

论文

地塞米松和吲哚美辛对基质金属蛋白酶-9的抑制作用及其机制研究

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摘要:

目的研究地塞米松和吲哚美辛对U937细胞中基质金属蛋白酶-9(MMP-9)活性的影响及抗炎作用机理。方法明胶酶谱法测定MMP-9的活性;Western blot法测定细胞培养上清液中MMP-9蛋白;RT-PCR法测定MMP-9 mRNA的表达。结果地塞米松和吲哚美辛可显著抑制PMA诱导的U937细胞培养上清液中MMP-9的活性,且抑制强度随浓度的增大而增加;地塞米松和吲哚美辛可显著抑制PMA诱导的的U937细胞MMP-9蛋白分泌及mRNA表达,且变化趋势与活性变化一致。结论对MMP-9活性的抑制作用可能是地塞米松和吲哚美辛抗炎作用的机理之一。

关键词: 基质金属蛋白酶-9 地塞米松 吲哚美辛 抗炎作用

Inhibition of dexamethasone and indomethacin on matrix metalloproteinase-9 and the mechanism of inhibition

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Abstract:

AimTo study the inhibitory effect of dexamethasone and indomethacin on matrix metalloproteinase-9 (MMP-9) and investigate their mechanism of MMP-9 inhibition on the level of protein and mRNA. MethodsU937 cells were cultured in RPMI 1640 medium with 10% fetal calf serum (FCS). After U937 cells were exposed to 1×10^{-8} mol·L⁻¹ phorbol 12-myristate 13-acetate (PMA) for 24 hours without FCS, the activity of MMP-9 in the supernatant was analyzed by gelatin zymography. The MMP-9 protein secreted from U937 in serum-free conditional media was detected by Western blot using special polyclonal antibodies. The mRNA expression of MMP-9 was investigated by RT-PCR. ResultsGelatin zymography showed that MMP-9 activity in U937 cells supernatant increased significantly after exposed to 1×10^{-8} mol·L⁻¹ PMA for 24 hours without FCS. Dexamethasone at 1×10^{-5} , 1×10^{-7} , 1×10^{-9} mol·L⁻¹ and indomethacin at 1×10^{-5} , 1×10^{-6} , 1×10^{-7} mol·L⁻¹ can inhibit this increase. Western blot showed that MMP-9 secretion from U937 cells in serum-free conditional media was increased under the same stimulating condition, Dexamethasone and indomethacin can inhibit MMP-9 secretion in U937 cells stimulated by 1×10^{-8} mol·L⁻¹ PMA and the inhibitory effect was increased as their concentration increased. RT-PCR showed that MMP-9 mRNA expression of U937 cells was also inhibited and the inhibitory effect was increased as their concentration increased. ConclusionInhibition of MMP-9 activity may be one of the anti-inflammatory mechanisms of dexamethasone and indomethacin; the inhibition of MMP-9 activity is coherent with the inhibition of MMP-9 secretion and mRNA expression.

Keywords: dexamethasone indomethacin Anti-inflammatory effect matrix metalloproteinase-9

收稿日期: 2002-01-04 修回日期 网络版发布日期

DOI:

基金项目:

通讯作者: 程桂芳

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