Fighting the "Rust" of Aging: Can Exercise Restore the Redox Balance?

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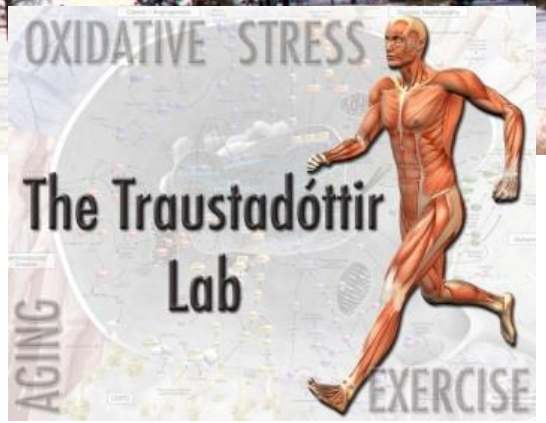
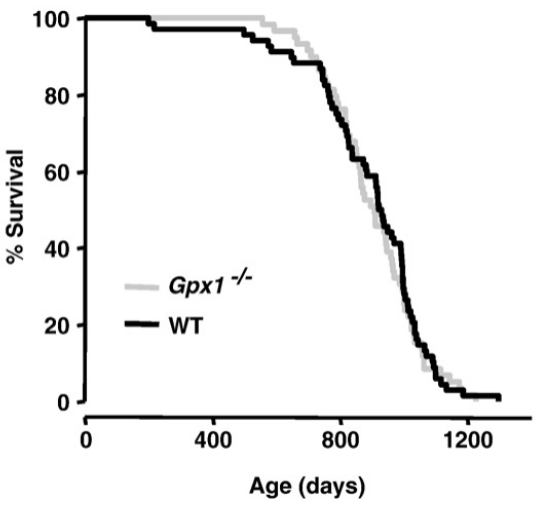
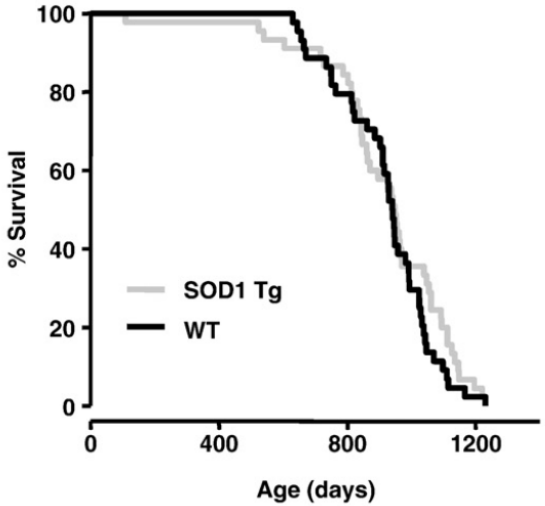


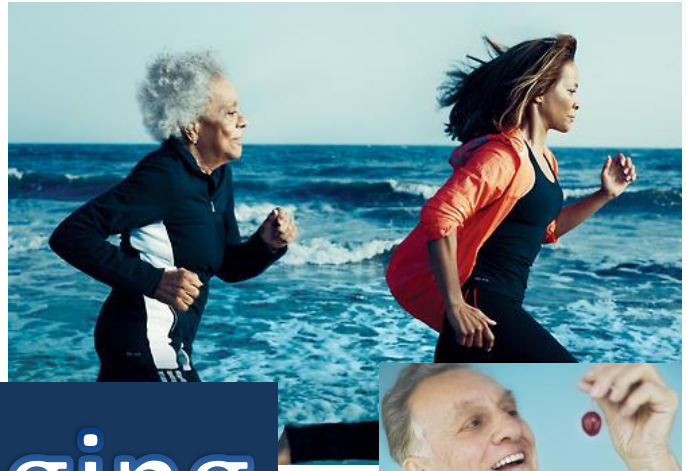
"Fighting the Rust of Aging"

Is the oxidative stress theory of aging dead?

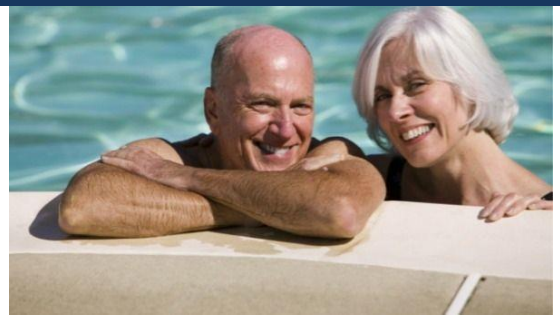
Viviana I. Pérez [a,b], Alex Bokov [a,c], Holly Van Remmen [a,b,d,f], James Mele [d], Qitao Ran [a,b], Yuji Ikeno [a,e,f], Arlan Richardson [a,b,f,*]

