# ROLE OF MITOCHONDRIAL DYSFUNCTION IN DIABETIC NEPHROPATHY

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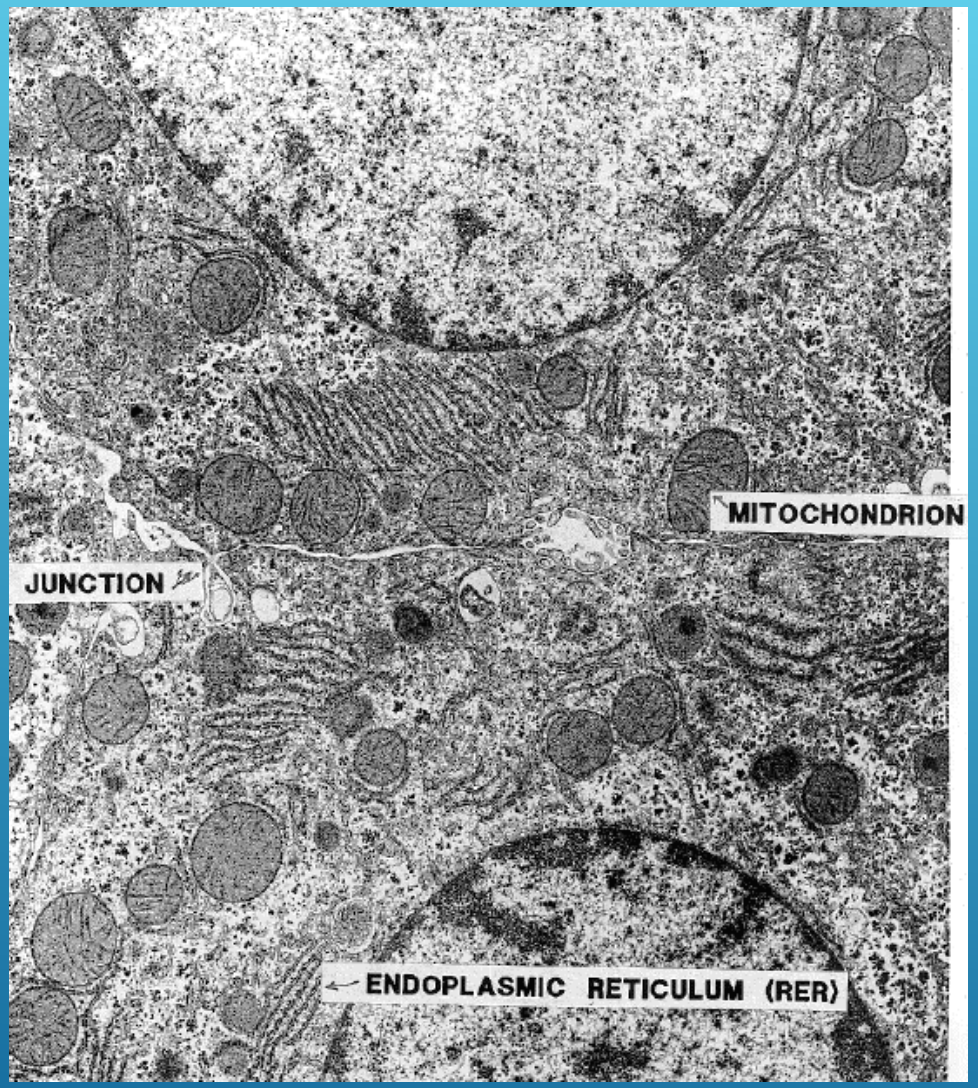
