

Age-related muscle weakness

Dr Graeme L. Close
School of Clinical Sciences

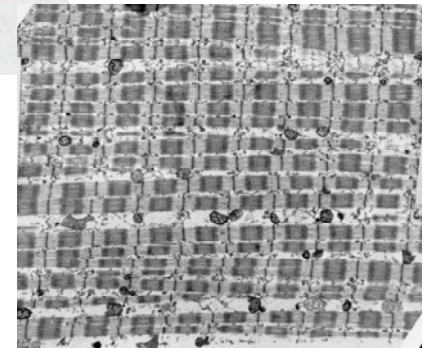
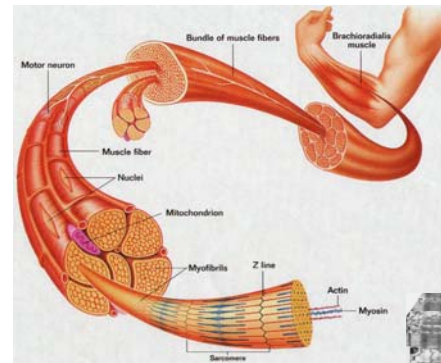


UNIVERSITY OF
LIVERPOOL

Who am I?



Muscular Pathophysiology Group



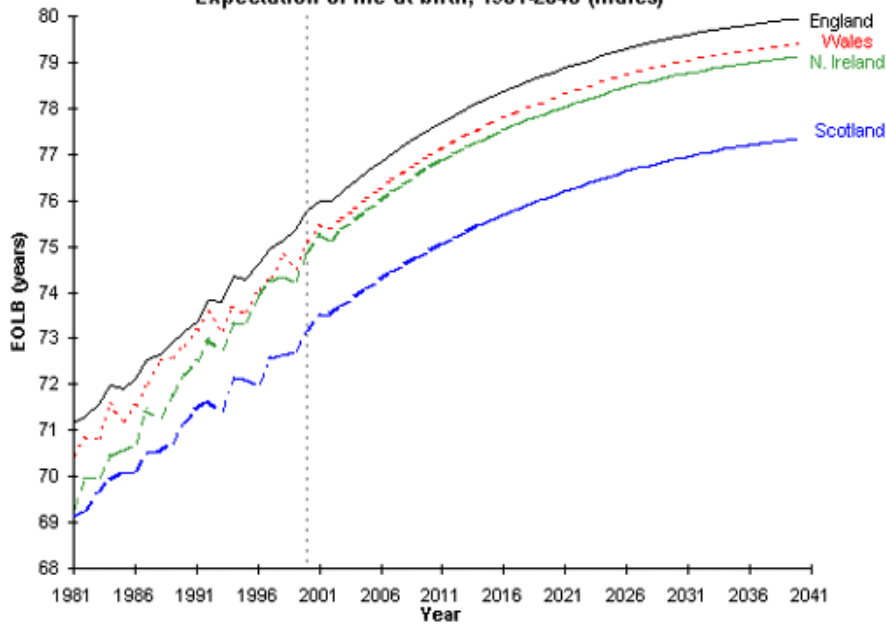
The bigger picture...



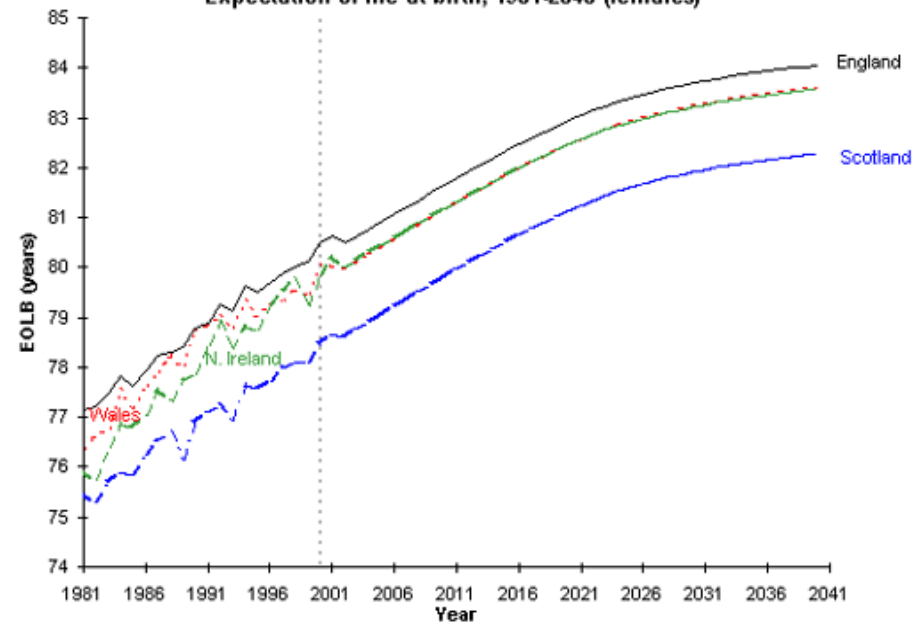
HELP THE AGED WE WILL®

Life Expectancy at Birth

Expectation of life at birth, 1981-2040 (males)

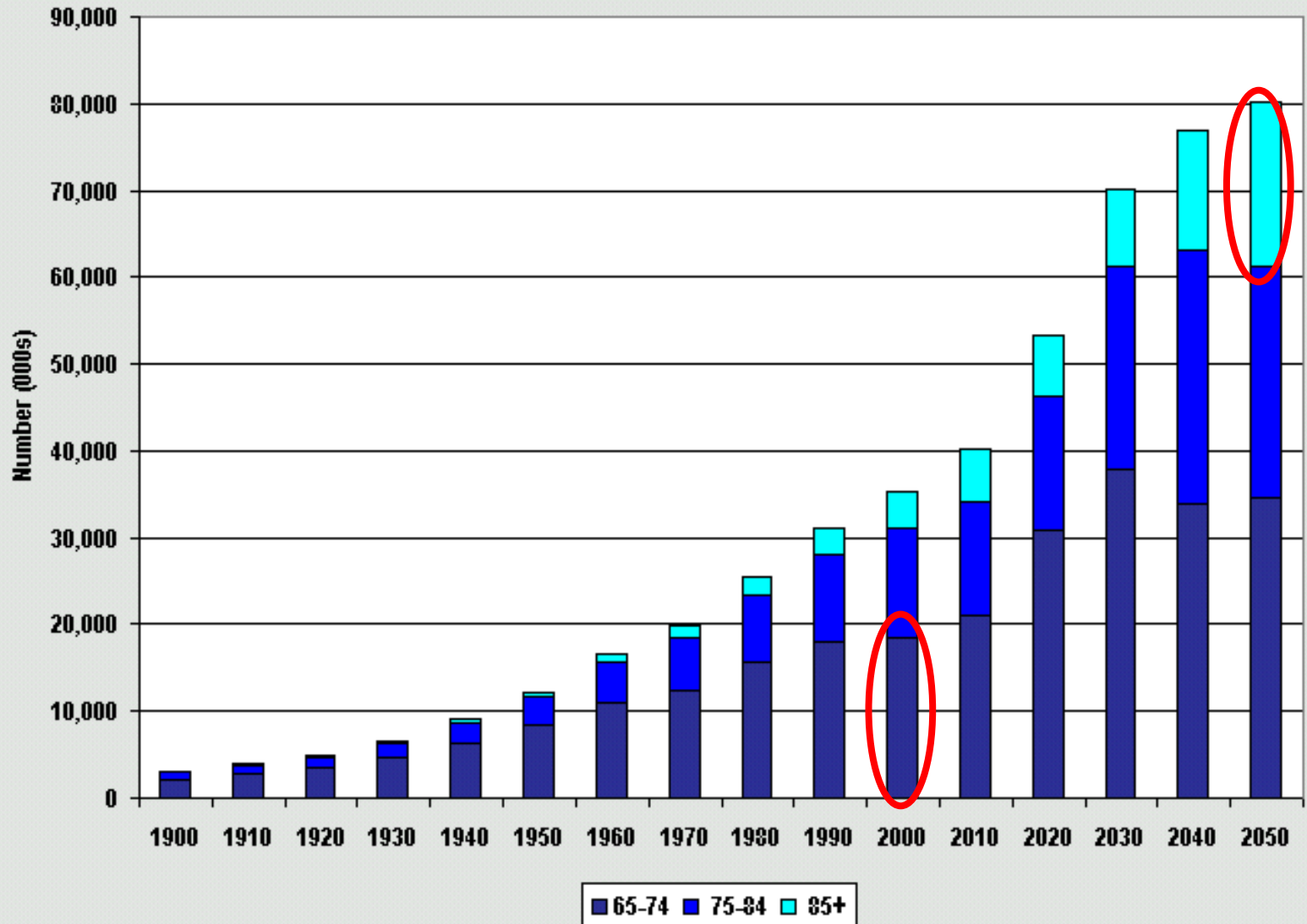


Expectation of life at birth, 1981-2040 (females)

