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雌激素激活GPER-EGFR-ERK通路促进人乳腺癌SKB

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Title: Estrogen activates GPER-EGFR-ERK pathway to promote the proliferation of human breast cancer cell line SKBR-3

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关键词: 雌激素; GPER ; SKBR-3; 增殖

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摘要: 目的 探讨G蛋白偶联雌激素受体（G protein-coupled estrogen receptor,GPER）介导雌激素对人乳癌细胞系SKBR-3增殖的影响。 方法 激光共聚焦显微镜扫描检测钙离子探针标记的细胞内钙离子浓度随时间的变化，CCK-8法观测细胞的增殖生长，流式细胞术检测细胞周期，Western blot 检测磷酸化细胞外信号调节激酶（phospho-extracellular regulate kinase，p-ERK）的相对表达量。 结果 17-β雌二醇（E_2）与GPER激动剂（G1）（E_2、G1处理组）刺激SKBR-3细胞后，细胞内钙离子浓度从120 s开始迅速升高，细胞增殖与对照组相比显著增加，CCK-8测定的（E_2、G1处理组）相对细胞数分别是对照组的（2.08±0.07）倍和（2.00±0.04）倍；流式细胞术检测E_2、G1处理组细胞增殖指数（PI）（E_2、G1处理组）为（43.12±0.38）%、（42.43±0.52）%，较对照组（29.19±0.29）%明显增加（P<0.05）；Western blot 检测结果显示E_2处理组p-ERK表达量显著高于对照组（P<0.05）。GPER特异性抑制剂G15、EGFR拮抗剂AG1478、ERK拮抗剂U0126均可抑制E_2、G1触发的相应变化，PI3K拮抗剂WM则不能。 结论 雌激素激活GPER-EGFR-ERK通路促进人乳腺癌SKBR-3细胞系增殖。

Abstract: Objective To explore the effect of estrogen on the proliferation of human breast cancer cell line SKBR-3 mediated by G protein-coupled estrogen receptor (GPER). Methods Calcium influx, cell growth ability and cell cycle were

examined by confocal laser scanning microscopy, CCK-8 assay and flow cytometry in the presence of different concentrations of drugs, respectively. The relative expression level of phospho-extracellular signal-regulated kinase (p-ERK) was detected by Western blotting. Results After the cells were treated with 17-β estradiol (E_2) or GFER specific agonist (G1), intracellular calcium ion concentration shifted quickly from 120 seconds, and cell proliferation increased significantly with the relative cell numbers (2.08±0.07) times and (2.0±0.04) times more than those of the control group. The proliferation index (PI) (43.12±0.38)% and (42.43±0.52)% at S phase and G2-M phase increased significantly as compared to the control group (29.19±0.29)% (P<0.05). The protein level of p-ERK was higher in the treatment group than in the control group (P<0.05). GFPE antagonist G15, EGFR antagonist AG1478 and ERK antagonist U0126 rather than PI3K antagonist wortmannin could inhibit the changes induced by E_2 or G1. Conclusion Estrogen activates GPER-EGFR-ERK pathway to promote the proliferation of human breast cancer cell line SKBR-3.

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