

昆明山海棠诱导人白血病细胞HPRT基因突变的研究 Molecular Analysis of THH-Induced Mutations at the HPRT Locus in Human Promyelocytic Leukemia Cells by Multiplex Polymerase Chain Reaction

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摘要 为研究昆明山海棠(THH)的遗传毒性和药理作用, 采用单细胞克隆培养, 双向筛选计数, 多重PCR扩增与电泳分析, 研究了THH诱导HL-60细胞HPRT基因突变率及分子突变谱。发现随着染毒剂量的增加, 细胞接种存活率逐渐下降, 突变频率明显升高; THH诱发突变主要由缺失和点突变两部分组成(46.6%和53.4%), 而自发突变几乎全是点突变(92.3%); HPRT基因突变位点在各个外显子的分布较集中于基因的3'末端, 且外显子1缺失只出现于全基因缺失中, 外显子7/8与9多表现为连锁缺失(71.4%)。结果提示, THH具有明确的诱导HPRT基因突变的作用, 且诱发突变与自发突变的分子图谱不一样, 这可能与其作用机制有关。上述发现有助于阐明THH遗传毒性作用机理。

Abstract: The genotoxicity and pharmacologic activity of a Chinese medicinal herb, *Tripterygium hypoglaucum* (Lévl) Hutch (THH), was investigated by methods of single cell clone culture, two-way screening count, multiplex PCR amplification and electrophoresis technique. THH showed clear cytotoxicity and mutagenesis in human promyelocytic leukemia (HL-60) cells. When doses were increased, cell plating efficiency reduced and mutation frequency increased. The analysis showed that the spectra of spontaneous and THH-induced mutants were different. 46.6% of THH-induced genetic changes were deletions, whereas the majority of spontaneous mutants (92.3%) exhibited point mutations. Mapping of all intragenic deletion breakpoints showed a random distribution of breakpoints in 9 exons, but toward the 3' end of the HPRT gene. Exon 1 deletion only appeared in total gene deletion, and exon 7/8 and 9 deletion often showed chain deletion (71.4%).

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