PEDF下调 HIF-1α表达抑制缺氧状态下NSCLC细胞增殖、迁移的作用机制

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Title: The mechanism of PEDF down-regulating HIF-1α expression inhibiting proliferation and migration of NSCLC cells under hypoxia

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摘要: 目的：研究色素上皮衍生因子（PEDF）对缺氧状态下非小细胞肺癌（NSCLC）细胞增殖、迁移和缺氧诱导因子-1α（HIF-1α）表达的影响。方法：体外培养NSCLC细胞A549，氯化钴（CoCl2）100 μmol/L 模拟缺氧环境。实验分为4组：正常对照组（A组）、氯化钴干预组（B组）、氯化钴＋PEDF 50 ng/ml干预组（C 组）及氯化钴＋PEDF 200 ng/ml干预组（D组）。MTT检测各组细胞增殖能力，进行划痕实验，在光镜下观察实验组和对照组细胞的移行情况；进行Transwell小室侵袭实验，计算细胞穿透数；进行ELISA法检测各组细胞培养液上清中HIF-1α、血管内皮生长因子（VEGF）蛋白表达水平。结果：细胞增殖能力：B组较A组增加，C组较B组降低，D组较C组降低，各组间差异均具有统计学意义（P<0.05）；细胞迁移能力：B组较A组增加，C组较B组降低，D组较C组降低，各组间差异均具有统计学意义（P<0.05）；细胞穿透数：B组较A组增多，C组较B组减少，D组较C组减少，各组间差异均具有统计学意义（P<0.05）；HIF-1α和VEGF的表达水平：B组较A组升高，C组较B组下降，D组较C组下降，各组间差异均具有统计学意义（P<0.05）。结论：肺癌A549细胞在缺氧环境较常氧具有更强的增殖力和移行能力；可以分泌HIF-1α，HIF-1α对VEGF的表达有一定的促进作用。PEDF对缺氧状态下A549细胞高表达的VEGF具有一定抑制作用，且该抑制作用可能与PEDF调控HIF-1α有关。

Abstract: Objective：To study the effects of PEDF on the proliferation，migration and expression of HIF-1α in hypoxia NSCLC cells.Methods：In vitro culture of NSCLC cells A549，cobalt chloride(CoCl2) 100 μmol/L simulated hypoxia environment.The experiment was divided into 4 groups：Normal control group(group A)，cobalt chloride intervention group(group B)，cobalt chloride+PEDF 50 ng/ml intervention group(group C) and cobalt chloride + PEDF 200 ng/ml intervention group(group D).MTT detected cell proliferation ability in each group.Conduct scratch experiments and observe the movement of cells in each group under the microscope.The Transwell cell invasion experiment was carried out to calculate the cell penetration number.HIF-1α and VEGF protein expression levels in cell culture solution by ELISA were detected.Results：Cell proliferation ability，B group was higher than A group.C group was lower than B group.D group was lower than C group，and the difference between groups was statistically significant（P<0.05）.Cell migration ability,increased in group B compared with group A，decreased in group C compared with group B and decreased in group D compared with group C（P<0.05）.The number of cell penetration,increased in group B compared with group A，decreased in group C compared with group B,and decreased in group D compared with group C.There were significant differences among groups（P<0.05）.The expression levels of HIF-1α andVEGF were higher in group B than in group A，lower in group C than in group B，and lower in group D than in group C（P<0.05）.Conclusion：Lung cancer A549 cells have stronger growth and mobility than oxygen in hypoxia environments.Hypoxia can regulate the secretion of HIF-1α by A549 cells，and HIF-1α has a certain effect on

the expression of VEGF.PEDF has a certain inhibitory effect on the high expression of VEGF in A549 cells in hypoxia，and this inhibition may be related to the regulation of HIF-1α by PEDF.

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