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左旋门冬酰胺酶杀伤MOLT-4细胞的机制研究

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MOLT-4 Cell Apoptotic Mechanism Induced by L-asparaginase in Amino Acid Response

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全文: PDF (919 KB) HTML (1 KB) 输出: BibTeX | EndNote (RIS) 背景资料

摘要 以左旋冬酰胺酶诱导MOLT-4 T淋巴细胞白血病细胞发生氨基酸反应为模式，观察左旋门冬酰胺酶对MOLT-4细胞CHOP，ASNS，Bax以及Bcl2基因表达的影响，探讨可能存在的凋亡机制。方法：左旋门冬酰胺酶作用MOLT-4细胞，于不同时间点搜集细胞样品，并提取RNA，相对定量PCR法检测CHOP，ASNS，Bcl2，Bax mRNA相对表达水平；台盼蓝拒染法检测细胞存活率。结果：在左旋门冬酰胺酶用药后的8 h和18 h CHOP与ASNS mRNA出现两次表达高峰，18 h后CHOP mRNA水平维持在较高水平，ASNS mRNA开始逐渐下降，Bax/Bcl2的比值也于18 h后显著升高；细胞存活率于24 h后下降明显，细胞存活数在0～12 h缓慢增加，随后开始下降，24 h开始下降最为显著。结论：左旋门冬酰胺酶杀伤MOLT-4细胞可能存在下列机制：CHOP通过上调Bax/Bcl2比值激活线粒体凋亡途径；CHOP通过抑制抗凋亡基因ASNS的表达杀伤细胞。

关键词： 左旋门冬酰胺酶 氨基酸应激反应 ASNS CHOP/GADD153 Bax/Bcl2

Abstract: The aim of our work is to observe the expression of CHOP protein, asparagine synthetase (ASNS), Bax, and Bcl2 genes at the mRNA level, and to explore the potential mechanism involved in MOLT-4 cell apoptosis. Methods: Amino acid deprivation is induced by transferring the cells to a culture medium containing L-Asparaginase (L-Asp). A total of 1 IU/mL of L-Asp was added to the culture medium at different time intervals. Cell samples were then collected, and RNA was extracted. Relative quantitative RT-PCR (qRT-PCR) analysis was performed, and the expression of SYBR Green I was detected. Results: Two peaks were observed at 8 h and 18 h after L-Asp administration. At 18 h after L-Asp administration, CHOP mRNA remained at a high level, and the Bax / Bcl2 ratio increased significantly, whereas ASNS mRNA decreased gradually. The percentage of viable cells decreased markedly after 24 h of medication. The absolute number of viable cells slowly increased until 12 h after administration, and then gradually decreased, with most significant decrease after 24 h of medication. Conclusion: The potential mechanisms underlying L-Asp-induced MOLT-4 cell apoptosis may involve the activation of the mitochondrial pathway through CHOP, thus upregulating Bax / Bcl2. This mechanism may induce cell death by inhibiting the expression of the anti-apoptotic gene ASNS.

Key words: L-asparaginase Amino acid response ASNS CHOP / GADD153 Bax / Bcl2

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