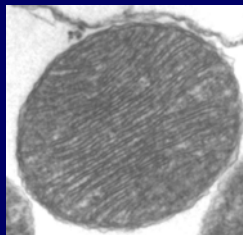


Mitochondrial ROS: Integrators of Protective and Pathologic Cell Signaling

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Mitochondrial Reactive Oxygen Species Formation

Loschen G, Flohe L, Chance B.

Respiratory chain linked H_2O_2 production in pigeon heart mitochondria.

FEBS Lett., 1971 18:261-264.

(Effects of different respiratory states)

Boveris A, Chance B.

The mitochondrial generation of hydrogen peroxide. General properties and effect of hyperbaric oxygen.

Biochem. J., 1973 134:707-716.

(Effects of respiratory inhibitors rotenone and antimycin)

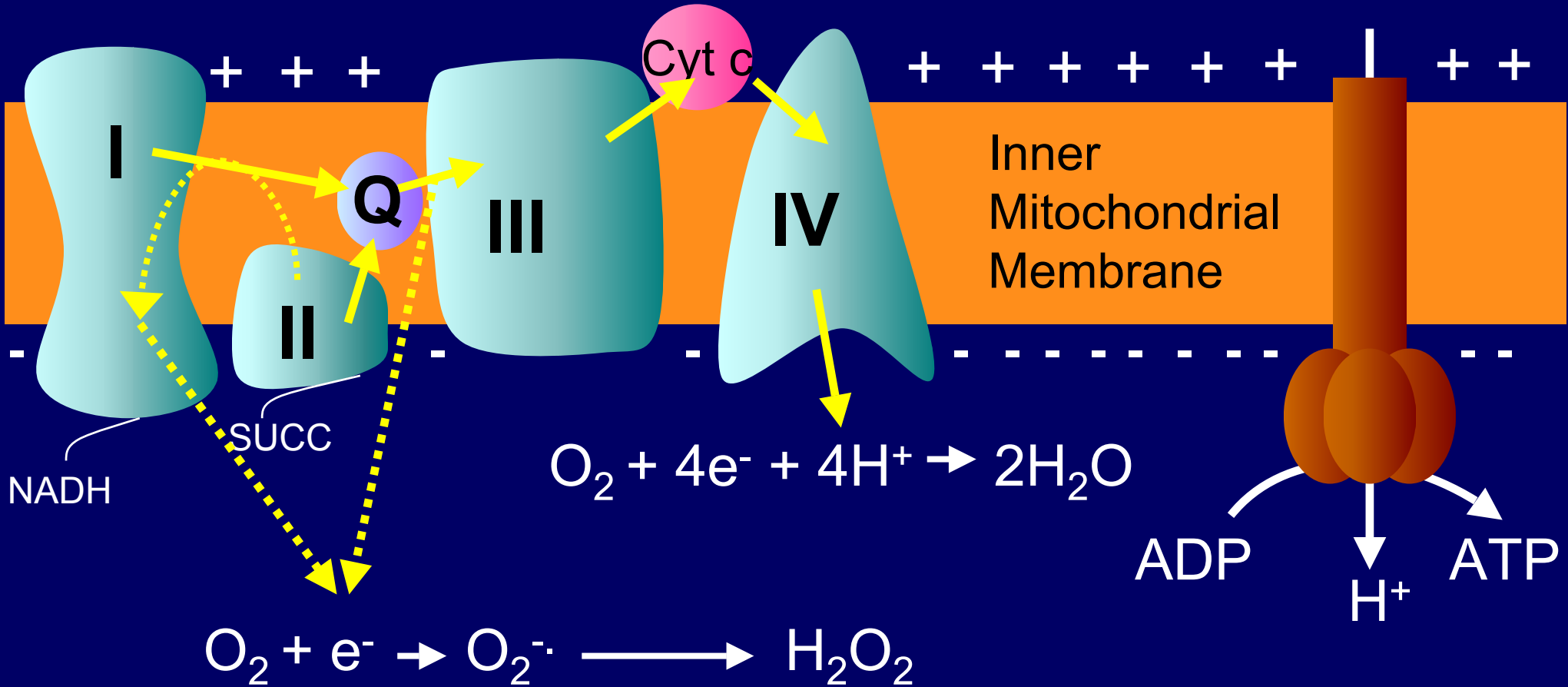
Dionisi O, Galeotti T, Terranova T, Azzi A.

Superoxide radicals and hydrogen peroxide formation in mitochondria from normal and neoplastic tissues.

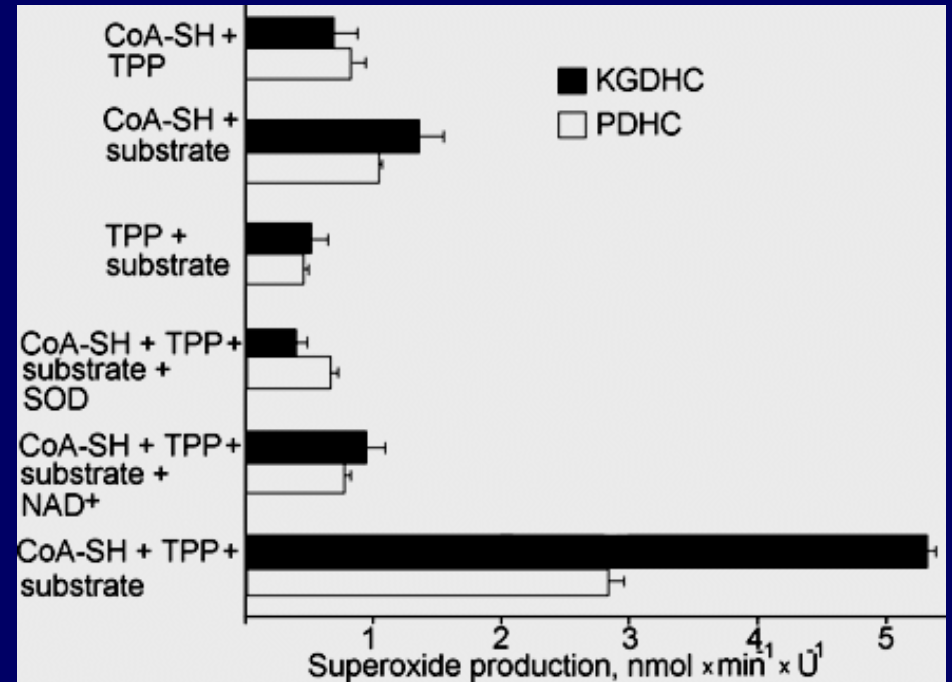
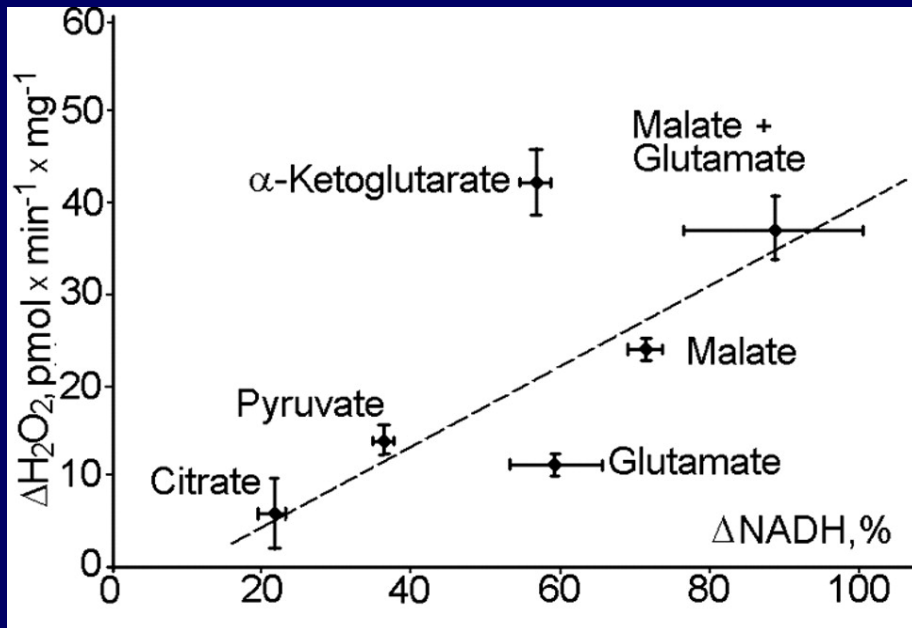
Biochim. Biophys. Acta 1975 403:292-300.

(Detection of superoxide radicals)

