Discussion
Mitochondrial functions and Nutrition

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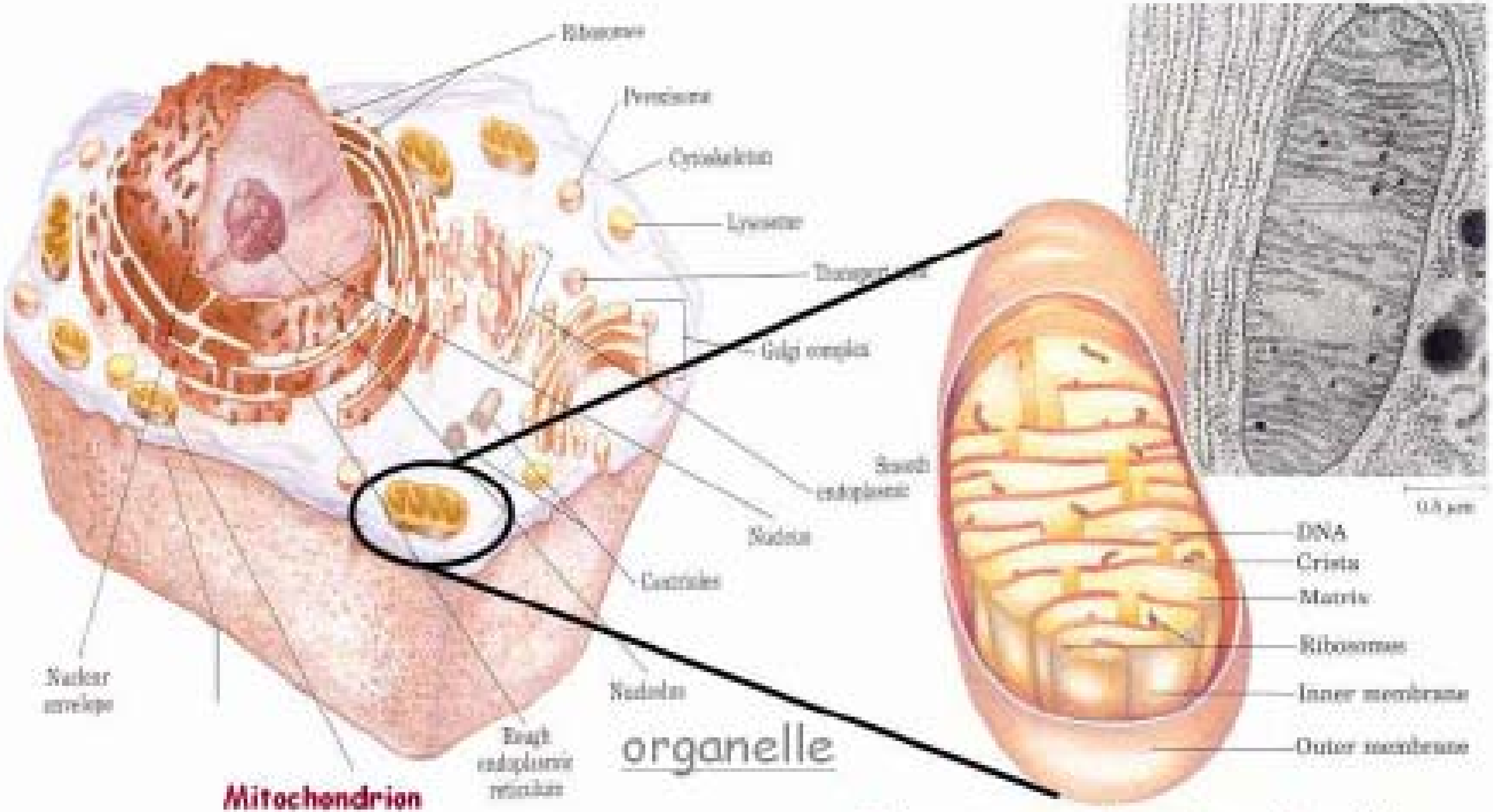
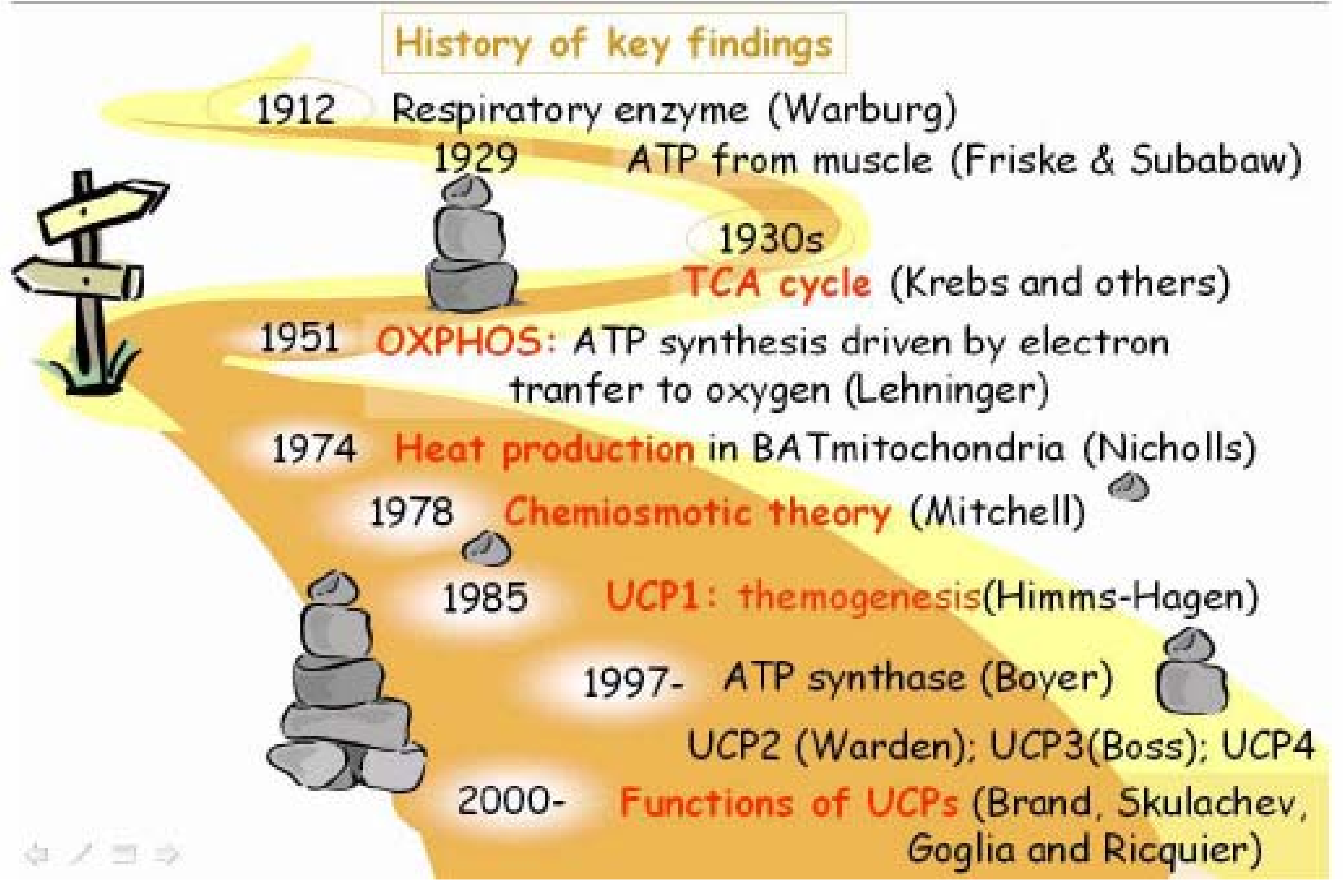
Mitochondria



Energy production of cell
(powerhouses)

Adapted from Lehninger's Principles of Biochemistry, 2[nd] ed.


History of key findings
1912 Respiratory enzyme (Warburg)
1929 ATP from muscle (Friske & Subabaw)
1930s
TCA cycle (Krebs and others)
1951 OXPHOS: ATP synthesis driven by electron tranfer to oxygen (Lehninger)
1974 Heat production in BATmitochondria (Nicholls)
1978 Chemiosmotic theory (Mitchell)
1985 UCP1: themogenesis(Himms-Hagen)
1997- ATP synthase (Boyer)
UCP2 (Warden); UCP3(Boss); UCP4
2000- Functions of UCPs (Brand, Skulachev, Goglia and Ricquier)

Main physiological functions of mitochondria

Energy conservation = ATP production

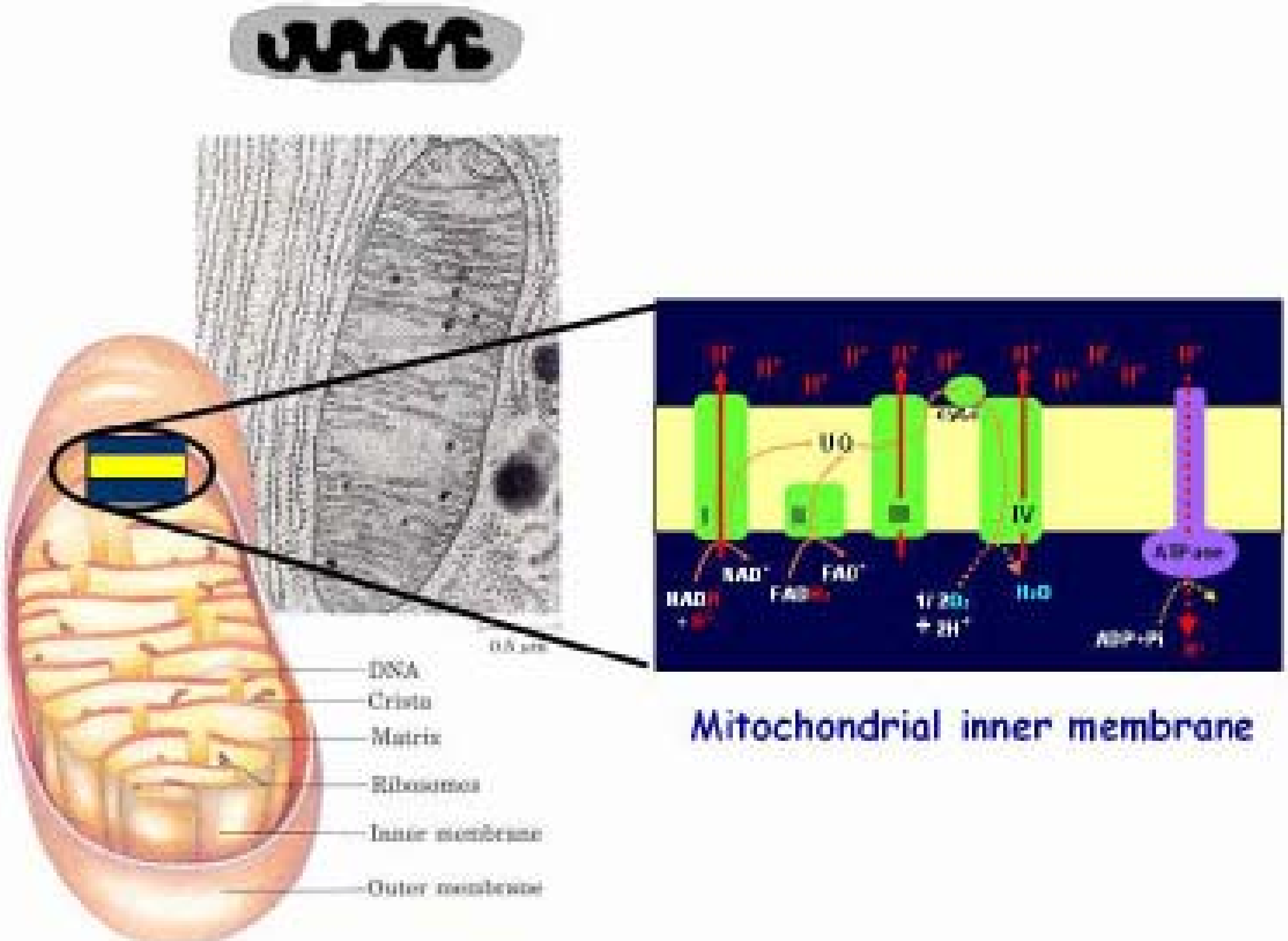
Thermoregulatory = energy dissipation as heat

Substrate production & decomposition

Reactive oxygen species (ROS)

Skulachev(1998)

