The activation of mouse hepatic stellate cells is suppressed by DIF-1, a morphogen produced by cellular slime molds.

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Hepatic stellate cells (HSCs), located in the gap of hepatocytes and sinusoidal endothelial cells, transdifferentiate from quiescent form (qHSCs) into myofibroblast-like activated one (aHSCs) during liver injury. The expression of α-smooth muscle actin (α-SMA) and the production of type Ⅰ collagen are up-regulated in aHSCs. Therefore, the activation of HSCs is responsible for liver fibrosis and inhibiting the activation can be a novel therapeutic target for the fibrosis. In the present study, we show that differentiation-inducing factor-1 (DIF-1) that is a low molecular weight compound derived from the cellular slime mold, *Dictyostelium discoideum*, has a suppressive effect on HSC activation. qHSCs were isolated from ddY mice and cultured in DMEM supplemented with 10% FBS. We treated qHSCs with DIF-1 on the next day after isolation and analyzed the effect of DIF-1 on HSC activation. DIF-1 significantly suppressed the up-regulation of α-SMA. However, the effect of DIF-1 was abolished in the presence of TWS119, an activator of Wnt/β-catenin signal pathway. DIF-1 reduced the levels of non-phosphorylated β-catenin (activated β-catenin) and phosphorylated GSK3β. These results suggest that DIF-1 inhibits the Wnt/β-catenin signal pathway through dephosphorylating GSK3β, thereby suppressing HSC activation.