Caffeine induces the reversion of activated hepatic stellate cells via antagonizing adenosine receptors.

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During liver injury, quiescent hepatic stellate cells (qHSCs) are activated by various cytokines and transdifferentiated into myofibroblast-like activated HSCs (aHSCs), which produce collagen, leading to liver fibrosis. Accordingly, the reversion of aHSC is expected to be a therapeutic target for liver fibrosis. Several epidemiological reports have suggested that the intake of caffeine decreases the risk of liver fibrosis. In the present study, therefore, we investigated the effect of caffeine on the reversion of aHSCs into qHSC. We used aHSC which was isolated from mice as qHSC and activated by culturing in DMEM supplemented with 10% FBS for 7 days. Caffeine (0.1–10 mM) decreased the expression of α-smooth muscle actin (α-SMA) and type I collagen a1 (COLIa1), an index of aHSC, in a concentration-dependent manner. Caffeine also increased the expression of matrix metalloproteinase-9 (MMP-9), an index of qHSC. Similarly to caffeine, the adenosine receptor inhibitor CGS-15943 had also significant effects on the expression of α-SMA, COLIa1 and MMP-9. These results suggest that caffeine induces the reversion of aHSC in a concentration-dependent manner via antagonizing adenosine receptors.