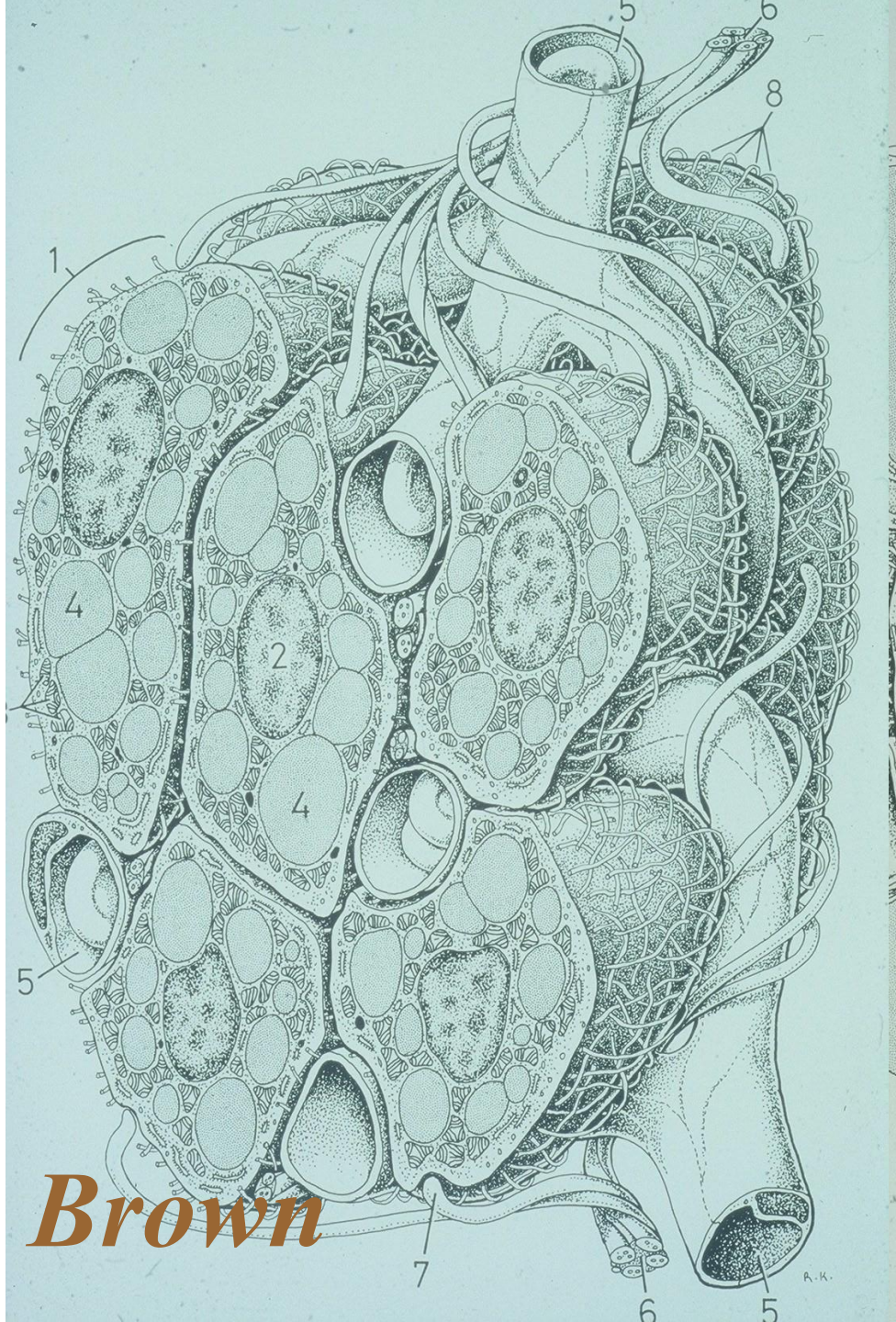
WP 3:

