肿瘤防治研究
Cancer Research on Prevention and Treatment

三氧化二砷联合5-杂氮-2′-脱氧胞苷对U937细胞SHP-1、JAK3、TYK2基因表达的影响

张小坤1，罗建民2，孙 杰1

1. 054000河北邢台，河北医科大学附属邢台市人民医院血液科；2.河北医科大学第二医院血液科 血液病河北省重点实验室

Effects of 5-Aza-2′-deoxycytidine Combined with Arsenic Trioxide on SHP-1, JAK3, TYK2 Expression in U937 Cells

ZHANG Xiaokun1,Luo Jianmin2,Sun Jie1

1. Department of Hematology, Xingtai People's Hospital of Hebei Medical University, Xingtai 054000,China;2. Department of Hematology, The Second Hospital, Hebei Medical University

摘要 目的 探讨甲基化抑制剂5-杂氮-2′-脱氧胞苷（5-Aza-2′-deoxycytidine，5-aza-CdR）联合三氧化 二砷（As2O3）对白血病细胞株U937中JAK3、TYK2和造血细胞磷酸酶SHP-1表达水平的影响，并探讨它 们在白血病发病中的作用。方法 5-aza-CdR、As2O3单用及联合处理U937细胞，5-aza-CdR浓度为0.5、1、2 μmol/L，As2O3的浓度为1、2.5、5 μmol/L，As2O3 1μmol/L + 5-aza-CdR 0.5μmol/L、As2O32.5 μmol/L + 5-aza- CdR 1 μmol/L、As2O3 35 μmol/L + 5-aza-CdR 2 μmol/L 及不加药物组，分别处理24、48、72 h后提取细胞总 RNA，荧光实时定量PCR（Real-time Quantitative Polymerase Chain Reaction，RQ-PCR）检测JAK3、TYK2 及SHP-1的表达。结果 As2O3和5-aza-CdR单独作用及两药合用时，SHP-1 mRNA在U937细胞中的表达呈 剂量及时间依赖性，其表达逐渐升高；JAK3 mRNA的表达呈剂量及时间依赖性，其表达逐渐降低；TYK2 mRNA的表达呈剂量及时间依赖性，其表达逐渐降低；SHP-1与JAK3、TYK2负相关，JAK3所受影响较 TYK2更为显著。结论 （1）甲基化抑制剂5-aza-CdR和As2O3可使SHP-1表达升高，JAK3、TYK2表达降 低，与浓度及作用时间有关。（2）SHP-1基因的重新表达与其发生去甲基化有关，对JAK/STAT通路有负调 控作用。

关键词 ： 甲基化抑制剂， 5-杂氮-2′-脱氧胞苷， SHP-1， JAK3， TYK2

Abstract : Objective To investigate the influence of methylation inhibitor of arsenic trioxide (As2O3) combined with 5-Aza-2′-deoxycytidine (5-aza-CdR) on the expression of JAK3, TYK2 and hematopoietic cell phosphatase SHP-1 in chronic myeloid leukemia cell line U937, and to explore the effects of the combination in leukemia pathogenesis. Methods 5-aza-CdR, As2O3 and the combined treatment were applied on U937 cells. As2O3 1 μmol/L and 5-aza-CdR 0.5μmol/L group, As2O3 2.5 μmol/L and 5-aza-CdR 1 μmol/L group, As2O3 5 μmol/L and 5-aza-CdR 2 μmol/L group and no chemical substances group were treated for 24, 48, 72 h, respectively. Then total cellular RNA was extracted. Real-time Quantitative PCR was used to detect the expression of JAK3, TYK2 and SHP-1. Results With the application of As2O3, 5-aza-CdR and the combination, SHP-1 mRNA expression in U937 cells was increased gradually, while JAK3 and TYK2 mRNA expression were decreased, in a dose- and time-dependent manner. SHP-1 was negatively correlated with JAK3 or TYK2. JAK3 was affected more obviously than TYK2. Conclusion (1) With the application of methylation inhibitor of As2O3 and 5-aza-CdR, the expression of SHP-1 was increased, while the expressions of JAK3 and TYK2 were decreased in a dose- and time- dependentmanner.(2)The reexpression of SHP-1 gene is related to its methylation and has a negative regulation role of JAK/STAT pathway.

Key words : Methylation inhibitor;5-Aza-2′-deoxycytidine SHP-1;JAK3;TYK2

ZTFLH: R733.71 (../article/showArticleBySubjectScheme.do?code=R733.71)

作者简介: 张小坤（1982-），女，硕士，主治医师，主要从事细胞内信号转导与恶性血液病的诊断与治疗

张小坤，罗建民，孙 杰. 三氧化二砷联合5-杂氮-2′-脱氧胞苷对U937细胞SHP-1、JAK3、TYK2基因表达的影响[J]. 肿瘤防治研究, 10.3971/j.issn.1000-8578.2014.07.009.
ZHANG Xiaokun,Luo Jianmin,Sun Jie. Effects of 5-Aza-2′-deoxycytidine Combined with Arsenic Trioxide on SHP-1, JAK3, TYK2 Expression in U937 Cells. Cancer Research on Prevention and Treatment, 2014, 41(07): 728-733.

链接本文:

http://www.zlfzyj.com/CN/10.3971/j.issn.1000-8578.2014.07.009 (http://www.zlfzyj.com/CN/10.3971/j.issn.1000-8578.2014.07.009) **或**
http://www.zlfzyj.com/CN/Y2014/V41/I07/728 (http://www.zlfzyj.com/CN/Y2014/V41/I07/728)

地址：武汉市洪山区卓刀泉南路116号
电话：027-87670126
邮编：430079
Email：zlfzyjzz@vip.163.com

杂志官网

微信公众号：zlfzyjzz