

**Apoptosis**

Referred to as programmed cell death, apoptosis involves a series of events resulting in cellular morphological changes and subsequent death, including cell shrinkage, blebbing, nuclear fragmentation, and chromatin condensation. One of its key features is that, unlike a necrotic cell, the cellular contents do not spill out due to phagocytic cells engulfing the apoptotic cell, which is a primary reason why apoptotic cell death does not result in inflammation.

**Carbohydrates**

These organic molecules contain only carbon, hydrogen, and oxygen, with the ratio of hydrogen to oxygen usually being 2:1. Important circulating carbohydrate energy sources for myocardial metabolism include glucose ( $C_6H_{12}O_6$ ) and lactate ( $C_3H_6O_3$ ).

**Electron transport chain**

This encompasses a series of five inner mitochondrial membrane protein complexes that allow electron transfer between electron donors (i.e., NADH/FADH<sub>2</sub>) and electron acceptors such as O<sub>2</sub> (these four protein complexes themselves act as both electron acceptors and then subsequent electron donors as they pass electrons to the following complex). The transfer of electrons between these complexes causes the transfer of protons from inside the mitochondrial matrix outside into the mitochondrial inner membrane space, which drives an electrochemical proton gradient used to drive ATP synthesis in the process of oxidative phosphorylation.

**Flip-flop mechanism**

This term describes the movement of fatty acid molecules across the phospholipid bilayer that comprises the cell membrane. Flip-flop involves reorientation of a fatty acid molecule such that the polar carboxyl moiety originally interacting with the lipid-aqueous interface of the external leaflet and the extracellular space subsequently interacts with the lipid-aqueous interface of the internal leaflet and cytosolic space. Following this reorientation, the fatty acid molecule can dissociate from the inner leaflet of the phospholipid bilayer and completely enter the aqueous cytosolic compartment.

**Glycolysis**

Glycolysis is the series of biochemical reactions occurring in the cytosolic compartment that converts a glucose molecule into two molecules of pyruvate. In the presence of oxygen (i.e., the aerobic setting), pyruvate is transported into the mitochondria, and undergoes oxidative decarboxylation yielding acetyl-CoA. In the absence of oxygen (i.e., the anaerobic setting), pyruvate is reduced to lactate by the enzyme lactate dehydrogenase, which generates NAD<sup>+</sup> required to maintain flux through glycolysis.

**Hibernating myocardium**

This state, in which segments of myocardium are viable but exhibit abnormalities in contractile function, is often observed in chronic ischemia.

**Phosphorylation**

Phosphorylation involves the addition of a phosphate ( $PO_4^{3-}$ ) to a protein/organic molecule via the action of enzymes known as kinases. Protein phosphorylation is one of the primary cellular mechanisms by which enzyme activity can be modified post-translationally.

**PPAR $\alpha$** 

Peroxisome proliferator activated receptor  $\alpha$  is a member of the ligand-activated nuclear hormone receptor superfamily. Fatty acids function as ligands for PPAR $\alpha$ , and fatty acid-bound PPAR $\alpha$  forms heterodimers with the retinoid X receptor. The PPAR-retinoid X receptor heterodimer can then translocate to the nucleus where it binds to PPAR response elements present in the promoter regions of target genes, including those involved in regulating fatty acid metabolism. PPAR $\alpha$  is predominantly expressed in tissues that exhibit a high capacity to oxidize fatty acids including the liver, skeletal muscle, and heart.

**Transporters**

These are integral membrane proteins involved in mediating the movement of molecules across the cell membrane. Facilitative transporters move molecules down a concentration gradient, while active transporters couple the hydrolysis of ATP to the movement of molecules against their concentration gradient. •