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• 計畫中文名稱	介白質-1 對牙齦纖維母細胞老化之影響及其在分子細胞學上之作用機轉
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• 研究人員	周幸華 Chou, Hsin-Hua
• 中文關鍵字	第一介白質；牙齦組織；牙周纖維母細胞；老化；基因表現；熱休克蛋白
• 英文關鍵字	Interleukin 1；Gingival tissue；Periodontal fibroblast；Aging；Gene expression；Heat shock protein
• 中文摘要	牙周軟組織之大部分是由人類牙周纖維母細胞所構成,牙周纖維母細胞具有維持牙周結締組織之完整性及功能性的作用,體外培養之纖維母細胞因爲有一定之壽命,長久以來已被研究者設定爲研究細胞老化之實驗模型。近年來,有研究發現高齡者由來之低繼代纖維母細胞及年輕者由來之高繼代纖維母細胞均會自發性地分泌介白質-1(Interleukin-1),因而誘導膠原蛋白？、Stromyelysin 及錳超氧化物歧化？等基因之表現。另有報告指出這三種基因表現亦可能與細胞之衰老(Senescence)有關。 本計畫的研究目的是探討在體外培養之牙周纖維母細胞在老化過程中所分泌之介白質-1 對其本身之增生及衰老的影響,並研究其在分子及細胞學上之作用機轉。本計畫分爲三部分進行。首先,利用基因導入的方法將第二型之介白質-1 接受器過剩表現於細胞上來拮抗介白質-1 對細胞之作用。其次,我們比較未轉形細胞、轉形細胞及過剩表現轉形細胞之增生。最後,我們分析熱休克蛋白 27 及與細胞衰老有關的三種基因(膠原蛋白？、Stromyelysin 及錳超氧化物歧化？)的表現情形來探討介白質-1 對細胞衰老之作用機轉。 本研究的結果發現隨著細胞老化,高繼代纖維母細胞之錳超氧化物歧化及 Stromyelysin 基因之表現比低繼代纖維母細胞之基因表現爲強。比較轉形細胞及第二型介白質-1 接受器過剩表現轉形細胞之增生,發現第二型介白質-1 接受器過剩表現轉形細胞之增生受到抑制。第二型介白質-1 接受器過剩表現轉形細胞之熱休克蛋白 27 的表現雖較轉形細胞之表現爲高,但是兩群細胞與細胞衰老有關的三種基因(膠原蛋白？、Stromyelysin 及錳超氧化物歧化？)的表現情形並無顯著之差異。第二型介白質-1 接受器過剩表現轉形細胞之增生受到抑制之作用機轉仍需進一步之研究來解明。
• 英文摘要	Human diploid fibroblasts (HDFs) are the major components of gingival connective tissues and play pivotal roles in maintaining the

functional integrity of gingival tissues. The lifespan of HDFs before senescence in vitro is inversely proportional to the age of the donor in vivo, suggesting that cellular senescence in vitro reflect aging in vivo. Recently, age-associated increases in production of Interleukin-1 (IL-1; IL-1.alpha. and IL-1.beta.) have been reported to be correlated with overexpression of IL-1-induced genes in late-passage HDFs obtained from young tissue donors and in early-passage of HDFs obtained from old tissue donors. These IL-1-induced genes including collagenase, stromyelysin and a scavenger enzyme of anion, manganese superoxide dismutase (Mn SOD). Though, there are increasing evidences of the biological significance of age-associated IL-1 in HDFs in vitro, there is little known about the underlying mechanisms of its effects. The goal of this grant application is to characterize the roles of age-associated IL-1.beta. in the regulation of biological aging and cellular proliferation in HGFs, and to understand the underlying molecular mechanisms. To do this, we analyzed the production of IL-1.beta. and in young- and late-passage cells of non-transformed HGFs, vector-transfected HGFs and RII-transfected HGFs. Then, we compared the proliferation rate of cell in these HGFs. Finally, to investigate the molecular mechanisms of the effects of age-associated IL-1.beta. on HGFs, we examined the expression of hsp 27 and the senescence-related genes in these HGFs by reverse transcriptase-polymerase chain reaction (RT-PCR). The data showed a decreased proliferation rate of the RII-transfected GF than that of the vector-transfected GF. As the cell grew older, an increased gene expression of MnSOD and stromyelysin were detected in late-passage GF. Although there was no significant difference in the expression of these genes in RII-transfected GF and the vector-transfected GF, an increased basal level of hsp 27 in RII-transfected GF was detected. These results suggest that IL-1RII overexpressing on GF might play a role in regulation of cell proliferation, but the underlying mechanisms of this regulation need to be further investigated.