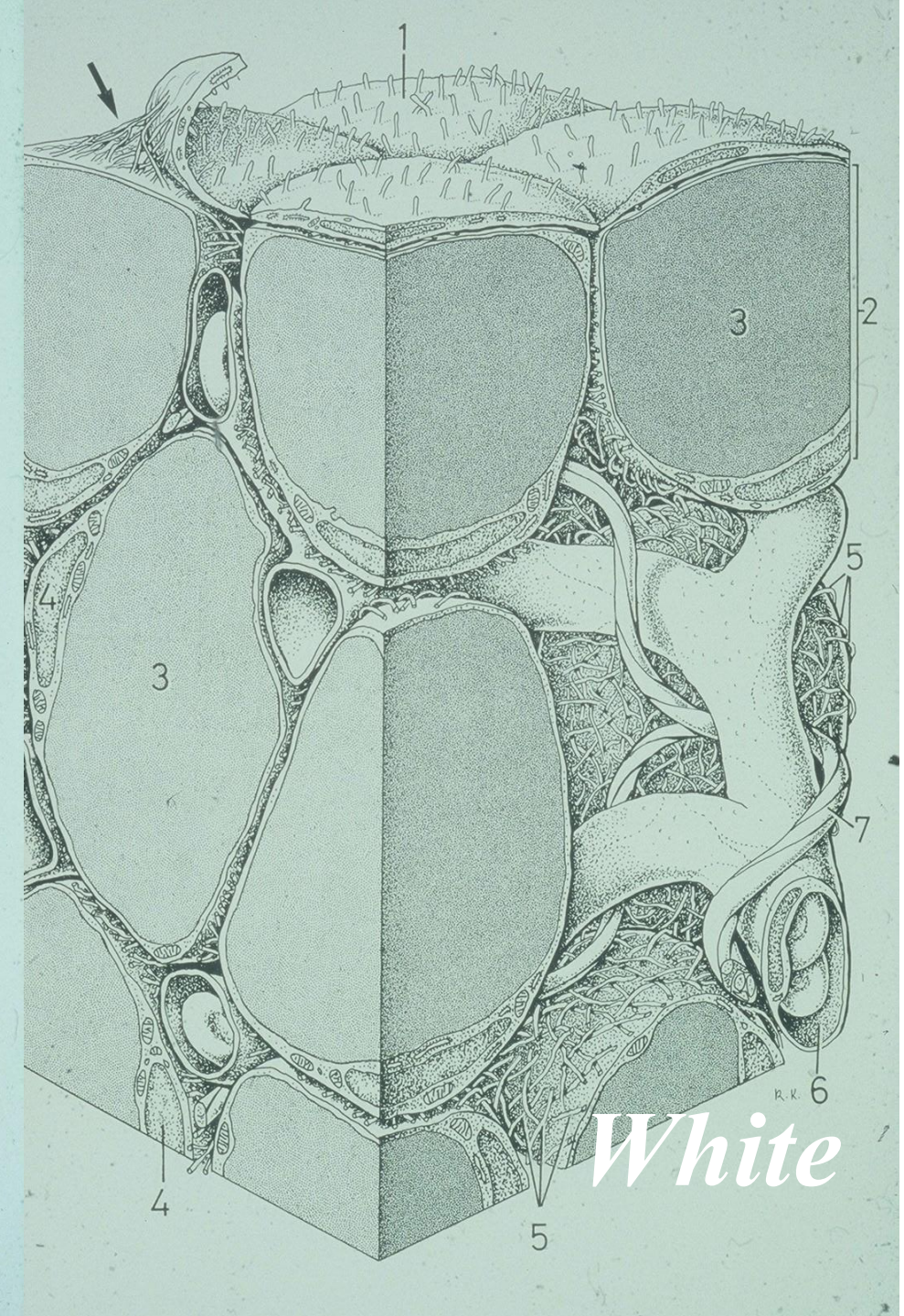
White fat, brown fat, neural and liver

Jan Nedergaard - fat
Vilma Borutaite - neural
Zuzana Cervinkova - liver

Not all mitochondria are created equal!

Consider the physiology!


1
2
4
4
5
5
6
7
8
Brown


1
2
3
3
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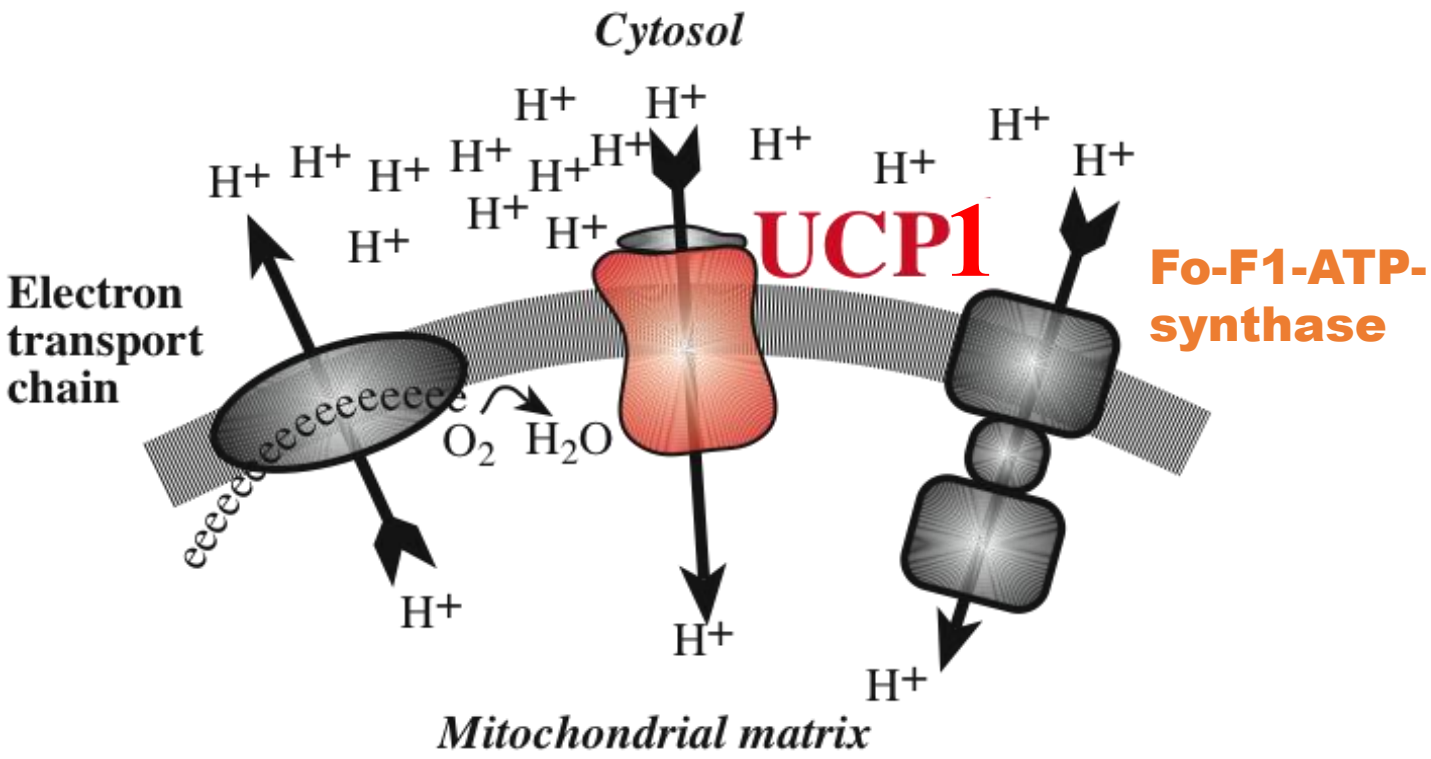
7
White