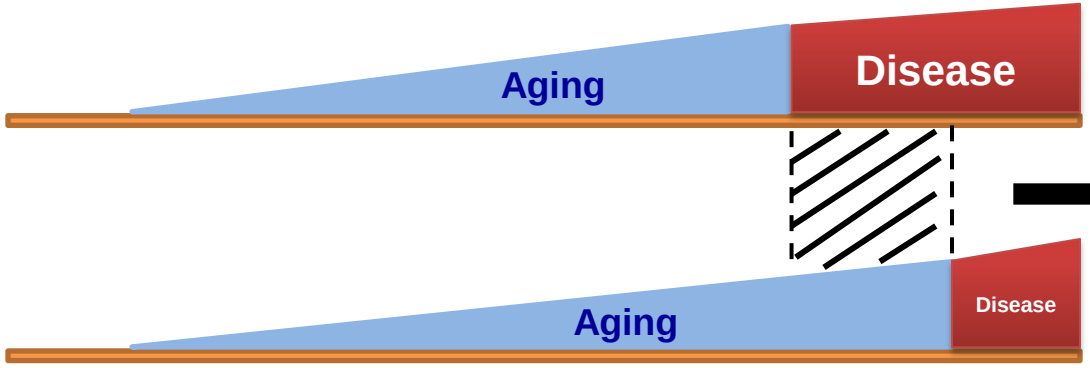






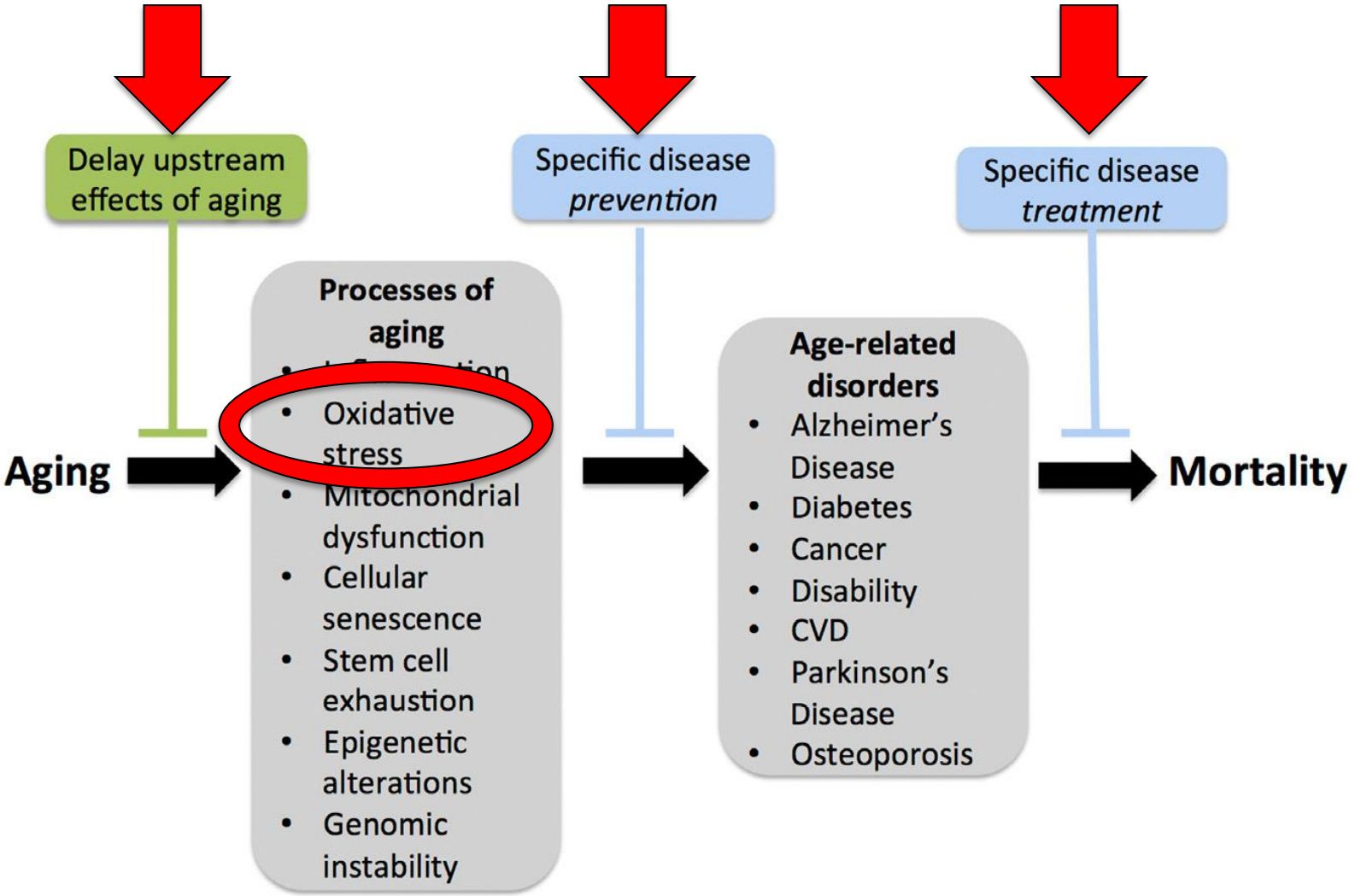
Successful Aging





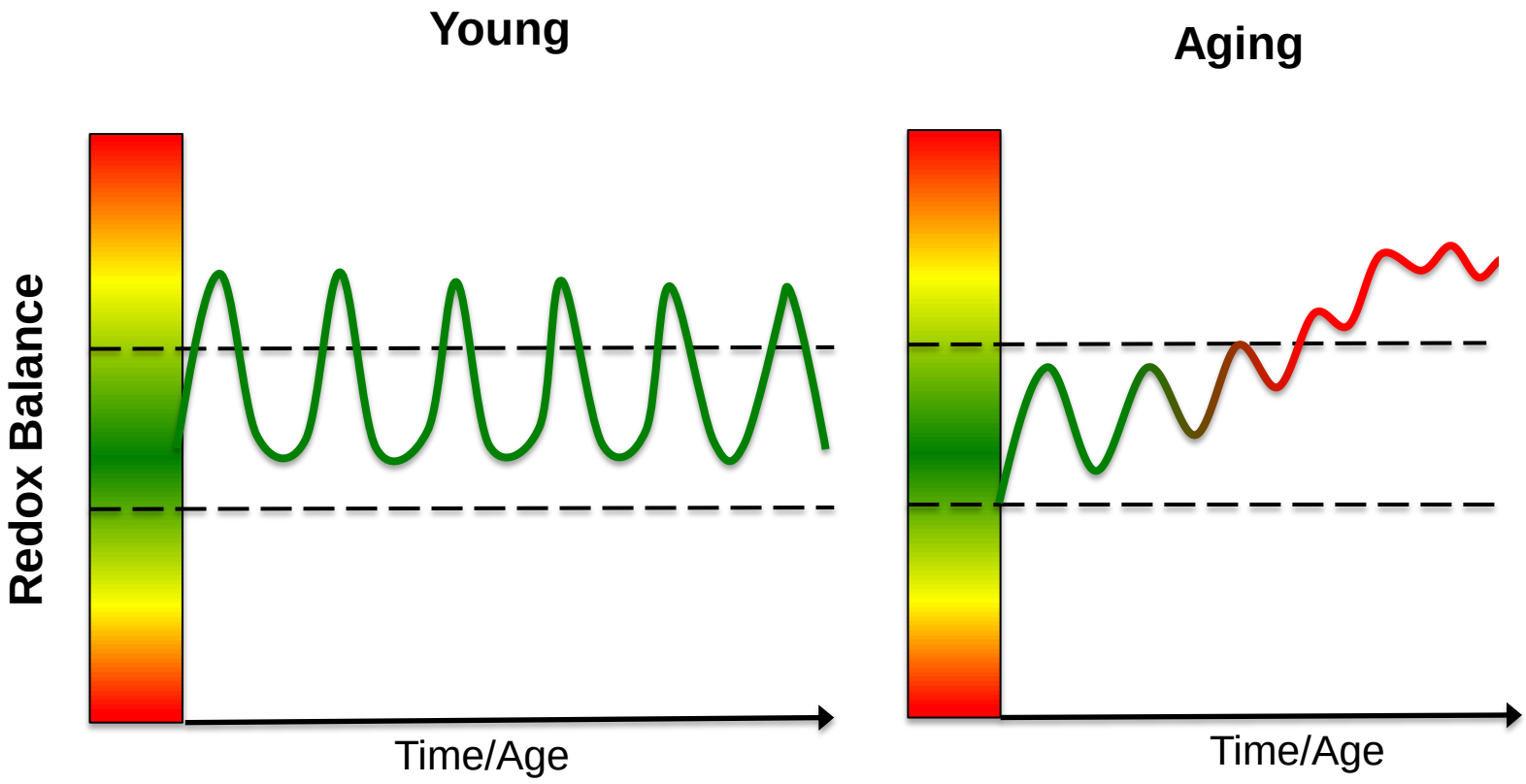
Increased Health span

Points of Intervention

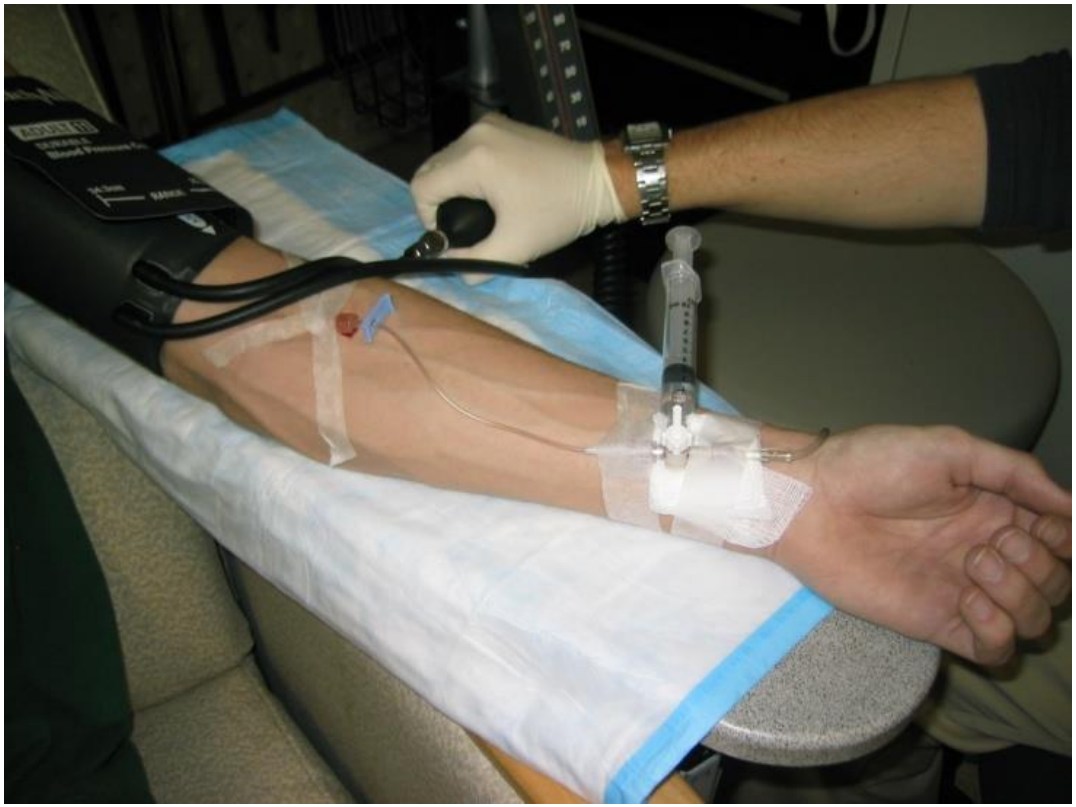


Seals, et al. (AGING 2014)

