Fibroblast growth factor 2 modulates purine metabolic enzymes through MAPK pathway in rat spinal cord astrocytes

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Extracellular adenosine (ADO) is mainly produced by metabolism of ATP released from astrocytes in the central nervous system and mediates neuroprotective effect under pathological conditions. In the previous study, we showed that fibroblast growth factor 2 (FGF2) upregulates purine metabolic enzymes, ecto-5'-nucleotidase (CD73) and adenosine deaminase (ADA), in rat spinal cord astrocytes. In this study, we investigated the intracellular signaling pathway of CD73 and ADA modulation by FGF2 in astrocytes.

Cultured astrocytes isolated from rat spinal cord were treated with FGF2. Enzymatic activity for purine metabolism was measured by incubation with artificial cerebrospinal fluid containing AMP or ADO and measurement of those metabolites with high-performance liquid chromatography. The expressions of CD73 and ADA were measured by western blotting.

In cultured astrocytes, FGF2 increased the expression and activity of CD73 and ADA in a concentration- and time-dependent manner. An FGF receptor inhibitor, SU5402 (5 μM), inhibited the increase in the expression and activity of CD73 and ADA by FGF2. FGF2 increased the phosphorylation of ERK and JNK, which is inhibited by SU5402 and MAPK inhibitors. In addition, U0126 (10 μM), a MEK inhibitor, also inhibited the increase in the expression and activity of CD73 and ADA.

These results indicate that FGF2 upregulates the expression and activity of CD73 and ADA through FGF receptor/MAPK pathway. Furthermore, it is suggested that mainly MEK/ERK pathway contribute to the upregulation of CD73 and ADA.