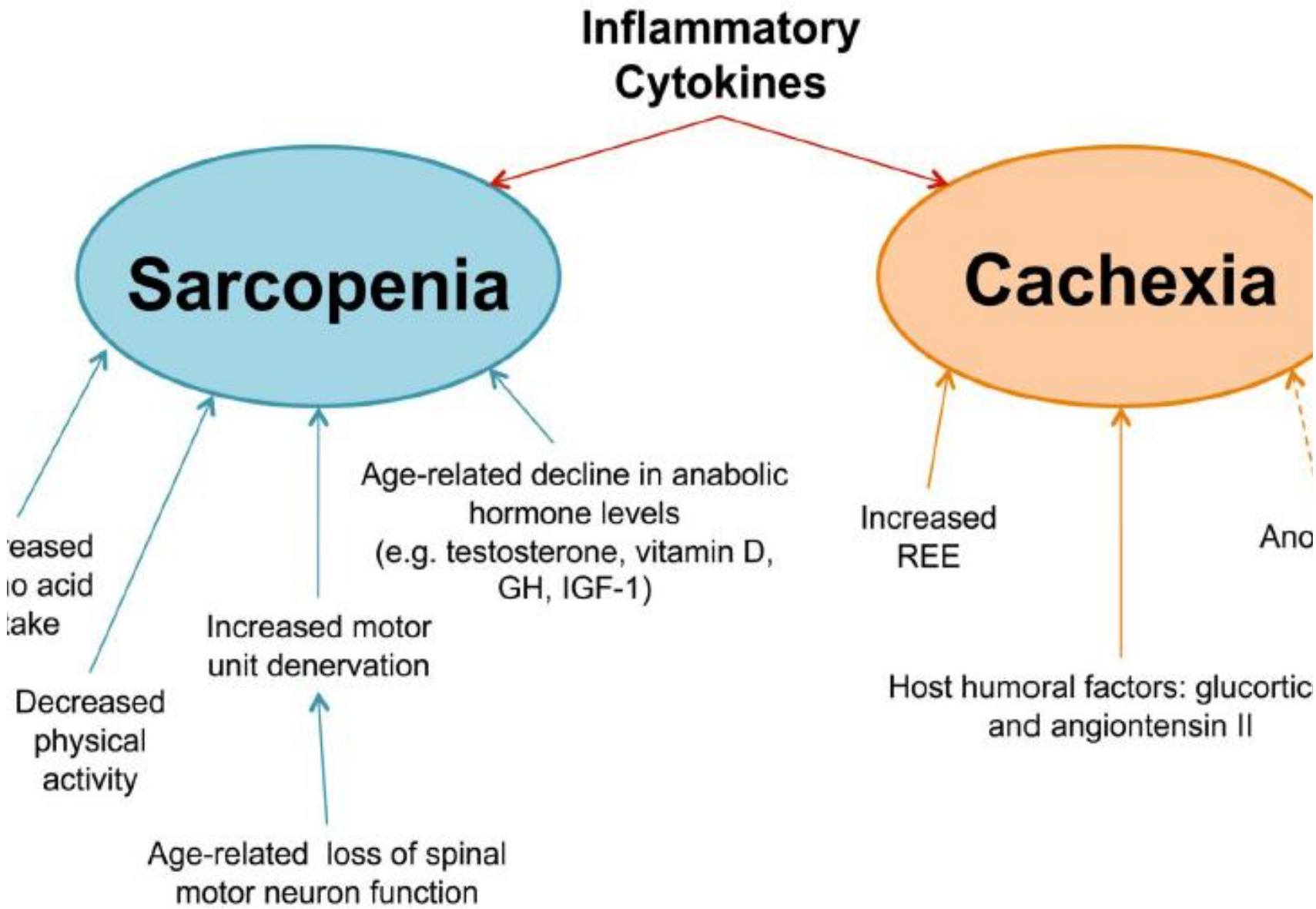
Aging and exercise

- As we age muscles atrophy.
- There is reduction in muscle fiber cross section area.
- Loss of muscle fibers by apoptosis
- Reduced nerve connections.

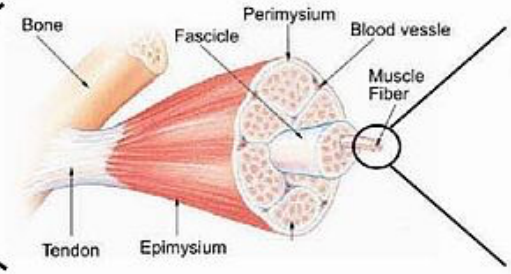
- CAN WE SLOW THE EFFECT?

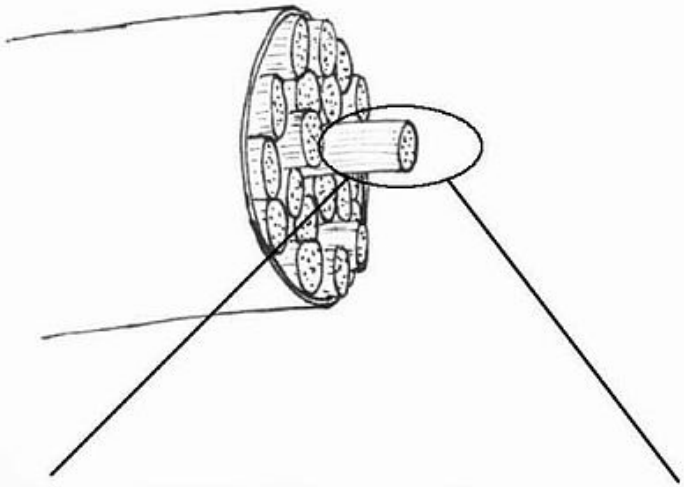
- This age-related muscle atrophy, termed **sarcopenia**, is associated with muscle weakness and can have significant effects on an individual's health and quality of life.
- affects a growing population, occurring in 10-25% of individuals under the age of 70 and in more than 40% of the elderly over the age of 80.

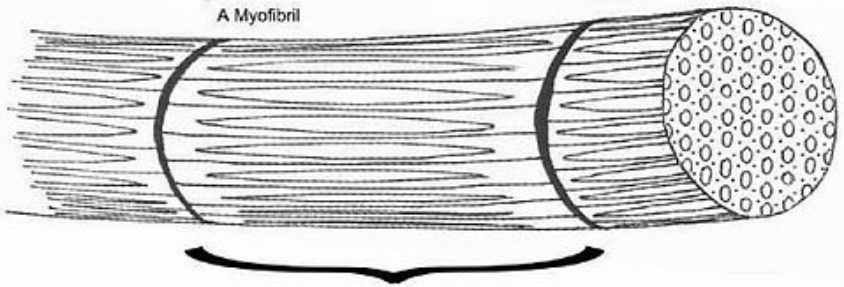
- specific skeletal muscles may undergo a ~40% decline in muscle mass between the ages of 20 and 80 years.
- 25% decrease in cross-sectional area of vastus lateralis is consistently seen in comparisons of 70- to 75-year-olds with 20- to 30-year-olds. Large declines also occur in the number of fibers.