Oxidative phosphorylation { coupling ⟺ uncoupling



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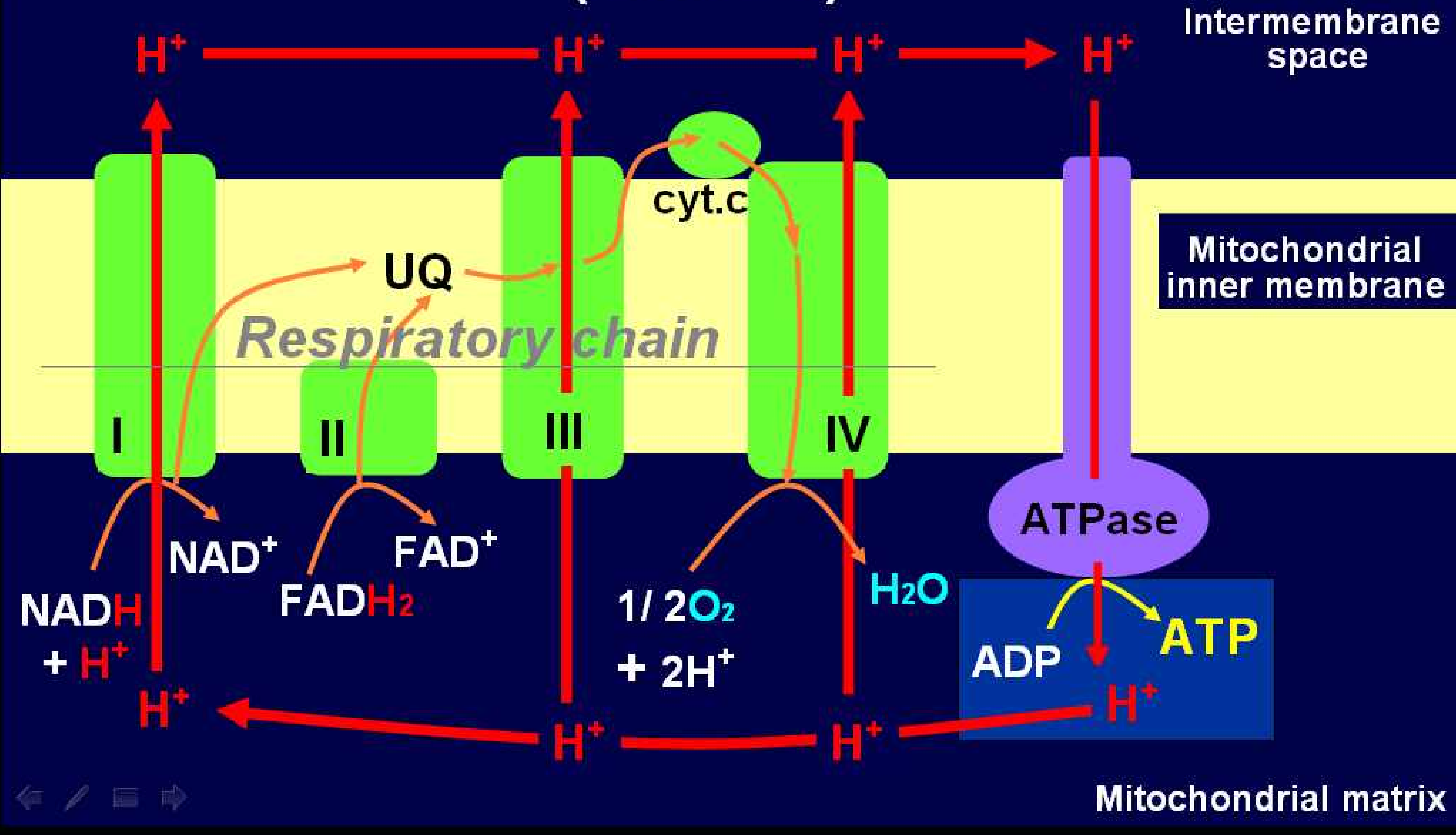
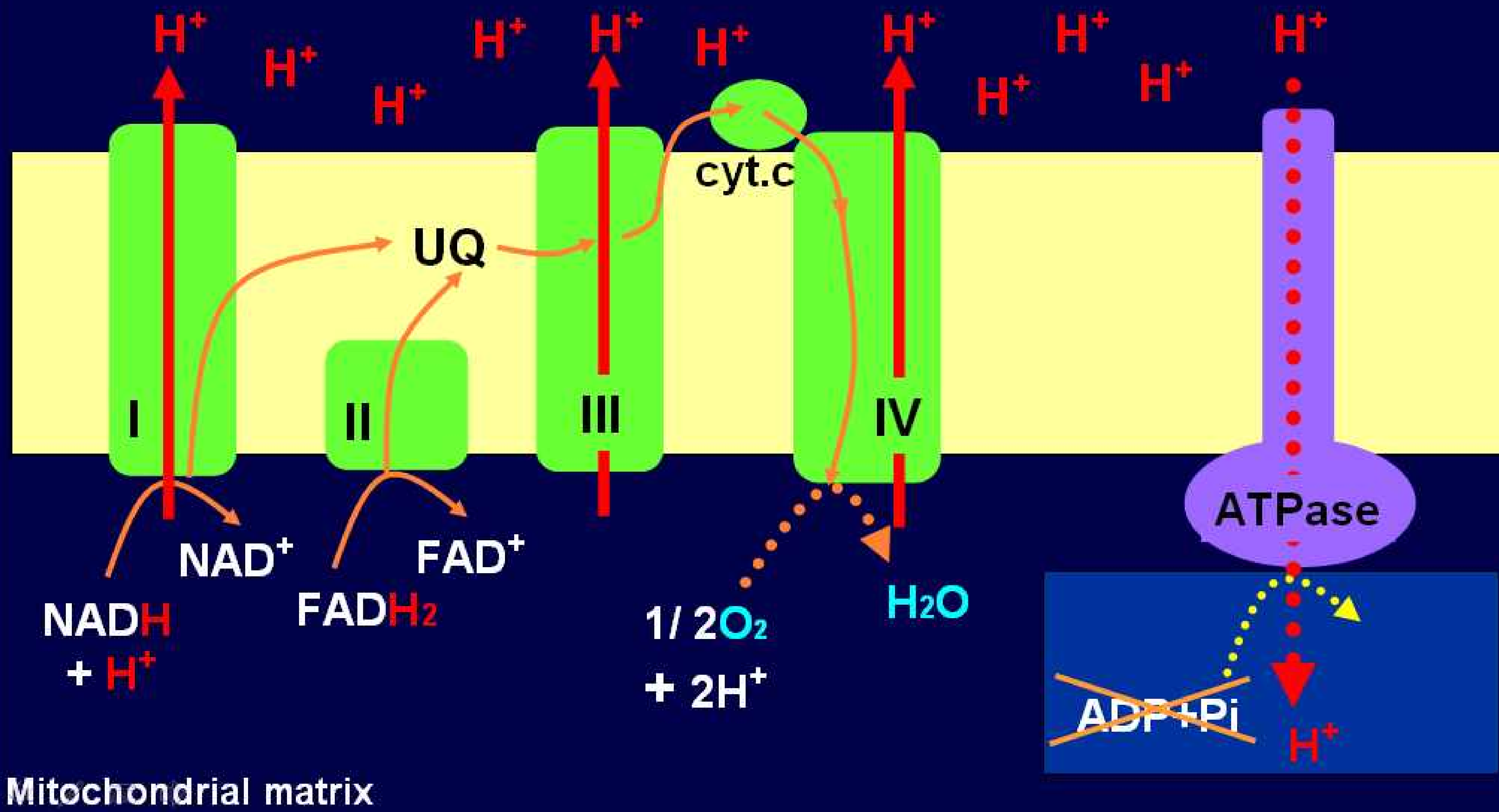
Oxidative phosphorylation in mitochondria

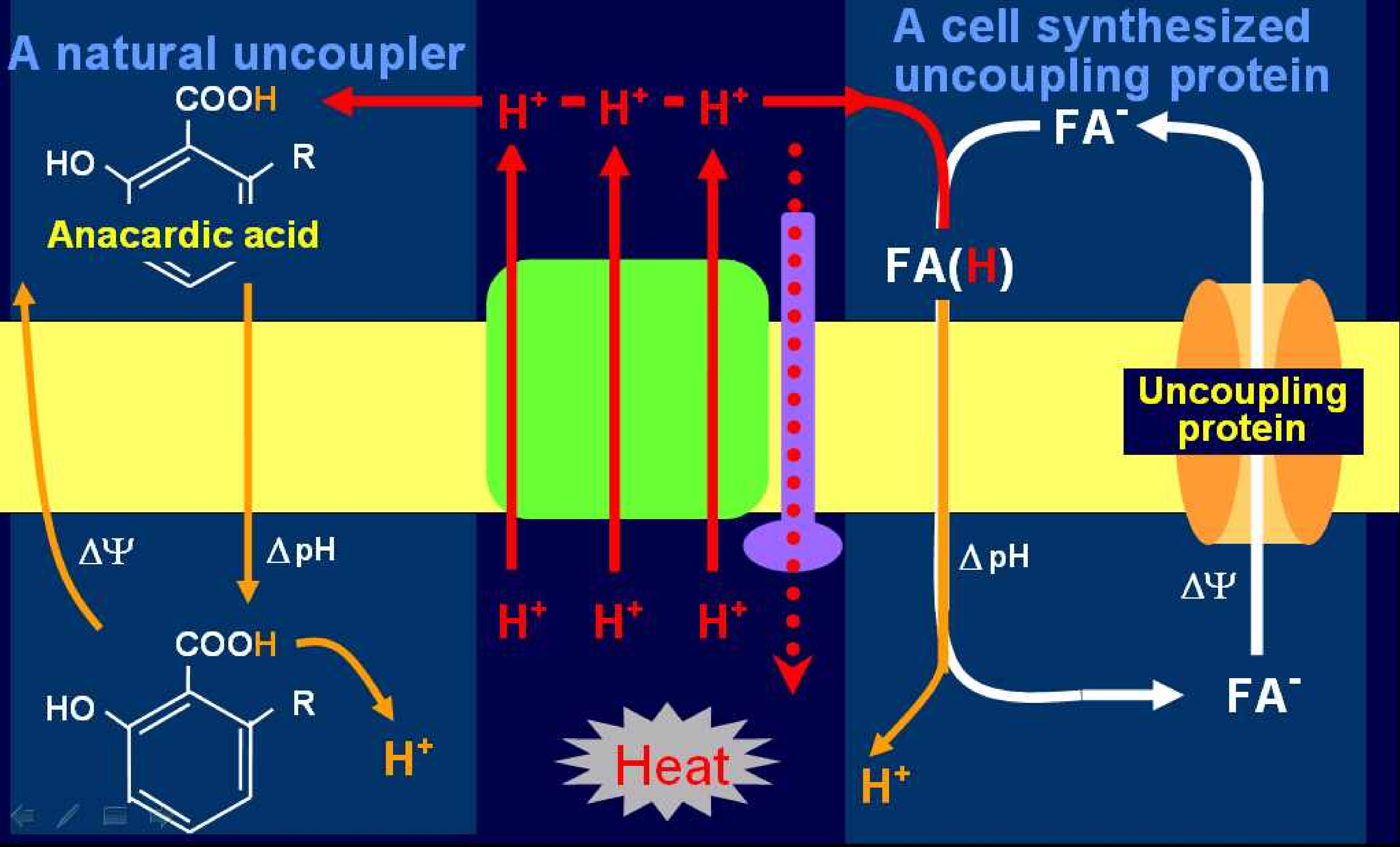
(STATE 3)

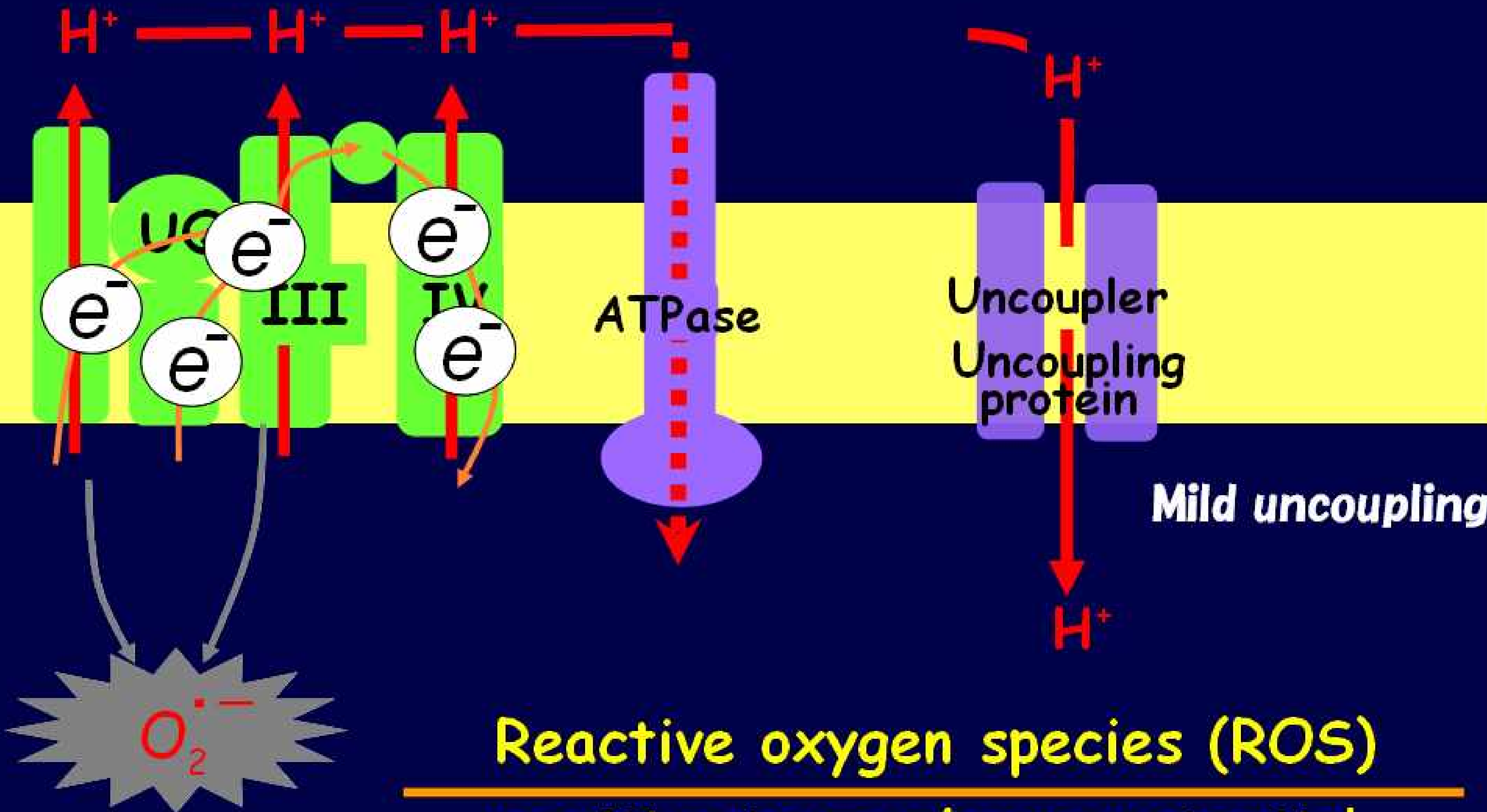


ADP Absent: Phosphorylation does not occur.
(STATE 4)



