JUSTUS-LIEBIG-
UNIVERSITÄT
GIESSEN

Physiologisches Institut

Reactive oxygen species: Importance for ischemia/reperfusion (injury)

Prof. Dr. Rainer Schulz

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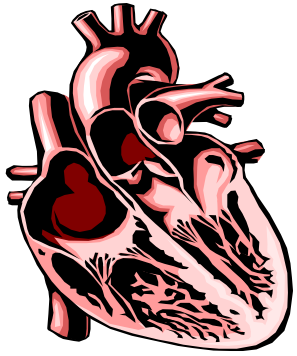
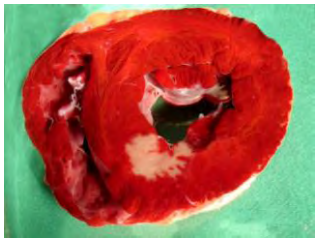
OF GIESSEN
CARDIOVASCULAR
RESEARCH CENTER

Reactive oxygen species (ROS) in ischemia/reperfusion injury (IRI)



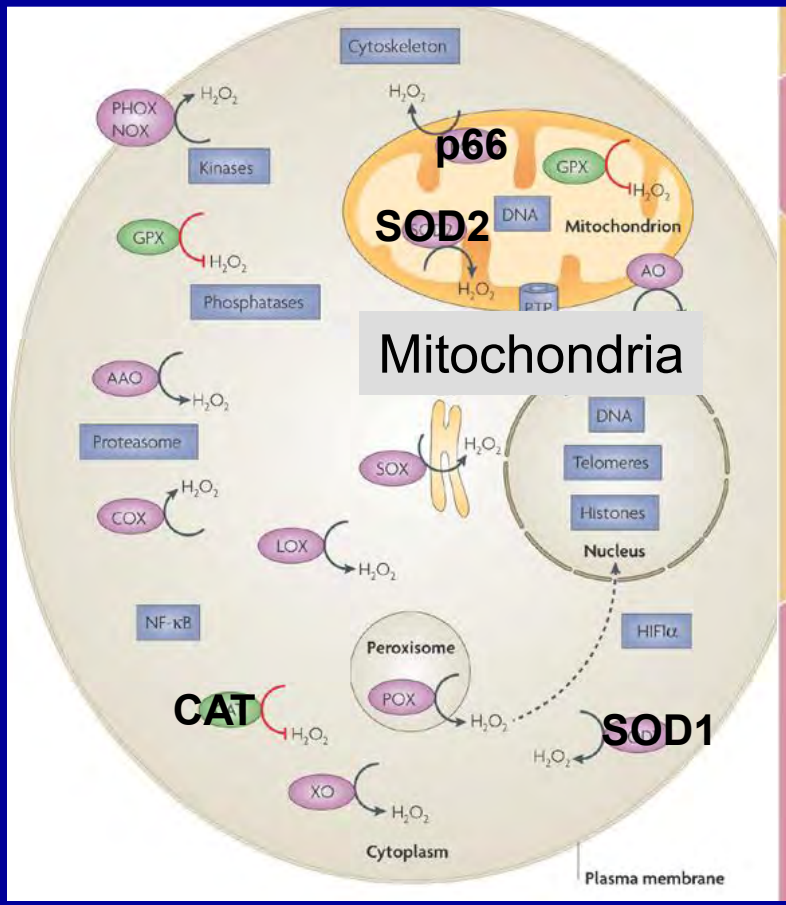
GOOD: Endogenous protection



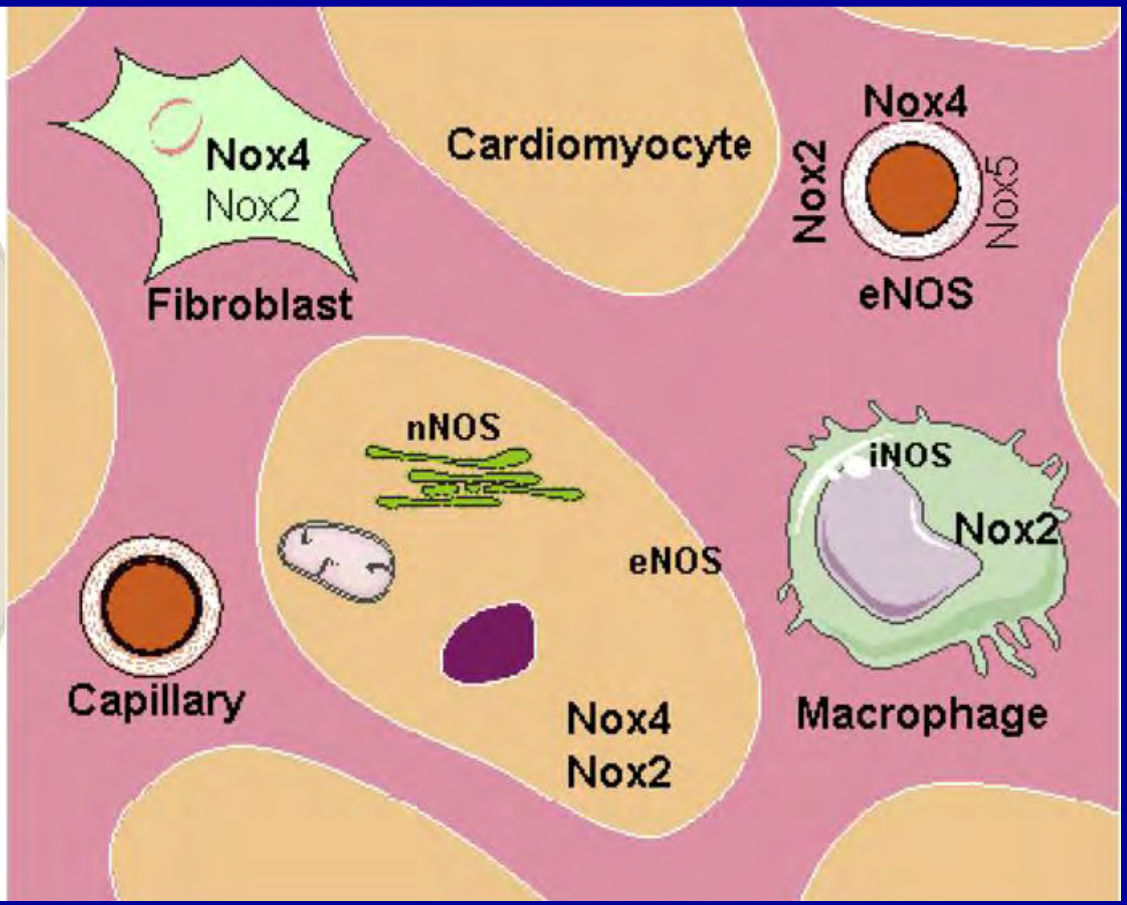
BAD: Infarction

Potential sources of ROS

Cardiomyocytes



Other cell types

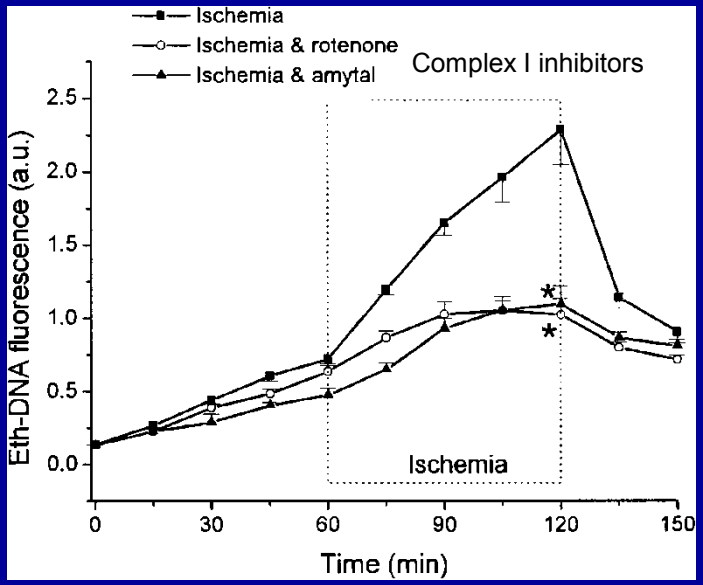


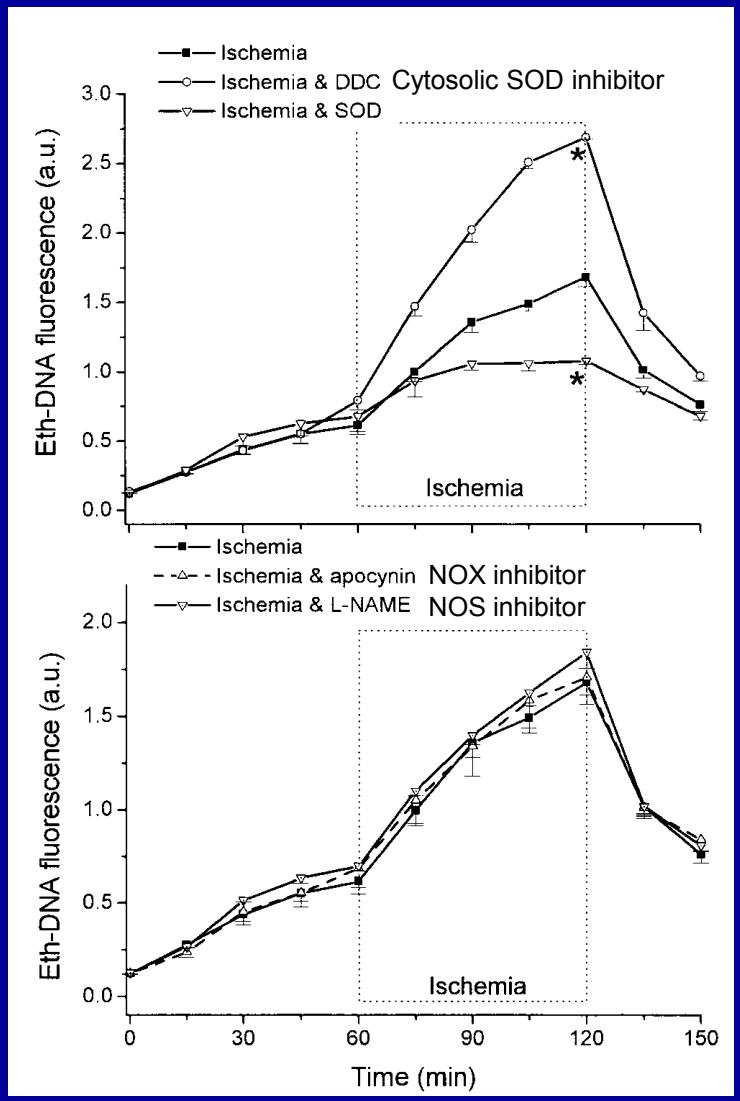
Giorgio et al., Nat Rev Mol Cell Biol, 8:722-728, 2007; Akki et al., J Mol Cell Cardiol 47: 15–22, 2009

Rat cardiomyocytes

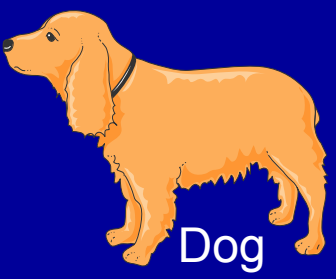
Formation of ROS during ischemia

ROS formation during (low-flow) ischemia appears to be primarily caused by mitochondria!

