Role and Function of Mitochondria

How to Cite this Article: Zamani GR. Mitochondrial Disease. Iran J Child Neurol Autumn 2012;7:4 (suppl.1):3-4.

Gholamreza ZAMANI MD

Mitochondrial diseases are a group of disorders caused by pathologic dysfunction of the mitochondrial respiratory chain. They present with a wide range of clinical expression. Although neurologic impairment is a common manifestation but they can affect other systems, either exclusively or in combination.

Mitochondria are intracellular organelles found in almost all human cells. They are responsible for aerobic metabolism through oxidative phosphorylation, which leads to energy production in the form of adenosine triphosphate (ATP). Each human cell contains on average hundreds to thousands of mitochondria. The exception is mature red blood cells, which rely exclusively on anaerobic metabolism and contain no mitochondria.

Mitochondria have four main compartments:

1. The outer membrane, 2.The intermembranous space, 3.The inner membrane, 4.The matrix. In addition to ATP generation through the respiratory chain, mitochondria perform multiple other metabolic functions, including pyruvate oxidation, the Krebs cycle, fatty acid oxidation, and amino acid metabolism. All of these tasks take place in the matrix. Although any abnormality in the above pathways could be technically designated as a mitochondrial disorder, only defects in the respiratory chain are traditionally referred to as primary mitochondrial diseases. The respiratory chain is composed of five enzyme complexes (complex I, II, III, IV, V) that are involved in receipt and transfer of electrons through these compartments .Oxidative phosphorylation takes place along the inner mitochondrial membrane, which contains the respiratory chain proteins.

Mitochondria are under the dual control of mitochondrial DNA and nuclear DNA. Mitochondrial DNA has several characteristics that distinguish them from their nuclear counterparts. These include: Maternal inheritance, heteroplasmy (e.g. some pathologic DNA copy, mitochondria or cells mixed with healthy ones), threshold effect (A minimal number of mutated cells needed before respiratory chain and cellular dysfunction occur), Mitotic segregation (e.g. since organelles are randomly distributed at the time of cell division, a change in the amount of mutant DNA in a cell occurs and surpass its threshold, therefore clinical phenotype can be changed in a previously unaffected tissue). Post mitotic replication (Mitochondrial DNA replication is not linked to the cell cycle. This allows for post mitotic mitochondrial DNA replication in terminally differentiated cells such as neurons or muscle in response to specific stimuli (exercise, increased metabolic demand). This explains how the symptomatic threshold can be exceeded later in life in previously asymptomatic tissues).

In contrast to mitochondrial DNA, nuclear DNA mutations affecting the mitochondria follow Mendelian genetics. Most of the nuclear genes that are

Pediatric Neurology Department, Children's Medical Center, Tehran University of Medical Sciences, Tehran, Iran

Corresponding Author:
Zamani GR MD
Children's Medical Center,
Gharib Ave, Tehran, Iran
Tel: +98 2166935848
Fax: +9821 66930024
Email:ghrzamani@yahoo.com

important in mitochondrial control are only starting to be recognized. Thus, in many patients with a suspected nuclear DNA-based mitochondrial disorder, no specific genetic mutation can be identified. Nevertheless, nuclear gene mutations are thought to be the major cause of mitochondrial disease in children and infants. Mitochondrial disorders can be classified according to whether the causative mutations affect mitochondrial DNA or nuclear DNA, further subdivided into: Mutations of genes that directly encode respiratory chain proteins and those that encode the ancillary machinery required for the synthesis of the respiratory chain proteins. Although essential for understanding the pathophysiology of these disorders (and perhaps important as a basis for future therapies), this genetic classification of mitochondrial disorders has limited clinical relevance at the present time.

Keywords: Mitochondria; Structure; Function; Genetic