Uncoupler and Uncoupling protein

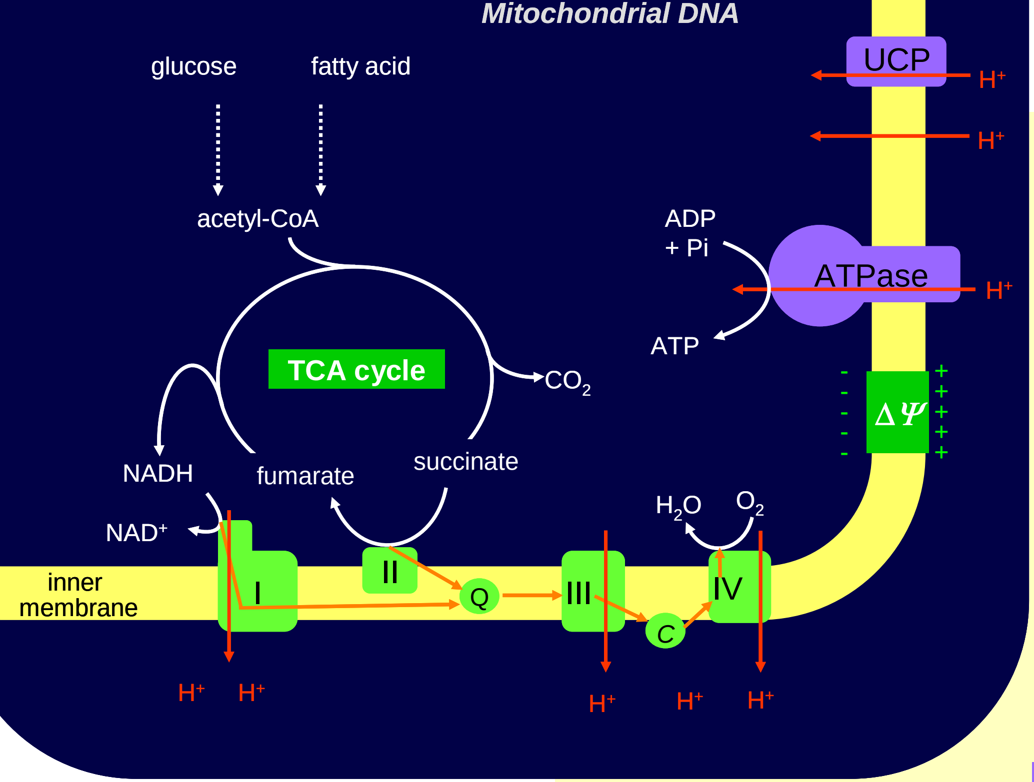


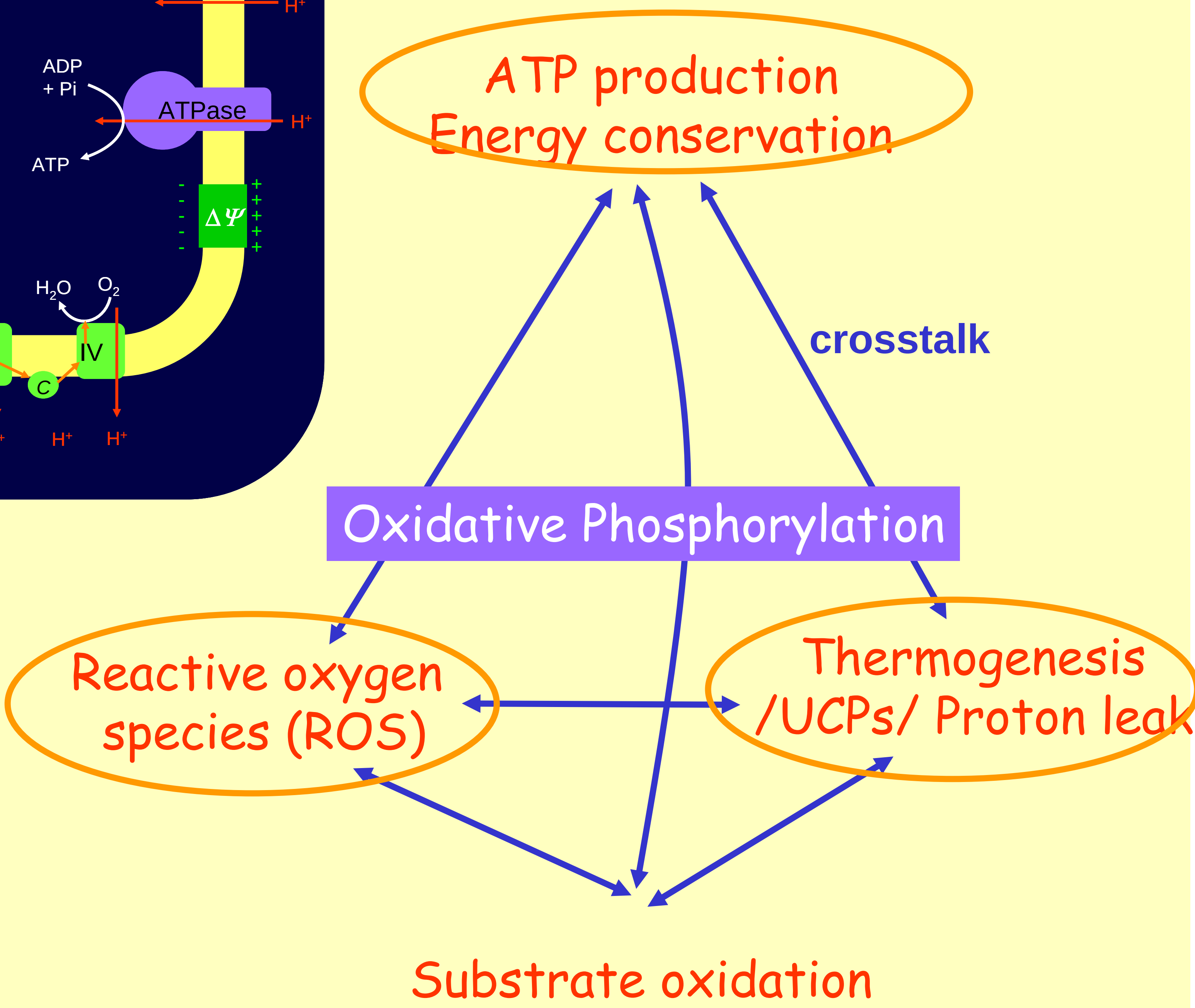


Reactive oxygen species (ROS)

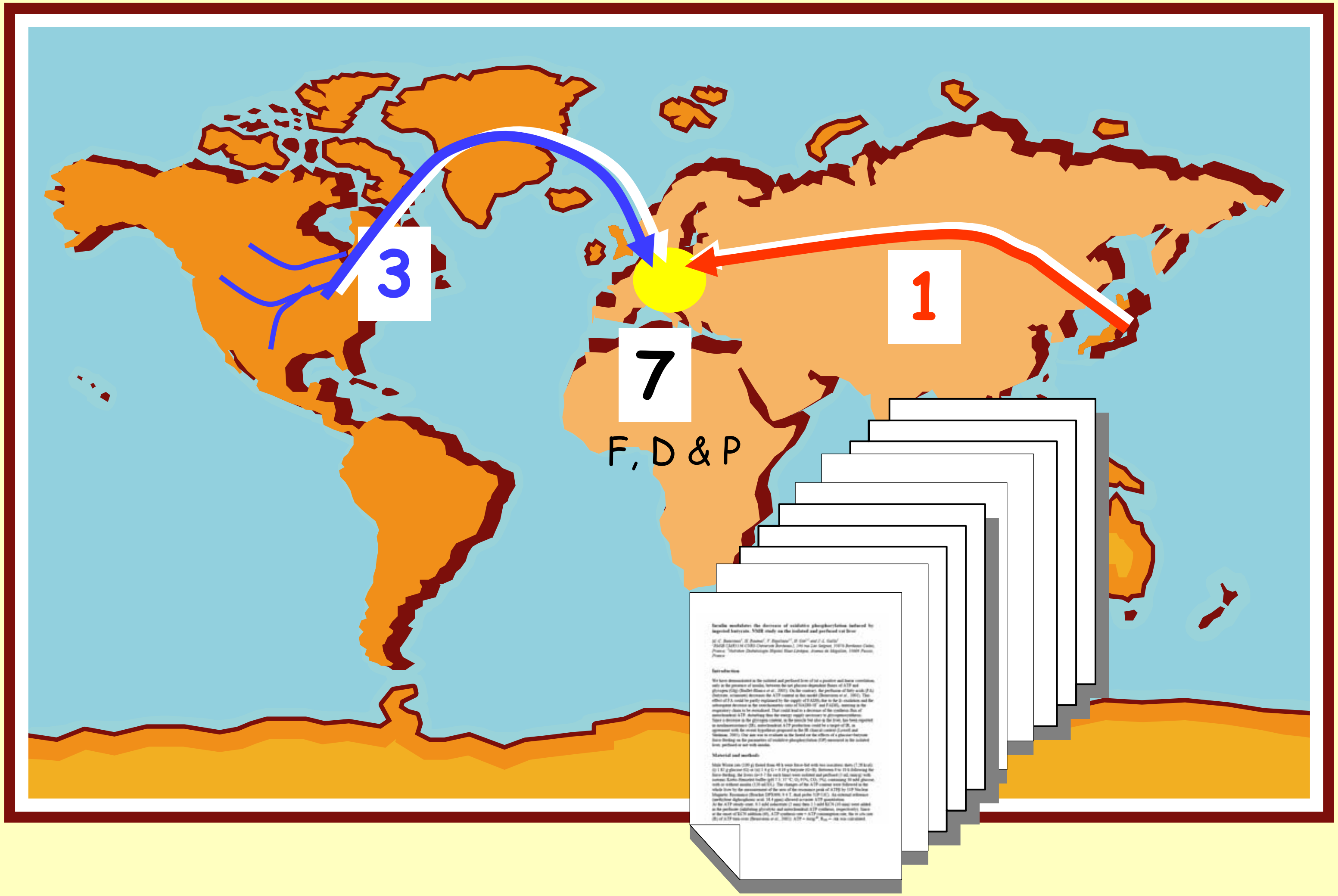
sensitive to membrane potential

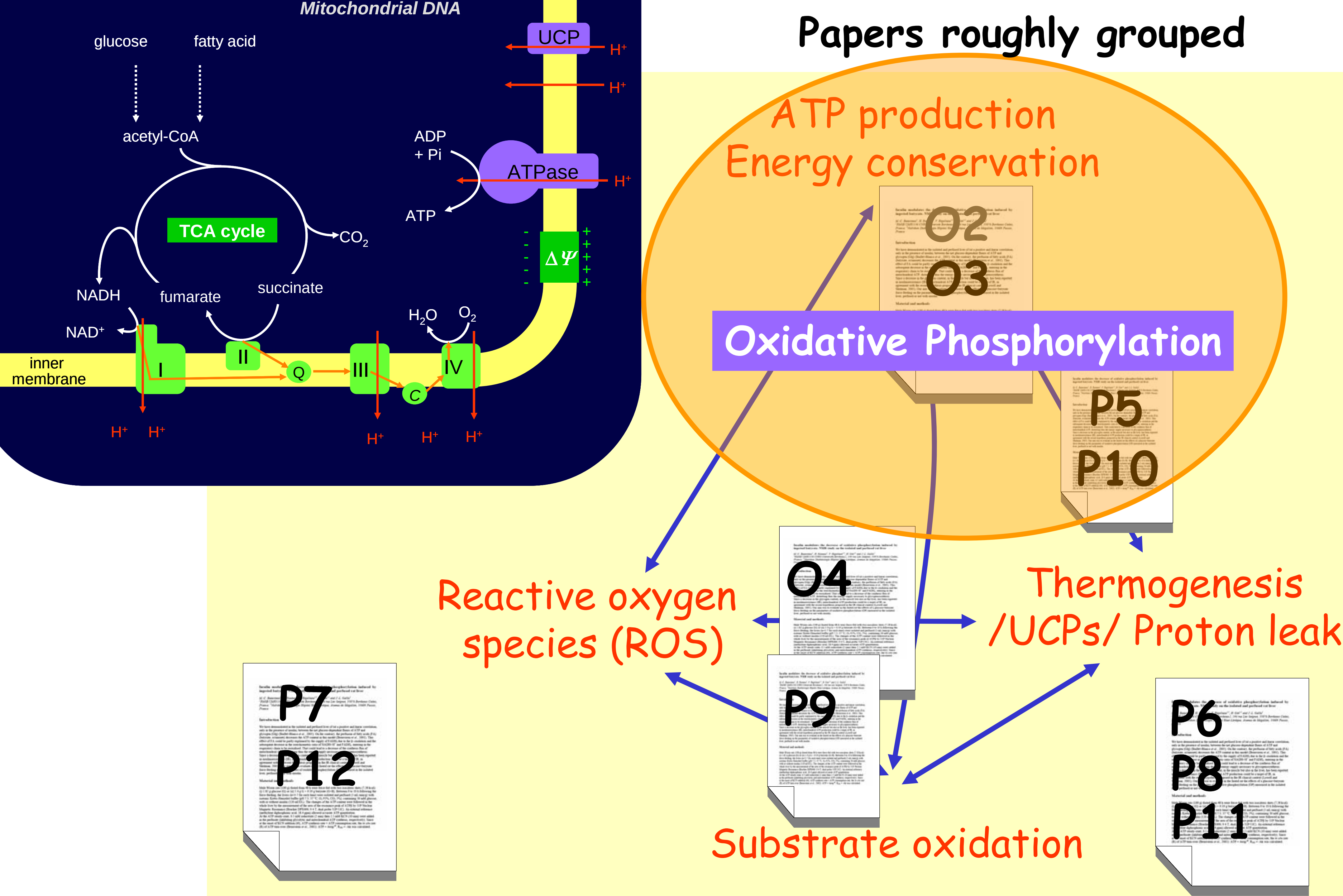
Mitochondria play key roles:





In this section




Papers roughly grouped
Mitochondrial DNA
glucose
fatty acid
acetyl-CoA
TCA cycle
CO_2
NADH
NAD^+
fumarate
succinate
UCP
H^+
ADP
+ Pi
ATPase
ATP
ΔΨ
H_2O
O_2
inner
membrane
I
II
Q
III
C
IV
ATP production
Energy conservation
O2
O3
Oxidative Phosphorylation
P5
P10
Reactive oxygen
species (ROS)
O4
P9
Thermogenesis
/UCPs/ Proton leak
P7
P12
Substrate oxidation
P6
P8
P11

#03 Effects of a diet enriched in *trans* fatty acids (*trans* MUFA) on muscle mitochondrial functions and development of insulin resistance in rodents Tardy et al, INRA, France

Wistar rats (400g)

fed different fat sources:

oleic acid	:C18:1-9 *cis*, OLE
elaidic acid	:C18:1-9 *trans*, ELA
vaccenic acid	:C18:1-11 *trans*, VAC