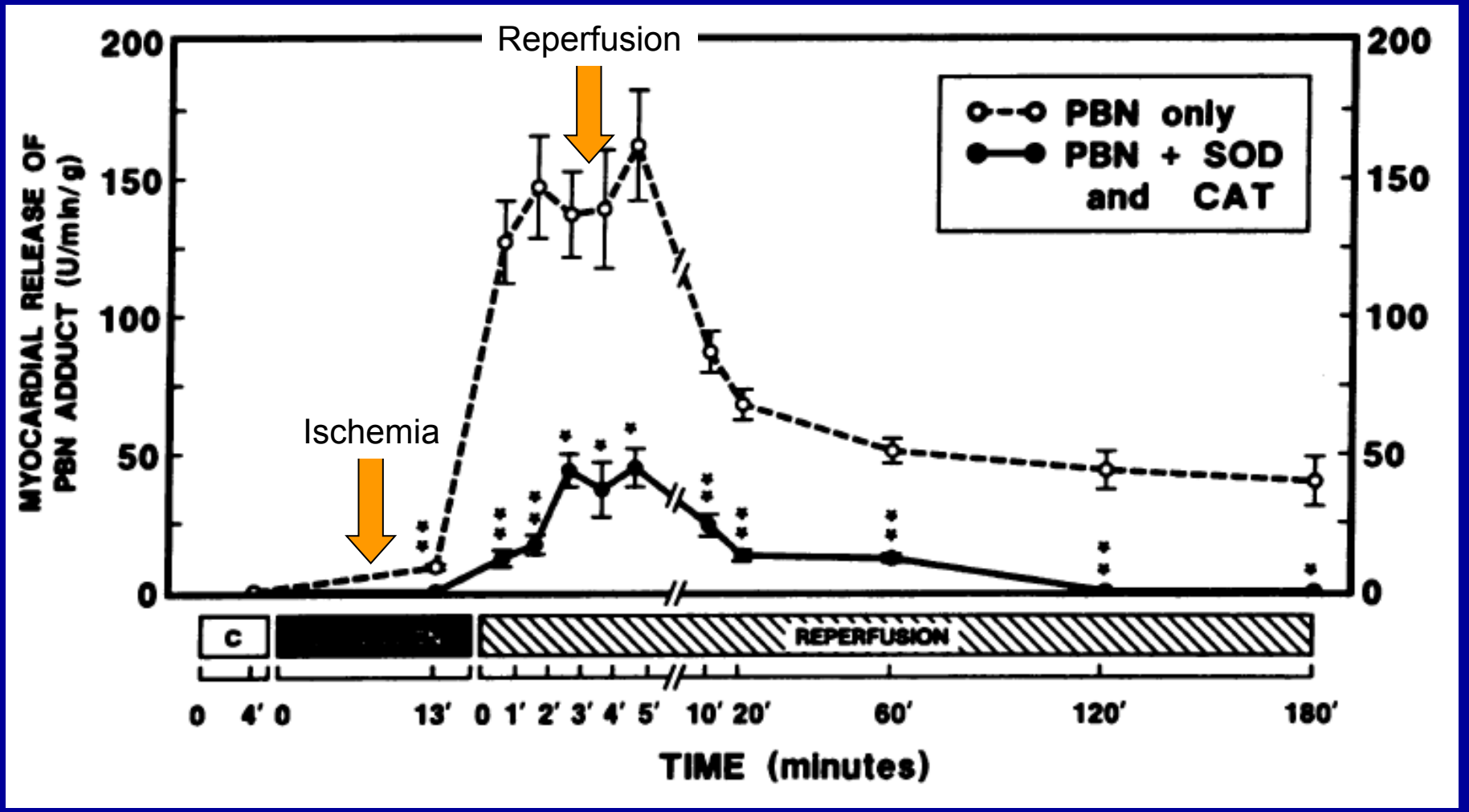




Becker et al., Am J Physiol 277 Heart Circ Physiol 46: H2240–H2246, 1999

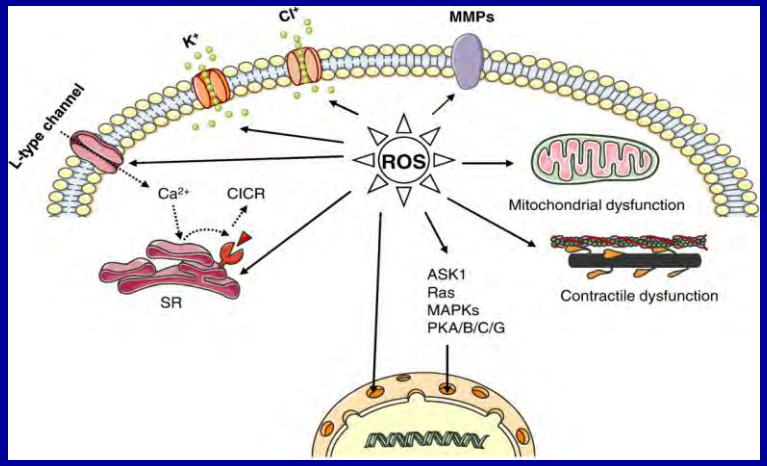


Formation of ROS during ischemia/reperfusion



Bolli et al., Proc Natl Acad Sci USA 86: 4695-4699, 1989

ROS during IRI



contribute to cellular damage

Function

Morphology

(Postischemic Reperfusion, Heart Failure)

contribute to cellular protection

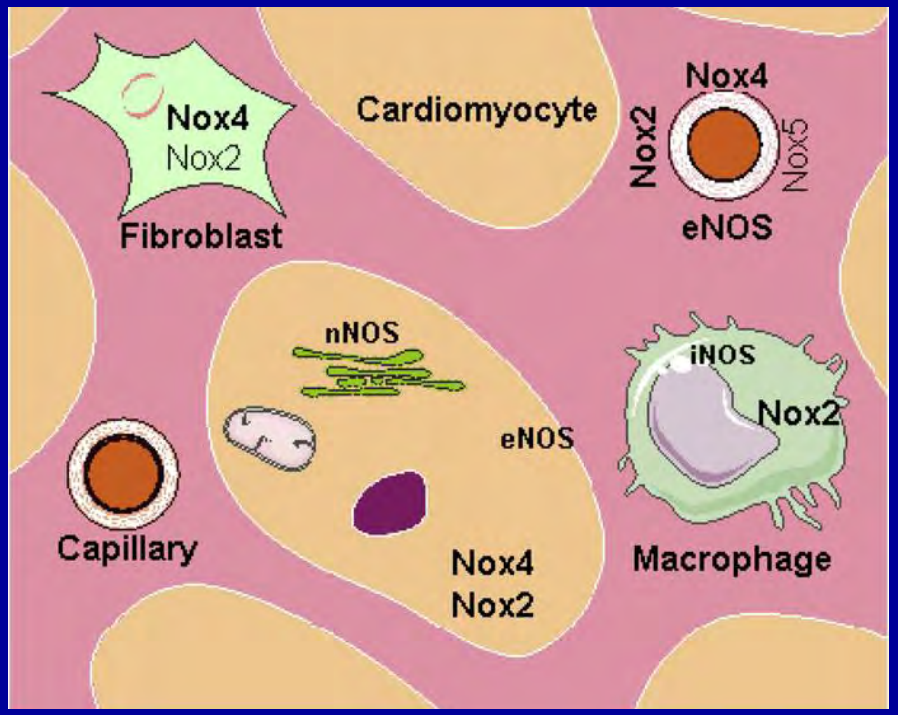
Function

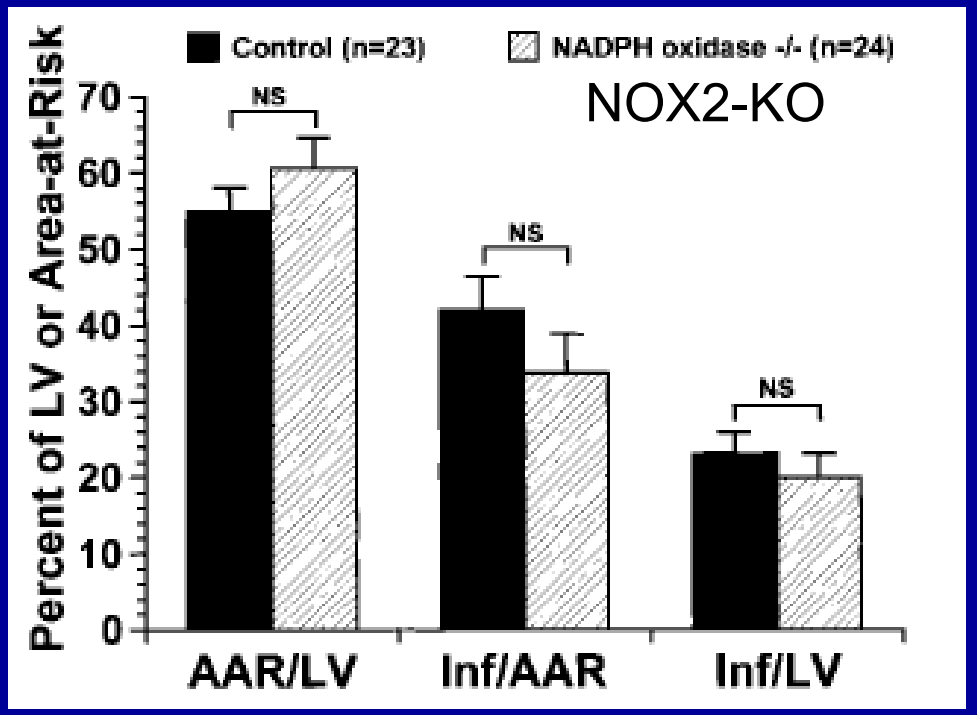
Morphology

(Ischemia/Reperfusion Injury)

