Senescence and odontoblastic differentiation of dental pulp cells

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論 文 名　：Senescence and odontoblastic differentiation of dental pulp cells

（歯髄細胞の老化と象牙芽細胞分化について）

区　　分　：甲

論 文 内 容 の 要 旨

Cellular senescence has been suggested to be involved in physiological changes of cytokine production. Previous studies showed that the concentration of tumor necrosis factor-α (TNF-α) is higher in the blood of aged people compared with that of young people. So far, the precise effects of TNF-α on odontoblastic differentiation of pulp cells has been controversial. Therefore, we aimed to clarify how this cytokine affected pulp cells during aging. Human dental pulp cells (HDPCs) were cultured until reaching the plateau of their growth, and the cells were isolated at actively (yHDPCs) or inactively (sHDPCs) proliferating stages. sHDPCs expressed senescence-related molecules while yHDPCs did not. When these HDPCs were cultured in odontoblast-inductive medium, both young and senescent cells showed mineralization, but mineralization in sHDPCs was lower compared with yHDPCs. However, the administration of TNF-α to this culture medium altered these responses: yHDPCs showed downregulated mineralization, while sHDPCs exhibited significantly increased mineralization. Furthermore, the expression of TNFR1, a receptor of TNF-α, was significantly upregulated in sHDPCs compared with yHDPCs. Downregulation of *TNFR1* expression led to decreased mineralization of TNF-α-treated sHDPCs, whereas restored the reduction in TNF-α-treated yHDPCs. These results suggested that sHDPCs preserved the odontoblastic differentiation capacity, and TNF-α promoted odontoblastic differentiation of HDPCs with progress of their population doublings through increased expression of *TNFR1*. Thus, TNF-α might exert a different effect on odontoblastic differentiation of HDPCs depending on their proliferating activity. In addition, the calcification of pulp chamber with age may be related with increased reactivity of pulp cells to TNF-α.