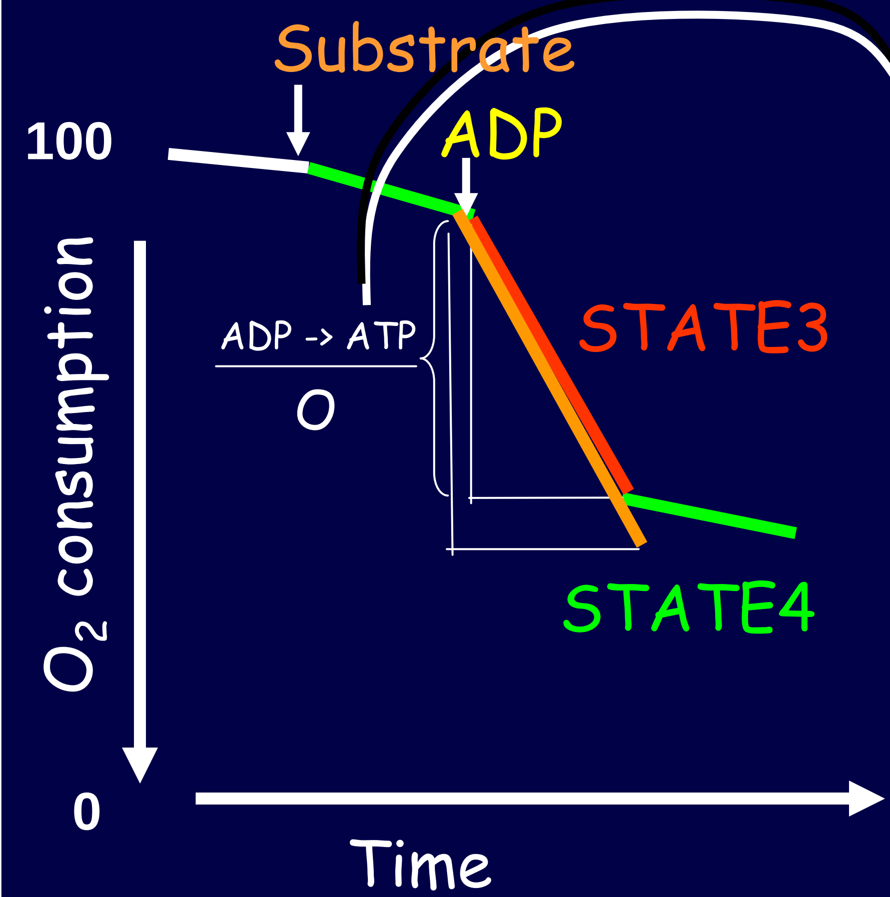
4% of total energy
for 8 wks

OXPHOS capacities
glutamate, malate +succinate
Enzyme activities
ROS production

Results with muscle mitochondria

	C18:1-9 *cis*		C18:1-9 *trans*	C18:1-11 *trans*
State 3	214	=	225	204
State 4	55	=	51	50
ATP	656	>	479	499
P/O	3.06	>	2.21	2.66

Oxygen consumption rates of mitochondria



	C18:1-9 cis	C18:1-9 trans	C18:1-11 trans
Results	(cis-fed)	(trans-fed)	
State 3	214 =	225	204
State 4	55 =	51	50
ATP	656 >	479	499
P/O	3.06 >	2.21	2.66

decrease

Reasons:

1) could be from uncoupling
2) may be the possibility of reduced integrity of the ATPase

#05 Relationships between hepatic mitochondrial function and residual feed intake in growing beef calves Lancaster et al, Texas A&M Univ., Washington State Univ., Ohio State Univ., USA

Two strains' calves

Angus heifers (n=29; BW=256kg)

Santa Gertrudis steers (n=119; initial BW=308.4 kg)

Growing calves with low and high Residual feed Intake (RFI) were selected

after feeding for 70 d

Exp.1/2 Group	Angus heifers Low RFI	Angus heifers High RFI	Angus heifers SE
Final BW, kg	326	322	9
ADG, kg/d	1.31	1.33	0.05
DMI, kg/d	less 8.94[a]	10.32[b]	0.33

Mitoc

C

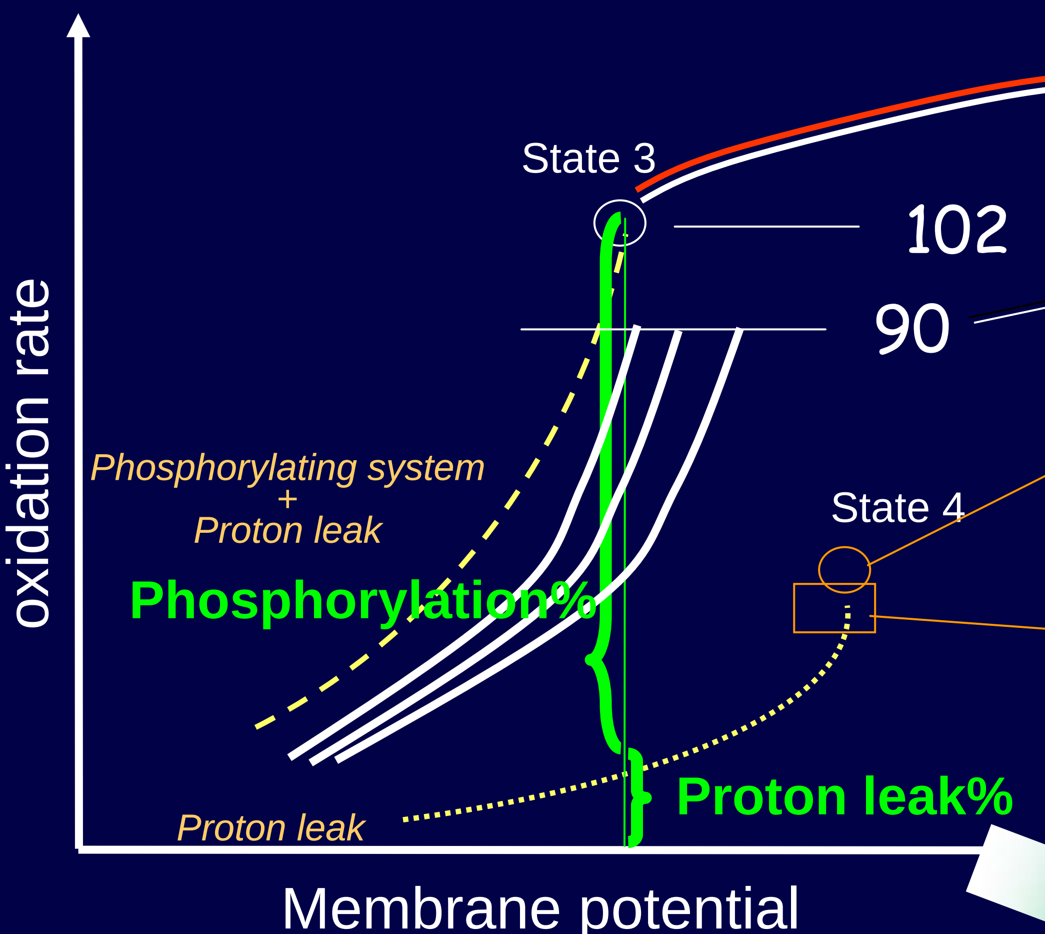
/

F

Gordo

Conclusion: These data suggest that ADP may have greater metabolic control of mitochondrial respiration in calves with low RFI (more efficient)

Efficiency of oxidative phosphorylation



Growing calves with low and high Residual feed Intake

DMI kg/d 8.9 *vs* 10.3

OXPHOS capacities of liver mitochondria

State 3	102	90
State 4	21	21

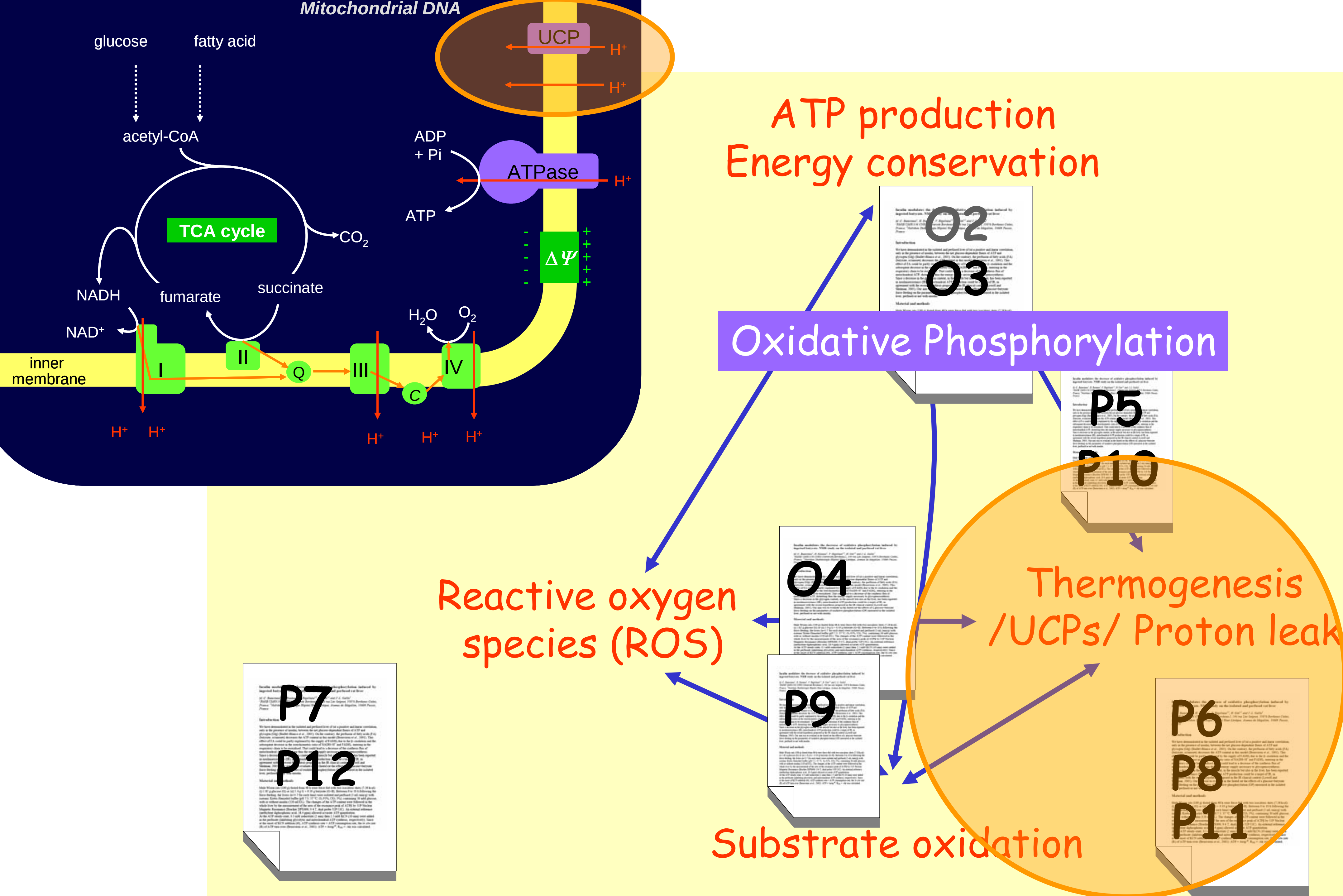
numerically

Membrane potetial

mV	192	195
O_2	Proton leak	
	19	19

Efficiency of OXPHOS

$$= \frac{O_2 \text{ consumption for phosphorylation}}{\text{total } O_2 \text{ consumption}}$$



