The Role of Mitochondrial tRNA Fragments (tRFs) in Cancer Metastasis

Rowland, Jonas (School: Shawnee Mission Northwest High School)

Metastatic cancers behave in an extremely aggressive manner. They move and spread all throughout the body and are very hard to predict and treat. The process which metastatic cancer develops is referred to as the metastatic cascade. Cancer has an inherently genetic origin. However, many people do not realize that humans have two separate genomes; nuclear (nDNA) and mitochondrial (mtDNA). However, the number of proteins encoded in mtDNA pales in comparison to proteins encoded in nuclear DNA (> 20,000), and as a result, mtDNA is viewed as far less important in cancer biology and metastasis. Metabolic changes mitochondria provide are significant to tumor formation, growth, and spread. Single nucleotide polymorphisms (SNP) potentially play a large role in metastasis regulation. To study the role of mitochondrial genetics, mitochondrial nuclear exchange (MNX) mice were developed. Communication between nuclear-mitochondrial DNA is extremely important and relevant to complex diseases, and changes in mtDNA have selective effects on the nDNA. There are a total of 7 SNPs in the mitochondrial genome. The goal of this research was to determine the role of two SNPs, located within mt-tRNAArg, tRNA Fragments (tRFs). Fragmentation of tRNAs redirects them from conventional protocols such as protein synthesis to new structure which come with new function. RNA from MNX mouse tissue was isolated, assessed, and ligated before being amplified using Stem-loop (SL) RT-qPCR. Detection, separation, and quantification of all three tRFs, tRNAArg (FL), RL3, and Ri, was successful using SL RT-qPCR. SL RT-qPCR proved to be an effective method by which to analyze tRFs in a way that Northern blots are not. The data presented is novel and significant to future studies and the cancer biology field.

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