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MEK/ERK对HT-29结肠癌细胞分化、侵袭迁移及NDRG1基因表达的影响

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Effect of MEK/ERK on Differentiation，Invasion/Migration and NDRG1 Gene Expression of Colon Cancer Cell Line HT-29

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摘要 目的

探讨MEK/ERK在结肠癌细胞NDRG1基因表达调控和体外侵袭、迁移中的作用；分析ERK通路、NDRG1基因、肿瘤侵袭及迁移三者间的潜在联系。方法将MEK/ERK抑制剂与HT-29结肠癌细胞共培养，光学显微镜下观察细胞形态变化；透射电子显微镜观察细胞超微结构变化；24孔-小室法检测癌细胞体外侵袭、迁移能力的改变；免疫细胞化学染色、Western blot检测NDRG1基因表达情况。结果与抑制剂共培养后，HT-29结肠癌细胞及胞核形态、大小趋于一致，排列多呈腺样结构。细胞表面微绒毛、高尔基复合体、线粒体增多，粗面内质网丰富，胞质内微腺腔常见，同时可见凋亡细胞。与对照组相比，加抑制剂组在侵袭迁移实验中穿过微孔膜的细胞数减少，差异有统计学意义($P<0.05$)。免疫细胞化学结果显示，HT-29组与DMSO组NDRG1表达较少，加抑制剂组表达显著增多；Western blot结果显示，加抑制剂各组均出现NDRG1蛋白表达条带，而HT-29组与DMSO组则未见有NDRG1蛋白的表达。结论阻断ERK通路可诱导HT-29结肠癌细胞发生分化且促进细胞凋亡，同时可抑制其体外侵袭及迁移能力并明显上调其NDRG1蛋白的表达。

关键词： 肿瘤 HT-29 MAPK NDRG1 侵袭

Abstract： Objective

To characterize the mechanism of NDRG1-induced colon cancer aggressiveness including NDRG1-induced colon cancer cell migration and invasion.MethodsHT-29 human colorectal cell，was employed to detect cell migration and invasion using transwell assays.The role of ERK in NDRG1-mediated cell migration and invasion was also evaluated by employing the MEK/ERK inhibitor.Change of cell morphology was microscopically examined.Transmission electron microscope was also used to examine the effect of ERK inhibitor on HT-29 ultra structure change.Results Treatment with ERK inhibitor changed HT-29 cell morphology.The size，appearance of the cells and nuclei were inclined with uniformity；the arrangement of the cells was glandule-like texture.There were more microvilli on the cell surface and the numbers of Golgi complexes，mitochondria were increasing；there were also more rough endoplasmic reticula；intracytoplasmic lumen was frequently seen；cells treated with ERK inhitors also induced cell apoptosis.Comparing with control groups，cell migratory ability was significantly inhibited by the inhibitors.Using an immunocytochemical staining approach，we demonstrated that increased NDRG1 protein was elevated in cells treated with the inhibitors，than that in control cells.Western blot confirmed this observation.ConclusionOur data indicate that blocking the MAPK pathway induces differentiation and apoptosis of the HT-29 colorectal cancer cells.In addition，inhibition of MAPK pathway also suppresses cancer cell invasive/migratory abilities through up-regulation of NDRG1 protein.

Key words： Neoplasm HT-29 MAPK NDRG1 Invasion

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