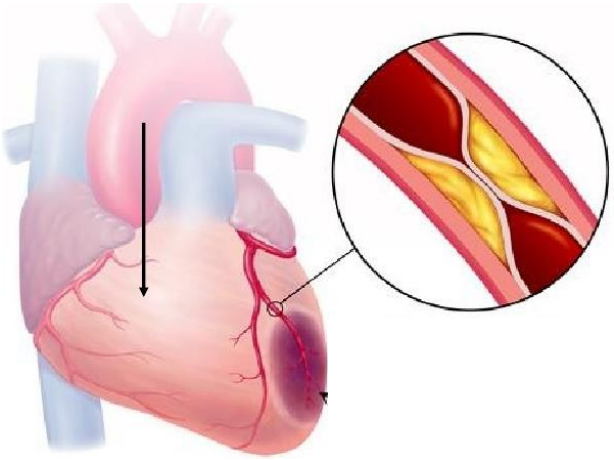
Redox Balance and Signaling

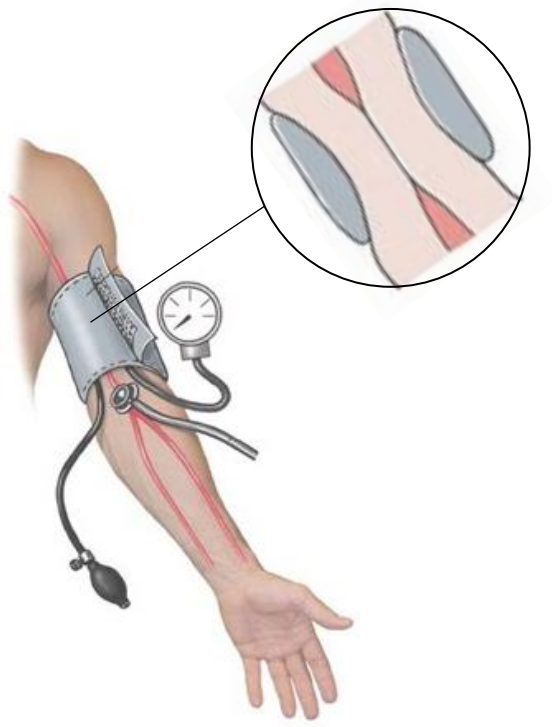


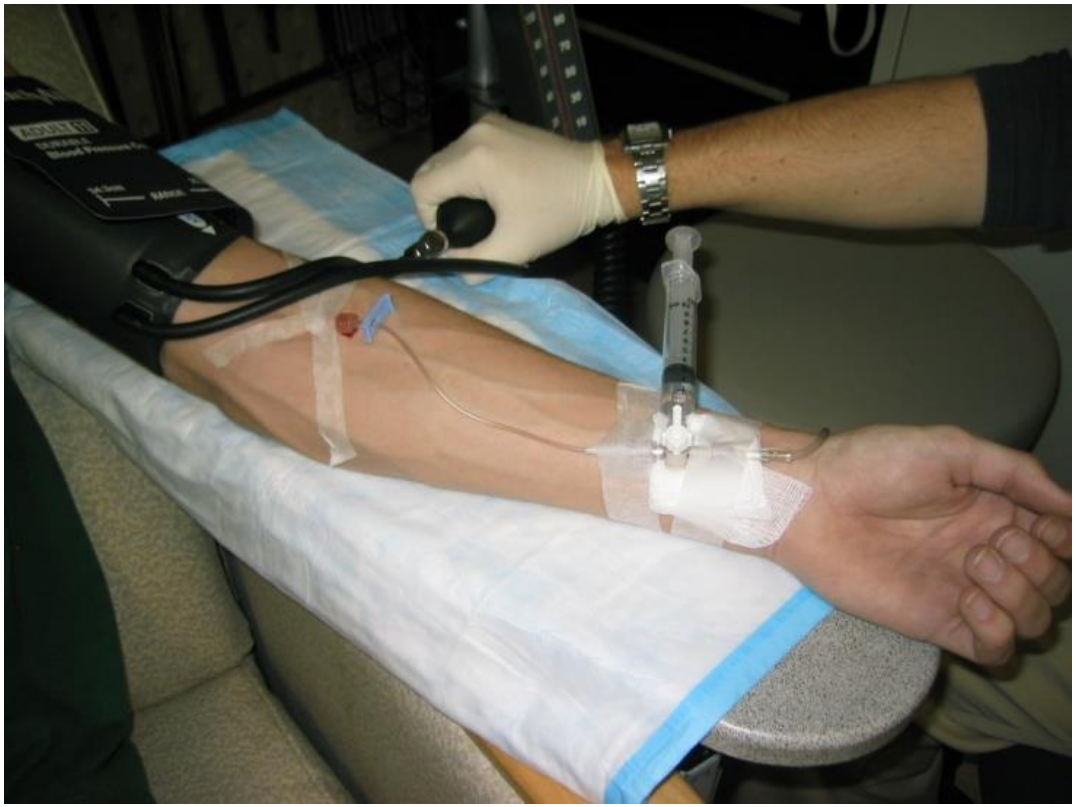
ACUTE EXERCISE



FOREARM ISCHEMIA/REPERFUSION

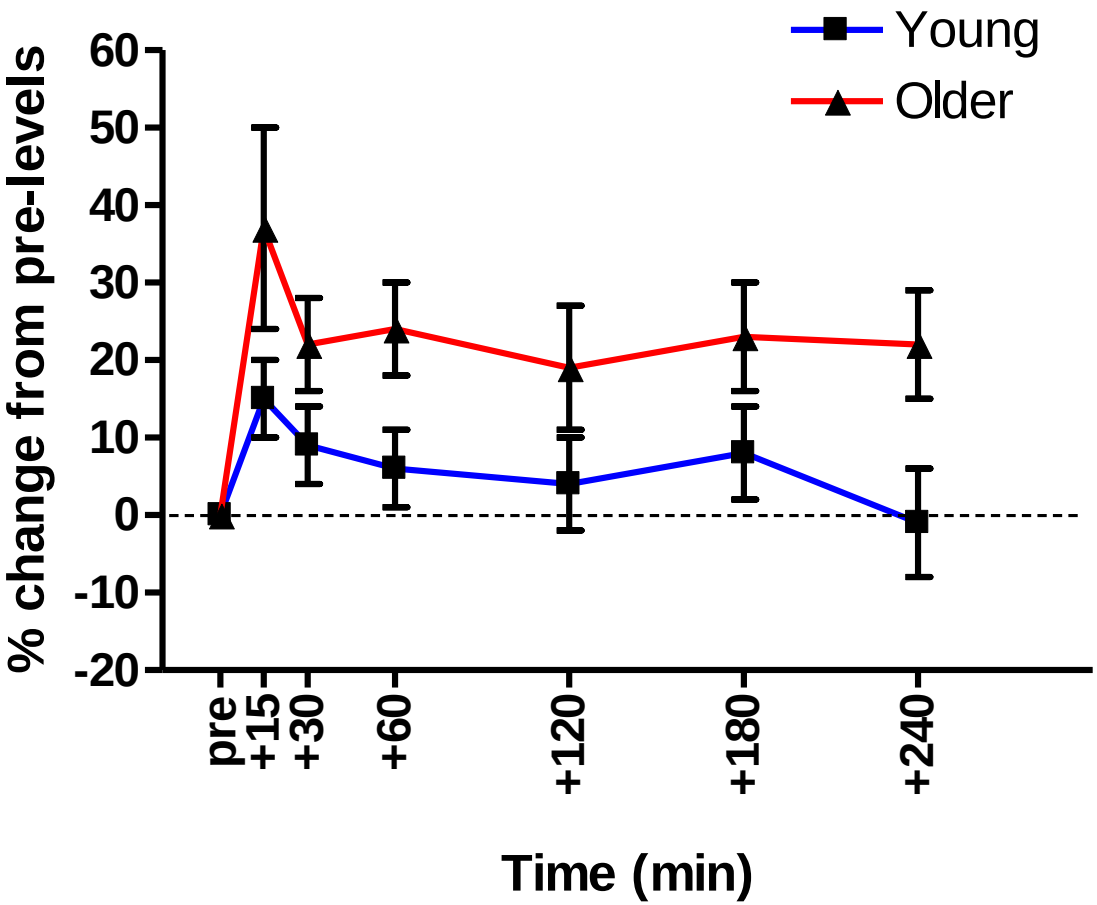


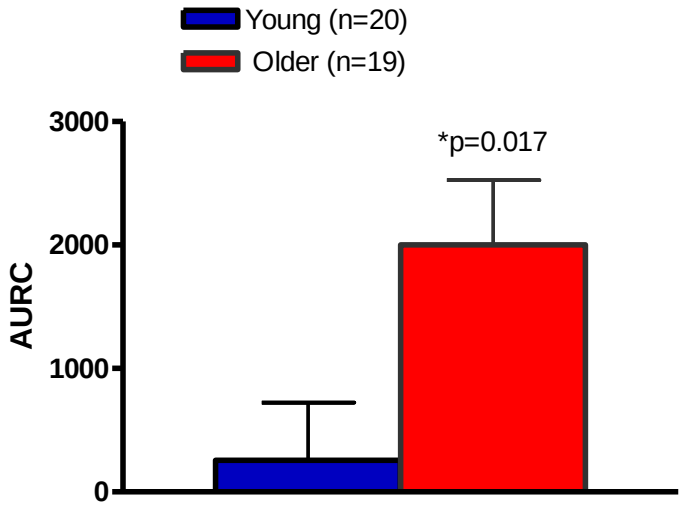




FOREARM ISCHEMIA/REPERFUSION

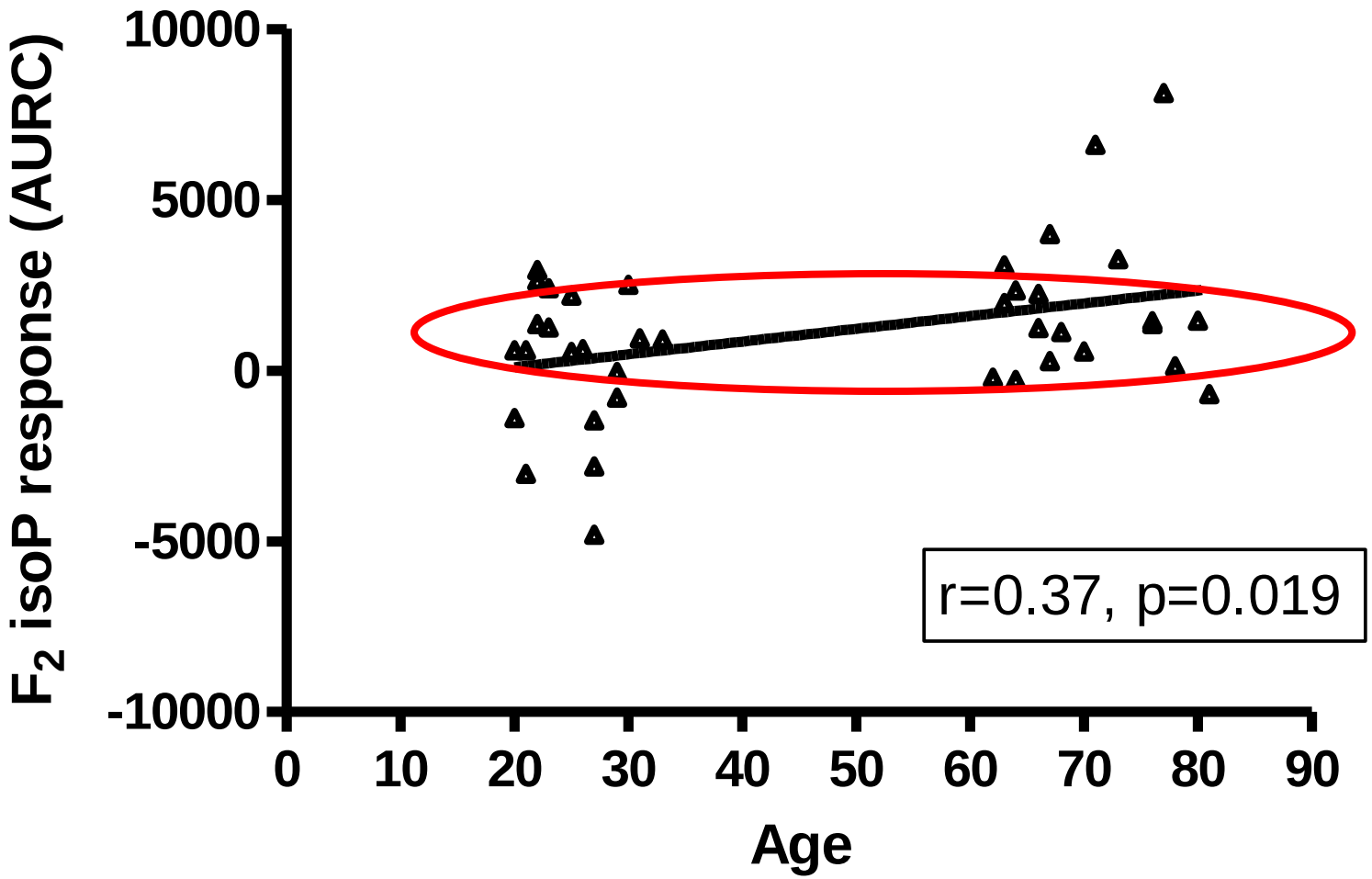
The capacity to resist oxidative stress is diminished with aging





Davies, et al. (FRBM 2009)

I/R Trial - Individual Responses by Age



Is resistance to oxidative stress modifiable in older adults?

Screening, Informed Consent, Health History, Blood Chemistry, Physical Exam

I-R Trial (#1)

Tart cherry juice (n=6)

14-day Intervention
Day 10-14 – daily morning urine sampling

Placebo (n=6)

I-R Trial (#2)

WASH-OUT PERIOD (4-WKS)

I-R Trial (#3)

Placebo (n=6)

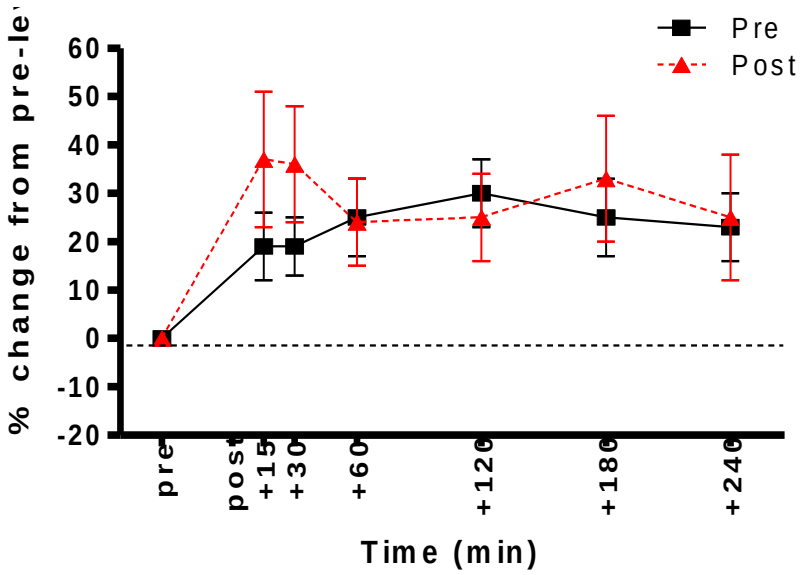
14-day Intervention
Day 10-14 – daily morning urine sampling

Tart cherry juice (n=6)

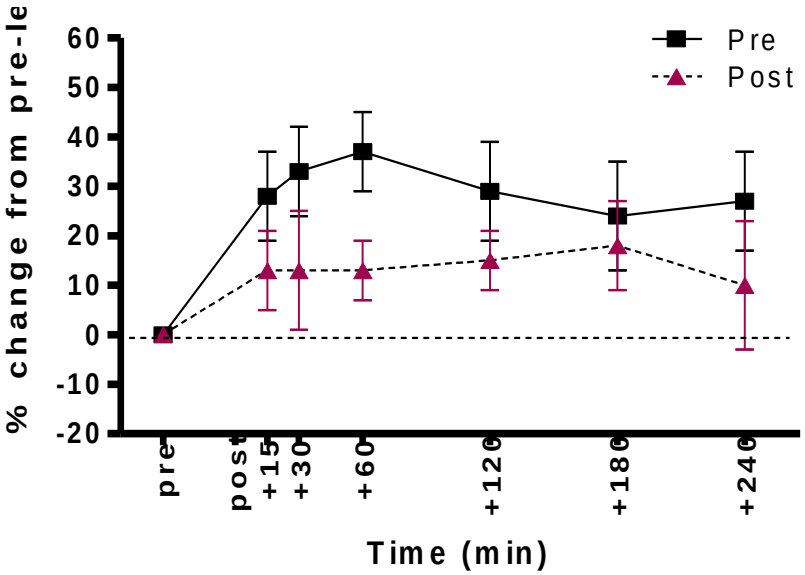
I-R Trial (#4)

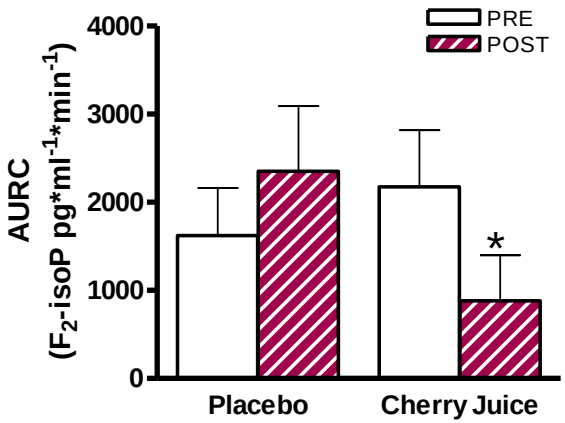
Tart cherry juice increases resistance to oxidative stress

PLACEBO



TART CHERRY JUICE

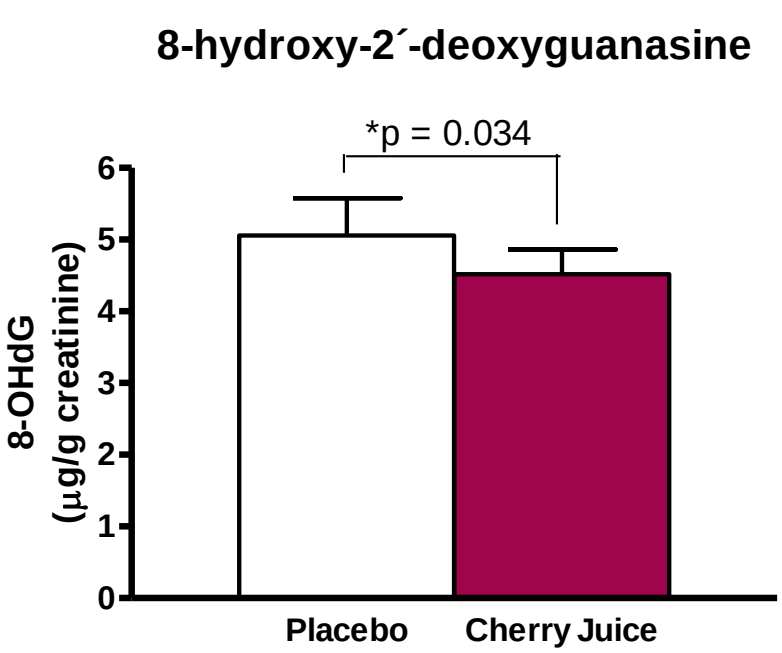


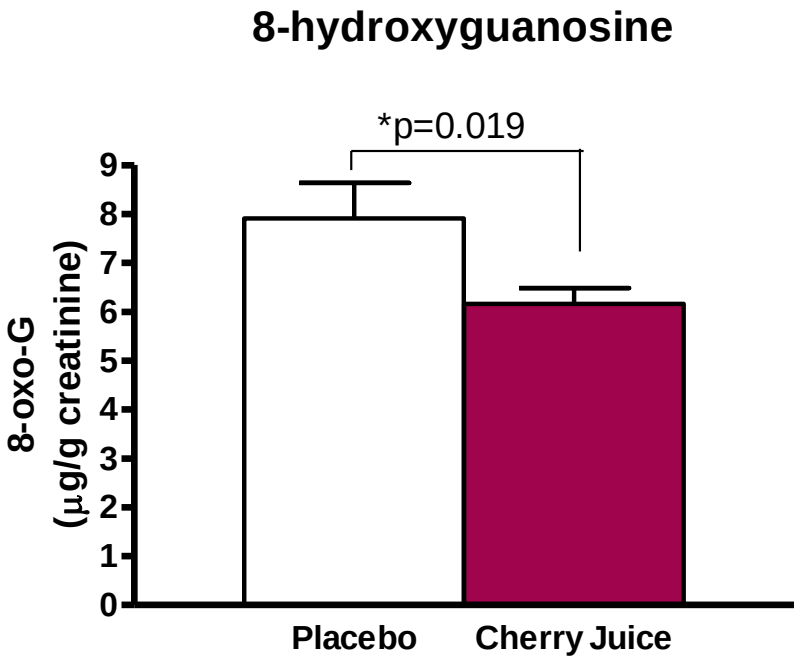


Treatment-by-Trial: p=0.024

Traustadóttir, et al. (J Nutr 2009)

