609~614.抑制CXCR4活性对乳腺癌骨转移影响的体内外研究[J].肖丹,刘寿贵,刘磊,郭善禹.中国肿瘤生物治疗杂志,2012,19(6)

抑制CXCR4活性对乳腺癌骨转移影响的体内外研究

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基金项目：上海市教育委员会科研基金资助项目（No. 09yz79）

DOI：10.3872/j.issn.1007-385X.2012.6.008

摘要：

目的：应用特异性抑制剂AMD3100抑制人乳腺癌骨高转移MDA-MB-231SA-rfp细胞中CXCR4的活性，探讨CXCR4在乳腺癌骨转移的机制。方法：CCK8法和Transwell法检测AMD3100对MDA-MB-231SA-rfp细胞体外增殖和迁移能力的影响。构建MDA-MB-231SA-rfp细胞裸鼠骨转移模型，同质量浓度的AMD3100处理后，X线影像观察骨转移情况，进一步利用MicroPET进行半定量分析，并应用H-E染色检测骨转移灶的骨质破坏程度，Western blotting检测AMD3100对MDA-MB-231SA-rfp细胞和移植瘤转移灶组织中CXCR4蛋白表达的影响。结果：AMD3100能明显抑制MDA-MB-231SA-rfp细胞的增殖和迁移（P<0.05），较高质量浓度（2 000 ng/ml）的AMD3100效果更明显（P<0.01）。成功构建MDA-MB-231SA-rfp细胞裸鼠骨转移模型，不同浓度AMD3100处理后，小鼠下肢骨骨质破坏程度降低；MicroPET分析发现，对照组、低剂量AMD3100组、高剂量AMD3100组SUV分别为9.44±0.25、 2.18± 0.47（P<0.01）；组织病理检测证实为乳腺癌骨转移灶。Western blotting结果显示，AMD3100作用前后骨转移灶标本中CXCR4蛋白表达无明显变化。结论：AMD3100降低CXCR4的活性能抑制乳腺癌MDA-MB-231SA-rfp细胞体外增殖和迁移，减少骨转移灶的形成。

关键词：CXC趋化因子受体4 AMD3100 乳腺癌 骨转移 MicroPET

In vivo and in vitro studies of blocking CXC chemokine receptor-4 on bone metastasis of breast cancer

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Fund Project:Project supported by the Research Foundation from Shanghai Education Committee (No. 09yz79)

Abstract:

Objective:To investigate the effect and mechanism of CXC chemokine receptor-4 (CXCR4) in the proliferation and migration of breast cancer MDA-MB-231SA-rfp cells in vitro and in vivo by a specific small CXCR4 inhibitor, AMD3100. Methods:MDA-MB-231SA-rfp cells were treated with AMD3100, and the proliferation and migration were detected by CCK-8 and Transwell assay. MDA-MB-231SA-rfp cells were inoculated into nude mice to establish a model of breast cancer bone etastasis xenograft. AMD3100 at different concentrations was delivered to mice. X-ray was taken to observe breast cancer bone metastasis and MicroPET was used to perform semi-quantitative analysis of breast cancer bone metastasis. H-E staining was used to further determine the location of breast cancer bone metastasis. Western blotting was performed to determine CXCR4 protein expression in MDA-MB-231SA-rfp cells as well as in xenograft tissues before and after AMD3100 administration. Results: The cell proliferation and migration of MDA-MB-231SA-rfp cells line induced by SDF-1α were significantly inhibited by AMD3100 (P<0.05) and 2 000 ng/ml AMD3100 showed much more significant inhibition of the cell proliferation (P<0.01). The model of breast cancer bone metastasis xenograft was successfully established. Bone erosion of the lower limbs was decreased after AMD3100 treatment of different concentrations . MicroPET images demonstrated that SUV of the control group, low concentration AMD3100 group and high concentration AMD3100 group were respectively 9.44±0.53, 2.18±0.47 (P<0.01). H-E staining detection confirmed the bone metastasis of breast cancer. No significant difference was found in CXCR4 expression in MDA-MB-231SA-rfp cells and bone metastasis tissues before and after AMD3100 administration. Conclusion: Blocking CXCR4 activity by AMD3100 can inhibit the proliferation and migration capacity of breast cancer MDA-MB-231SA-rfp cells and bone metastasis in xenograft in vivo in nude mice.

Keywords:CXC chemokine receptor 4 AMD3100 breast cancer bone metastasis MicroPET

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