

论文

铂类络合物引起的DNA O⁶-AGT的耗竭及染色体损伤

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摘要:

本文测定了KB,CHL,HL-60和L1210细胞DNA鸟嘌呤O⁶-烷基转移酶(O⁶-AGT)活性。结果表明,KB细胞有较高的O⁶-AGT活性,系Mer⁺细胞。而CHL,HL-60和L1210细胞的O⁶-AGT活性低,属于Mer⁻细胞。在此基础上我们观察了顺铂(DDP)、宁辛铂(樟脑胺氯乙酸铂,CCP)和碳铂(JM-8)对KB(Mer⁺)细胞O⁶-AGT的影响及Mer⁺和Mer⁻细胞的杀伤及微核的诱发作用。结果表明,三种络合物在等毒性浓度下对O⁶-AGT耗竭程序是CCP>DDP>JM-8,但这种耗竭与杀细胞作用无明显相关性而与微核诱发作用相关。此结果提示铂类络合物对DNA鸟嘌呤O⁶的损伤可能是其致痛致突变的原因之一。

关键词: 宁辛铂 Mer细胞 DNA鸟嘌呤O⁶-烷基转移酶 染色体损伤

DEPLETION OF O⁶-ALKYLGUANINE ALKYLTRANSFERASE AND CHROMOSOME DAMAGE INDUCED BY CISPLATIN, NING XIN PLATIN AND CARBOPLATIN

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Abstract:

O⁶-Alkylguanine- DNA- alkyltransferase (O⁶- AGT) is a very important DNA repair protein known to carry out the transfer of alkyl groups from the O⁶ position of guanine in alkylated DNA to a cysteine acceptor site contained within its own protein sequence. In this work, the activity of O⁶- AGT in different cell lines and the relationship between the depletion of the enzyme and the frequency of micronuclei induced by cisplatin (DDP), Ning Xin platin (camphoramine chloroacetic platinum, CCP) or carboplatin (JM-8) in KB and CHL cells were studied. Experiments indicate that KB cells showed higher O⁶- AGT activity (> 400 dpm/300µg protein extracts) which belonged to Mer⁺ cells, but CHL, HL-60 and L1210 cells showed very low O⁶- AGT activity (<50 dpm/300µg protein extracts) which can be considered to be Mer⁻ cells. Cytotoxicity studies indicated that no mer⁻ selection was observed in these platinum complexes for KB, HL-60, CHL and L1210 cells. However, a good relationship between the depletion of O⁶- AGT and the frequency of micronuclei induced by the platinum complexes was obtained. CCP caused the highest depletion of the enzyme and exhibited highest potency in damaging chromosome.

Keywords: Mer cells O⁶- Alkylguanine-DNA- alkyltransferase Chromosome damage Ning xin platin

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