Urinary markers of nucleic acid oxidative damage





Traustadóttir, et al. (J Nutr 2009)

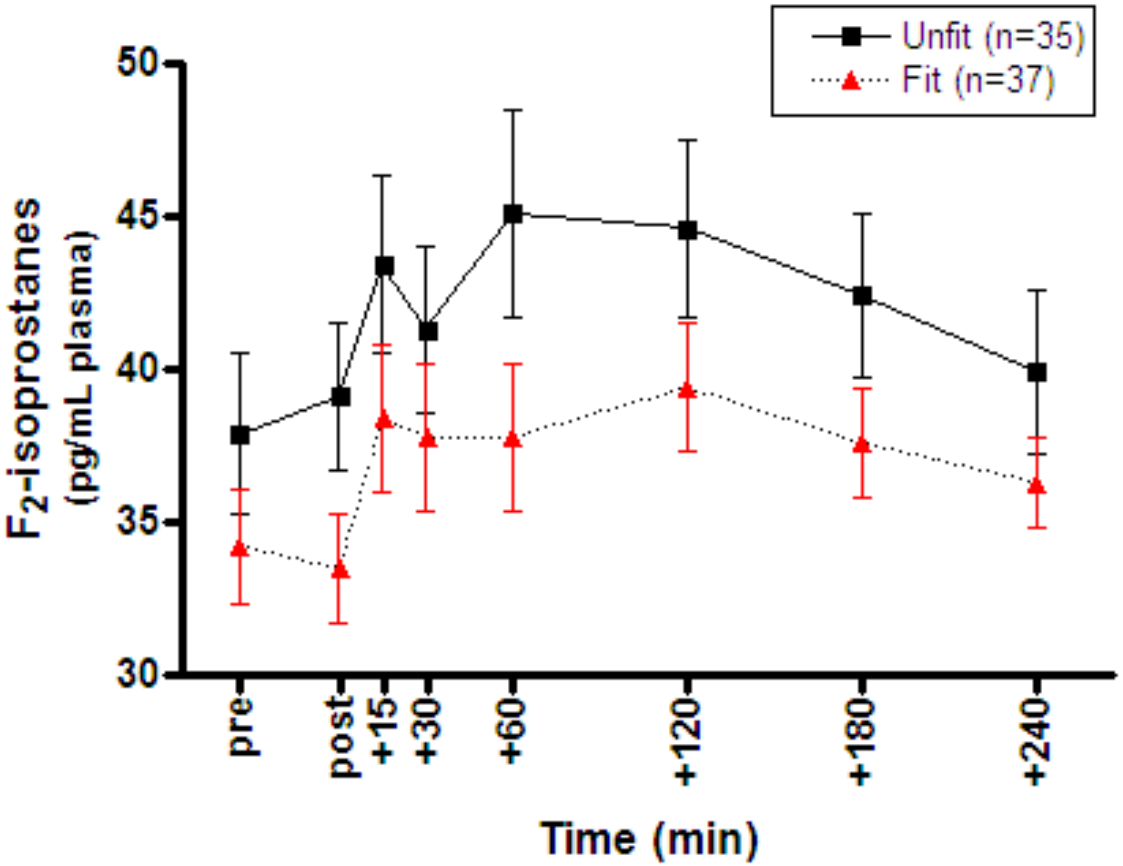
Does regular exercise prevent the lowering of resistance to oxidative stress with aging?

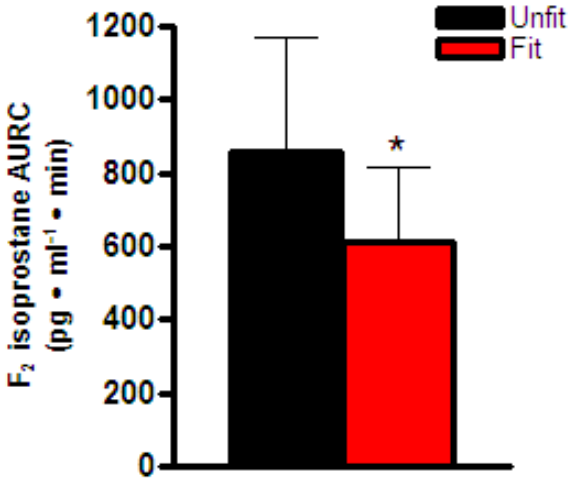
Stress Resilience Study: Fit vs. Unfit

SUBJECT CHARACTERISTICS

	UNFIT (n=35)	FIT (n=37)
Age (yrs)	68 ± 4	65 ± 5*
Height (cm)	168 ± 11	170 ± 10
Weight (kg)	78.2 ± 17.1	71.6 ± 14.4
BMI (kg/m^2)	27.3 ± 3.7	24.5 ± 3.0**
Waist circ. (cm)	94 ± 11	85 ± 12**
SBP (mm Hg)	124 ± 13	120 ± 11
DBP (mm Hg)	78 ± 7	75 ± 8
$VO_{2\ max}$ (ml/kg/min)	18.6 ± 3.1	30.0 ± 6.7†
Leg power (w/kg)	11.9 ± 2.7	16.8 ± 4.5†
HLPA score (0-4)	2.3 ± 1.0	3.4 ± 0.5†

Capacity to resist oxidative stress is higher in fit individuals





The fit group had significantly lower F_2-isoP responses to the I/R trial compared to the unfit ($P < 0.05$) after adjusting for covariates

Traustadóttir, et al. (*AGE,* 2011)

Exercise Hormesis Model

→ **∆ in Redox Balance**

↓

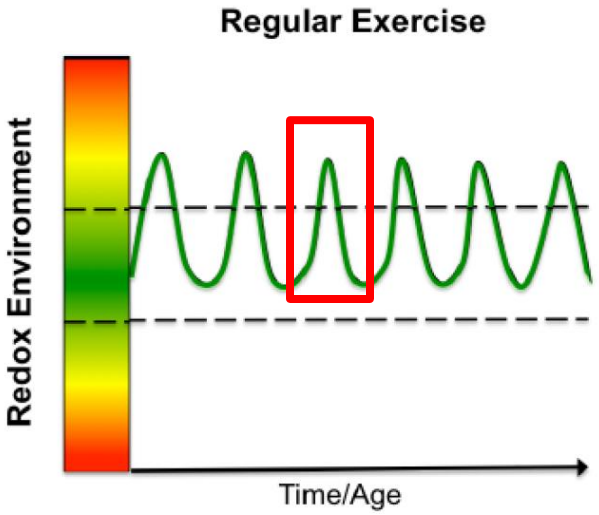
(+) Signal Transduction Pathways

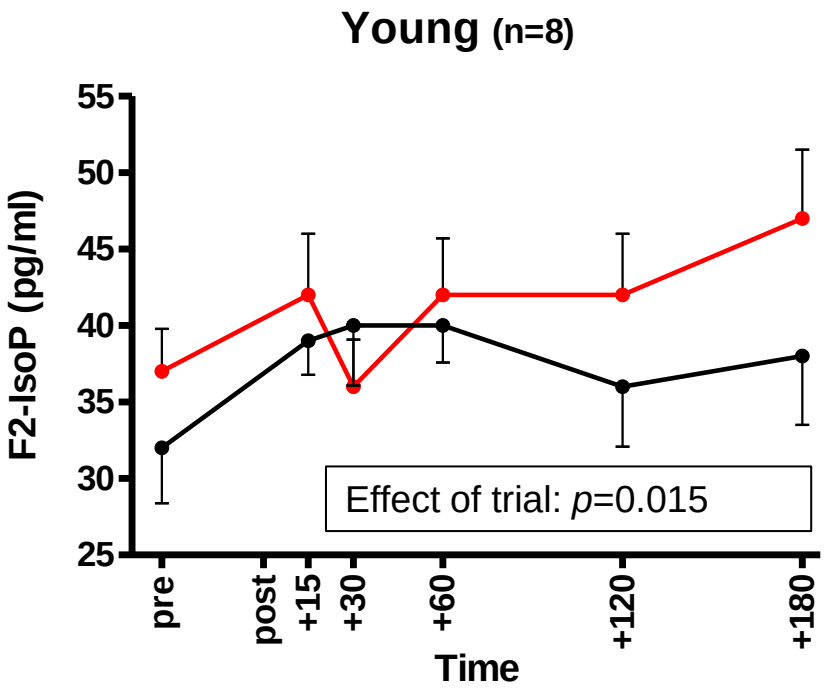
↓

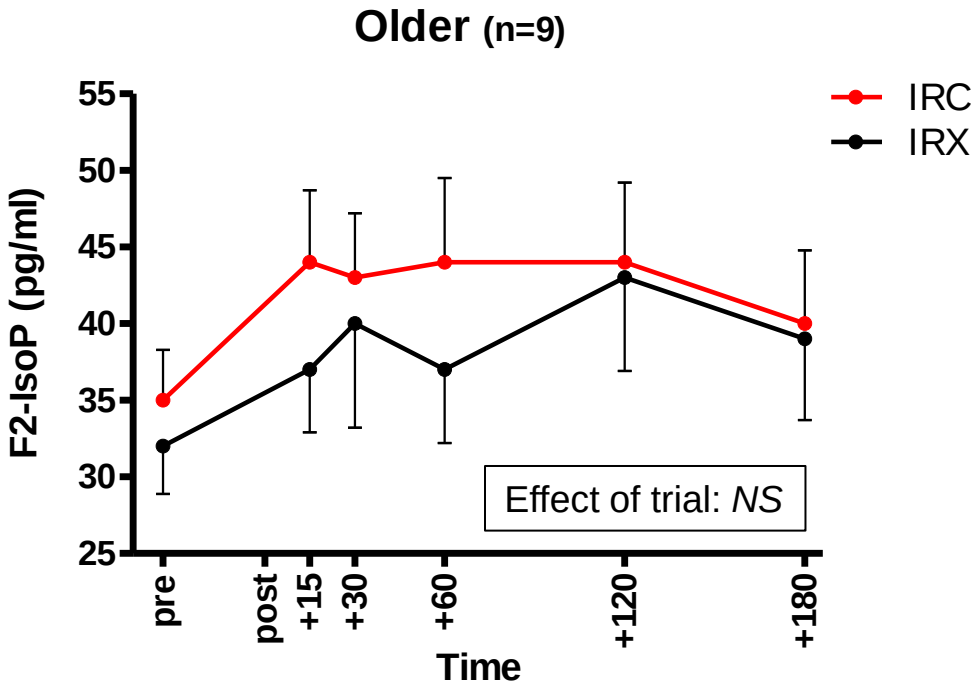
↑ Endogenous Antioxidant Systems

↓ **?**

↑ protection against subsequent non-exercise oxidative challenge (forearm ischemia/reperfusion)







Nordin, et al. (*AGE,* 2014)

Exercise Hormesis Model

→ **∆ in Redox Balance**

↓

(+) Signal transduction pathways

↓

↑ Endogenous Antioxidant Systems

↓

↑ protection against subsequent non-exercise oxidative challenge (forearm ischemia/reperfusion)

