MONASH University
Engineering

PhD Research Project

Are there different therapeutic benefits of native MSCs and MSCs differentiated from pluripotent stem cells? A study in graft-versus-host disease

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Description

Mesenchymal stem cells are multipotent stem cells that can differentiate into a number of cells of the mesodermal lineage such as bone, cartilage and fat cells. They have enormous clinical potential, particularly because they also have immunosuppressive and immunomodulatory properties which can aid tissue regeneration. Mesenchymal stem cells act to regenerate tissues in a number of ways, such as differentiating into certain cell types and become part of an existing tissue or by migrating to sites of inflammation and releasing agents which have potent effects on the innate and adaptive immune systems. Well known factors expressed by MSCs, are cytokines such as EFG, BEGF, PDGF, IL8 and TGF-β. However, more recently a variety of other potentially important factors such as small RNA molecules via extracellular vesicles is becomingly more widely understood.

Due to the limited supply of these cells from donors and the difficulties of generating large numbers of cells in a manufacturing process, there is significant interest in generating MSCs from a more primitive cell types that can be generated essentially indefinitely, such as embryonic stem cells or induced pluripotent stem cells. As a result a number of groups have been working towards the aim of creating well-defined mesenchymal cells using a range of published differentiation protocols. However, it is not established yet whether these differentiated MSCs have the same therapeutic potential as native MSCs. In addition, in certain disease states, it is not known exactly what molecules delivered by MSCs are important in modulating the disease state such as graft versus host disease. In this project we will compare and contrast the release of potential therapeutic molecules in MSCs from both sources (tissue and differentiated PSCs) and test in both *in vitro* models and in animal models of diseases for which MSCs have a purported therapeutic benefit. The initial focus will be cytokine release profiles. We will also investigate whether the material properties of the cell culture substrate (elasticity, ligand type etc) influences the cytokine (and other potential therapeutic molecules) release profiles of MSCs from both sources.