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论著

叶酸、核黄素缺乏及MTHFR A1298C多态性对人类淋巴细胞基因组遗传稳定性的影响

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摘要 背景与目的： 叶酸代谢涉及DNA合成及甲基化等重要生化过程，对维持人类遗传稳定性意义重大。亚甲基四氢叶酸还原酶(methylene tetrahydrofolate reductase,MTHFR)对上述两个生化过程之间的分支走向发挥着关键作用，核黄素作为MTHFR的重要辅助成分，亦可能干涉MTHFR的功能，进而影响到遗传稳定性。本研究拟探讨叶酸、核黄素缺乏以及MTHFR基因1298位点多态性对人类淋巴细胞基因组稳定性的综合影响。 材料与方法： 采用胞质分裂阻断微核分析法研究叶酸(20、200 nmol/L，即LF、HF)和核黄素(1、500 nmol/L，即LR、HR)不同浓度组合以及MTHFR A1298C多态性对培养9 d的人类淋巴细胞基因组稳定性的影响。 结果： 各MTHFR基因型淋巴细胞在低叶酸高核黄素组合培养条件下的遗传损伤程度均高于所有其它组合，而高叶酸低核黄素组达最低 (P<0.01)，各基因型淋巴细胞在高叶酸条件下的微核化双核细胞(MNed BNC)、核质桥(NPB)和核芽(BUD)频率分别为低叶酸条件的46.5%、22%和42.3%；而高核黄素条件下的相应指标则比低核黄素高约6.3%～12.4%；MTHFR 1298AA型遗传稳定性显著高于突变纯合子MTHFR 1298 CC(P<0.01)；叶酸对MNed BNC、NPB、BUD的变异贡献率分别达到91.61%、73.72%和78.07%(P<0.01)；核黄素及MTHFR A1298C多态性对遗传损伤的变异贡献虽接近或达到显著水平，但均不及叶酸；叶酸、核黄素和MTHFR基因型之间的交互作用对上述遗传损伤标记没有显著影响。 结论： 叶酸、核黄素和MTHFR A1298C多态性都在一定程度上对基因组稳定性有影响，但相比之下，叶酸在我们的研究中是影响基因组稳定性的主导因素。

关键词 叶酸； 核黄素； 亚甲基四氢叶酸还原酶； 基因多态性； 胞质阻断微核分析 基因组稳定性

Impacts of Folic Acid, Riboflavin Deficiency and MTHFR A1298C Polymorphism 、on Human Lymphocytes Genomic Stability

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Abstract BACKGROUND & AIM: Folic acid (FA) is a key factor that is involved in DNA methylation and DNA synthesis. Methylene tetrahydrofolate reductase (MTHFR) is a critical enzyme which determines the balance between the above two processes. Riboflavin(RF) is the precursor of flavin adenine dinucleotide (FAD) which is the coenzyme of MTHFR, consequently, low concentration of RF may affect MTHFR activity. MATERIALS AND METHODS: Cytokinesis_block micronucleus assay (CBMN) was employed to assess the effects of different combinations of FA(20 and 200 nmol/L, i.e. LF and HF) and RF (1 and 500 nmol/L, i.e. LR and HR) and MTHFR A1298C polymorphism on genomic stability of 9_day old cultured human lymphocytes. RESULTS: The result showed that the genetic damage was significantly higher in LFHR groups regardless of the genotypes(P<0.01).The optimal levels of genomic stability were identified in all HFLR groups. The frequencies of MNed BNC, NPB and BUD in HF groups were 46.5%,22% and 42.3%, respectively, of those in LF. These biomarkers levels were 6.3%－12.4% lower in LR groups than in HR groups. FA accounted for 91.61%， 73.72% and 78.07% for MNed BNC,NPB and BUD respectively. RF and MTHFR A1298C polymorphism did contribute to the variations of the above indexes but the impact was relatively trivial compared with that of FA. No interactions among these three factors that affected the genomic stability were found. CONCLUSION:All of FA,RF and MTHFR A1298C polymorphism could affect genomic stability, with FA being the dominant factor in our system.

Keywords folic acid riboflavin MTHFR polymorphism cytokinesis_block micronucleus assay genomic stability

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