↓ *Aging*

Exercise Hormesis Model

→ **Δ in Redox Balance**

(+) Signal transduction pathways

↓ ***Aging***

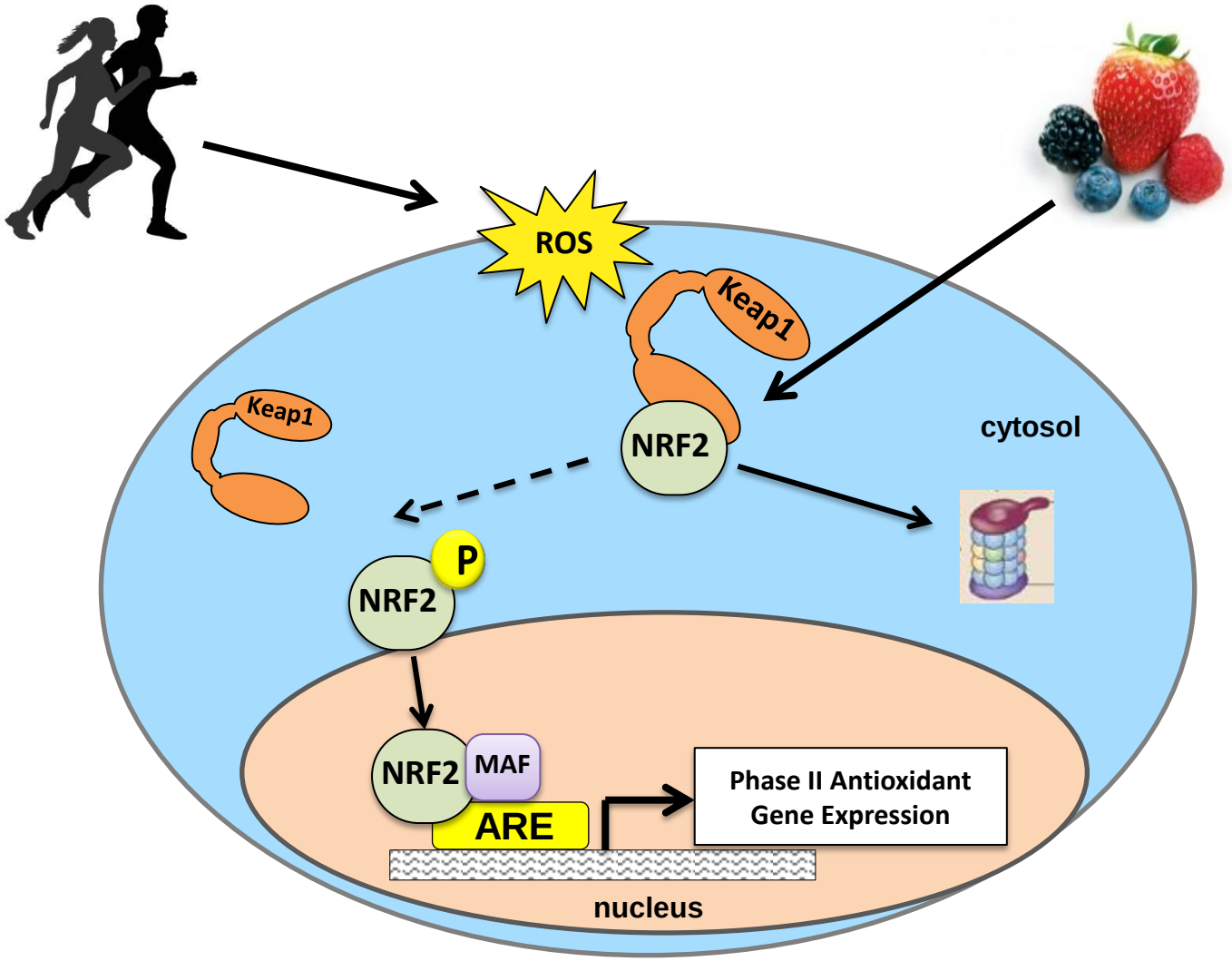
↑ Endogenous Antioxidant Systems

↓

↑ protection against subsequent non-exercise oxidative challenge (forearm ischemia/reperfusion)

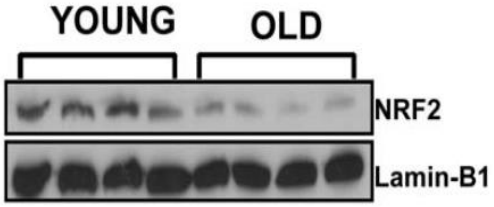
Nrf2 (Nuclear factor, erythroid-2-related factor 2)

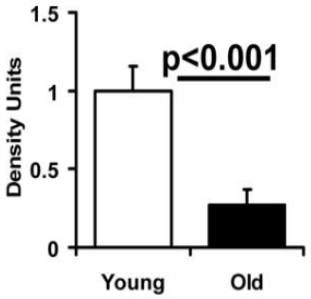
"The master regulator of antioxidant defense"

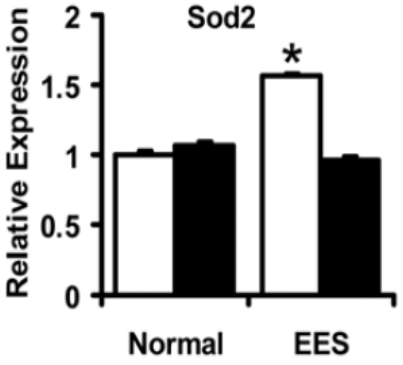


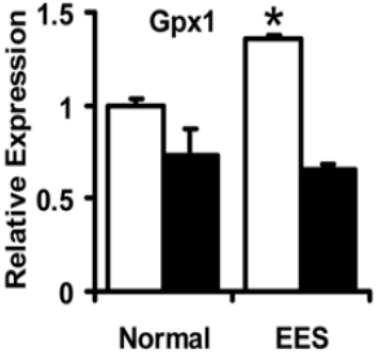
Is there evidence for changes in Nrf2 and related signaling with age?

Nrf2 signaling, aging, and exercise; Existing Literature…

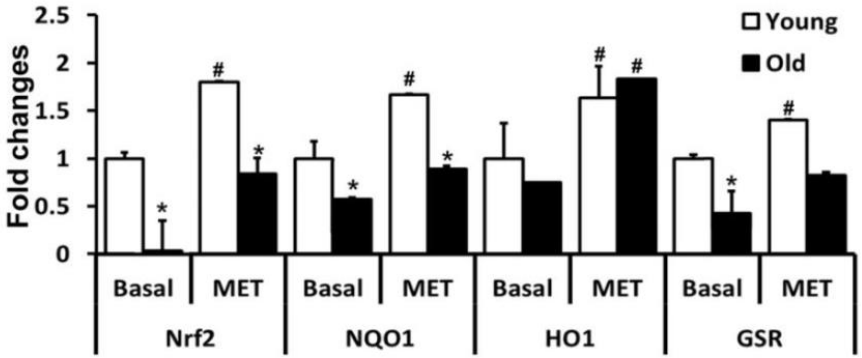


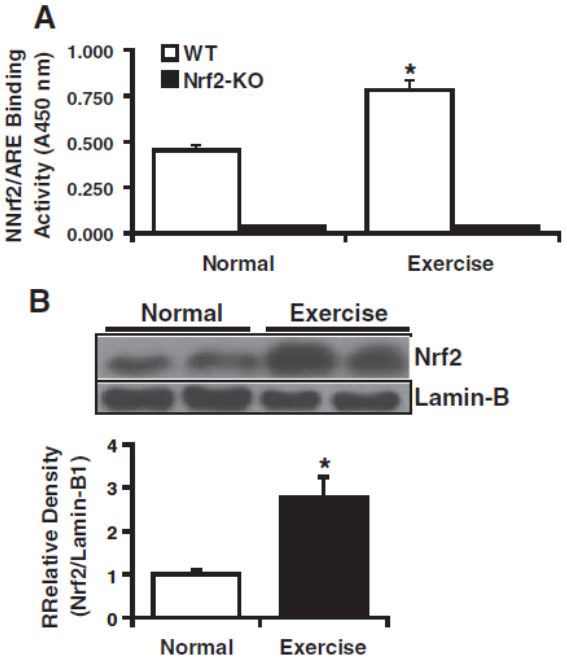






Gounder et al., PLoS One 2012, 7:e45697

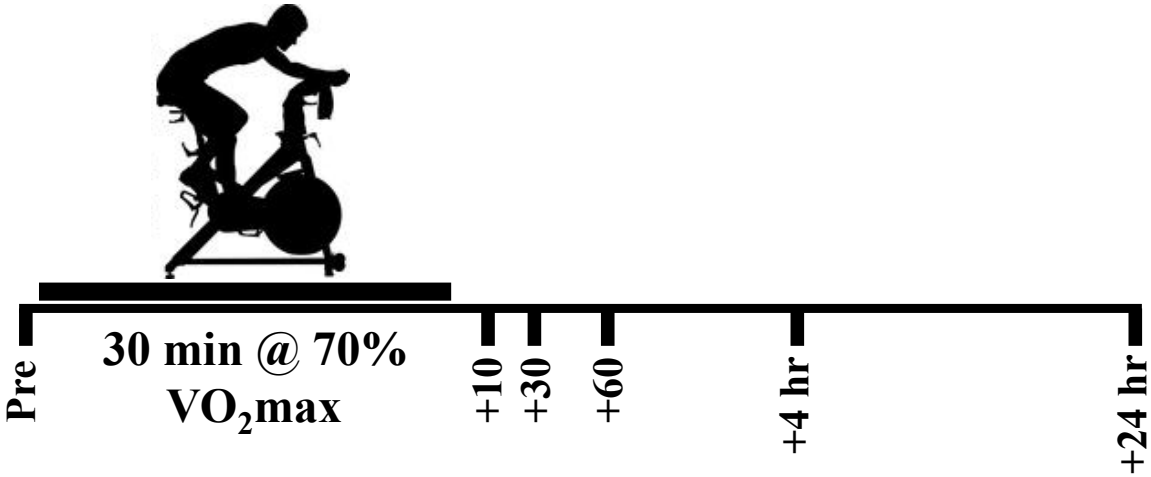




Muthusamy et al., FRBM 2012, 52:366

Nrf2 signaling: Effects of age

- 10 young (18-30y) and 10 older (≥55y) men
- Response to acute cycling exercise:



- *Measures in **isolated PBMCs**:*
  - Gene expression (qPCR): **SOD1, NQO1, HMOX**
  - Protein content (Western blot): **NRF2, SOD1, HMOX**

OMICS A Journal of Integrative Biology
Volume 15, Numbers 1 and 2, 2011

DOI: 10.1089/omi.2010.0073

Original Articles

Validation of the Use of Peripheral Blood Mononuclear Cells as Surrogate Model for Skeletal Muscle Tissue in Nutrigenomic Studies

Iwona Rudkowska,[1] Catherine Raymond,[1] André Ponton,[2] Hélène Jacques,[1,3] Charles Lavigne,[1,4] Bruce J. Holub,[5] André Marette,[1,4] and Marie-Claude Vohl[1,3,6]

http://informahealthcare.com/bmk
ISSN: 1354-750X (print), 1366-5804 (electronic)

Biomarkers

Biomarkers, 2015; 20(2): 97–108
 DOI: 10.3109/1354750X.2014.1002807

informa
healthcare

REVIEW ARTICLE

Blood reflects tissue oxidative stress: a systematic review

Nikos V. Margaritelis[1], Aristidis S. Veskoukis[1], Vassilis Paschalis[2,3], Ioannis S. Vrabas[1], Konstantina Dipla[1], Andreas Zafeiridis[1], Antonios Kyparos[1], and Michalis G. Nikolaidis[1]#

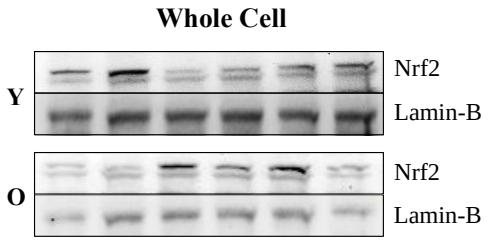
Subject Demographics

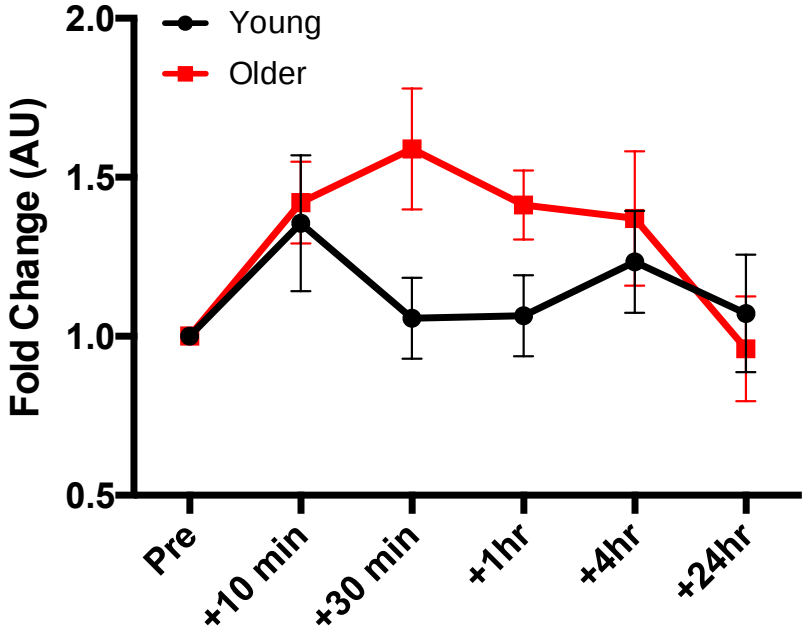
	Young (n=10)	Older (n=10)	*P*
Age (yrs)	23 ± 2	63 ± 4	<.001
BMI (kg/m^2)	26.3 ± 3.9	26.6 ± 3.0	NS
Waist circ. (cm)	79 ± 30	100 ± 12	NS
SBP (mm Hg)	125 ± 8	123 ± 14	NS
DBP (mm Hg)	78 ± 8	83 ± 10	NS
VO_2 max (mL/kg/min)	45.6 ± 5.0	30.7 ± 5.3	<.001
% VO_2 max – acute EX	68 ± 4	69 ± 6	NS
% HR max – acute EX	81 ± 6	76 ± 11	NS