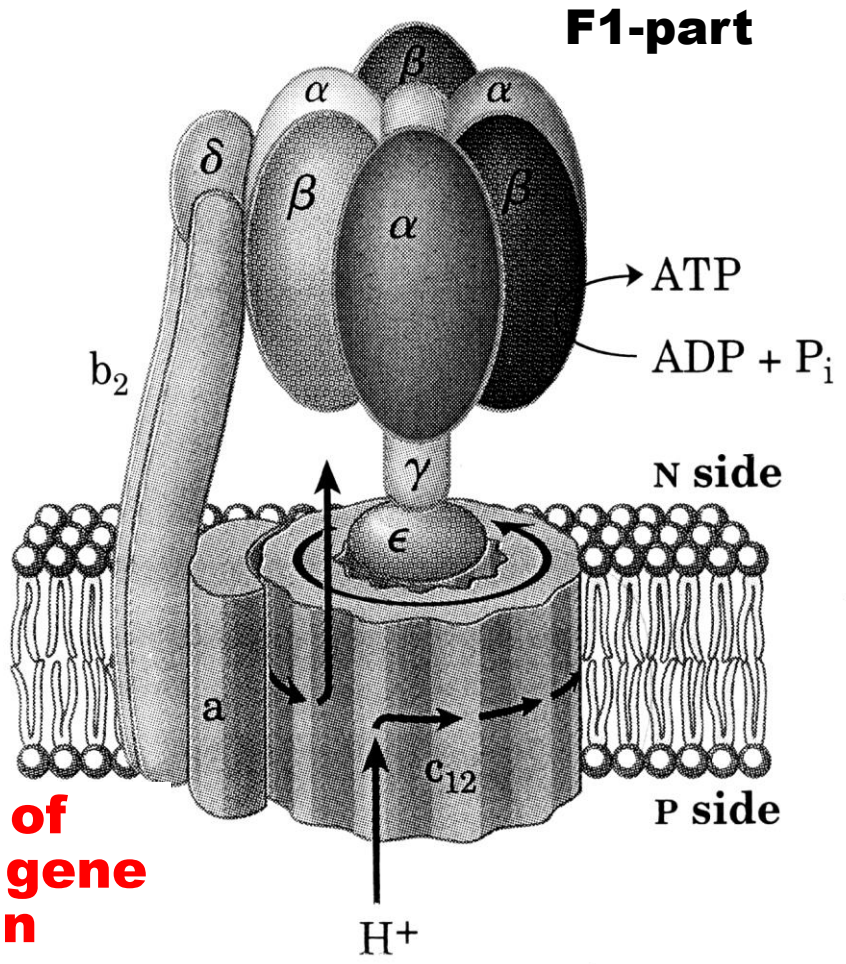
Brown fat mitochondria



Energy of transmembrane potential

could be used by UCP1 and released as heat
and
could be used by Fo-F1-ATP-synthase and released as ATP

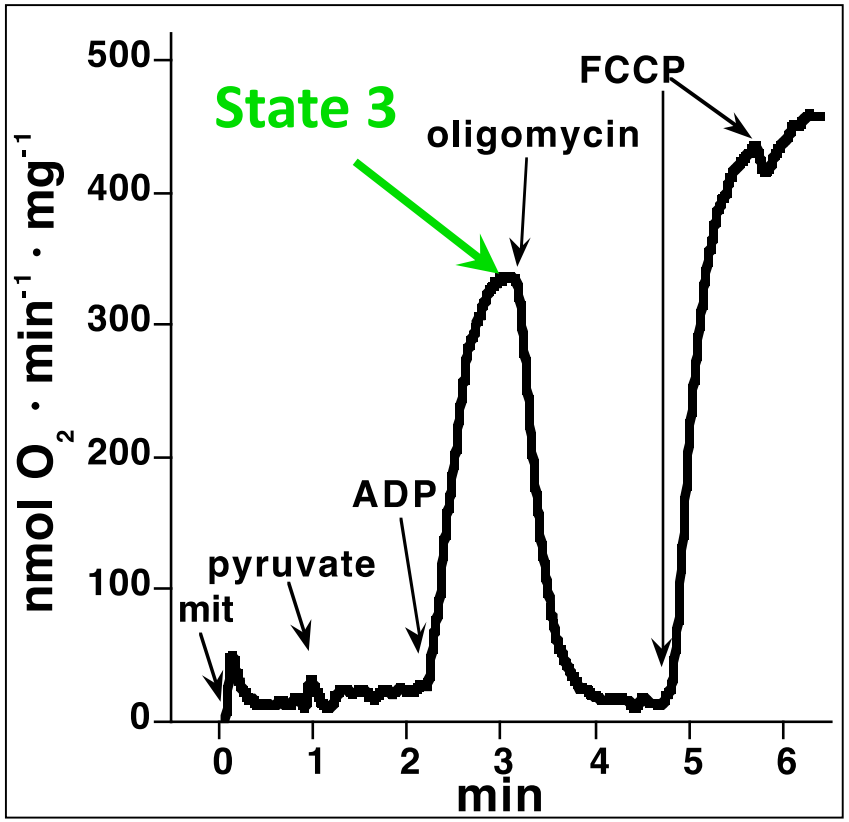
Content of Fo-F1-ATP-synthase in brown fat mitochondria is remarkably low