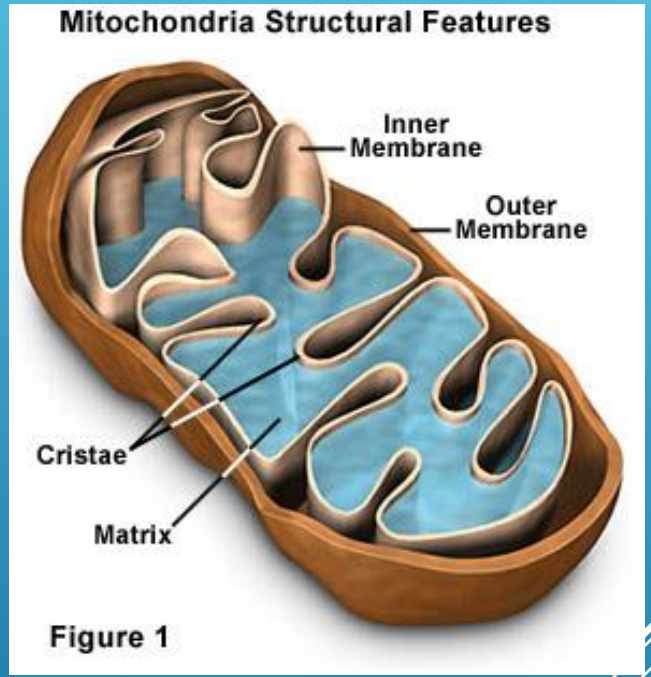
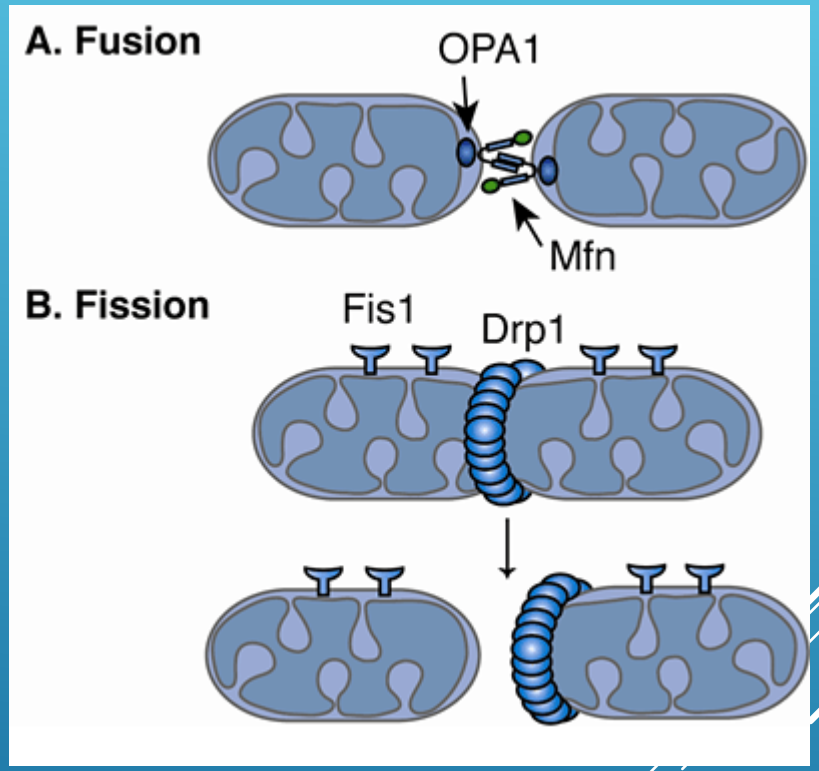
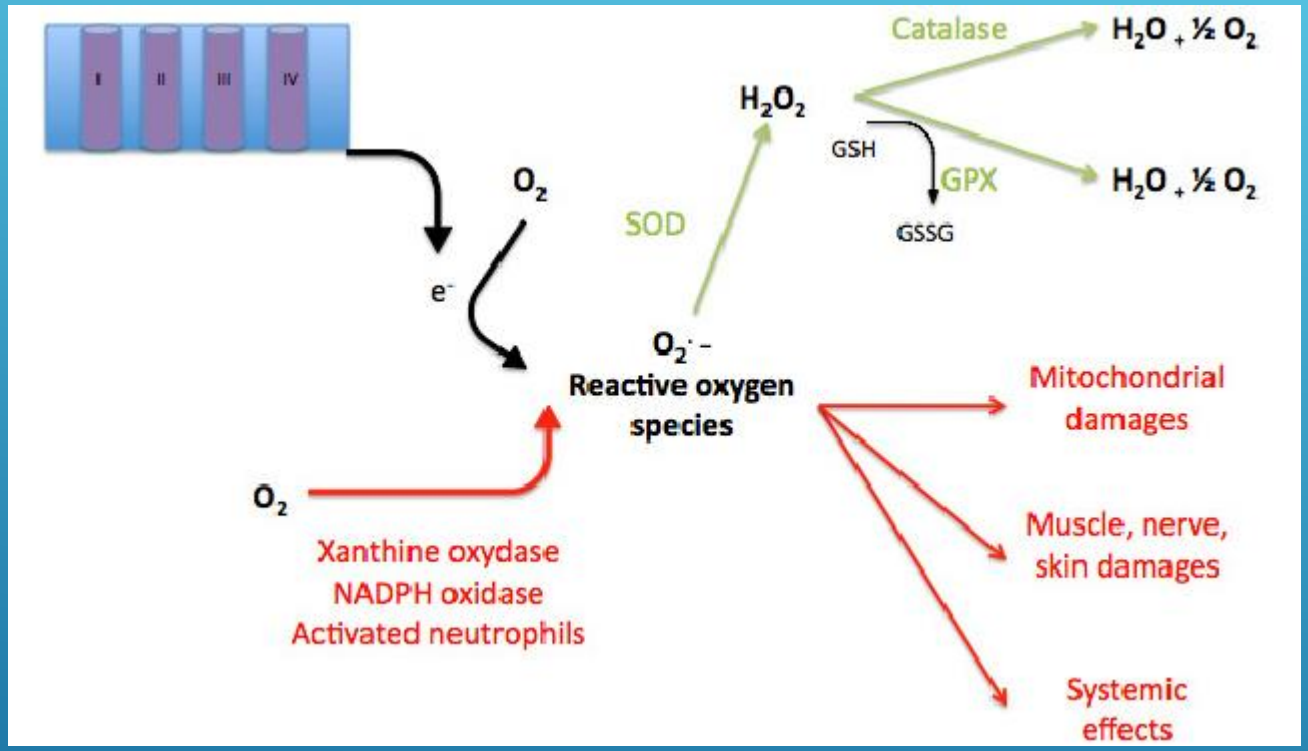
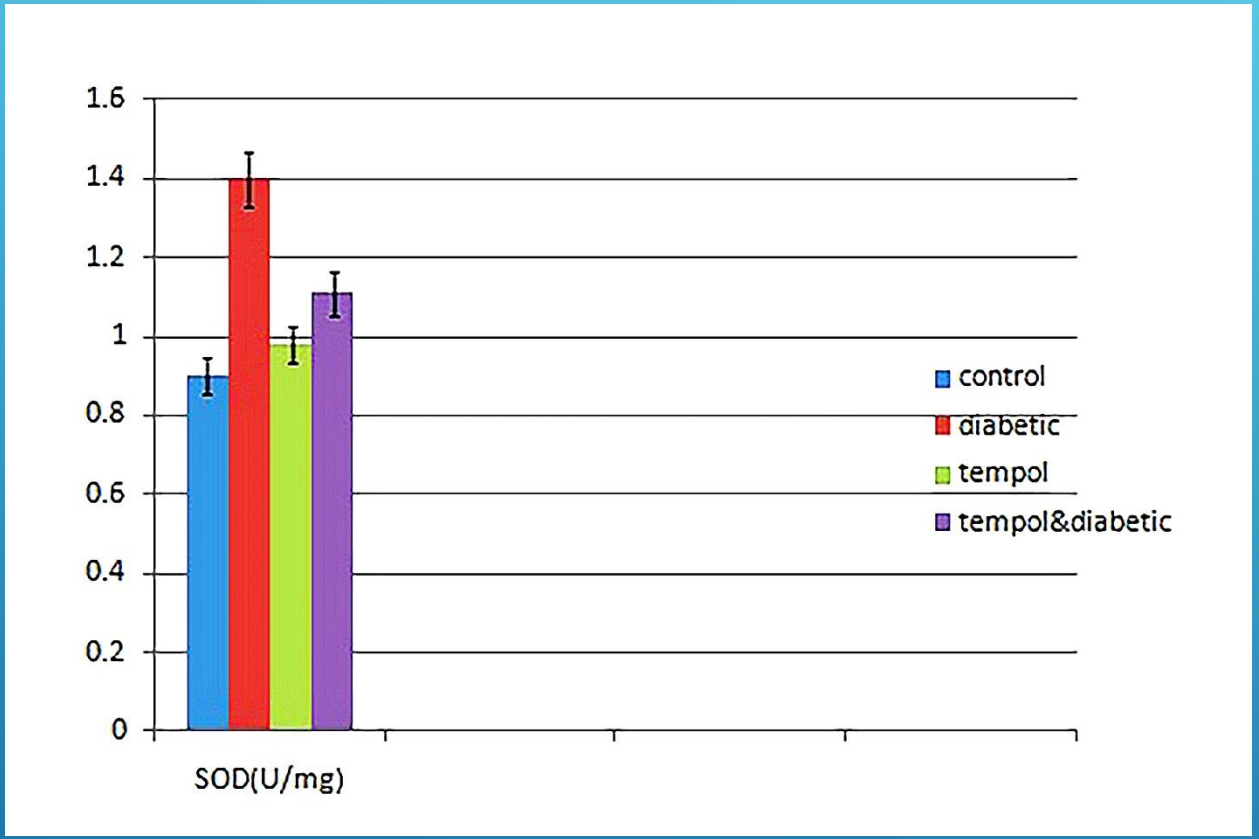
NEPHROLOGIST