Data are presented as mean ± SD

Done et al., FRBM 2016

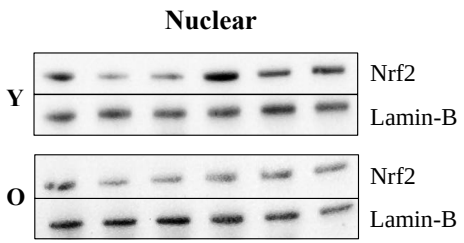
Nrf2 Response to Exercise

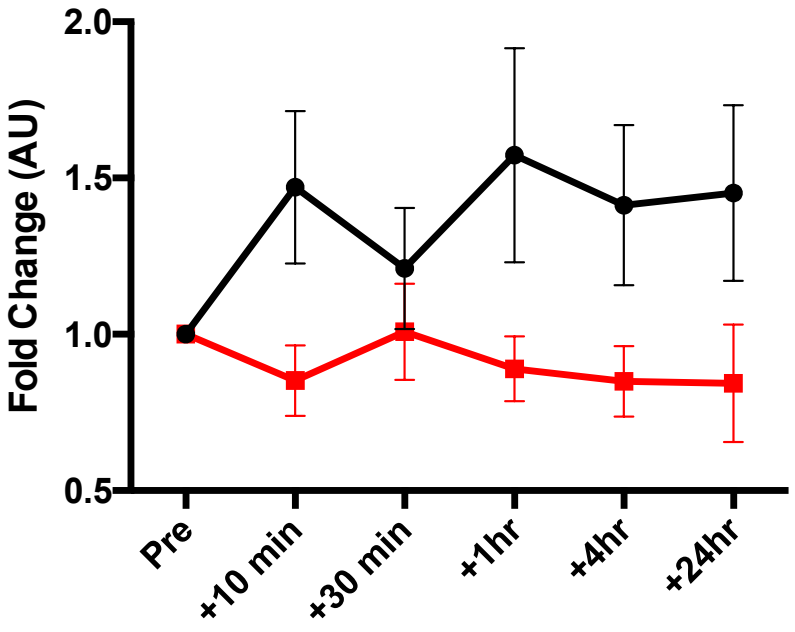




Age: *p*=0.313

Time: *p*=0.003**



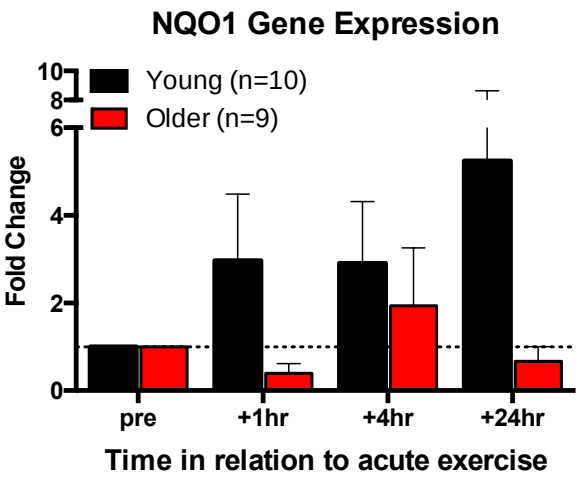


Age: *p*=0.031*

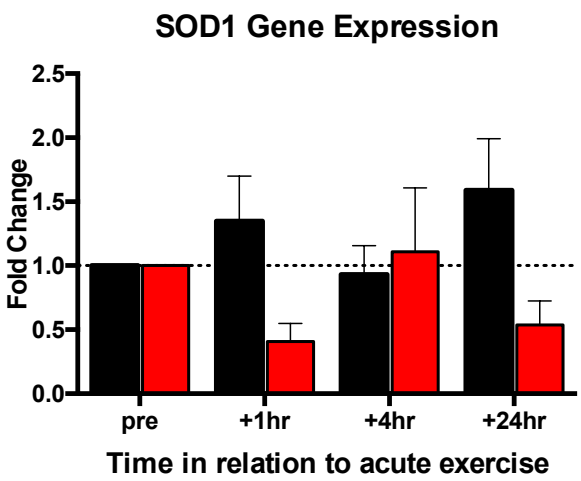
Time: *p*=0.785

Done et al., FRBM 2016

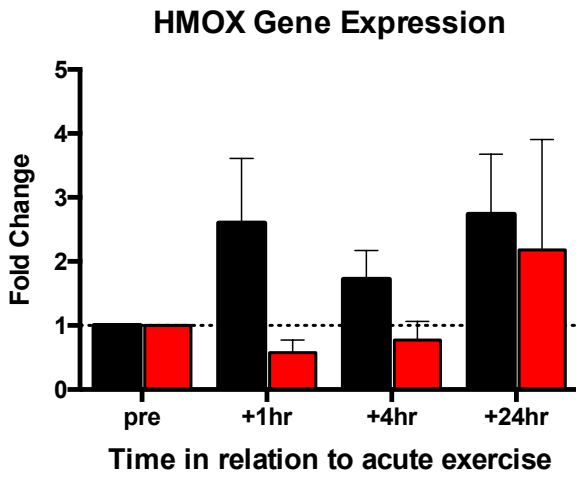
Target Gene Response to Exercise



Age: *p*=0.05†
Time: *p*=0.07†
Interaction: *NS*



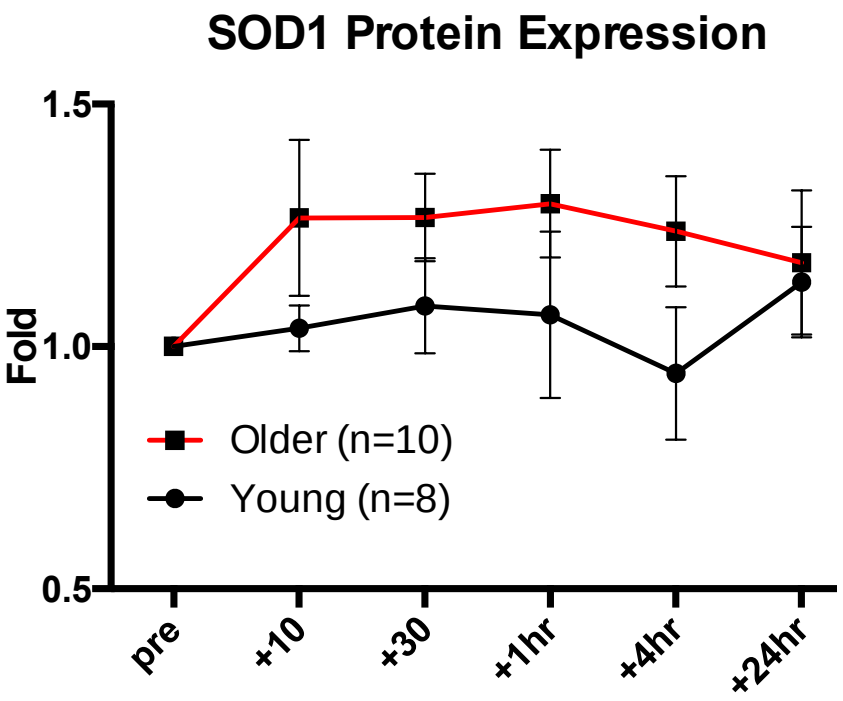
Age: *p*=0.131
Time: *p*=0.097†
Interaction: *NS*

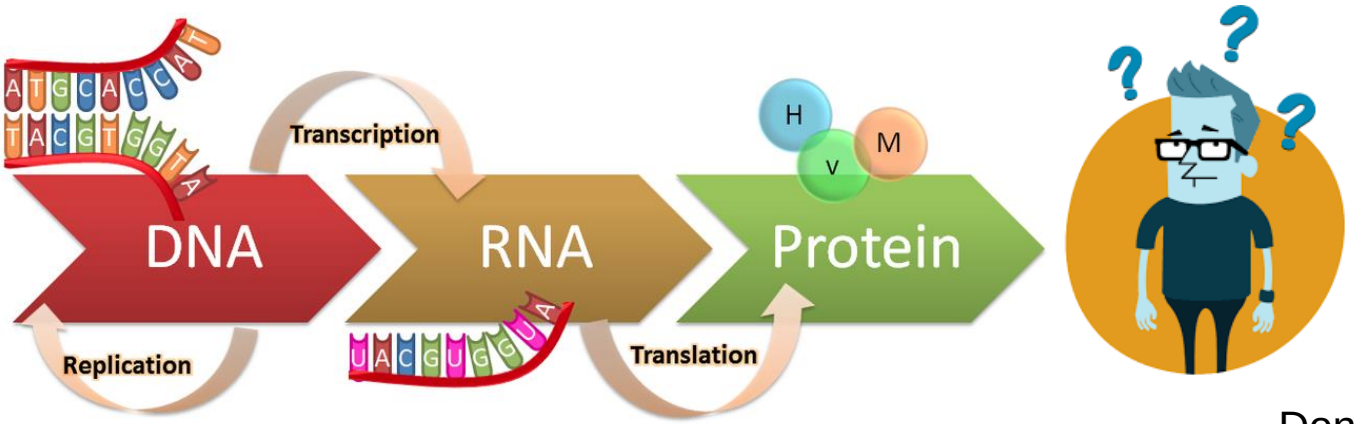


Age: *p*=0.006**
Time: *p*=0.540
Interaction: *NS*

Done et al., FRBM 2016

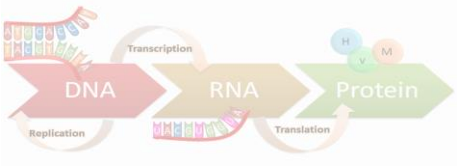
Antioxidase Protein Response to Exercise