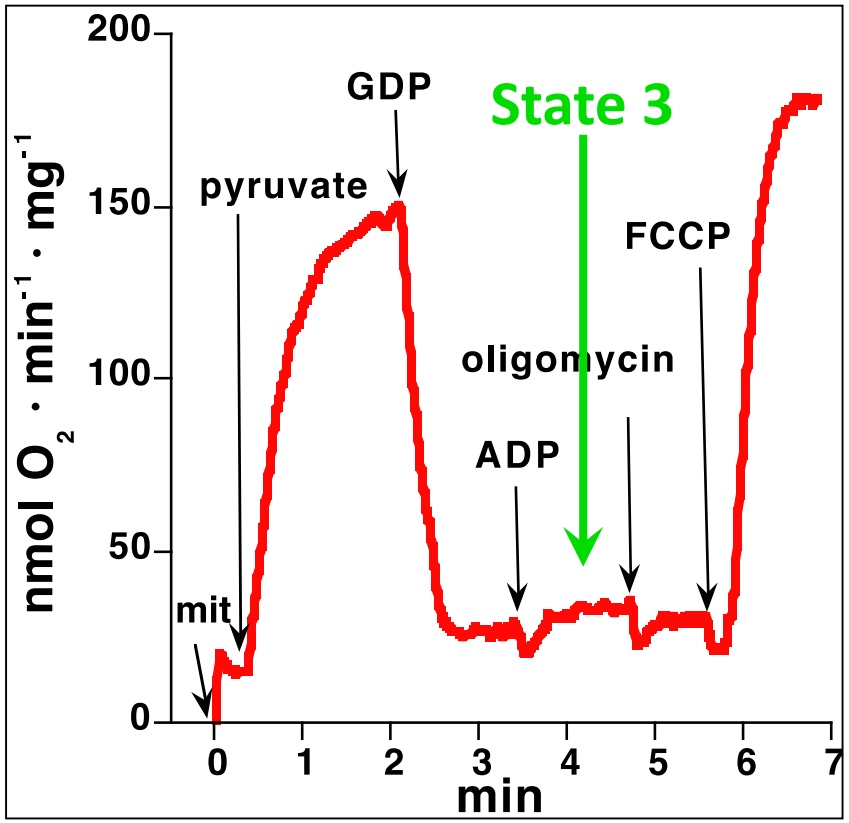


Low level of subunit *c* gene expression

Kramarova T, Shabalina IG ..... and Cannon B. ***FASEB J. 22, 55– 63 (2008)***

Skeletal muscle mitochondria	Brown fat mitochondria



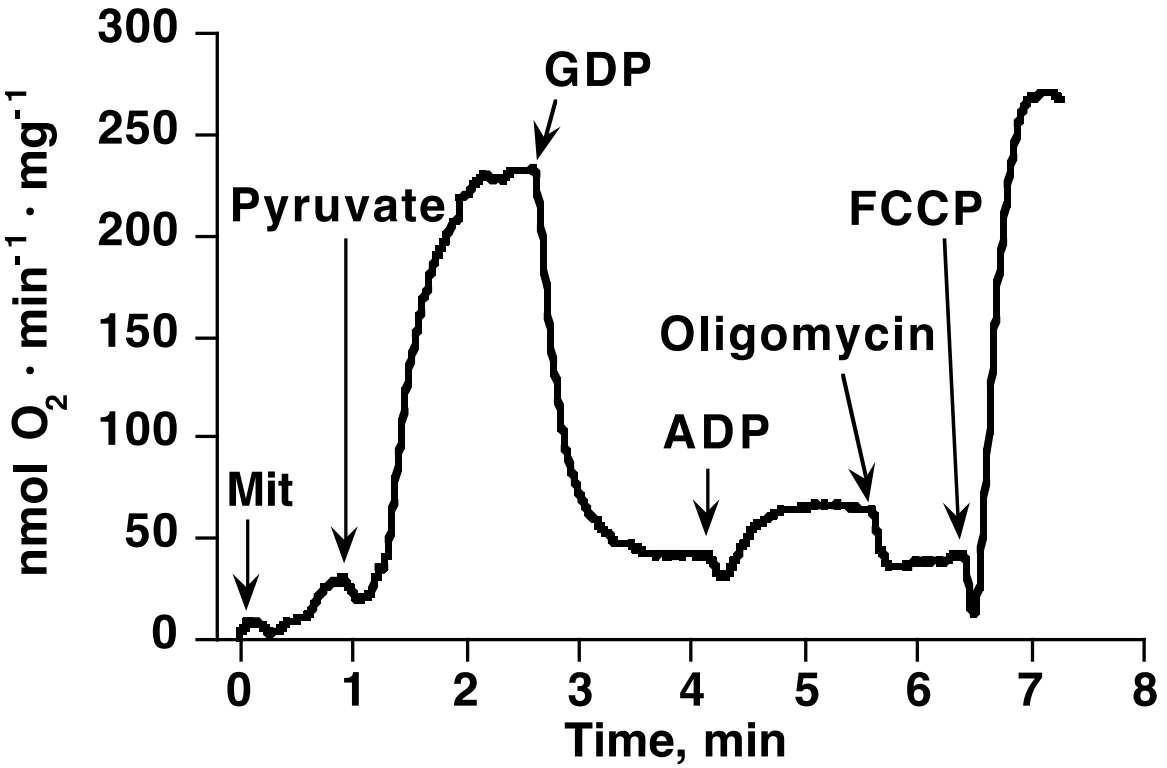


(Low amount of ATP synthase determined by
low amount of mRNA for P1 isoform of subunit c.)

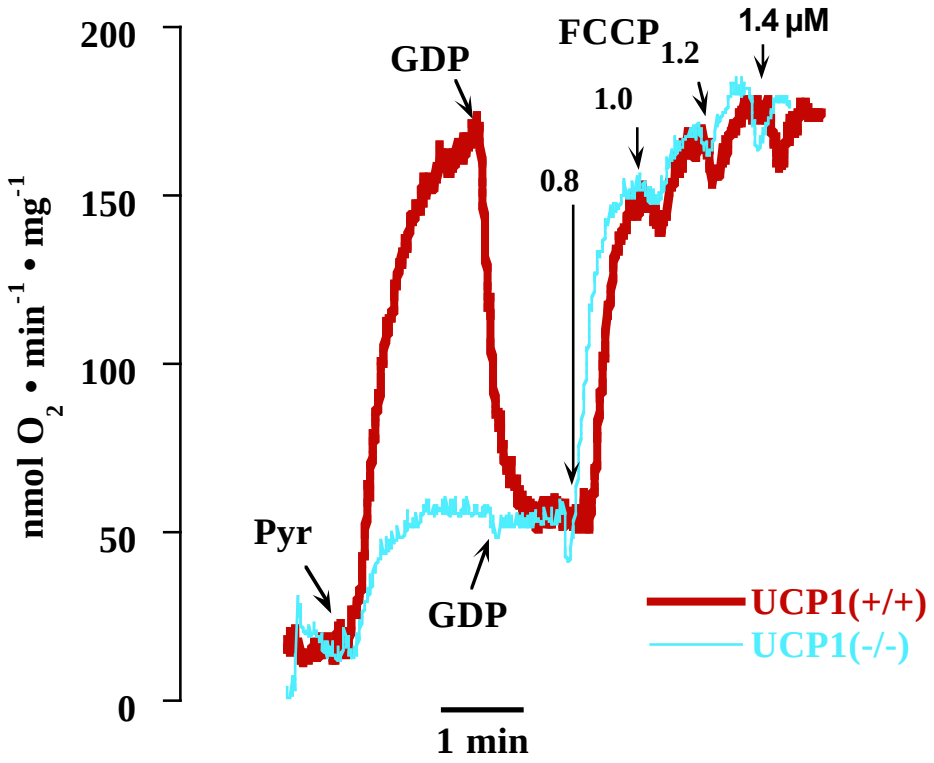
Kramarova T, Shabalina I, ….Cannon B., ***FASEB J.* 22, 55– 63, (2008)**