Mice

NOX2 and irreversible IRI



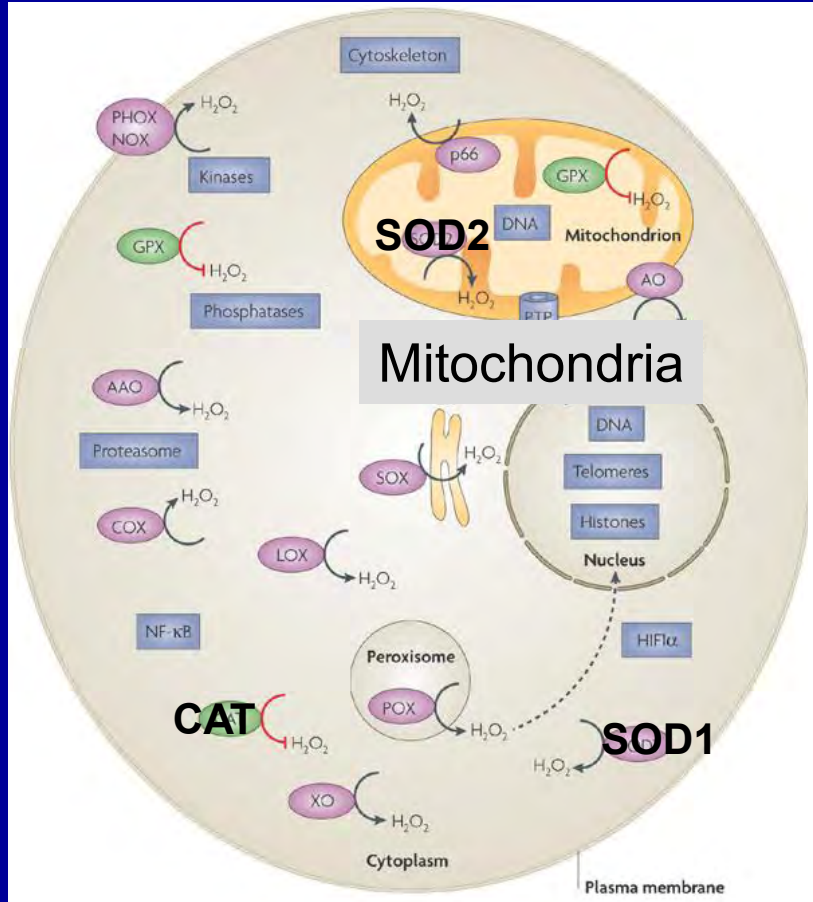


Hoffmeyer et al., Circ Res 87: 812-817, 2000

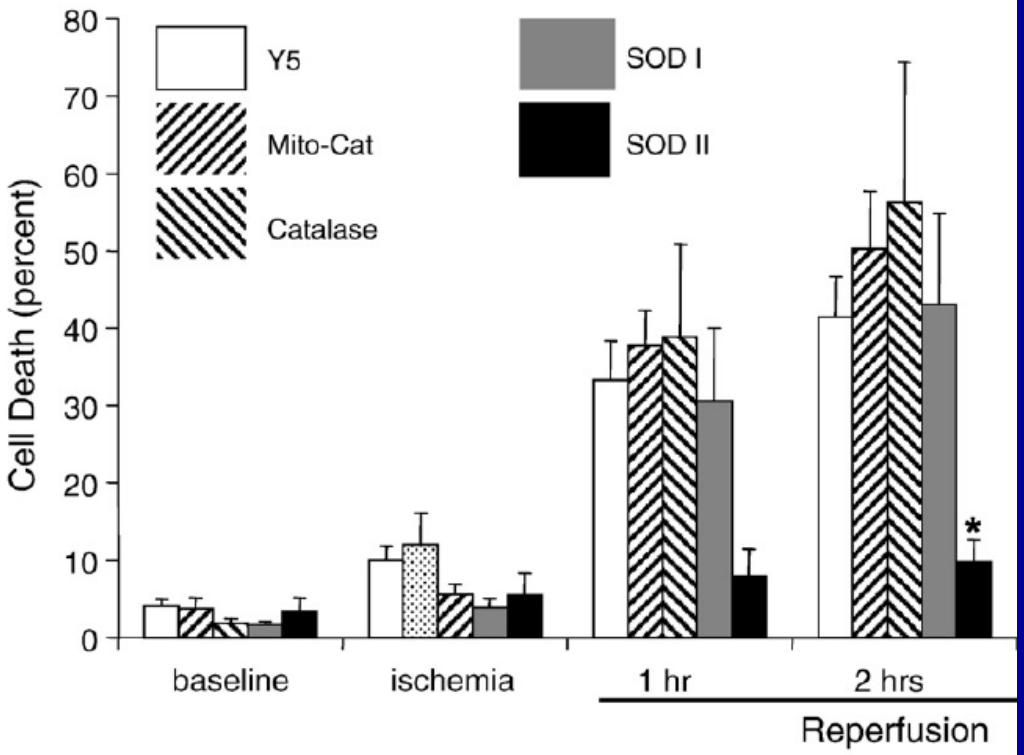
Mice

Catalase (CAT), superoxid dismutase (SOD) and irreversible IRI

Cardiomyocytes



Cardiomyocytes



Giorgio et al., Nat Rev Mol Cell Biol, 8:722-728, 2007

Loor et al., Biochem Biophys Acta 2011

Mice

GSH during ischemia/reperfusion

THE JOURNAL OF BIOLOGICAL CHEMISTRY VOL. 282, NO. 26, pp. 19133–19143, June 29, 2007
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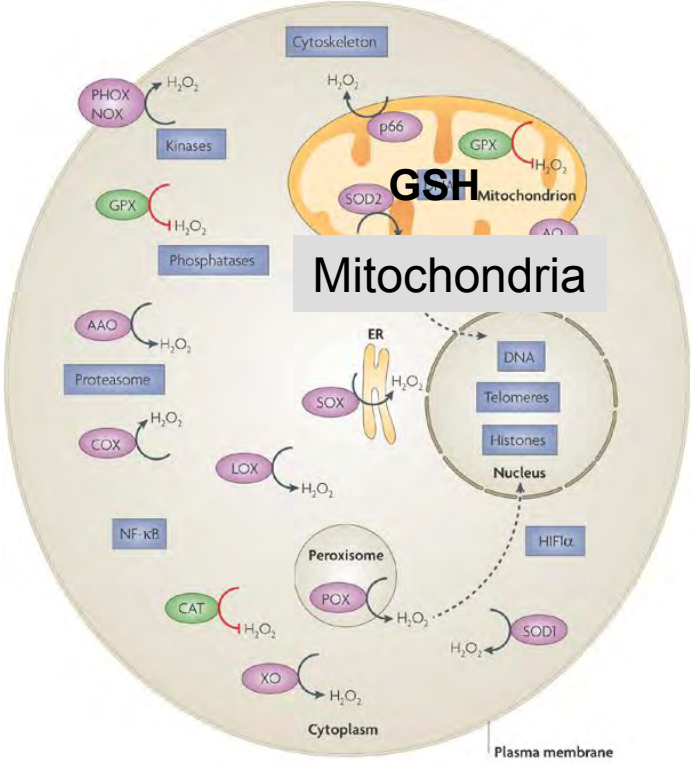
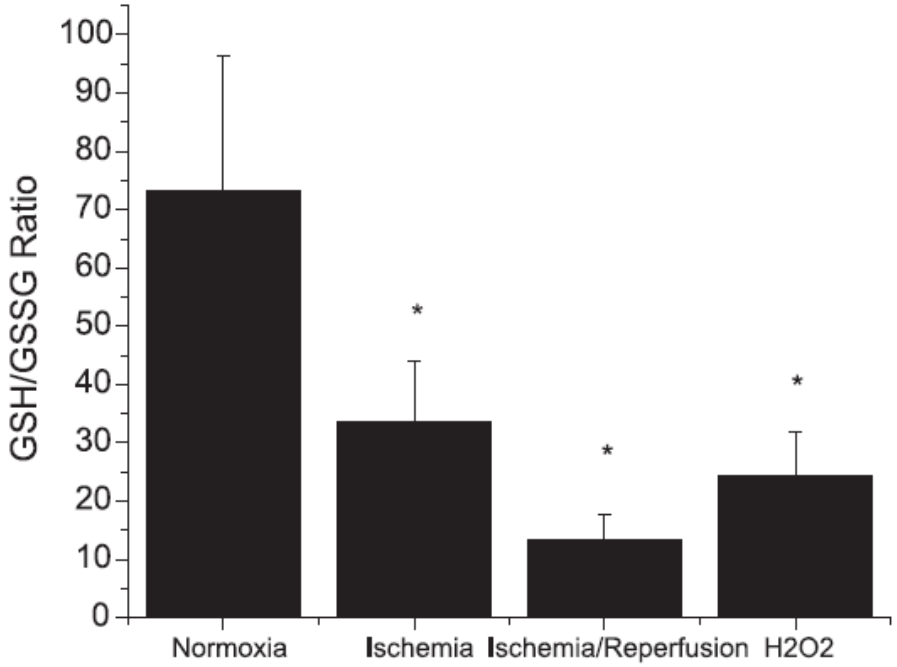
Oxidant Stress during Simulated Ischemia Primes Cardiomyocytes for Cell Death during Reperfusion*

Received for publication, March 5, 2007, and in revised form, April 16, 2007 Published, JBC Papers in Press, May 7, 2007, DOI 10.1074/jbc.M701917200

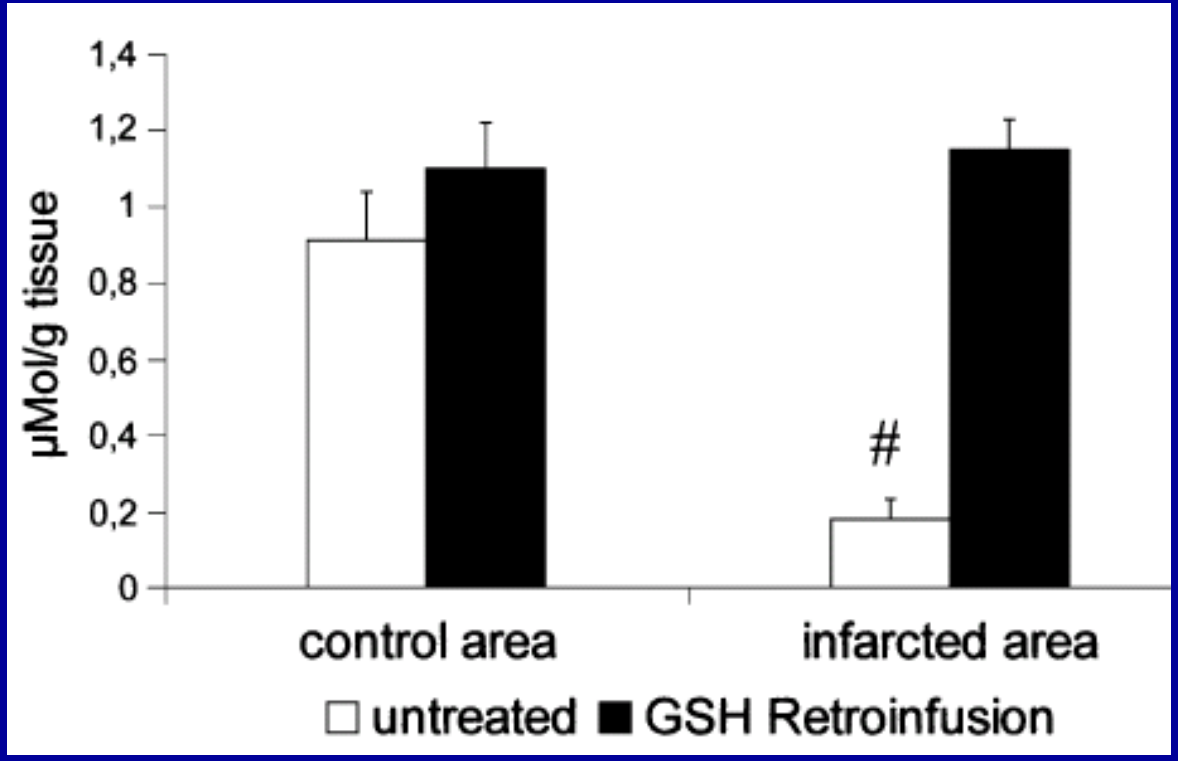
Emmanuel Robin[‡1], Robert D. Guzy[§], Gabriel Loor[¶], Hirotaro Iwase[‡], Gregory B. Waypa[§], Jeremy D. Marks[‖],

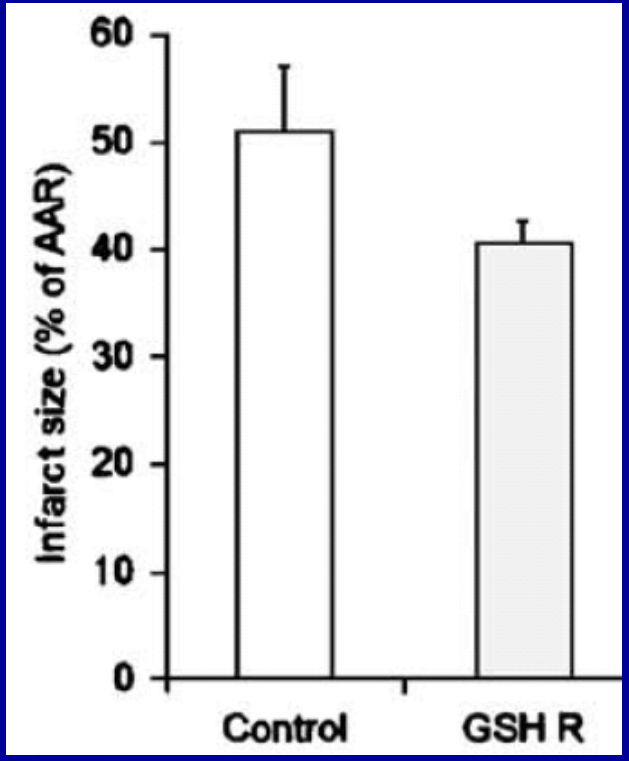




Pig

GSH and irreversible IRI





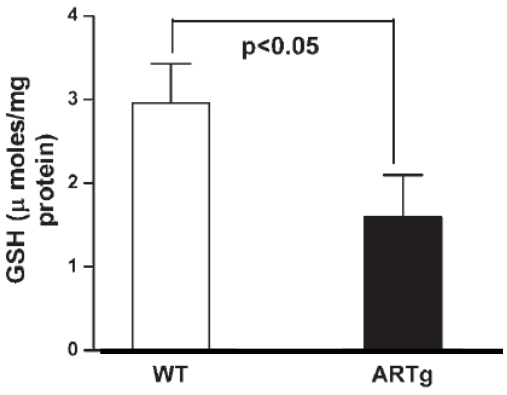
Kupatt et al., Cardiovasc Res 61: 530-537, 2004

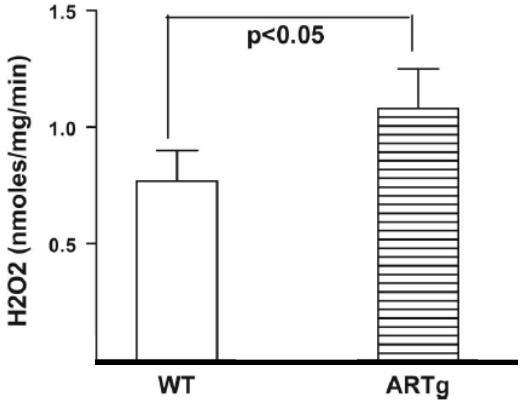
Aldolase reductase and irreversible IRI

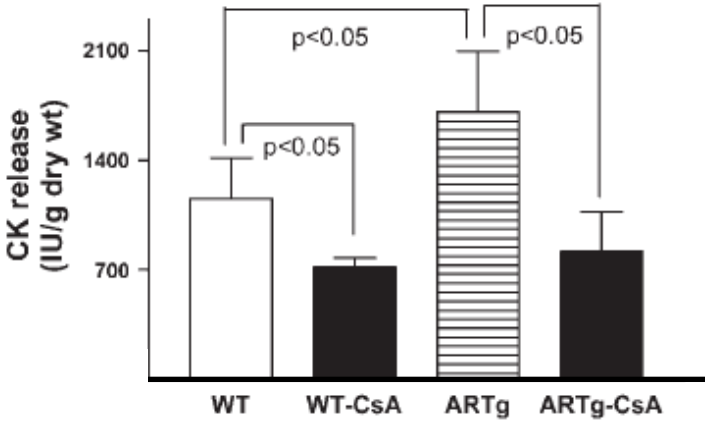
Am J Physiol Heart Circ Physiol 296: H333–H341, 2009.
First published December 5, 2008; doi:10.1152/ajpheart.01012.2008.