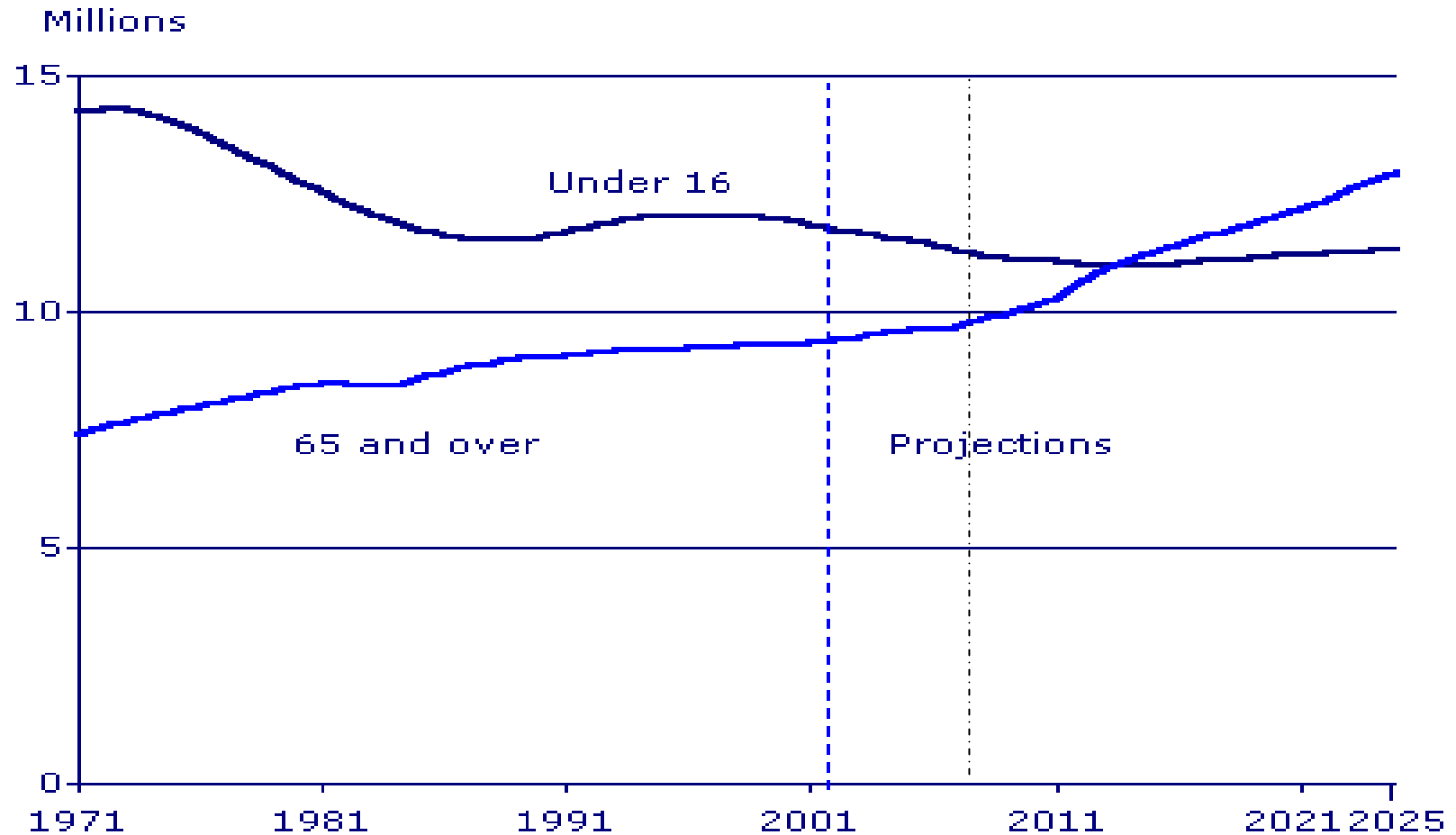


Older Population by Age: 1900-2050

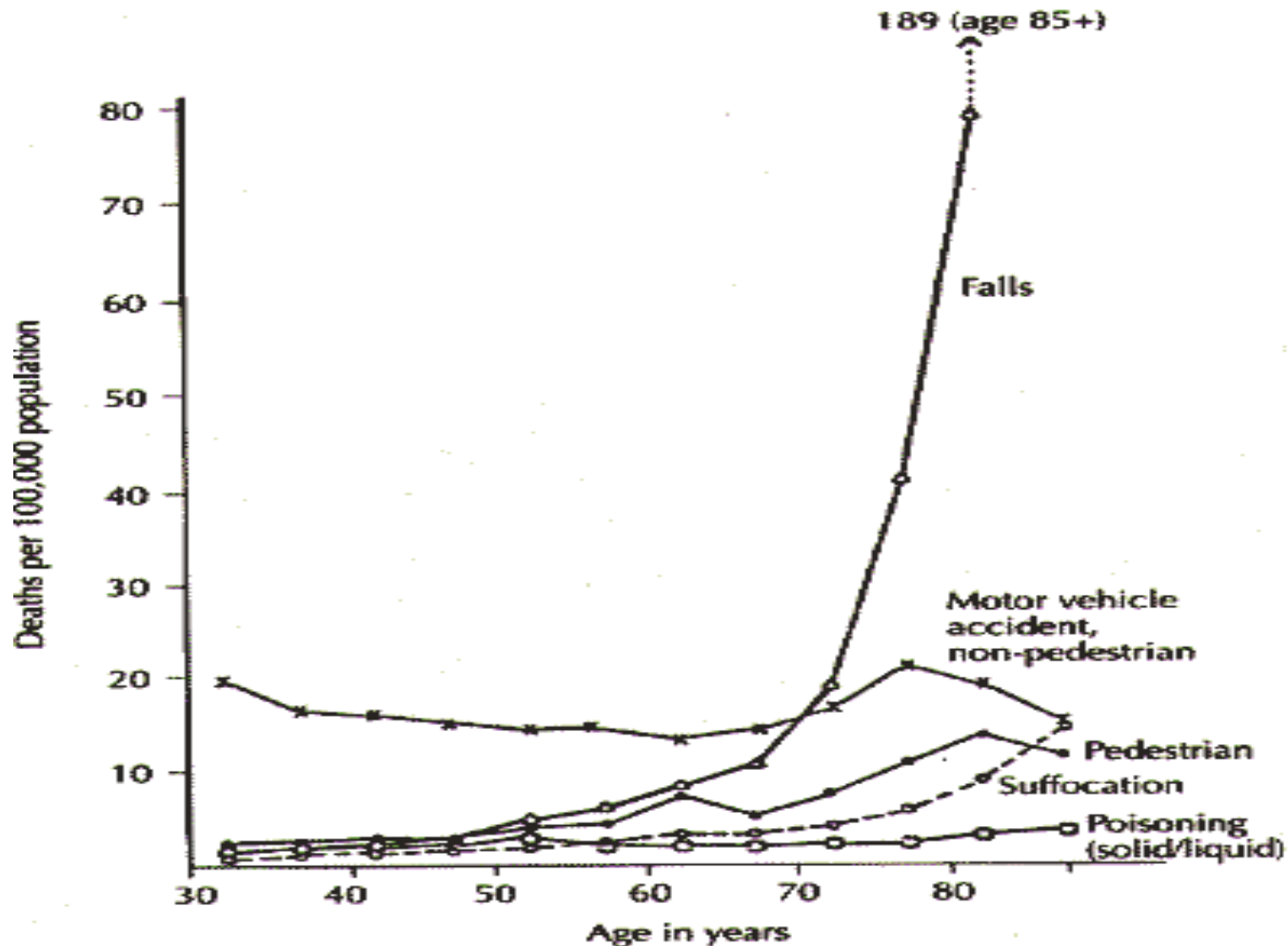
Source: U.S. Bureau of the Census



Percentage of under 16 to over 65

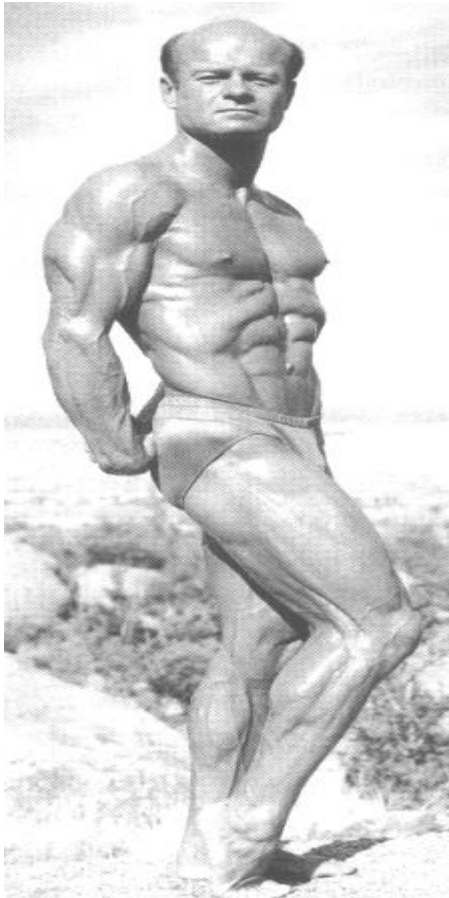


Incidence of Falls per 100,000 population increases rapidly with increasing age.

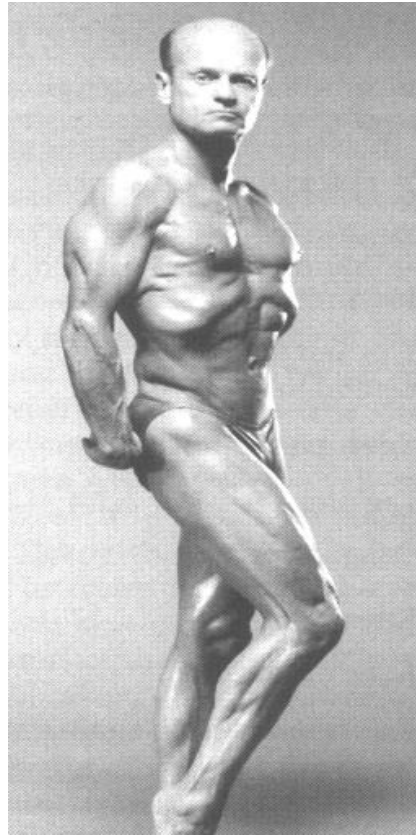


Sarcopenia – A problem for all.

