Summary

Stem cells offer a promising avenue to therapy for a wide range of human diseases. However, for this potential to be realized, a consistent and plentiful supply of well-characterized stem cells is essential. To date, there has been relatively little progress in the development of new culture technologies for the large-scale manufacture of mesenchymal stem cells (MSCs).
Current obstacles to the large-scale manufacture of MSCs suitable for therapeutic use in humans include: a lack of standards for the characterization, isolation or identification of MSCs; the absence of standard protocols for differentiation of MSCs to various lineages; a lack of specificity for surface markers used for MSC characterization ; the absence of standardized cryopreservation protocols; the requirement of current production methods to use animal-derived serum resulting in major contamination implications.

Following my first experiments with low fetal bovine serum containing media and experimental work with dental pulp stem cells I was invited to be a part of the collaborative 7FP EU project - PurStem. As a team leader I was personally responsible for the work package focused on serum-free isolation, growth and differentiation of MSCs. Objectives, standard operating protocols and results summarized in this thesis are in relation to this project.

PurStem project set out to identify the MSC “receptome” and use this repertoire of growth factor receptors to develop novel serum-free media suitable for large-scale MSC production. Furthermore, the PurStem project aimed to create novel antibody reagents for specific MSC characterization and contribute to Good Manufacturing Practice (GMP) standards to enable rapid progression to production of serum-free MSC for clinical, therapeutic applications.

Goals of this thesis and PurStem project were achieved by: developing and validating a collaborative, standardized procedure for the isolation, culture and cryopreservation of MSCs that produced consistent cell types even when grown in different laboratories; using the wealth of information obtained from characterisation of the MSC “receptome” to develop low and serum-free culture conditions where MSCs can survive and proliferate, thereby reducing or eliminating potential contamination issues associated with current serum-based culture methods.

These results will contribute to the optimization of GMP manufacturing and banking of cells for use in clinical trials initially and ultimately as a commercial product. Furthermore, this thesis and related PurStem project have also advanced our basic understanding of MSC biology by defining the surface “receptome”, setting the stage for the development of next generation therapies which will exploit the self-repair potential of adult stem cells or stem cell targeting.

Stem cell therapeutics are expected to lead to the treatment of diseases with no current effective treatment options, as well as contribute to tissue engineering of new tissues or organs for replacement purposes. The findings of this work and PurStem project will enable the translation of promising stem cell therapies, initially in the area of osteoarthritis and autoimmune diseases. These novel regenerative therapies will reduce the economic and social costs of disease to the European Community. The primary social benefits from this work and PurStem will accrue from improvements in treatment options for a range of diseases. These improved treatments will improve patient quality of life and reduce the economic burden associated with chronic diseases.