Mitochondrial DNA
glucose
fatty acid
acetyl-CoA
UCP
H+
H+
ADP
+ Pi
ATPase
H+
ATP
TCA cycle
CO_2
ΔΨ
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inner membrane
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H+
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H+
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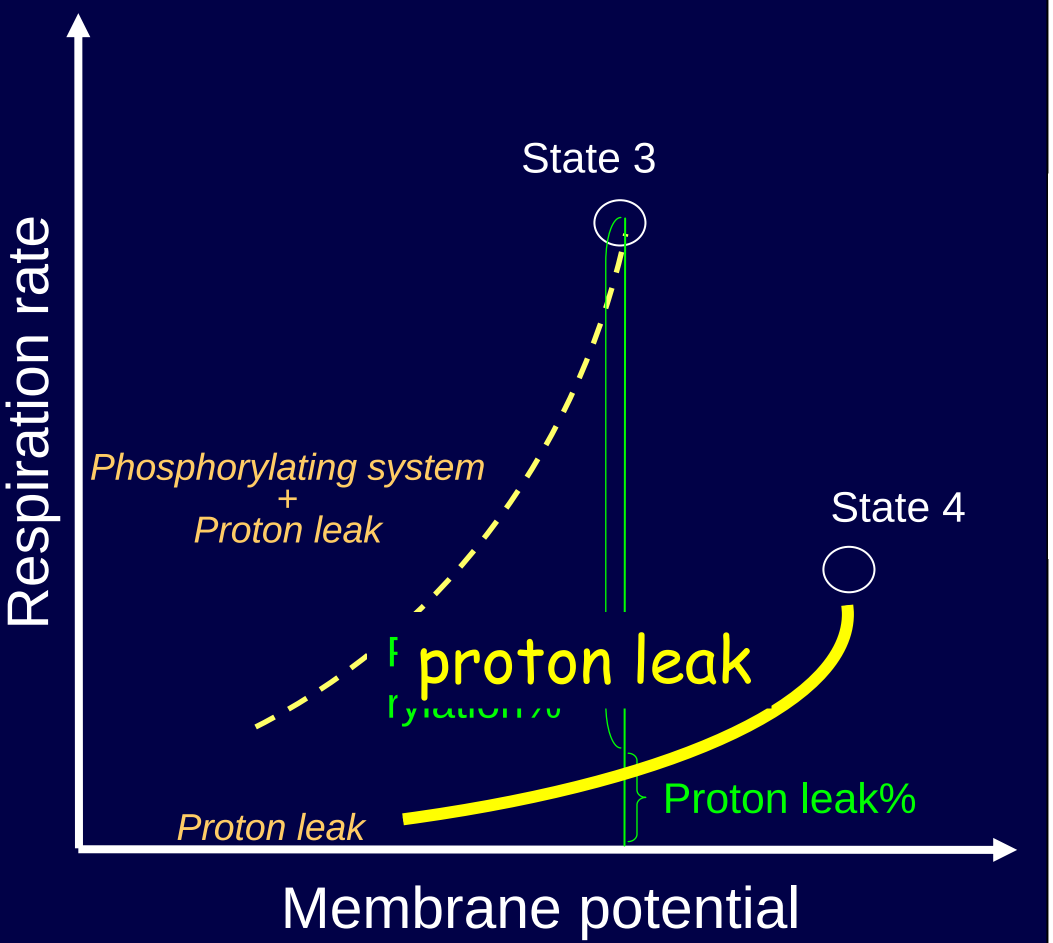
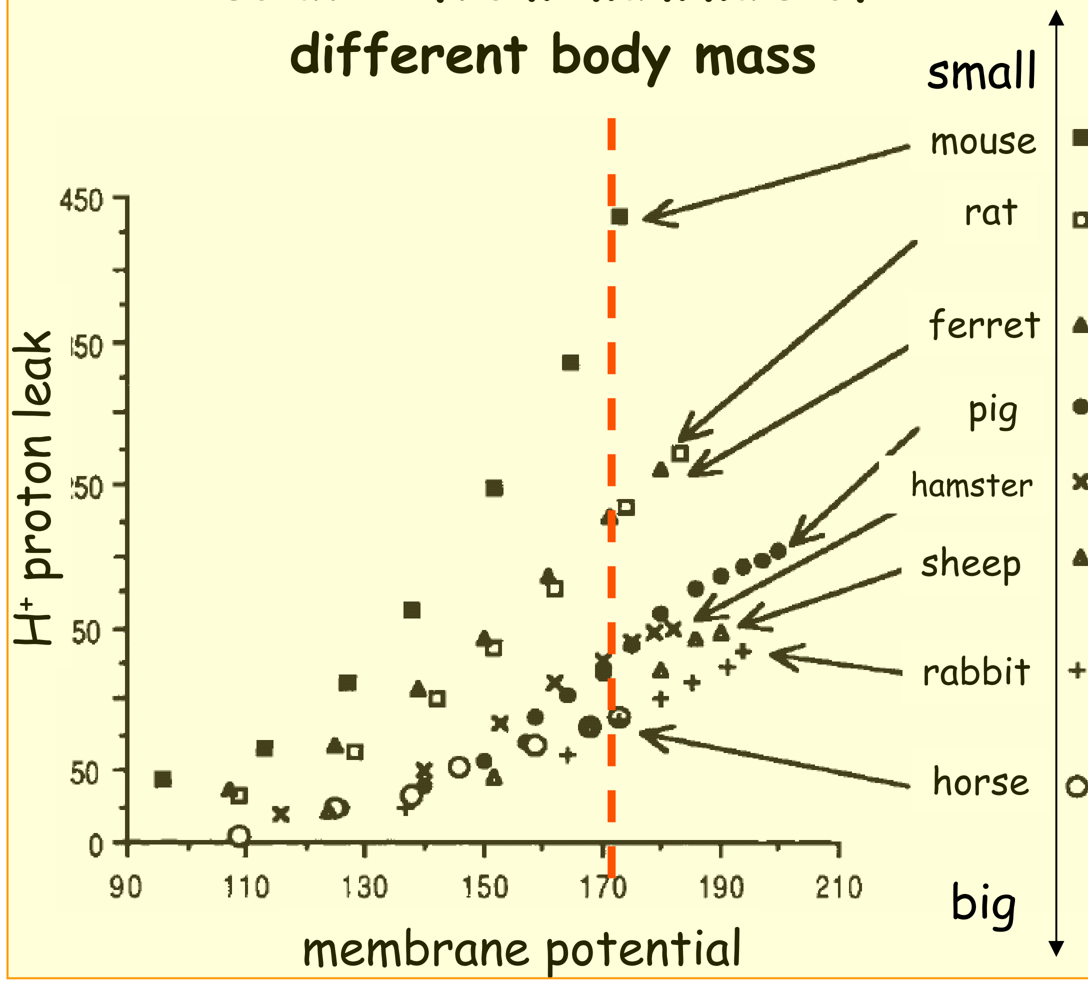
Substrate oxidation



Porter & Brand, **Nature** 362: 628 (1993)

Proton leak kinetics in <u>liver mitochondria</u> isolated from mammals of different body mass



Differences in proton leak may partly explain the differences in metabolic rate between mammals of different mass.

#P10 Variation in animal energy expenditure and mitochondrial function and protein expression *(among* Angus, Holstein, Wagyu)

Michal et al, Washington State Univ., USA

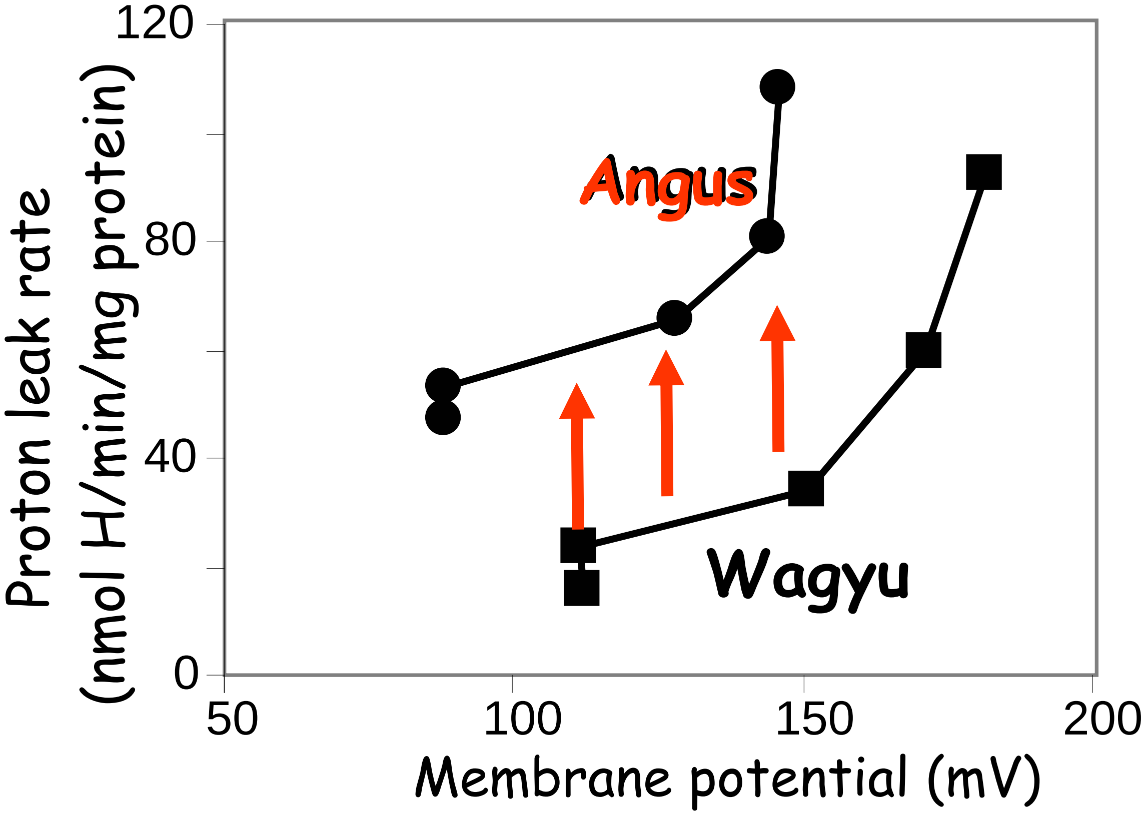
Angus, Holstein, Wagyu heifers
(n=8/breed; 10 mo)

Angus and Wagyu heifers at the Low level of intake were studied for mitochondrial function

Mitochondria: liver biopsy samples

simultaneous measurement of
- oxygen consumption
- membrane potential

Kristen A. Johnson



	Angus	Wagyu
MEm, kcal/kg$^{.75}$	113.5 >	105.2
UCP3	2.17	1.17

#P08 Expression of uncoupling proteins and mitochondrial activity are dependent on muscular fibre type in rabbits and chickens

Joubert et al, INRA, France

Chicken

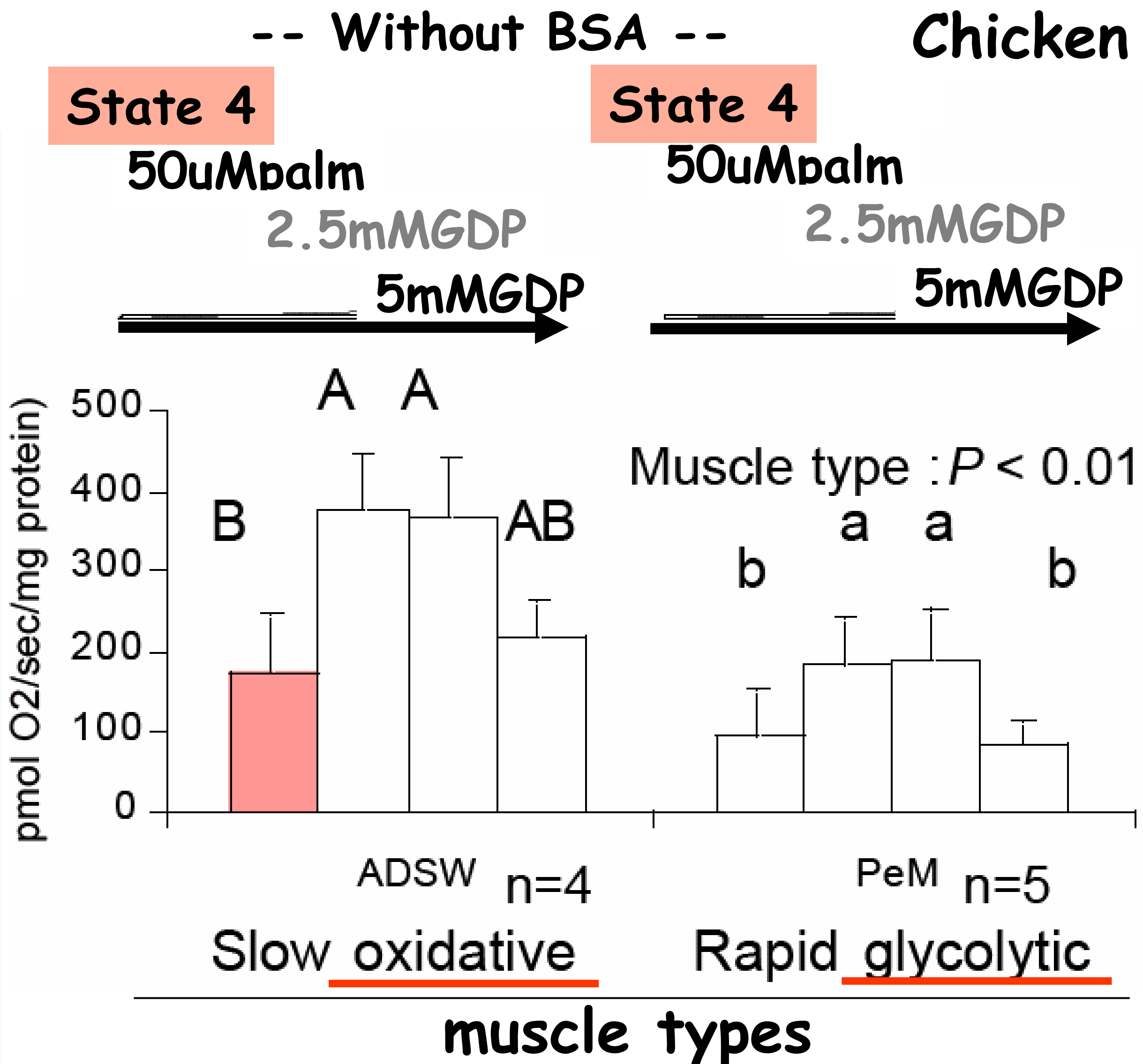
Slow: Adductor superficialis
Fast : Pectoralis major

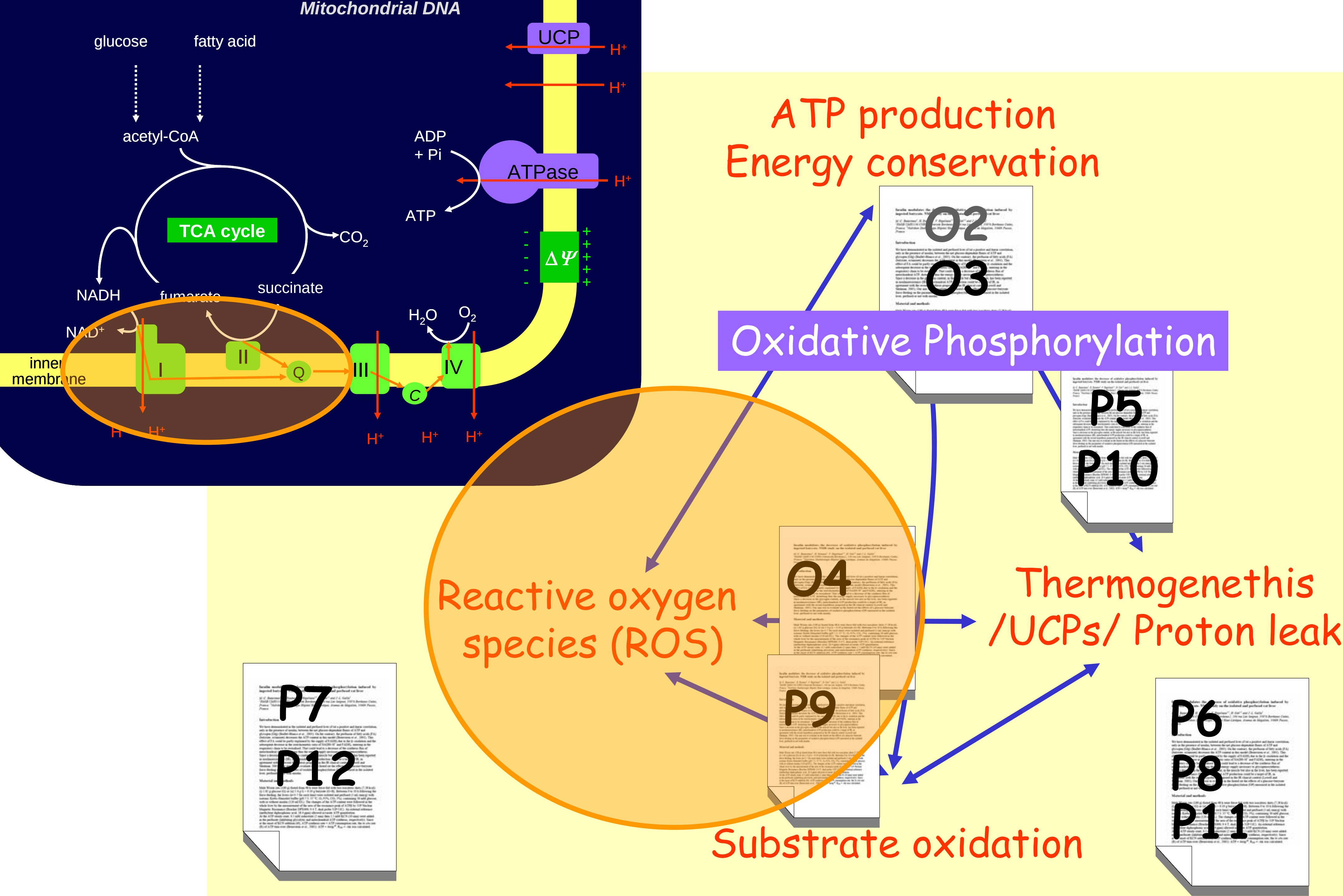
Rabbit

Slow: Semi-membranosus proprius
Fast : Psoas major

Mitochondrial respiration study:
- isolated permeabilised fibres
- isolated mitochondoria
  - Palmitate/Hydroxynonenal HNE
  - GDP