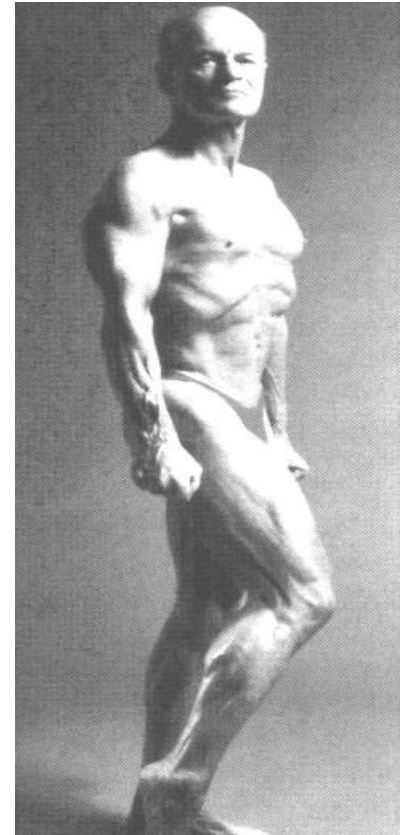
Clarence Bass



43



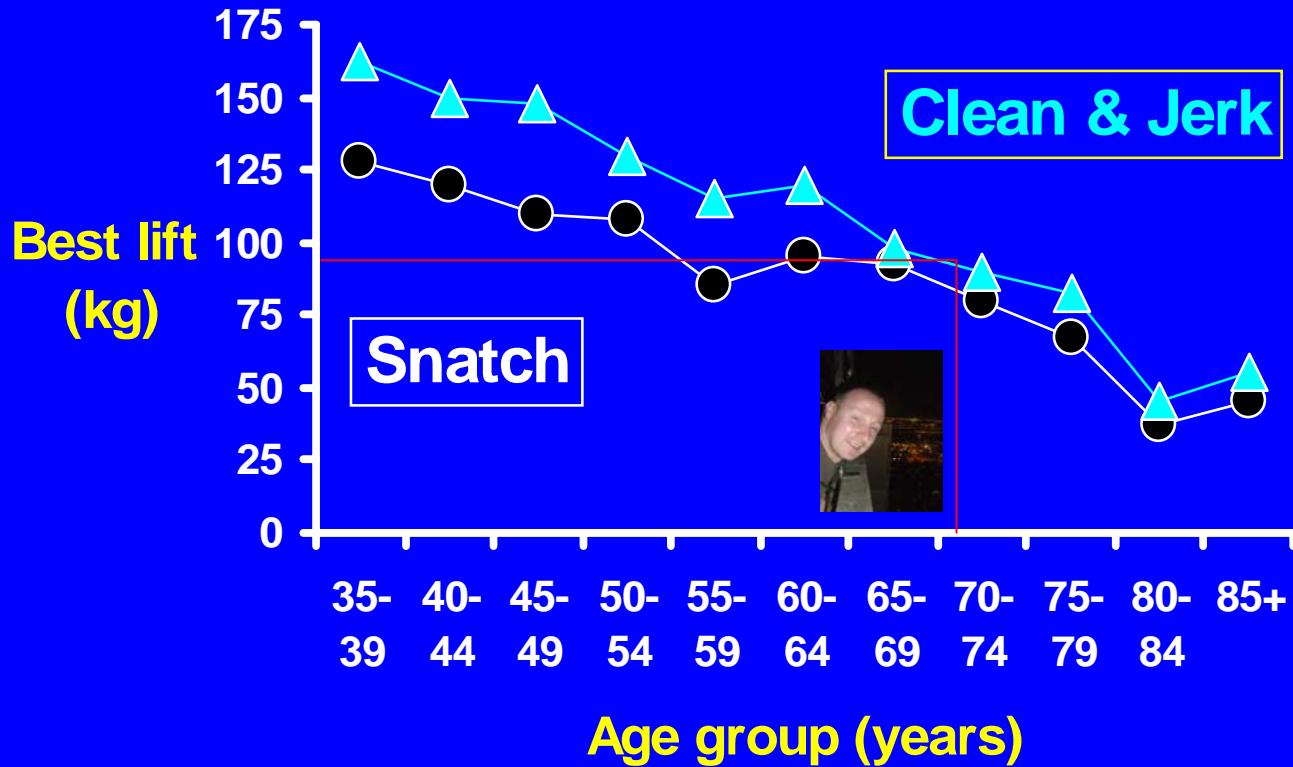
55



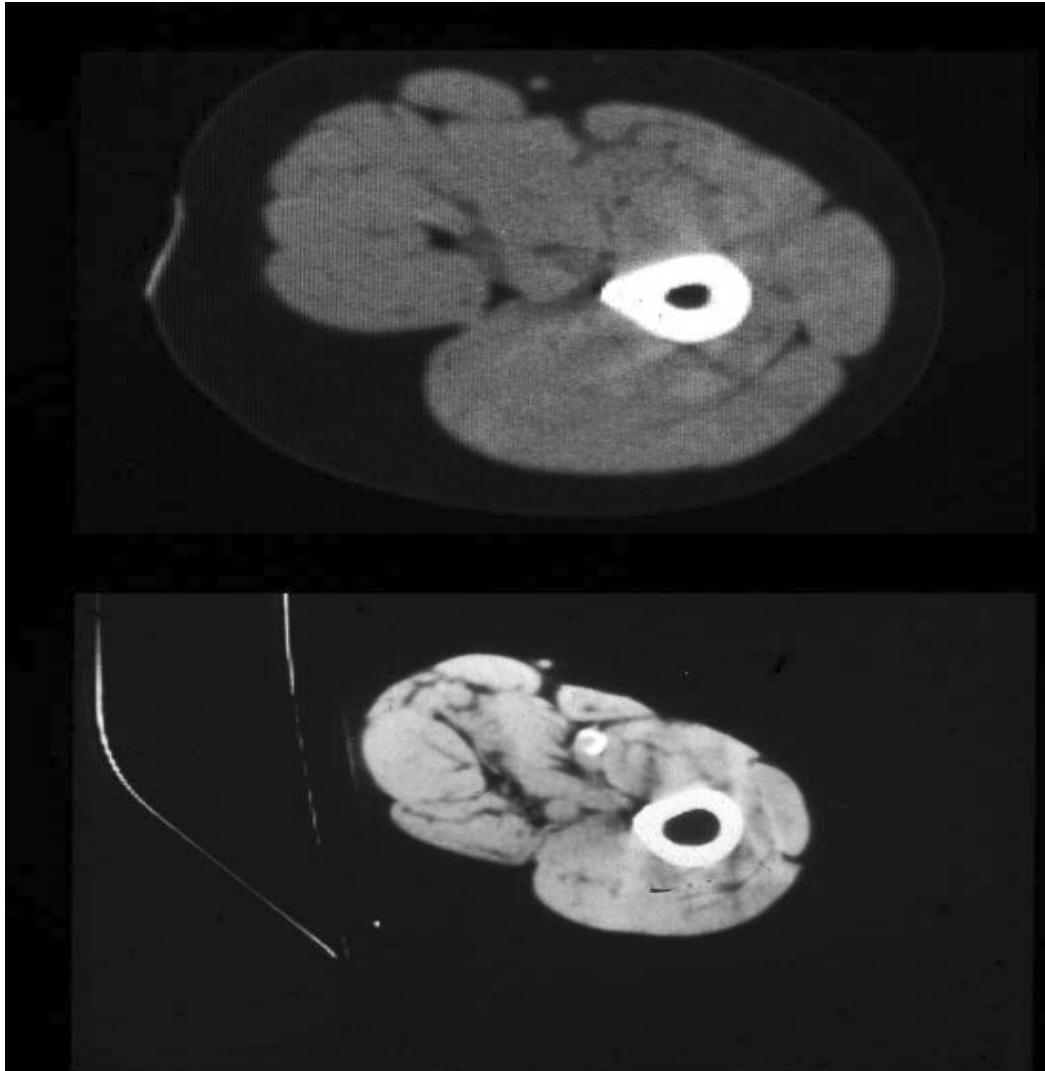
60

Data courtesy of Prof A. Young

World Masters Weightlifting Championships 1999 Men (<85 kg)



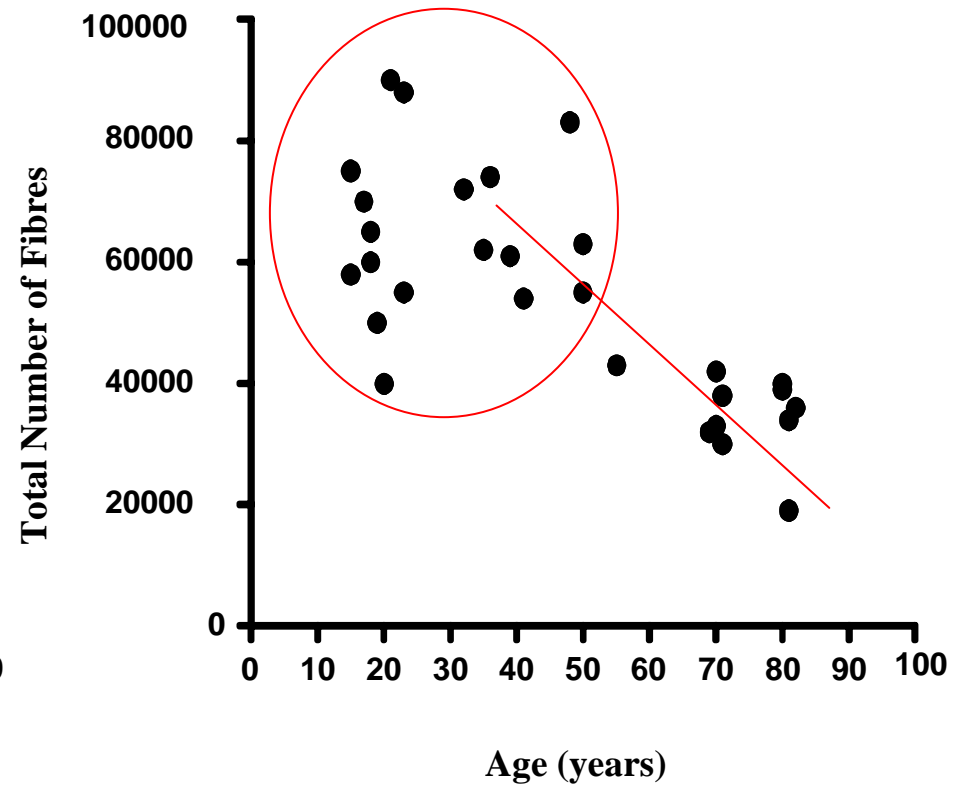
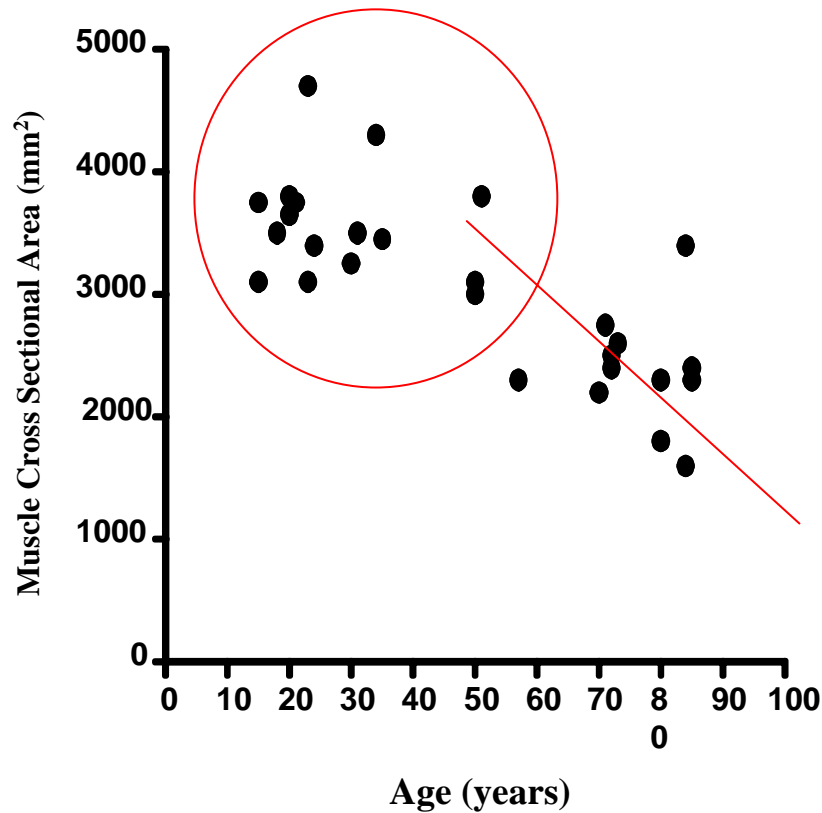
Data Courtesy of Prof A Young