Electron Transport, OxPhos and ROS

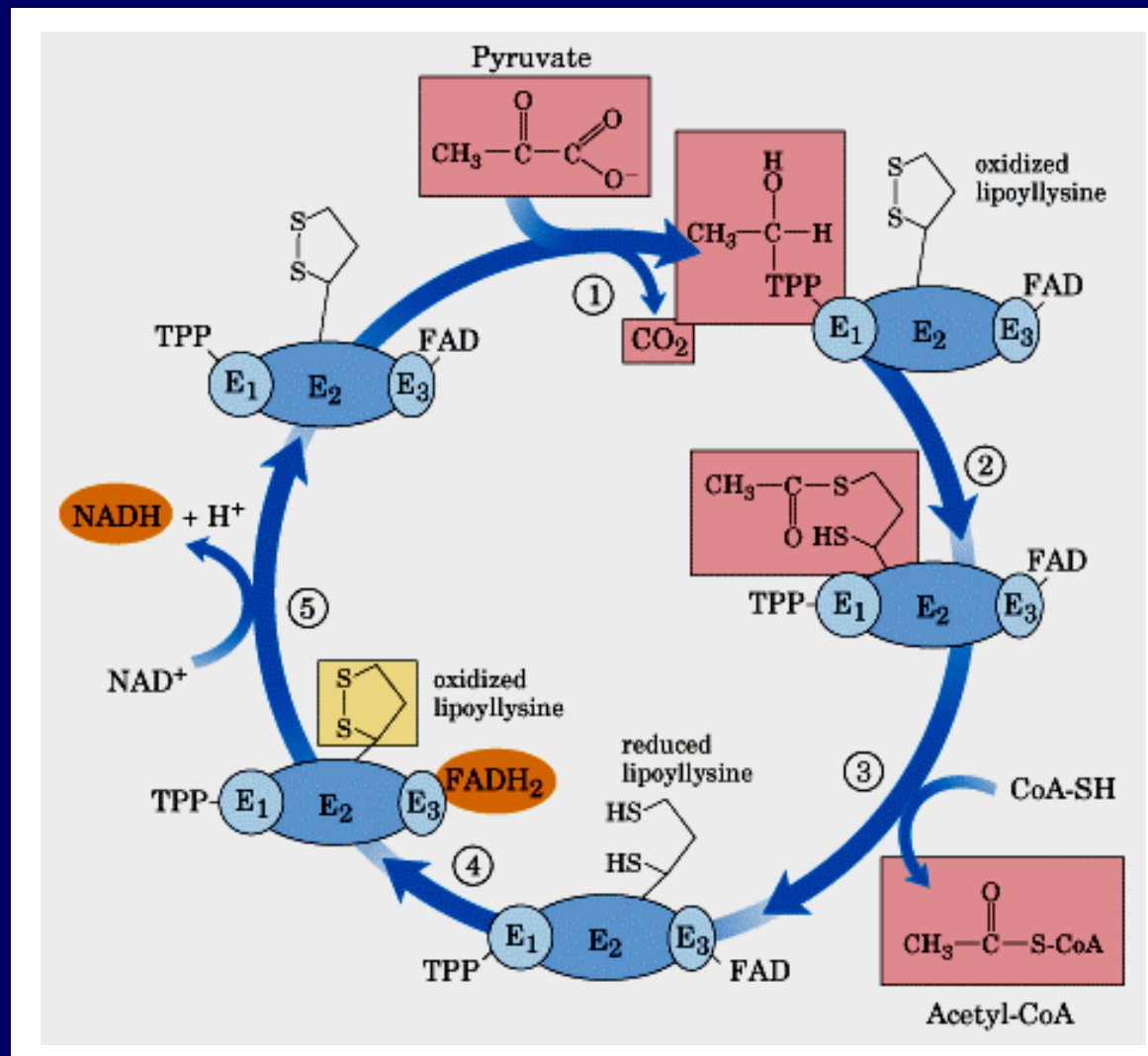


α -KG Dehydrogenase Generates ROS

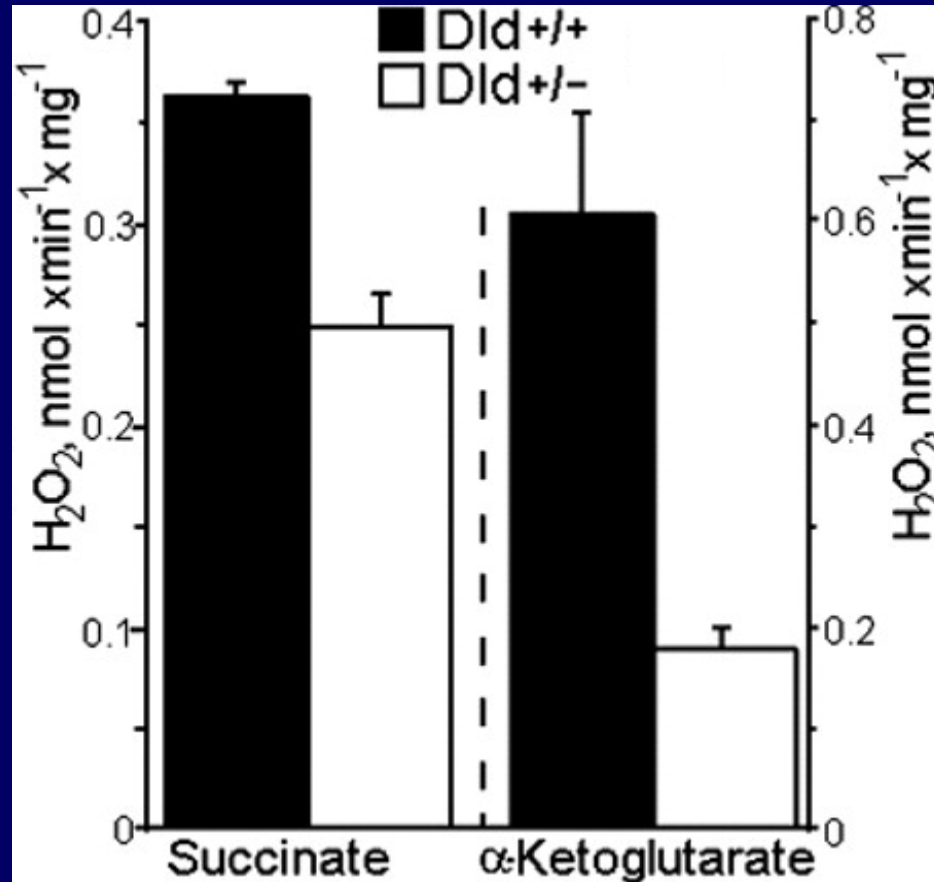


Tretter and Adam-Vizi J. Neurosci. 2004, 24:7771-7778.
 Starkov et al. J. Neurosci. 2004, 24:7779-7788.

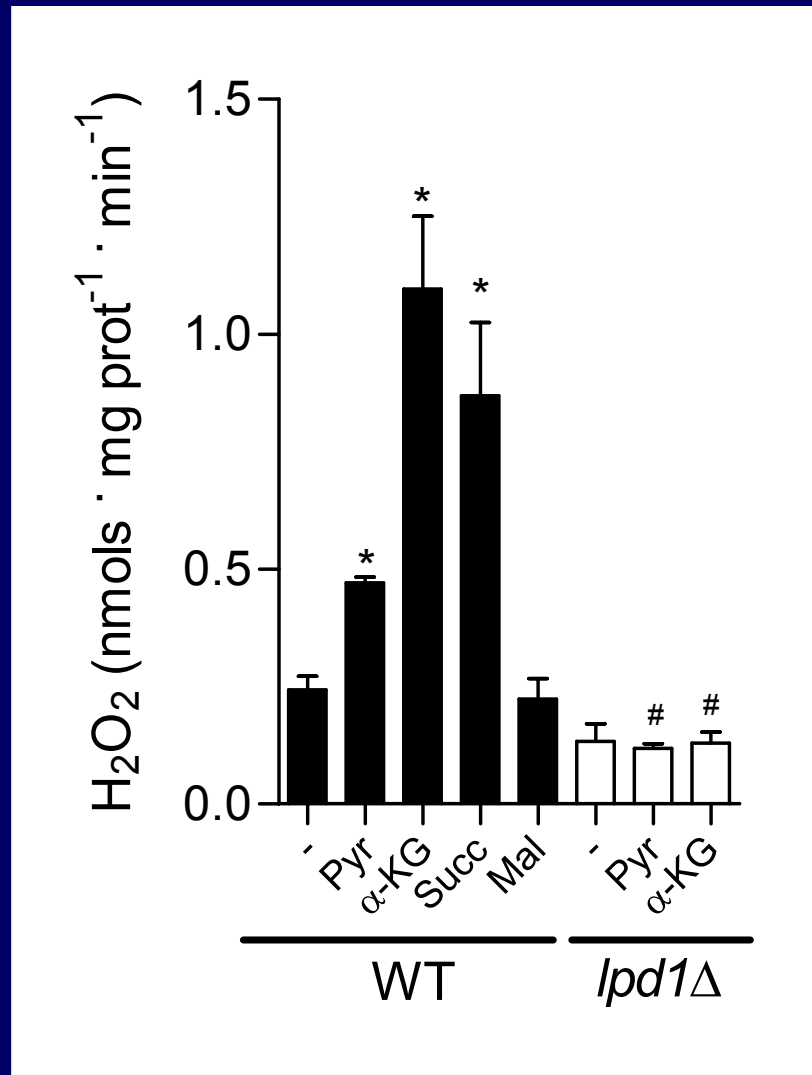
Dihydrolipoyl Dehydrogenase Generates ROS