UCPmRNA expression study:
- Real-time RT-PCR




Mitochondrial DNA
glucose
fatty acid
acetyl-CoA
TCA cycle
CO_2
NADH
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inner membrane
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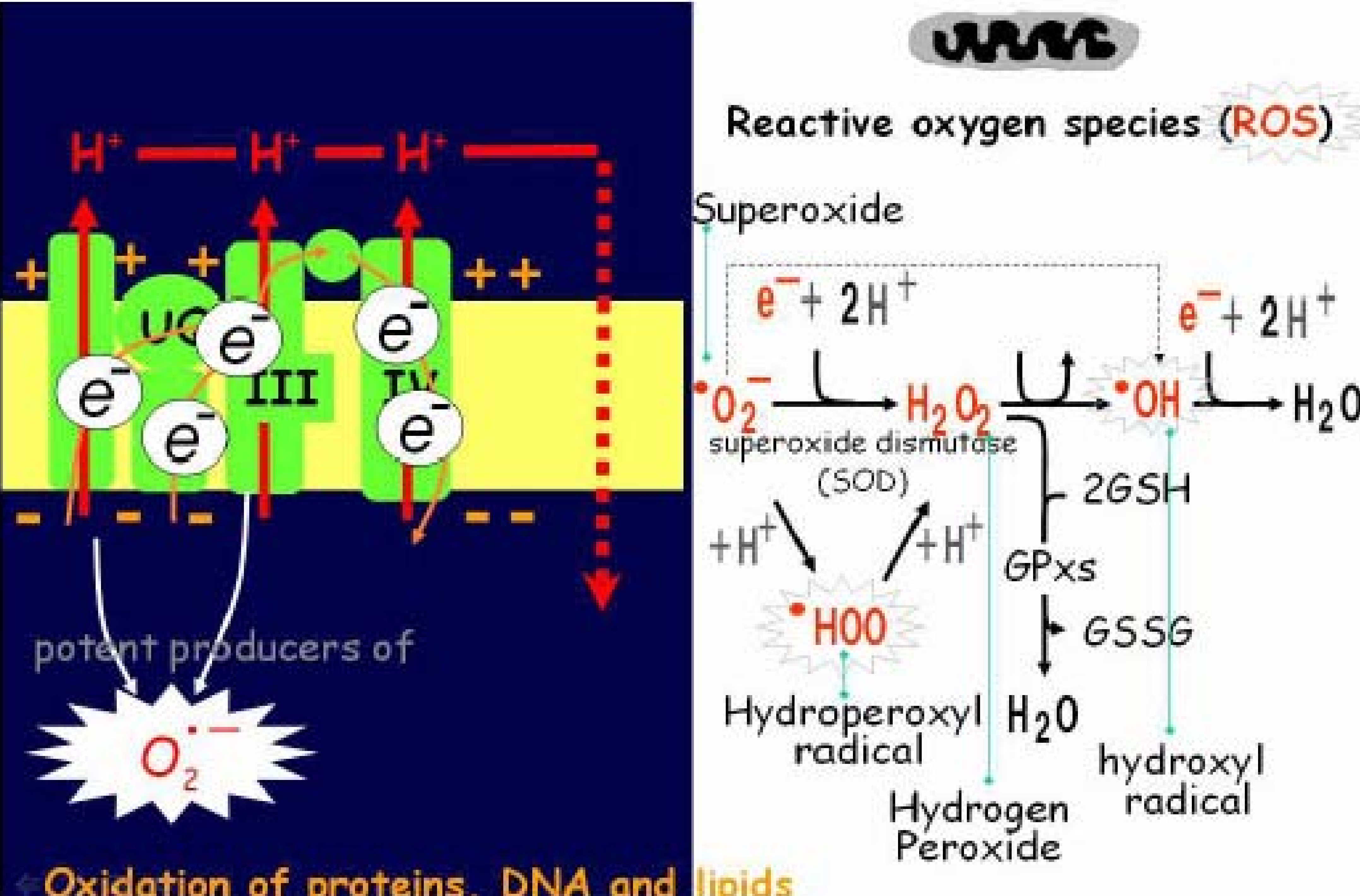
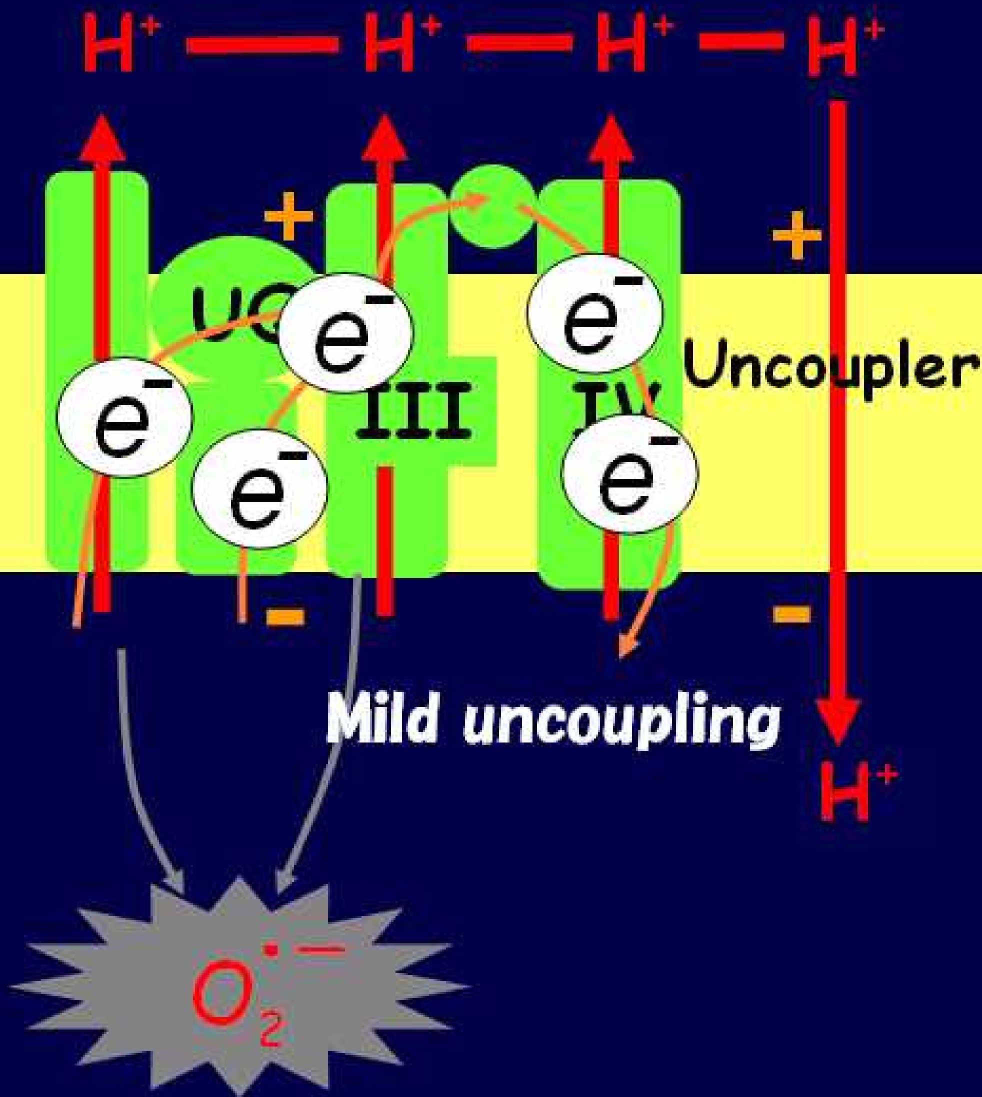
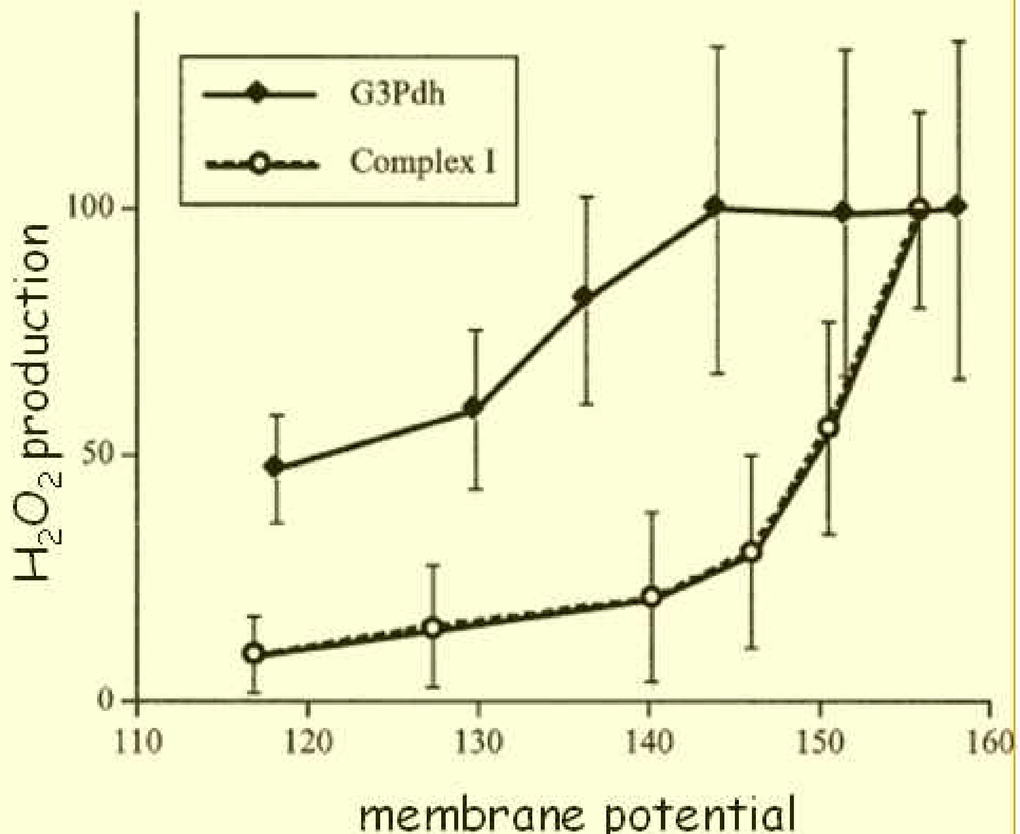


H+ H+ H+
UQ
III
IV
e-
potent producers of
O2•−
Reactive oxygen species (ROS)
Superoxide
e− + 2H+
•O2−
superoxide dismutase (SOD)
H2O2
•OH
H2O
+H+
•HOO
2GSH
GPxs
GSSG
Hydroperoxyl radical
Hydrogen Peroxide
hydroxyl radical
Oxidation of proteins, DNA and lipids

