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Correlation of MSH3 polymorphisms with response and survival in advanced non-small cell lung cancer patients treated with first-line platinum-based chemotherapy

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ABSTRACT. Mismatch repair (MMR) genes, as well as the nucleotide excision repair genes, play an important role in removing cisplatin-DNA adducts, and the mutation of MMR genes in tumors can lead to a decreased response to platinum-based therapies. We examined MutS homolog 3 (MSH3), a mismatch repair gene, and whether polymorphisms of MSH3 were associated with response and survival in advanced non-small cell lung cancer (NCSLC) patients who were treated with platinum-based chemotherapy. The peripheral blood of 180 advanced NCSLC patients who were treated with first-line platinum-based chemotherapy was collected to determine the patients' genotypes of MSH3. The three genotypes of the MSH3 polymorphisms rs26279, rs1650697 and rs1105524 were investigated. A statistically significant association was observed between the polymorphism

rs26279 (Ala1054Thr) and sensitivity to platinum-based chemotherapy (P = 0.014). A significant correlation was found between rs1105524 and progression-free survival (PFS), with the G/A and A/A genotypes (median survival time: 14.27 months; 95%CI = 9.80-18.75) suffering shorter survival than patients with the G/G genotype (median survival time: 26.37 months; 95%CI = 15.03-37.71) (P = 0.04). Our results showed that single nucleotide polymorphisms in MSH3 had an impact on the chemotherapy response and prognosis of advanced NCSLC patients who were treated with platinum-based chemotherapy.

Key words: MutS homolog 3; Single nucleotide polymorphism; Platinum-based chemotherapy; Non-small cell lung cancer