牙周病主要致病菌 **Porphyromonas gingivalis** 促使人類牙齦纖維母細胞細胞增生及其相關蛋白降解現象探討

Studies on the Phenomena of Proliferation and Related Protein degradation by Porphyromonas gingivalis in Human Gingival Fibroblast

中文摘要

Porphyromonas gingivalis （P. gingivalis）是一株主要造成牙周病的主要致病菌之一，而牙周病是因爲細菌感染所引起的慢性發炎。文獻報導指出 P. gingivalis 在宿主上皮細胞中會促使 anti-apoptosis 的基因表現及蛋白產生。這種現象與另一隻牙周致病菌 Actinobacillus actinomycetemcomitans 是很不一樣的表現。本研究藉由觀察 P. gingivalis 對人類牙齦纖維母細胞造成的影響，來探討長期的慢性發炎下，其巨觀的細胞生長情形與微觀的分子調控之改變。結果顯示，在受到長期 MOI = 100 的 P. gingivalis 感染之下，細胞會被促使增生，且在剛感染的初期，就可以發現被感染的細胞比正常情況的細胞更早進入細胞週期；而在基因調控方面，亦可以很明顯的發現 NF- B 被活化，進一步促使 AKT/PKB、cyclin D1、CDK2 等基因活化、蛋白合成。另一方面，在初期感染時，由於 P. gingivalis 具有能黏附細胞表面的能力，造成 cyclin D1、cyclin D3、cyclin A、cyclin E、p53、p27、CDK 1、CDK 2 及 AKT 等蛋白的降解，而這個現象在細菌侵入後，會被調控回來。然而，如果抑制 P. gingivalis 侵入細胞，cyclin D1、cyclin D3、cyclin A、cyclin E、p53、p27、CDK 1 及 AKT 調控回來的時間會被延後。在更長期的重複感染之下，原本回復的 p53、 p27 等蛋白會再次消失。因此，藉由探討牙周病致病菌對人類牙齦纖維母細胞的細胞生長週期之影響，期望將來能由致病機轉找出長期慢性發炎與癌化之間的相關性。

英文摘要

Porphyromonas gingivalis (P. gingivalis) is an major oral pathogen of periodontal disease, which can causes a chronic inflammatory disease. Recent studies indicate that P. gingivalis can promotes anti-apoptosis gene and protein expression in the host cell. The phenomenon induced by P. gingivalis is very different from the other pathogens Actinobacillus actinomycetemcomitans. In this study, we infected Human gingival fibroblast (HGF) with P. gingivalis to observe the macrocosm of proliferation and the microcosm of molecular change. Our results demonstrate that P. gingivalis enhanced the proliferation of HGF,and infected cell will entered into cell cycle faster in the early phases. The triggering of the signal pathways in P. gingivalis-infected HGF was demonstrated with rapid phosphorylation of I B , followed by nuclear

translocation of p65. In addition, NF- B induced enhanced expression of AKT, cyclin D1 and CDK 2 . In the other side, in the early stage of infection, since P. gingivalis could adhere to cell surface, cyclin D1, cyclin D3, cyclin A, cyclin E, p53, p27, CDK 1, CDK and AKT would be degraded, and the phenomenon was regulated by P. gingivalis invasion. But, P. gingivalis invasion which inhibited by cytochalasin D or heat-killed, the regulation of those protein will be delayed. The influence of P. gingivalis in the long term, we found p53, p27 which were degraded in the early phases would be degraded again at fourth day. To expect, the relationships and mechanisms through which infection and inflammation increase cancer risk and promoter tumor development could be found by the influence of P. gingivalis in HGF in the long stage.