Inhibition of transcription factor OASIS attenuated kidney fibrosis

Ayaha Yamamoto[1], Masanori Obana[1], Takafumi Nakae[1], Yoshiaki Miyake[1], Sayuri Mitsuoka[1], Makiko Maeda[2], Kazunori Imaizumi[3], Kotaro Matsumoto[1], Yasushi Fujio[1]

[1]Laboratory of Clinical Science and Biomedicine, Grad. Sch. Pharm., Osaka Univ., [2]Education and Research Project for Pharm.D, Grad. Sch. Pharm., Osaka Univ., [3]Department of Biochemistry, Grad. Sch. Biomed. & Health Sci., Hiroshima Univ.

[Background] Since kidney fibrosis is a common pathway to many kidney diseases, prevention of kidney fibrosis could be a therapeutic strategy for kidney diseases. Previously, we reported that old astrocyte specifically induced substance (OASIS), a transcription factor, promotes proliferation of renal myofibroblasts, analyzed by *in vitro* assay. However, the pathophysiological significance of OASIS in kidney fibrosis *in vivo* remains to be elucidated.
[Methods/Results] C57BL/6J mice were subjected to unilateral ureteral obstruction (UUO) to cause kidney fibrosis, analyzed by Sirius red staining and hydroxyproline assay. AEBSF, an inhibitor of OASIS, suppressed kidney fibrosis at day 7 after UUO. Moreover, kidney fibrosis was ameliorated in OASIS KO mice compared with WT mice, accompanied by decreased proliferation of myofibroblasts. To explore the downstream of OASIS, DNA microarray was performed using myofibroblasts from OASIS KO mice. Interestingly, it was found that bone marrow stromal antigen 2 (BST2) was a candidate downstream gene of OASIS. Anti-BST2 antibody treatment attenuated UUO-induced kidney fibrosis.
[Conclusion] OASIS contributes to the develop of kidney fibrosis by promoting the proliferation of myofibroblasts, in part, through increased BST2 expression. OASIS could be a therapeutic target against kidney fibrosis.