

论著

## 丹参素对肝星状细胞TGF- $\beta$ 信号转导的影响

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**摘要** 目的: 观察丹参素对转化生长因子 $\beta$ 1 (TGF- $\beta$ 1) 诱导活化的大鼠肝星状细胞(HSCs)Smad信号转导通路的影响。方法: 体外分离、培养大鼠肝HSCs,用不同浓度丹参素作用于HSCs,检测丹参素对HSCs增殖和TGF- $\beta$ 1刺激后HSCs增殖的影响; 观察丹参素对TGF- $\beta$ 1刺激HSCs表达 $\alpha$ -SMA的影响; 观察HSCs转化生长因子受体(T $\beta$ R I、II)的表达; 观察丹参素和TGF- $\beta$ 1作用HSCs后,其Smad2、Smad3、Smad7 mRNA表达的变化。结果: (1)丹参素在0.0625 mmol/L-1 mmol/L时,对HSCs的生长增殖具有抑制作用(P<0.05); 丹参素对TGF- $\beta$ 1诱导的HSCs增殖也具有明显的抑制作用(P<0.05)。(2)丹参素0.25 mmol/L作用HSCs能下调 $\alpha$ -SMA的表达(P<0.05),也能下调TGF- $\beta$ 1诱导的HSCs的 $\alpha$ -SMA表达(P<0.05)。(3)HSCs中T $\beta$ R I、II的表达定位于细胞膜上,丹参素能下调活化HSCs中T $\beta$ R I、II的表达(P<0.05或P<0.01)。(4)TGF- $\beta$ 1促进HSCs中Smad2、Smad3、Smad7 mRNA的表达(P<0.01);丹参素能下调TGF- $\beta$ 1诱导的HSCs内Smad2、Smad3 mRNA的表达(P<0.05),并能上调Smad7 mRNA表达(P<0.05)。结论: 体外细胞实验表明,丹参素能通过下调活化HSCs细胞膜上T $\beta$ R I、II蛋白的表达来抑制HSCs的活化增殖。丹参素能上调HSCs内Smad7 mRNA表达,并下调Smad2、Smad3 mRNA表达,抑制HSCs活化,并抑制TGF- $\beta$ 1诱导的HSCs活化。

**关键词** 肝星状细胞 丹参素 转化生长因子 $\beta$  受体,转化生长因子 Smads通路

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## Role of danshensu on TGF- $\beta$ signal transduction in rat's hepatic stellate cells

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### Abstract

<FONT face=Verdana>AIM: To investigate the role of danshensu on Smad signal transduction in rat hepatic stellate cells (HSCs) stimulated with transforming growth factor (TGF- $\beta$ 1). METHODS: The rat HSCs was isolated with collagenase by in situ-liver recirculation perfusion and cultured in vitro. MTT colorimetric assay was used to detect proliferation of HSCs treated with different concentration of danshensu. The expressions of  $\alpha$ -SMA and T $\beta$ R I and II were observed by immunocytochemistry, indirect immunofluorescent staining and Western blotting when HSCs stimulated with TGF- $\beta$ 1 and with different concentrations of danshensu for 24 h. RESULTS: (1) Danshensu at the concentration from 0.0625 mmol/L to 1 mmol/L prevented the proliferation of HSCs in a dose-dependent manner (P<0.05). Danshensu also inhibited the proliferation of HSCs induced by TGF- $\beta$ 1 in a dose-dependent manner (P<0.05). (2) At concentration of 0.25 mmol/L, danshensu down-regulated  $\alpha$ -SMA protein expression in HSCs with or without stimulation of TGF- $\beta$ 1 (P<0.05), and the activation of HSCs was inhibited also. (3) Danshensu down-regulated the protein expression of T $\beta$ R I and II in HSCs stimulated with TGF- $\beta$ 1 (P<0.05, or P<0.01), these effects were correlated with the concentration. (4) TGF- $\beta$ 1 increased the mRNA level of Smad2, 3, and 7 in HSCs (P<0.01). Danshensu down-regulated the mRNA level of Smad2, 3 (P<0.05) and up-regulate the mRNA level of Smad7 in HSCs induced by TGF- $\beta$ 1 (P<0.05). CONCLUSION: Danshensu inhibits the activation and proliferation of HSCs through down-regulating the expression of T $\beta$ R I and II located in cellular membrane of HSCs. Danshensu suppresses the activation of HSCs, and also inhibits the activation of HSCs stimulated by TGF- $\beta$ 1 through up-

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regulation of Smad7 mRNA and down-regulation of Smad2, Smad3 mRNA expression in HSCs.</FONT>

**Key words** [Hepatic stellate cells](#) [Danshensu](#) [Transforming growth factor beta](#) [Receptors](#) [transforming growth factor](#) [Smads pathway](#)

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