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Editor's note...

The Role of Exercise and Mitochondrial Biogenesis in Aging Process

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Aging can be defined as the progressive accumulation of changes with time associated with increasing vulnerability to disease and death which accompanies advancing age. The time related changes are attributed to aging process (Harman, 1981). There are growing evidences that a number of the detrimental free radical reactions are continuously occur throughout the cells of the body constitutes the prominent contributor to aging process (Harman, 1981). This theory was extended to mitochondrial theory of aging, suggesting that mitochondria is the main source and target of reactive oxygen species (ROS) produced in association with aging processes and degenerative diseases (Payne and Chinnery, 2015). Mitochondria has a pivotal roles in multiple cellular processes such as oxidative phosphorylation (OXPHOS), apoptosis, -oxidation of fatty acids, steroid biosynthesis, calcium homeostasis, intermediary metabolism, and cell signaling (Yin and Cadenas, 2015). Recent studies indicated that oxidative damage due to accumulation of ROS result from mitochondria production were associated with multiple pathologies, including neurodegenerative diseases, diabetes, cancer, and premature aging (Cedikova et al., 2016).

Mitochondria are the organelles reside within cell, has double membranes and several hundreds of proteins and 2–10 copies of mitochondrial DNA (mtDNA) in the matrix enclosed by mitochondrial inner membrane (Lee and Wei, 2005). Owing to environmental stressor, mitochondria are able to grow and divide to more numerous number, size, and mass and becoming abundance in cell through mitochondrial biogenesis. Mitochondrial biogenesis is defined as the growth and division of pre-existing mitochondria to increase their individual mitochondrial mass and copy number to increase the production of ATP as a response to greater energy expenditure (Lee and Wei, 2005; Jornayvaz and Shulman, 2010). According to this concept, mitochondrial count in muscle and cardiac cell is the largest amongst cells in the body. It is plausible since muscle and cardiac cells are continually used to move the body and heart contraction respectively. Consequently, they require large energy (ATP) and only can be supplied by the great number of mitochondria producing energy and unfortunately ROS as byproduct via OXPHOS. (Sun, Youle and Finkel, 2016).

ROS concentration may be increased by dysfunction of mitochondrial electron transporting system, which in turn results in mitochondrial DNA (mtDNA) mutations causing compromised function of mitochondrial protein and therefore increase oxygen radicals production (Cedikova et al., 2016). Interestingly, as reported by Fayet G, et al. that mitochondrion dysfunctional is determined by mtDNA mutation caused by ROS (Fayet et al., 2002; Theurey and Pizzo, 2018). In this context, mitochondria served as a biologic clock, meaning that premature aging may be occur when mitochondrial function particularly in neuron, endocrine, and immune cells will decrease below a critical level (De la Fuente and Miquel, 2009). However, aerobic exercise will increase ROS in certain level which is capable of inducing mitochondrial biogenesis and repair mitochondrial function particularly in muscles (Gomes, Silva and Oliveira, 2012). Accordingly, the increased mitochondrial biogenesis, is seen as a very desirable way to drive cellular function, and it can even be used as a potential mitochondrial therapy and subsequently induce cells and tissues rejuvenation (Viscomi, Bottani and Zeviani, 2015). Fortunately, mitochondrial biogenesis can easily be triggered by external stimuli, such as dietary restriction and physical exercise (Jornayvaz and Shulman, 2010; Kauppila, Kauppila and Larsson, 2017).

Physical exercise can be defined as any planned structured activity that leads to increase in energy expenditure and heart rate (Gomes, Silva and Oliveira, 2012). Several studies showed that exercise is able to increase ROS production, in some circumstance lead to detrimental effect in cells. However, ROS, which is produced during times of exercise have essential role in muscle adaptation. In addition, ROS also activate signaling pathway and induce mitochondrial network branching and elongation (Gomes, Silva and Oliveira, 2012). A study reported by Pesce et al. indicated that mitochondrial biogenesis was characterized by increased in mtDNA copy number and mitochondrial mass was in accordance with increasing levels of ROS in aging skeletal muscle (Pesce et al., 2005). Moreover, mitochondrial biogenesis is activated by numerous different signals and tightly controlled by transcription

factor, such as nuclear respiratory factor-1 and - 2 (NRF-1 and NRF-2) and co activators such as peroxisome proliferators activated receptor c coactivator-1a (PGC-1α). (Moyes and Hood, 2003; Yin and Cadenas, 2015). Recently, numerous studies showed that treatment with exogenous ROS is invariably followed by the increased in expression of PGC-1α (Gomes, Silva and Oliveira, 2012). There is growing evidence that ROS resulted from exercise also capable of increasing PGC-1α promoter activity and expression through both adenosine monophosphate activated protein kinase-dependent (AMPK) and AMPK independent pathways (Irrcher, Ljubicic and Hood, 2009).

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