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研究论文

SHIP-1对SR3Y1细胞的MMP2分泌和侵润能力的影响

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摘要

SHIP-1是一个含有SH2结构域的肌醇5磷酸酶，在造血过程中起负调节作用。为了调查SHIP-1对癌细胞的迁移能力和MMP2分泌是否有影响，我们制作了鼠SHIP-1的3种突变体△SH2-SHIP-1, △Ptase-SHIP-1, △Cter-SHIP-，并与其野生型全长cDNA一起分别插入到真核表达载体pcDNA3中，分别转染src转化的3Y1细胞系(SR3Y1)，Western blot筛选稳定转染并表达SHIP-1的克隆。对这些克隆的MMP2、MMP9和细胞侵润能力的测定结果显示，野生型全长SHIP-1转染3Y1和SR3Y1不影响其MMP2的分泌，但能诱导MMP9分泌。但其3种突变体SHIP-1转染却都能显著地抑制SR3Y1细胞的MMP2和MMP9分泌，并抑制其侵润能力。野生型全长SHIP-1也能抑制SR3Y1的侵润能力。研究结果肯定了SHIP-1对转化细胞的迁移和侵润是一个负调节因子，并且它的3个结构域都参与了这种负调节作用。

关键词 SHIP-1；转染；SR3Y1细胞；侵润；MMP2

分类号

Effect of SHIP-1 on MMP2 secretion and invasion of SR3Y1 cells

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Abstract

<P>SHIP-1 is an SH2 domain containing inositol-5-phosphatase that appears to be a negative regulator of hematopoiesis. To the potential effects of SHIP-1 on MMP2 secretion and migration of cancer cells, three murine SHIP-1 mutants were made: △SH2-SHIP-1, △Ptase-SHIP-1, △Cter-SHIP-1. These mutant forms were subcloned as well as the wild type (WT) of murine SHIP-1 cDNA were subcloned into pcDNA3 expression vector, then transfected into and overexpressed SHIP-1 and its mutants in a Src-transformed 3Y1 cell line (SR3Y1). The results showed that overexpression of wild type of SHIP-1 does not affect the MMP2 secretion in both SR3Y1 and 3Y1 cells, but can induce MMP9 secretion, while either WT SHIP-1, the SH2 domain, phosphatase domain, or C terminus deletion mutants could significantly block the MMP2 and MMP9 secretion in SR3Y1 cells and suppress cell invasion ability. The results confirmed SHIP-1 as a negative regulator for cell migration and invasion in transformed cells, and im-plied that it may function through each of its three domains.</P>

Key words SHIP-1 transfection SR3Y1 invasion MMP2

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