Title	Collagen scaffold remodeling by human mesenchymal stem cells
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Citation	The 2011 Meeting of the Days of Molecular Medicine (DMM), Hong Kong, 10-12 November 2011
Issued Date	2011
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82] COLLAGEN SCAFFOLD REMODELING BY HUMAN MESENCHYMAL STEM CELLS

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Type I collagen has been widely used as scaffold for tissue engineering because of its excellent biocompatibility and negligible immunogenicity. We previously have developed a collagen microencapsulation technology entrapping many cells including human mesenchymal stem cells (hMSCs) in microspheres made of nanofibrous collagen meshwork. Nevertheless, little is understood about how stem cells interact with and remodel the collagen meshwork. This study aims to investigate collagen remodeling by human mesenchymal stem cells (hMSCs) in terms of degradation, new matrix synthesis, and re-organization. We hypothesized that human MSCs have the ability to remodel collagen fibrils through both extracellular and intracellular pathways. To test this hypothesis, hMSCs were seeded on 2D culture dishes in the presence of fluorescently labeled soluble collagen or within 3D DQ FITC labeled collagen microspheres. After a short period of time, hMSCs degraded collagen molecules and fibrils through extracellular pathway mediated by MMPs and uptake collagen via endocytosis. This indicates that hMSCs may also degrade collagen through intracellular pathway. To determine roles of each degradation pathway, intracellular or extracellular degradation pathways were blocked by protease inhibitors (E64D or GM6001 respectively). Interestingly, blocking the extracellular degradation resulted in formation of thicker and denser fibril networks than the non-treated control while blocking the intracellular pathway resulted in less fibril formation than the control. More interestingly those fibrils seemed to grow from intracellular sites. When inducing chondrogenesis of hMSCs in 3D collagen scaffolds by TGF b3, immunohistochemical examination revealed that type I collagens was replaced with type II collagens. Immunofluorescent staining indicates that type I collagen in a scaffold may be recycled to synthesize new matrix, e.g. type II collagen. In future we will examine whether the collagen degradation processes affect the stem cell differentiation and integration of old and newly synthesized collagen.