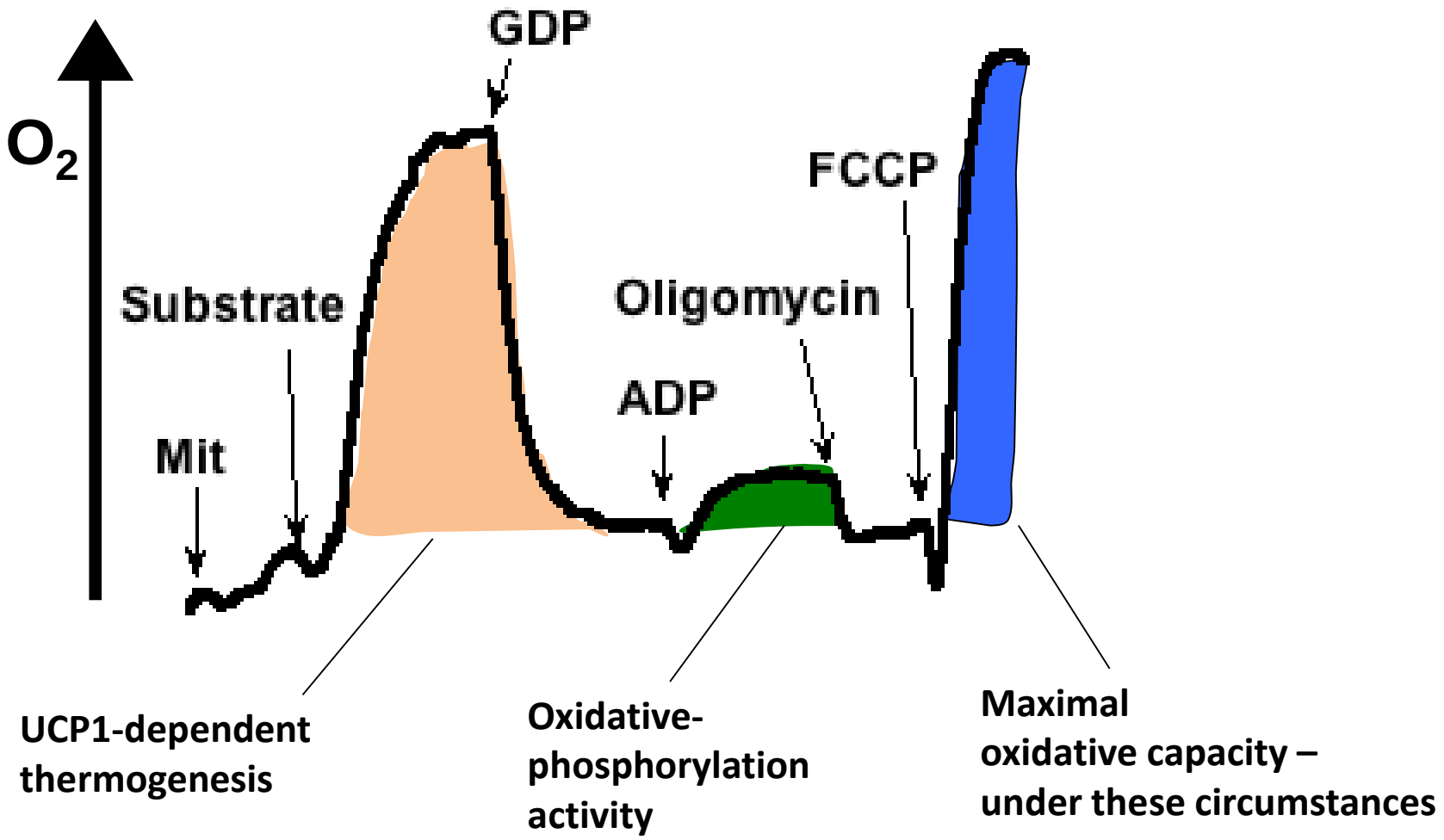
129sv

Brown adipose tissue mitochondria

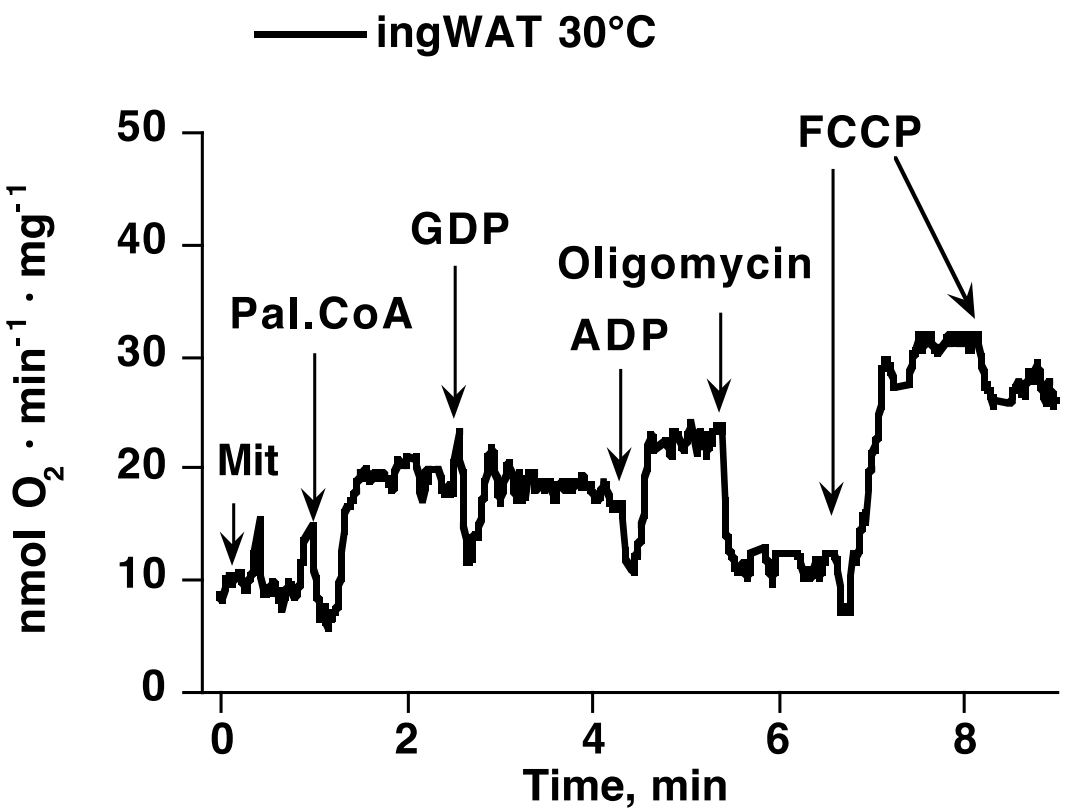


Innate uncoupling
GDP Inhibition
Low phosphorylation
High oxidative capacity

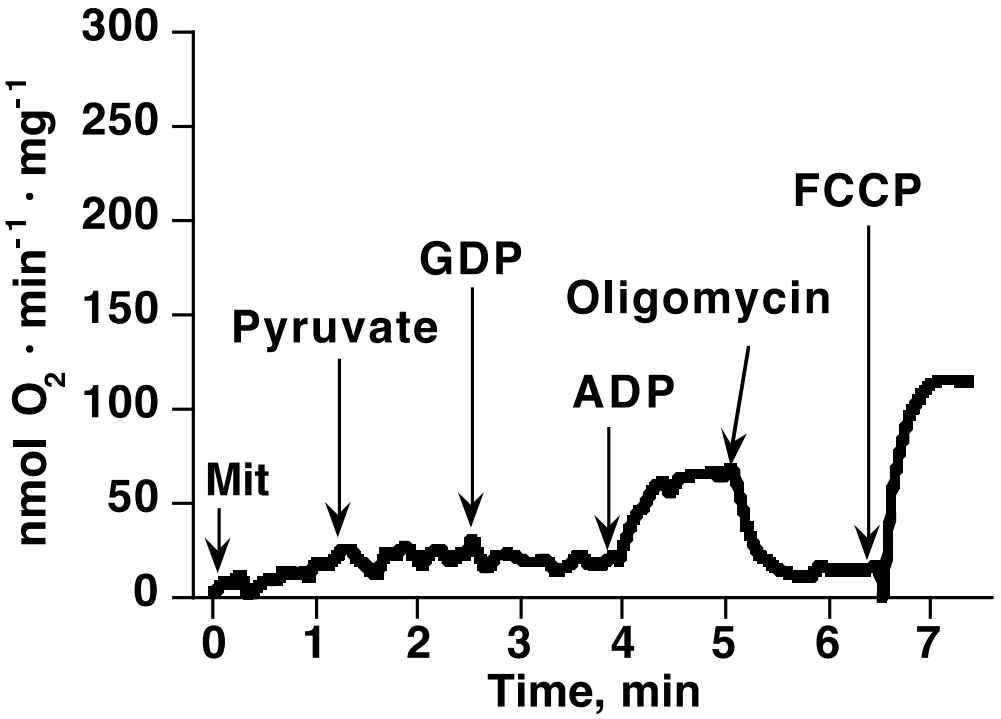

200
150
100
50
0
nmol O2 • min-1 • mg-1
GDP
FCCP
1.2
1.4 µM
1.0
0.8
Pyr
GDP
1 min
UCP1(+/+)
UCP1(-/-)


O_2
GDP
FCCP
Substrate
Oligomycin
ADP
Mit
UCP1-dependent thermogenesis
Oxidative-phosphorylation activity
Maximal oxidative capacity – under these circumstances

Inguinal fat mitochondria from mice housed at 30 °C



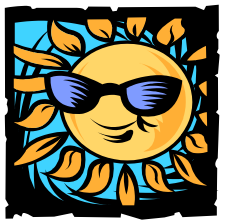
