

NEW EVIDENCE CONFIRMS THAT THE MITOCHONDRIAL BOTTLENECK IS GENERATED WITHOUT REDUCTION OF MITOCHONDRIAL DNA CONTENT IN EARLY PRIMORDIAL GERM CELLS OF MICE.

Liqin Cao^{1,2}, Hiroshi Shitara¹, Michihiko Sugimoto², Jun-Ichi Hayashi³, Kuniya Abe², Hiromichi Yonekawa¹

¹The Tokyo Metropolitan Institute of Medical Science (Rinshoken), Tokyo 156-8506, Japan. ²BioResource Center (BRC) RIKEN Tsukuba Institute, Ibaraki 305-0074, Japan. ³University of Tsukuba, Ibaraki 305-8572, Japan.

Mutations of mtDNA are responsible for many types of mitochondrial diseases in humans, including myopathy and neurological disorders. Females carrying a mixture of mutant and wild-type mtDNA variants transmit a variable amount of mutant mtDNA to each offspring. The proportion of mutated mtDNA inherited from the mother determines the onset and severity of diseases. Previous studies have suggested that the mtDNA genome is transmitted through a bottleneck, but the underlying mechanism remains controversial. We have previously determined mtDNA copy number in single germ cells and shown that the bottleneck occurs without the reduction of mtDNA content in germline. Recently one study suggested that the bottleneck is driven by a remarkable decline of mtDNA copies in early primordial germ cells (PGCs), while another study reported that the mtDNA genetic bottleneck results from replication of a subpopulation of the mtDNA genome during postnatal oocyte maturation and not during embryonic oogenesis despite that they detected a reduction in mtDNA content in early PGCs. To resolve these controversies, we examined the mtDNA copy number in PGCs isolated from transgenic mice expressing fluorescent proteins specifically in PGCs. Here we present solid evidence to confirm our previous findings; no significant reduction of mtDNA content occurs in early PGCs. This confirmation is important because the understanding of mtDNA content in female germ cells will facilitate the development of therapeutic strategies preventing the transmission of mitochondrial diseases from mother to offspring.

Keywords:

mtDNA copy number; Single cells; Bottleneck; Mouse