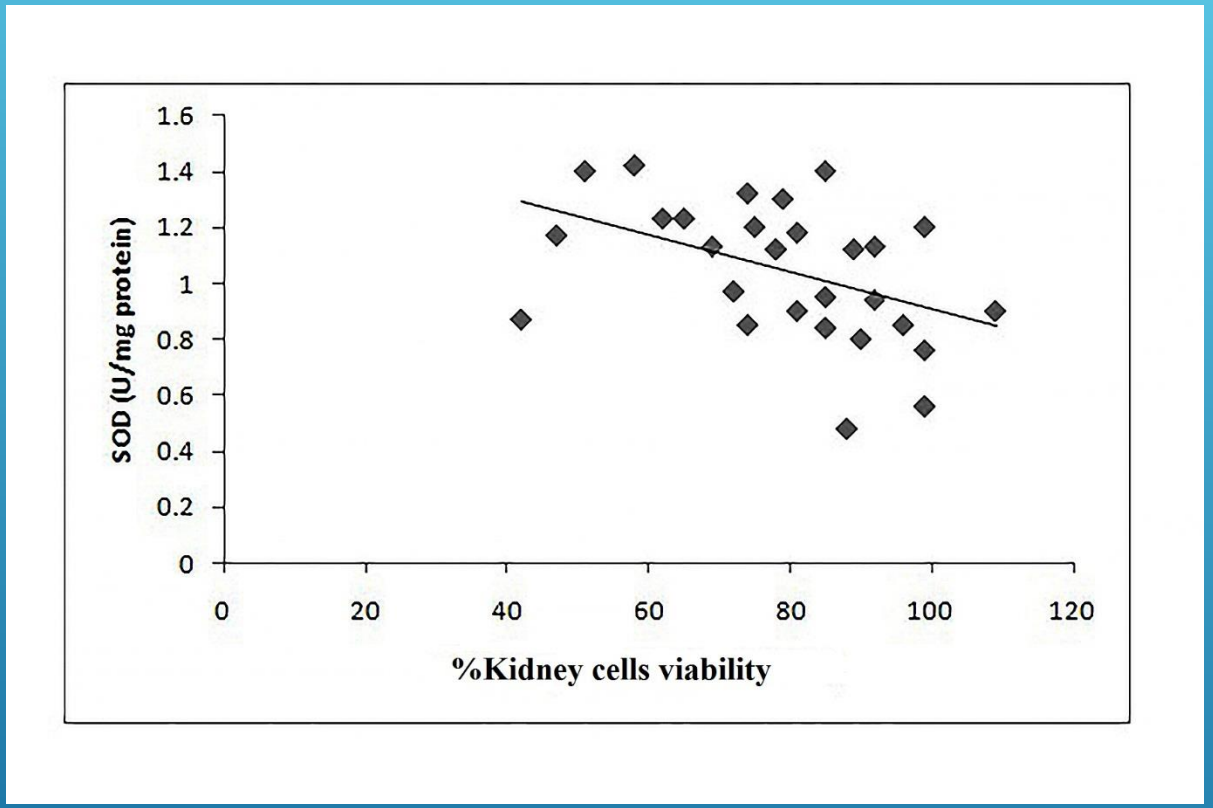

MITOCHONDRION
JUNCTION
ENDOPLASMIC RETICULUM (RER)