Epididymal fat mitochondria

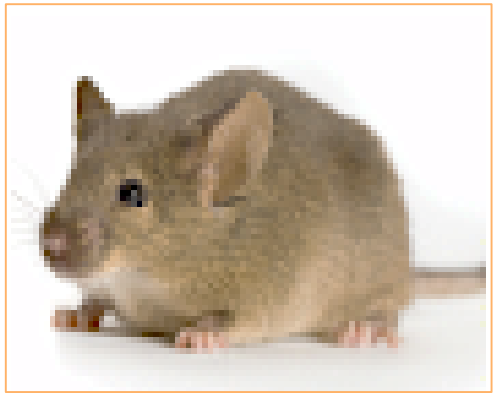


No innate uncoupling
No GDP Inhibition
Normal phosphorylation
Low oxidative capacity

Brite/beige adipocytes are recruited in inguinal white adipose tissue during cold adaptation

30° C





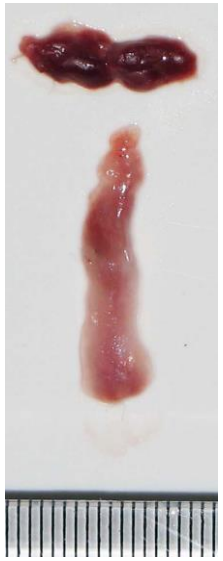
5 weeks

129sv

4° C

BAT

ingWAT



BAT

ingWAT

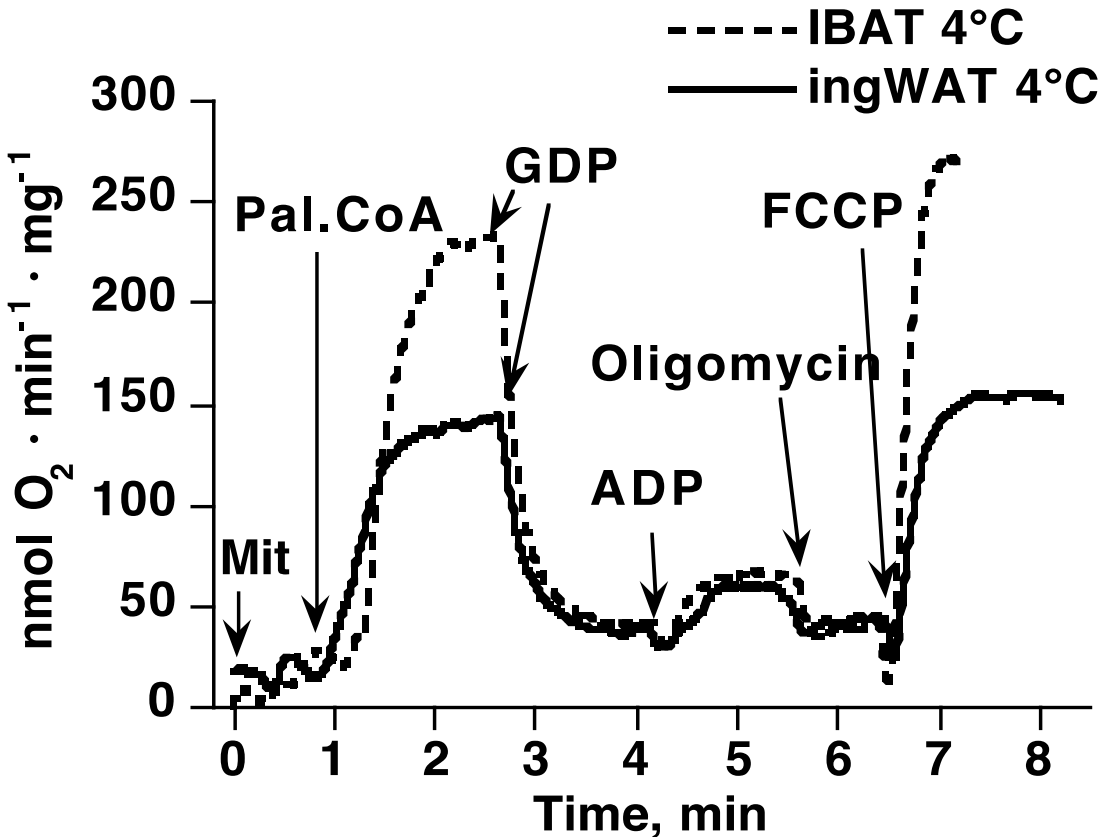
Remember the half-life of mitochondria when you change the conditions!

Normally in brown fat, about 15 days; in the cold about 7 days.

So you will have a mixed population if you do an experiment after only one week!

