AUTOMATED MANUFACTURING FOR IPSC-DERIVED RETINAL PIGMENT EPITHELIAL CELLS

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Cell manufacturing, which is the most critical steps to realize the transplant of cell-based products for cell therapy or regenerative medicine, will be done in terms of safety, stably and cost-saving under the aseptic environment in the cell processing facility (CPF). The cell processing is regarded as the system consisting of target process, input and output, and there are several fluctuations derived from extrinsic noises (environmental errors) against the system, input quality such as starter cells and materials (medium, reagents, substrate, vessel etc.), and intrinsic disorders (in-process errors) from the behavior variance in manual operation (Fig.1). Especially, intrinsic disorders cause the difficulty to make consistency and robust process for stable quality because the cells have uncertainty accompanied by time-dependent and time-delay properties. Therefore, environmental, material, and operational standardizations are required to realize consistency of processes. In addition, long manufacturing period and small lot size for cell production make the low productivity, causing the high cost production.

Cell manufacturability is defined to be "manufacturing design of cell-based products in such a way that they are easy to manufacture through simple, safe and efficient (cost-saving) process with stable product quality and secure to customer by considering transpiration and hospital preparation outside factory". Based on the cell manufacturability, the realization of 3S (safe, stably and cost-saving) is desired for the industrialization, leading to the affordability of the final cell-based products.

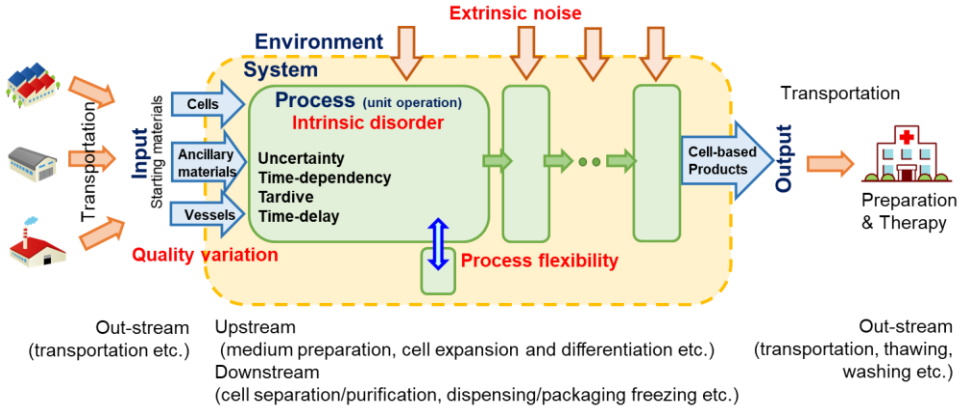

Figure 1 The cell processing system

In the present study, the novel isolator system based on a flexible Modular Platform (fMP) was designed to realize that the individual modules can connect and disconnect flexibly with keeping the aseptic environment in each module(Fig.2). The fMP isolator system may reduce equipment and maintenance/operation costs while providing a reliable aseptic environment for the CPFs handling different cell-based materials. The system performs 4-month culture processing of iPS cells and the derived retinal pigment epithelial cells (RPECs), successfully by considering the cell manufacturability. In addition, the gravity forces in manual handlings were measured by using motion sensor and the set-up of the motion in robotic arm handling. This teaching leads to the stability of cell culture in differentiation of iPSCs to RPECs to realize the automated cell manufacturing, preventing from the intrinsic disorder in cell processes.

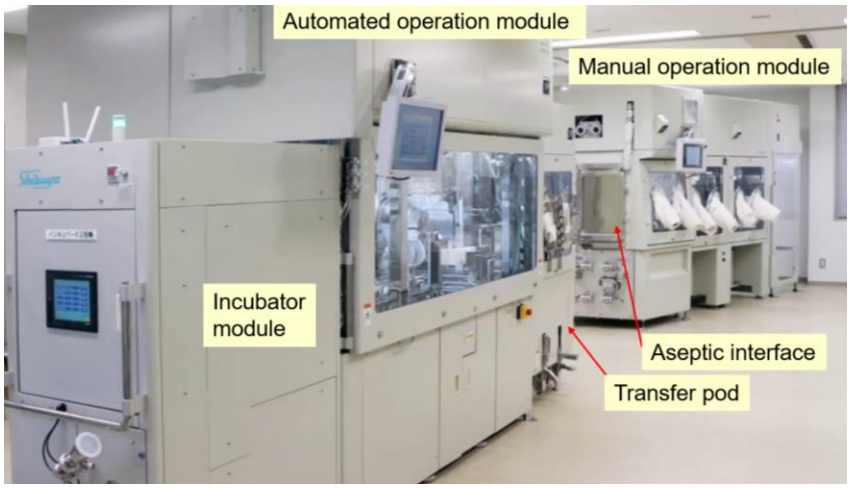

Figure 2 The novel cell processing system based on the fMP