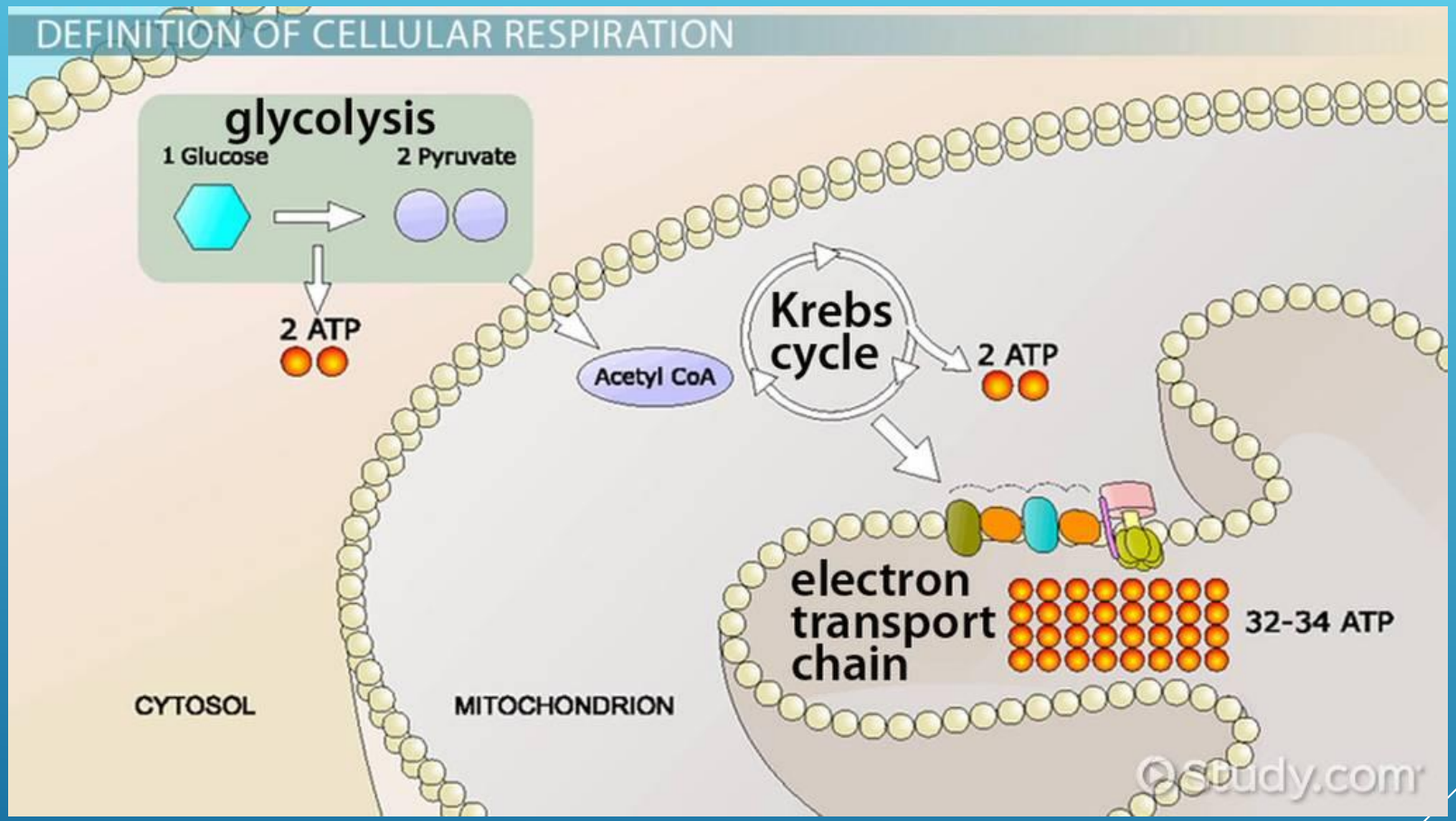

Mitochondria Structural Features
Inner Membrane
Outer Membrane
Cristae
Matrix
Figure 1

