介白質-1 對兔子軟骨細胞之第二型膠原蛋白基因表現的調控

The Regulation of Type II Collagen Gene Expression by Interleukin-1 in Rabbit Chondrocytese

中文摘要

關節炎的主要特徵是關節軟骨組織之細胞外間質持續及不可逆的發生損壞。當關節損壞至失去功能時，置入人工關節是現今唯一的治療方法。但是，這些金屬性的人工關節經過長期使用後，亦可能造成磨損，有些甚至併發關節黏連的症狀。因此，本實驗室著手研發一種膠原蛋白模板的生物材料，它可以使受損的關節軟骨再生。在關節軟骨組織之細胞外間質產生發炎及退化性損壞的過程中，介白質-1 被認為扮演極重要的角色。且介白質-1 對培養的軟骨細胞的影響，已被廣泛的研究。綜合先前的研究結果顯示，介白質-1 會降低關節軟骨專屬之膠原蛋白信使核醣核酸及蛋白質的產量；同時，使第一型及第三型膠原蛋白信使核醣核酸及蛋白質的產量增加。為了瞭解植入膠原蛋白模板後，關節組織再生的機轉，本研究嘗試分析介白質-1 對軟骨細胞之第二型膠原蛋白基因表現的調控機制，而後，再針對以手術引發關節炎的動物，分析膠原蛋白模板植入與否與介白質-1 變化量間的關係。實驗中針對介白質-1、前列腺素 E1、前列腺素 E2，對軟骨細胞第二型膠原蛋白基因之調控的影響進行分析探討。在另一方面，嘗試比較單層培養與懸浮培養的軟骨細胞之特性，以建立較能模擬人體環境的軟骨細胞人工培養模式。實驗結果顯示，介白質-1 會抑制人類軟骨細胞第二型膠原蛋白基因的表現。在人類軟骨細胞第二型膠原蛋白基因表現上，可由介白質-1 與引朵甲阿辛共同引發產生抑制，亦可被前列腺素 E1 及前列腺素 E2 反轉回來，且此反轉現象與前列腺素的劑量成正比。在軟骨細胞之培養模式方面，以單層法培養出的軟骨細胞，在外形上傾向類纖維母細胞般的立方形，且第二型膠原蛋白的分泌量減少，轉而分泌第一型膠原蛋白。以懸浮法培養出的軟骨細胞，在外形上仍然維持多角形的外貌；雖然分裂的速度較慢，但卻能持續保持分泌第二型膠原蛋白的性質與產量。

英文摘要

Progressive and irreversible destruction of the extracellular matrix in articular cartilage is a major feature of arthritis. When the joint is destroyed, the prothesis of artificial joint is indicated. However, the metallic joint prothesis often causes severe ankylosis and some complications such as wear problems. Therefore, a biomaterial, collagen template, manufactured in this laboratory was designed to regenerate the

articular cartilage.IL-1 is thought to play a major role in the inflammatory and destructive processes associated with the breakdown of cartilage matrix. The regulation of interleukin-1 on cultured chondrocytes was extensively studied. According to previous studies, the synthesis of cartilage-specific collagen is decreased while the synthesis of type I and III collagen are increased in protein and mRNA levels. In order to understand the mechanism of tissue regeneration by implants of the collagen template, the regulatory meIn this study, the regulation of type II collagen gene expression by IL-1, PGE1 and PGE2 in the chondrocyte was determined. In the same time, the suspension cultured chondrocytes for mimicking in vivo cell model also be established.According this study, the expression of type II collagen gene in human chondrocytes is suppressed by IL-1 alone. And IL-1 with indomethacin induced suppression of type II collagen gene expression by human chondrocytes is partially reversed by exogenous prostaglandins (PGE1, PGE2) in a dose-dependent manner. In cell model study, the monolayer cultured chondrocytes assume a fibroblast-like cuboid morphology and may secrete little cartilage-specific intercellular matrix material (they express type I rather t