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论著

TNF-α上调单核巨噬细胞MMP-9的活性与类风湿关节炎关节破坏的关系

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摘要 目的： 探讨TNF-α对单核巨噬细胞基质金属蛋白酶9（MMP-9）的表达与酶活性的影响以及与类风湿关节炎患者关节破坏的关系。方法：用双抗体夹心ELISA法检测类风湿关节炎患者组（RA）和对照组血清和关节滑液中TNF-α、MMP-9的含量，观察MMP-9与X线表现积分（Larsen）的关系。体外将佛波酯（TPA）和不同浓度（0、1、10、20 μg/L）TNF-α共同孵育THP-1细胞24 h后，运用Western blotting方法检测MMP-9蛋白的表达，明胶酶谱法检测MMP-9活性，侵蚀小室法观察分化前后THP-1细胞的侵蚀力。结果：RA患者组血清和关节滑液中TNF-α、MMP-9的水平明显高于对照组（P＜0.05），且血清和滑液MMP-9与Larsen积分显著相关（r＝0.37和r＝0.32，P＜0.01）；体外细胞实验中，TNF-α上调分化的THP-1中MMP-9的表达和酶活性，并且增强分化的THP-1细胞的侵蚀性，并与TNF-α呈浓度依赖性。结论：TNF-α上调单核巨噬细胞MMP-9表达及活化，增强了炎症细胞的侵蚀力，可能在RA关节破坏机制中起着重要的作用。

关键词 肿瘤坏死因子 单核细胞 关节炎,类风湿 基质金属蛋白酶-9

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Association of TNF-α upregulation of MMP-9 activation in monocyte-derived macrophages with progression of joint damage in patients with rheumatoid arthritis

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Abstract

<FONT face=Verdana>AIM: To explore the expression and activation of matrix metalloproteinase-9 (MMP-9) from monocyte-derived macrophages induced by tumor necrosis factor-α (TNF-α) and to investigate its association with progression of joint damage in patients with rheumatoid arthritis. METHODS: TNF-α and MMP-9 in serum and synovial fluid from patients with early RA and controls were tested with a double-antibody enzyme-linked immunosorbent assay. The correlation between MMP-9 and Larsen score over the first 12 months was analyzed. THP-1 cells differentiated by the treatment with TPA were stimulated with increasing concentration of TNF-α for 24 h in vitro. The protein expression of MMP-9 was determined by Western blotting. The activity of MMP-9 was measured by gelatinolytic zymography. Boyden chamber-matrigel in vitro invasion assay was used to detect the invasive capacity. RESULTS: The levels of TNF-α and MMP-9 in serum and synovial fluid of RA patients were significantly higher than those in controls (P<0.05). Serum and synovial fluid levels of MMP-9 correlated significantly with Larsen score (r=0.37 and 0.32, P<0.01). The MMP-9 activity and invasive ability of co-cultured THP-1 cells with TNF-α and TPA were higher than those of non-TNF-α treatment. CONCLUSION: TNF-α upregulates MMP-9 activation and promotes infiltration of monocyte-derived macrophages, indicating that TNF-α play an important role in the pathogenesis of RA.</FONT>

Key words Tumor necrosis factor Monocytes Arthritis rheumatoid Matrix metalloproteinase-9

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