Cross sectional
CT scan of upper
thigh from healthy
20 year old female

Cross sectional CT
scan of upper thigh
from healthy 80 year
old female

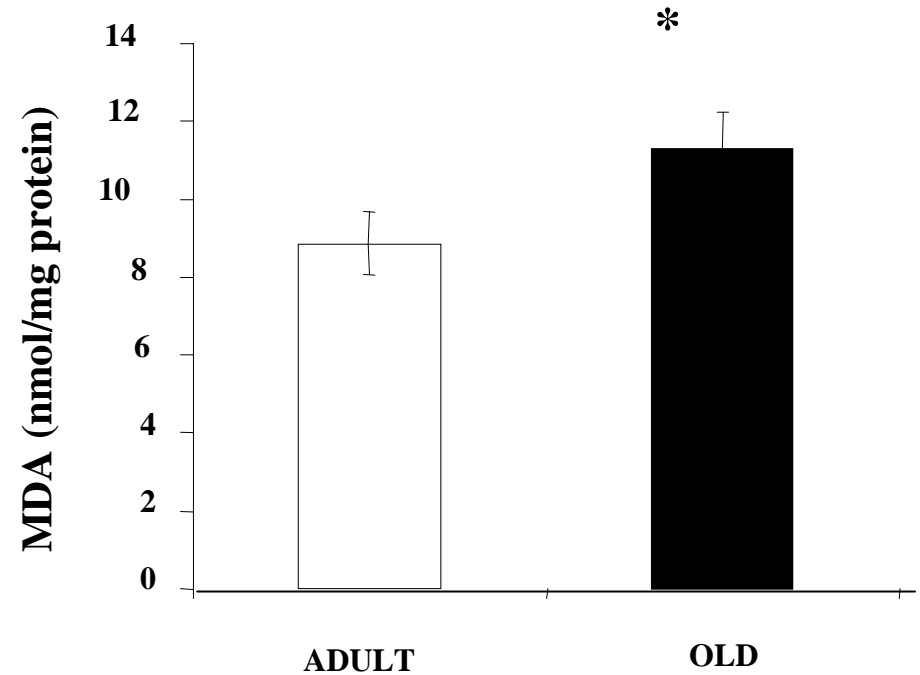
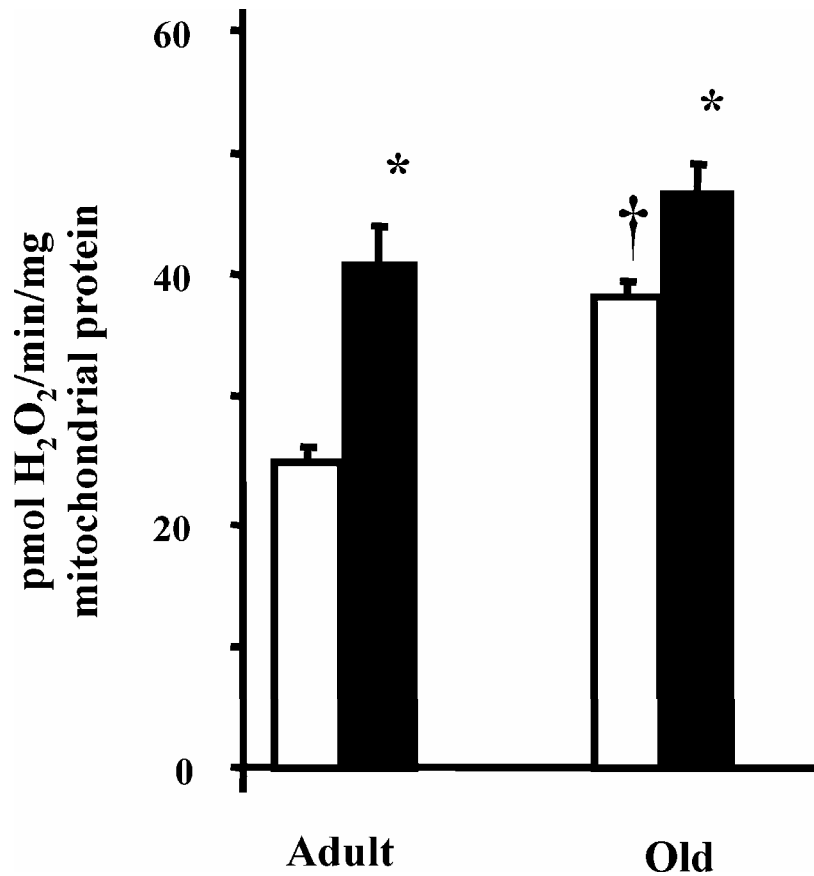
“As we age our muscles become smaller and weaker”



Why do aged muscles weaken?

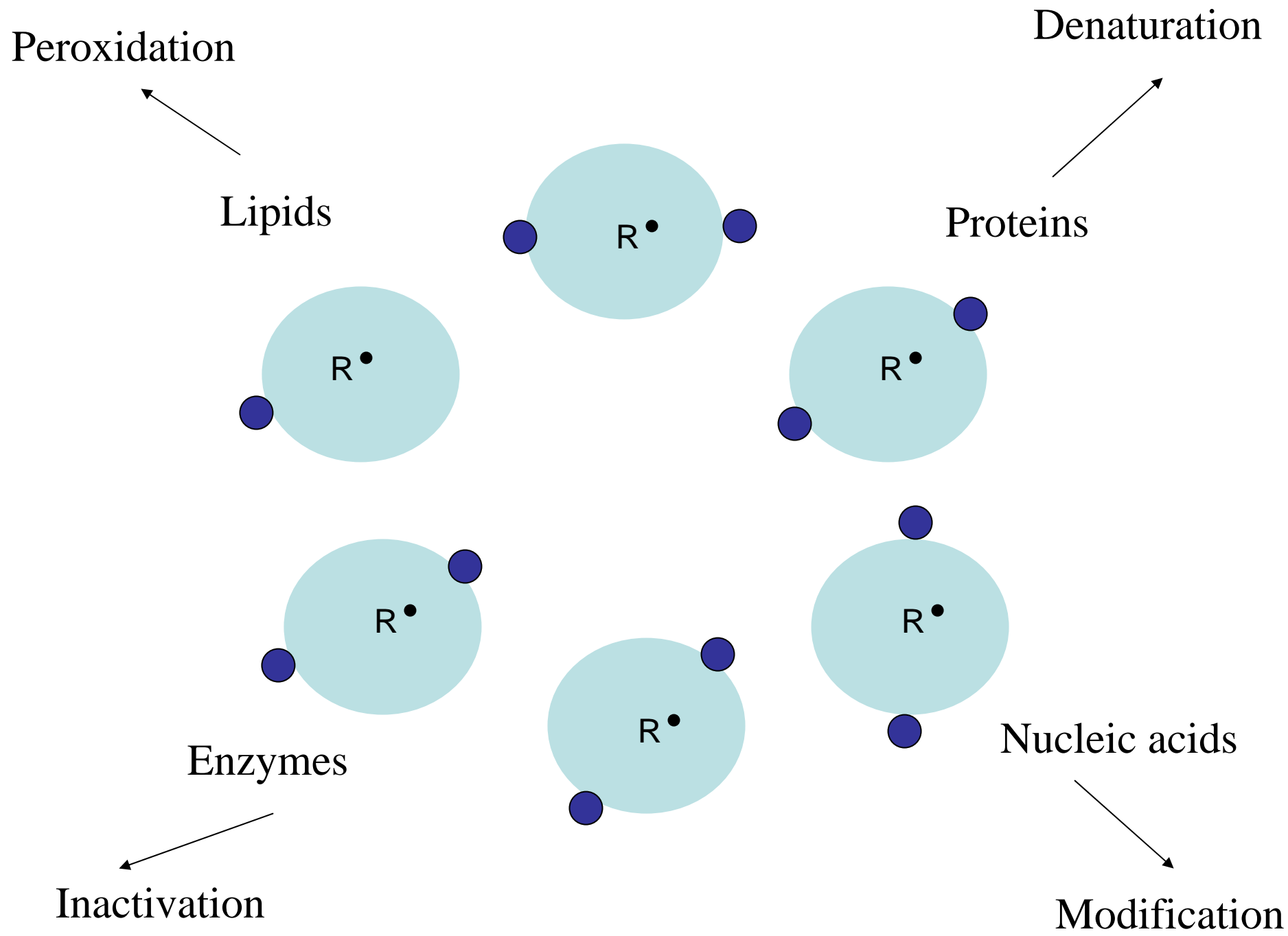
- Million dollar question and this is what our group has been interested in for a number of years.
- Malcolm Jackson – Free radical theory
- Anne McArdle – originally a postdoctoral fellow with RIA and now a professor holding RIA programme grant investigated protective proteins.
- Graeme Close – Insulin resistance