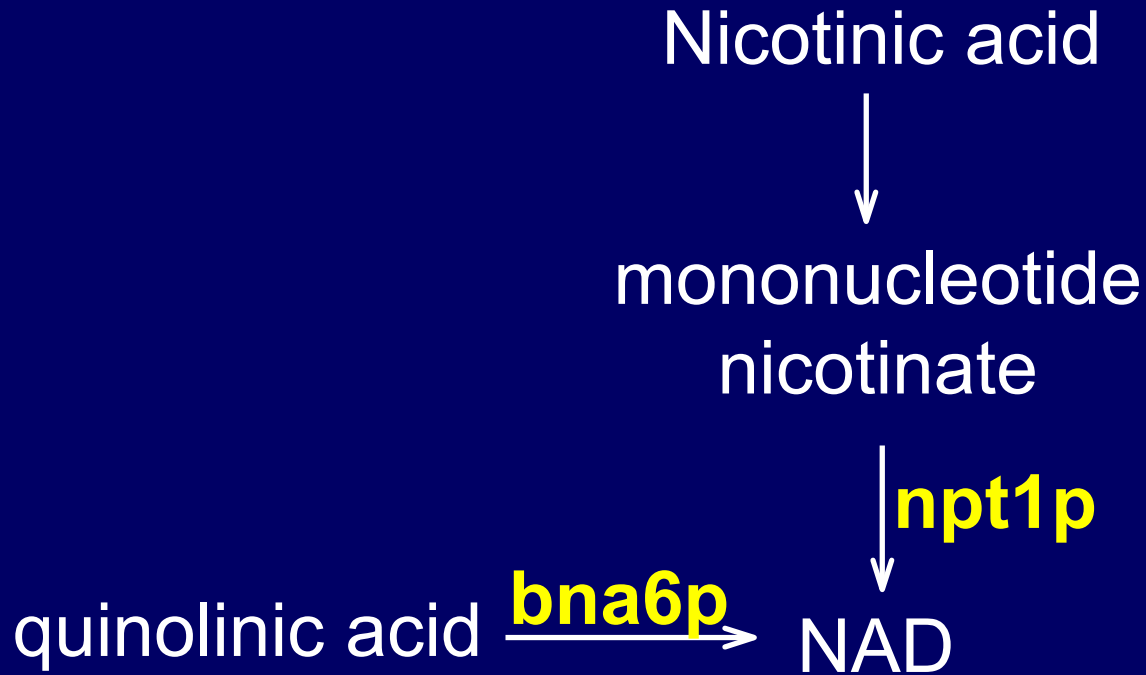
α -KG Dehydrogenase Generates ROS



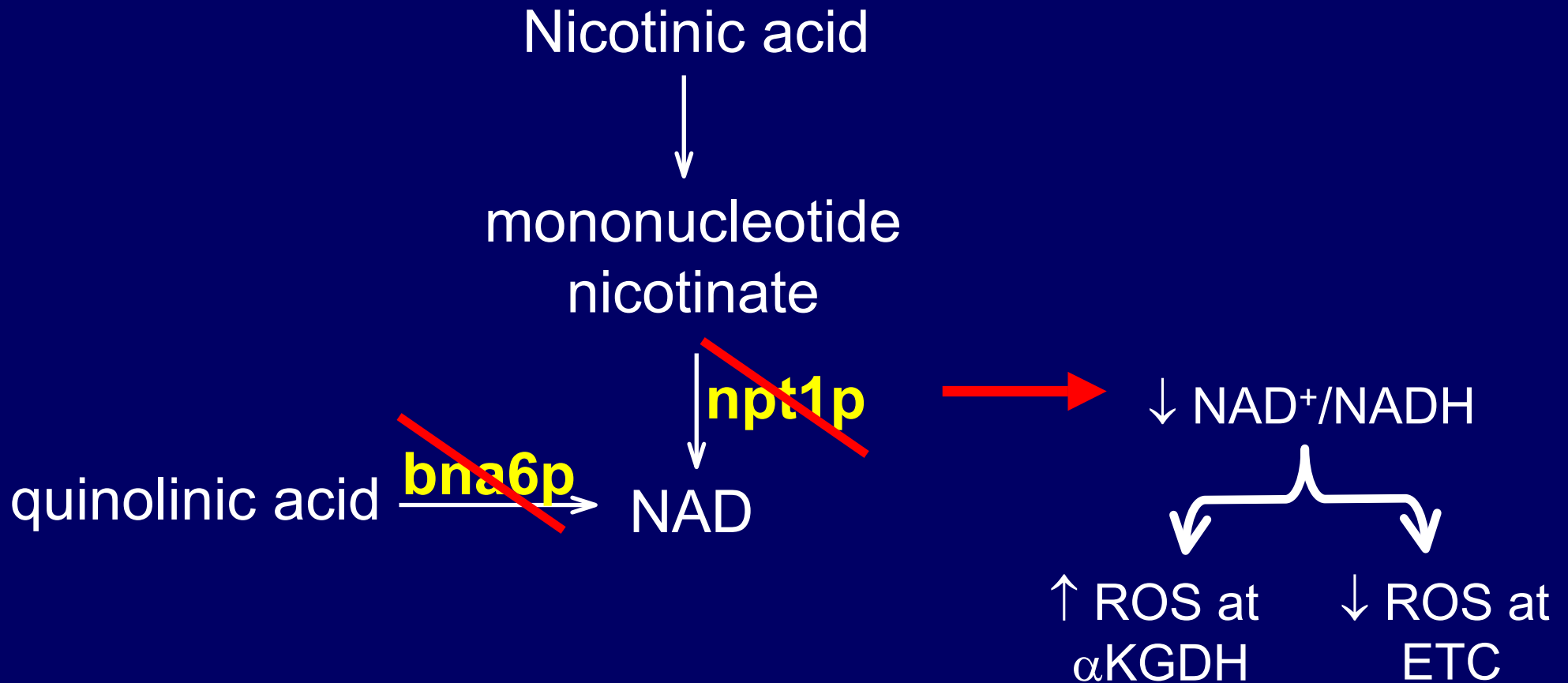
Matrix Dehydrogenases Generate ROS



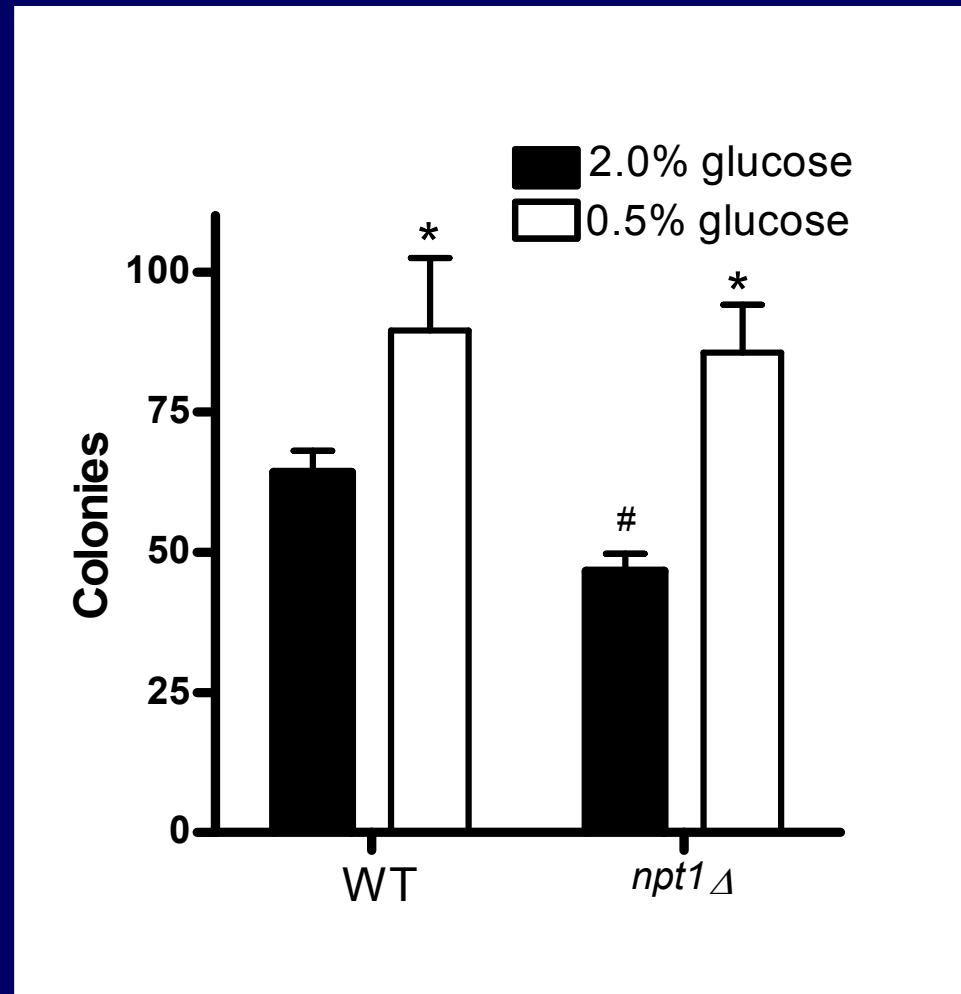
NAD⁺ Metabolism in *S. cerevisiae*



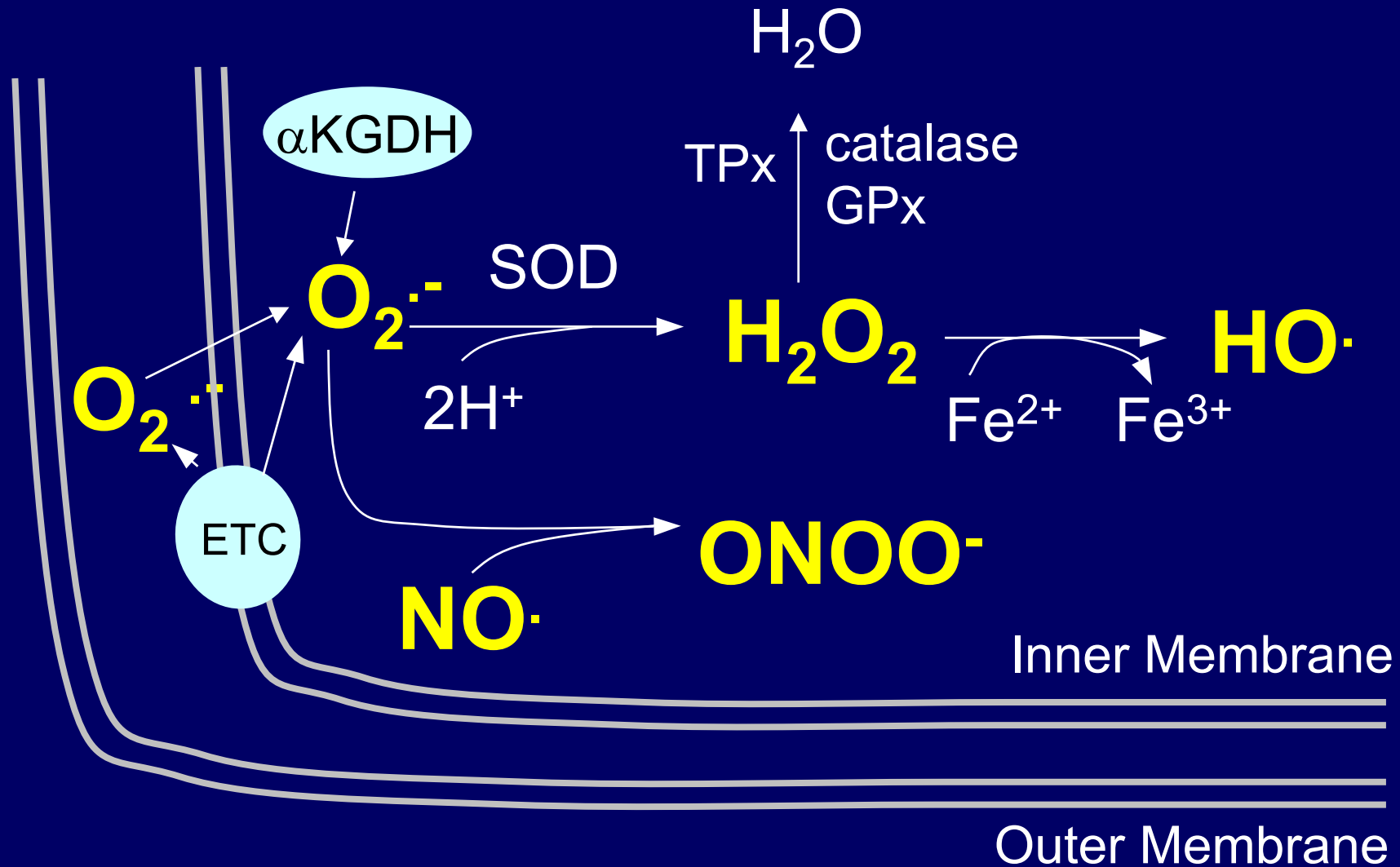
NAD⁺ Metabolism in *S. cerevisiae*



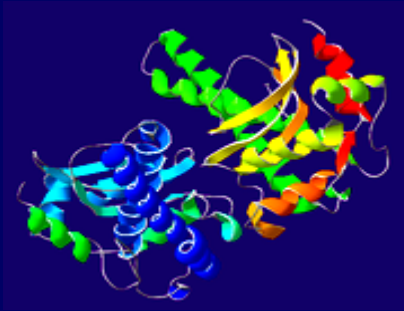
Matrix Dehydrogenase ROS Limit Life Span



ROS Detected in Mitochondria



Mitochondrial SODs



1969 - McCord and Fridovich characterize SOD

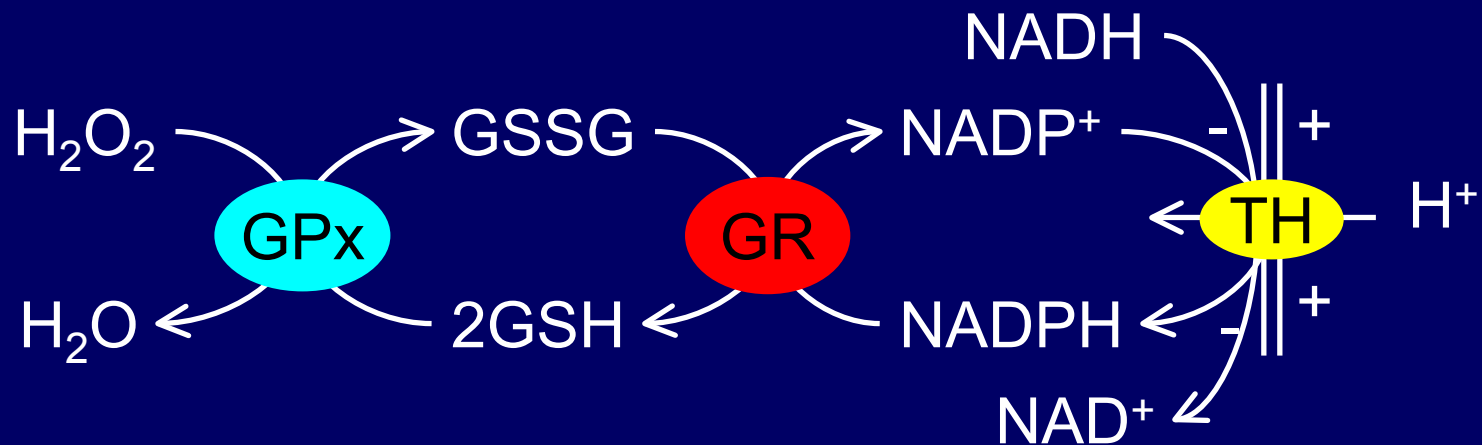
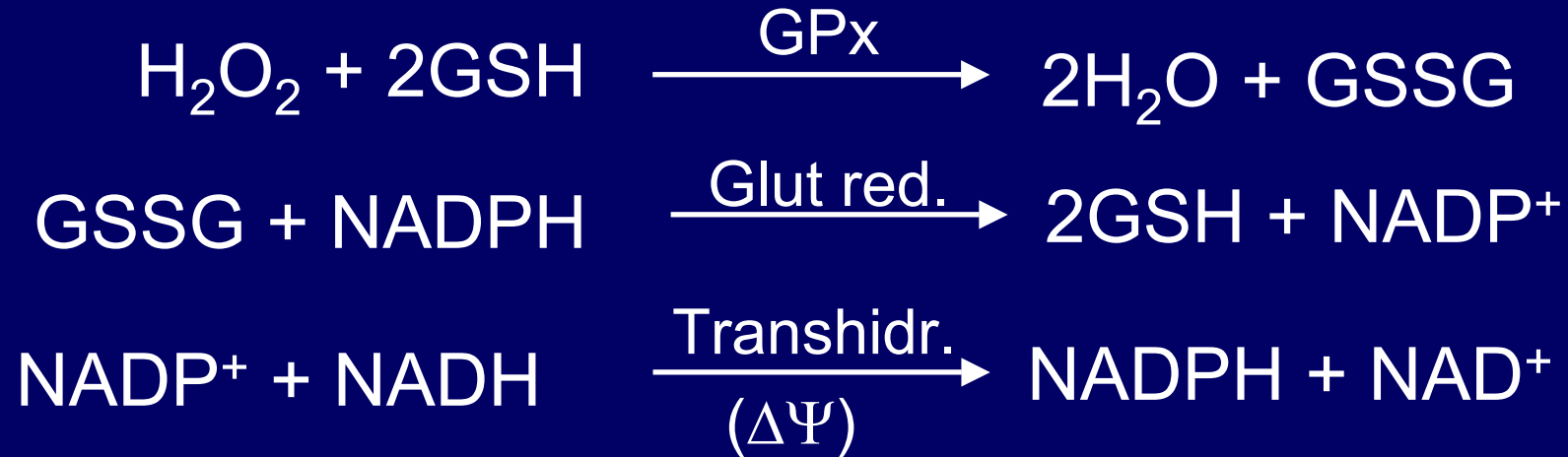


- MnSOD in the matrix, CuZnSOD in the intermembrane space
- Mutant MnSOD (-/-) animals do not survive (MnTBAP)

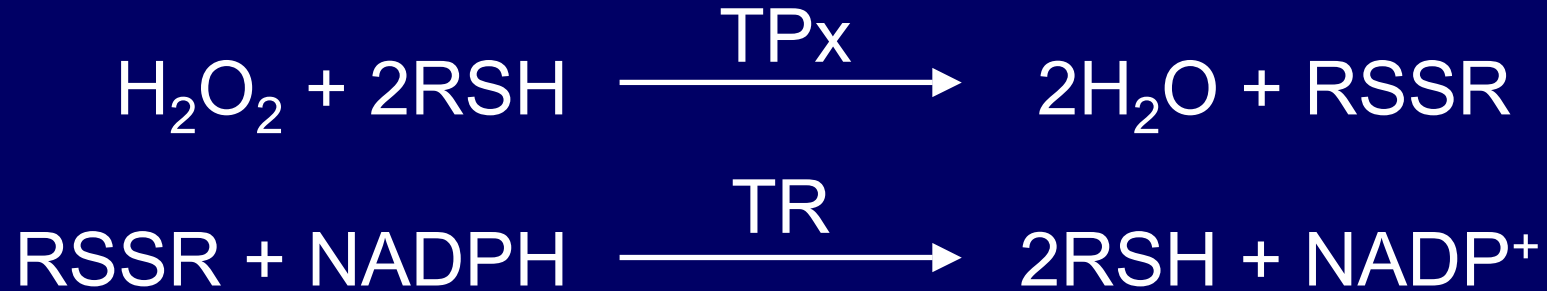
Weisiger and Fridovich J. Biol. Chem. 1973, 248:4793-4796.
Sturtz et al J. Biol. Chem. 2001, 276:38084-38089.

