PC009

Fasudil Suppresses Head and Neck Squamous Carcinoma Growth by Stimulating Gene Expression and Secretion of the Chemokine CXCL14/BRAK

C Miyamoto, S Ozawa, SS Takahashi, SW Takahashi, F Yoshino, MC Lee, RI Hata, Y Maehata

Kanagawa Dental Univ., Yokosuka, Japan

Ras-homologous small GTPase (RhoA) and Rho-associated coiled-coil-containing protein kinase (ROCK) are key regulators of the endocytic and exocytic trafficking of molecules in cells. Activation of this pathway promotes tumor invasion and metastasis (1). Fasudil is a specific inhibitor of ROCK, which has been approved for the treatment of cerebral vasospasm (2). We previously reported that fasudil has anti-tumor activity by stimulating Chemokine CXCL14/BRAK secretion in fibrosarcoma cells (3). But effect of Head and Neck Squamous Carcinoma cells (HNSCC) are not clear. Here, we investigated the effects of Fasudil on BRAK secretion and gene expression in HNSCC cells.

We examined the effect of Fasudil on tumor growth, HSC-3 cells were inoculated subcutaneously into both sides of the dorsolateral regions of female mice (5 weeks old). These mice were daily-administered Fasudil, i.p. (50mg/kg/day). Animal experiment protocols were approved by Institutional Animal Care Committees (Kanagawa Dental College, Yokosuka, Japan). Fasudil suppressed the growth of tumors (n=6) [fig.1].

We examined the effects of fasudil on the secretion of BRAK by using ELISA in HSC-3 cells. The secretion of BRAK was significantly increased (22.83±3.18 vs 73.26±2.91 (pg/10^5 cells)) by treatment with fasudil (25µM) in HSC-3 cells. In order to determine the effects of Fasudil on the and expression of BRAK by using qPCR in HSC-3 cells. The expression of BRAK was significantly increased (101.52±11.86 vs 289.68±47.87%) by treatment with Fasudil (25µM) in HSC-3 cells [fig.2]. Results are expressed as mean ± standard deviation (S.D.). Statistical analysis was performed using Student's t-test or one-way analysis of variance (ANOVA). P values less than 0.05 were considered to be statistically significant.

These results indicate that Fasudil inhibits tumor growth by stimulating BRAK secretion and gene expression in the HNSCC cells and suggests that therapy using fasudil may have clinical efficacy.
