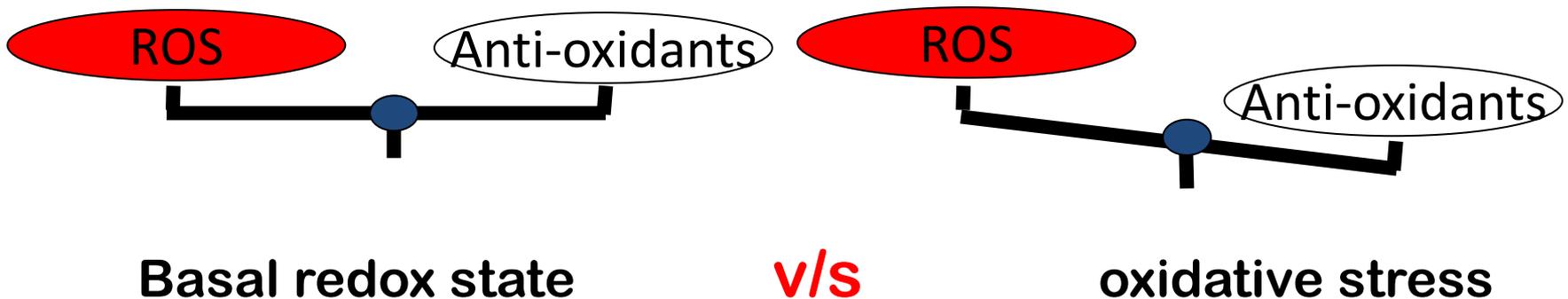


Significance of the Redox Environment

- Role of mitochondria
- Activation of oxidases
- Induction of nitric oxide synthases
- $\uparrow\downarrow$ Antioxidants



John Seawright's discussion of Azzam's slide -

The mitochondria are typically referred to as "the powerhouse of the cell." Mitochondria are used by eukaryotic cells to produce the cellular currency, ATP, by passing electrons across the electrical transport chain (ETC). Some electrons may "leak" out of the mitochondrial ETC and reduce oxygen molecules to the reactive oxygen species (ROS), superoxide, (O_2^-). O_2^- may then diffuse throughout the cell and react with other molecules in the cell, damaging their associated proteins or DNA. Mitochondrial produced superoxide augments the superoxide produced by the hydrolysis of water that accompanies ionizing radiation exposure.

The cell contains oxidase proteins labeled Superoxide Dismutases (antioxidants) that are responsible for removing superoxide from the cell. Superoxide is converted into less reactive hydrogen peroxide and then eventually water. The cell also contains nitric oxide synthase, (NOS), an enzyme responsible for producing the signaling molecule, nitric oxide (NO).

McKinney 1998, showed that ionizing radiation can induce nitric oxide synthase to produce NO.

The balance between superoxide and nitric oxide is important when considering the redox state of the cell. Increases in nitric oxide are important for cell signaling and have been proposed as a molecule responsible for bystander or non-targeted effects, where non-irradiated cells show evidence of radiation-induced damage similar to irradiated cells in their environment. Superoxide can degrade nitric oxide, producing peroxynitrite. In addition to reducing the amount of nitric oxide available in the cell, peroxynitrite is also a reactive molecule that nitrosylates proteins in the cell also damaging them and impairing their function. An abundance of superoxide in the cell shifts the redox balance in favor of oxidative stress following ionizing radiation exposure.