[1]张闻宇,黄文栋,娄桂予.胆汁酸 G-蛋白偶联受体通过p38 MAPK 通路诱导巨噬细胞IL-1β、TNF-α和IL-6的转录[J].第三军医大学学报,2012,34(07):597-601.

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Title: TGR5 induces IL-1β, TNF-α and IL-6 mRNA transcription by p38 MAPK pathway in mouse macrophages

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关键词: 胆汁酸G-蛋白偶联受体; 齐墩果酸; RAW264. 7细胞株; 枯否细胞; 促炎因子

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摘要: 目的 观察胆汁酸G-蛋白偶联受体（G protein-coupled receptor for bile acids, TGR5）被齐墩果酸（oleanolic acid，OA）激活后对RAW264. 7 细胞白细胞介素-1（interleukin-1β, IL-1β）、肿瘤坏死因子-α（tumor necrosis factor α，TNF-α）和白细胞介素-6（interleukin-6，IL-6）转录的影响及其机制的探讨。 方法 通过实时荧光定量（Real-time）PCR 法检测OA作用不同时间RAW264. 7 细胞和原代枯否细胞IL-1β、TNF-α和IL-6 mRNA的表达；并进一步分析在RAW264. 7 细胞中加入3种不同信号通路的抑制剂对上述3种炎症因子mRNA表达的影响。OA作用RAW264. 7 细胞和原代枯否细胞不同时间后，Western blot 分析p38 MAPK 的磷酸化水平。 结果 OA刺激RAW264. 7细胞6、12、24 h后，IL-1β、TNF-α和IL-6 mRNA表达明显升高。OA作用于分离的原代枯否细胞 3 h 和 6 h 后，也可观察到相同的结果。p38 MAPK 特异性抑制剂SB203580可以明显地抑制OA诱导的RAW264. 7 细胞内IL-1β、TNF-α和IL-6 mRNA的表达，但PKA和NF-κB的抑制剂无此作用。RAW264. 7 细胞和原代枯否细胞经OA刺激后，p38 MAPK磷酸化水平明显增强。 结论 TGR5可能通过活化 p38 MAPK 磷酸化诱导炎症细胞 IL-1β、TNF-α和IL-6 mRNA的表达，提示TGR5在无其他刺激因素作用下，具有诱导炎症因子表达的作用。

Abstract: Objective To determine the effect of plasma membrane-bound G protein-coupled receptor for bile acids (TGR5) activation by oleanolic acid (OA) on the expression of interleukin-1β （IL-1β）, tumor necrosis factor-α（TNF-α） and interleukin-6（IL-6）in mouse macrophages. Methods Real-time PCR was used to detect the expression of IL-1β, TNF-α and IL-6 at mRNA level after rat macrophage RAW264.7 cells and Kuffer cells were incubated with OA in different time periods. And the expression of these inflammatory factors were further analyzed by the same method when RAW264.7 cells were stimulated by inhibitors of 3 different signal pathway plus OA. The phosphorylation level of p38 MAPK was measured by Western blotting. Results Treatment of RAW264.7 cells with OA resulted in a robust increase in IL-1β, IL-6 and TNF-α transcripts at 6, 12 and 24 h compared with untreated control cells. Similarly, an up-regulation of IL-1β, IL-6 and TNF-α expression was also observed in isolated Kupffer cells at 3 and 6 h. Pre-treatment of RAW 264.7 cells with a p38 MAPK inhibitor SB203580 markedly reduced the OA-induced increase of IL-1β and TNF-α transcription, but not for PKA or NF-κB inhibitors. p38 phosphorylation was increased by OA treatment in both RAW 264.7 cells and Kupffer cells. Conclusion TGR5 activation induces IL-1β, IL-6 and TNF-α expression through p38 MAPK activation, indicating that TGR5 possesses pro-inflammatory properties when without any other stimulus.

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备注/Memo: -