Aldose reductase mediates myocardial ischemia-reperfusion injury in part by opening mitochondrial permeability transition pore

Radha Ananthakrishnan, Michiyo Kaneko, Yuying C. Hwang, Nosirudeen Quadri, Teodoro Gomez, Qing Li, Casper Caspersen, and Ravichandran Ramasamy



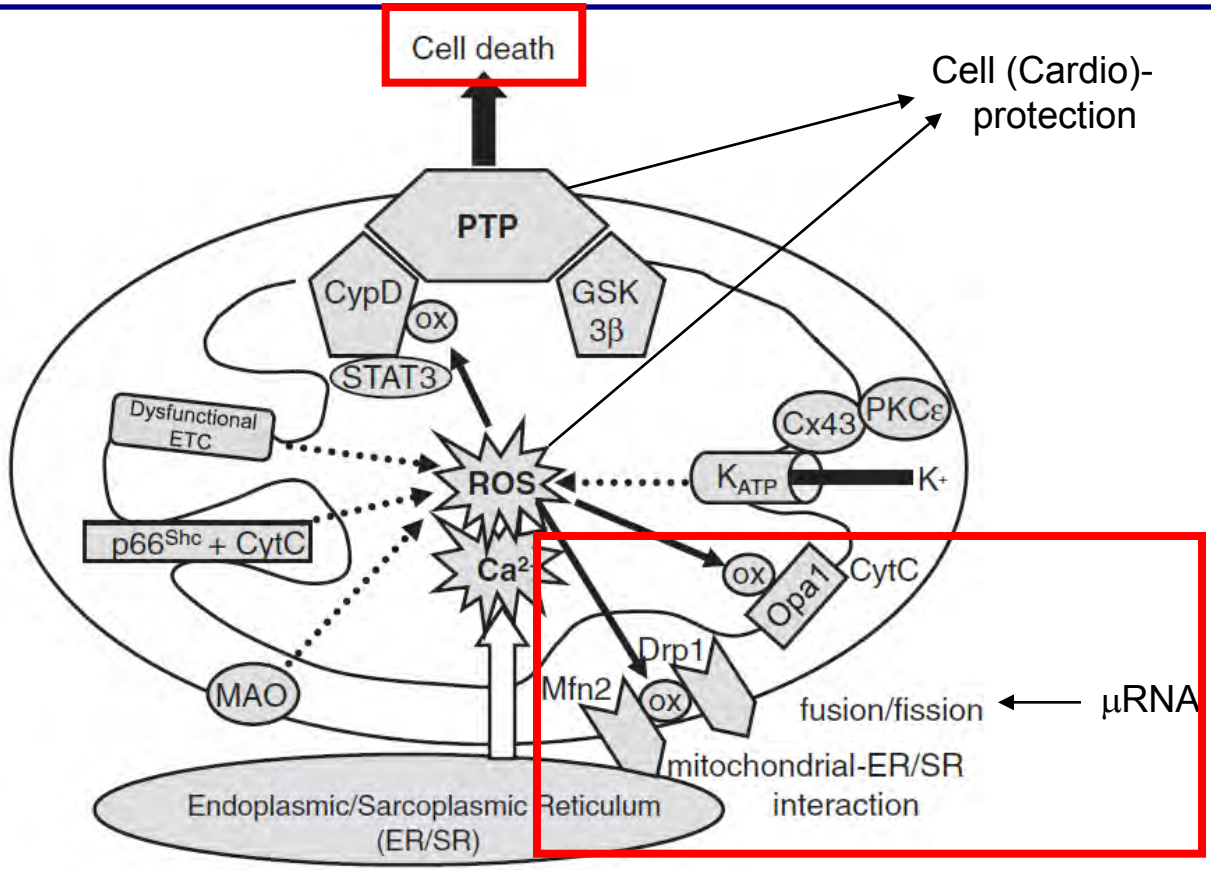




ROS and mitochondrial morphology

Nuclear-encoded mitochondrial proteins and their role in cardioprotection ☆

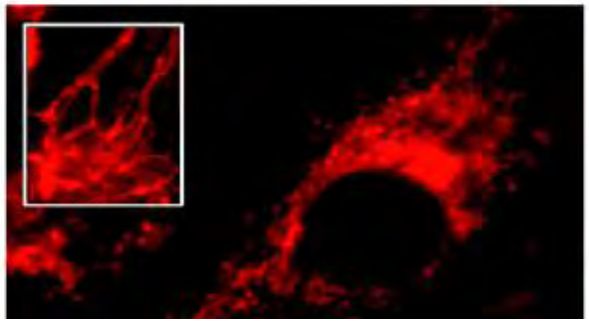
Kerstin Boengler [a,*], Gerd Heusch [a], Rainer Schulz [b]

