

LIVE-CELL REAL-TIME IMAGING REVEALS ROLE OF ENDOTHELIAL NITRIC OXIDE SYNTHASE AND MITOCHONDRIA IN HMSC ADIPOGENIC DIFFERENTIATION

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Mitochondria play critical roles in human health and diseases. In addition to providing energy for life functions, mitochondria serve as platforms and regulators for many cellular signalling pathways. Mitochondrial dysfunction is associated with a wide range of diseases, including cancer, metabolic, cardiovascular, and neurodegenerative diseases. Intercellular transfer of mitochondria has been proposed as an attractive approach for organelle-based therapy. Uptake of healthy mitochondria and subsequent functional recovery of the recipient cells have been reported. However, studies on live-cell, real-time, cell-to-cell transfer of mitochondria remain scarce. It is well known that nitric oxide (NO) generated by endothelial nitric oxide synthase (eNOS) acts as an upstream regulator of mitochondrial biogenesis. We reported previously that eNOS-derived NO plays distinct and separable roles in white and brown adipogenesis. In the brown adipocytes, eNOS up-regulates the expression of thermogenic gene program. In white adipocytes, eNOS-derived NO is required for adipocyte differentiation and mitochondrial biogenesis. To better understand the role of NO in mitochondria function during adipocyte differentiation, we examined the impact of siRNA knockdown (KD) of eNOS on mitochondrial effect in human mesenchymal stem cell (hMSC) adipogenic differentiation, using live-cell real-time fluorescence imaging. Our studies demonstrated that mitochondria can be transferred from one cell to another, indicating that human mitochondria may possess the innate ability for intercellular exchange. Our results show that transfer of healthy mitochondria to eNOS deficient cells restores mitochondrial function in adipogenic differentiation, suggesting that mitochondria remodeling can be a novel approach for the treatment of diseases associated with mitochondrial dysfunction. Thus, live-cell real-time imaging of mitochondria dynamics at the cellular and subcellular levels would be a useful tool to monitor the biological, pathological and therapeutic roles of mitochondria.

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