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论著

ST14/MT-SP1影响MT2-MMP和TIMP-2的表达而增强结直肠癌细胞的侵袭力

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摘要 目的： 膜型丝氨酸蛋白酶（ST14 / MT-SP1）和它的同源物在细胞迁移和肿瘤转移中起重要作用。本研究目的是评估ST14/MT-SP1过度表达如何影响结直肠癌细胞的侵袭能力。
方法: 全长人ST14/MT-SP1基因被瞬时转染到结直肠癌细胞系RKO。表达产物由Ni2+-亲和层析柱纯化并通过明胶酶谱法分析蛋白的明胶酶活性。用ECM体外侵润试验确定细胞的体外侵袭力。用cDNA微阵列法测定ST14/MT-SP1转染细胞中MMPs和TIMPs表达变化情况。用实时定量PCR 来验证这些基因表达的变化。
结果: 人全长ST14/MT-SP1基因被转染到结直肠癌细胞系RKO后，纯化表达的蛋白具有明胶酶的活力。RKO细胞过度表达ST14/MT-SP1 后其体外侵润转移能力显著增强(P<0.01),而ST14/MT-SP1蛋白被阻断后使SW480和SW620细胞的侵袭能力降低(P<0.01)。进一步发现，ST14/MT-SP1 过度表达使RKO 细胞的MT2-MMP(MMP-15)表达显著上调（约2.5倍） 和TIMP2表达下调（约0.35倍）。
结论: ST14/MT-SP1 过度表达导致了结直肠癌细胞侵袭力增强，这种能力的增强是由于ST14/MT-SP1自身具有明胶酶的活性和ST14/MT-SP1 能上调 MT2-MMP与下调TIMP-2的表达。因此,ST14/MT-SP1过度表达可能增强结直肠癌细胞的侵袭能力。

关键词 ST14/MT-SP1 丝氨酸内肽酶类 基质金属蛋白酶15 金属蛋白酶2组织抑制剂 结直肠肿瘤 肿瘤转移

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ST14/MT-SP1 influences expression of MT2-MMP and TIMP-2 to promote invasiveness of colorectal cancer cells

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Abstract

<FONT face=Verdana>AIM: To evaluate how ST14/MT-SP1 overexpression alters invasiveness of colorectal cancer cells.
METHODS: Human full length ST14/MT-SP1 gene was transiently transfected into colorectal cancer (RKO) cell lines.The expression products were purified by chromatography on Ni2+-affinity resin column and analyzed for gelatinase activity by gelatin zymography.Cell invasion and migration were determined by ECM invasion assay in vitro.RNA was isolated from stable ST14-transfected RKO cells and a cDNA microarray was utilized to detect the change in expression of MMPs and TIMPs.Real-time quantitative PCR was used to validate the change of expression.
RESULTS: The full length ST14/MT-SP1 was transfected and expressed in RKO cells.The expressed protein showed a gelatinase activity.In addition,invasiveness of RKO was significantly enhanced by ST14/MT-SP1 overexpression (P<0.01).Blockage of ST14/MT-SP1 resulted in a decrease in the invasiveness of SW480 and SW620 (P<0.01).Furthermore,MT2-MMP (MMP-15) expression was significantly up-regulated (2.5-fold change) and TIMP2 down-regulated (0.35-fold change) by ST14/MT-SP1 overexpression in RKO.
CONCLUSION: ST14/MT-SP1 overexpression results in an increase in invasiveness of colorectal cancer RKO cells.Increased invasiveness is due to an increase in the gelatinase activity of ST14/MT-SP1 and a change in up-regulated MT2-MMP and down-regulated TIMP-2 expression.Therefore,ST14/MT-SP1 overexpression enhances invasiveness of colorectal cancer cells.</FONT>

Key words ST14/MT-SP1 Serine endopeptidases Matrix metalloproteinase-15 Tissue-inhibitor of metalloproteinase-2 Colorectal neoplasms Neoplasm metastasis

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