Ageing results in an increased production of free radicals

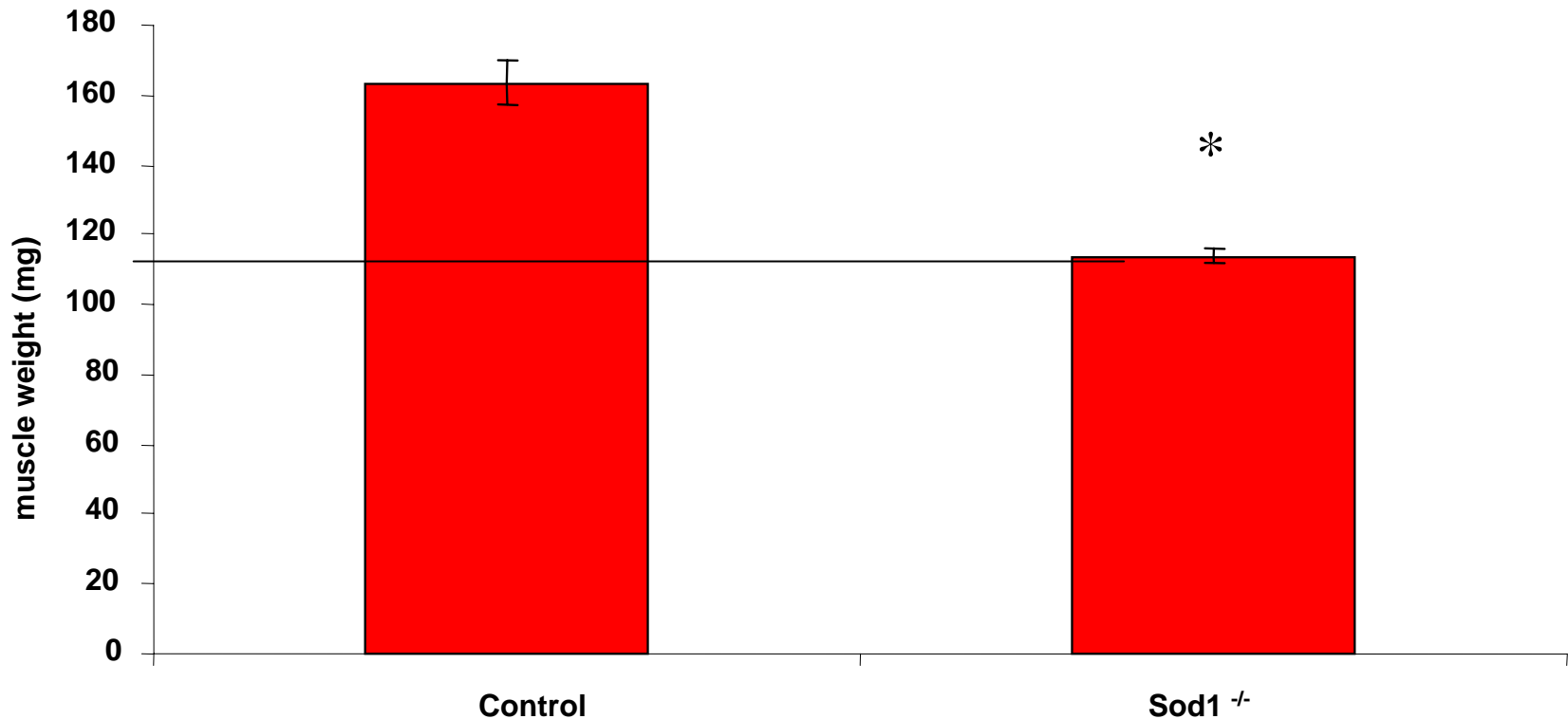


What are Free radicals – I will let 'M'
tell you





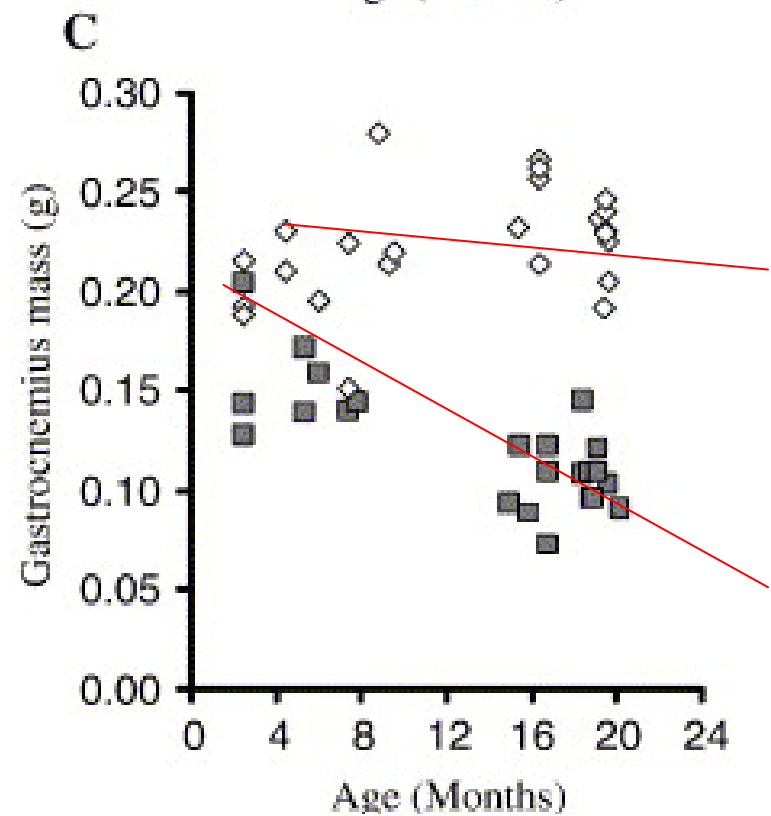
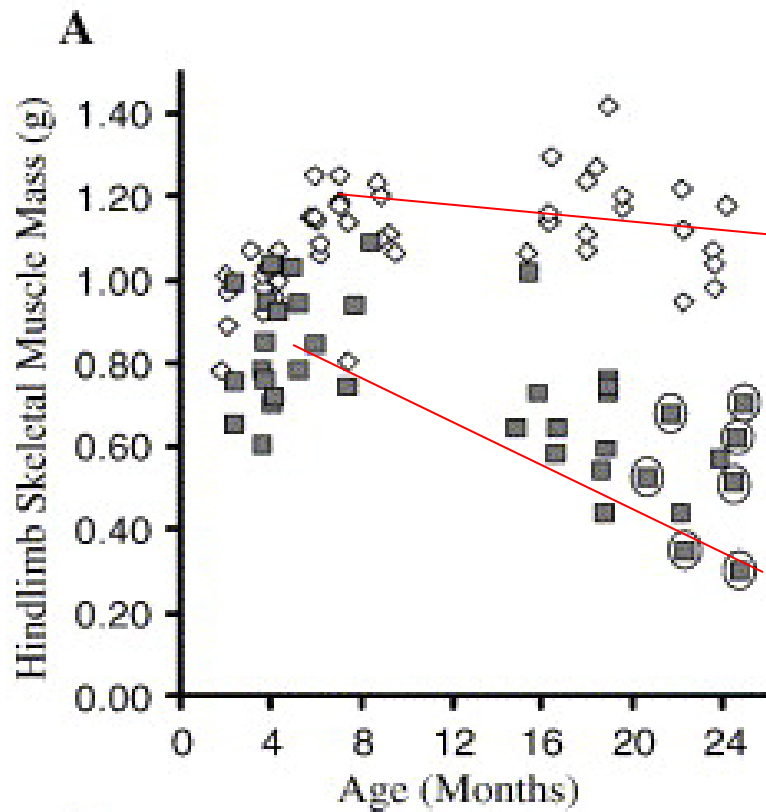
...but can increased free radical production result in losses of muscle mass and function?



Vasilaki et al

Muscles that have been modified to produce increased free radicals

Muller et al., 2006

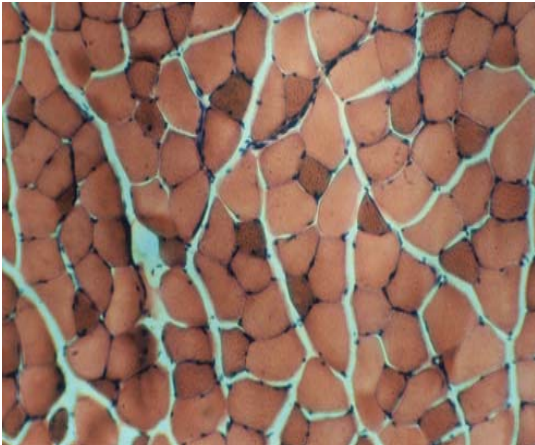
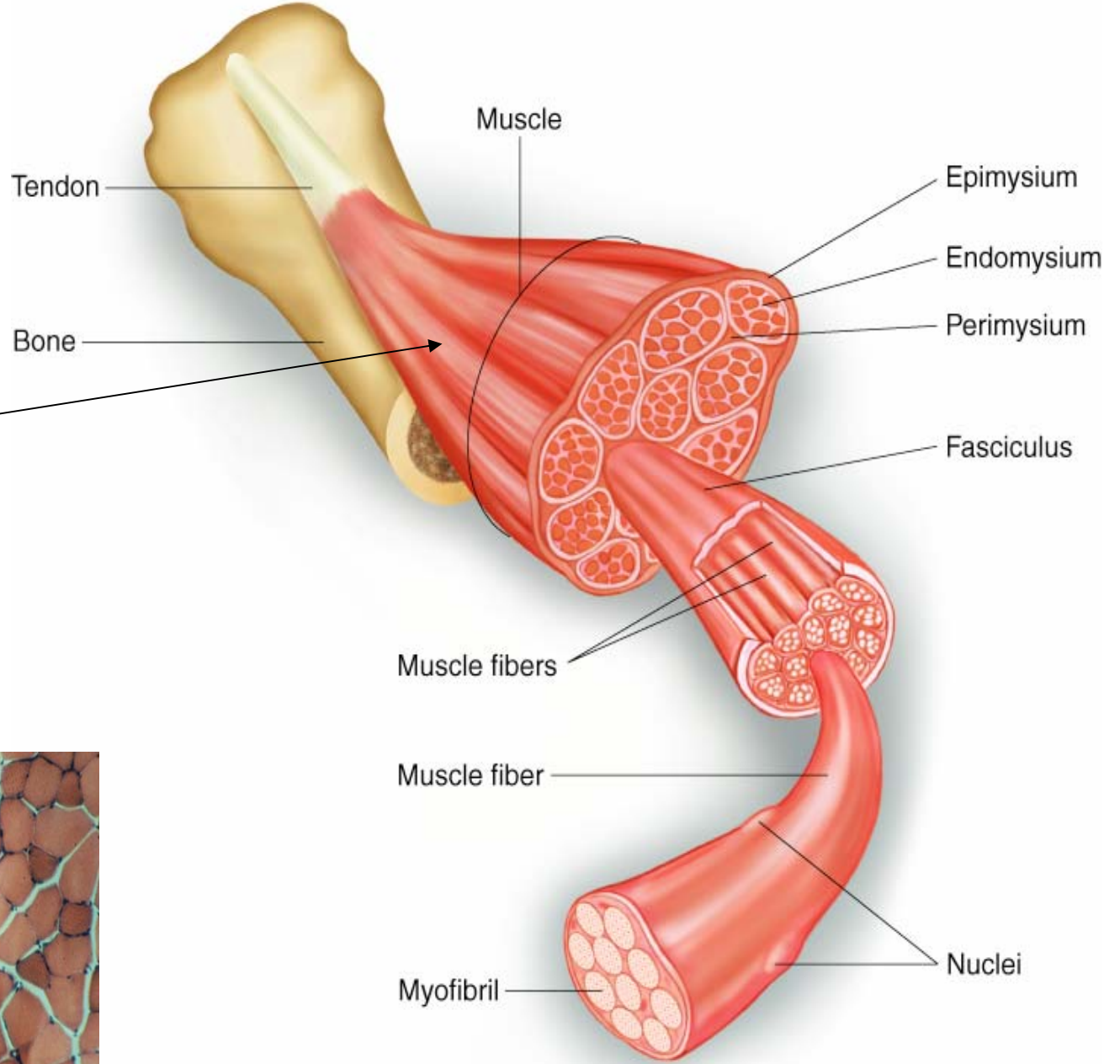


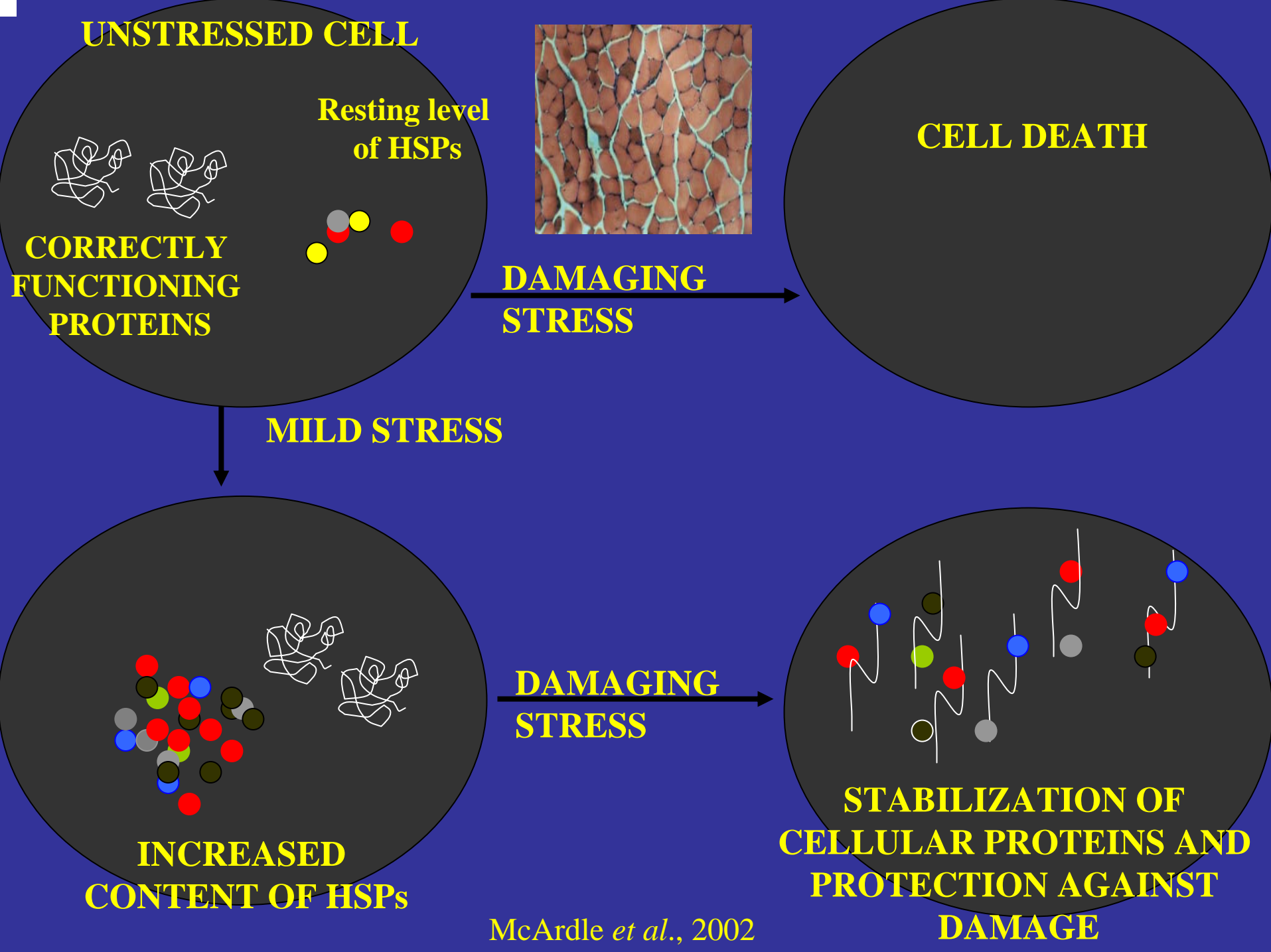
Aged muscle fails to produce protective proteins

- Aged muscle produces increased free radicals but how does this lead to accelerated ageing of skeletal muscles?
- Number of suggestions but one that we have given a great deal of attention to is the role of protective proteins, known as heat shock proteins (HSPs).

