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

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【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.