[1]李振华,涂刚,李维东,等.MCF-7细胞他莫昔芬耐药过程中F-actin细胞骨架的重构促进细胞迁移[J].第三军医大学学报,2013,35(14):1475-1479.

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MCF-7细胞他莫昔芬耐药过程中F-actin细胞骨架的重构促进细胞迁移(PDF)

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Title: Rearrangement of filament actin cytoskeleton promotes cell migration in MCF-7 cells during tamoxifen-induced resistance

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摘要: 目的 研究人乳腺癌细胞MCF-7获得他莫昔芬(tamoxifen，TAM)耐药过程中发生的肌动蛋白细胞骨架重构及其对细胞迁移能力的影响，并探讨相关分子机制。 方法 采用高浓度短时间4-羟基他莫昔芬(4-hydroxytamoxifen，OHT)冲击法诱导人乳腺癌MCF-7/TAM耐药细胞株（Tam-R）。运用FITC标记的鬼笔环肽染色观察纤维状肌动蛋白（F-actin）动态变化，免疫荧光分析E-钙粘蛋白在野生型MCF-7细胞（MCF-7W）及Tam-R细胞中的表达及分布，pull-down和Western blot检测小GTP酶Rac1活性，Transwell细胞迁移实验评估F-actin骨架重构对Tam-R细胞迁移能力的影响。 结果 MCF-7W细胞中F-actin富集于毗邻细胞膜周边，呈典型鹅卵石形态，E-钙粘蛋白分布与F-actin相似，可在毗邻细胞膜周边形成完整的黏附连接；而Tam-R细胞中F-actin纤维出

现板状伪足和应力纤维两种异常形态，细胞外围不能通过E-cadherin与周围细胞形成完整的黏附连接。在Tam-R细胞中，PI3K抑制剂Wortmannin（WM）可抑制OHT引起的F-actin骨架重构、Rac1的活化和细胞迁移(P<0.05)，而ERK1/2抑制剂U0126对OHT引起的F-actin骨架重构无明显影响。　　结论　　OHT可能激活PI3K，促进Rac1活化，通过诱导F-actin骨架重构促进Tam-R细胞迁移。

Abstract:　Objective　To investigate the rearrangement of filament actin（F-actin） cytoskeleton during the development of tamoxifen resistance in human breast cancer MCF-7 cells.　Methods　MCF-7 tamoxifen-resistant (Tam-R) cells were derived from wild-type MCF-7 (MCF-7W) cells by exposure to a high concentration of 4-hydroxytamoxifen (OHT) for a short period. The dynamic change of F-actin was visualized by FITC-Phalloidin staining. Immunofluorescence staining was used to evaluate the expression and distribution of E-cadherin in MCF-7W and Tam-R cells. Pull-down assay and Western blot analysis were utilized to analyze the activity of small GTPases Rac1. Transwell assay was used to evaluate the effects of F-actin cytoskeleton rearrangement on migratory ability of Tam-R cells.　Results　In MCF-7W cells, F-actin concentrated along the cell membrane like pebbles, and E-cadherin, distributed like F-actin, formed strong intercellular adhesion junction. In contrast, abnormal lamellipodia, stress fiber and reduced E-cadherin-mediated cell-cell adhesion were observed in Tam-R cells. Additionally, the PI3K inhibitor Wortmannin (WM) attenuated the activity of Rac1, rearrangement of actin cytoskeleton and cell migration（P<0.05） induced by tamoxifen in Tam-R cells. The inhibitor of ERK, U0126, had few effects on the actin cytoskeleton rearrangement induced by OHT.　Conclusion　OHT probably activates PI3K and promotes Rac1 activation, and to promote the migration in Tam-R cells by inducing the rearrangement of actin cytoskeleton.

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