Okado-Matsumoto and Fridovich J. Biol. Chem. 2001, 276:38388-38393

Glutathione Peroxidase/Reductase System



Thioredoxin Peroxidase/Reductase System

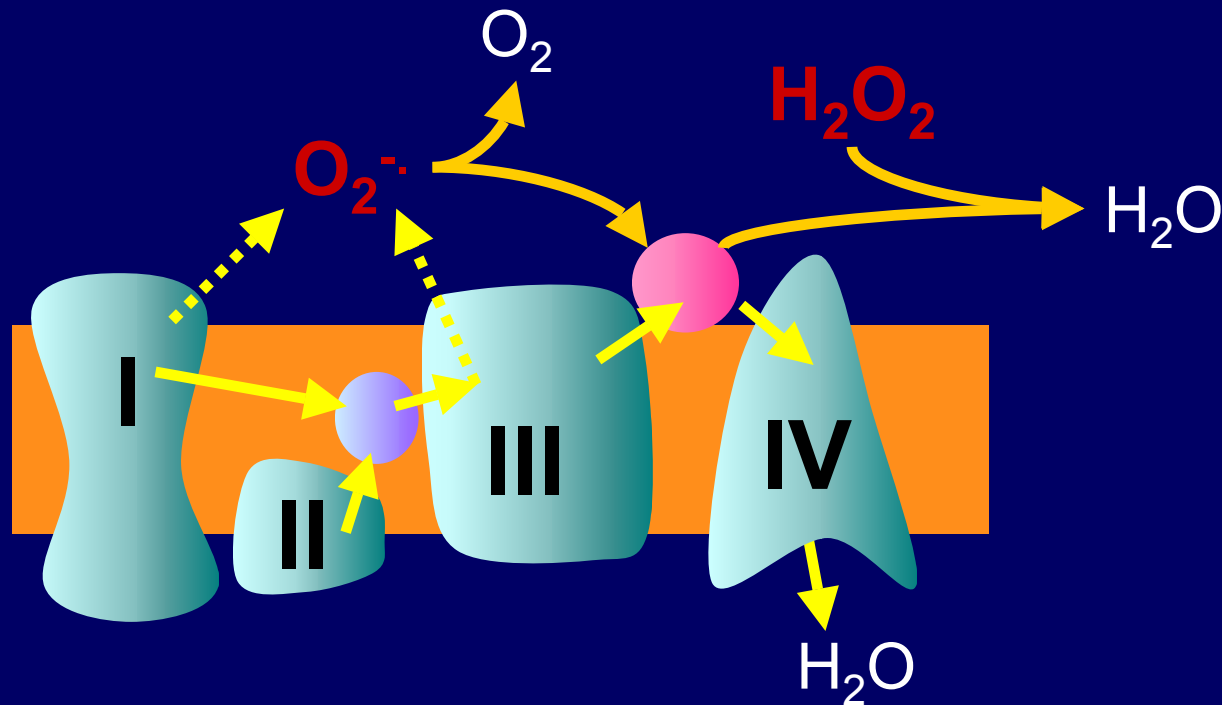


Watabe et al. Eur. J. Biochem. 1997, 249:52-60.

Catalase



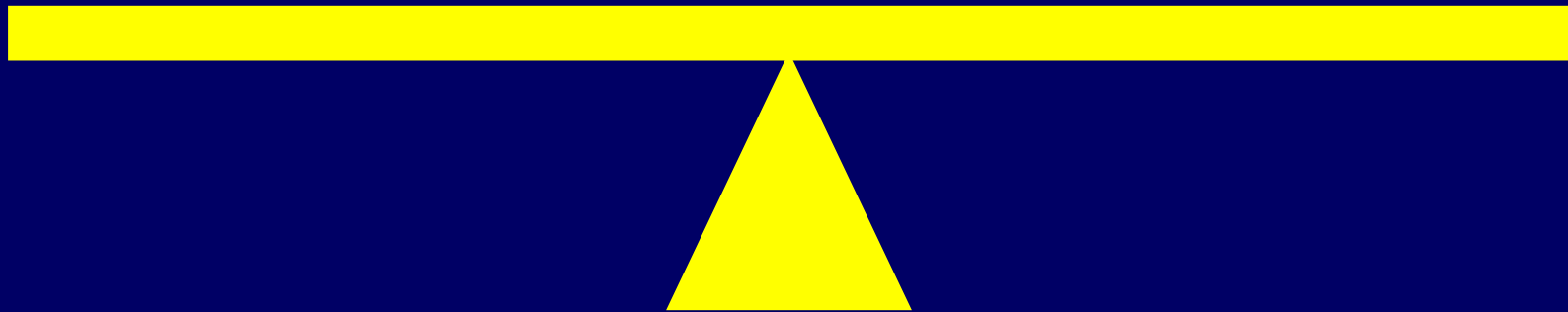
Cytochrome c



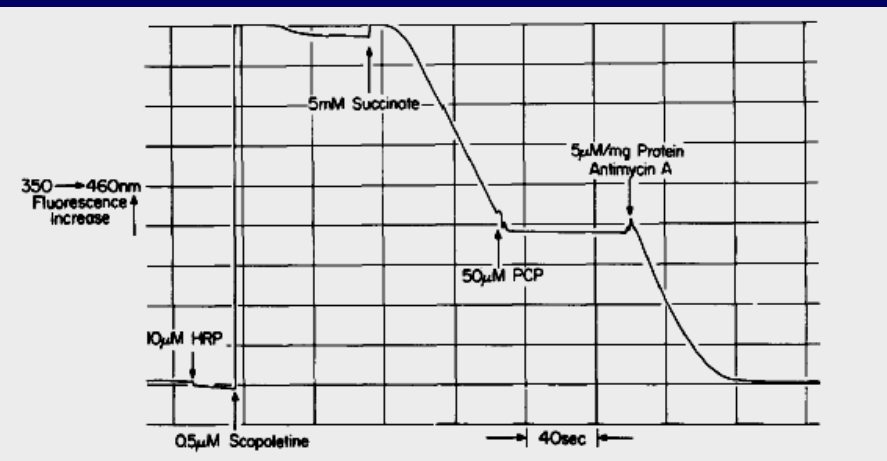
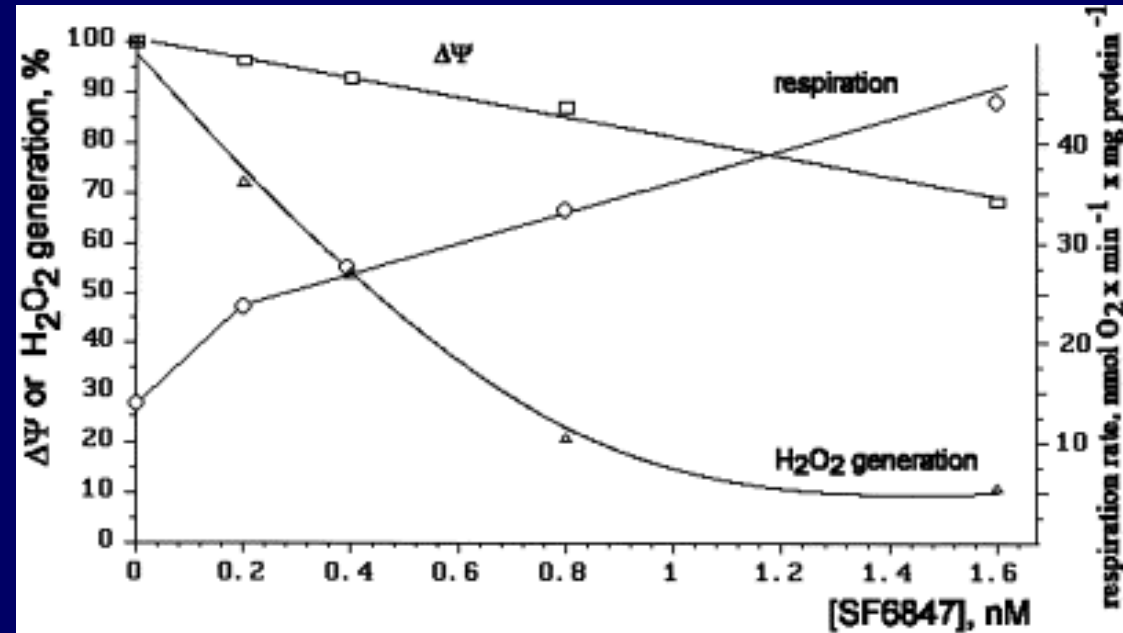
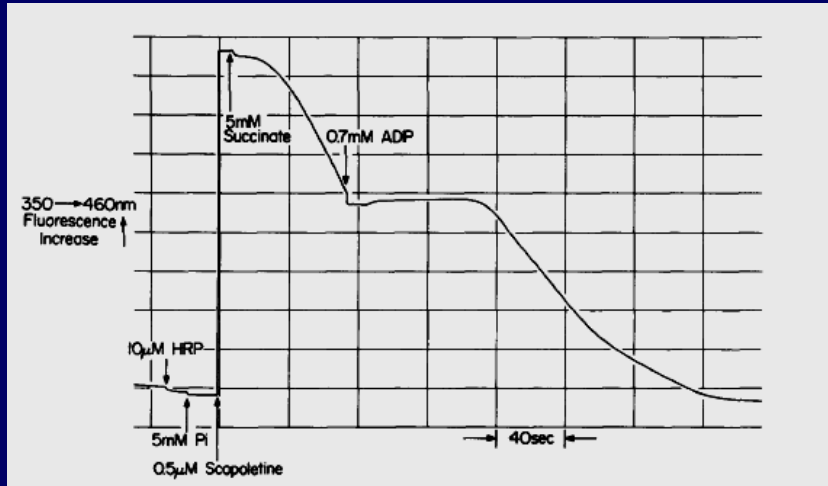
Redox Balance

ROS

Antioxidants



Mild Uncoupling Decreases ROS Release



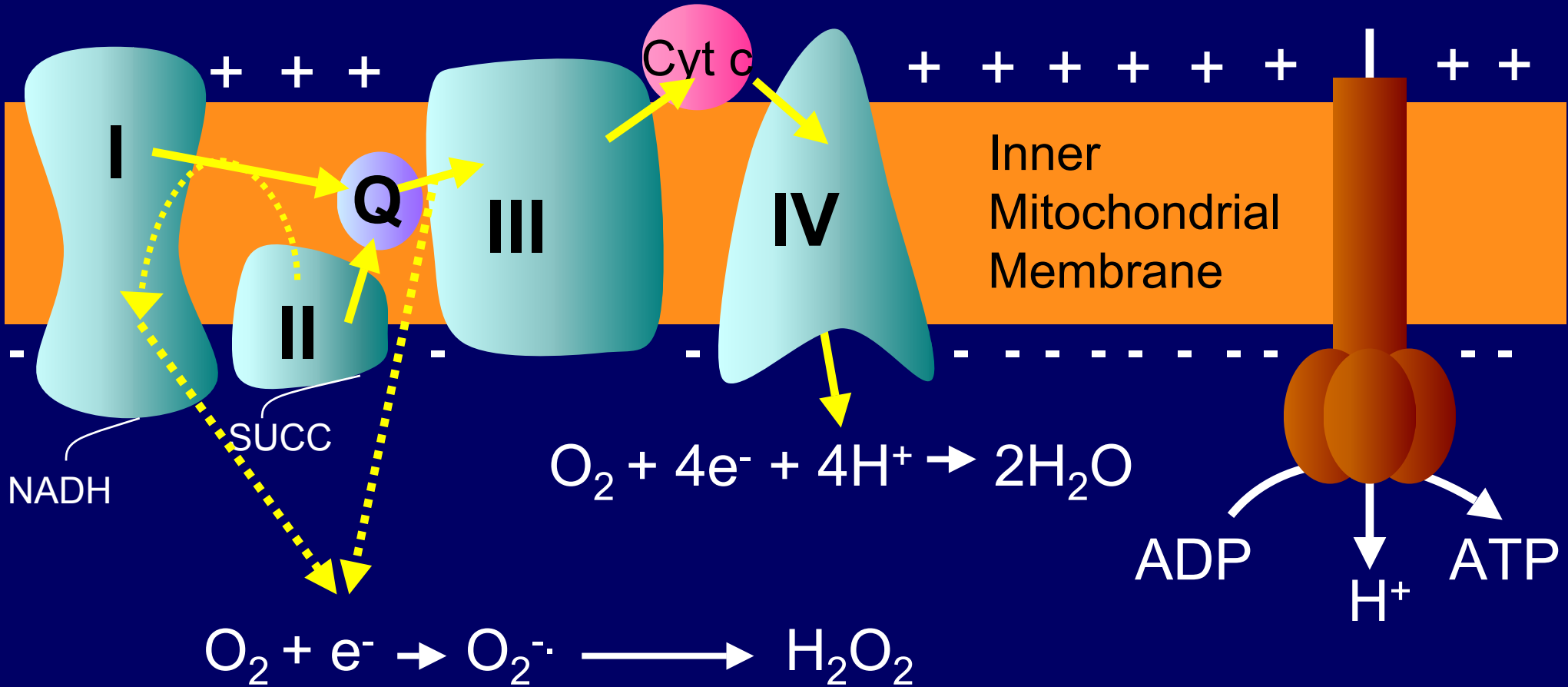
Loschen et al. FEBS Lett. 1971, 18:261-264.

