جامعة المستقبل
AL MUSTAQBAL UNIVERSITY

كلية العلوم
قسم الكيمياء الحياتية

LECTURE (7)

Subject :**Pathologies Related to Energy and Membrane Dysfunction**

Level: second

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Pathologies Related to Energy and Membrane Dysfunction

Pathologies like mitochondrial diseases, transport disorders, and metabolic syndromes.

mitochondrial processes

General roles of mitochondria in metabolism

The traditional definition of the mitochondrion is the energy-generating organelle of the cell, responsible for the **final steps of metabolizing organic substances to produce energy** for the cell in the form of adenosine triphosphate **(ATP).**

In mammalian cells, most of the redox potential used for generating ATP arrives at the mitochondrion in the form of the **nicotinamide adenine dinucleotide (NADH)** and **flavin adenine dinucleotide (FADH2).**

Mitochondria most readily produce ATP by the oxidation of NADH and FADH2 yielded from the breakdown of **sugars such as glucose**

interactions between **mitochondria** and the **ER(Endoplasmic Reticulum)** have been implicated in almost all mitochondrial processes, further adding to the complexity of mitochondrial function in health and in pathogenesis.

the core function of the mitochondrion is to act as the metabolic hub of the cell. when mitochondrial respiratory activity becomes impaired, symptoms are visible on a systemic level.

Diseases associated with functional or genetic mitochondrial defects

Mitochondrial myopathy

Mitochondrial myopathy (also**: mitochondrial encephalomyopathy**) is a disease in which mitochondria within muscle fibers exhibit **defects in function and dynamics,** leading to weakness of the muscle and accumulation of mitochondria within the fiber, giving rise to the characteristic "ragged red" fibers seen upon Gömöri trichrome staining. Some patients experience mitochondrial myopathy as constant muscle weakness, while others only experience weakness upon more intense exercise, and in some forms is accompanied by other more intense symptoms, such as epilepsy . Mitochondrial myopathies most commonly arise from mtDNA mutations leading to defects in oxidative phosphorylation, resulting in the accumulation of mitochondria within fibers and the "ragged red" phenotype.

Chronic lactic acidosis

Mutations in genes encoding mitochondrial proteins required for the assembly and function of ETC complexes, as well as the use of certain prescription drugs and other physiological stress conditions have all been associated with the onset of LA (Lactic acidosis) (LA) is characterized by the buildup of lactate due to decreased mitochondrial respiration, which can lead to the acidification of tissues.

Patients suffering from high lactate levels can suffer from tissue acidification if left untreated. The acidification of tissues can cause system-wide disturbances in physiological function, and thus it is critical that chronic LA is detected and treated. Currently available treatments include the administration of ion-containing fluids to help raise systemic pH back to near-normal levels.

Altered mitochondrial function in cancer

In addition to strictly metabolic disorders, mitochondrial activity is affected in cancer patients. Often, tumor progression is associated with increased mitochondrial respiration (due to rapidly growing cells) and therefore increased ROS production. MtDNA mutations are thus a hallmark of many cancer patients. A large portion of mutations occurs in the noncoding D-loop region of the mtDNA, which is responsible for the initiation of replication

The role of mitochondrial dysfunction in heart failure

In a mechanism similar to mitochondrial dysfunction in cancer, mitochondrial dysfunction has also been implicated in heart failure . The role of mitochondria in cardiac muscle is paramount due to its function as an organ of high-energy demand. Previously, studies on patients with chronic heart

disease revealed decreased ETC complex activity, and identified a non-pathological point mutation in the mtDNA-encoded