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Age-related accumulation of somatic mitochondrial DNA mutations in adult-derived human iPSCs

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The genetic integrity of iPSCs is an important consideration for therapeutic application. In this study, we examine the accumulation of somatic mitochondrial genome (mtDNA) mutations in skin fibroblasts, blood and iPSCs derived from young and elderly subjects (24-72 years). We found that pooled skin and blood mtDNA contained low heteroplasmic point mutations but a panel of ten individual iPSC lines from each tissue or clonally expanded fibroblasts carried an elevated load of heteroplasmic or homoplasmic mutations, suggesting that somatic mutations randomly arise within individual cells but are not detectable in whole tissues. The frequency of mtDNA defects in iPSCs increased with age, and many mutations were non-synonymous or resided in RNA coding genes and thus can lead to respiratory defects. Our results highlight a need to monitor mtDNA mutations in iPSCs, especially those generated from older patients, and to examine the metabolic status of iPSCs destined for clinical applications.

Biography

Taosheng Huang is a Physician-Scientist. Currently, he is a Professor with tenure in Human Genetics, Director, Program of Mitochondrial Medicine, and Associate Director of the Molecular Diagnostic Laboratory at Cincinnati Children's Hospital Medical Center (CCHMC). He has been actively engaged in many programs in China. He is an Honorable Professor of Peking Union Medical School, a member of the special committee for Yusheng Yuyou of People's Republic of China, Advisory Board Member to Chinese Ministry of Health for targeted therapy and a Principal Investigator for Birth Defect Control Program of Chinese Ministry of Health.

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