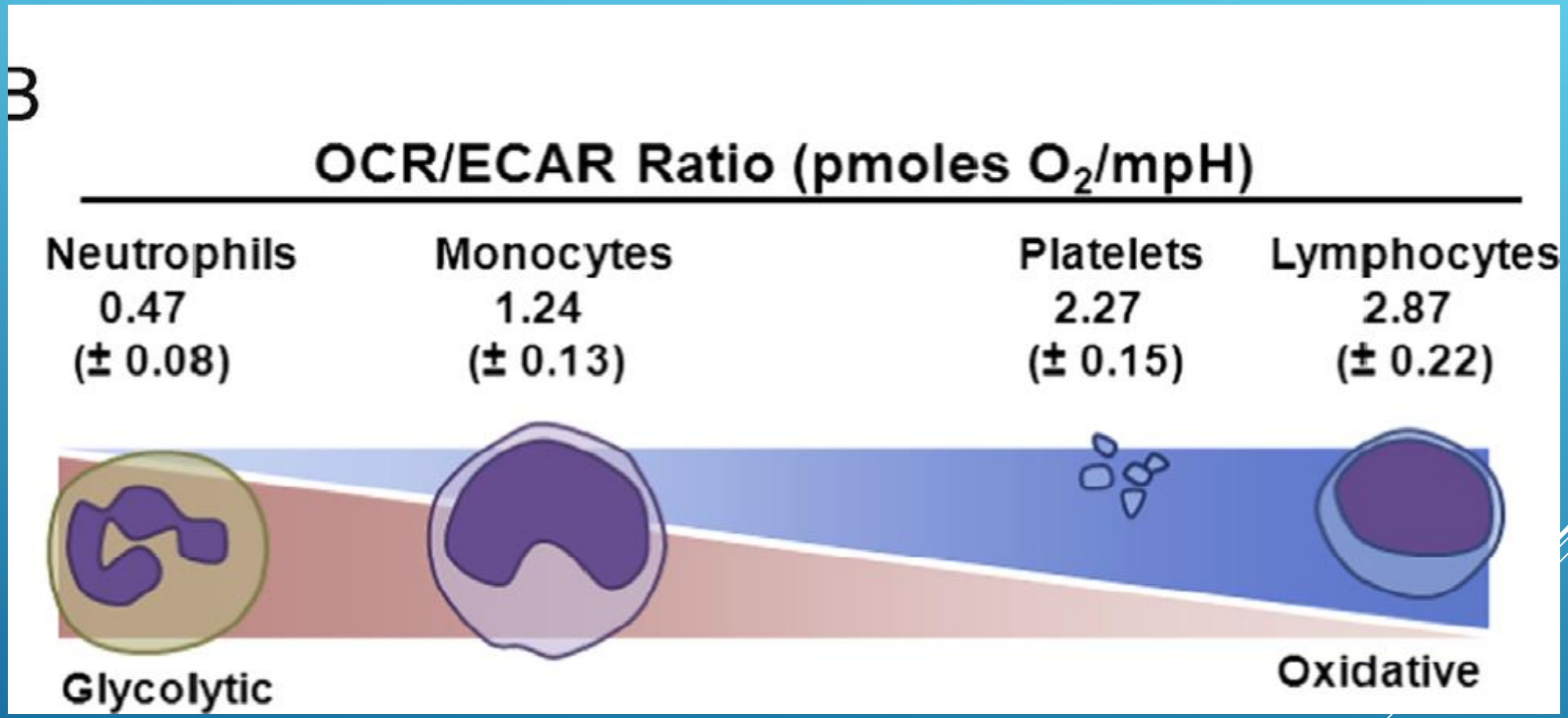

A. Fusion
OPA1
Mfn
B. Fission
Fis1
Drp1

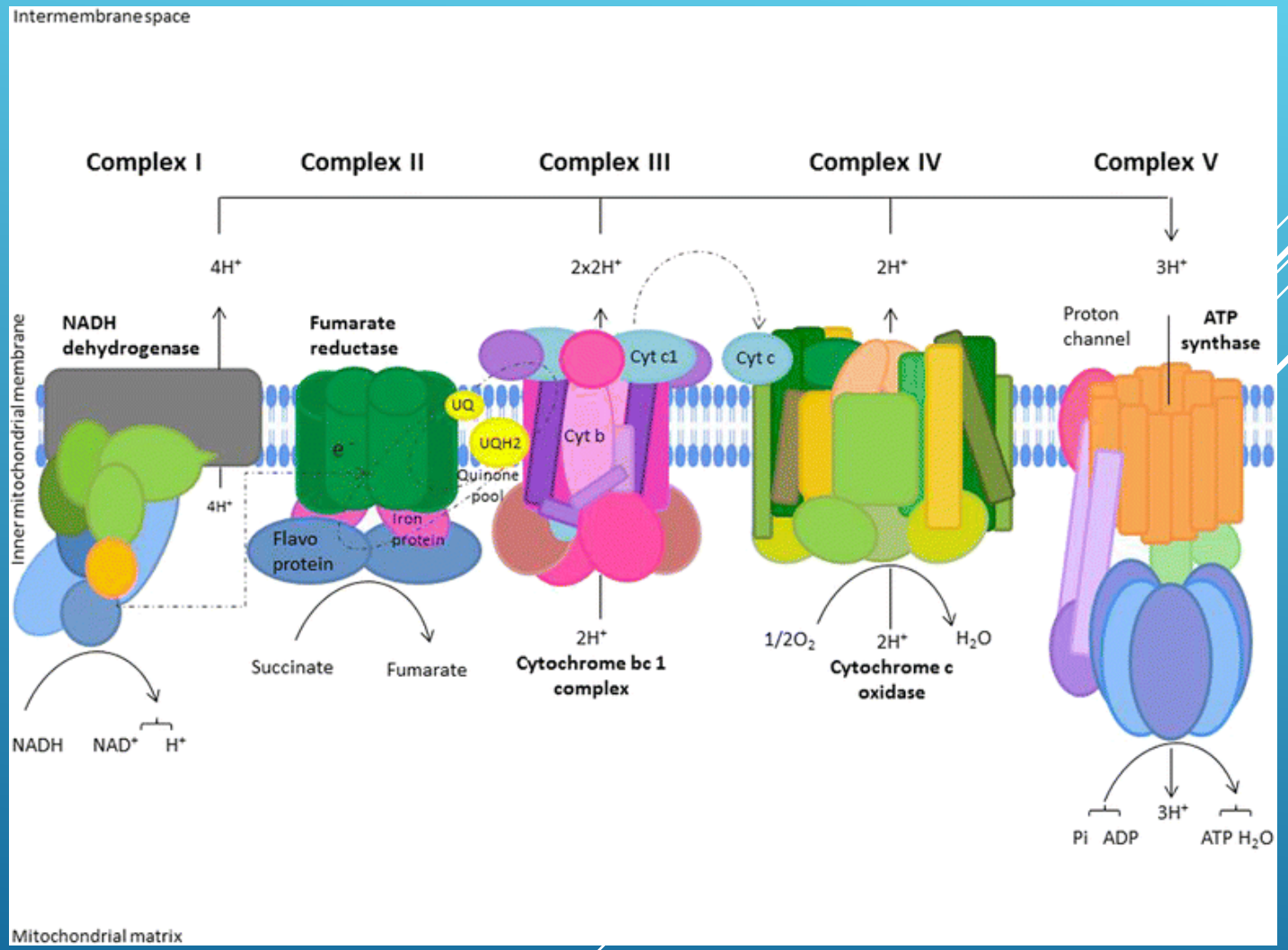

I
II
III
IV
$O_2$
$e^-$
SOD
$H_2O_2$
Catalase
$H_2O + ½ O_2$
GSH
GPX
GSSG
$H_2O + ½ O_2$
$O_2^{\cdot -}$
Reactive oxygen species
$O_2$
Xanthine oxydase
NADPH oxidase
Activated neutrophils
Mitochondrial damages
Muscle, nerve, skin damages
Systemic effects


1.6
1.4
1.2
1
0.8
0.6
0.4
0.2
0
SOD(U/mg)
control
diabetic
tempol
tempol&diabetic


SOD (U/mg protein)
1.6
1.4
1.2
1
0.8
0.6
0.4
0.2
0
0
20
40
60
80
100
120
%Kidney cells viability