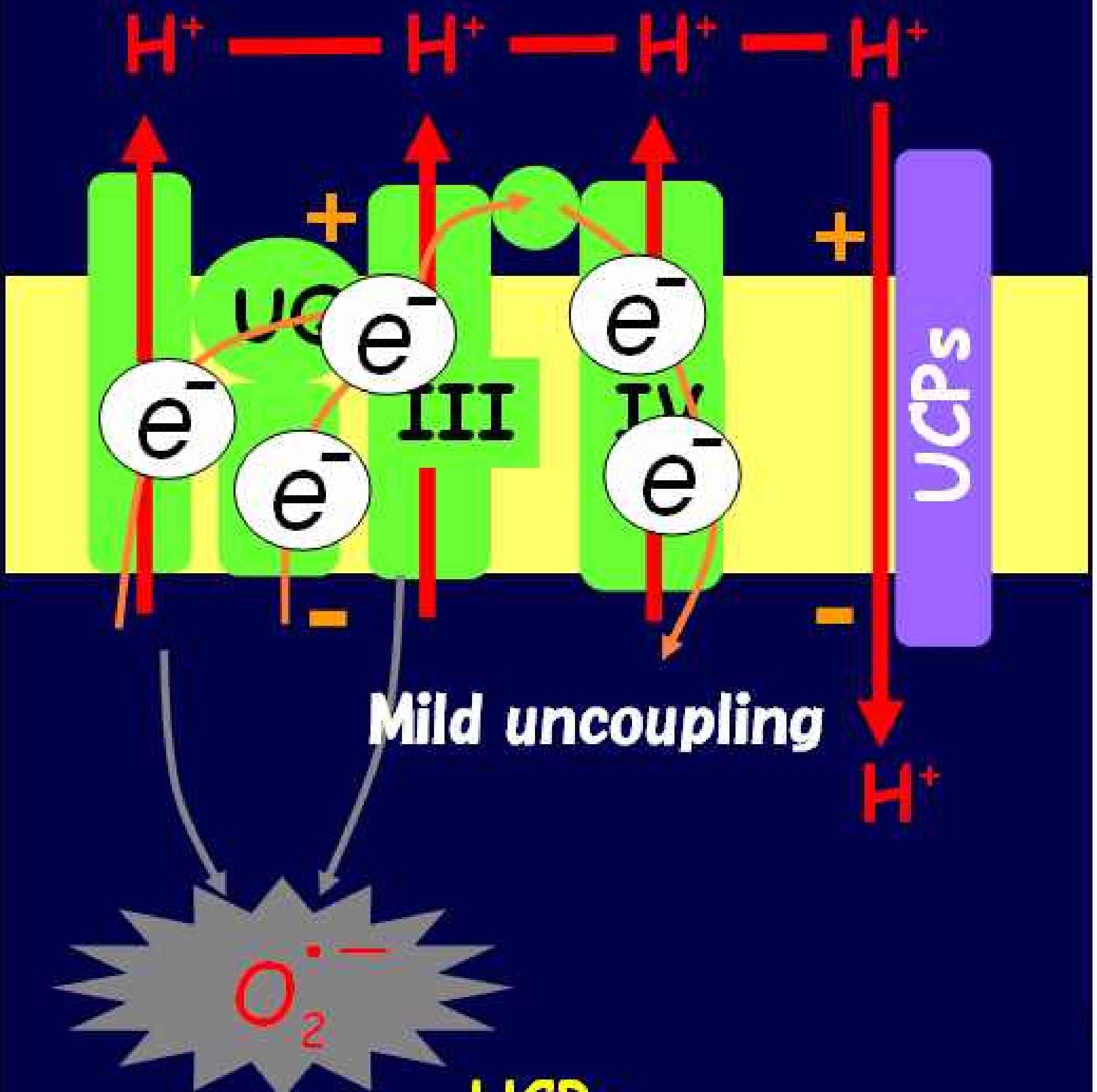
Miwa & Brand, **BST** 31: 1300 (2003)



Dependence on membrane potential of ROS at complex I and G3P-dh by isolated *Drosophila* mitochondria



ROS production is sensitive to $\Delta\Psi$

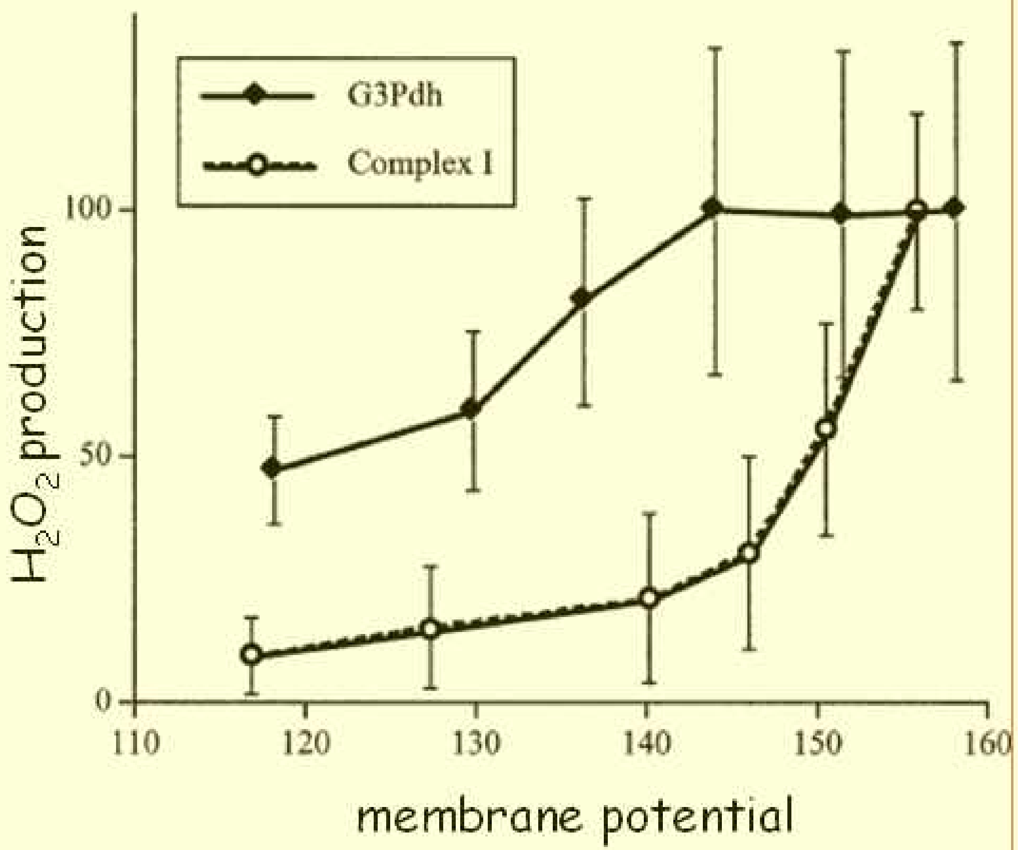


UCPs

Role in controlling ROS production

Miwa & Brand, **BST** 31: 1300 (2003)

Dependence on membrane potential of ROS at complex I and G3P-dh by isolated *Drosophila* mitochondria



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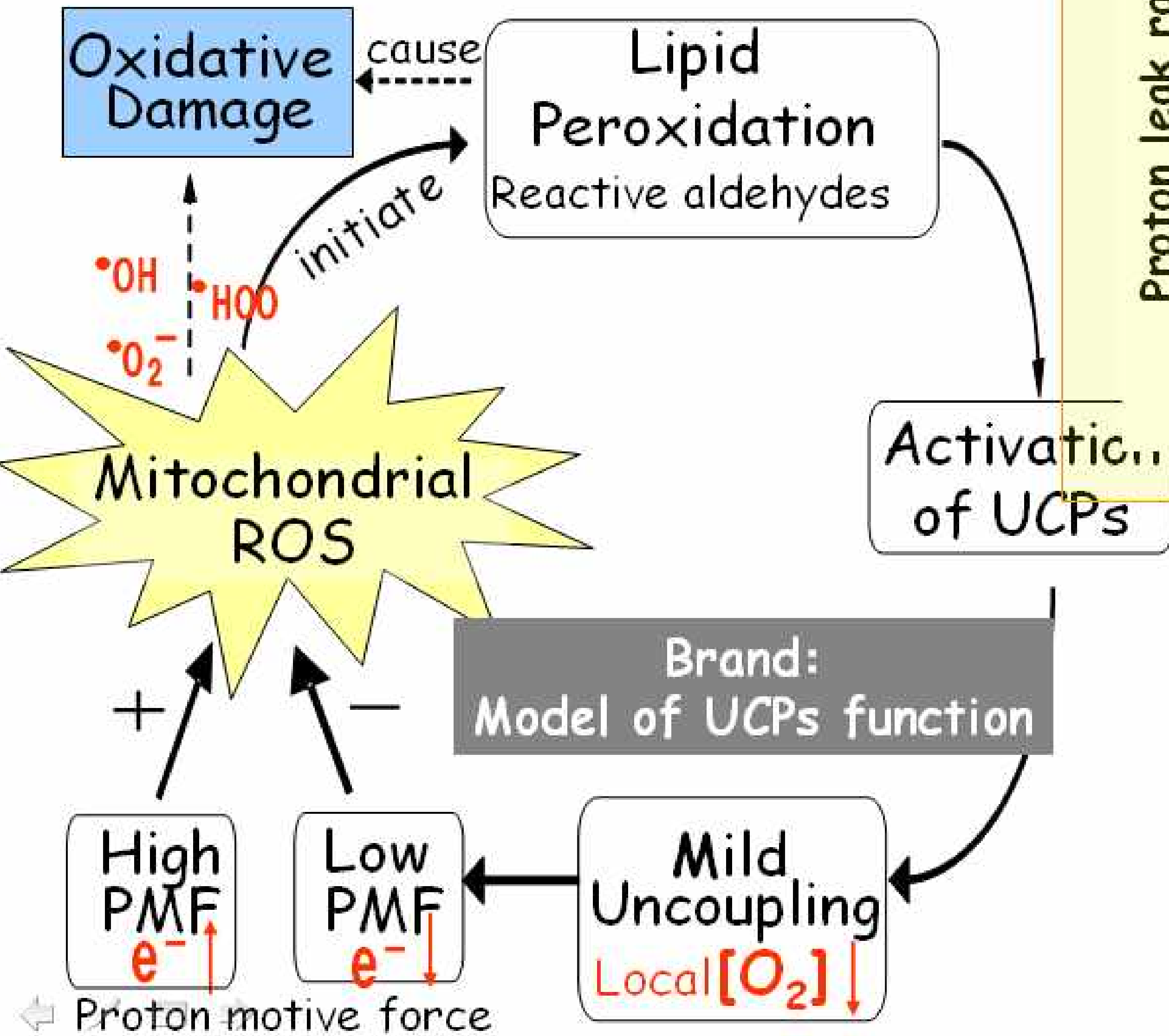
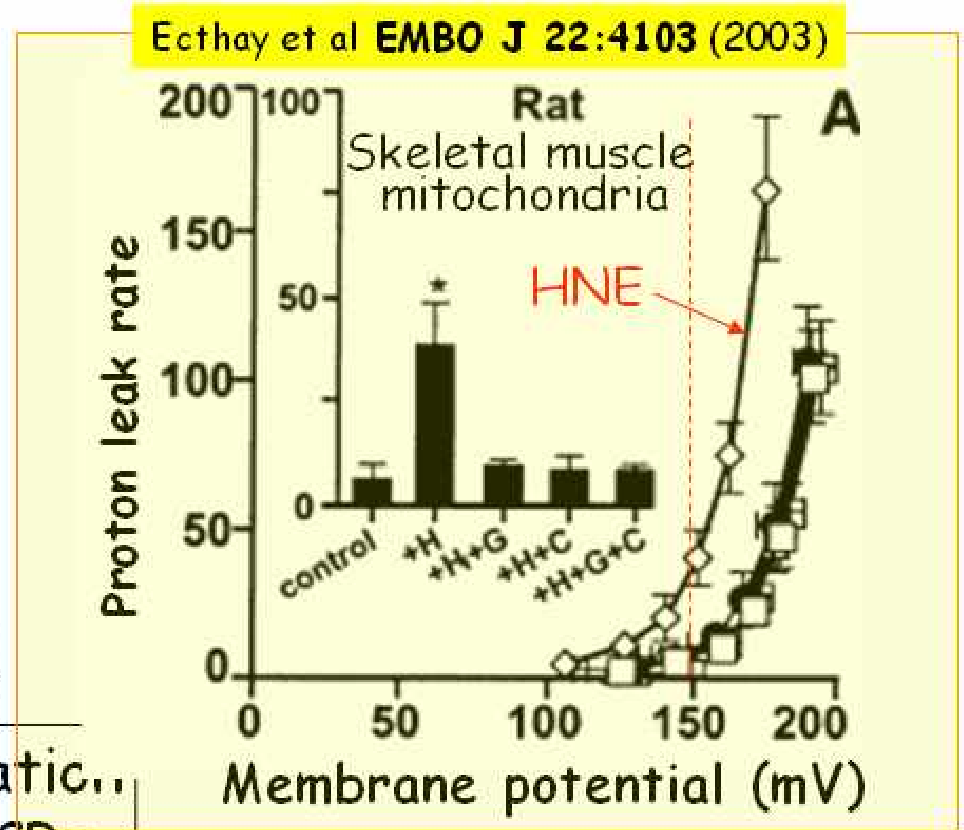
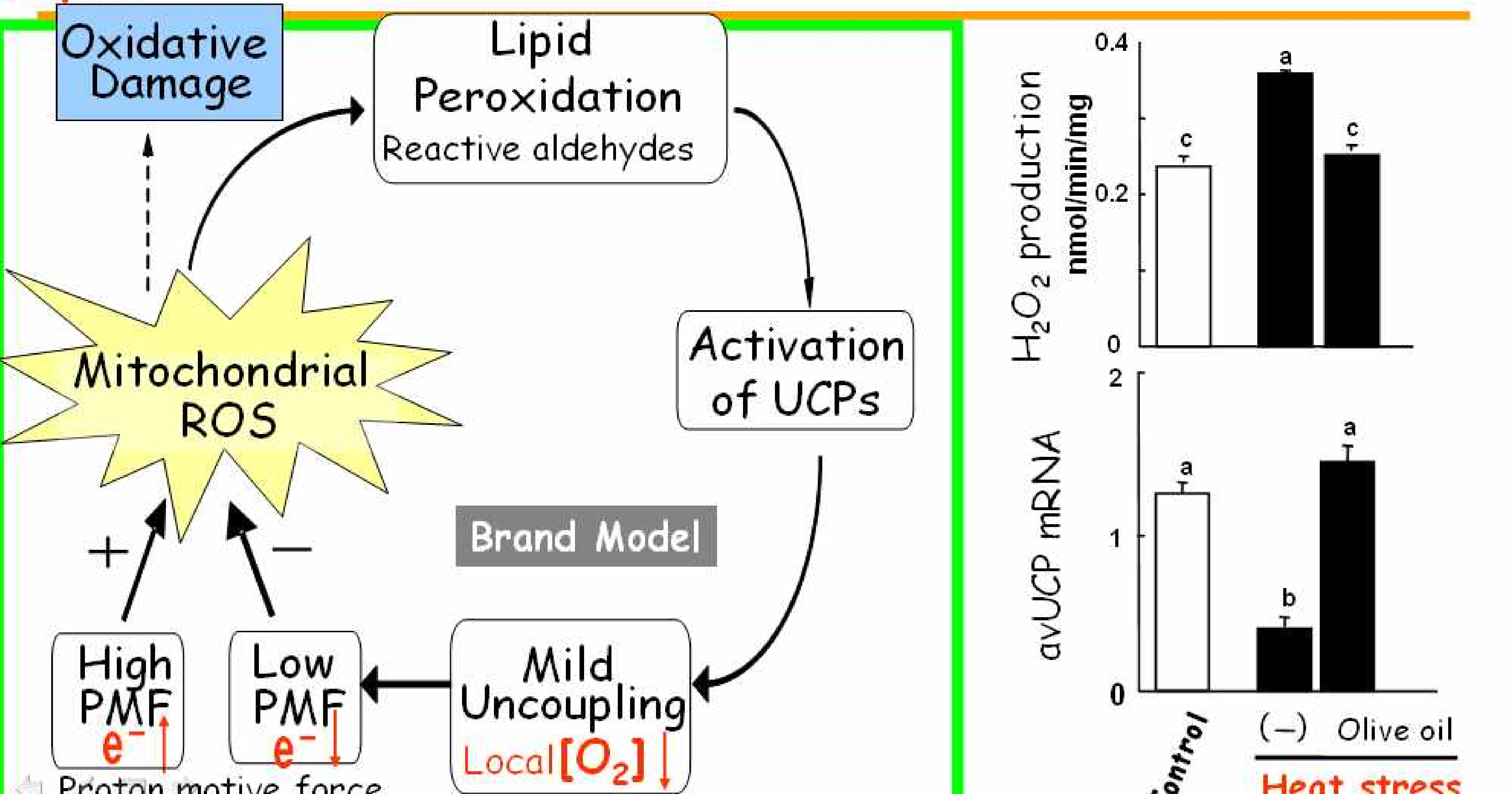




Negative feedback loop

#O04 Up-regulation or activation of avian UCP attenuates mitochondrial ROS production and oxidative damage in broiler chickens exposed to acute heat stress Mujahid et al, Tohoku Univ Japan.