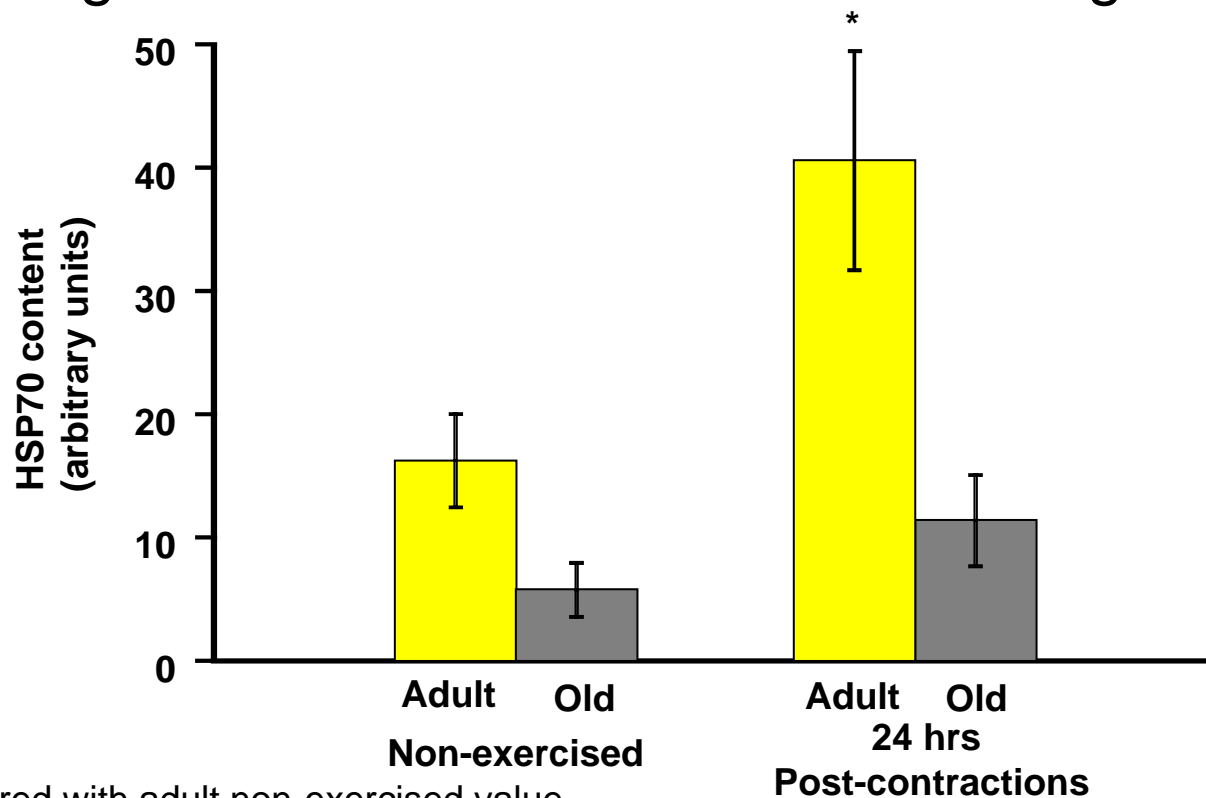
Why do aged muscles weaken?

- Million dollar question and this is what our group has been interested in for a number of years.
- Malcolm Jackson – Free radical theory
- Anne McArdle – originally a postdoctoral fellow with RIA and now a professor holding RIA programme grant investigated protective proteins.
- Graeme Close – Insulin resistance





- Adult muscle adapts following exercise by the increased production of Heat Shock Proteins (HSPs).
- This increased content of HSPs has been shown to protect muscles from damage following contractile activity.
- Ageing attenuates HSP induction following exercise.

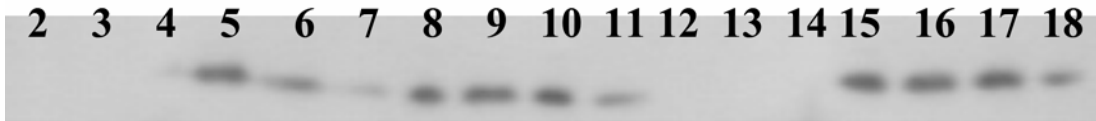
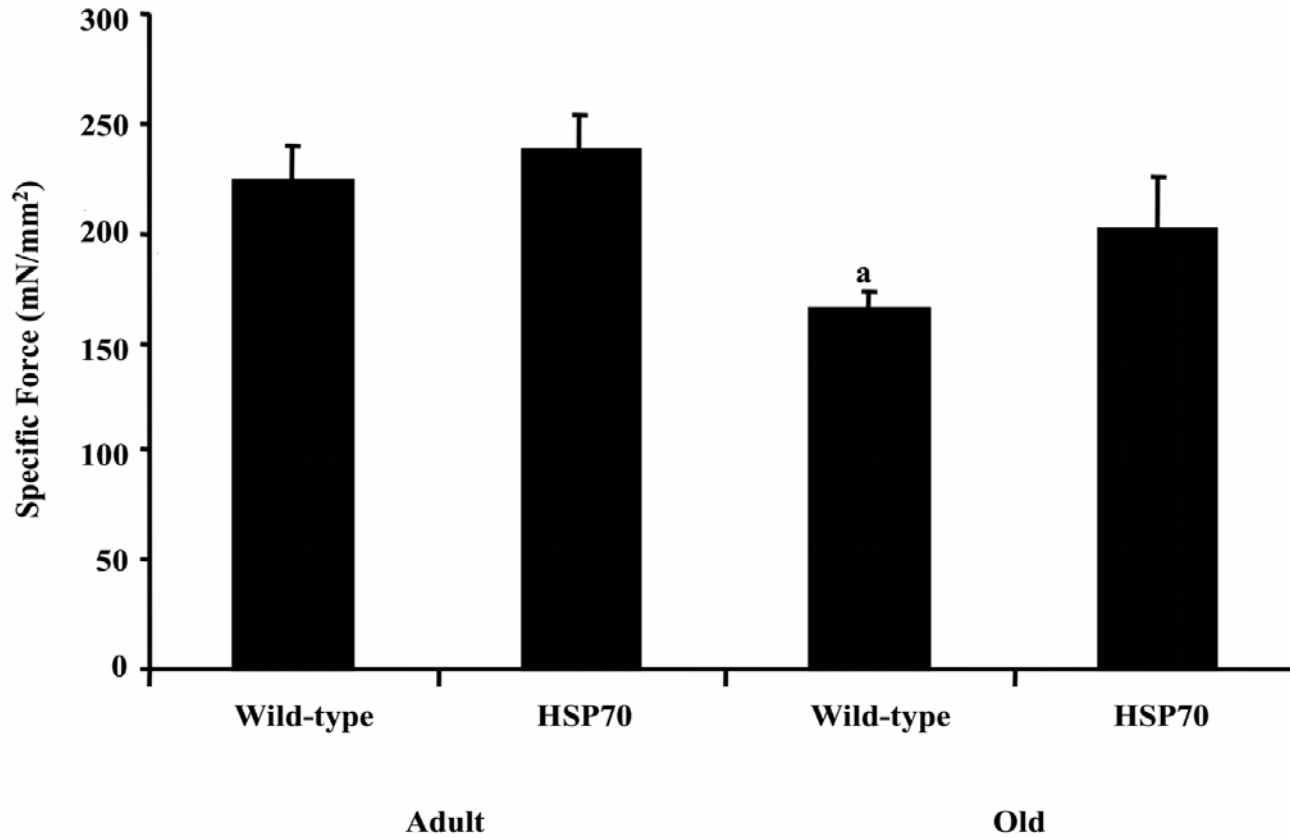


* P<0.05 compared with adult non-exercised value

We are attempting to correct this

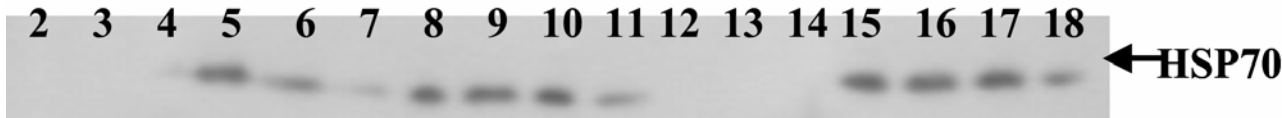
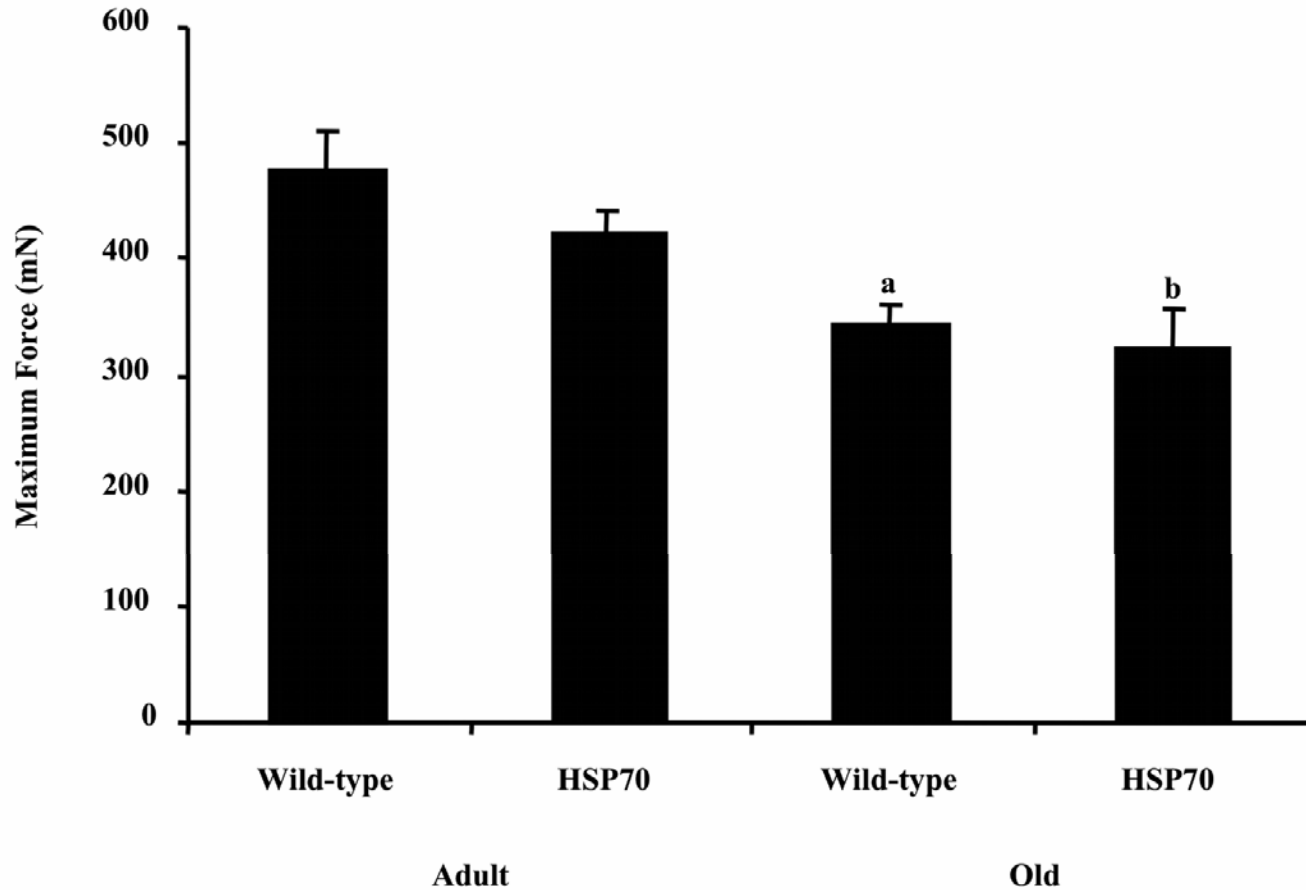
- Genetic approaches
- Drugs
- Exercise (short and long term)

