

Glossary

Gary Lopaschuk

Adenine nucleotide translocator and/or the voltage dependent anion channel

The adenine nucleotide translocator (ANT) is a mitochondrial membrane protein that carries ATP from the matrix into the inter-membrane space and transports ADP back. ANT is also a component of a mitochondrial voltage dependent anion channel. The ANT/voltage dependent anion channel can contribute to apoptosis via its capacity to become a lethal pore.

Cardiolipin

Cardiolipin is a glycerol lipid containing two phospholipids, and is an important and abundant lipid component of the inner mitochondrial membrane. Cardiolipin has an important function as a stabilizer of mitochondrial protein complexes important to the electron transport chain. Mutations in the biosynthesis of cardiolipin can result in Barth syndrome, a rare genetic disorder in which mitochondria are abnormal, and affected individuals cannot sustain adequate production of ATP. Cardiomyopathy and general weakness is common to these patients.

Catalase

Catalase is a common enzyme that functions to catalyze the decomposition of hydrogen peroxide to water and oxygen. Catalase is an important anti-oxidant enzyme that protects the cell from free radical injury.

Delayed rectifier channel (I_{Kr})

The human ether-a-go-go-related gene (hERG) encodes a channel that conducts the rapidly activating delayed rectifier K(+) current (I_{Kr}) which is important for cardiac repolarization. Mutations in hERG reduce I_{Kr} and cause congenital long QT syndrome (LQTS).

Electrogenic NCX (3Na⁺/2Ca²⁺)

The Na⁺/Ca²⁺ exchanger is a membrane ion transporter that exchanges Na⁺ for Ca²⁺.

Because the exchange involves 3 Na⁺ for 2 Ca²⁺, the current exchange is not equal, and therefore the exchange is considered electrogenic.

Fab

Antibodies are immune system-related proteins that consists of four polypeptides– two heavy chains and two light chains joined to form a “Y” shaped molecule. The amino acid sequence in the tips of the “Y” give the antibody its specificity for binding antigen. Treating the antibody with a protease cleaves this region, producing Fab or fragment antigen binding.

Glutathione S-transferase (GST)

Glutathione S-transferase (GST) is a cytosolic, mitochondrial, and microsomal protein that catalyses the conjugation of reduced glutathione via the sulfhydryl group, to electrophilic centres on a wide variety of substrates. GST can detoxify peroxidised lipids, and therefore acts as an anti-oxidant.

Glutathione peroxidase

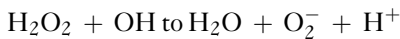
Glutathione peroxidase is a peroxidase found in cells that helps to prevent lipid peroxidation of the cell membrane. The function of glutathione peroxidase is to reduce lipid hydroperoxides to their corresponding alcohols and to reduce free hydrogen peroxide to water.

Gly671Val variant of MRP1 and with the Val1188Glu-Cys1515Tyr haplotype

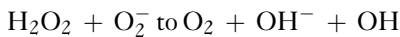
Anthracycline-induced cardiotoxicity (ACT) is a condition mainly presenting as arrhythmias or congestive heart failure. This cardiotoxicity can be associated with a mutation in multi drug resistance proteins (MRP1 or MRP2) responsible for doxorubicin transport. This can involve mutation in the MRP1 gene consisting of a Gly671Val variant and a mutation in the MRP2 gene involving a Val1188Glu-Cys1515Tyr haplotype. These genetic variants in doxorubicin transport increase an individual risk of developing ACT.

Haber-Weiss reaction

The Haber-Weiss reaction is a chemical reaction that can produce highly toxic hydroxyl (OH[•]) radicals. The reaction consists of the following two reactions:



and



This reaction is often catalyzed by iron, creating a source of oxidative stress in tissues. The second part of this reaction is a source of very toxic hydroxyl radicals.

Human ether-a-go-go related gene

A gene was discovered in *Drosophila* called the ether-a-go-go gene, since mutations in the gene caused the legs of the ether anesthetized *Drosophila* to shake. A human related ether-ago-go gene encodes a voltage-gated potassium channel. Abnormalities in this channel may lead to either Long QT syndrome (with loss of function mutations) or Short QT syndrome (with gain of function mutations). Both long and short QT syndromes can cause potentially fatal cardiac arrhythmia, due to repolarisation disturbances of the cardiac action potential.

(Na⁺/K⁺) Mg-ATPase (NKA)

Na/K-ATPase is an ion pump that is involved in the transport of ions across membranes. This ATPase pumps Na⁺ and K⁺ against their concentration gradient, and therefore energy is required, which is provided by the hydrolysis of ATP, the main energy currency in cells (hence the name ATPase). Na/K-ATPase pumps Na⁺ out of cells, while simultaneously pumping K⁺ into cells. In the heart this helps to re-establish ionic changes that occur during the action potential, in which Na⁺ flows into the heart cell, and K⁺ flows out of the heart cell.

Oxygen-derived free radicals

Oxygen-derived free radicals are usually either oxygen or hydroxyl groups that have an unpaired electron. These free radicals are unstable and react

with lipids, proteins, or DNA and RNA. This can result in tissue damage.

p53 pathway

P53 is a tumour suppressor protein that has the important function of inhibiting abnormal growth of cells. P53 helps to ensure genomic integrity and has important functions, such as DNA repair, promoting apoptosis, and inhibition of angiogenesis. p53 is a nuclear transcription factor that binds to defined consensus sites within DNA as a tetramer and affects the transcription of its target genes. Activation of p53 results in translocation of the protein to the nucleus where it induces transcriptional changes in proteins that prevent cell division and cause apoptosis.

Redox activation

A chemical reactions in which atoms have their oxidation number (oxidation state) changed is considered a redox reaction (shorthand for oxidation/reduction reaction). Oxidation describes the loss of electrons by a molecule, while reduction describes the gain of electrons by a molecule. This can involve simple molecules such as carbon or complex molecules. If a molecule is undergoing reduction/oxidation the process is often called redox activation.

Superoxide dismutase (SOD)

Superoxide is a free radical, that is an oxygen molecule that has an unpaired electron. This molecule can react with lipids, proteins, DNA, and RNA, causing tissue damage. Superoxide dismutase is an enzyme that “detoxifies” superoxide by converting superoxide radicals to hydrogen peroxide.

Xenobiotics

A xenobiotic is a chemical which is found in an organism but which is not normally produced or expected to be present in it. An example of a xenobiotic are antibiotics drugs because the human body does not produce them. The term xenobiotic can also refer to organs transplanted from one species to another.