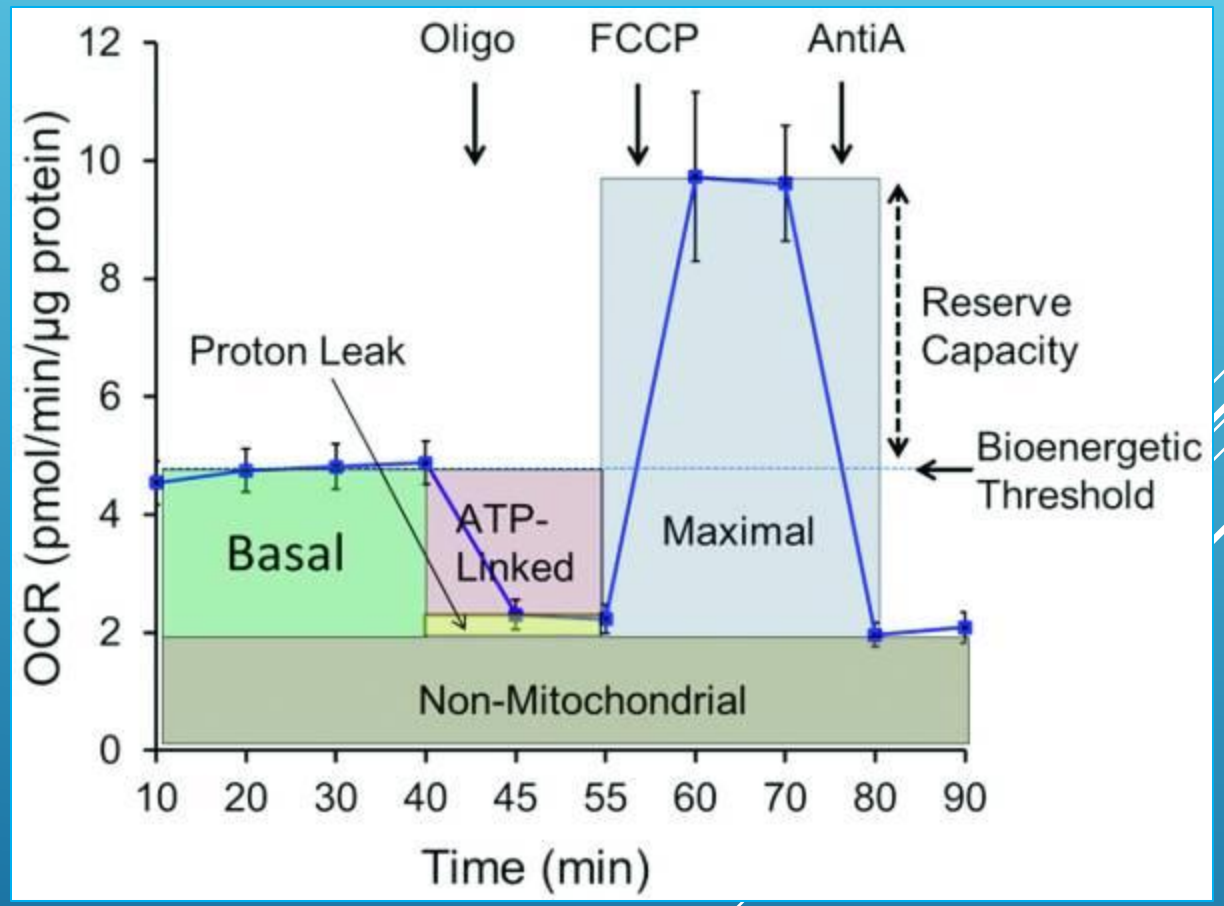

DEFINITION OF CELLULAR RESPIRATION
glycolysis
1 Glucose
2 Pyruvate
2 ATP
Acetyl CoA
Krebs cycle
2 ATP
electron transport chain
32-34 ATP
CYTOSOL
MITOCHONDRION
Study.com


B
OCR/ECAR Ratio (pmoles $O_2$/mpH)
Neutrophils
0.47
(± 0.08)
Monocytes
1.24
(± 0.13)
Platelets
2.27
(± 0.15)
Lymphocytes
2.87
(± 0.22)
Glycolytic
Oxidative

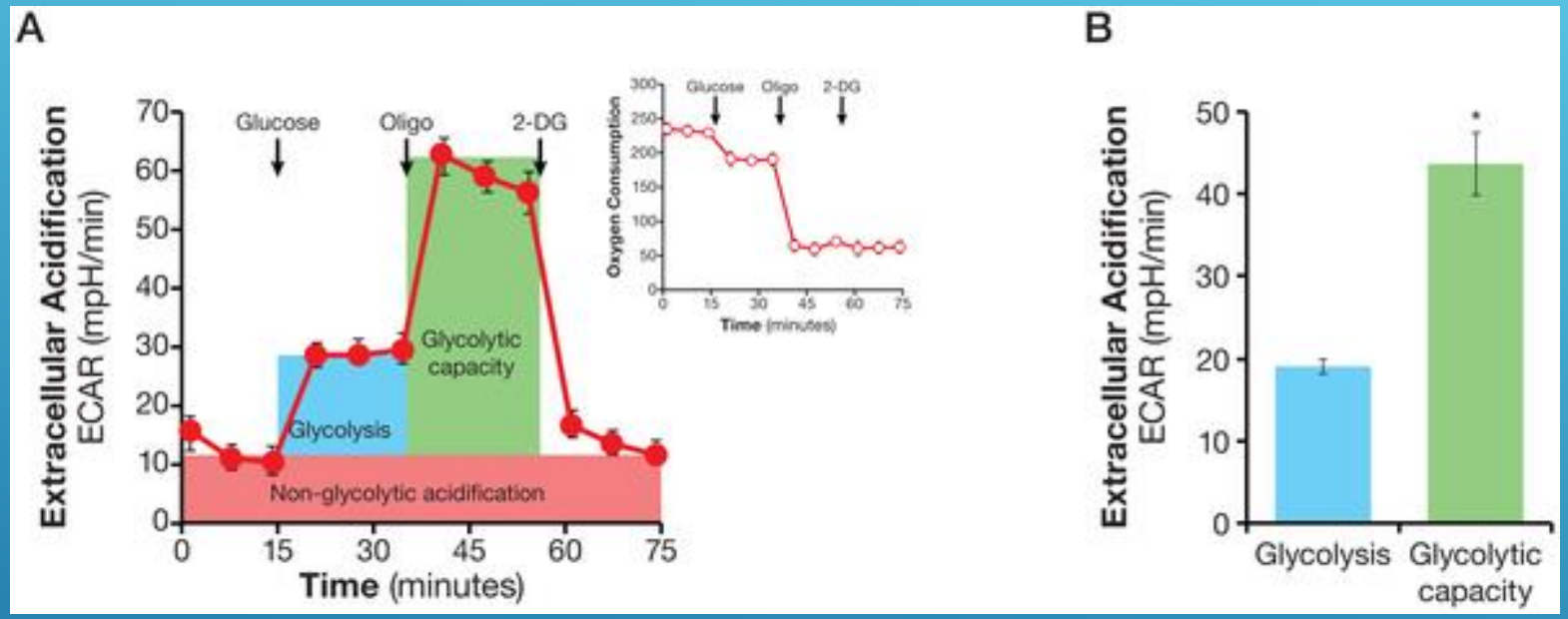

Intermembrane space
Complex I
Complex II
Complex III
Complex IV
Complex V
4H+
2x2H+
2H+
3H+
Inner mitochondrial membrane
NADH dehydrogenase
Fumarate reductase
Cyt c1
Cyt c
Proton channel
ATP synthase
UQ
UQH2
Cyt b
Quinone pool
4H+
Flavo protein
Iron protein
2H+
Cytochrome bc 1 complex
1/2O2
2H+
H2O
Cytochrome c oxidase
Succinate
Fumarate
NADH
NAD+
H+
3H+
Pi
ADP
ATP
H2O
Mitochondrial matrix

- OCR :oxygen consumption rate
- ECAR : extracellular acidification rate
- BHI : bioenergetic health index

