[1]张霹雲,王斌,王军,等.5-甲基胞嘧啶羟化酶TET1在肝再生时卵圆细胞向肝细胞分化过程中的作用[J].第三军医大学学报,2014,36(08):797-801.

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5-甲基胞嘧啶羟化酶TET1在肝再生时卵圆细胞向肝的作用(PDF)

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Title: Effect of TET1 on hepatocytic differentiation of oval cells in liver regeneration

作者: 张霹雲; 王斌; 王军; 魏艳玲; 孙文静; 吴林; 罗茜; 陈东风
第三军医大学大坪医院野战外科研究所消化内科

Author(s): Zhang Piyun; Wang Bin; Wang Jun; Wei Yanling; Sun Wenjing; Wu Lin; Luo Xi; Chen Dongfeng
Department of Gastroenterology, Institute of Surgery Research, Daping Hospital, Third Military Medical University, Chongqing, 400042, China

关键词: 肝脏再生; 卵圆细胞; 细胞分化; TET1

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摘要: 目的 研究5-甲基胞嘧啶羟化酶TET1在肝脏再生时卵圆细胞向肝细胞分化过程中的作用。 方法 采用SD大鼠2-乙酰氨基芴（2-AAF）灌胃加2/3肝切除法建立肝脏再生模型，胶原酶灌注联合percoll 密度梯度离心法提取纯化大鼠原代卵圆细胞，免疫荧光实验鉴定卵圆细胞特异性标志物OV6的表达；RT-PCR和Western blot检测肝切后不同时间（3、6、9、12、15 d）TET1 mRNA和蛋白表达变化。培养WB-F344卵圆细胞，SCF 20 μg/L、HGF 10 μg/L、EGF 10 μg/L、地塞米松1.0×10^{-7} mol/L和 DMSO 1.5%处理7 d，诱导其向肝细胞样细胞分化（对照细胞不加任何细胞因子）。倒置相差显微镜观察卵圆细胞形态变化，RT-PCR和Western blot检测TET1表达变化。 结果 ①成功建立肝再生动物模型，分离获得大鼠原代卵圆细胞，其OV6阳性率≥80 %。②与对照细胞相比，卵圆细胞被诱导分化后，细胞形态由圆形变为梭形。③与对照细胞相比，卵圆细胞被诱导分化后， TET1 mRNA和蛋白水平均显著下降($P<0.01$)，此时肝细胞特异性标记物ALB表达升高，卵圆细胞分化为肝细胞样细胞。 结论 5-甲基胞嘧啶羟化酶TET1可能参与了卵圆细胞增殖和肝再生过程。

Abstract: Objective To investigate the effect of ten-eleven-translocation 1 (TET1) a 5-

methylcytosin hydroxylase, on the hepatocytic differentiation of oval cells in liver regeneration. Methods A liver regeneration model was established by gavage of 2-acetylaminofluorine (2-AAF) and surgical resection of 70% liver in SD rats. The expression of TET1 was analyzed by RT-PCR and Western blotting at 3, 6, 9, 12, and 15 d after liver resection. Primary rat oval cells were isolated by collagenase perfusion, purified by density-gradient centrifugation and stained for OV6 detection by immunofluorescence assay. WB-F344 oval cells were treated by dexamethasone 1.0×10^{-7} mol/L and DMSO 1.5%, with or without a mixture of cytokines including SCF 20 μg/L, HGF 10 μg/L, and EGF 10 μg/L, for 7 d. Cell differentiation was examined by detection of morphological changes and differentiation maker such as ALB. The expressions of TET1 were further determined. Results A large number of primary rat oval cells were obtained, with 80% $OV6^{+}$ oval cells. After induced differentiation for 7 d, oval cells showed a shape change from round to polygonal. Furthermore, induced differentiation resulted in reduce of TET1 expression (P<0.01) and dramatically increased expression of ALB (P<0.01), suggesting oval cells underwent hepatocytic differentiation. Conclusion TET1 participates in the proliferation of oval cells and liver regeneration possibly.

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