

SCALABLE MANUFACTURE OF PLURIPOTENT STEM CELL DERIVED THERAPEUTICS

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Human pluripotent stem cells (PSC) hold great promise as a source of starting material for the further production of therapeutic cell products. However, PSC are typically cultivated in planar formats that severely constrain scalability and hence restrict the quantities of cells that can be generated. Such formats are largely uncontrolled, require open processing, are labour intensive, and have an unfavourable risk profile. Manufacture of PSC in a suspension bioreactor format would alleviate scale-up constraints and simultaneously provide the benefits of sophisticated process monitoring and control, labour reduction, and process closure. We have developed a platform process for the expansion of PSC as aggregates in stirred tank reactors (STR's), and demonstrated scale-up to a 10 L single-use Xcellerex XDR10 bioreactor system.

PSC themselves are of no value as a cell therapy, and it is the differentiated progeny that are desired. We have demonstrated scalable differentiation of suspension cultured PSC to cardiomyocytes, as aggregates in STR's. PSC expanded to the 10 L scale differentiated to cardiomyocytes with an efficiency of 97% and yield (cardiomyocyte:PSC) of > 5.