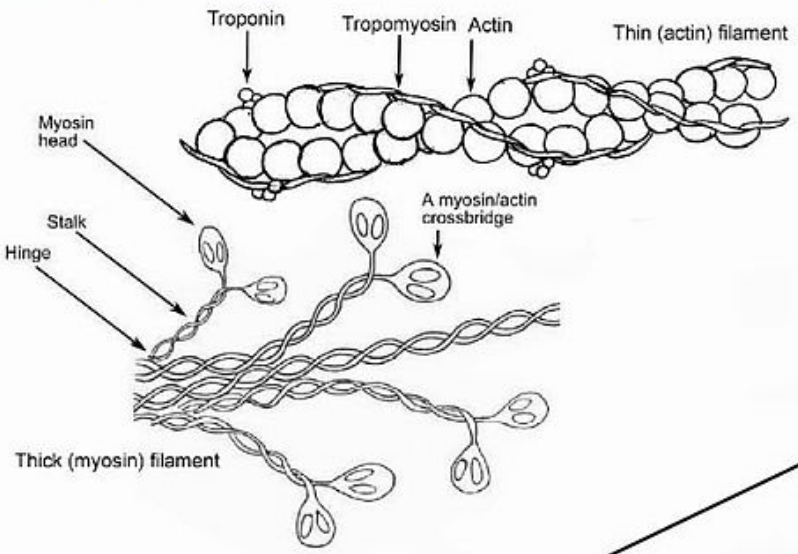

Inflammatory Cytokines
Sarcopenia
Cachexia
eased
o acid
ake
Decreased physical activity
Increased motor unit denervation
Age-related loss of spinal motor neuron function
Age-related decline in anabolic hormone levels (e.g. testosterone, vitamin D, GH, IGF-1)
Increased REE
Host humoral factors: glucortic and angiontensin II
Ano

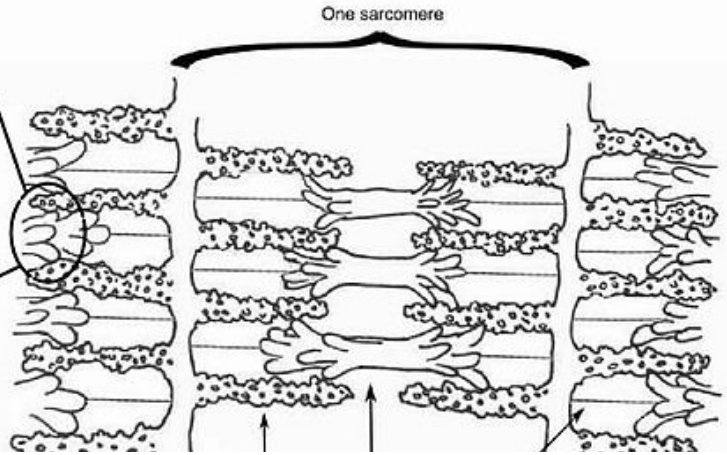
- MUSCLE ACTION REVISITED

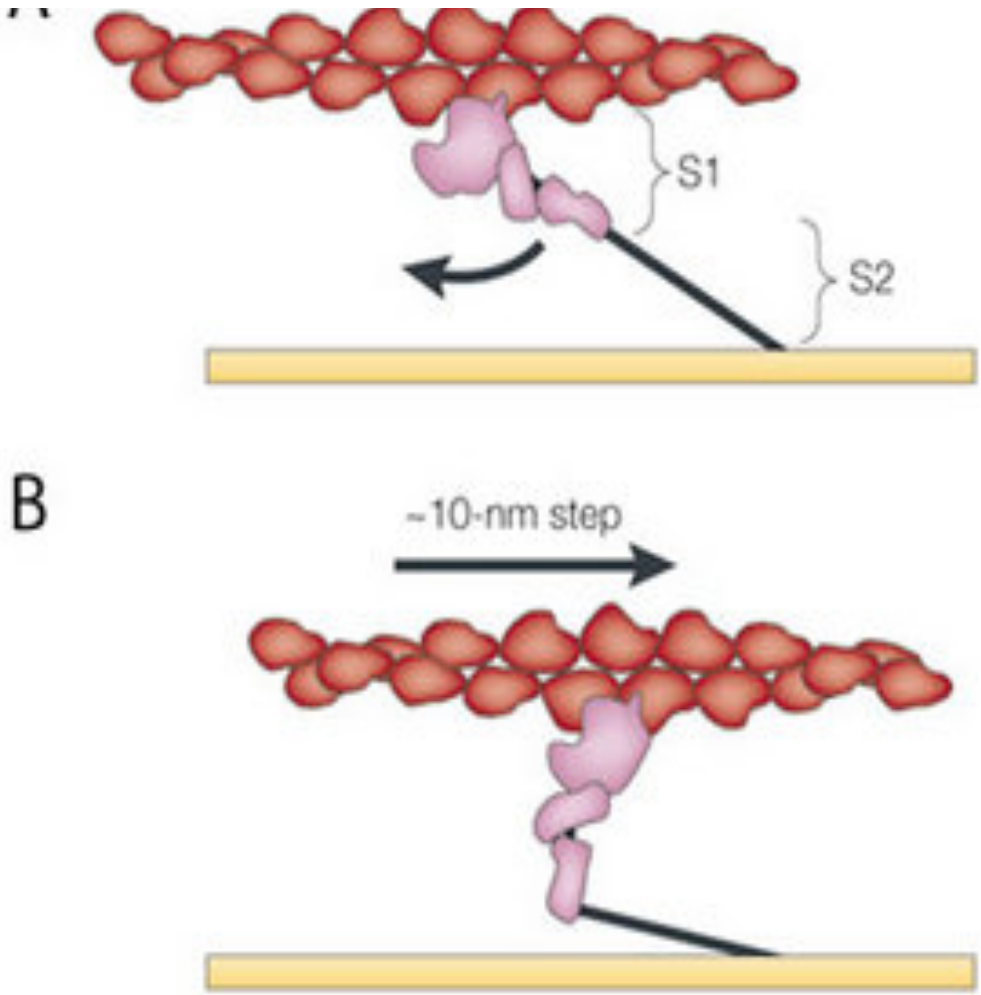

Bone
Fascicle
Perimysium
Blood vessle
Muscle Fiber
Tendon
Epimysium



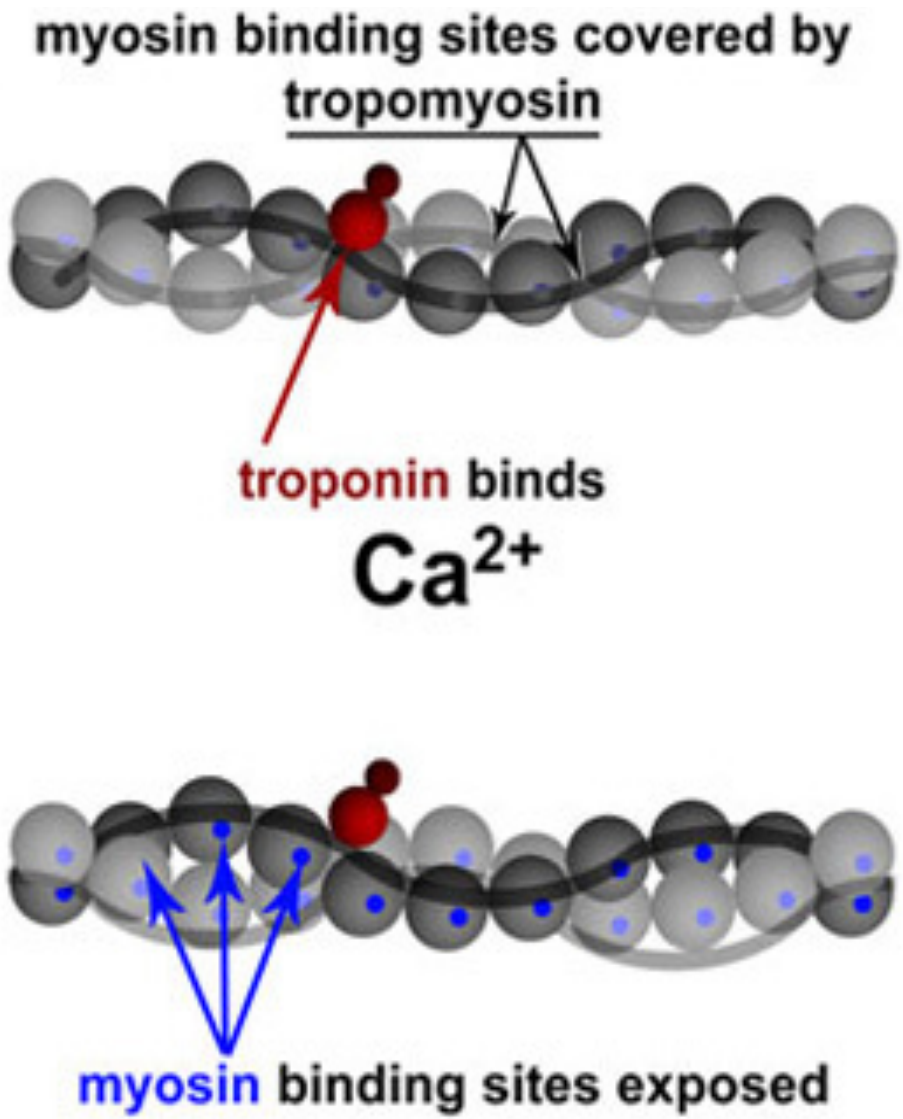

A Myofibril


Troponin
Tropomyosin
Actin
Thin (actin) filament
Myosin head
Stalk
Hinge
A myosin/actin crossbridge
Thick (myosin) filament

