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论著

美洛昔康对骨形态发生蛋白9诱导间充质干细胞骨向分化的抑制作用

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摘要 目的 探讨美洛昔康对骨形态发生蛋白9(BMP 9)诱导间充质干细胞成骨分化的影响。方法 用BMP 9编码序列的重组腺病毒感染C3H10T1/2细胞，并同时加入美洛昔康5，10和20 μmol·L^{-1}对BMP9的作用进行干预。采用化学发光法检测第5天、第7天和第9天的碱性磷酸酶(ALP)活性，RT-PCR方法分别于第9天和第11天检测骨钙蛋白mRNA表达以及第1天、第3天和第5天Dlx-5 mRNA表达，于第14天和第20天采用茜素红S染色法检测钙盐沉积。另用荧光素酶报告质粒检测BMPR-Smad信号的转录活性。结果 与正常C3H10T1/2细胞组相比，第5~第9天BMP9组ALP活性明显增加(P<0.01)，但加入美洛昔康5，10和20 μmol·L^{-1}后，ALP活性随美洛昔康浓度增加而明显降低(P<0.05)。与正常C3H10T1/2细胞组相比，BMP9组骨钙蛋白素和Dlx-5 的mRNA表达水平及钙盐沉积明显增加，美洛昔康则明显抑制BMP9诱导的骨钙蛋白素和Dlx-5 mRNA的表达及钙盐沉积(P<0.05)。BMP9促进C3H10T1/2细胞中BMPR-Smad报告质粒的荧光素酶活性增加(P<0.01)，美洛昔康能够抑制BMP9对BMP-Smad信号的活化作用(P<0.05)。结论 美洛昔康对BMP9诱导的间充质干细胞成骨化有明显的抑制作用，其机制可能与抑制BMP-Smad信号激活有关。

关键词 美洛昔康 骨形态发生蛋白9 间充质干细胞 成骨分化 Smad信号转导

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Inhibitory effect of meloxicam on osteogenic differentiation in mesenchymal stem cells induced by bone morphogenetic protein 9

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Abstract

OBJECTIVE To investigate the effect of meloxicam on bone morphogenetic protein 9 (BMP9) induced osteogenic differentiation in mesenchymal stem cells. **METHODS** The infected C3H10T1/2 cells with BMP9 recombinant adenovirus were interfered with meloxicam 5, 10 and 20 μmol·L^{-1}. The alkaline phosphatase activity (ALP) on day 5, day 7 and day 9 after treatment was determined. The mRNA expression of osteocalcin (OCN) was detected on day 9 and day 11 by RT-PCR, and so did the Dlx-5 mRNA on day l, day 3 and day 5. The matrix mineralization with alizarin red S staining on day 14 and day 20 was assayed. The transcriptional activity of BMP-Smad signaling with Smad binding site luciferase reporter was measured. **RESULTS** ALP in BMP9 group was much higher than in normal control group (P<0.01) on day 5, day 7 and day 9, but the ALP activities were reduced when treated with BMP9 combined with meloxicam (P<0.05). Compared with normal control group, the mRNA expression of osteocalcin and Dlx-5 apparently increased in BMP9 group. However, the function of BMP9 was attenuated by combination with meloxicam (P<0.05). Compared with normal control group, the matrix mineralization in BMP9 group was increased, but decreased when BMP9 combined with meloxicam. Compared with normal control group, BMP9 promoted the firefly luciferase activities of BMPR-Smad reporter plasmids in C3H10T1/2 cells (P<0.01), but decreased when BMP9 and meloxicam were combined (P<0.05). **CONCLUSION** Meloxicam can inhibit osteogenic differentiation induced by BMP9 in mesenchymal stem cells, which may be mediated by inhibiting the BMP-Smad signaling activation.

Key words meloxicam bone morphogenetic protein 9 mesenchymal stem cell osteogenic differentiation Smad signal transduction

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