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2,5-Dimethylcelecoxib attenuates cardiac fibrosis after cryoinjury-induced myocardial infarction by suppressing the fibroblast-myofibroblast differentiation

Eigo Ikushima[1], Shin Ishikane[1], Tomohiro Takiguchi[2], Yumiko Toyohira[1], Fumi Takahashi[1]

[1]Department of Pharmacology, University of Occupational and Environmental Health, Japan, [2]Dep. Clin. Pharm., Grad. Sch. Med., Kyushu Univ.

【Background】
Cardiac fibrosis is associated with heart diseases, such as myocardial infarction (MI), and activated fibroblasts (myofibroblasts) play a main role during fibrosis progression. Although we reported that 2,5 dimethylcelecoxib (DM-C) prevents cardiac fibrosis, the molecular mechanism, including the effect on myofibroblast differentiation, is not clarified yet.
【Objective】
We investigate the effect of DM-C on MI-caused fibrosis and fibroblast-myofibroblast differentiation using *in vivo* and *in vitro* models.
【Methods】
In vivo: Cryoinjury-induced MI (CMI) mouse model was employed. In DM-C group, the mice received DM-C for 4 weeks from 3 days before the operation. Cardiac function was evaluated with transthoracic echocardiography every week. Four weeks after operation, the heart was removed and the fibrosis area was evaluated.
In vitro: The effect DM-C on myofibroblast-differentiation induced by TGF-b using SD rat dermal fibroblast was examined.
【Results】
In DM-C group, the ejection fraction was increased than control group and, according with this, the fibrosis area is reduced. Further, DM-C significantly suppressed aSMA expression (myofibroblast marker) and the phosphorylation level of Akt, GSK-3b and Smad2/3.
【Conclusion】
These results suggest that DM-C attenuates cardiac fibrosis after MI through inhibition of fibroblast-myofibroblast differentiation. DM-C also inhibited the TGF-b /SMAD2/3 signaling pathway by Akt inhibition. Therefore, DM-C has a potential as the novel drug for treatment of cardiac fibrosis after MI.