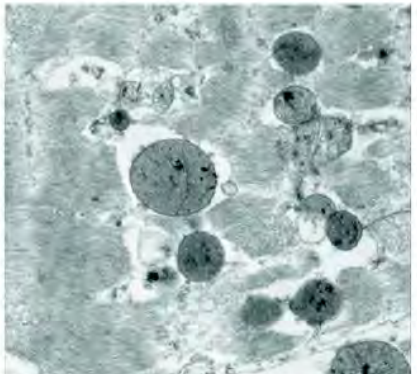


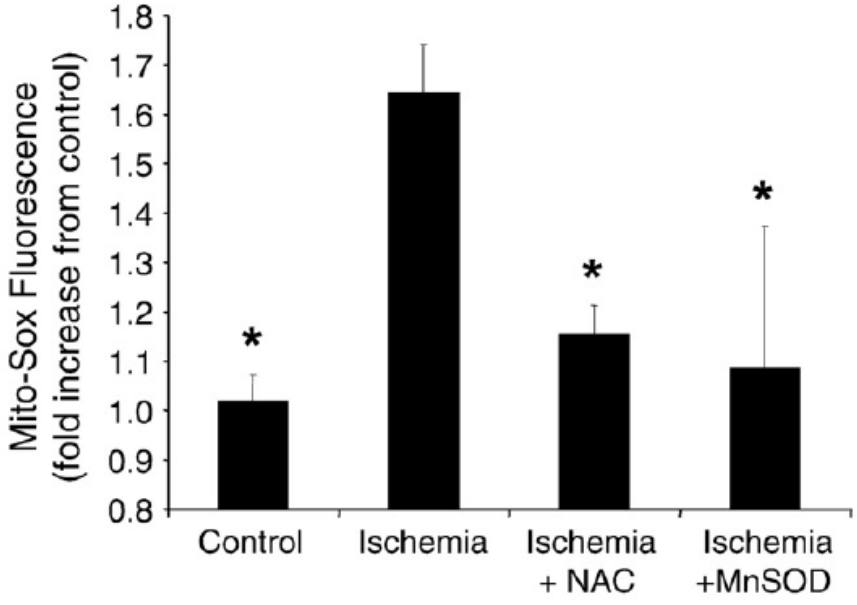
BBA 2011

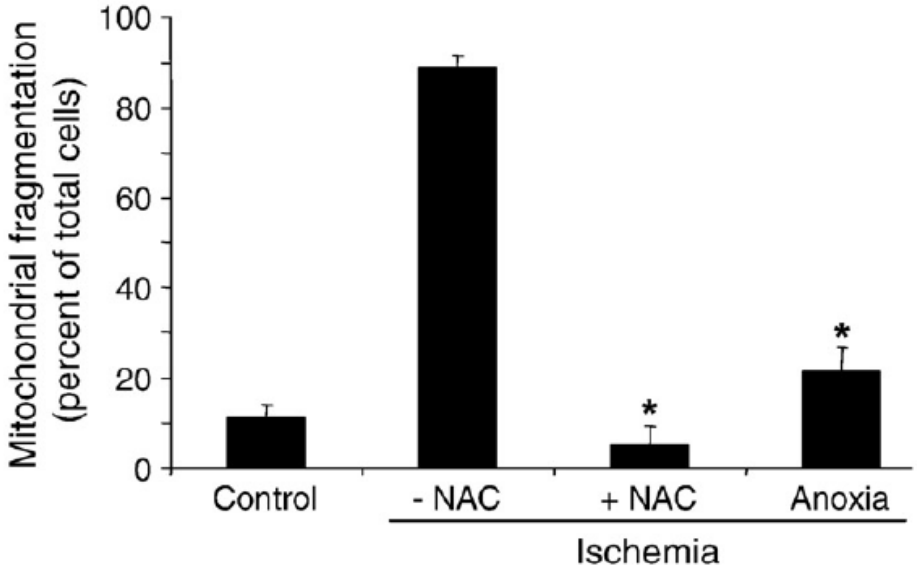
Mice

ROS and mitochondrial morphology



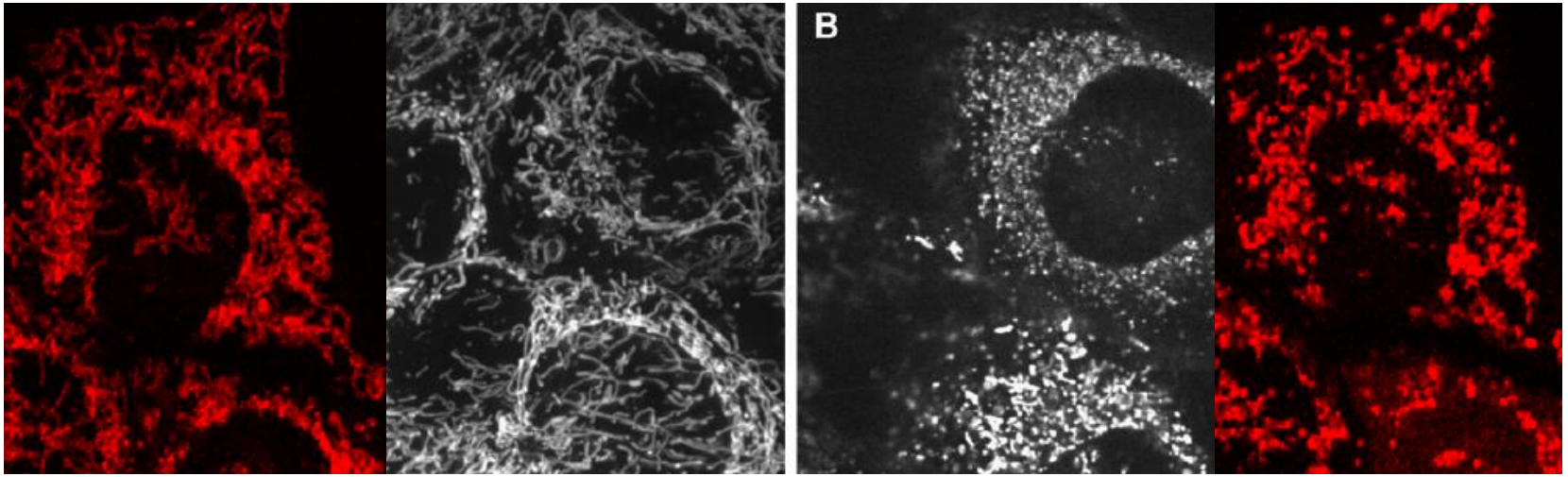






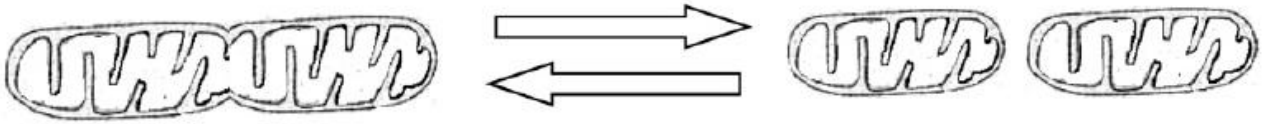
Loor et al., Biochem Biophys Acta 2011

ROS and mitochondrial morphology



Dnm1 Drp1 Fis1 Mdv1,2

Fission

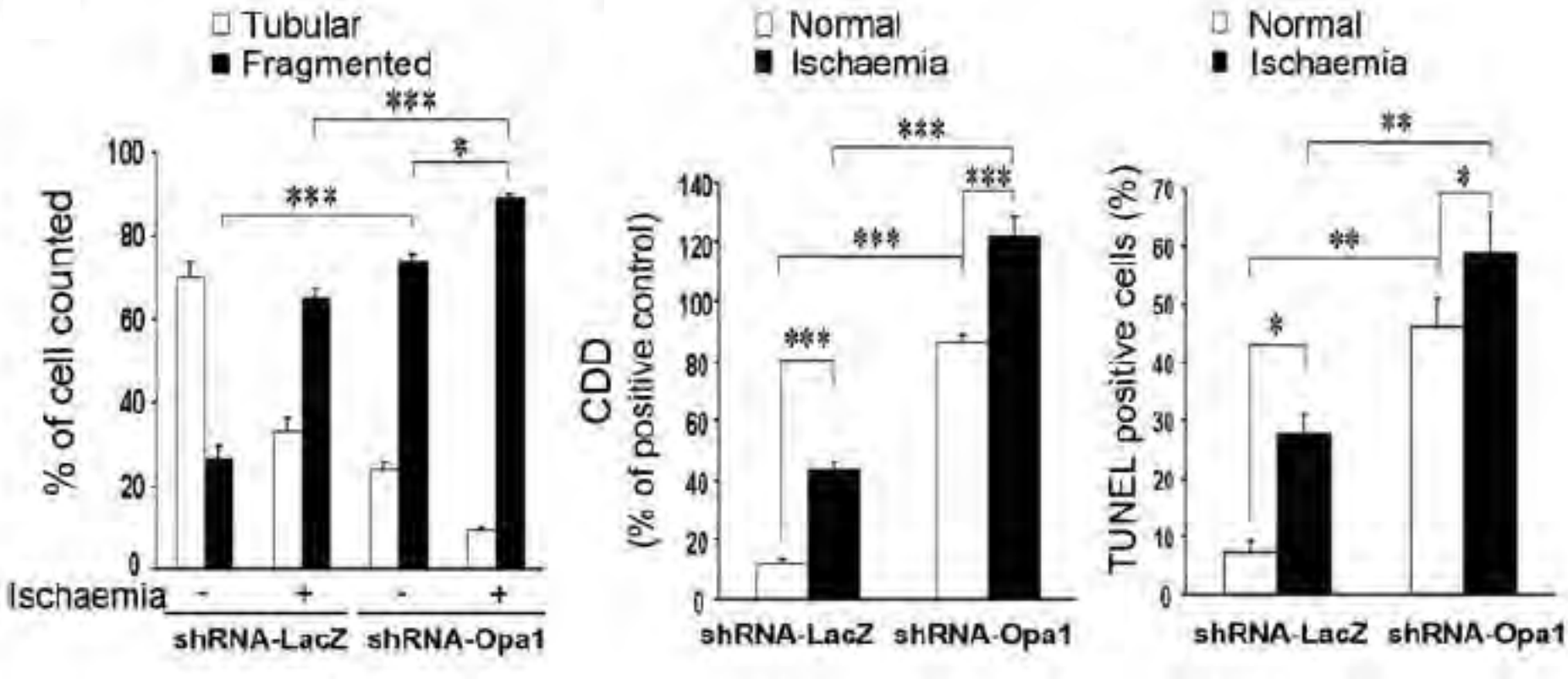


Fusion

OPA1 Mfn1,2 Fzo1 Mgm1

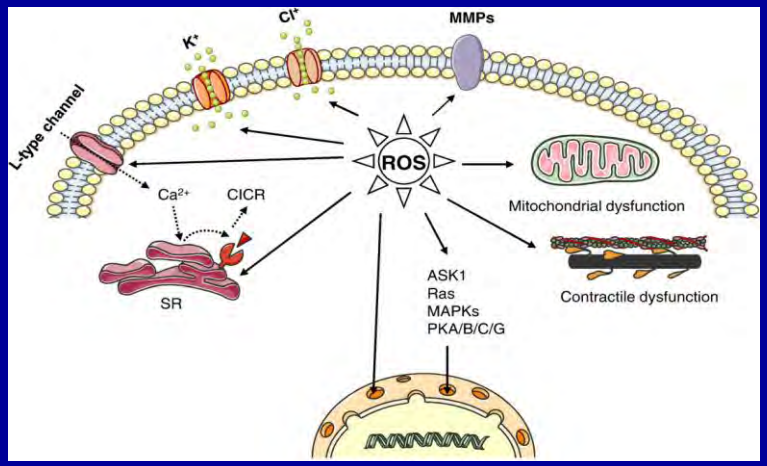
Kuznetsova et al, Int J Biochem & Cell Biol 41: 1928–1939, 2009

OPA1, mitochondrial morphology and IRI



Chen et al., Cardiovasc Res 84: 91-99, 2009

ROS during IRI and protection from it



contribute to cellular damage

Function

Morphology

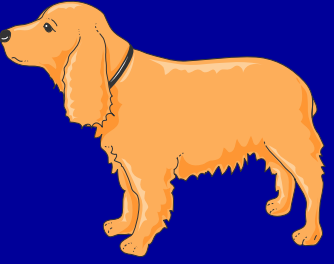
(Postischemic Reperfusion, Heart Failure)

contribute to cellular protection

Function

Morphology

(Ischemia/Reperfusion Injury)



Dog

Ischemic pre- and post-conditioning

Coronary occlusion

Control

60 min 3h

Precon (Ischemia/ Drugs)

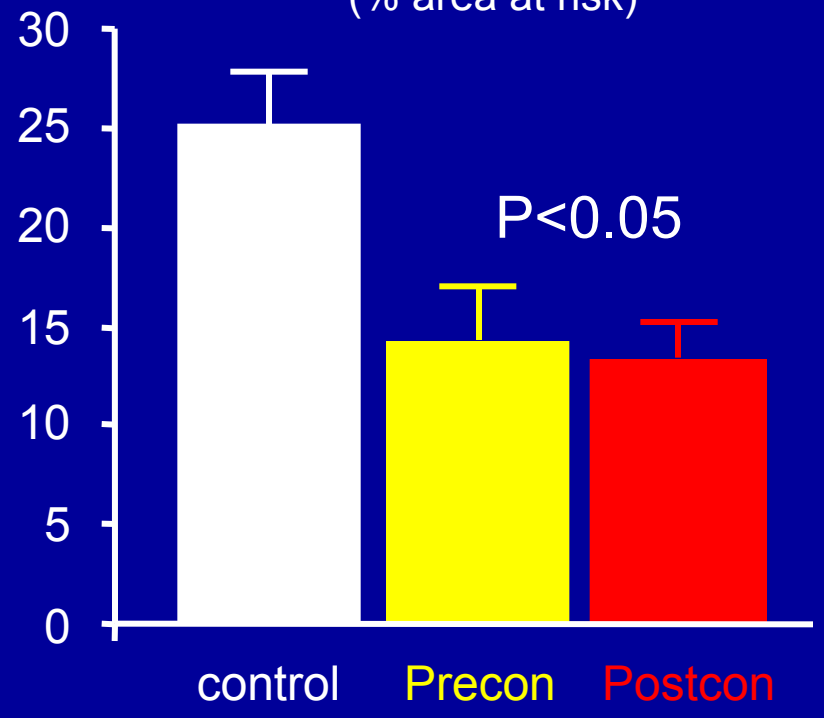
5 10 min 3h

Postcon

3h

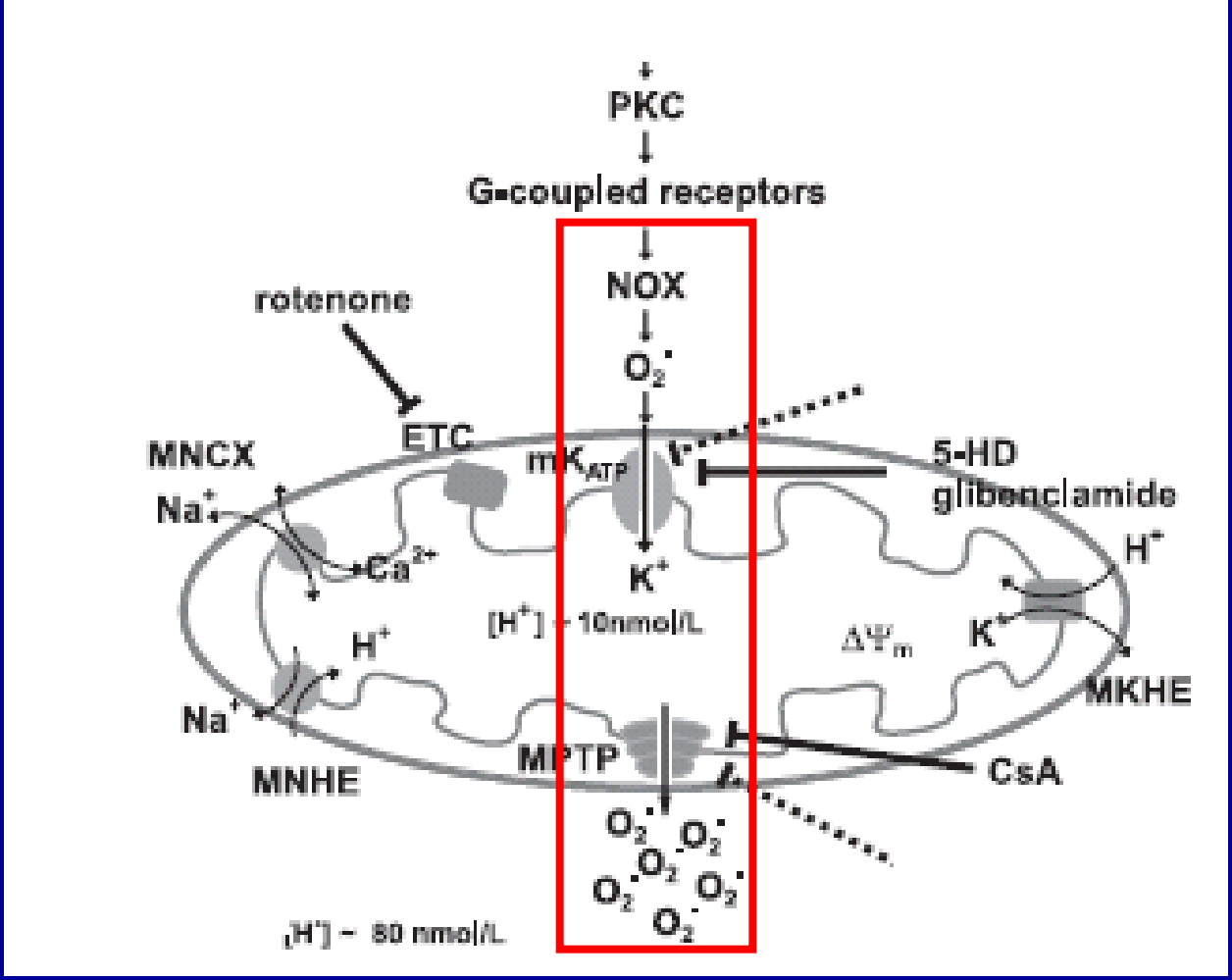
Infarct size

(% area at risk)