Korshunov et al. FEBS Lett. 1997, 416:15-18.

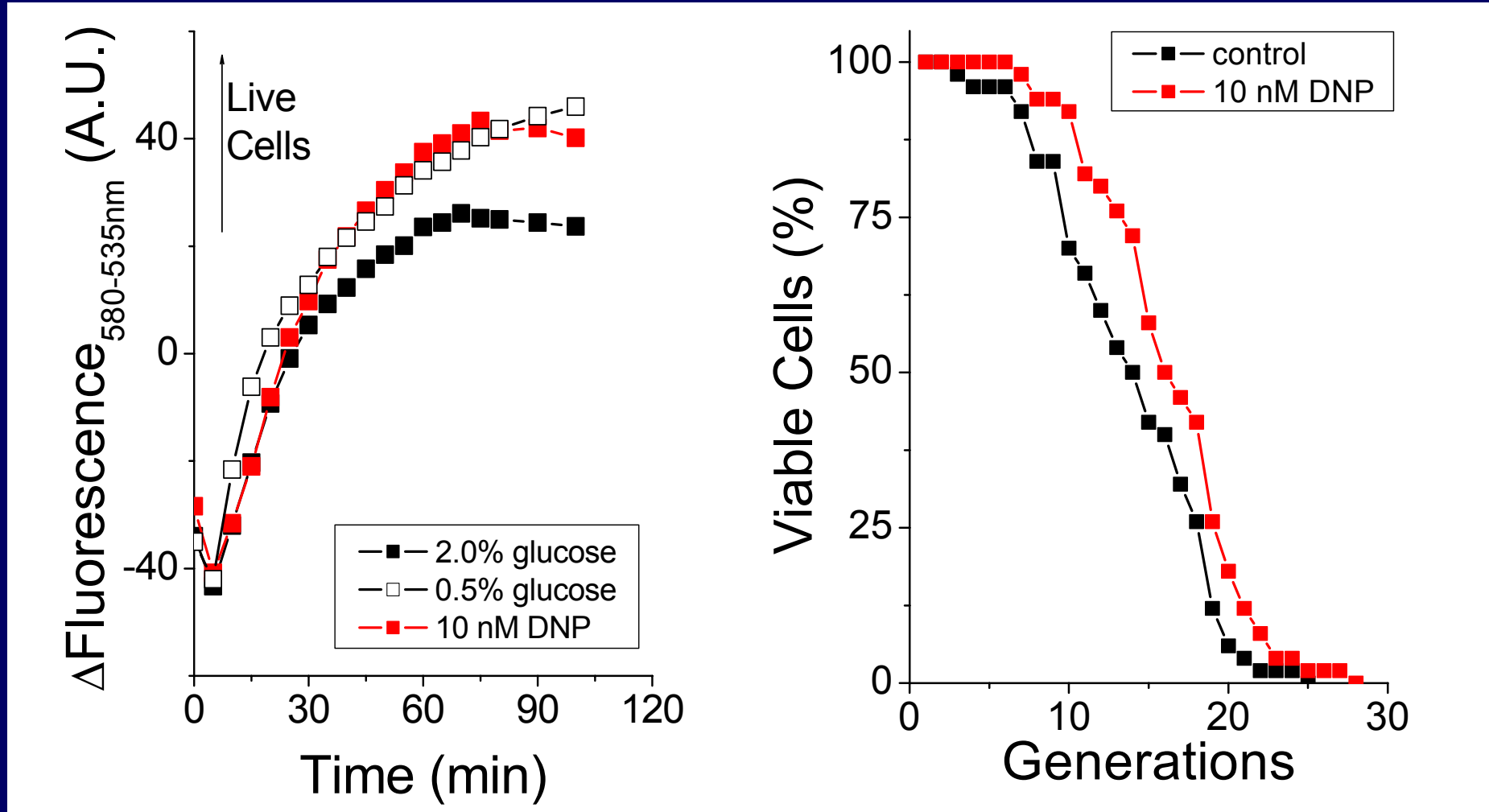
SFRBM 2006

Sunrise Free Radical School

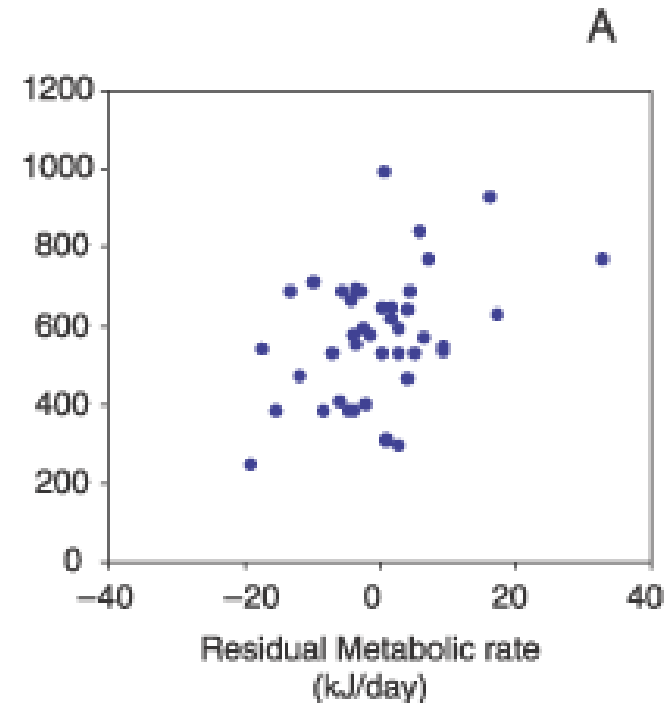
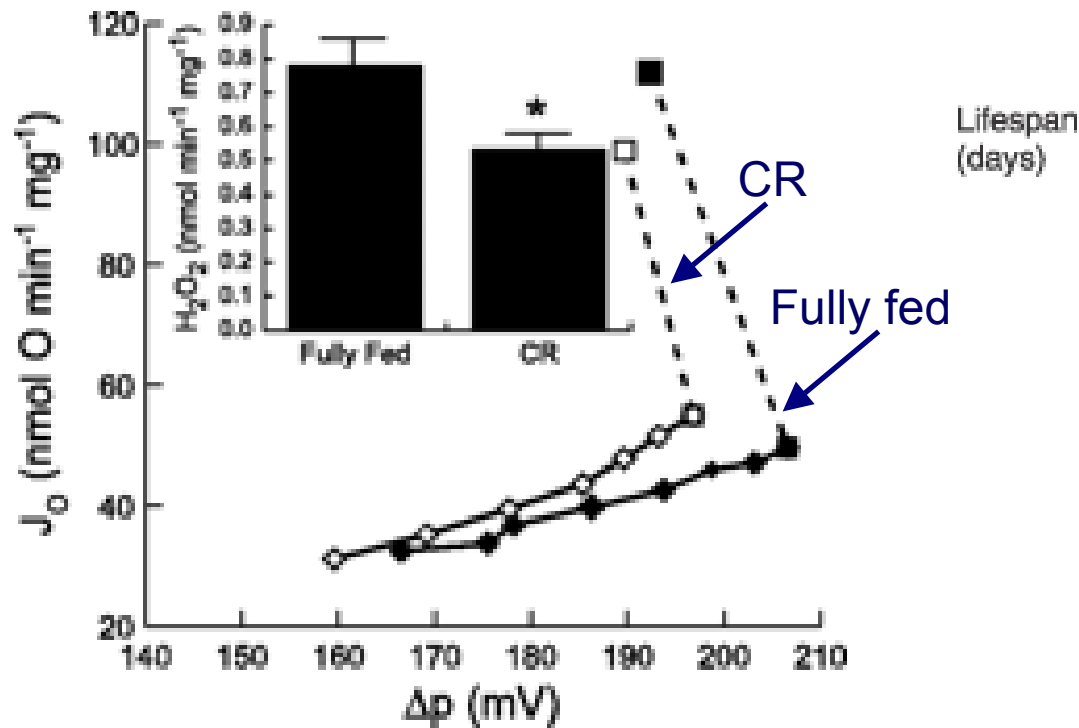
Electron Transport, OxPhos and ROS