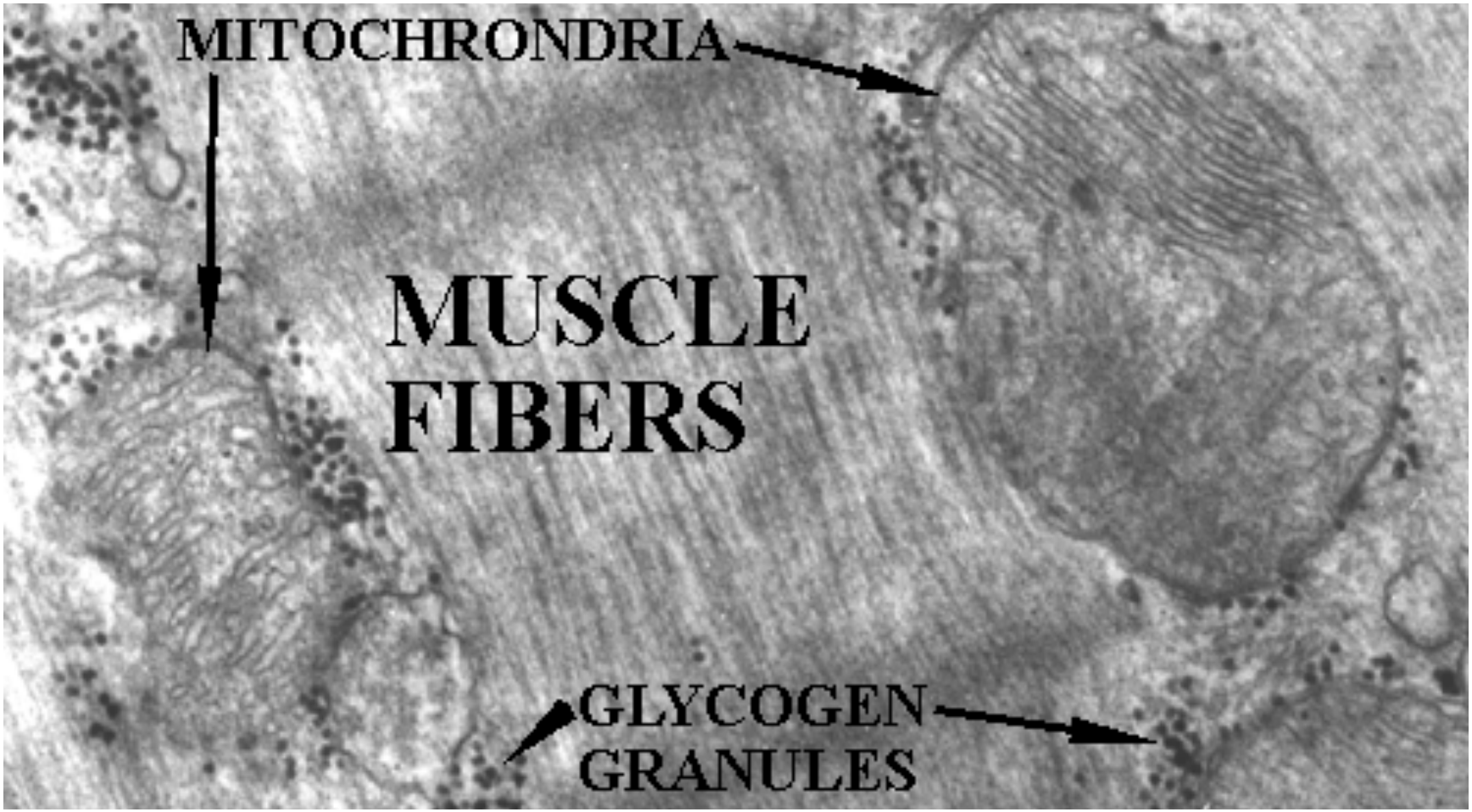

One sarcomere



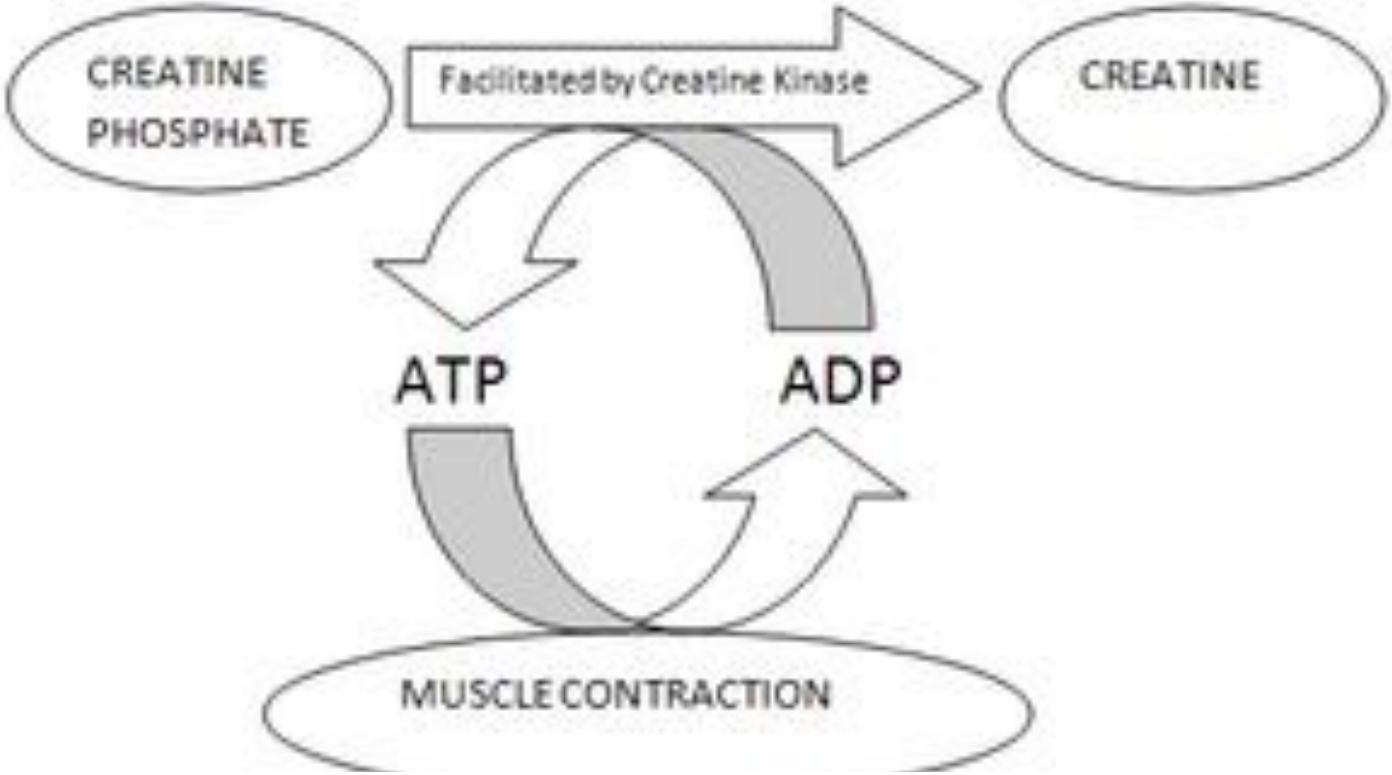
Nature Reviews | Molecular Cell Biology

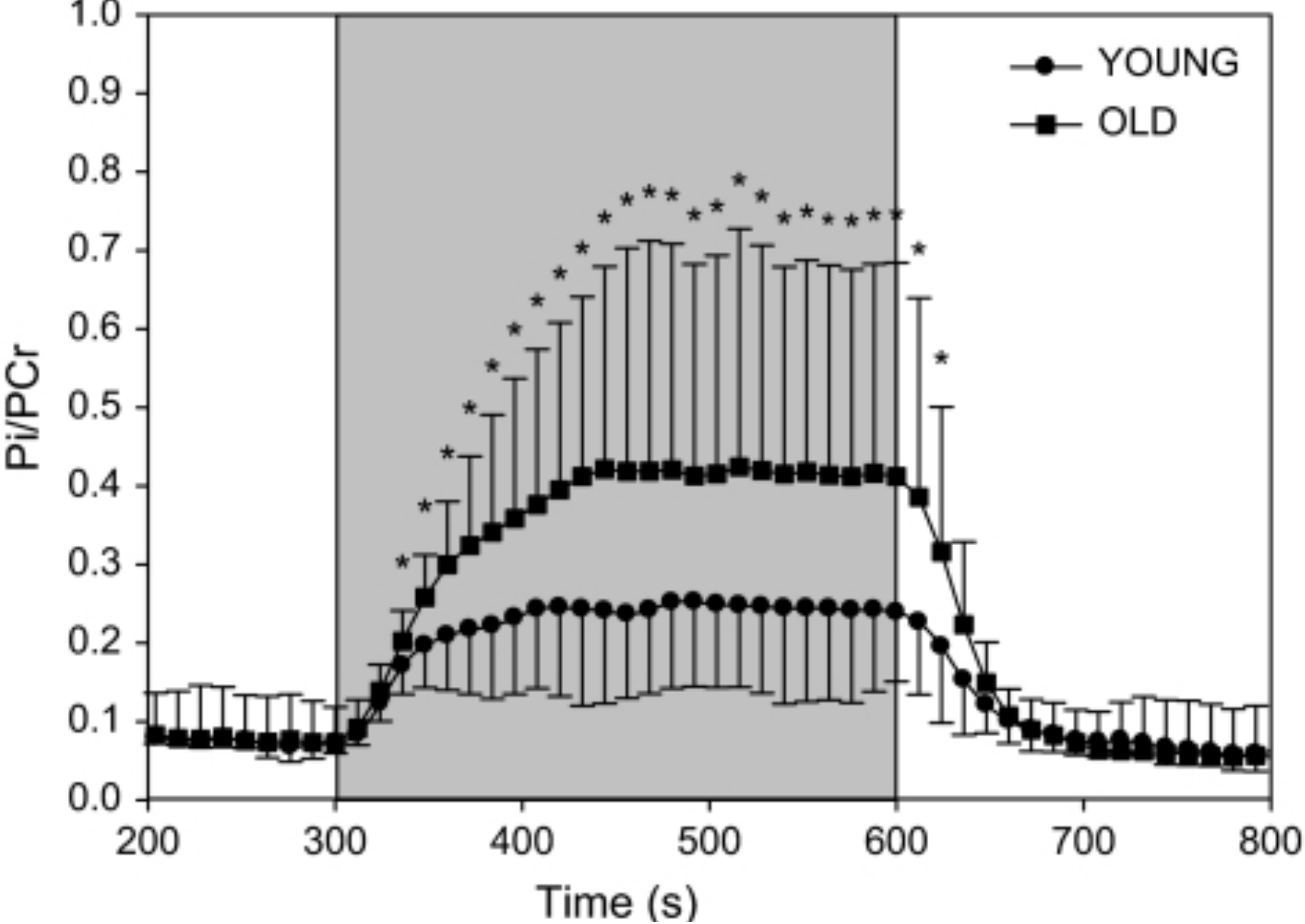

myosin binding sites covered by
tropomyosin
troponin binds
Ca^{2+}
myosin binding sites exposed