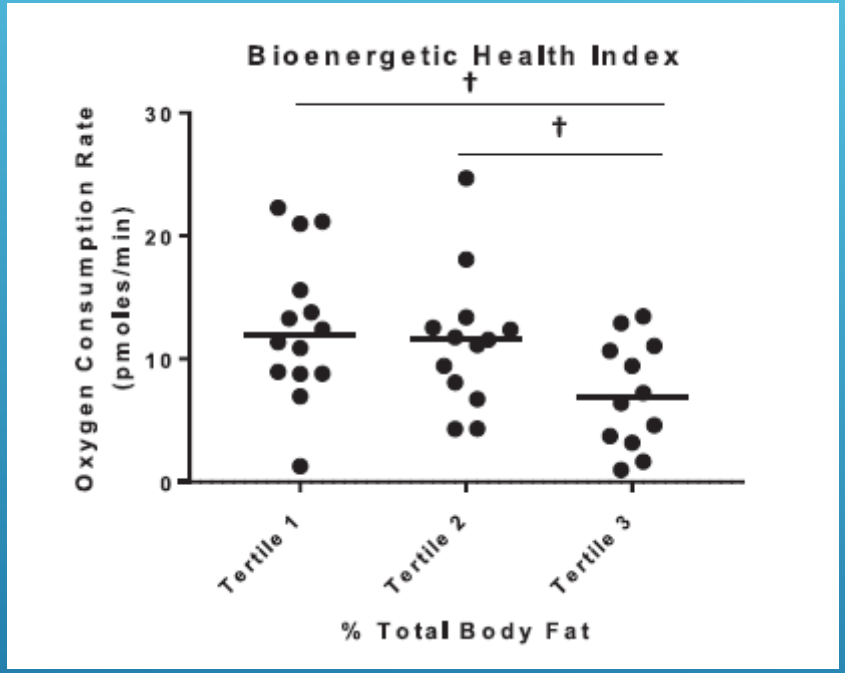
# SEAHORSE XF ANALYSER

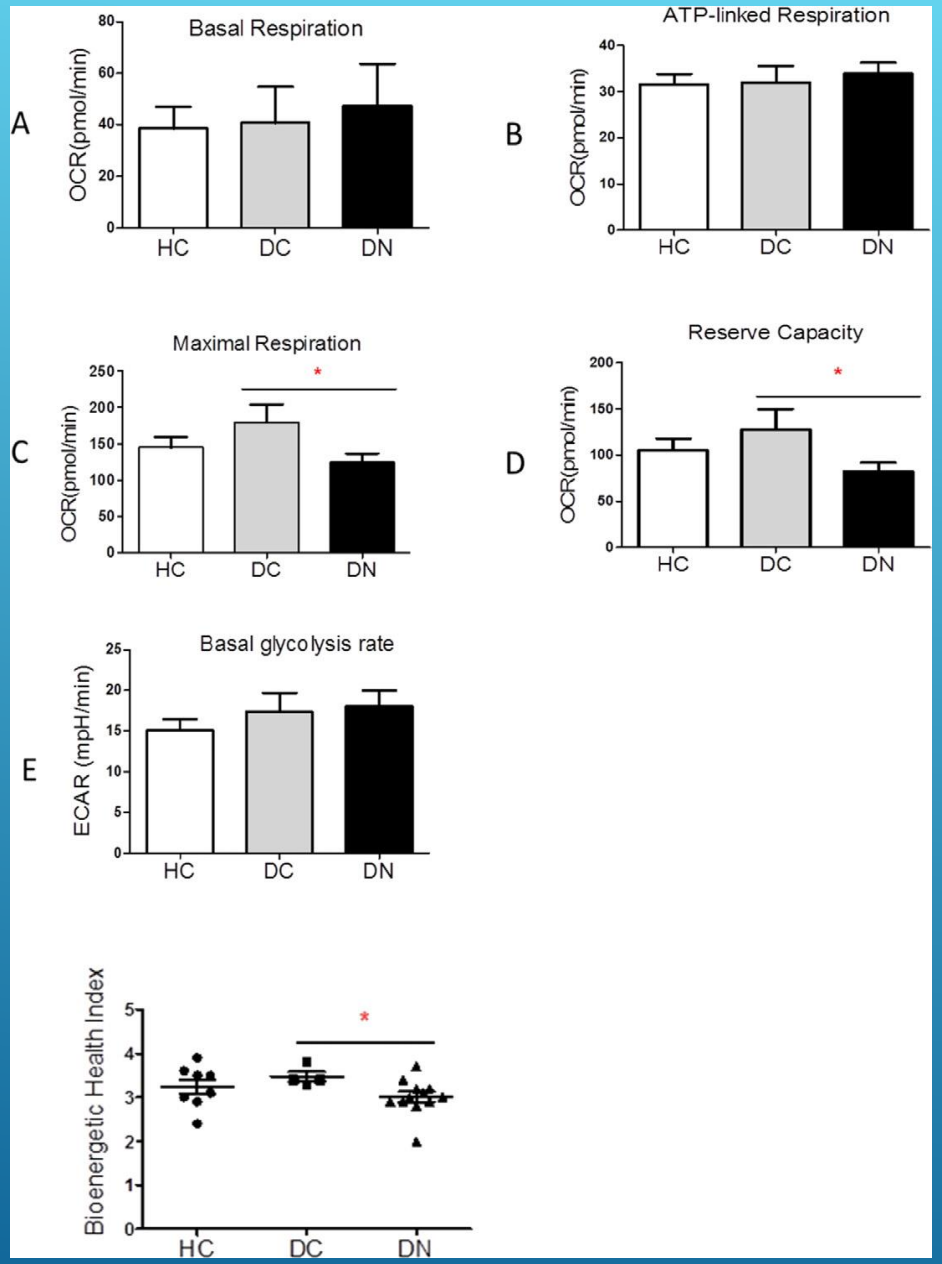

Oligo
FCCP
AntiA
12
10
8
6
4
2
0
OCR (pmol/min/µg protein)
Proton Leak
Reserve
Capacity
Bioenergetic
Threshold
Basal
ATP-
Linked
Maximal
Non-Mitochondrial
10
20
30
40
45
55
60
70
80
90
Time (min)

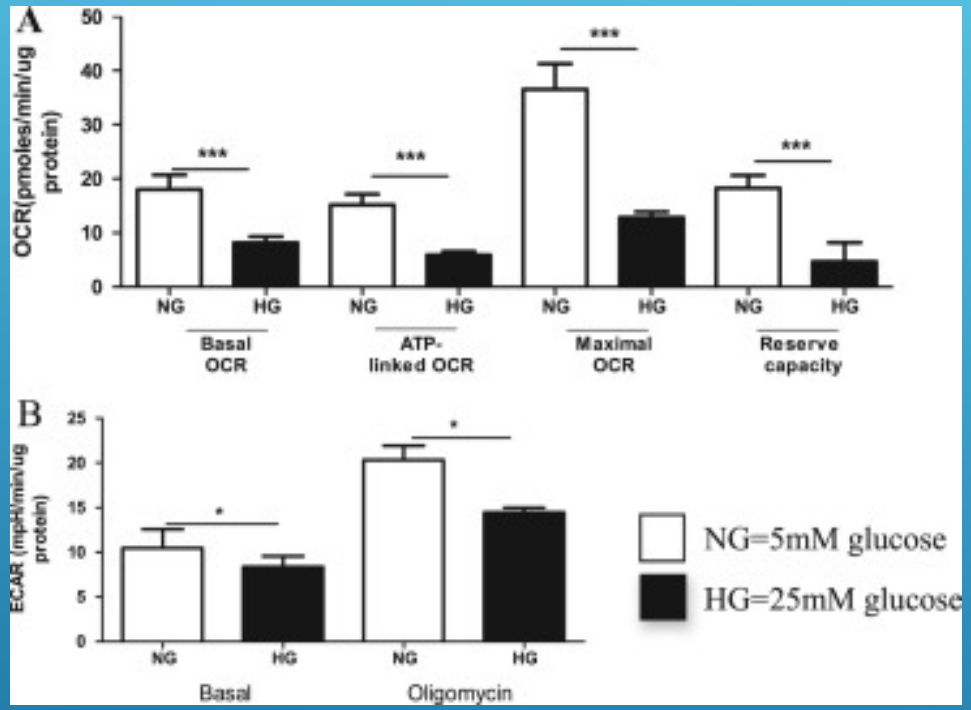
$$\mathrm{BHI} = \log \frac{(\text{reserve capacity})^a \times (\text{ATP-linked})^b}{(\text{non-mitochondrial})^c \times (\text{proton leak})^d}$$