Uncoupling Enhances Lifespan



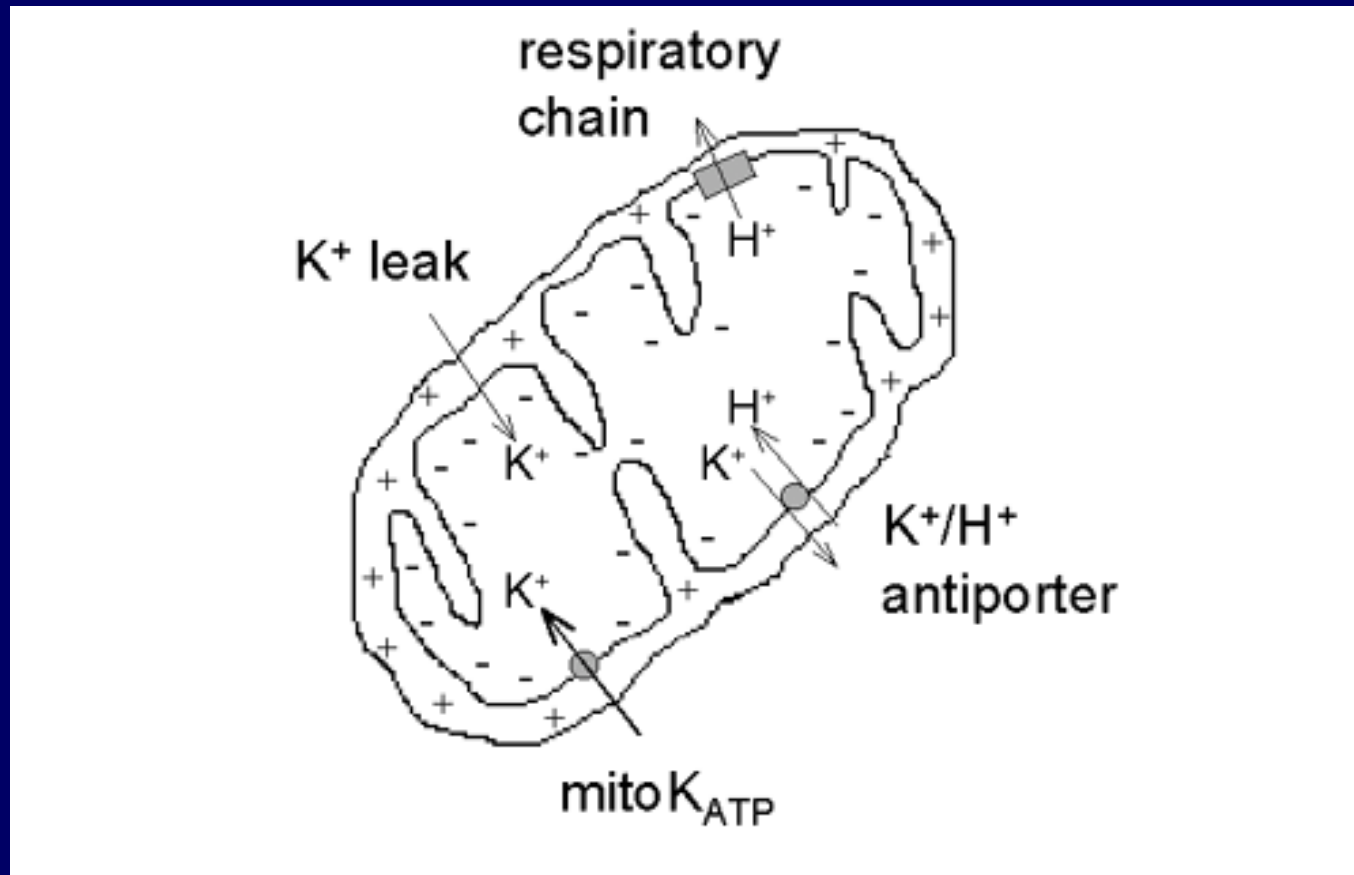
Uncoupling Enhances Lifespan



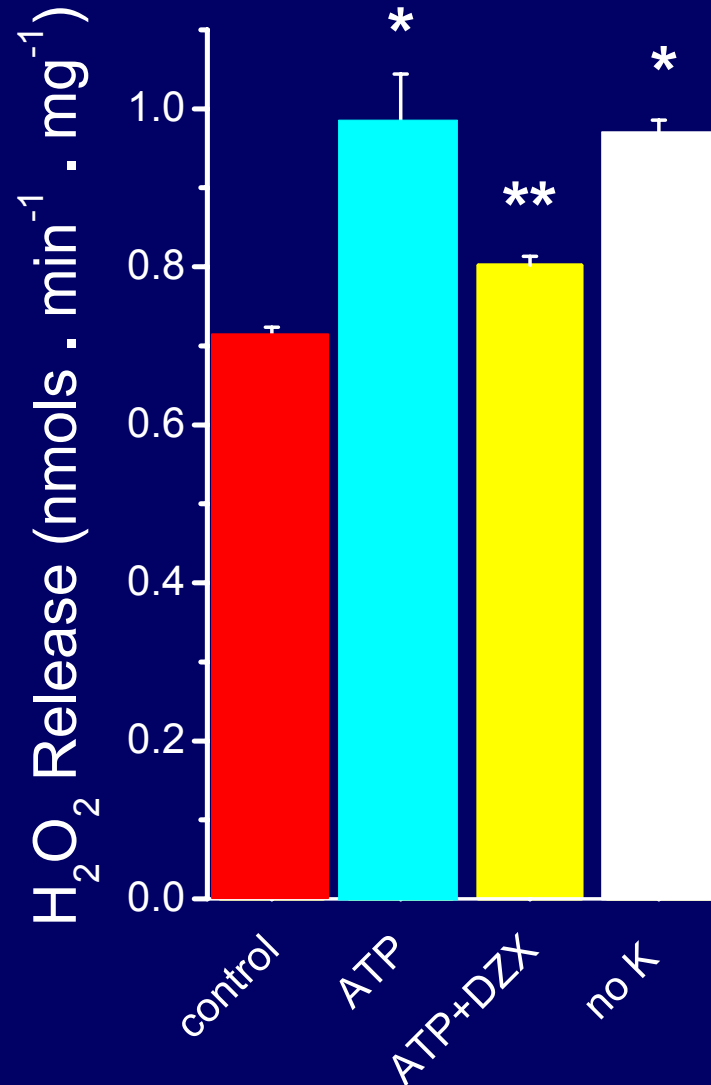
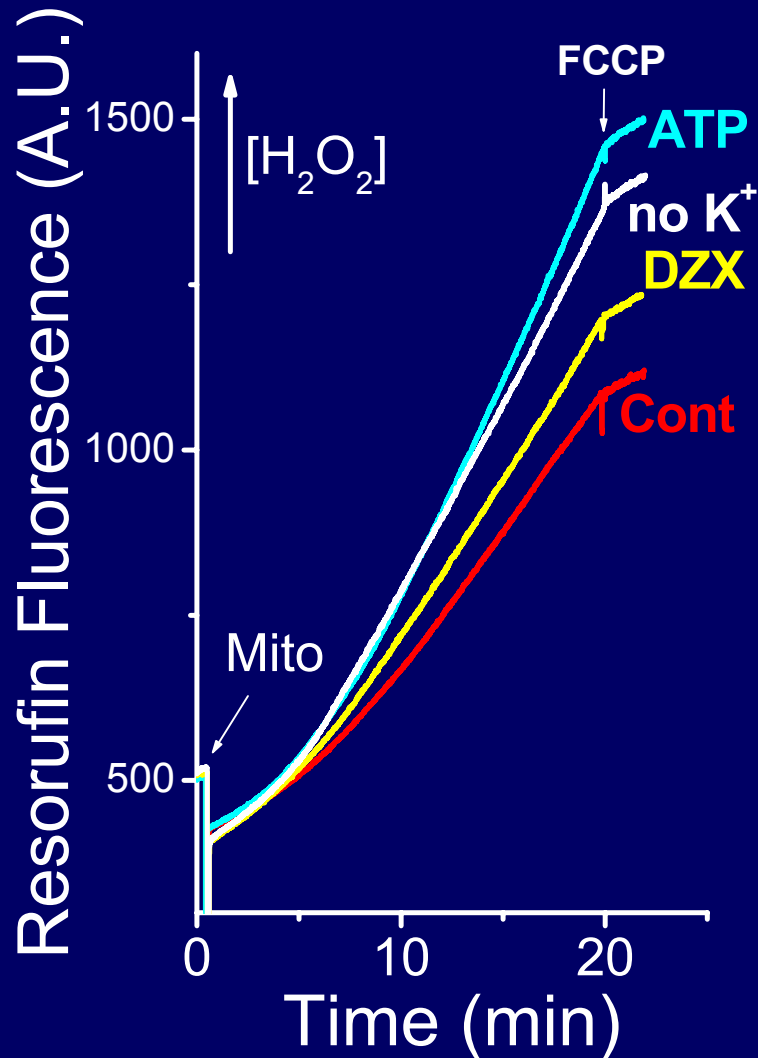
Lambert and Merry
Am J Physiol 2004 286:R71-9

Speakman JR et al.
Aging Cell 2004 3:87-95.

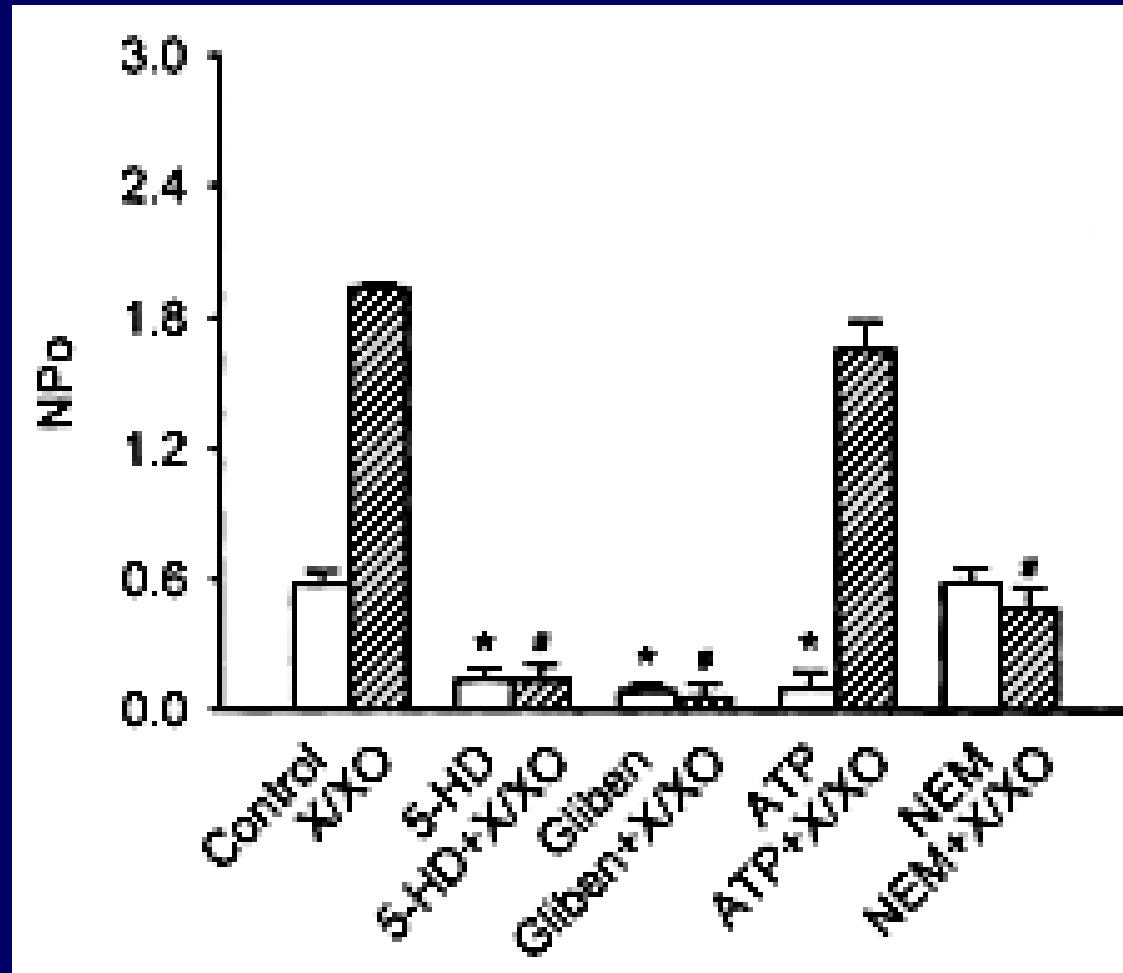
MitoK_{ATP} Promotes Mild Uncoupling



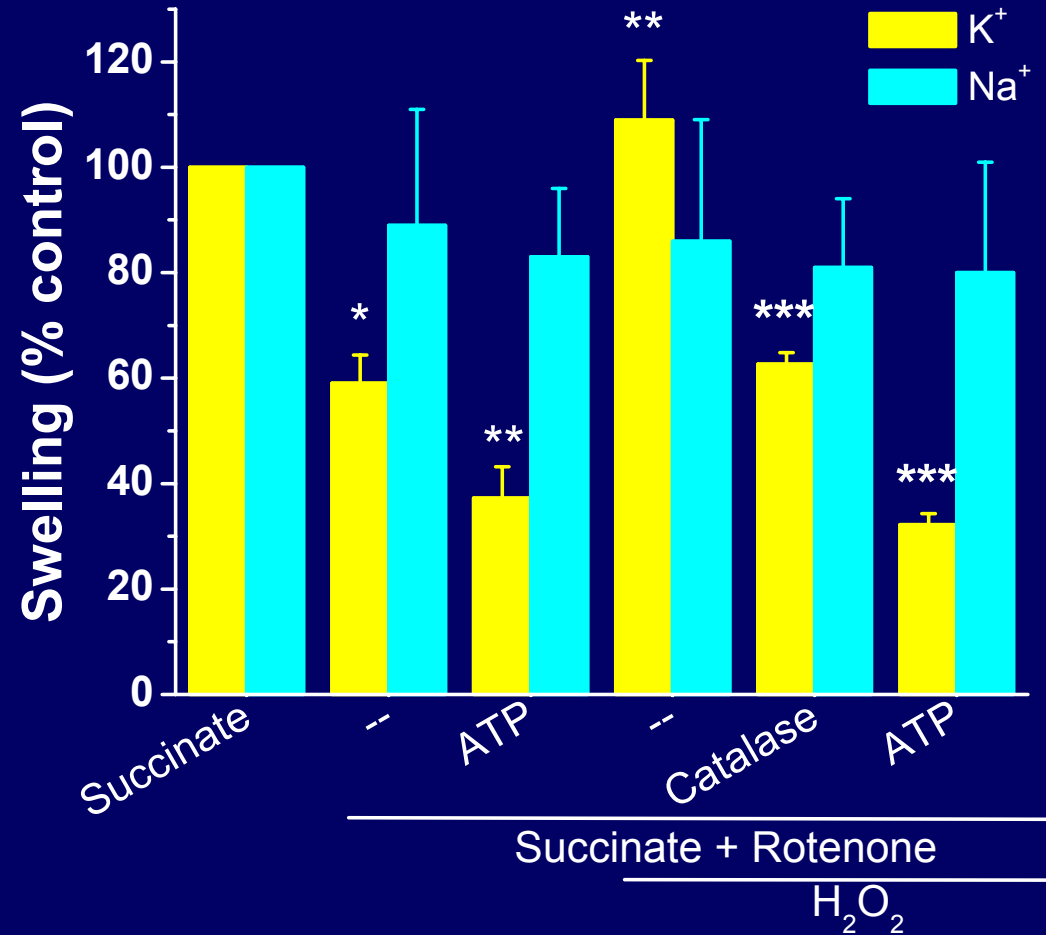
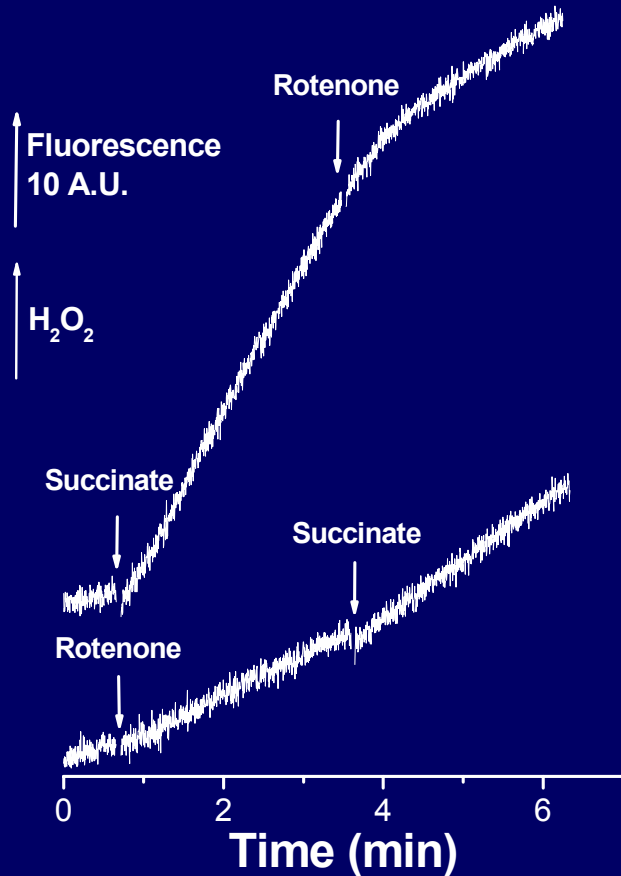
MitoK_{ATP} Decreases ROS Release



