硼替佐米调控内质网应激诱导人急性T淋巴细胞白血病细胞株凋亡的机制探讨

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Title: The mechanism of Bortezomib on apoptosis of human T cell acute lymphoblastic leukemia by modulation of endoplasmic reticulum stress

作者: 沈 杰; 王瑞环; 苏国宏
沧州市中心医院血液内科，河北 沧州 061000

Author(s): Shen Jie; Wang Ruihuan; Su Guohong
Department of Hematology，Cangzhou Central Hospital，Hebei Cangzhou 061000，China.

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摘要: 目的：探讨硼替佐米对人急性T淋巴细胞白血病（T cell acute lymphoblastic leukemia，T-ALL）细胞株Molt-4细胞凋亡的影响。方法：硼替佐米（0、100、200和400 nmol/L）处理人急性T淋巴细胞白血病细胞株Molt-4细胞后，运用MTT法测定Molt-4细胞活力；使用Hoechst 33258染色法观察凋亡细胞形态；采用荧光定量PCR法测定Bax以及Bip mRNA水平；运用Western blot法测定Bax以及Bip蛋白水平。结果：100、200和400 nmol/L的硼替佐米处理Molt-4细胞24 h后，可浓度依赖性地降低细胞活力。100、200和400 nmol/L的硼替佐米作用细胞24 h后，Molt-4细胞核发生固缩或裂解。硼替佐米（100、200和400 nmol/L）处理细胞24 h后，Molt-4细胞的Bax mRNA和蛋白表达水平明显增加且可显著上调Bip mRNA和蛋白表达水平。结论：硼替佐米可诱导人急性T淋巴细胞白血病细胞株Molt-4细胞凋亡，作用机制可能与它调控内质网应激有关。

Abstract: Objective：To investigate the role of Bortezomib on cell apoptosis of human T cell acute lymphoblastic leukemia cell line Molt-4 cells.Methods：After adminstration of Molt-4 cells with different concentrations of Bortezomib（100，200 and 400 nmol/L） for 24 h，cell viability was detected using MTT assay.The morphological of apoptotic cells was observed under a fluorescence microscope using Hoechst 33258 staining.The expression levels of Bax as well as Bip mRNA were measured by quantitative real-time PCR.The expression levels of Bax as well as Bip protein were measured by Western blot.Results：Compared with the 0 nmol/L group，Bortezomib obviously decreased the viability of Molt-4 cells in a dose dependent way.Additionally，after treating with Bortezomib（100，200 and 400 nmol/L），the occurrence of apoptotic morphology and the expression levels of Bax mRNA as well as protein in Molt-4 cells were significantly elevated.The expression levels of Bip mRNA as well as protein in Molt-4 cells were obviously increased after treating by Bortezomib for 24 h.Conclusion：Bortezomib can induce cell apoptosis of human T cell acute lymphoblastic leukemia cell line Molt-4 cells，which may be associated with regulating endoplasmic reticulum stress.

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