

SUMMARY OF REACTIVE OXYGEN SPECIES (ROS) AND THE ROLE OF VITAMIN E:

- 1) Our metabolism is based on the movement of electrons (e^-). O_2 accepts 4 e^- in the electron transport chain to become 2 H_2O , allowing for the formation ATP.
- 2) Sometimes O_2 will “accept” single electrons (e^-) to form free radicals.
- 3) When O_2 accepts 1 e^- it becomes a superoxide radical ($O_2^{\cdot-}$), which is not reactive enough to directly attack cellular structures. This e^- comes from a leaky electron transport chain.
- 4) $O_2^{\cdot-}$ is reduced by superoxide dismutases (which uses either Cu^+ or Zn^{2+} as electron donors) to form hydrogen peroxide (H_2O_2). While producing H_2O_2 may seem like a bad idea, it is a step in the right direction to reduce the number of modestly reactive radicals in a cell.
- 5) H_2O_2 can be detoxified by glutathione peroxidase (GSH Peroxidase), which adds 2 e^- from 2 glutathione (GSH) molecules, producing 2 H_2O and the oxidized dimer, GSSG. GSH is regenerated from GSSG by glutathione reductase through the transfer of 2 e^- from NADPH (remember, NADPH is created by the pentose phosphate pathway and requires niacin).
- 6) If not detoxified, H_2O_2 can receive 1 e^- from either reduced iron (Fe^{2+}) or another e^- from the leaky electron transport chain to form a hydroxyl radical ($\cdot OH$), which is extremely reactive.
- 7) $\cdot OH$ is the real bad guy, and will damage proteins, DNA and lipids.
- 8) Lipid peroxidation is INITIATED by $\cdot OH$ grabbing a H^+ (with 1 e^-) from a PUFA in the plasma membrane.
- 9) The resulting PUFA free radical reacts with O_2 to form the PUFA peroxy radical.
- 10) The PUFA peroxy radical grabs a H^+ from a neighboring PUFA, leading to a destructive chain reaction (PROPAGATION) that can end up peroxidizing all of the PUFAs in the membrane. The PUFA peroxy radical that grabbed the H^+ is converted into a PUFA hydroperoxide, while the PUFA that lost its H^+ is now a PUFA free radical. And the vicious cycle begins.
- 11) However, tocopherol (Vitamin E) can sacrifice itself by donating an e^- . This still forms a PUFA hydroperoxide, but it **BREAKS THE VICIOUS CYCLE** and prevents extensive membrane peroxidation. The tocopherol radical can dimerize and leave the body through bile, or be converted to a quinone and leave through urine. There is test tube evidence that Vitamin E could be regenerated by Vitamin C.
- 12) Note that the PUFA hydroperoxide still needs to be dealt with by the cell. FA Peroxidase transfers electrons from 2 GSH to convert the PUFA hydroperoxide into a PUFA alcohol. The PUFA alcohol is harmless. If this doesn't happen, the PUFA hydroperoxide will be broken down into toxic short chain aldehydes that are toxic to a cell. So it's important to remember that the FA peroxidase is also critical to prevent cell death.