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论著

# 高浓度他克莫司抑制人骨髓间质干细胞增殖及向成骨细胞分化

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**摘要** **目的** 探讨他克莫司（FK506）对人骨髓间质干细胞（hBMSCs)增殖及向成骨细胞分化的影响。**方法** FK506 0.001～5 μmol·L$^{-1}$处理hBMSCs细胞中，雌二醇0.01 μmol·L$^{-1}$或咖啡因100 μmol·L$^{-1}$为阳性对照组，作用24 h后用BrdU掺入法检测细胞增殖，在促成骨细胞分化液中作用8 d后用比色法检测碱性磷酸酶（ALP）活性，作用12 d后用邻甲酚酞络合法检测钙沉积量；通过检测磷酸盐释放量间接反映钙调神经磷酸酶（CaN）活性，Western印迹法检测核心结合因子α1亚基（Cbfα1)表达。**结果** 与DMSO对照组相比， FK506 0.001～0.01 μmol·L$^{-1}$促进细胞增殖，但对ALP活性及钙沉积量无影响；FK506 0.5～5 μmol·L$^{-1}$则呈浓度依赖性地抑制细胞增殖，显著抑制ALP活性及减少钙沉积量($P$<0.05)。此外，FK506 0.1～5 μmol·L$^{-1}$ 呈浓度依赖性地降低CaN活性，与相同浓度FK506 呈浓度依赖性地下调Cbfα1的表达效应相一致。**结论** 高浓度FK506可通过CaN/Cbfα1通路抑制hBMSCs增殖及向成骨细胞成骨分化。

**关键词** 他克莫司 人骨髓间质干细胞 钙调神经磷酸酶 核心结合因子α1亚基

**分类号** R979.5

# High concentration of tacrolimus inhibits proliferation and osteoblastic differentiation of human mesenchymal stem cells

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**Abstract**

**OBJECTIVE** To investigate the effect of tacrolimus on cell proliferation and osteoblastic differentiation of primary human bone marrow-derived mesenchymal stem cells (hBMSCs). **METHODS** hBMSCs were cultured with tacrolimus 0.001-5 μmol·L$^{-1}$. BrdU incorporation was used to assess the cell proliferation while cellular alkaline phosphatase (ALP) activity and calcium deposition were measured to evaluate the osteoblastic differentiation of hBMSCs cultures. The calcineurin (CaN) activity was also examined using commercial CaN assay kit, and core binding factor 1 alpha subunit (Cbfα1) protein level was determined by Western blotting. **RESULTS** Tacrolimus 0.001-0.1 μmol·L$^{-1}$ promoted BrdU incorporation but had no effect on ALP activity and calcium deposition, whereas tacrolimus 0.5-5 μmol·L$^{-1}$ resulted in significant decrease in both cell proliferation and osteoblastic maturation, by reducing BrdU incorporation, ALP activity, and calcium deposition of hBMSCs cultures in a concentration-dependent manner. In addition, tacrolimus 0.5-5 μmol·L$^{-1}$ led to concentration-dependent decrement in CaN activity, which was consistent with down- regulated Cbfα1 protein in the tacrolimus treated cells. **CONCLUSION** High concentration of tacrolimus might inhibit the cell proliferation and osteoblastic differentiation of hBMSCs cultures through a CaN/Cbfα1 pathway.

**Key words** tacrolimus human bone marrow derived mesenchymal stem cells calcineurin core binding factor alpha1 subunits

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