Done et al., FRBM 2016

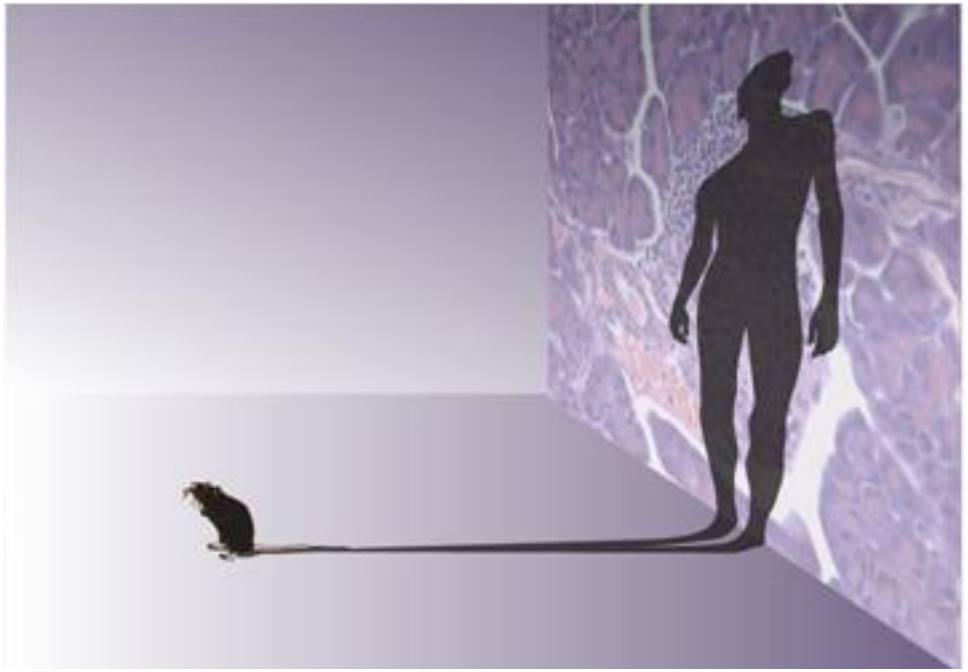
Protein Response to Exercise



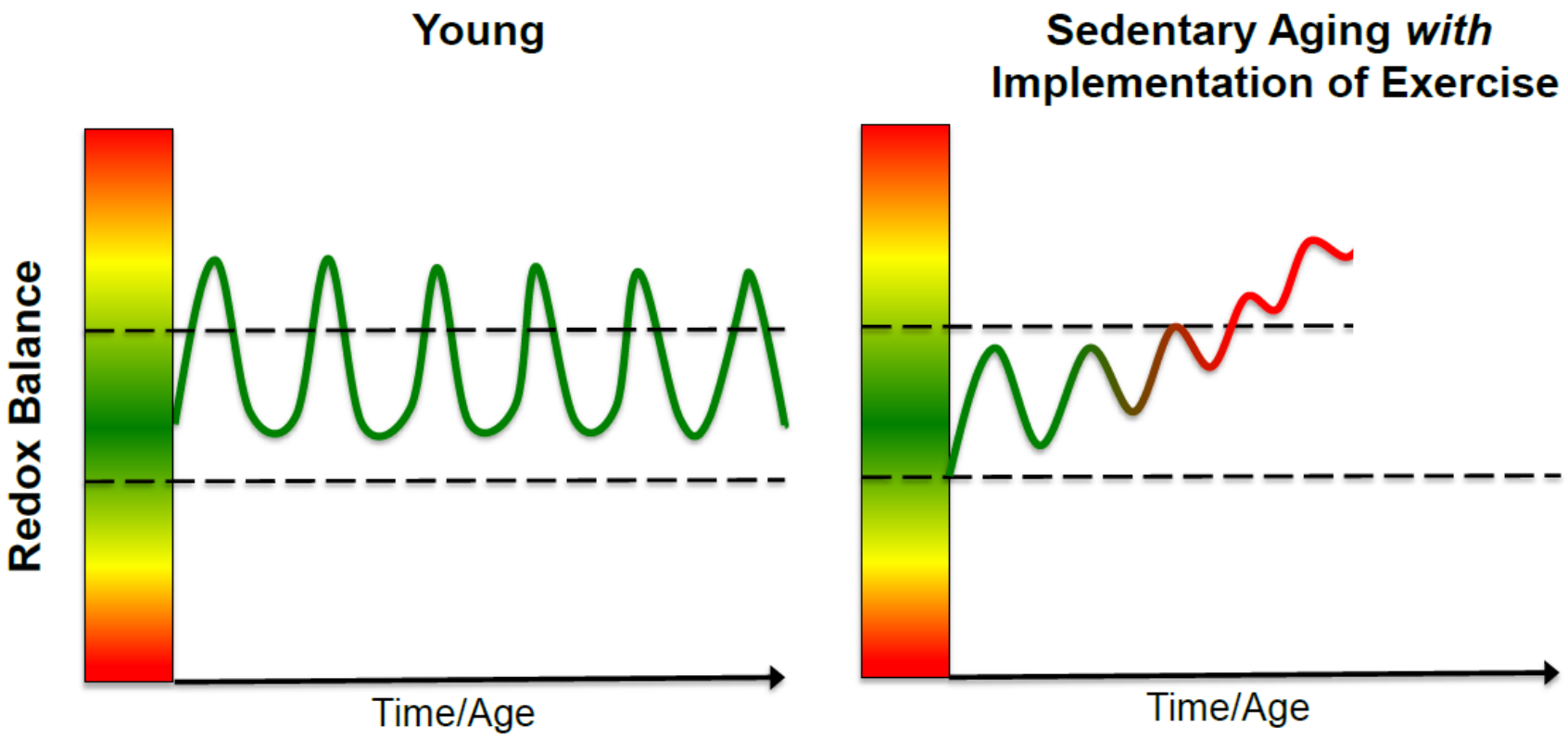
(measure 4- and 24-hours post each)

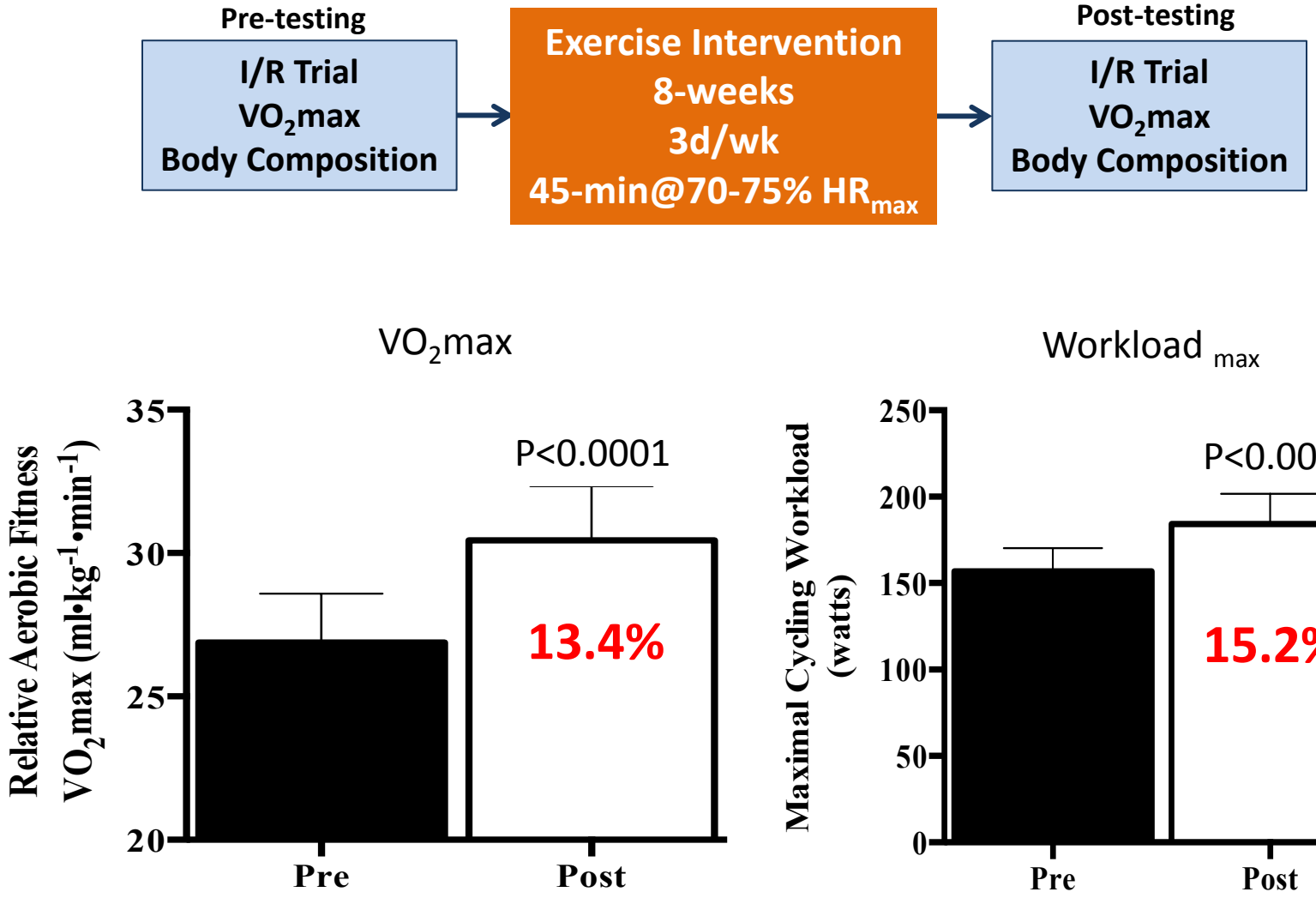
Perry et al., (2007)

Summary



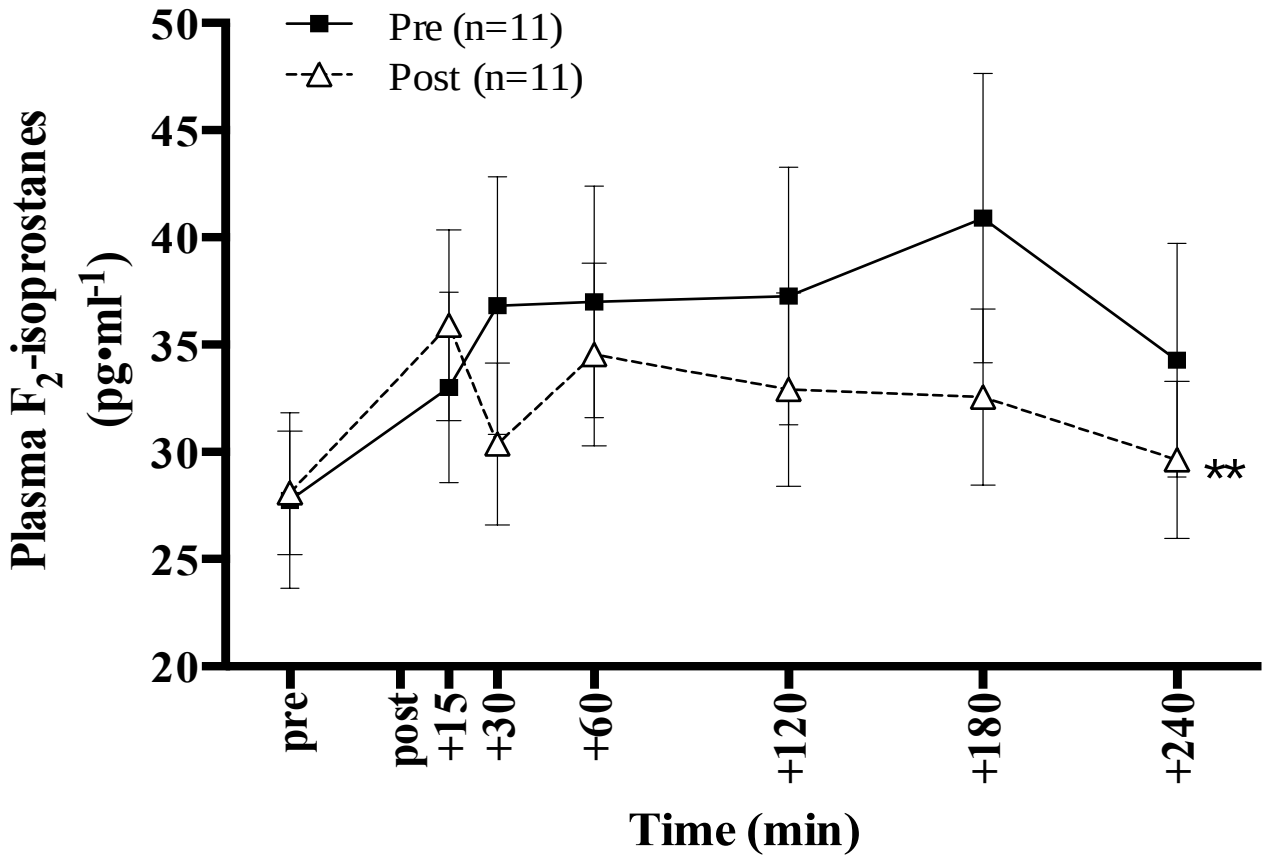
Can regular exercise overcome the age-related impairment In Nrf2 signaling?