- Muscle building as a normal process involves myocytes that become myofibers.
- Myocytes are progenitor cells and their ability to differentiate is reduced in aging.


MITOCHRONDRIA
MUSCLE
FIBERS
GLYCOGEN
GRANULES

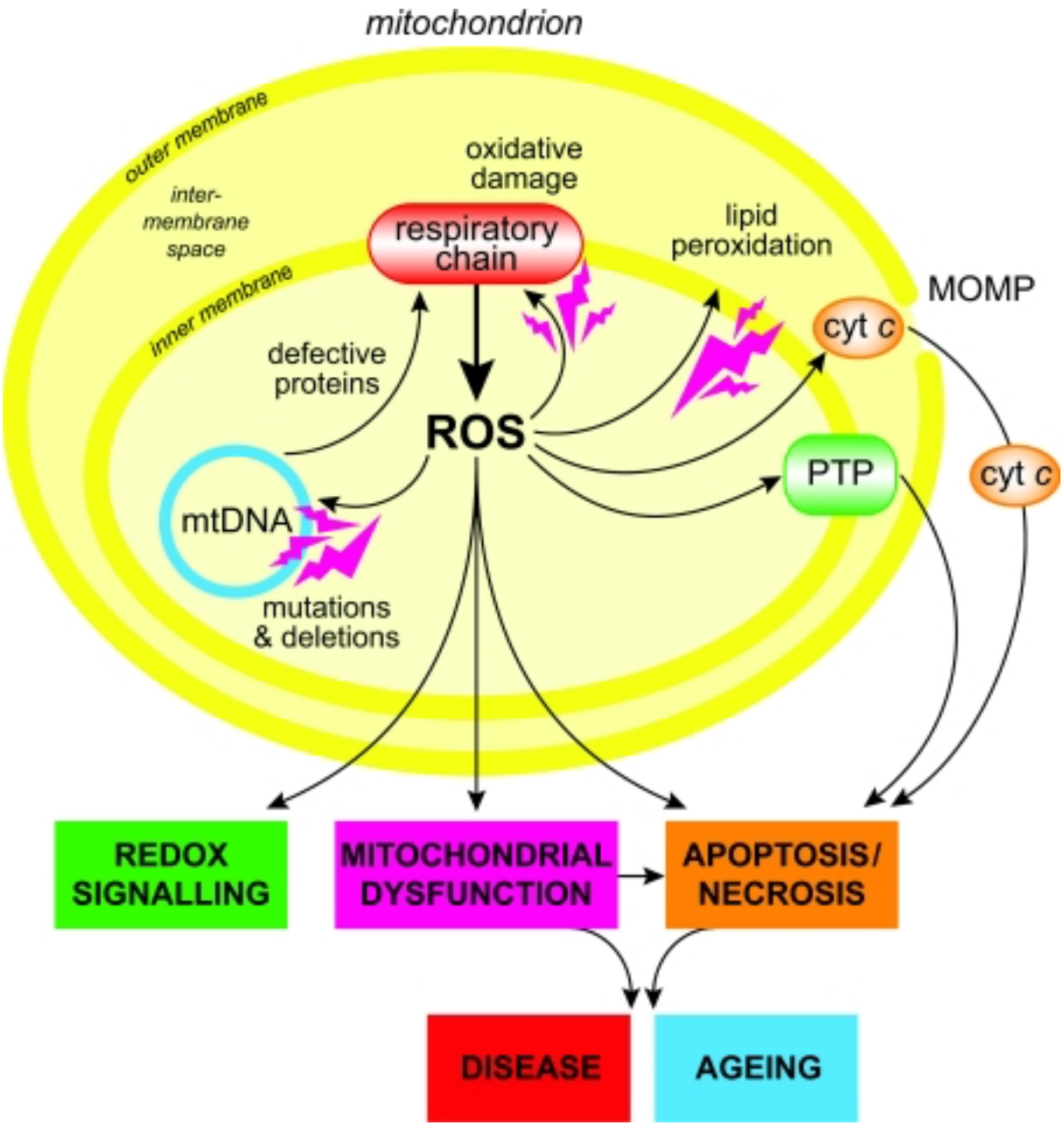
ENERGY IN MUSCLE CAN BE STORED BY REVERSIBLE TRANSFER OF THE TERMINAL PHOSPHATE OF ATP TO CREATINE

