中国寄生虫学与寄生虫病杂志 2001 19 (2): 87-89 ISSN: 1000-7423 CN: 31-1248/R

论著

恶性疟原虫二氢叶酸还原酶基因的突变

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收稿日期 修回日期 网络版发布日期 接受日期

摘要

目的 探测云南恶性疟原虫二氢叶酸还原酶基因 (dhfr)与乙胺嘧啶和双氯胍抗性有关的基因位点突变的情况。方法 应用特异性套式PCR和限制性酶切片段长度分析 (RFPS)检测采自现场的干滤纸血样。结果 检测到恶性疟原虫dhfr基因内 16 ,5 1,10 8和 16 4位氨基酸有不同程度的突变 ,以Asn 10 8和 Ile 5 1为甚 ,出现频率分别为 94.1%和 90 .1%。野生型 (3D7型)Ser 10 8出现较低频率 9.1% (6 / 6 6) ,而Ala 16出现频率较高 6 1.8%(42 / 6 8) ;突变型比例高 ,HB3型 ,7G8型 /FCR3型和 Cambodian型比例为 1:2 1:7.5。结论 首次在云南西双版纳州检测恶性疟原虫dhfr基因内 16 ,5 1,10 8和 16 4位氨基酸存在不同程度的突变 ,与乙胺嘧啶抗性有关的 7G8型突变率较高 ,而与双氯胍抗性有关的FCR3型则较低。

关键词 恶性疟原虫 二氢叶酸还原酶(dhfr)基因 基因突变

分类号

Gene Point Mutation in the Dihydrofolate Reductase-thymidylate Synthase Gene of Plasmodium falciparum

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Abstract

Objective To investigate the gene point mutation in the dihydrofolate reductase thymidylate synthase (dhfr) gene of Plasmodium falciparum isolate from Yunnan Province strongly associated with pyrimethamine and cycloguanil resistance. Methods Nested PCR and restriction endonuclease digestion were applied to detect the gene mutation using dried blood filter paper collected from the fields in Yunnan Province. Results Different mutations were found in 4 amino acids at positions 16, 51, 108 and 164 of dhfr gene, particularly, Asn 108 and Ile 51, the mutaiton frequency being 94.1% and 90.1%, respectively. The frequency of the wild type genotype (3D7 type) Ser 108 appeared lower (9.1%) , while the frequency of the Ala 16 was high(61.8%); the mutation type was very high, the ratio of HB3 type, 7G8 type/FCR3 type and Cambodian type was 1:21:7.5. Conclusion The investigation first demonstrated that Plasmodium falciparum Yunnan isolate dihydrofolate reductase thymidylate synthase gene(dhfr) at positions 16, 51 ,108 and 164 exhibited different degrees of point mutation. The frequency of mutation of the 7D8 type involved in pyrimethamine resistance was higher, while that of the FCR3 type involved in cycloquanil resistance was lower.

Key words Plasmodium falciparum dihydrofolate reductase thymidylate synthase (dhfr)gene gene mutation

DOI:

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