the lab environment, which will be well controlled.
f. ***Ergonomics:*** The bioreactor must be simple to use.
g. ***Size:*** The bioreactor will be a standalone unit, meaning it will operate independently from other equipment within the lab environment. It will use a 100 mL vessel volume to contain the cell culture. All of the components of the bioreactor should be able to be transported from building to building.
h. ***Weight:*** The weight should be light enough so that one person can lift the bioreactor.
i. ***Materials:*** The materials on the inside of the bioreactor must not be cytotoxic. The bioreactor vessel and elements exposed to the cell culture must be cytophobic or coated in a material that prevents cell adhesion. The material must be impermeable to small molecules and gas to create a closed system.

**2) Production Characteristics**

a. ***Quantity:*** 1
b. ***Target Product Cost:*** Indeterminate

**3) Miscellaneous**

a. ***Customer:*** The customer would like this to be eventually used for human adult cells to be reprogrammed into iPSCs. However, we are initially going to design the bioreactor to use MEFs due to the existing protocols being readily available in literature.
b. ***Competition:*** Bioreactors exist in the market for specific applications, but the commercially available bioreactors are not tailored to the specific needs to reprogram cells into iPSCs or for later differentiation of those cells.