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## 宫颈鳞癌中基质细胞衍生因子-1、CXC趋化因子受体4、基质金属蛋白酶-2和Ki-67的

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Title: Expression and Significance of Stromal Cell Derived Factor 1, Chemokine CXC Motif Receptor 4, Matrix Metalloproteinase 2 and Ki 67 in Cervical Squamous Cancer

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关键词: 宫颈肿瘤; 基质细胞衍生因子 1; CXC趋化因子受体4; 基质金属蛋白酶类; Ki 67; 免疫组织化学

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摘要: 目的 探讨基质细胞衍生因子(SDF) 1、CXC趋化因子受体(CXCR) 4、基质金属蛋白酶(MMP) 2和Ki 67在宫颈鳞癌中的表达,以及SDF 1对MMP 2和Ki 67表达的影响。方法 选取2010年1月至2012年9月在青岛大学医学院第二附属医院接受宫颈鳞癌手术(初治)的60例宫颈鳞癌患者的60例切除癌组织标本(术后经组织病理学检查证实均为颈鳞癌)纳入研究组,选取同期在该院因子宫肌瘤行子宫切除术的60例患者的正常宫颈组织标本60例纳入对照组。两组患者的年龄等一般临床资料比较,差异无统计学意义( $P > 0.05$ ) (本研究遵循的程序符合青岛大学医学院第二附属医院人体试验委员会制定的伦理学标准,得到该委员会批准,分组征得受试对象的知情同意,并与之签署临床研究知情同意书)。采用免疫组化SP法检测SDF 1、CXCR4、MMP 2和Ki 67在两组标本中的表达,并进行相关性分析。结果 SDF 1、CXCR4、MMP 2和Ki 67在研究组标本中阳性表达率分别为90.00%、63.33%、70.00%、86.67%,显著高于对照组的40.00%、8.33%、13.33%、1.67%,且差异均有统计意义( $\chi^2=9.63, 7.04, 4.00, 4.00; P < 0.05$ );在研究组中,SDF 1、CXCR4、MMP 2和Ki 67的表达水平在淋巴结转移呈阳性标本中的表达均显著高于淋巴结转移呈阴性者( $\chi^2=16.692, P < 0.001; \chi^2=8.496, P < 0.01; \chi^2=4.762, P < 0.001; \chi^2=6.125, P < 0.05$ );SDF 1的表达水平与CXCR4、MMP 2和Ki 67的表达水平呈正相关( $r=0.586, P=0.002; r=0.419, P=0.025; r=0.645, P < 0.001$ )。结论 SDF 1、CXCR4、MMP 2和Ki 67的表达水平与宫颈鳞癌的发生、侵袭及淋巴结转移密切相关,或许可作为预测宫颈鳞癌淋巴结转移及预后的指标。SDF 1/CXCR4轴可通过加强肿瘤细胞MMP 2和Ki 67分泌的途径促进肿瘤的浸润和转移,提示SDF 1是药物治疗该病的重要靶点。

Abstract: Objective To study the expression of stromal cell derived factor (SDF) 1, chemokine CXC motif receptor(CXCR) 4, matrix metalloproteinase (MMP) 2 and Ki 67 and their association with clinical pathological features in human cervical squamous cancer tissues. Methods From January 2010 to September 2012, a total of 60 cases samples with squamous carcinoma of the cervix which were confirmed by histopathology were enrolled into this study (study group). At the same time, another 60 cases samples with benign uterine diseases were included into control group. There had no significant differences among age and other clinical information between two groups ( $P > 0.05$ ). The expression of SDF 1, CXCR4, MMP 2 and Ki 67 were detected between two groups by immunohistochemistry and the correlation analysis was conducted. The study protocol was approved by the Ethical Review Board of Investigation in Second Affiliated Hospital, Medical School of Qingdao University. Informed consent was obtained from all participates. Results The positive expression rates of SDF 1, CXCR4, MMP 2 and Ki 67 were 90.00%, 63.33%, 70.00% and 86.67% in study group, 40.00%, 8.33%, 13.33% and 1.67% in control group, respectively. Significant differences were observed between two groups ( $\chi^2=9.63, 7.04, 4.00, 4.00; P < 0.05$ ). Expressions of SDF 1, CXCR4, MM 2 and Ki 67 in cervical cancer tissues with pelvic lymph nodes metastasis were higher than those in cervical cancer tissues without pelvic lymph node metastasis, which were closely associated with pelvic lymph node metastasis ( $\chi^2=16.692, P < 0.001; \chi^2=8.496, P < 0.01; \chi^2=4.762, P < 0.001; \chi^2=6.125, P < 0.05$ ). The expression of SDF 1 was significantly correlated with CXCR4, MMP 2 and Ki67 ( $r=0.586, P=0.002; r=0.419, P=0.025; r=0.645, P < 0.001$ ). Conclusions Expressions of SDF 1, CXCR4, MMP 2 and Ki 67 of cervical squamous cancer tissues are involved in tumor genesis and associated with invasion and lymphnode metastasis of cervical cancer, which can serve as biomarkers for diagnosis and prediction of lymph node metastasis. Furthermore, the expression of SDF 1/CXCR4 in cervical cancer may promote the tumor invasion and metastasis through the secretion of MMP 2 and Ki 67, suggesting that SDF1 may be an important target for drug therapy.

### 参考文献/REFERENCES

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