[1]余腾骅,王智亮,赵晨晖,等.雌激素激活GPR30/ERK通路促进三阴性乳腺癌MDA-MB-468细胞迁移及侵袭[J].第三军医大学学报,2014,36(20):2077-2082.

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雌激素激活GPR30/ERK通路促进三阴性乳腺癌MDA及侵袭

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Title: Estrogen enhances migration and invasion in triple-negative breast cancer MDA-MB-468 cells *via* activating GPR30/ERK signaling pathway

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关键词：雌激素；GPR30/ERK通路；三阴性乳腺癌；细胞迁移及侵袭

Keywords: estrogen; GPR30/ERK pathway; triple-negative breast cancer; cell migration and invasion

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摘要：

目的　探讨雌激素/GPR30/ERK信号通路的激活对三阴性乳腺癌（triple-negative breast cancer，TNBC）MDA-MB-468细胞迁移及侵袭的影响。　方法　免疫荧光及Western blot检测MDA-MB-468细胞中雌激素受体GPR30的蛋白表达量及细胞内定位，Western blot检测药物处理后细胞中磷酸化细胞外信号调节激酶（phospho-extracellular regulate kinase，p-ERK）的蛋白表达变化，细胞划痕实验及Transwell小室实验分别检测细胞的迁移及侵袭能力的改变。　结果　雌激素受体GPR30在TNBC细胞系MDA-MB-468中高表达，且主要位于细胞胞浆部位。17-β雌二醇（E2）和GPR30特异性激动剂（G1）可以显著活化细胞中GPR30/ERK信号通路（$P<0.05$），上调p-ERK蛋白水平，其相对表达量分别是空白对照组的（2.07±0.11）倍和（1.98±0.06）

倍。E2及G1药物处理后的细胞迁移能力得到显著提高（P<0.05），24 h后迁移入划痕区域的相对细胞数分别为空白对照组的（2.10±0.20）倍和（2.14±0.34）倍。细胞侵袭实验也可得到类似结果。GPR30特异性拮抗剂（G15）以及ERK特异性抑制剂（U0126）均可显著抑制E2和G1引发的以上改变（P<0.05）。　结论　雌激素通过活化TNBC细胞MDA-MB-468中GPR30/ERK信号通路，促进细胞迁移及侵袭的恶性潜能。靶向雌激素/GPR30/ERK通路可能成为TNBC的有效治疗手段。

Abstract: Objective To explore the effects of activated estrogen/GPR30/ERK signaling on the migration and invasion of triple-negative breast cancer (TNBC) cell line MDA-MB-468. Methods Immunofluorescent assay and Western blotting were used to test the expression and localization of estrogen receptor GPR30 in MDA-MB-468 cells. The expression level of phospho-extracellular regulate kinase (p-ERK) was detected by Western blotting. The changes of cell migration and invasion ability were examined by wound-healing assay and Transwell assay, respectively. Results Estrogen receptor GPR30 was detected with high expression level in MDA-MB-468 cells and was mostly expressed in the cytoplasm. After treating with 17-β estradiol (E2) and GPR30 specific agonist (G1), the GPR30/ERK signaling was remarkably activated. The relative protein expressions of p-ERK in the E2 and G1 treatment groups were (2.07±0.11) and (1.98±0.06) times higher than those of the control group (P<0.05), respectively. Moreover, E2 and G1 significantly increased the ability of cell migration. The relative migrated cell numbers in the E2 and G1 treatment groups were 2.10±0.20 and 2.14±0.34 times higher than those of the control group (P<0.05), respectively. Transwell assays indicated the similar results as wound-healing assays. Interestingly, these changes induced by E2 and G1 could be significantly blocked by GPR30 specific antagonist (G15) and ERK specific inhibitor (U0126) (P<0.05). Conclusion Estrogen increases the ability of cell migration and invasion through activating GPR30/ERK signaling in TNBC cells. Inhibition of estrogen/GPR30/ERK signaling represents a novel targeted therapy in TNBC.

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