Zhao et al., Am J Physiol 285: H579-H588, 2004

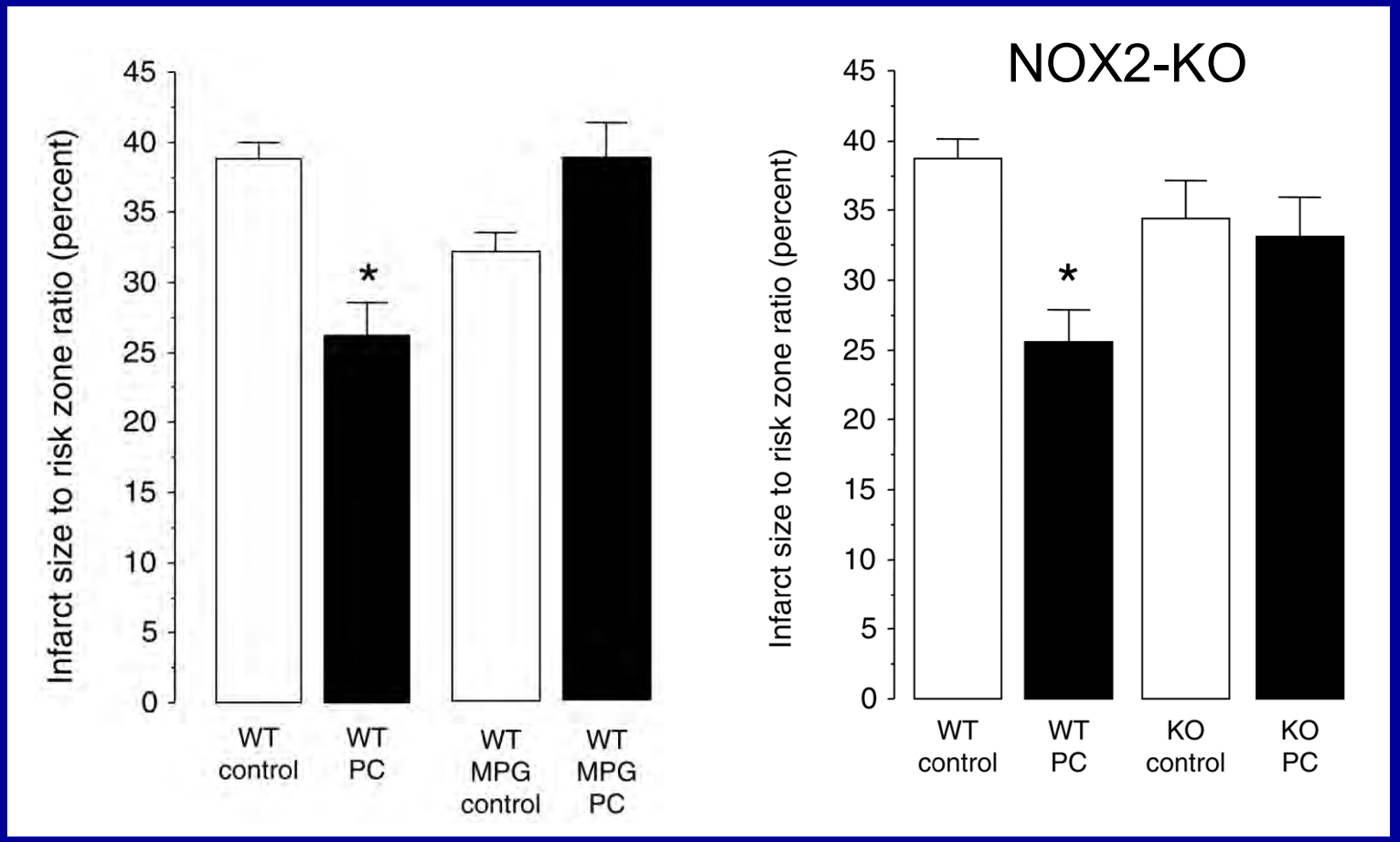
ROS and ischemic preconditioning



Garciarena et al., J Appl Physiol 105: 1706-1713, 2008

Mice

NOX2, ROS and ischemic preconditioning



Bell et al., FASEB J 2005

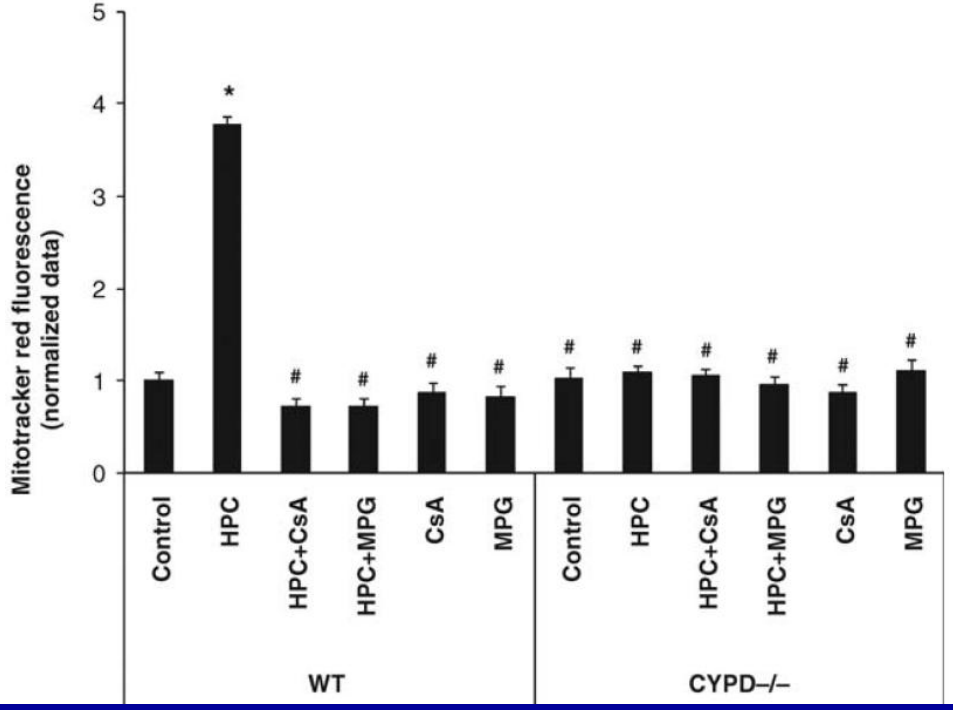
Cylophilin D, ROS and ischemic preconditioning

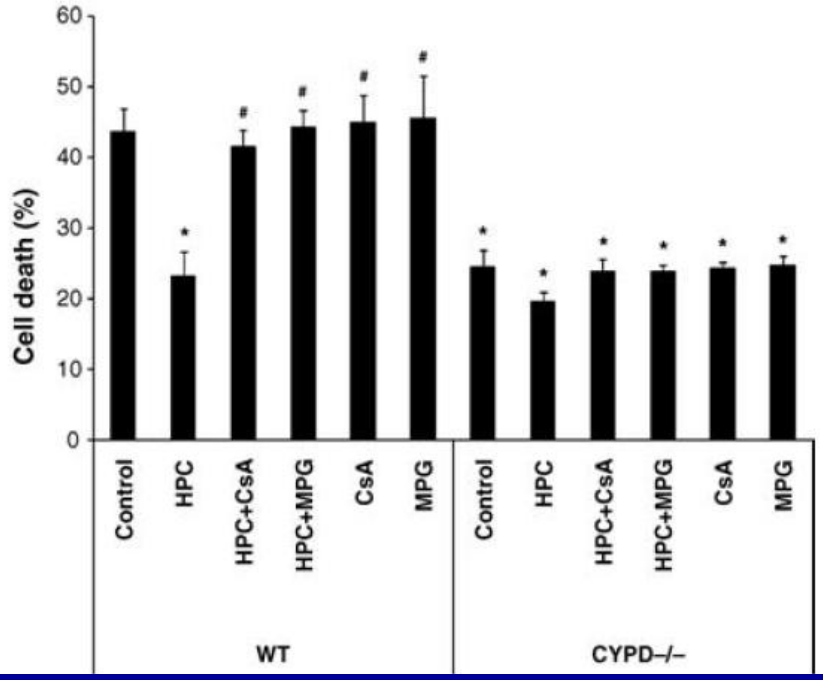
EUROPEAN SOCIETY OF CARDIOLOGY®

Cardiovascular Research (2010) **88**, 67–74
doi:10.1093/cvr/cvq113

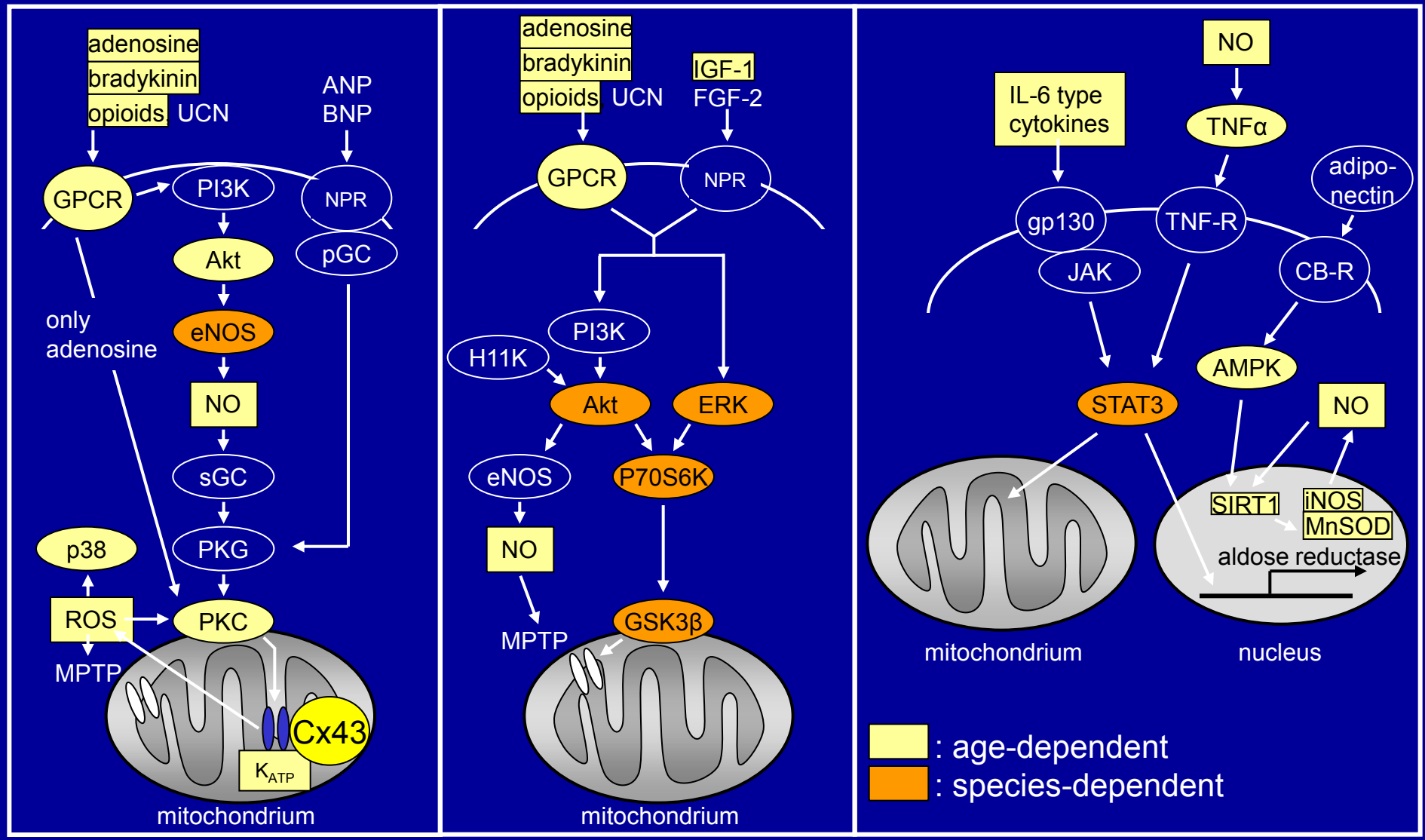
Mitochondrial cyclophilin-D as a critical mediator of ischaemic preconditioning

