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高血压相关的线粒体DNA突变

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摘要 线粒体DNA(mtDNA)突变是高血压发病的分子机制之一。已经报道的与原发性高血压相关的mtDNA突变包括: $tRNA^{Met}$ A4435G, $tRNA^{Met}$/$tRNA^{Gln}$ A4401G, $tRNA^{Ile}$ A4263G, T4291C 和 A4295G突变。这些高血压相关的mtDNA突变改变了相应的线粒体tRNA的结构, 导致线粒体tRNA的代谢障碍。而线粒体tRNAs的代谢缺陷则影响蛋白质合成, 造成氧化磷酸化缺陷, 降低ATP的合成, 增加活性氧的产生。因此, 线粒体的功能缺陷可能在高血压的发生发展中起一定的作用。mtDNA突变发病的组织特异性则可能与线粒体tRNAs的代谢以及核修饰基因相关。目前发现的这些高血压相关的mtDNA突变则应该作为今后高血压诊断的遗传风险因子。高血压相关的线粒体功能缺陷的深入研究也将进一步诠释母系遗传高血压的分子致病机制, 为高血压的预防、 控制和治疗提供依据。文章对高血压相关的mtDNA突变进行了综述。

关键词: 高血压 母系遗传 mtDNA突变 线粒体tRNA

Abstract: Mutations in mitochondrial DNA (mtDNA) are one of the molecular bases of hypertension. Among these, the $tRNA^{Met}$ A4435G, $tRNA^{Met}$/$tRNA^{Gln}$ A4401G, $tRNA^{Ile}$ A4263G, T4291C and A4295G mutations have been reported to be associated with essential hypertension. These mutations alter the structure of the corresponding mitochondrial tRNAs and cause failures in tRNA metabolism. These shortages of these tRNAs lead to an impairment of mitochondrial protein synthesis and a failure in the oxidative phosphorylation function. These result in a deficit in ATP synthesis and an increase of generation of reactive oxygen species. As a result, these mitochondrial dysfunctions may contribute to the development of hypertension. Furthermore, the tissue specificity of these pathogenic mtDNA mutations might be associated with tRNA metabolism and nuclear modifier genes. These mtDNA mutations should be considered as inherited risk factors for future molecular diagnosis. Thus, these findings provide new insights into the molecular mechanism, management and treatment of maternally inherited hypertension. This review summarized the association between mtDNA mutations and hypertension.

Keywords: hypertension, maternal inheritance, mtDNA mutation, mitochondrial tRNA

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