Specific Force



←HSP70

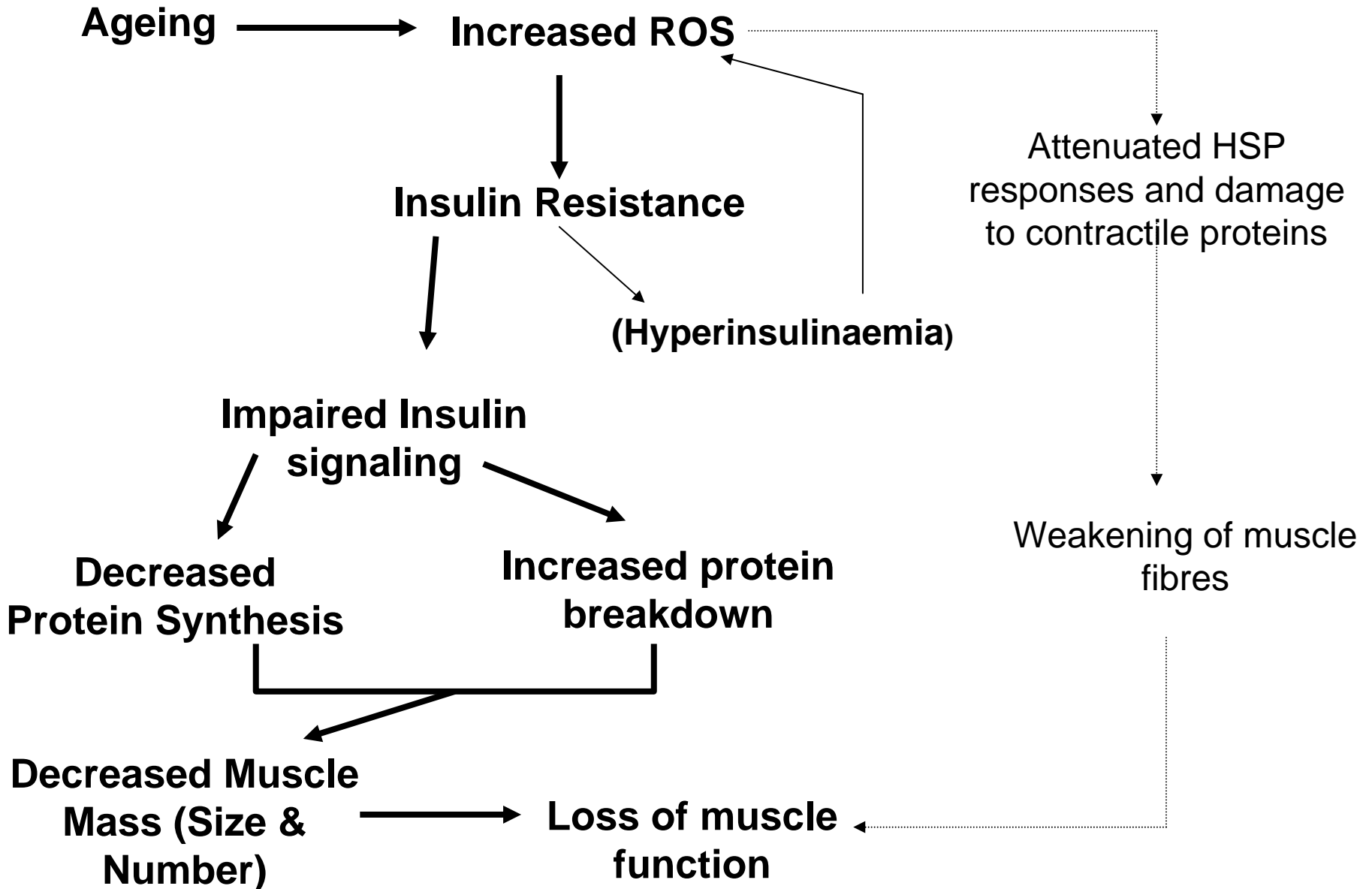
Maximum Force



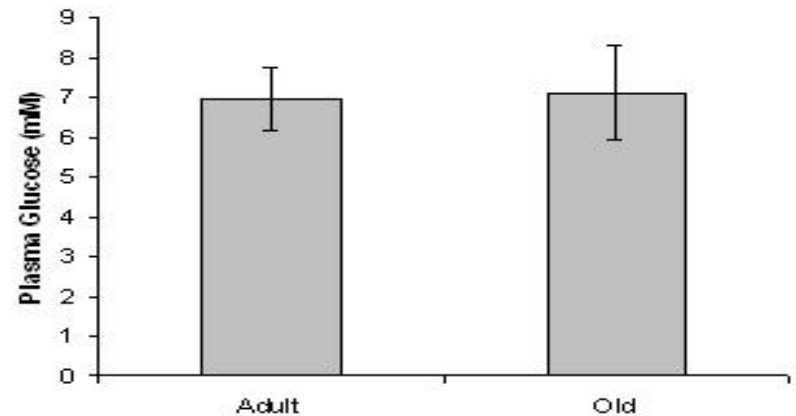
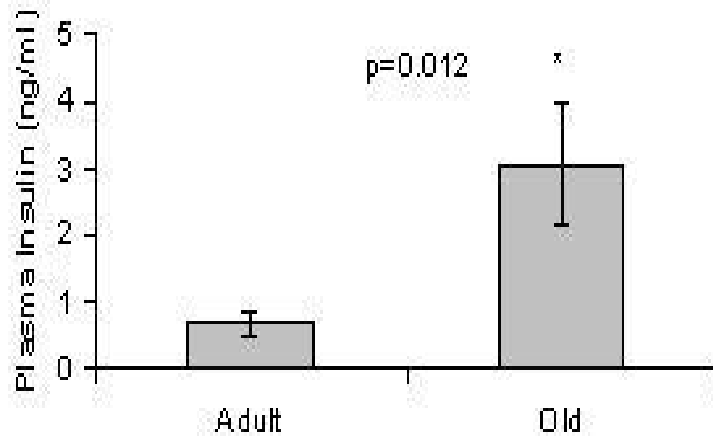
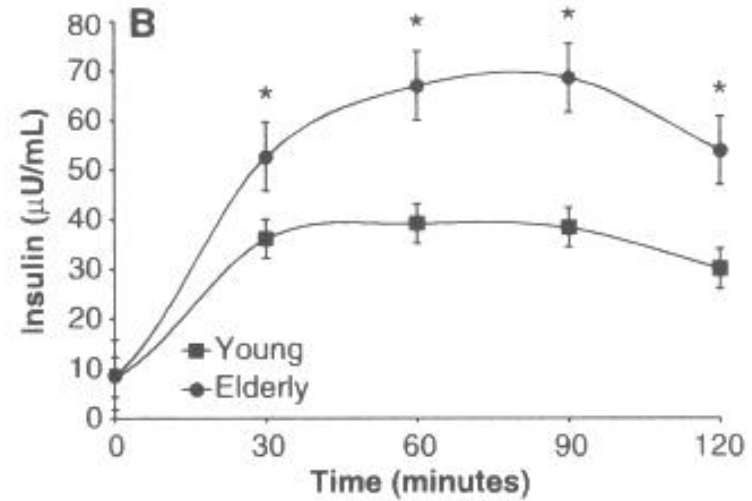
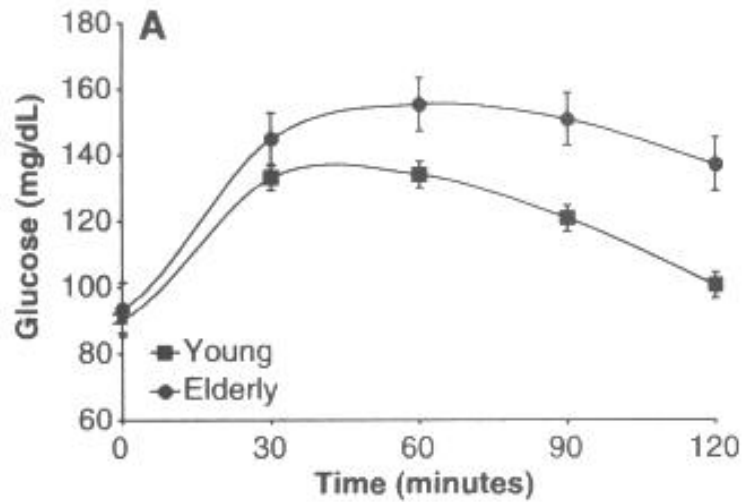
Why do aged muscles weaken?

