Diverse Pathophysiological Roles of Mitochondrial Fission and Fusion upon Nanophotodynamic Effect of Fullerene-induced Mitochondrial Oxidative Stress

Cheng-En Hsieh¹, and Mei-Jie Jou²

¹ School of Medicine, Chang Gung University, Kwei-Shan, Tao-Yuan, Taiwan
² Department of Physiology and Pharmacology, Chang Gung University, Kwei-Shan, Tao-Yuan, Taiwan

Abstract:
Mitochondrial fission and fusion machinery possesses vital function in maintaining the mitochondrial integrity and network, bioelectrical and chemical connectivity, turnover of mitochondria, and segregation and protection of mitochondrial DNA (mtDNA). Substantial evidence indicates that extensive mitochondrial fission occurs during oxidative insult, a key reason for various diseases and molecular aging, yet the detailed cellular functions and effects of such morphological response remain unclear. We investigated pathophysiological roles of mitochondrial fission and fusion machinery upon mitochondria-targeted reactive oxygen species (mROS) generation by the photodynamic effect (PDE) of a new class of water-soluble nanophotosensitizer carbon 60, tris-malonic acid carboxyfullerene (C₃), coupled with 543 nm laser in wild-type, fission enhanced and fusion enhanced 143B osteosarcoma cells. Mitochondrial level of dynamic alterations including morphology, oxidative strength, lipid peroxidation, ∆ψₘ, cardiolipin (CL), and mCa²⁺ were time-lapsed imaged using laser scanning confocal microscopy coupled with various fluorescent probes including MitoTracker Green, 2',7'-dichlorofluorescin diacetate (DCF), C11-BODIPY₅₈₁/₅₉₁, tetramethyl rhodamine methyl ester (TMRM), 10-N-nonyl acridine orange (NAO), and rhod-2. Our results revealed that fission of mitochondria reduced significantly mROS propagation for less lipid peroxidation and ∆ψₘ loss whereas fusion of mitochondria facilitated mitochondrial destruction. Whereas, fission of mitochondria accelerated and fusion decreased ∆ψₘ depolarization, CL peroxidation, mCa²⁺ overload, and eventual cell death upon lethal doses of mitochondrial oxidative insults. Thus, rearrangement of mitochondrial network via fission or fusion may provide potential diverse protection against or augmentation towards mitochondrial oxidative stress associated apoptosis.