

Inhibition of sonic hedgehog signaling pathway in ameloblastoma cell line

ザム, シャリファ ノファ アミザ

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氏 名	Syarifah Nova Amiza Zam			
論 文 名	Inhibition of sonic hedgehog signaling pathway in ameloblastoma cell line (エナメル上皮腫細胞株におけるソニックヘッジホッグシグナル経路の抑制)			
論文調査委員	主 査	九州大学	教授	清島 保
	副 査	九州大学	教授	前田 英史
	副 査	九州大学	教授	森 悦秀

論 文 審 査 の 結 果 の 要 旨

Ameloblastoma is a benign odontogenic tumor which is characterized by locally invasive growth into the jaw, and often recurs. The quality of life is reduced by resection of the jaw as a radical treatment. Therefore, development of new treatment is eagerly expected.

Sonic hedgehog (SHH) activates a membrane-receptor complex formed by patched (PTCH) and smoothened (SMO). Hedgehog signaling pathway has crucial roles in growth and patterning during organogenesis and tumorigenesis. In the present research, we demonstrated the necessity of the SHH signaling pathway in the growth of human ameloblastoma cell line, AM-1 cells, and the suppression of the proliferation by using inhibitors for SHH signaling pathway. We examined the effects of each inhibitor for SHH signaling pathway on growth in the AM-1 cells. We also examined the apoptotic cells by TUNEL and Annexin V assays. RT-PCR analysis revealed that SHH, PTCH, SMO, GLI1, GLI2, and GLI3 were expressed in AM-1 cells and these gene products were also detected by immunocytochemistry. The SHH signaling pathway inhibitors suppressed cellular proliferation of AM-1 cells. The TUNEL positivity in the cells treated with SHH signaling inhibitors was significantly higher than those in the untreated cells. Furthermore, it was confirmed immunocytochemically that BCL2 expression was decreased and BAX expression was increased in the treated AM-1 cells.

The results of this study can provide new information in which the inhibition of SHH signaling pathway is a strong target candidate for the novel treatment of ameloblastoma by growth inhibition and apoptosis induction. Based on this research, the candidate deserves to be conferred the degree of doctor of philosophy (Dental Science) in the Kyushu University Graduate School of Dental Science.