Effect of phenytoin on PI3K/Akt signaling pathway in human gingival fibroblasts

Hiroko Matsumoto[1], Reiri Takeuchi[2], Junichi Yamane[1], Hitoshi Nishimura[3], Masamichi Komiya[3]

[1]Dept. Pharmacol., Nihon Univ. Sch. Dent. Matsudo, [2]Dept. Biochem., Nihon Univ. Sch. Dent. Matsudo, [3]Dept. Oral Surg., Nihon Univ. Sch. Dent. Matsudo

Gingival overgrowth is caused in response to the antiepileptic drug, phenytoin (PHT). PHT-induced gingival overgrowth is characterized by the proliferation of fibroblasts and increased collagen formation in gingiva. Interleukin -1α (IL-1α) increases basic fibroblast growth factor (bFGF) production and influences the release of bFGF in human gingival fibroblasts (hGFs). We have previously reported that PHT induced gingival overgrowth to promote cell proliferation by ETS-1 expression and reduced apoptosis through SAPK/JNK pathway, since PHT enhanced Bcl -2 mRNA and protein expression in hGFs. The present study investigated the effect of PHT on PI3K/Akt signaling pathway in hGFs to clarify the mechanism of PHT-induced gingival overgrowth. Cultured hGFs were purchased from ScienCell Research Laboratories. hGFs were cultured to semi-confluence and treated with PHT and/or IL-1α for 1, 6, 24, and 96 hours. The expression and phosphorylation of Akt, GSK-3β, PTEN, PDK1, p21Waf1/Cip1, and p27 Kip1 were measured by Western blot analysis. IL-1α increased the phosphorylation of Akt (Ser473), however, PHT did not affect that of Akt (Ser473) and GSK-3β. On the other hand, PHT decreased the expression of p21Waf1/Cip1 and p27 Kip1. These results suggest that PHT may affect the expression of p21Waf1/Cip1 and p27 Kip1 through another pathway except Akt and GSK-3β signaling.