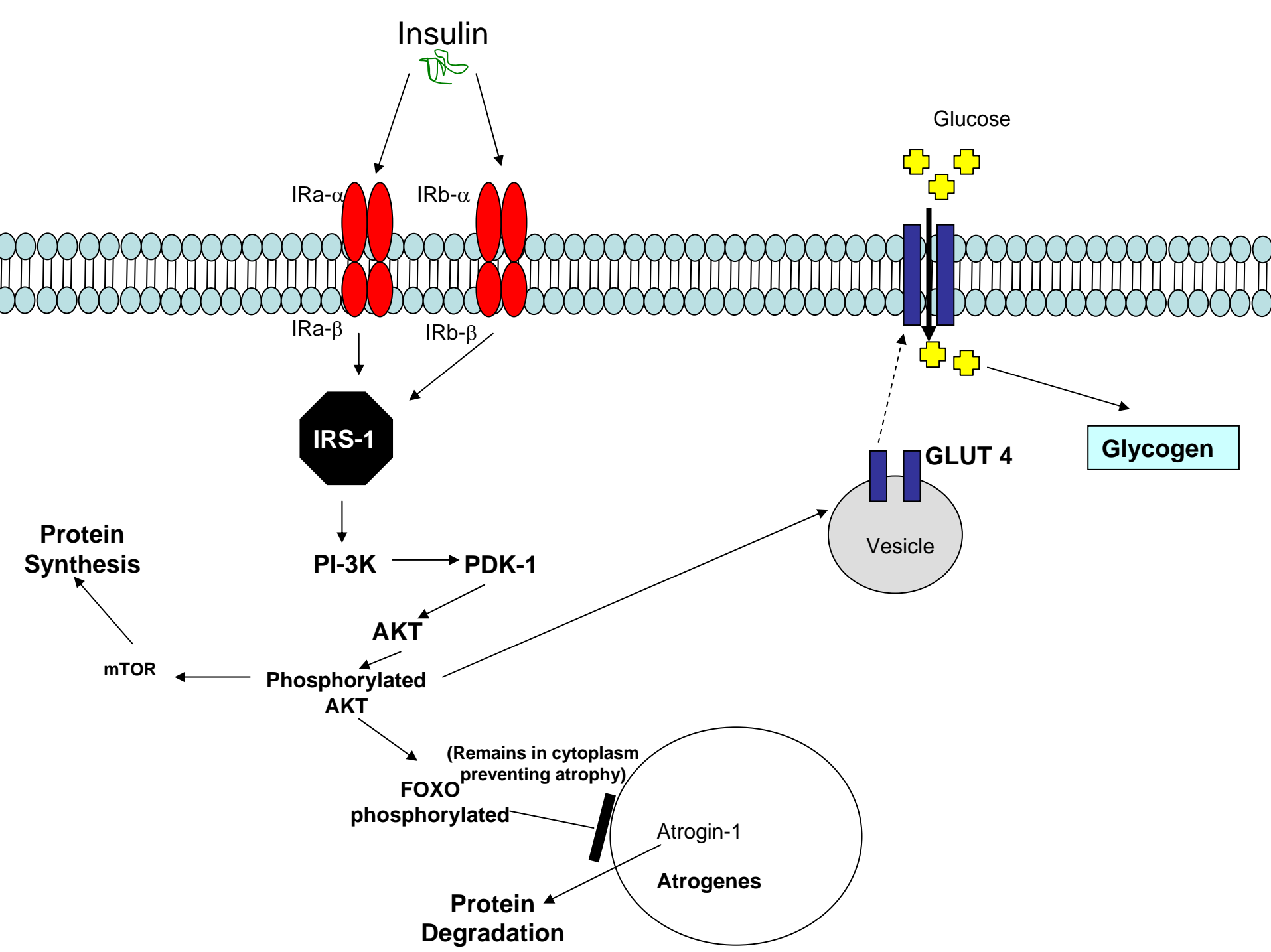
- Million dollar question and this is what our group has been interested in for a number of years.
- Malcolm Jackson – Free radical theory
- Anne McArdle – originally a postdoctoral fellow with RIA and now a professor holding RIA programme grant investigated protective proteins.
- Graeme Close – Insulin resistance

New hypothesis



Ageing results in insulin resistance.





Latest studies

- Correct insulin resistance using:
- Drugs (Metformin, rosiglitazone, resveratrol, rosuvastatin).
- Prolonged exercise
- Investigate early correction of insulin resistance on loss of muscle mass and function.
- These studies are part of my RIA fellowship plus my first PhD student.

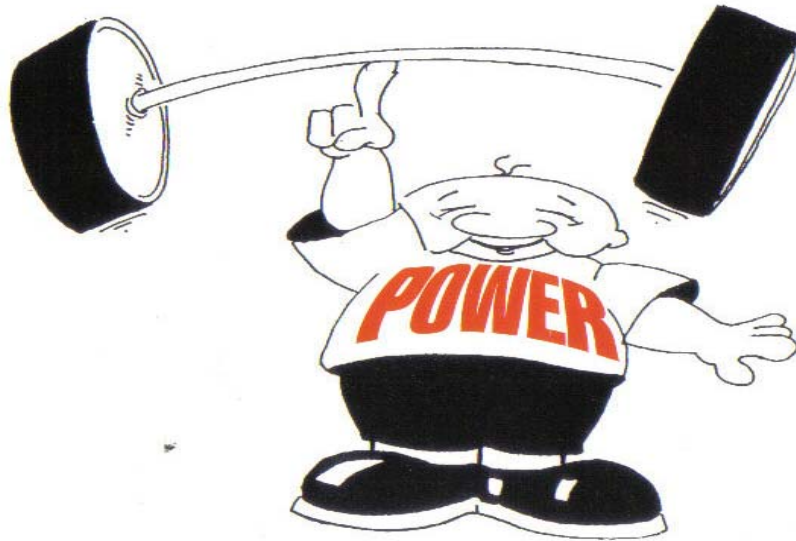
Lets finish on a high!

Age-related muscle weakness is
not completely beyond our
control

RESEARCH INTO **Ageing**

EXERCISE FOR HEALTHY AGEING

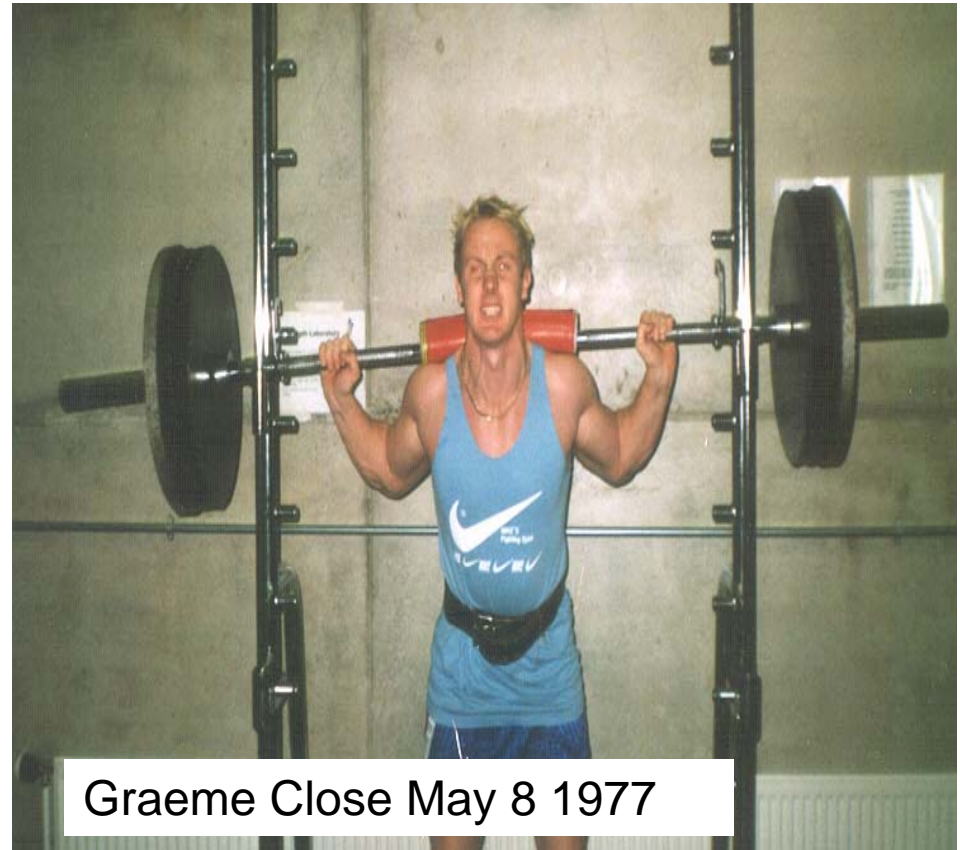
Dr Dawn Skelton



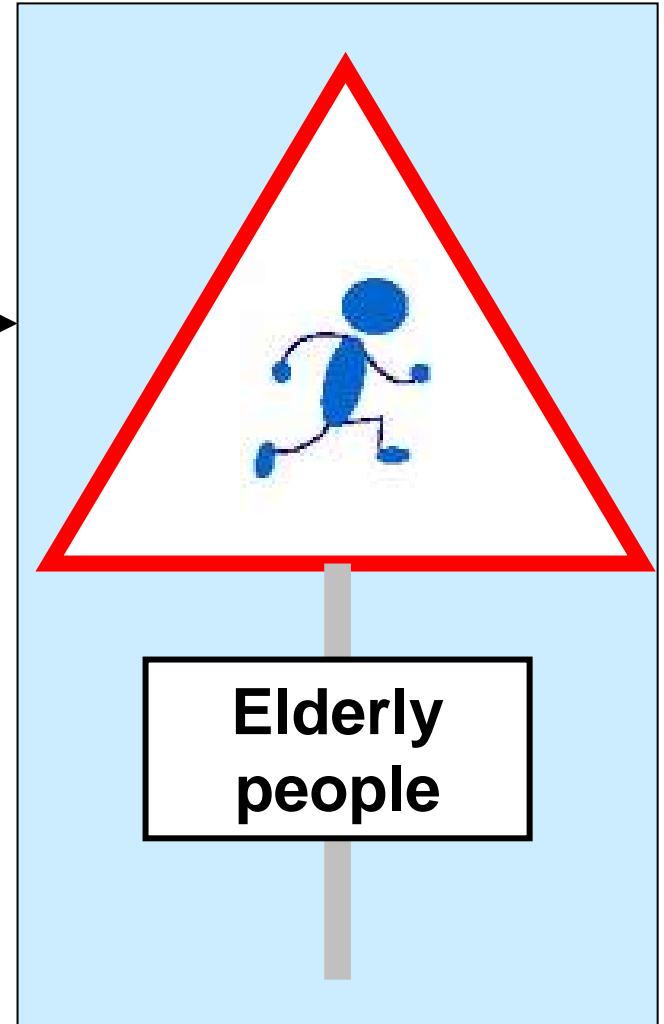
Exercise programmes
proven in research
to increase muscle strength

**REVISED & EXPANDED
SECOND
EDITION**

Musculoskeletal Achievements of the over 70's



Who knows what 3 years might bring...





UNIVERSITY OF
LIVERPOOL



Graeme L. Close
gclose@liv.ac.uk

Cellular Pathophysiology Group

Research Into Ageing ™

Body composition when there is a defect in insulin receptors

Table 2

Body composition in the control and MIRKO mice

		Tissue mass				
	<i>n</i>	Gastrocnemius and quadriceps muscles (mg)	Soleus muscle (mg)	EDL muscle (mg)	Heart muscle (mg)	Whole body fat pad (% of BW)
Control	7	608 ± 12	7.4 ± 0.2	9.9 ± 0.2	171 ± 4	27.5 ± 2.3
MIRKO	8	528 ± 11 ^A	5.4 ± 0.1 ^A	8.4 ± 0.1 ^A	123 ± 7 ^A	38.0 ± 6.4 ^A

^A*P* < 0.05 versus control group by two-tailed *t* test. EDL, extensor digitorum longus; BW, body weight.

Kim *et al.*, 2000