129sv
4°C

IBAT and ingWAT, 4°C



Brown mitochondria

Innate uncoupling
GDP Inhibition
Low phosphorylation
High oxidative capacity

BRITE mitochondria

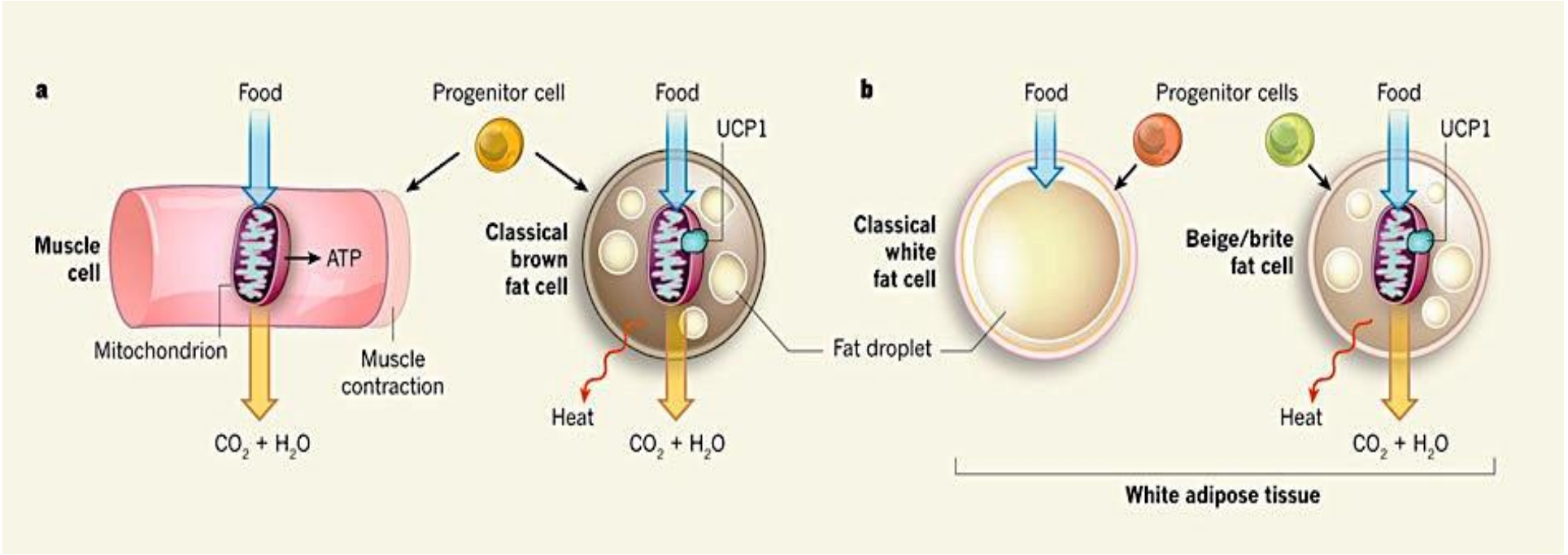
Innate uncoupling
GDP Inhibition
Low phosphorylation
Medium oxidative capacity

