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17β-雌二醇通过上调CXCR4表达促进骨髓间充质干细胞的趋化迁

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Title: 17β-estradiol promotes chemotaxis migration of bone mesenchymal stem cells by up-regulating CXCR4

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关键词: 雌激素; 骨髓间充质干细胞; SDF-1/CXCR4; 迁移

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摘要: 目的 研究17β-雌二醇（17β-estradiol,17β-E2）对体外骨髓间充质干细胞(bone mesenchymal stem cells, BMSCs) 趋化因子受体CXCR4表达的影响及CXCR4表达变化对BMSCs趋化迁移的调控情况。 方法 全骨髓法+贴壁法分离、培养BMSCs，不同浓度（10^{-10}、10^{-9}、10^{-8}、10^{-7}、5×10^{-7}、10^{-6}mol/L）的17β-雌二醇诱导经雌激素受体拮抗剂ICI 182780处理和未经处理的BMSCs后于不同时相点（24、48 h），用RT-PCR法和Western blot法分别检测细胞趋化因子受体CXCR4的表达情况，利用Transwell小室体外迁移体系观察10^{-7} mol/L 17β-雌二醇诱导前后的BMSCs对于不同浓度基质细胞衍生因子SDF-1的定向迁移情况，及采用AMD3100阻断SDF-1特异性受体CXCR4后对雌激素诱导前后BMSCs定向迁移的影响。 结果 BMSCs在不同浓度17β-雌二醇诱导24、48 h后，其CXCR4 mRNA的表达均有不同程度的升高，其中以24 h时10^{-7} mol/L组升高最为明显（$P<0.05$）。CXCR4蛋白表达在24 h各浓度组以升高为主，24 h时5×10^{-7} mol/L 组升高最为明显，48 h各浓度组以降低为主。雌激素受体拮抗剂ICI 182780能够明显抑制17β-雌二醇对CXCR4表达的影响（$P<0.05$）。BMSCs对SDF-1的定向迁移有明显的浓度依赖性，且相同条件下17β-雌二醇诱导后的BMSCs迁移细胞数显著高于未经诱导的BMSCs，而CXCR4阻断剂AMD3100可明显抑制17β-雌二醇干预前后BMSCs的趋化迁移（$P<0.05$）。 结论 17β-雌二醇在一定的诱导时间内可提高BMSCs CXCR4的表达，进而增强SDF-1对BMSCs的体外趋化作用。

Abstract: Objective To determine the effect of 17β-estradiol on the expression of CXC chemokine receptor 4 (CXCR4) and its expression on regulating directional migration in bone mesenchymal stem cells (BMSCs) *in vitro*. Methods Rat BMSCs were isolated and cultured by using whole bone marrow adherence method. After the BMSCs were treated in presence or absence of estrogen receptor antagonist ICI 182780, the cells were induced with various concentrations of 17β-estradiol (10^{-10}, 10^{-9}, 10^{-8}, 10^{-7}, 5×10^{-7}, 10^{-6}mol/L) for 24 or 48 h. Real-time PCR and Western blotting were used to detect the expression of CXCR4 at mRNA and protein levels in 17β-estradiol-treated and untreated BMSCs. Transwell chamber test was used to observe the migration of BMSCs before and after being treated with 10^{-7} mol/L of 17β-estradiol, which induced by different concentrations of stromal-derived factor-1 (SDF-1). Then the effect of CXCR4 antagonist AMD3100 on the directional migration of 17β-estradiol-treated and untreated BMSCs was investigated. Results Treated with various concentration of 17β-estradiol for 24 and 48 h,

the mRNA expression of CXCR4 was increased, and the peak amount appeared when the concentration was 10^{-7} mol/L for 24 hours' treatment (P<0.05). The CXCR4 protein was increased in the cells induced by 17β-estradiol for 24 h, in which the peak was with the concentration of 5×10^{-7} mol/L. But in the BMSCs treated by 17β-estradiol for 48 h, CXCR4 protein expression was reduced in most concentrations. The estrogen receptor antagonist ICI 182780 inhibited the effect of 17β-estradiol on the expression of CXCR4 (P<0.05). The BMSCs migration induced by SDF-1 depended on the concentration of SDF-1, and in the same conditions, the amount of migrated cells was significantly larger in the 17β-estradiol-treated cells than the cells untreated. The CXCR4 blocker AMD3100 inhibited the directional migration of BMSCs before and after 17β-estradiol inducement (P<0.05). Conclusion 17β-estradiol promotes the expression levels of CXCR4 in BMSCs within a certain time period, and enhances the directional migration of BMSCs induced by SDF-1.

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