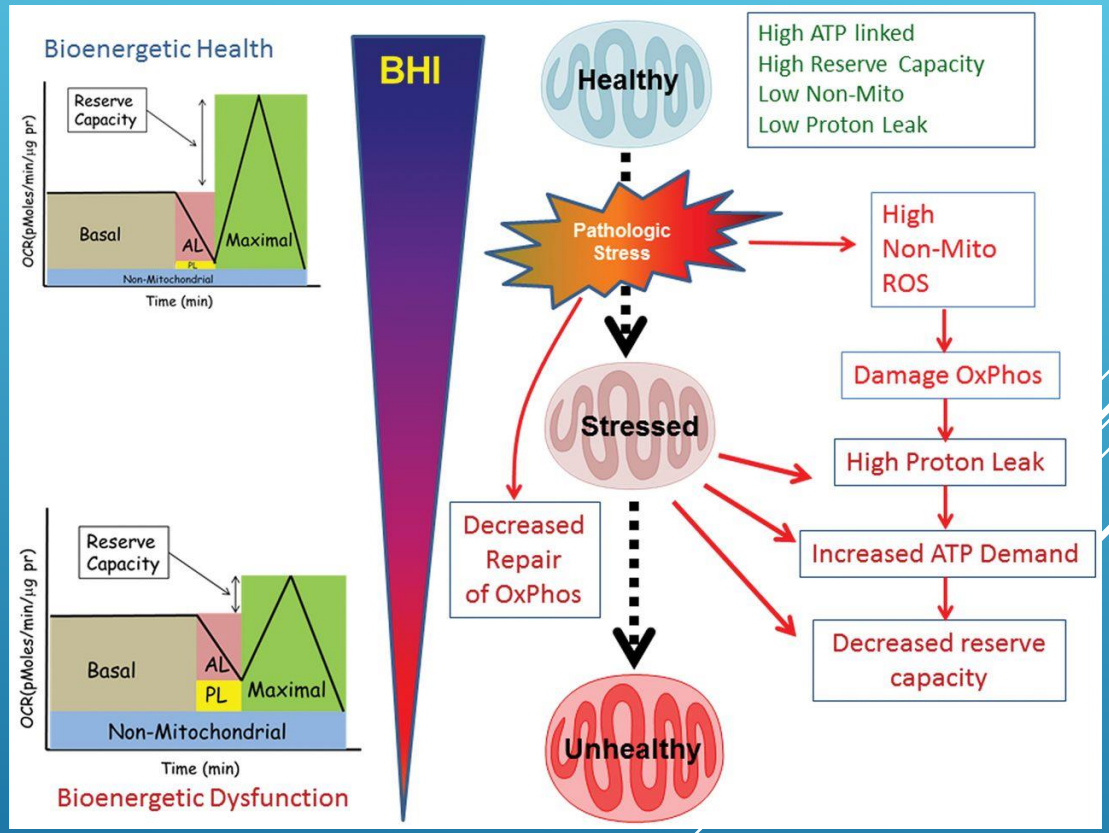

A
Extracellular Acidification
ECAR (mpH/min)
70
60
50
40
30
20
10
0
Glucose
Oligo
2-DG
Glycolytic capacity
Glycolysis
Non-glycolytic acidification
0
15
30
45
60
75
Time (minutes)
Oxygen Consumption
300
250
200
150
100
50
0
Glucose
Oligo
2-DG
0
15
30
45
60
75
Time (minutes)
B
Extracellular Acidification
ECAR (mpH/min)
50
40
30
20
10
0
*
Glycolysis
Glycolytic capacity

# BMI and BHI


Bioenergetic Health Index
†
†
Oxygen Consumption Rate (pmoles/min)
30
20
10
0
Tertile 1
Tertile 2
Tertile 3
% Total Body Fat


A
Basal Respiration
OCR(pmol/min)
80
60
40
20
0
HC
DC
DN
B
ATP-linked Respiration
OCR(pmol/min)
40
30
20
10
0
HC
DC
DN
C
Maximal Respiration
OCR(pmol/min)
250
200
150
100
50
0
*
HC
DC
DN
D
Reserve Capacity
OCR(pmol/min)
200
150
100
50
0
*
HC
DC
DN
E
Basal glycolysis rate
ECAR (mpH/min)
25
20
15
10
5
0
HC
DC
DN
Bioenergetic Health Index
5
4
3
2
1
0
*
HC
DC
DN


A
OCR(pmoles/min/ug protein)
50
40
30
20
10
0
***
***
***
***
NG
HG
NG
HG
NG
HG
NG
HG
Basal OCR
ATP-linked OCR
Maximal OCR
Reserve capacity
B
ECAR (mpH/min/ug protein)
25
20
15
10
5
0
*
*
NG
HG
NG
HG
Basal
Oligomycin
NG=5mM glucose
HG=25mM glucose


Bioenergetic Health
Reserve Capacity
Basal
AL
PL
Maximal
Non-Mitochondrial
OCR(pMoles/min/µg pr)
Time (min)
BHI
Healthy
High ATP linked
High Reserve Capacity
Low Non-Mito
Low Proton Leak
Pathologic Stress
High Non-Mito ROS
Damage OxPhos
Stressed
High Proton Leak
Decreased Repair of OxPhos
Increased ATP Demand
Decreased reserve capacity
Unhealthy
Bioenergetic Dysfunction

# THANK YOU