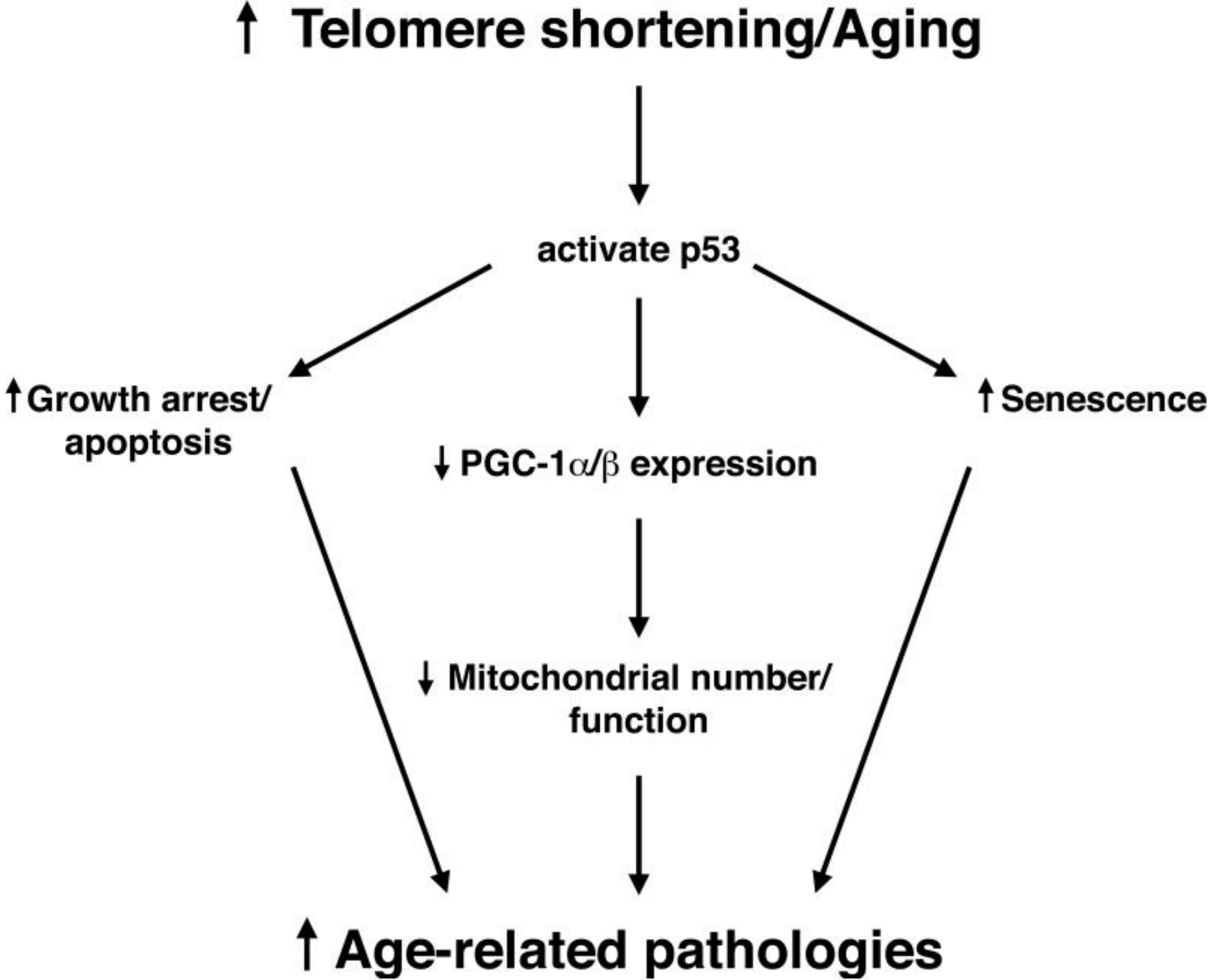



YOUNG
OLD
Pi/PCr
Time (s)
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0.0
200
300
400
500
600
700
800

THE MITOCHONDRIAL VICIOUS CYCLE THEORY

- Oxidative stress induces mutations in **mtDNA**
- This gives even higher ↑ in ROS production
- Leading to ↓ ETC activity Mito dysfunction
- And causing apoptosis.


mitochondrion
outer membrane
inter-membrane space
inner membrane
oxidative damage
respiratory chain
lipid peroxidation
MOMP
cyt c
defective proteins
ROS
PTP
cyt c
mtDNA
mutations & deletions
REDOX SIGNALLING
MITOCHONDRIAL DYSFUNCTION
APOPTOSIS/ NECROSIS
DISEASE
AGEING


↑ Telomere shortening/Aging
activate p53
↑Growth arrest/ apoptosis
↓ PGC-1α/β expression
↑Senescence
↓ Mitochondrial number/ function
↑ Age-related pathologies

Cytochrome c oxidase enzyme activity (average ± S.E.) in young and old in skeletal muscles, liver, and heart

Cytochrome c oxidase activity (µmol/min · g protein)

	Young	**Old**
Gastrocnemius medial	187 ± 62	162 ± 13
Gastrocnemius lateral	232 ± 22	166 ± 6[1-a]
Liver	455 ± 18	444+-11
Heart	1136 ± 60	1194 ± 61

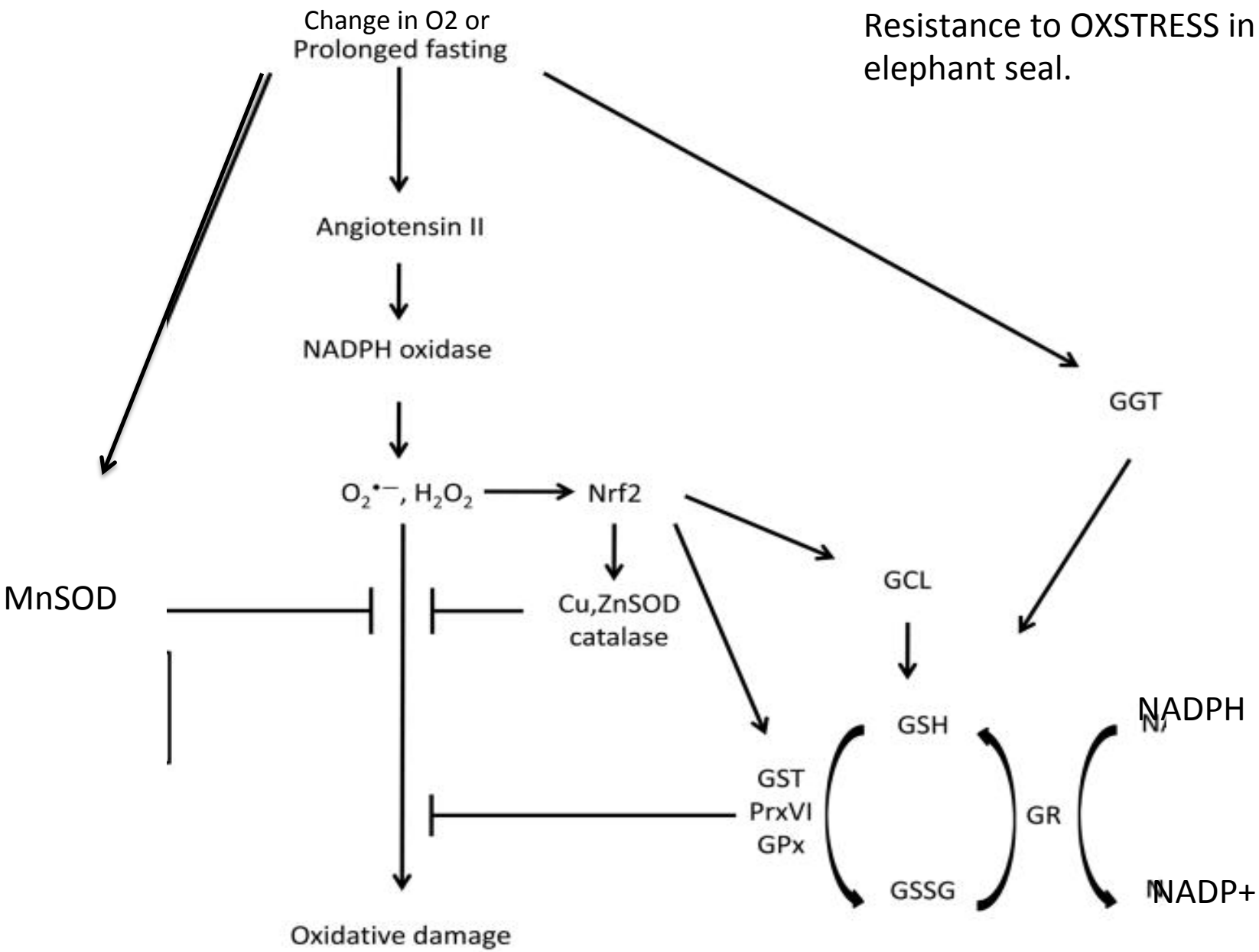
ROS is most highly generated in circumstances such as reperfusion and where O2 levels are increased after decreased, e.g. after going anaerobic by exercise and then re-oxygenating.

