EDITORIAL

Mitochondrial Dysfunction & Neurological Disorders

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Most of the living organisms derive their energy requirements from ingested food material through controlled metabolic reactions. Prokaryotes like bacteria obtain the ATP, the energy subunit from series of enzymatic reactions which occur in the cytosol [1]. In contrast to prokaryotes, eukaryotes have evolved a highly specialized double membrane organelles *i.e.,* mitochondria encompassing electron transport chain complexes to harness the electrochemical energy in the reducing equivalents to generate ATP [2]. Thus, mitochondria are vital organelles responsible for providing the energy currency in the form of ATP to sustain various cellular processes. Disturbances or damage to mitochondria results in altered bioenergetics, redox equilibrium and dynamics of cell and is thus identified to be the focal point of pathogenesis in many human diseases including neurological disorders [3].

Mitochondrial dysfunction is a broad term describing the series of maladaptive cellular events due to disturbed mitochondrial function. Such changes may include reduced ATP production from mitochondria, increased ROS output, altered proteastasis and cellular quality control [4]. Neurons have an increased susceptibility for mitochondrial dysfunction because of their critical requirement for ATP supply from mitochondria and increased demand for oxygen. Such critical requirement makes them vulnerable to leakage of electrons from electron transport chain resulting in free radical generation [5]. Intrinsically low level of antioxidant defences in the neurons further makes them susceptible to oxidative damage mediated by mitochondria. The matter of interest here is important here is that the large ROS output generated from mitochondria, not only damages the cellular bio molecules *i.e.,* DNA and proteins in the cell, but ROS also damages various mitochondrial components like mitochondrial DNA and other ETC components, which ensues loss of electrochemical gradient across the inner membrane of the mitochondria and reduces ATP production [6]. Mutations in mitochondrial DNA and oxidative stress are the important risk factors associated with age related neurodegeneration [7].

The current issue entitled "Mitochondrial Dysfunction & Neurological Disorders" is an attempt to summarize the various physiological and pharmacological aspects of mitochondrial dysfunction in myriad range of neurological diseases ranging from peripheral neuropathies to cancers. The article by Kumar *et al.* highlights the importance of maintaining mitochondrial equilibrium with respect to their biogenesis, turnover to keep redox, bioenergetic homeostasis in peripheral neurons affected by neuropathies [8]. The article by Naidu *et al.* discusses the mechanistic aspects of mitochondrial dysfunction in various glioblastomas and also enlists the most important phytochemicals which were proved to be effective against the mitochondria mediated apoptosis in Glioblastoma multiforme [9]. Another article by Kuhad *et al.* summarizes the mechanism of mitochondrial dysfunction in depression [10]. Sharma *et al.* have discussed the importance of Peroxisome proliferator-activated receptor-gamma coactivator (PGC)-1alpha mediated mitochondrial protection in cognitive decline associated with Parkinson's disease [11]. Tripathi *et al.* have elaborated involvement of mitochondria mediated oxidative stress, apoptosis, Ca^{2+} dyshomeostasis and bioenergetic dysfunction in neurodegenerative diseases. They have highlighted the importance of nutraceuticals for the therapeutic management of Parkinson's disease, Huntington's disease, Multiple sclerosis and Amyotrophic lateral sclerosis where neurodegenerative events are evident [12]. In addition to this, the role of mitochondrial involvement in neurogenesis and angiogenesis in cerebral

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ischemia and the actions of endothelin receptor anatagonists on the mitochondrial functions have been discussed by Gulati [13].

Articles present in this issue have indicated the possible pathogenic role of mitochondria in neurological diseases and the benefits of targeting it as a drug target would expect to yield better therapeutic outcome. Our knowledge of mitochondrial biology is still in infancy and it would require further exploration to unravel the molecular facets of mitotoxicity in neurological diseases. This can be achieved by studying the mitochondrial pathology in more detailed manner using specific knockout cellular, animal models and assessing the interorganellar association between mitochondria, nucleus and endoplasmic reticulum under neurodegenerative conditions. Nevertheless the huge interest by scientific groups across the globe towards the development of mitochondrial based therapeutics against the mitochondrial derangements observed in various diseases would definitely expected to yield fruitful results in the coming years.

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