EP_4 receptor regulates cell migration and apoptosis in oral cancer

Yumika Azuma[1], Masanari Umemura[1], Rina Nakakaji[1,2], Akane Nagasako[1], Kohei Osawa[1,2], Ryo Tanaka[1], Yoshihiro Ishikawa[1]

[1]Cardiovascular Research Institute, Sch. Med., Yokohama City Univ., [2]Department of Oral and Maxillofacial Surgery, Sch. Med., Yokohama City Univ.

【Background】The EP4 prostanoid receptors are one of the four receptor subtypes for Prostaglandin E2 (PGE2). EP4 plays an important role in cancer progression. Its inhibition is a potential strategy for cancer therapy. However, little information is available regarding cell apoptosis and cellular signaling pathway of EP4 in oral cancer. In current study, we examined that EP4 signal regulates cell apoptosis and chemotherapeutic resistance in oral cancer.

【Material and Method】Human-derived tongue squamous cell carcinoma cell lines, HSC-3 was used. Western blot analysis was performed to evaluate the proteins, which is associated with cell migration and apoptosis in cancer (E-cadherin, N-cadherin, claudin-1, ZEB1, ZO-1, galectin-3, fibronectin, Bcl-2, Bax). Cell apoptosis was evaluated by flowcytometry.

【Result】EP4 agonist (ONO-AE1-437) increased expression of galectin-3 in HSC-3 cells ($p<0.001$). EP4 agonist also increased claudin-1 expression. The other proteins were not changed by the EP4 agonist stimulation. Furthermore, EP4 agonist inhibited cisplatin-induced early apoptosis of oral cancer cells and decreased late apoptosis and necrosis.

【Conclusion】Activation of EP4 signal may increase the expression of galectin-3 and promote cell apoptosis, resulting in a chemotherapeutic resistance of oral cancer.