Derek J. Hausenloy*, Shiang Y. Lim, Sang-Ging Ong, Sean M. Davidson, and Derek M. Yellon





Pre- and Post-conditioning: Signal transduction

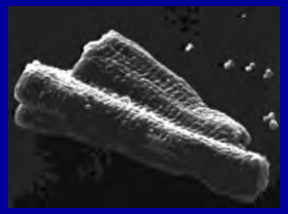


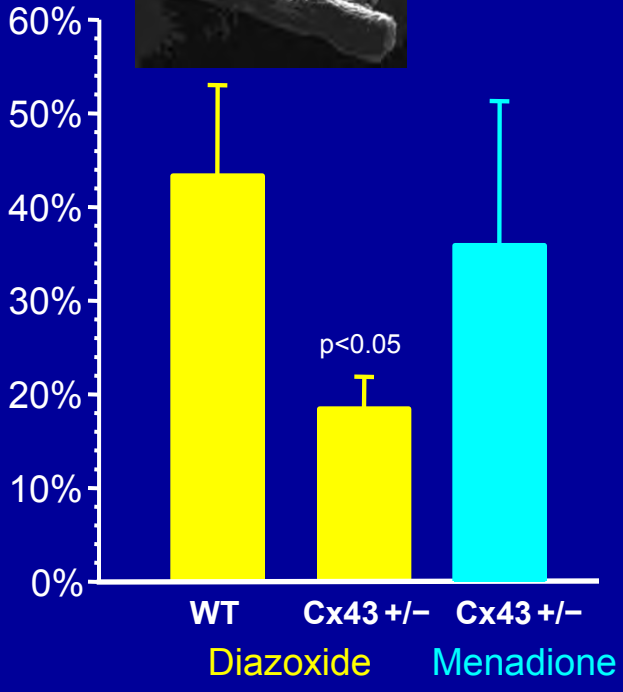
Heusch, Boengler, Schulz, Circulation 118: 1915-1919, 2008; Boengler, Schulz, Heusch, Cardiovasc Res 2009

Knockout mice

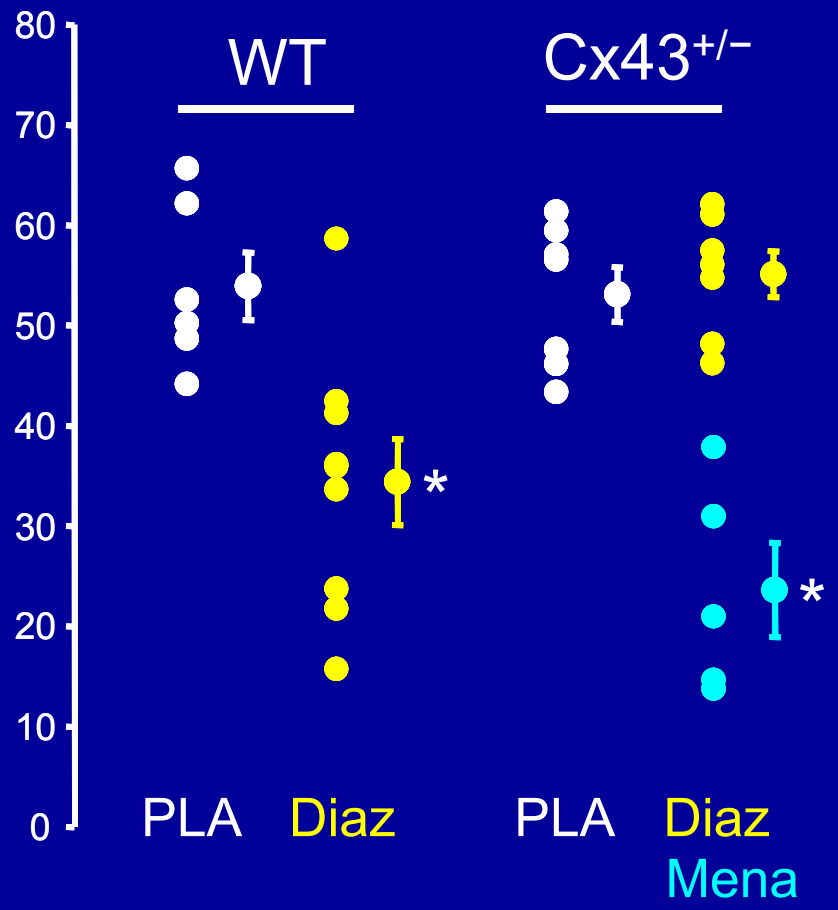
Connexin 43 (Cx43), ROS and ischemic preconditioning

MTR fluorescence
[% above control]





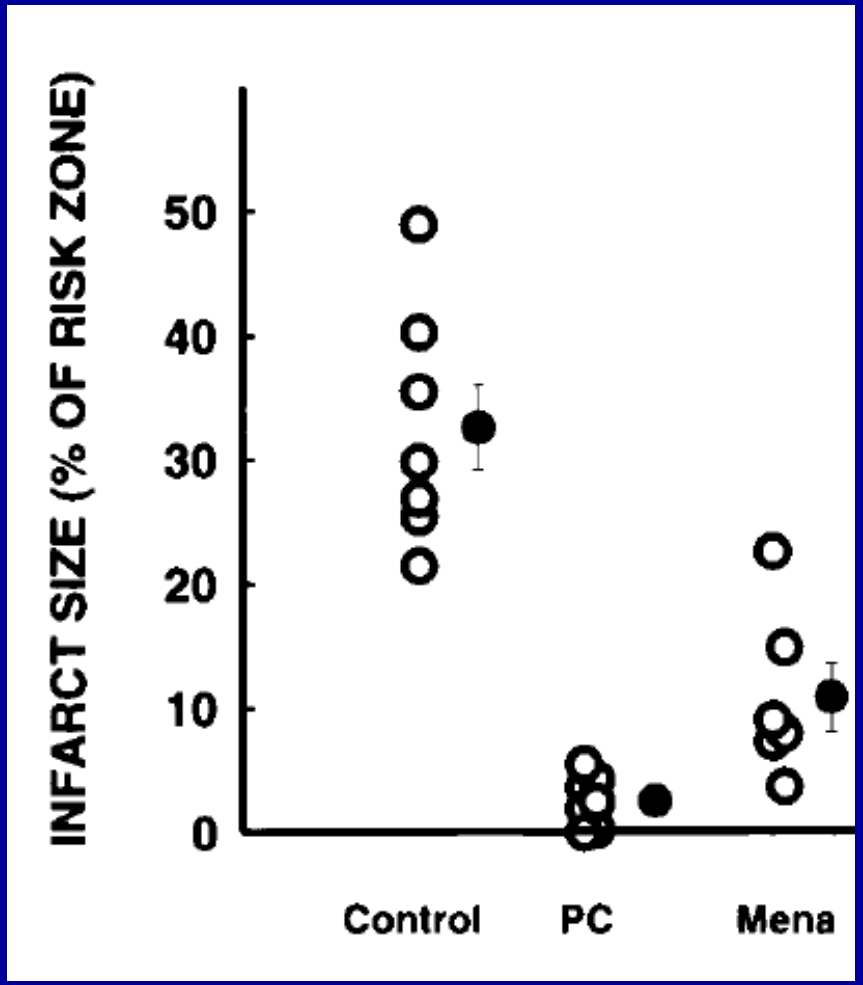
Infarct size (% area at risk)

