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Combination of Mitochondrial DNA content and G10398A polymorphism defines a group of distinct molecular subset indicative for non-small cell lung cancer with different prognosis

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Abstract

Mitochondrial DNA (mtDNA) is known for its high frequencies of polymorphisms and mutations, some of which are related to cancers. This study explored the mtDNA content and G10398A polymorphism in the prognosis of patients with non-small cell lung cancer (NSCLC). A total of 128 tissue samples were obtained from the tumor bank of Zhongnan Hospital of Wuhan University between 2004 and 2011.The mtDNA copy number was assessed by real-time PCR, PCR-RFLP was used to genotype at mtDNA G10398A, and their relationships to prognosis were analyzed. Low mtDNA content was more common in stage III and IV than in stage I and II ($\chi 2$=6.433; P=0.018). 10398A was found in 49.2% (63/128) NSCLC patients. Low mtDNA content patients had a marginally shorter survival time than high mtDNA patients (median survival time 27.9 months vs. 34.1 months; $\chi 2$=3.742; P= 0.0530). There was no survival difference when G10398A polymorphism was analyzed alone. However, when combining mtDNA content with G10398A polymorphism, overall survival in NSCLC patients was significantly shorter in patients with low mtDNA content plus 10398A than in patients with high mtDNA content plus 10398G(median survival time 26.3 months vs. 34.1 months; $\chi 2$=4.035; P= 0.0446). Cox-regression analysis showed that stage and mtDNA plus G10398A polymorphism were the two most independent prognostic factors in patients with NSCLC (χ^2=6.235, P=0.013; $\chi 2$=18.515, P<0.0005, respectively).The results highlight the complex relationships between mtDNA copy number and G10398A mutation in tumorigenesis. Changes in the expression of mtDNA plus G10398A polymorphism define a distinct subset of lung cancers. Patients with such cancers have poorer survival and require early treatment.