Sk Muscle

BAT

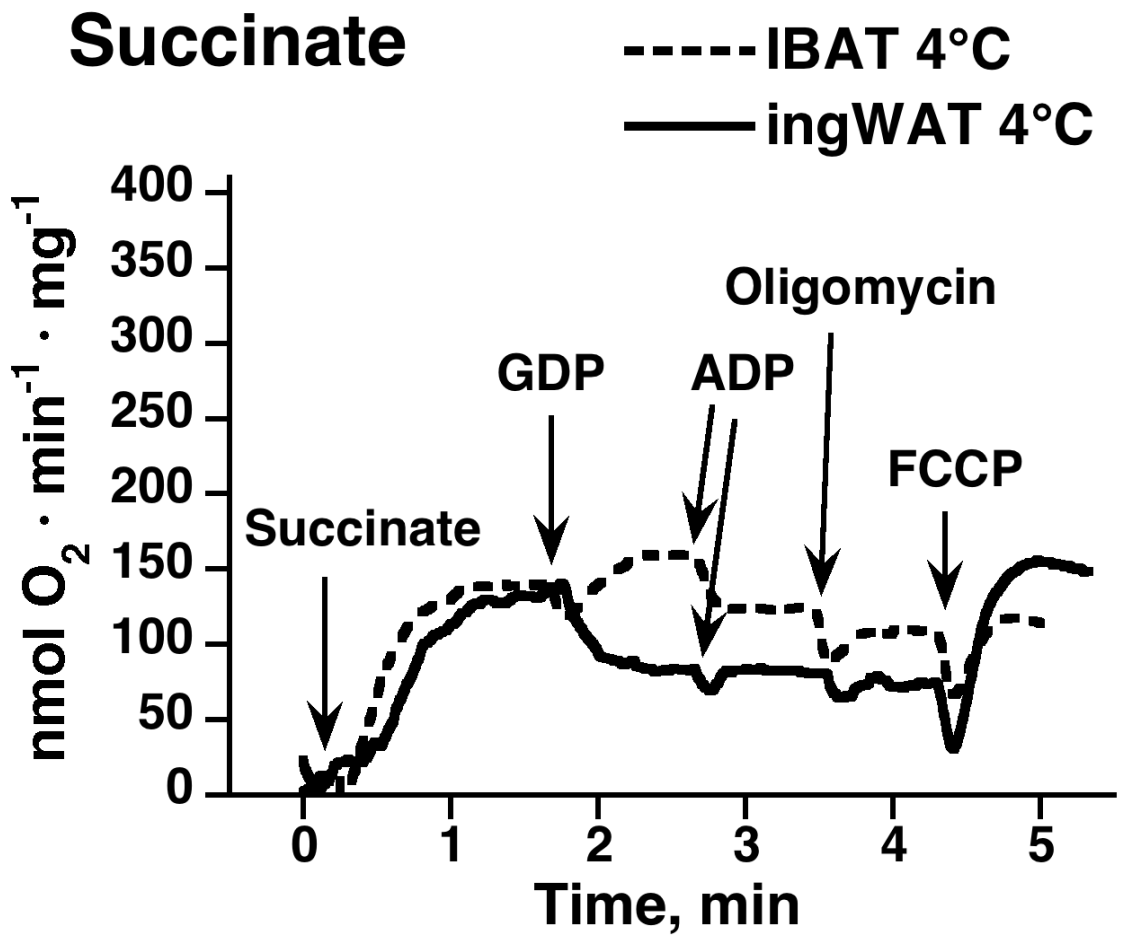
WAT

BRITE



129Sv

Succinate is a poor substrate for both brown and brite fat mitochondria

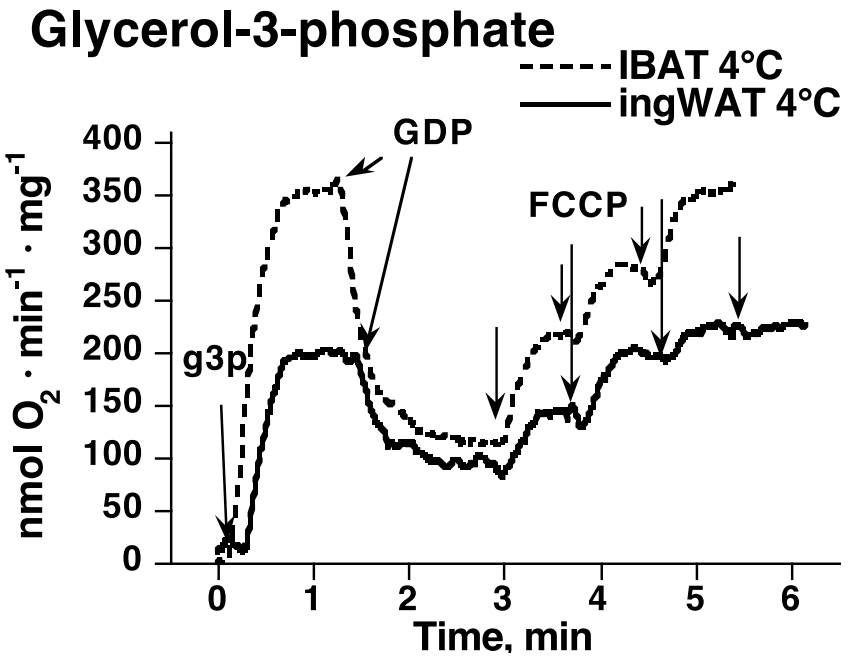


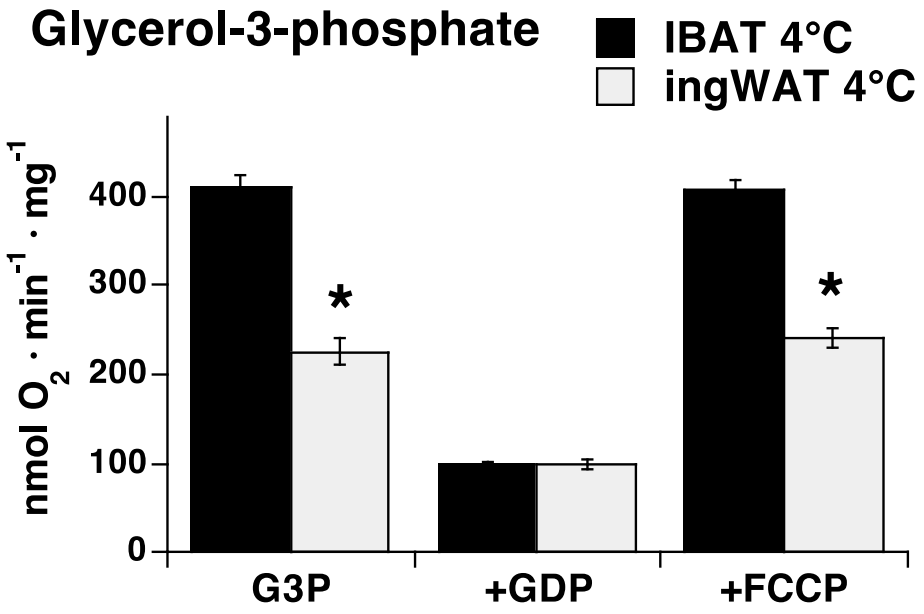
129sv

Brown mitochondria

BRITE mitochondria

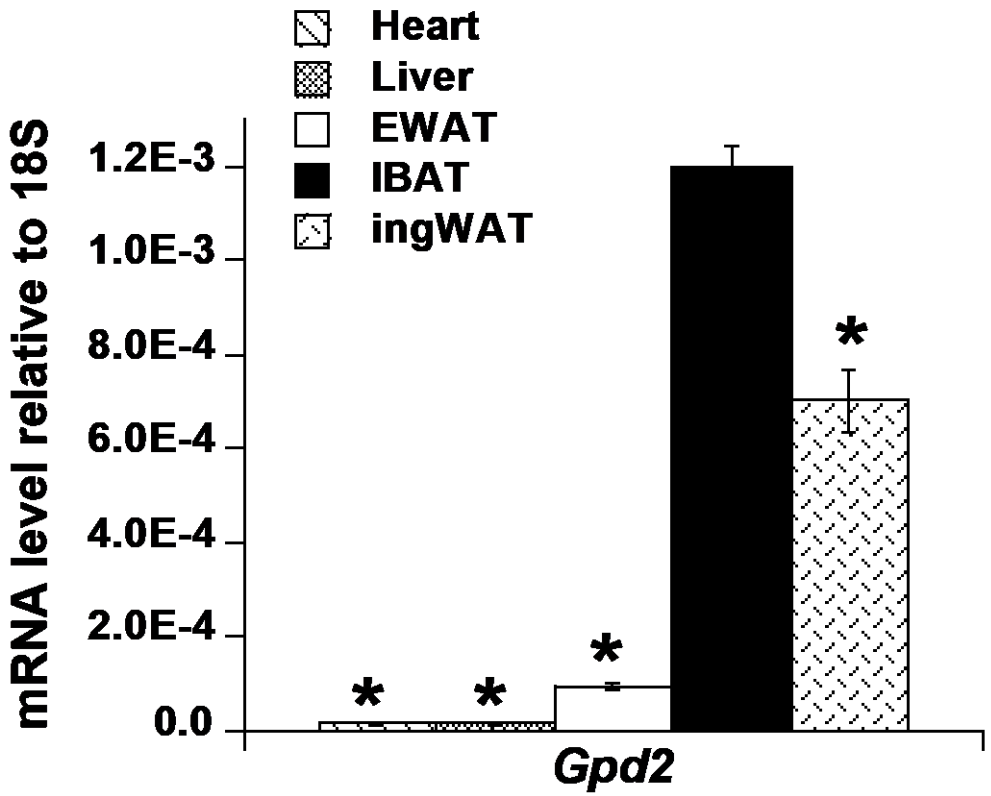
Glycerol-3-phosphate-supported oxygen consumption in recruited brite-fat mitochondria was 50 % of the level in BAT





129sv

The expression level of glycerol-3-phosphate dehydrogenase in recruited brite-fat was 50 % of the level in BAT



Limitation in transporting reducing equivalents from cytosol to mitochondria

Consider carefully your experimental animal.

Remember its physiology.

Choose relevant substrates.