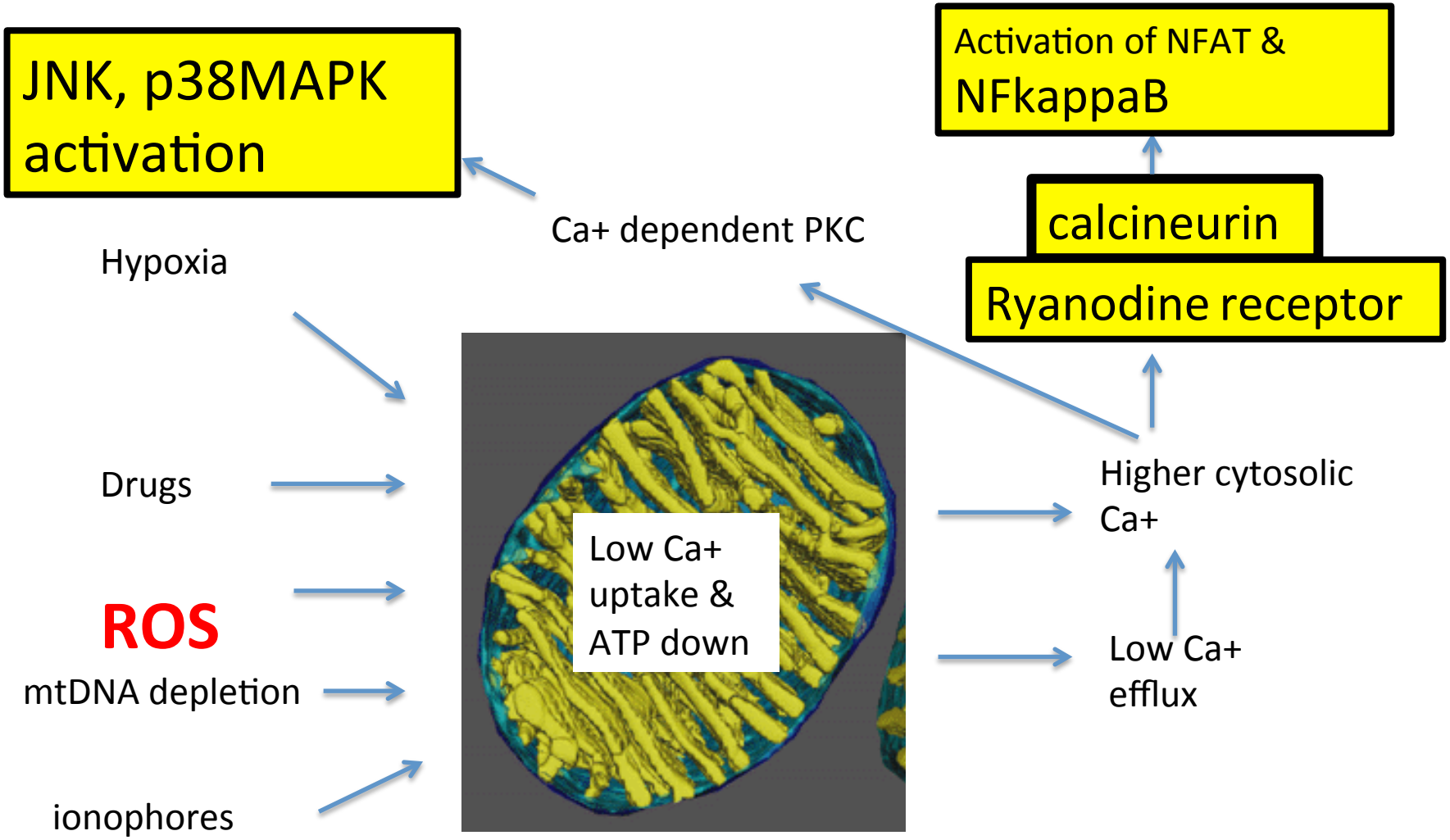
- **MANY ANIMALS ARE EXPOSED TO VARIABLE METABOLIC/ENERGY DEMANDS AND DIFFERENT OXYGEN TENSIONS, HOW DO THEY ADAPT?**

- Hibernation is characterized by a profound decrease in oxygen consumption and metabolic demand during torpor that is punctuated by periodic rewarming episodes, during which oxygen consumption increases dramatically. The surge in oxygen consumption during arousal increases production of reactive oxygen species, making hibernation a potentially injurious process.

- Elephant seals can go very deep in the ocean where O2 levels are low then rise to the surface quickly. Also they can fast for very long periods and then start metabolism on feeding HOW?

Resistance to OXSTRESS in the elephant seal.



