Bioprocessing of Human Brain Cancer Tumour Tissue

Krishna Panchalingam[1], Wendy Paramchuk[1], Greg Foltz[2], Anup Madan[2], Leo A. Behie[1].
[1]*Pharmaceutical Production Research Facility (PPRF), Schulich School of Engineering - University of Calgary*
[2]*Institute for Systems Biology*

It has been hypothesized that a rare, stem cell-like subpopulation, termed cancer stem cells (CSCs), in brain tumours are responsible for formation and sustaining growth of the tumour. Capable of self-renewal, but lacking proliferative control, the CSC subpopulation represents a unique and novel target for the development of cancer therapeutics. The scarcity of CSCs *in vivo* represents a major impediment to such research, as there is an insufficient supply for basic biochemical and genetic analyses. It is therefore necessary to develop methods to reproducibly expand brain CSC tissue in a controlled environment. To date, the expansion of human glioblastoma (GBM)-derived cells as non-adherent cell aggregates (termed tumourspheres) has been achieved in both static and 125 mL suspension bioreactors. Inoculated at 5.0×10^4 cells/mL, these cells were found to exhibit exponential growth in batch culture, where a maximum cell density of 2.4×10^6 cells/mL was attained after 24 days under high shear conditions with a 48-fold expansion and a doubling time of 85 h. Scale-up to 500 mL bioreactors under batch conditions yielded similar growth kinetics. In addition, fed-batch cultures in 125 mL suspension bioreactors achieved 4.5×10^6 cells/mL after 32 days with a doubling time of 88 h. Characterization of bioreactor expanded cells using both flow cytometry and differentiation assay indicated that bioreactor generated human GBM-derived tumourspheres have similar characteristics with the parental cell population and achieve > 90% CD133 expression.