DESIGNING A BANKING SCALE OF HUMAN INDUCED PLURIPOTENT STEM CELLS BASED ON SUSPENSION TIME-DEPENDENT QUALITY VARIATIONS IN FILLING AND CRYOPRESERVATION PROCESSES

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To establish a robust commercial production system for a cell product, it is necessary to investigate a lot of variable factors inside and outside of the system and discuss the cell manufacturability. In case of trying a scale-up of banking system for human induced pluripotent stem cells (hiPSCs), the process time to fill the cell suspension into vials before cryopreservation is prolonged. And that will cause the decay of the cell quality, because cryoprotective agent (CPA) including dimethyl sulfoxide has toxicity to cells. Based on such fluctuation of cell product quality derived from time-dependency in down-stream process, novel strategy to design a process time and a banking scale is required. In this study, four performance indexes, survival ratio of cells during suspension in CPA before cryopreservation (γ), survival ratio, attachment efficiency and specific growth rate of cells after cryopreservation (β, α and μ, respectively) are proposed to evaluate the cellular state and potential of the product. And, the quality variations of suspended cells in CPA are elucidated by changing the process time of suspension at room temperature and 4 °C.

At room temperature, γ decreased with process time (t_s) exponentially, being γ = 0.72 at t_s = 6 h. With respect to α, 4 hours suspension at room temperature had an insignificant effect, however, it dropped after the lag-time, being α = 0.73 at t_s = 6 h. In contrast, β and μ were kept high level of 0.80 and 5.3 × 10^{-2} h^{-1}, respectively, similarly to those without the process. In addition, the suspension at 4°C made the enhancement of γ and α at t_s = 6 h (γ = 0.88 and α = 1.08, respectively), suggesting that the suppression in cell activity during suspension is important to preserve the cell quality.

In conclusion, the proposed performance indexes are useful to estimate the state and potential of cell product in filling and cryopreservation processes, and the temperature control in filling process is one of the promising factors to maintain the cell product quality.

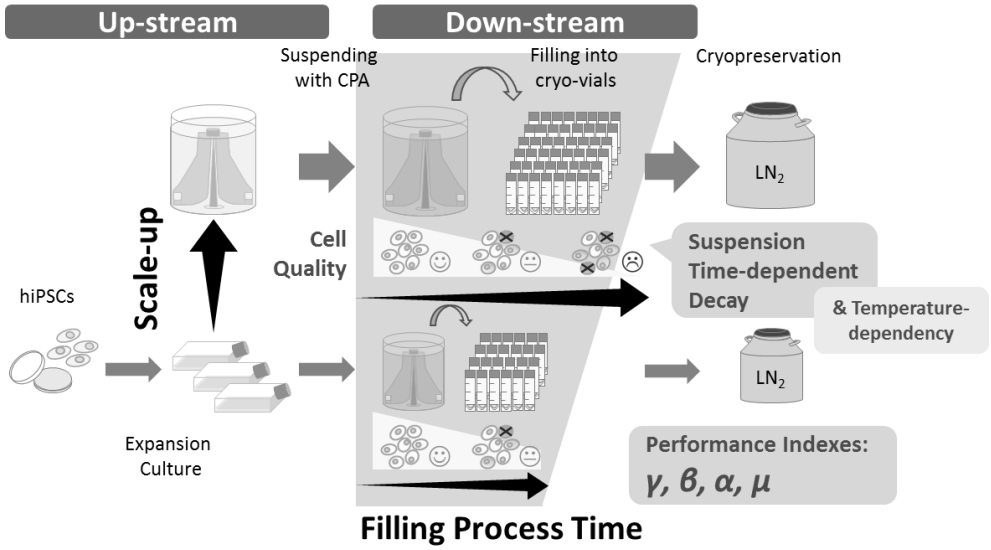

Figure 1 – Trade-off between scale-up in up-stream process and time-dependent quality variation in down-stream process