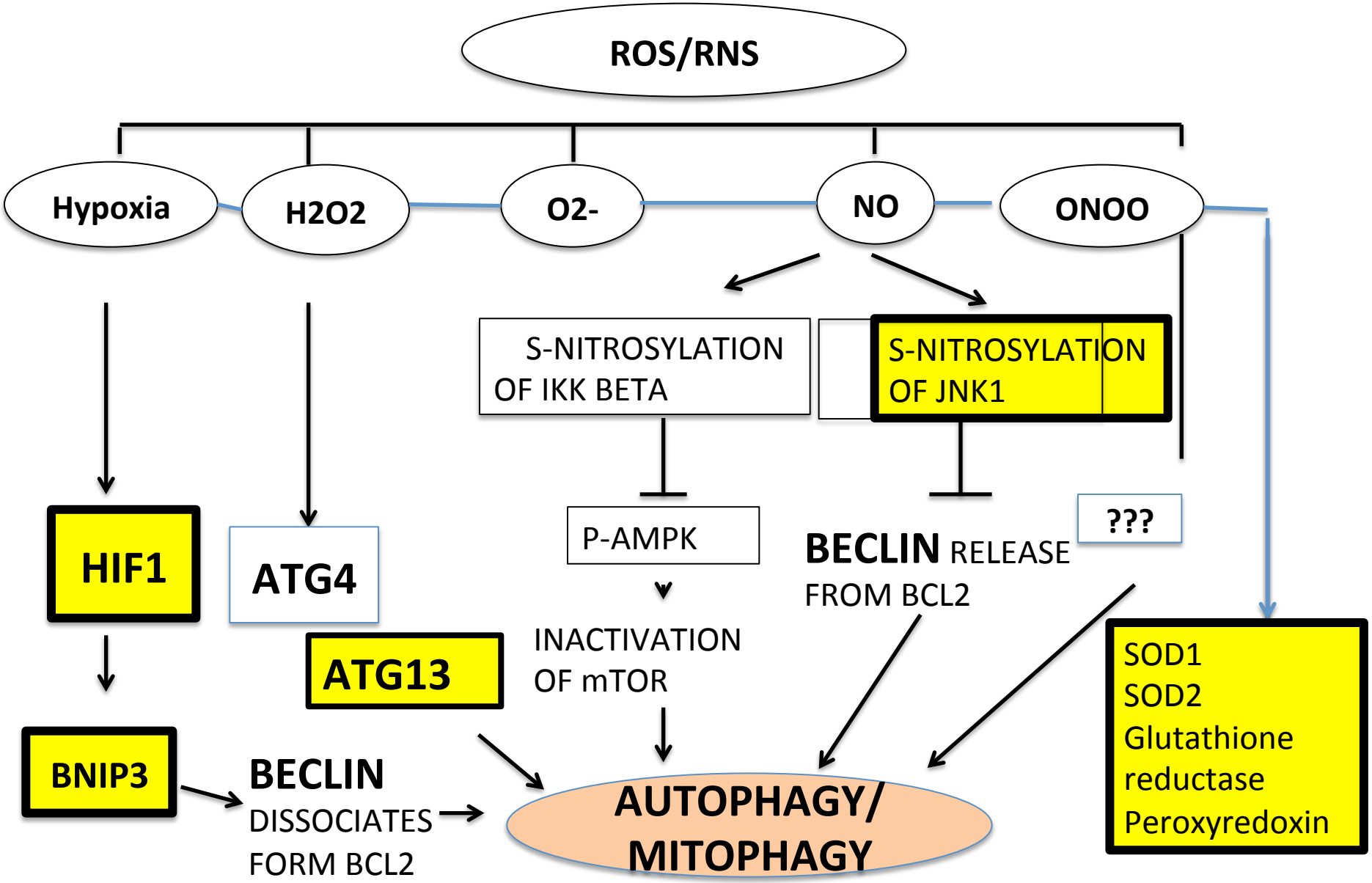


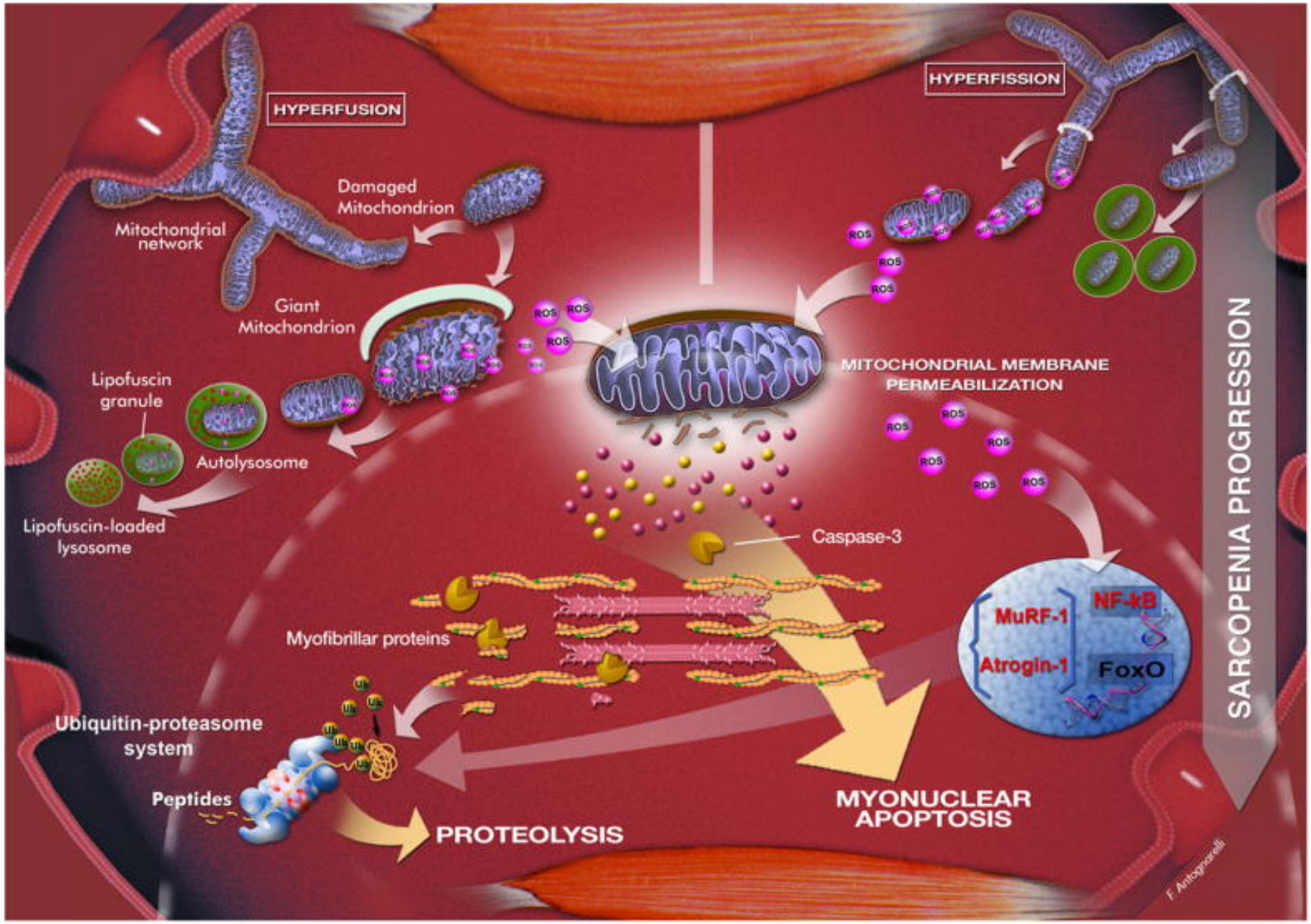
Ca+ induced mitochondrial retrograde response

Ca++ release from the ER (called sarcoplaasmic reticulum in muscle)causes activation of Ca++ channels in the plasma membrane which leads to loss of Ca++