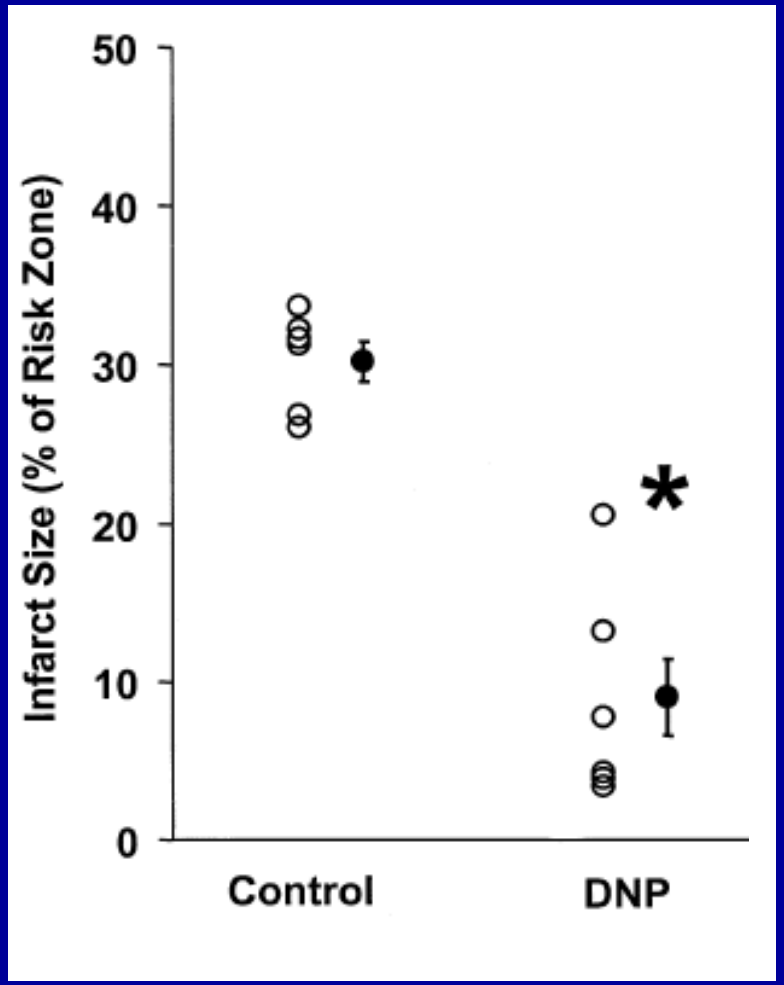


Heinzel et al., Circ Res 97:583-586, 2005

Rat heart in vitro

Mitochondrial uncoupling, ROS and IRI

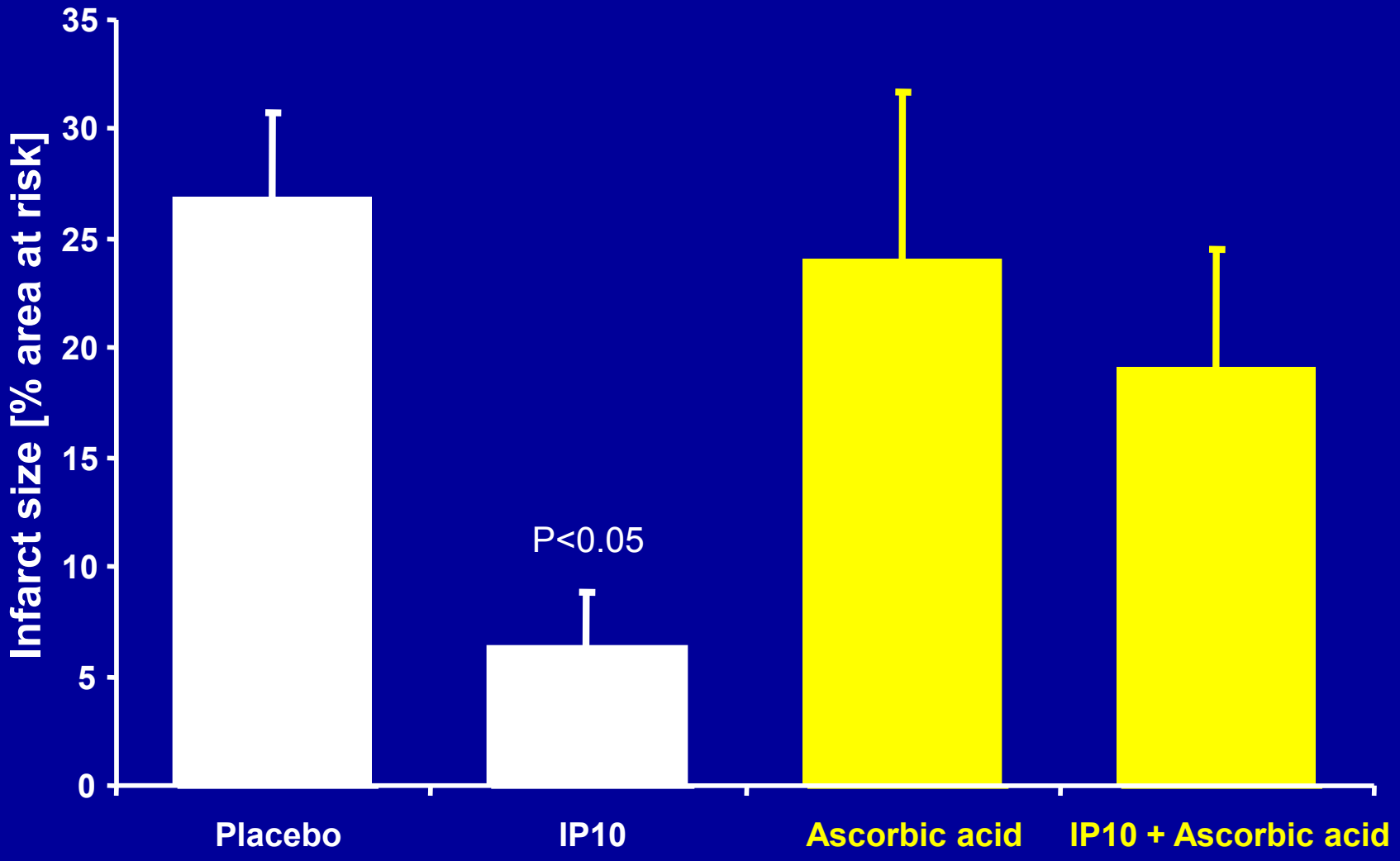




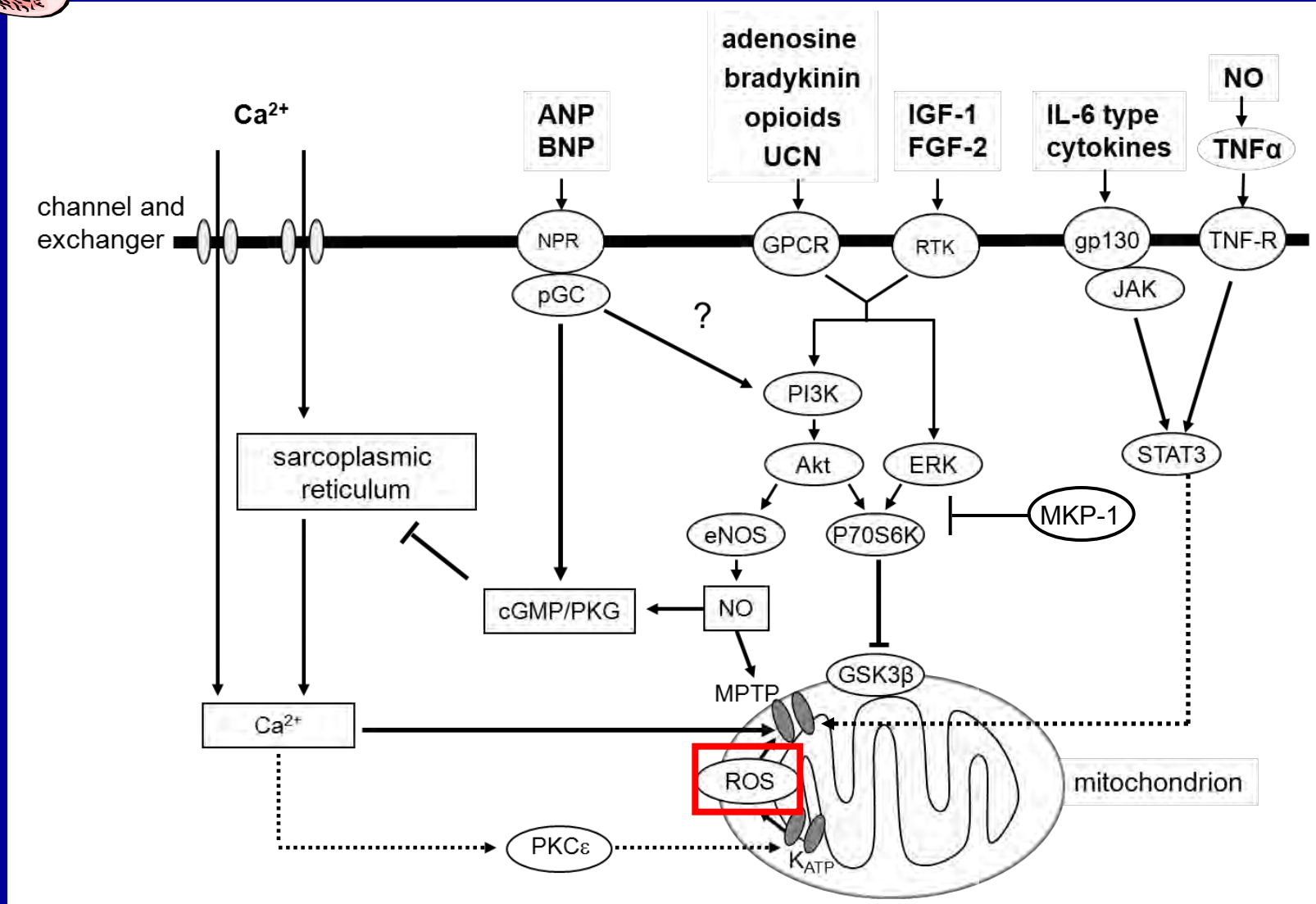
Yue et al., Am J Physiol 281: H590-H595, 2001

Minners et al., Cardiovasc Res 47: 68-73, 2000

ROS scavenging and ischemic preconditioning



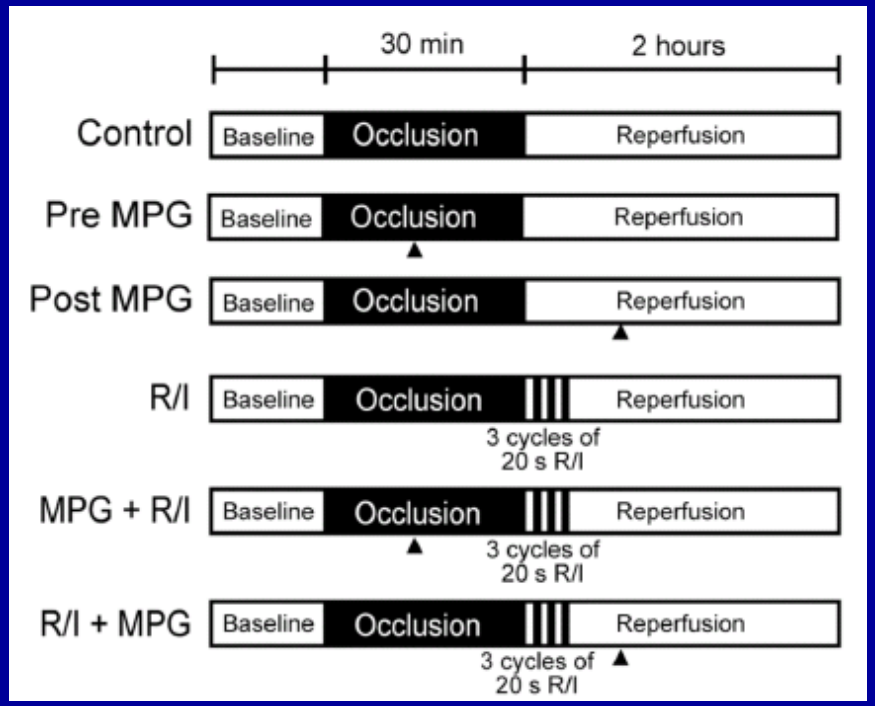
Ischemic Postconditioning: Signal transduction

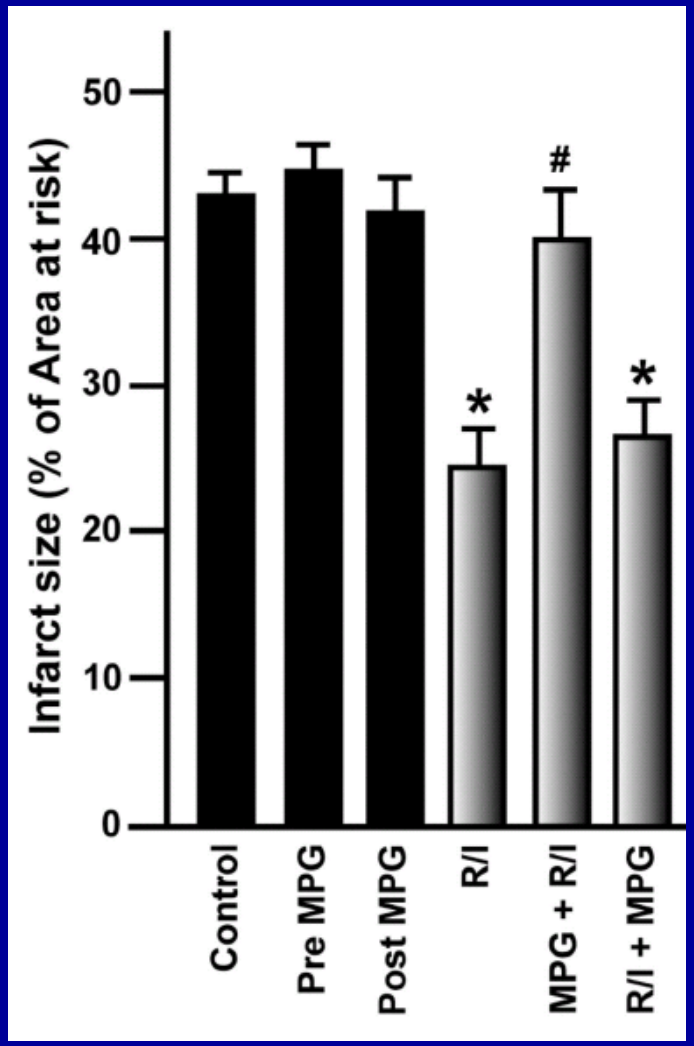


Ovize et al, Cardiovasc Res 87: 406-423, 2010

Mice

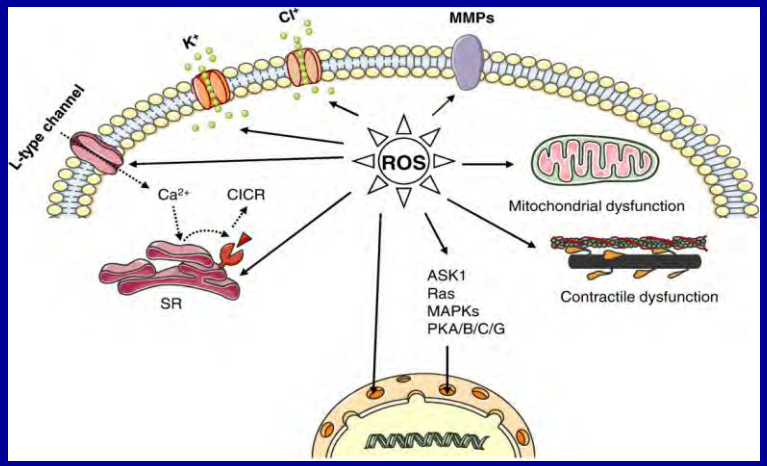
ROS scavenging and ischemic postconditioning





Tsutsumi et al., Life Sci 81: 1223-1227, 2007

ROS during IRI and protection from it



contribute to cellular damage

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Morphology

(Postischemic Reperfusion, Heart Failure)

contribute to cellular protection

Function

Morphology

(Ischemia/Reperfusion Injury)