#P09 Regulation of mitochondrial and tissue oxidations by thyroid hormones in chicken muscle

Collin et al, INRA, France; Katholieke Univ. Leuven, Belgium

Chicken

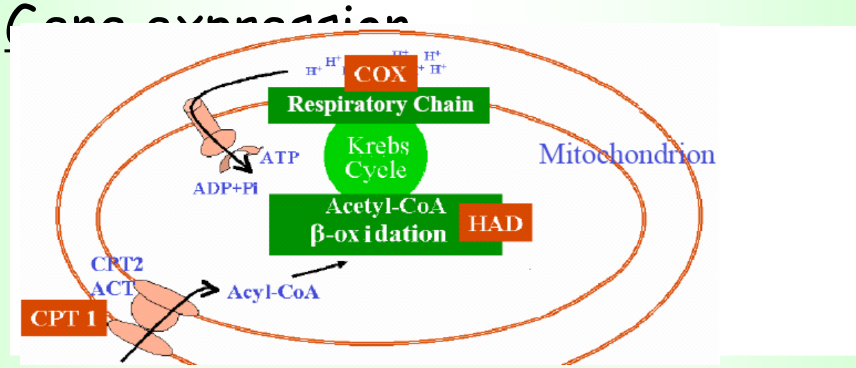
Chicken, 1-wk of age

Control

MMI: methimazole 1 g/kg feed
thyroid grand inhibitor

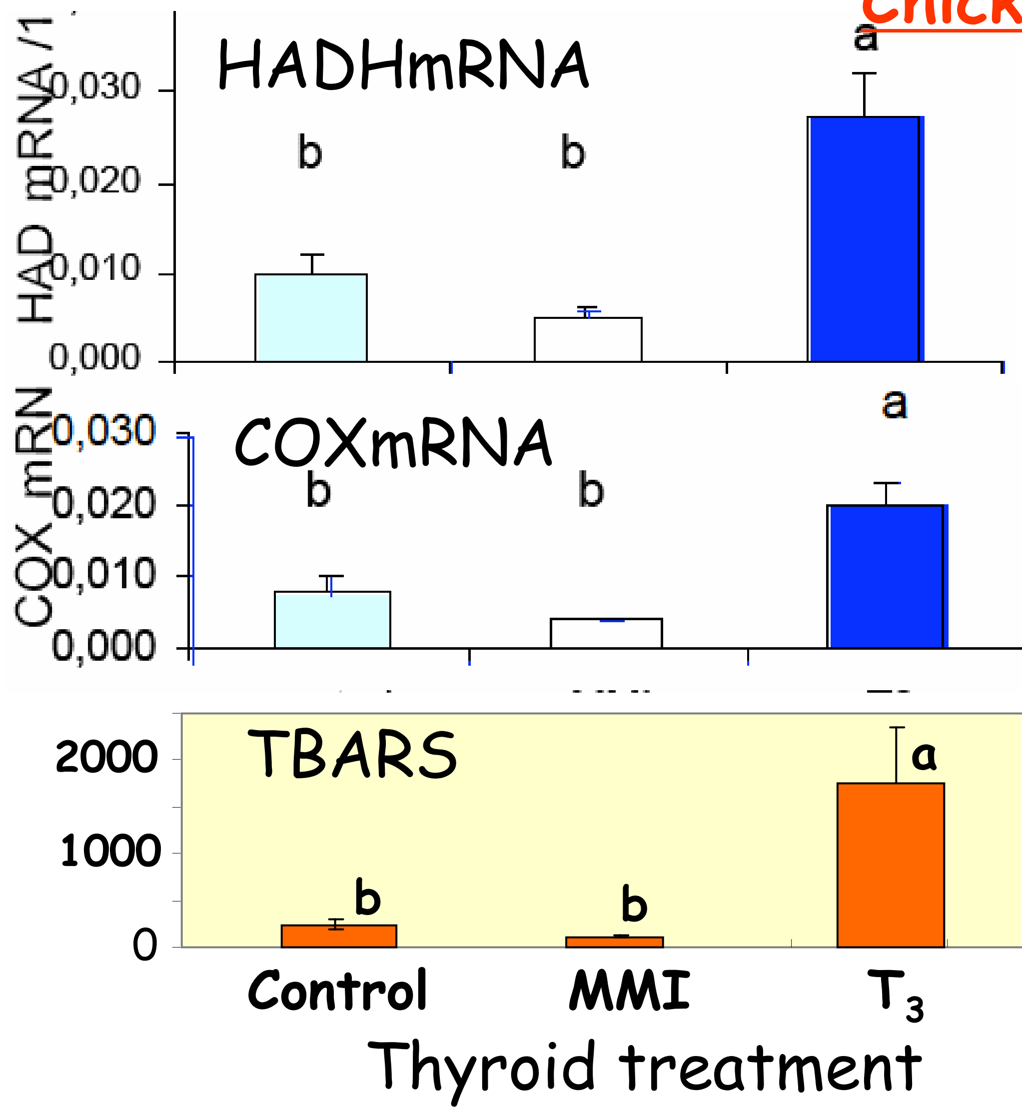
T_3: triiodothyronine 1 mg/kg feed
for 3 wks

Gene expression



AMPK assay

Oxidative stress



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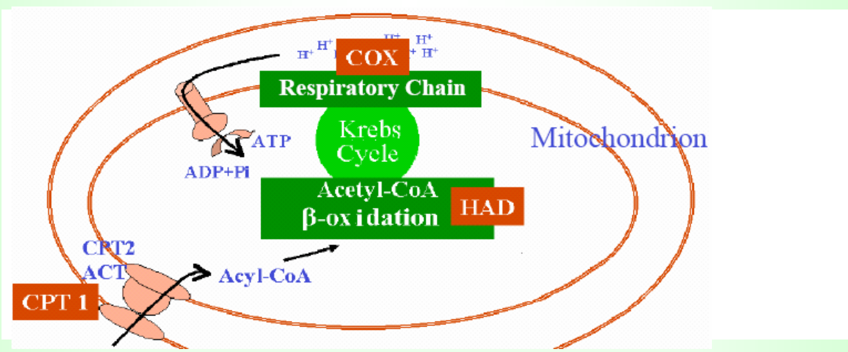
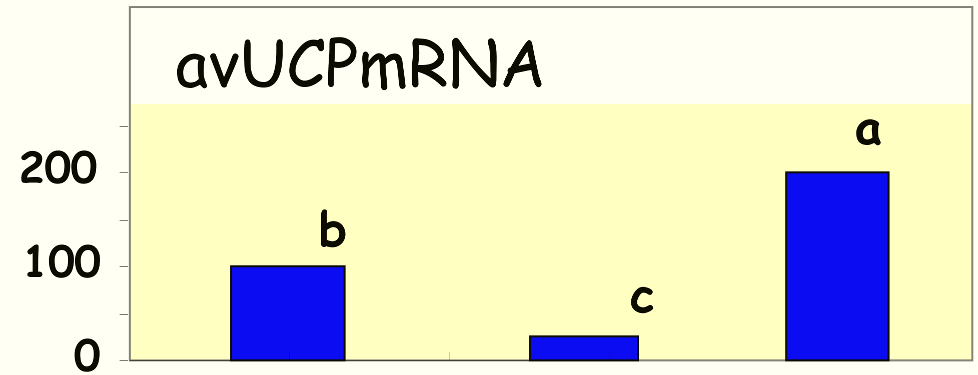
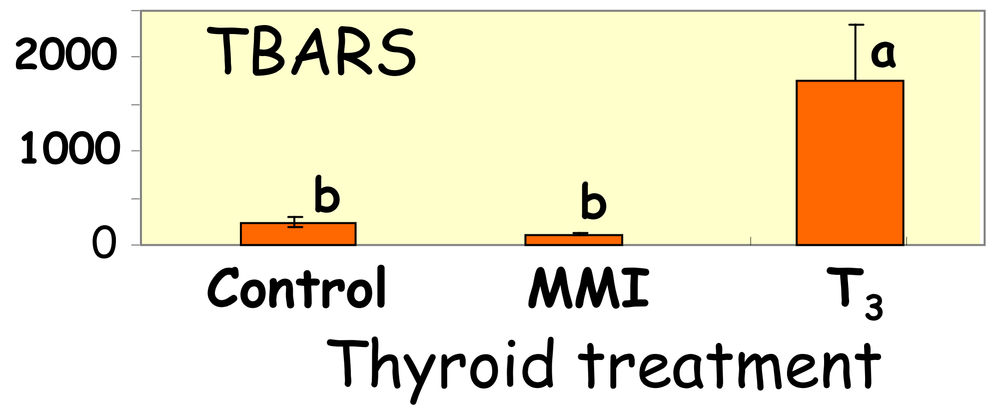


AMPK assay
Oxidative stress

Their previous results
Collin et al. AJP 284:E771 (2003)





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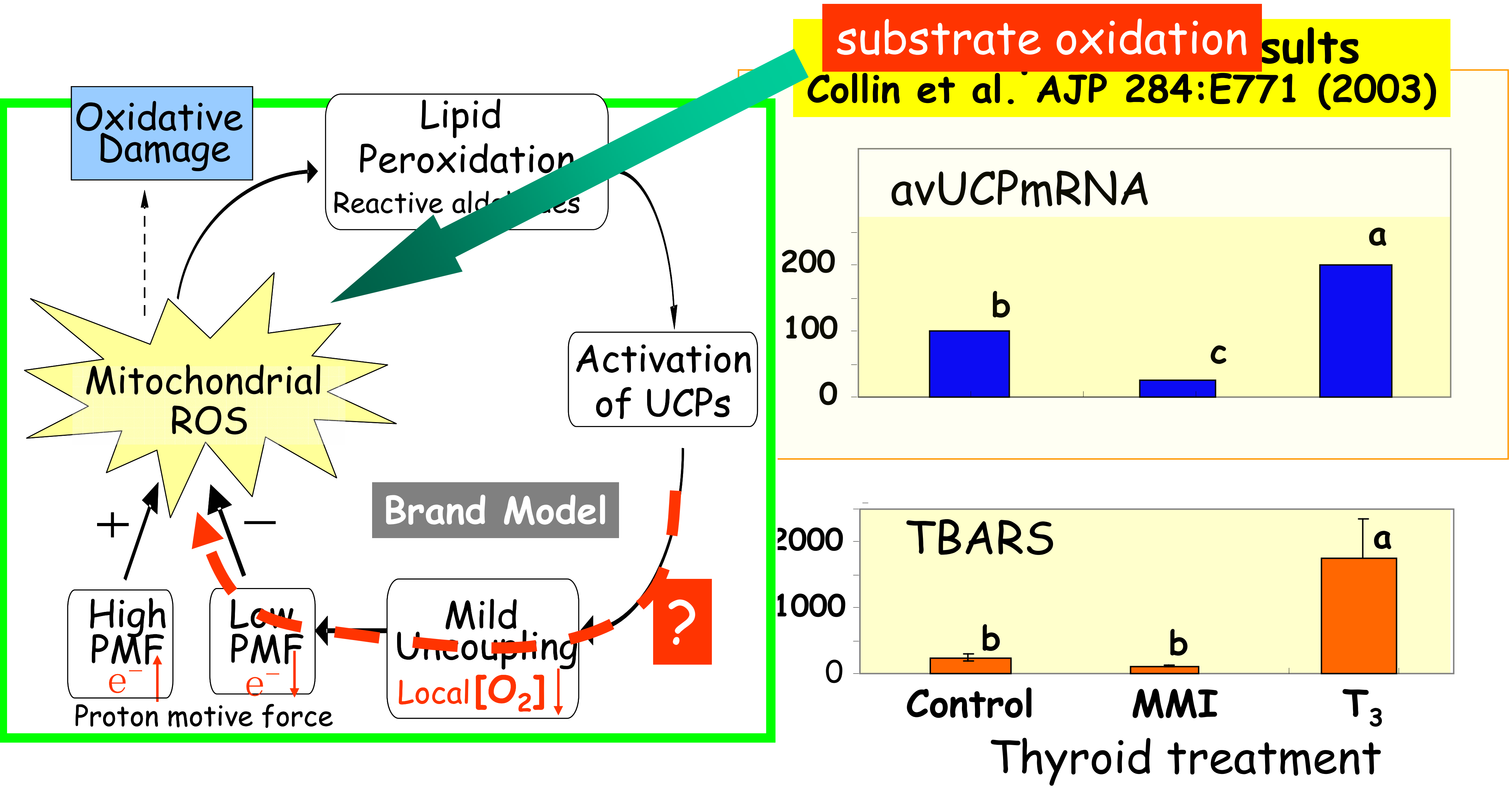


Many new ideas for research on mitochondria
Mitochondrial function
Thanks Professor Goglia
Substrate oxidation
Proton leak
ROS
ATP
the cellular level or the whole body
(Beauvieux's group demonstrated)
Metabolic processes of whole body