Ca++ is required for muscle functioning

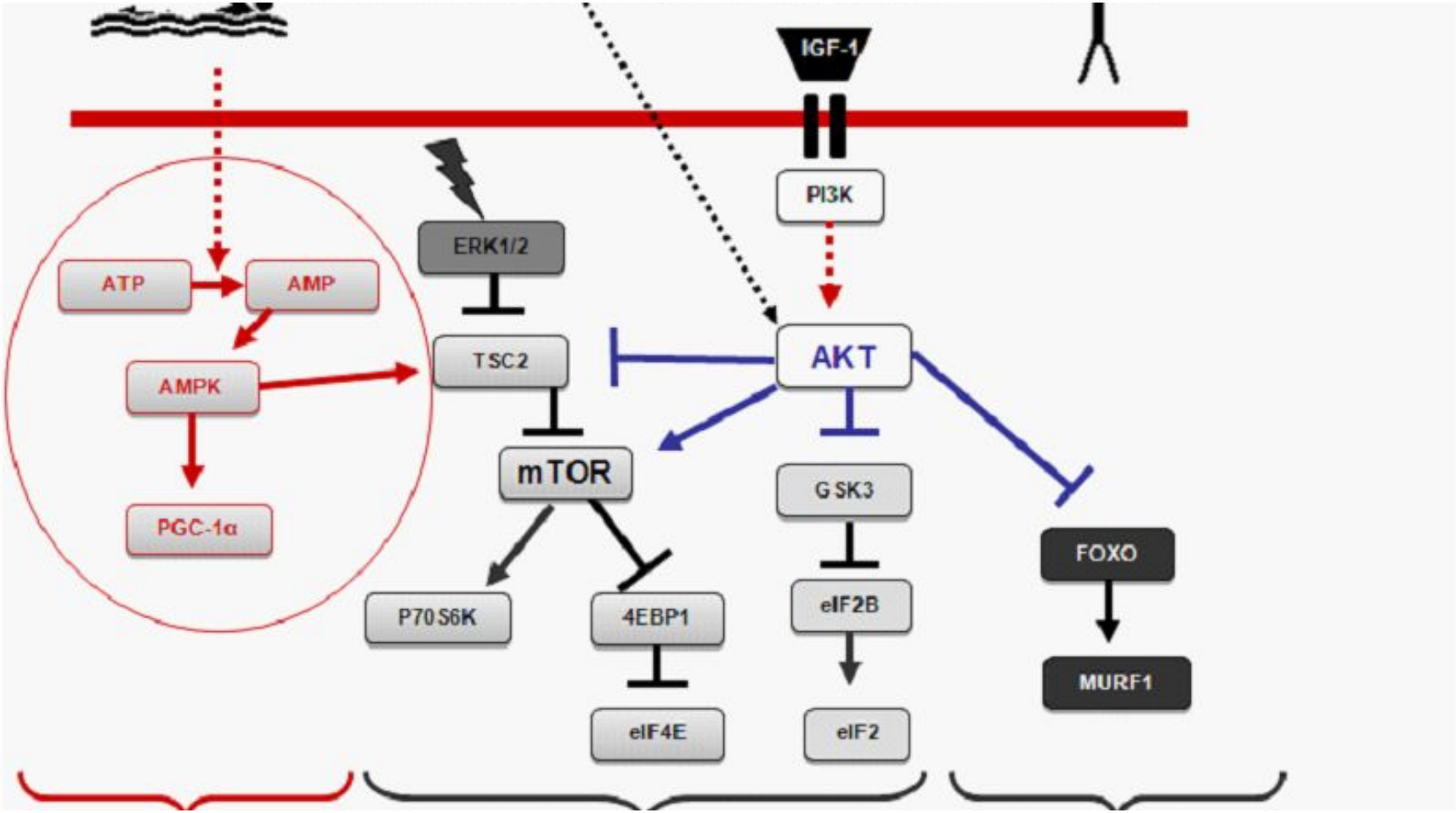
RETROGRADE SIGNALING INVOLVING ROS AND RNS




HYPERFUSION
HYPERFISSION
Damaged Mitochondrion
Mitochondrial network
Giant Mitochondrion
Lipofuscin granule
Autolysosome
Lipofuscin-loaded lysosome
ROS
MITOCHONDRIAL MEMBRANE PERMEABILIZATION
Caspase-3
Myofibrillar proteins
MuRF-1
NF-kB
Atrogin-1
FoxO
Ubiquitin-proteasome system
Peptides
PROTEOLYSIS
MYONUCLEAR APOPTOSIS
SARCOPENIA PROGRESSION
F. Antognarelli

- EXERCISE AND DIET: THE LINK TO A LONGER, HEALTHIER LIFE.

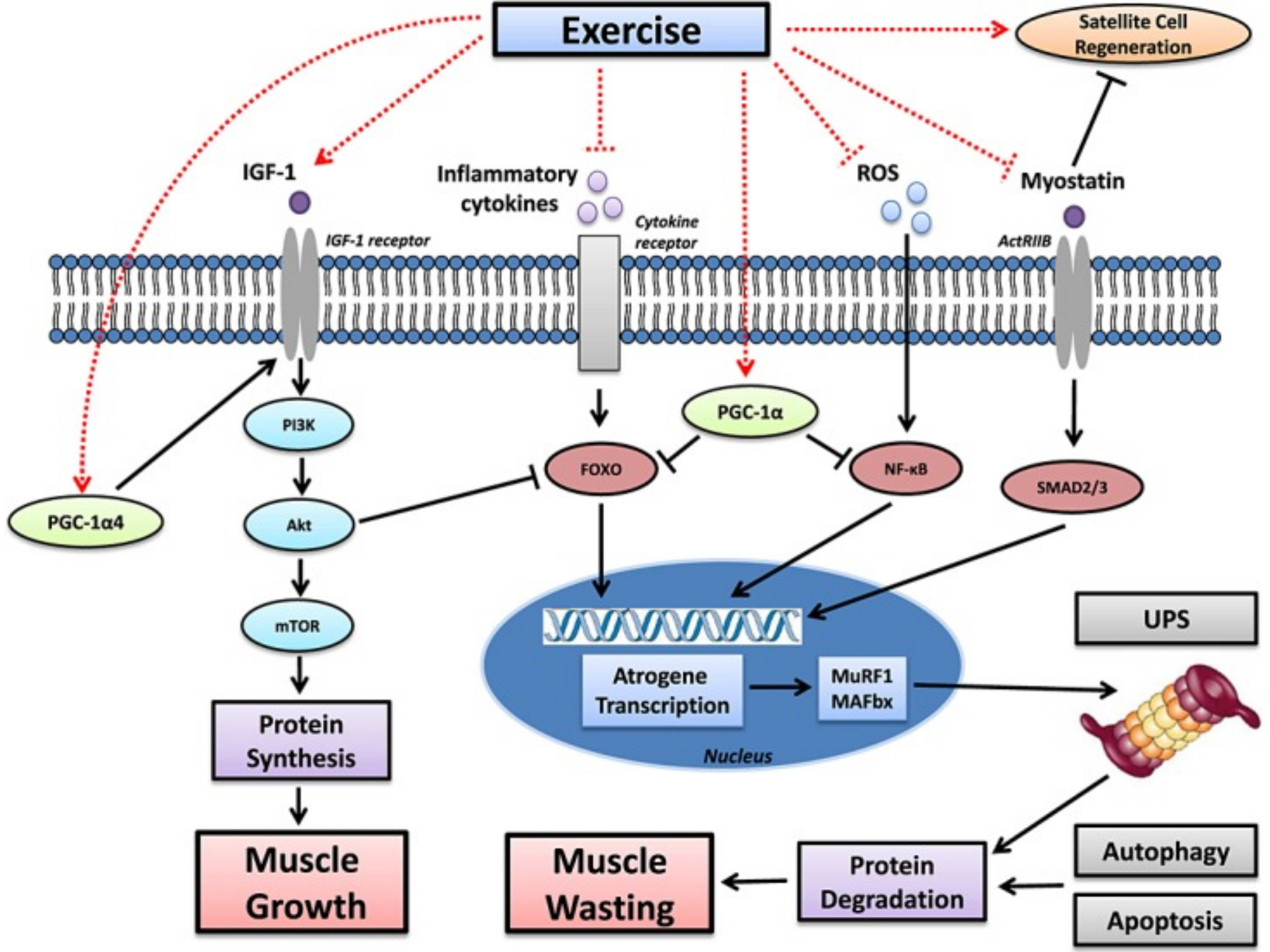

Exercise
Mechanical,
Metabolic Stress
IGF-1
Cytokines
(TNF-α, IL-18)
ERK
PI-3K
MnSOD
HSPs
NF-κB
activation
Akt
apoptosis



Mito biogenesis

Protein synthesis

Protein degredation


Exercise
Satellite Cell Regeneration
IGF-1
Inflammatory cytokines
ROS
Myostatin
IGF-1 receptor
Cytokine receptor
ActRIIB
PGC-1α4
PI3K
Akt
mTOR
PGC-1α
FOXO
NF-κB
SMAD2/3
Atrogene Transcription
MuRF1
MAFbx
Nucleus
UPS
Protein Synthesis
Muscle Growth
Muscle Wasting
Protein Degradation
Autophagy
Apoptosis

CREATINE SUPPLIMENTATION and HIGH INTENSITY EXERCISE

- Short term use of creatine with weight bearing exercises has been shown to improve muscle mass and fatigue resistance in the elderly. Also improves cognitive performance.

- Conjugated linoleic acid also improves muscle mass.

- RESVERITROL (RED WINE) AND HISTONE DEACETYLASE INHIBITORS REDUCE AGING EFFECTS IMPLYING A ROLE FOR SIRT 1 AND SIRT 3.