Receptor tyrosine kinase AXL in induced by chemotherapy drugs and overexpresion of AXL confers drug resistance in acute myeloid leukemia.

賴基銘

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摘要

Abstract

By using a novel profiling analysis of protein tyrosine kinases differentially expressed in the sensitive and refractory leukemia from the same patients we found that AXL was upregulated in drug-resistant leukemia. Furthermore, AXL could be induced by chemotherapy drugs in the acute myeloid leukemia U937 cells and this induction was dependent on the CCWGG methylation status of the AXL promoter. In U937 cells ectopically overexpressing AXL, addition of exogenous Gas6 induced AXL phosphorylation and activation of the Akt and ERK1/2 survival pathways. The Gas6-AXL activation pathway of drug resistance was associated with increased expression of Bcl-2 and Twist. These results show that upregulation of AXL by chemotherapy might induce drug resistance in acute myeloid leukemia in the presence of Gas6 stimulation.

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