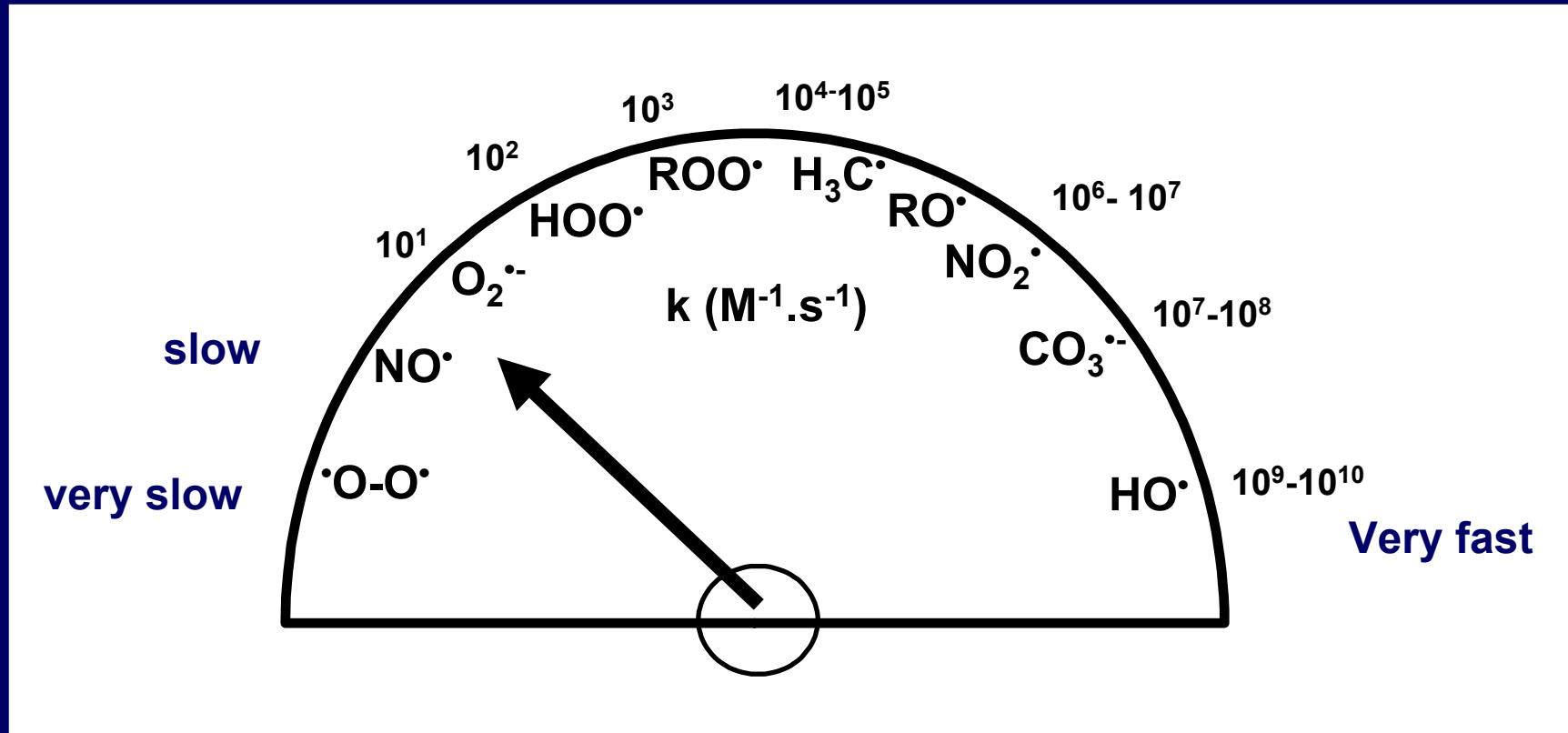
MitoK_{ATP} is Redox Sensitive



MitoK_{ATP} Is Activated by Mitochondrial ROS



ROS: Signaling Versus Damaging Roles



Ischemia/Reperfusion and Preconditioning

25 min wash 30 min ischemia 30 min reperfusion



↑ damage



↓ damage

+ antioxidants
+ mitoK_{ATP} agonists

IP



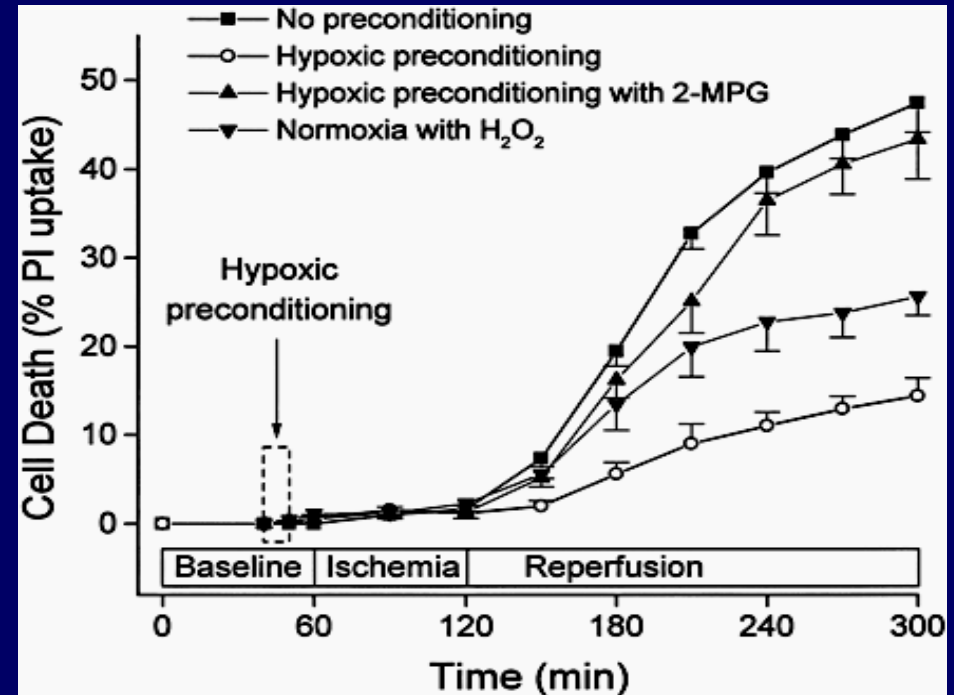
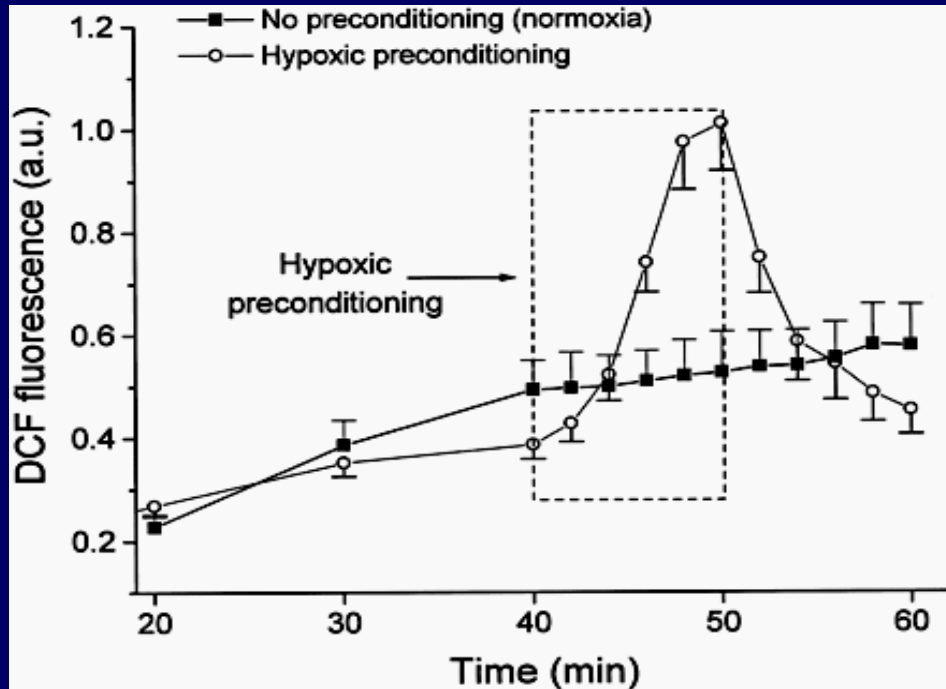
↓ damage



↑ damage

+ antioxidants
+ mitoK_{ATP} antagonists

Preconditioning and ROS



Preconditioning and MitoK_{ATP}

Garlid KD, Paucek P, Yarov-Yarovoy V, Murray HN, Darbenzio RB, D'Alonzo AJ, Lodge NJ, Smith MA, Grover GJ.

Cardioprotective effect of diazoxide and its interaction with mitochondrial ATP-sensitive K⁺ channels. Possible mechanism of cardioprotection.

Circ Res. 1997 81:1072-82.

Auchampach JA, Grover GJ, Gross GJ.

Blockade of ischaemic preconditioning in dogs by the novel ATP dependent potassium channel antagonist sodium 5-hydroxydecanoate.

