

Ex-vivo human mesenchymal stem cell expansion and differentiation for cellular therapies

(Expansão e diferenciação de células estaminais mesenquimatosas para terapias celulares)

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The major potential application of stem-cell technology is in cell-replacement therapies. Recent advances in developmental biology, the establishment of human embryonic, induced pluripotent and adult stem cell lines and the discovery of organ-specific stem cells with differentiation potential have substantially accelerated the potential of using these cells in human regenerative medicine. Before any clinical application, stem cells need to be isolated from various sources, cultivated and maintained in culture, possibly differentiated into committed tissue precursor cells, stored and transported to the bed-side of a patient.

The development of reliable *in vitro* systems for the growth of stem cells is a valuable tool to study the mechanisms controlling the expansion and the differentiation of stem cells *in vitro*. Successful *ex vivo* models will enable the study of the dynamics and mechanisms of cell differentiation and organ development in bioreactor systems. The need for improved cultivation methods is also driven by the fact that most potential therapeutic applications are limited by the availability of stem cells or their derivatives. The *in vitro* propagation of stem cell populations remains largely undeveloped and is considered a major technical challenge because of the complex kinetics of the heterogeneous starting culture population, the transient nature of the subpopulations of interest, and the complex interactions between the culture parameters. This lecture presents the fundamental concepts for bioprocess development towards the *ex-vivo* expansion, maintenance and differentiation of human mesenchymal stem cells stem cells, while maintaining their functional characteristics, for cell-based therapies in clinical use for cartilage repair. Additionally, recent developments in this area are also described and new approaches are discussed.