慶應医学会例会

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特任准教授

演題「腫瘍間質に依存するdiffuse-type胃癌進展機構の解明」

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東校舎1階　セミナー室

（要旨）

Cancer-associated fibroblasts (CAFs) enhance tumor progression through secretion of soluble factors. However, there have been no systematic studies of CAFs in diffuse-type gastric cancers (DGCs). We investigated the characteristics and functional roles of CAFs in DGCs using comprehensive genomic approach. We established primary fibroblasts from more than 100 GC patients. Normal fibroblasts (NFs)/CAFs were subjected to Exome and RNA sequencing, and the candidates for functional assay were selected and examined the roles for GC tumor progression. CAFs showed invasive molecular pattern and high motility in extracellular matrix (ECM). We identified RHBDF2 as a mediator of TGF-β signaling and an enhancer of CAF motility and demonstrated that RHBDF2 regulates type I TGF-β receptor (TβRI) cleavage through tumor necrosis factor (TNF)-α converting enzyme (TACE) activity. Moreover, high-motility CAFs confer on DGC cells the ability to invade ECM. Furthermore, we recently found that particular cytokines induce RHBDF2 up-regulation and subsequent cellular senescence in CAFs. The expression of these cytokines in GC tissues was significantly associated with poor prognosis of GC patients. Here, we will discuss about potential molecular mechanisms by which CAFs assist DGC progression.

（参考文献）

Ishimoto T, Miyake K, Nandi T, Yashiro M, Onishi N, Huang KK, Joyce LN, Kalpana R, Tay ST, Suzuki Y, Cho BC, Kuroda D, Arima K, Izumi D, Iwatsuki M, Baba Y, Oki E, Watanabe M, Saya H, Hirakawa K, Baba H, Tan P. Activation of Transforming Growth Factor Beta 1 Signaling in Gastric Cancer-associated Fibroblasts Increases Their Motility, via Expression of Rhomboid 5 Homolog 2, and Ability to Induce Invasiveness of Gastric Cancer Cells. ***Gastroenterology.*** (2017)

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