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骨唾液酸蛋白对乳腺癌 MDA-MB-231 细胞 PI3K-AKT 信号通路的影响 点此下载全文

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摘要：

目的：探讨骨唾液酸蛋白（bone sialoprotein，BSP）对乳腺癌 MDA-MB-231细胞 PI3K-AKT信号通路的影响。方法：BSP基因沉默的乳腺癌 MDA-MB-231细胞(简称231BO-BSP27)经重组人 BSP（recombinant human BSP，rhBSP）和PI3K-AKT抑制剂 LY294002处理后，Western blotting检测磷酸化AKT水平的变化，实时定量 PCR检测 caspase-3、cyclin D1 mRNA 表达水平，MTT法检测细胞增殖能力。结果：与BSP基因未沉默的对照组231BO-Scrambled细胞相比，BSP基因沉默的231BO-BSP27细胞BSP蛋白表达明显下调（74.32±2.18）%（P<0.01）；AKT磷酸化水平明显下降（33.30±2.61）%（P<0 01），而caspase-3和cyclin D1 mRNA表达分别上升和下降（1.000±0.000 vs 1.733±0.039，1.000±0.000 vs 0.370±0.012；均P<0.01）；231BO-BSP27细胞增殖能力显著下降（P<0. 05）。外源添加rhBSP蛋白分别上调 231BO-Scrambled和 231BO-BSP27细胞 AKT磷酸化水平（17.86±2.27）%和（33.78±1.5 1）%（均P<0.01），231BO-BSP27细胞 caspase-3 mRNA表达降低（1.000±0. 039 vs 0.541±0.091，P<0.01)、cyclin D1 mRNA表达升高（1.000± 0.000 vs 2. 921±0.032，P<0.01），促进 231BO-Scrambled和 231BO-BSP27细胞的增殖（均P<0.01）。LY294002则能逆转rhBSP对231BO-Scrambled和 231BO-BSP27细胞AKT磷酸化激活作用（P<0.05），使 231BO-BSP27细胞caspase-3 mRNA表达升高（P<0.01）、cyclin D1 mRNA表达降低（P<0.01），使该两种细胞增殖能力下降（均P<0.01）。结论：BSP通过 PI3K-AKT信号通路调控乳腺癌 MDA-MB-231细胞 caspase-3和 cyclin D1的表达，并影响细胞的增殖。

关键词：骨唾液酸蛋白 乳腺癌细胞 LY294002 PI3K-AKT信号通路

Effect of bone sialoprotien on PI3K-AKT signaling pathway of breast cancer MDA-MB-231 cells Download Fulltext

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Abstract:

Objective:To investigate the effect of bone sialoprotein (BSP) on the PI3K-AKT signaling pathway in breast cancer MDA-MB-231 cells. Methods: BSP-silenced MDA-MB-231 cells were treated with recombinant human BSP (rhBSP) and the PI3K-AKT specific inhibitor LY294002. Western blotting analysis was used to detect the phosphorylation of AKT, qPCR was conducted to evaluate caspase-3, cyclin D1 mRNA expressions, and the proliferation of cells was analyzed by MTT assay. Results: Compared with the 231BO-Scrambled cells in control group, BSP protein expression in BSP-silenced 231BO-BSP27 cells was significantly lower (74.32±2.18)% (P<0.01), and expression level of AKT phosphorylation was also significantly lower (33.30±2.61) % (P<0.01), resulting in up-regulation of caspase-3 mRNA level (1.000±0.000 vs 1.733±0.039, P<0.01) , down-regulation of cyclin D1 mRNA (1.000±0.000 vs 0 370±0.012, P<0. 01),and the inhibition of 231BO-BSP27 cells growth (P<0.05). After treatment with exogenous rhBSP, the phosphorylation of AKT was increased in both 231BO-Scrambled and 231BO-BSP27 cells \[(17.86±2.27)%, (33.78±1.51)%, P<0.01\]. rhBSP treatment decreased caspase-3 mRNA (1.000±0.039 vs 0.541±0.091, P<0.01) , and increased cyclin D1 mRNA (1.000±0.000 vs 2.921±0.032, P<0.01) expression in 231BO-BSP27 cells, and stimulated the proliferation of 231BO-Scrambled and 231BO-BSP27 cells (P<0.01). Furthermore, rhBSP-induced activation of AKT was reversed by LY294002 in 231BO-Scrambled and 231BO-BSP27 cells (P<0.05), with an increase in caspase-3 mRNA and decrease in cyclin D1 mRNA expression in 231BO-BSP27 cells (all P<0.01), causing proliferation inhibition in 231BO-Scrambled and 231BO-BSP27 cells (P<0.01). Conclusion: BSP can regulate the mRNA expressions of caspase-3 and cyclin D1, and affect the proliferation of breast cancer MDA-MB-231 cells through the PI3K-AKT signaling pathway.

Keywords:bone sialoprotein breast cancer cell LY294002 PI3K-AKT signaling pathway

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