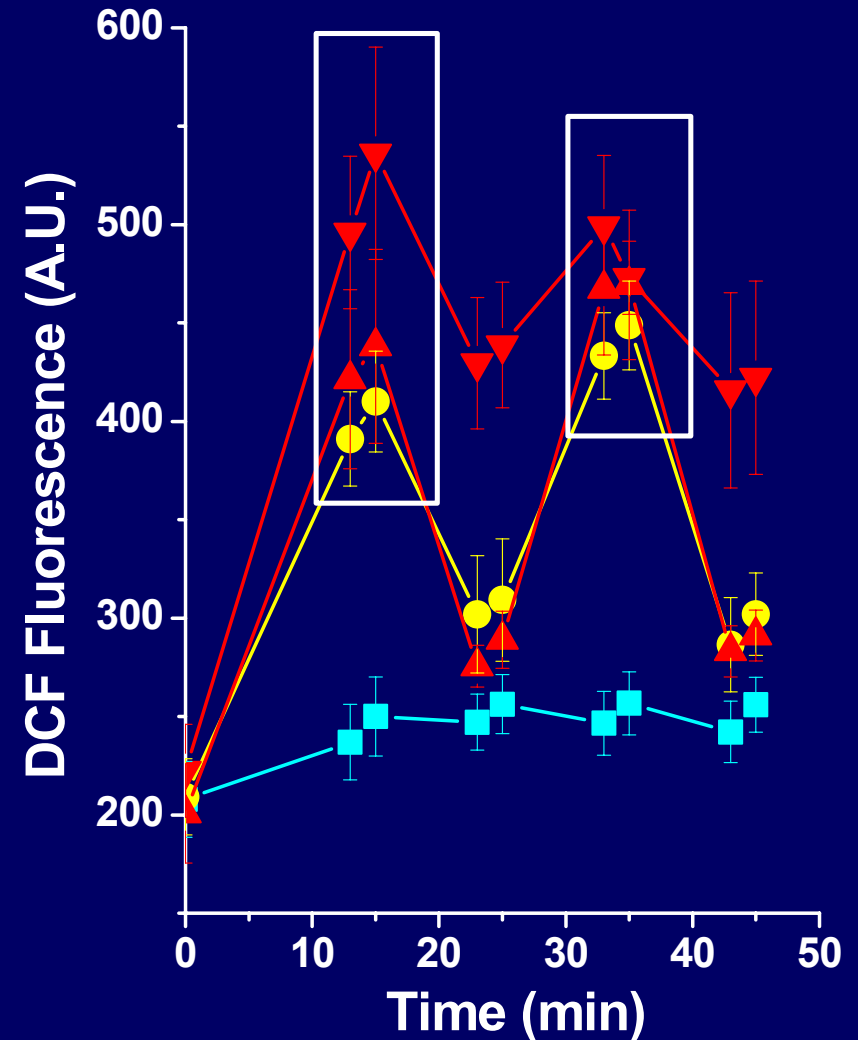
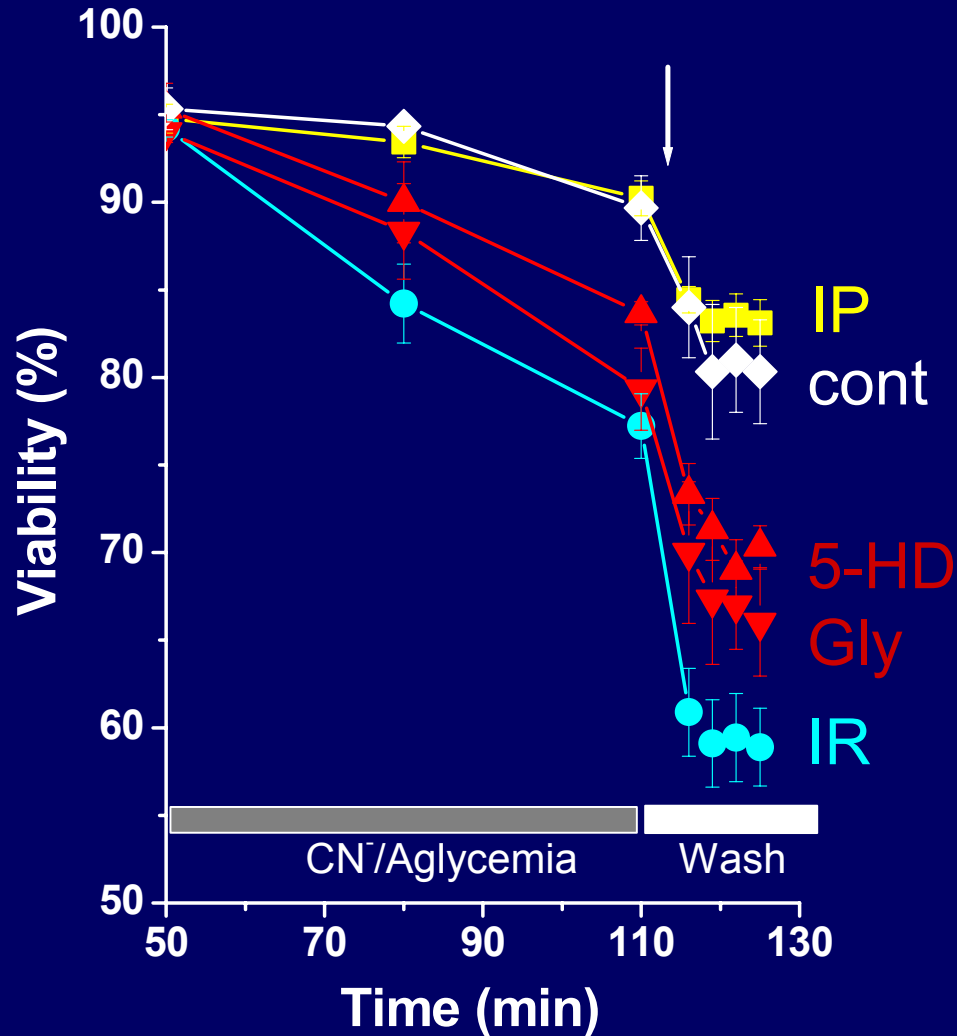
Cardiovasc Res. 1992 26:1054-62.

Jaburek M, Yarov-Yarovoy V, Paucek P, Garlid KD.

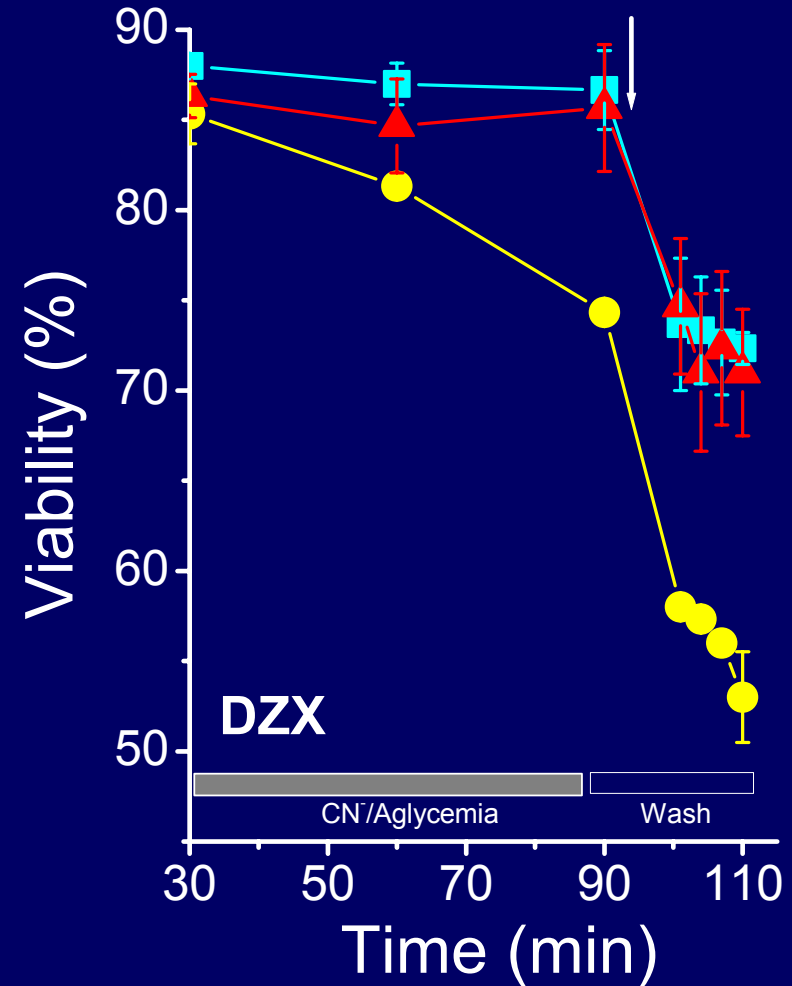
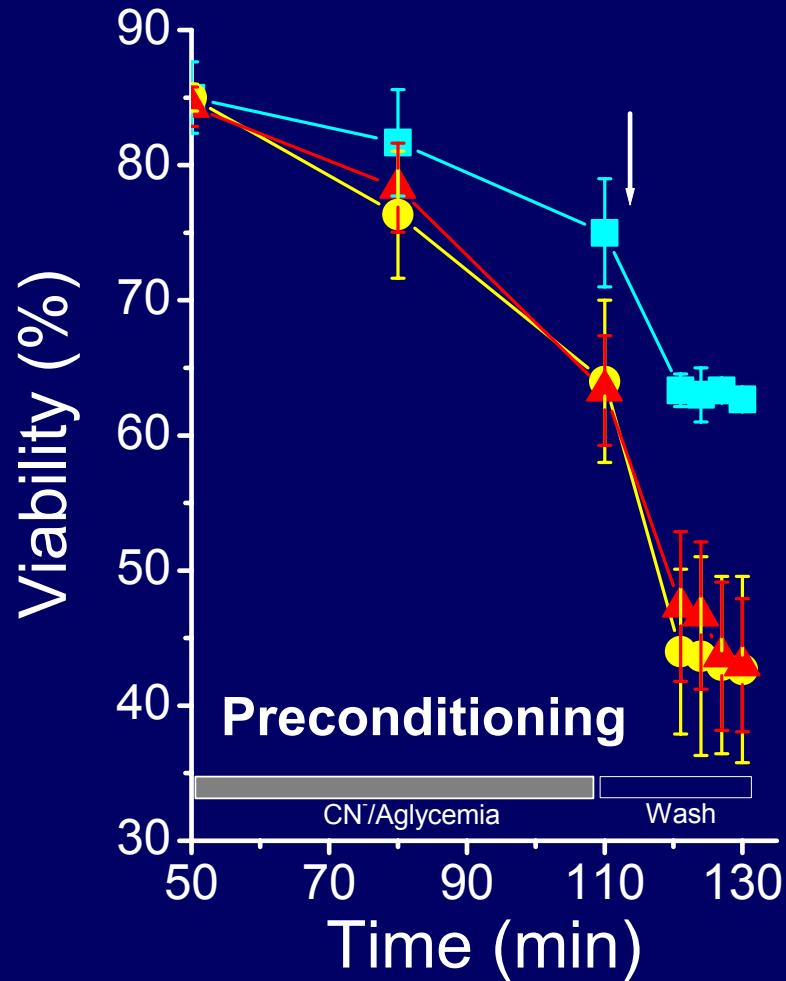
State-dependent inhibition of the mitochondrial K_{ATP} channel by glyburide and 5-hydroxydecanoate.

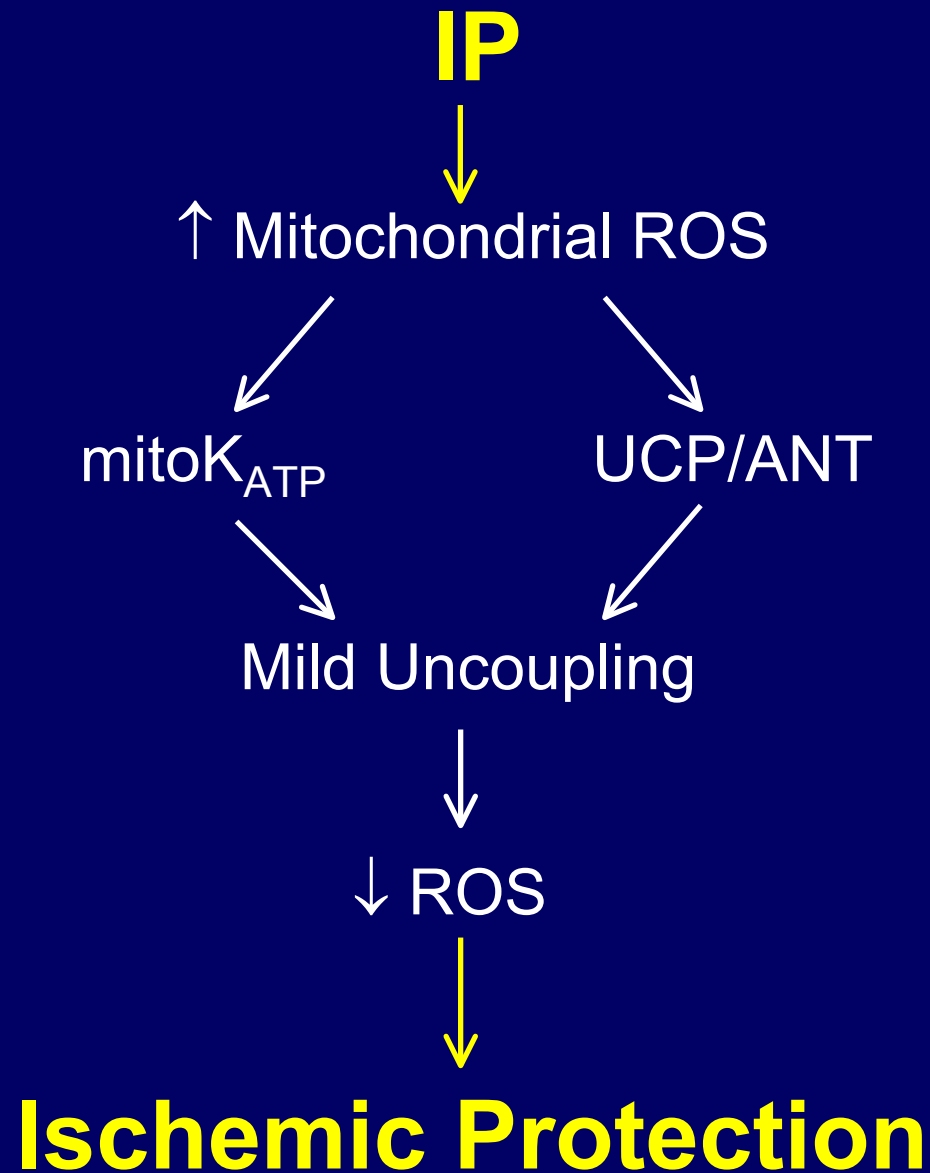
J Biol Chem. 1998 273:13578-82.

ROS Release Precedes MitoK_{ATP} Opening



DZX Protects Independently of ROS





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- Luis E. S. Netto
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