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

X.-L. Xu1,2*, Y.-L. Yao1*, W.-Z. Xu2, J.-G. Feng1 and W.-M. Mao1,2

1Key Laboratory on Diagnosis and Treatment Technology for Thoracic Cancer, Zhejiang Cancer Hospital (Zhejiang Cancer Research Institute), Hangzhou, Zhejiang Province, China
2Department of Medical Oncology, Zhejiang Cancer Hospital, Hangzhou City, China

*These authors contributed equally to the study.
Corresponding author: W.-M. Mao
E-mail: maowm1318@163.com

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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