Young
Sedentary Aging *with* Implementation of Exercise
Redox Balance
Time/Age
Time/Age



Done & Traustadóttir (*AGE 2016*)

Aerobic Exercise Intervention Restores Redox Balance in Older Adults



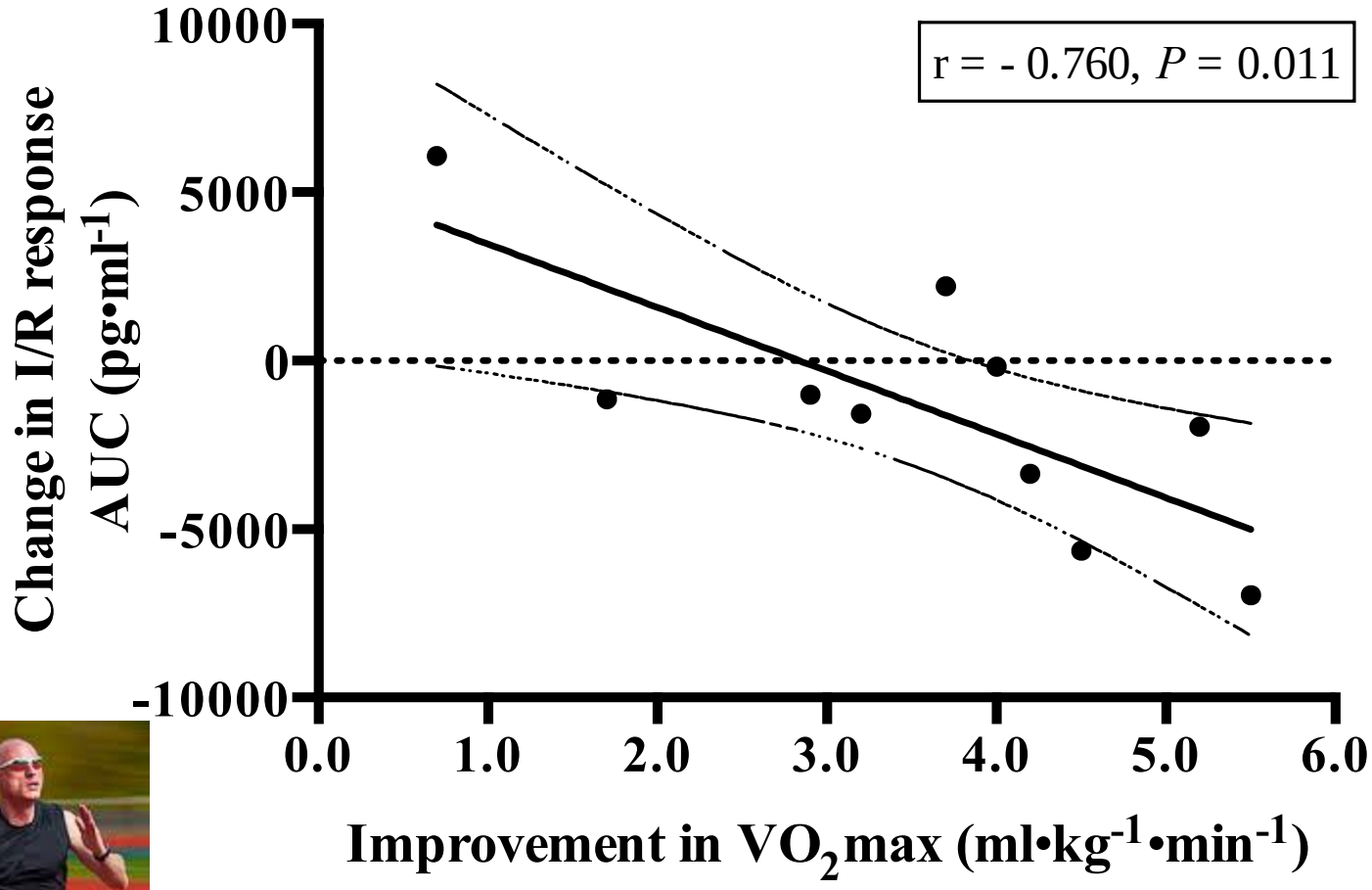
Trial: p = .42

Trial* Time: p =.043

Time: p = .00487

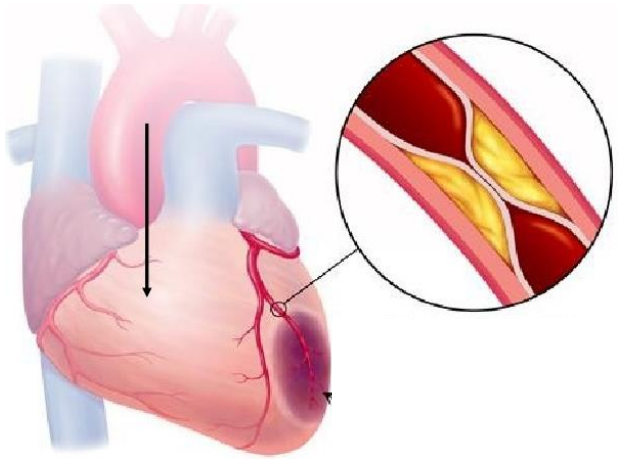
Done & Traustadóttir (*AGE 2016)*

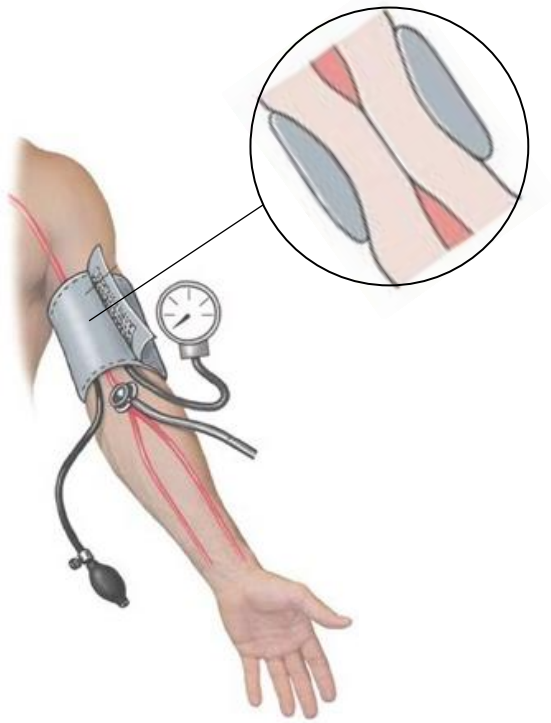
Fitness matters!



Done & Traustadóttir (*AGE 2016)*

Clinical Implications

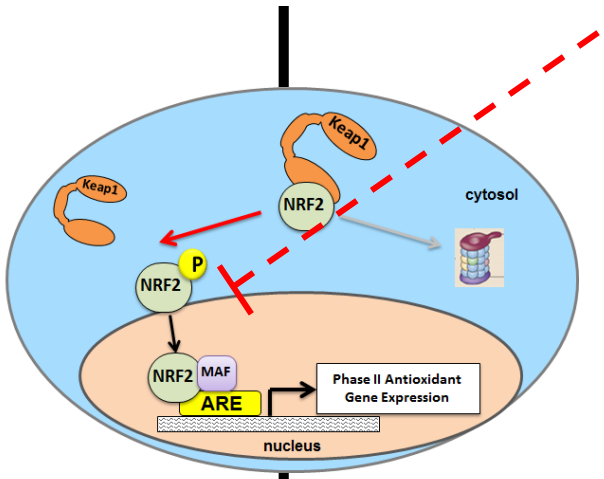


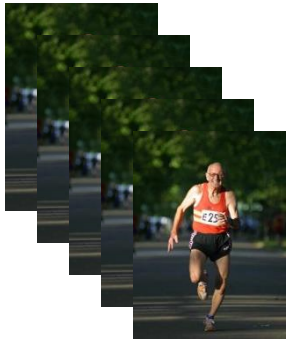


So what have we learned
&
what next??

Exercise Hormesis Model

→ **Δ in Redox Balance**





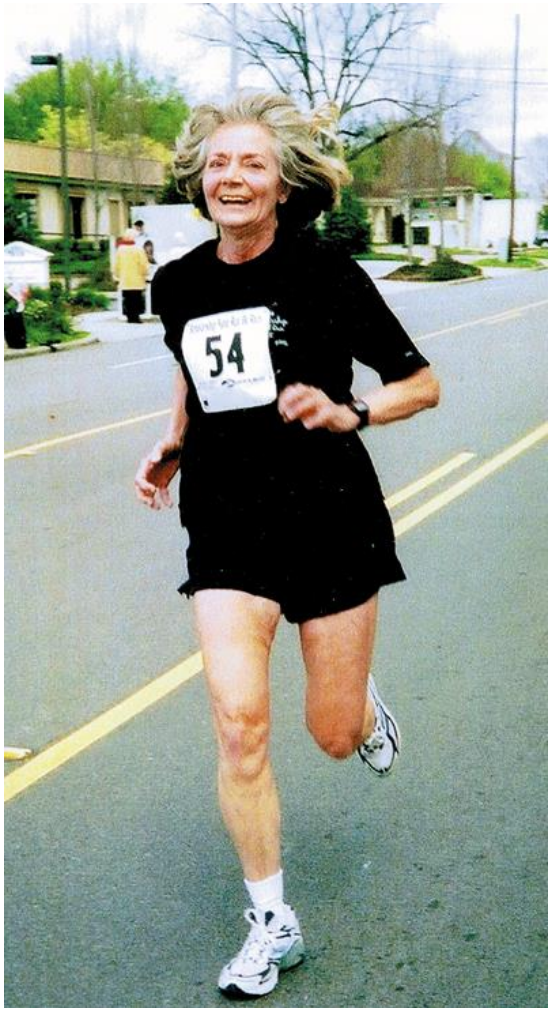
↑ Endogenous Antioxidant Systems

↑ protection against non-exercise oxidative challenge

? →

↑ protection against diseases associated with oxidative stress

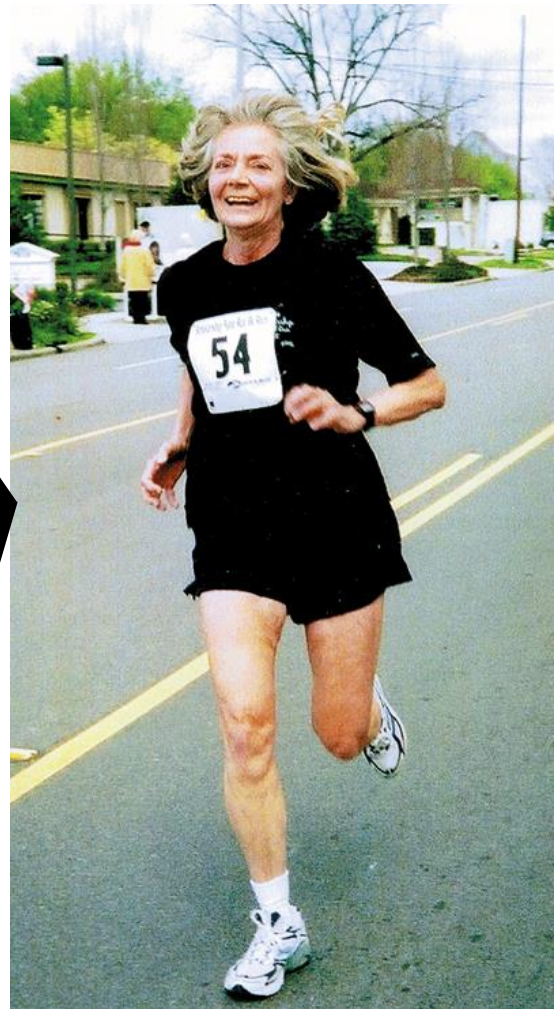
The ultimate pleiotropic medicine…



INTENSITY

DOSE RESPONSE

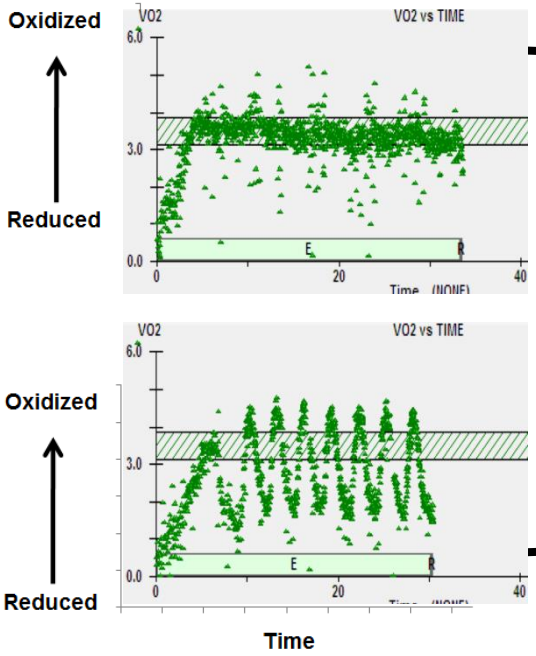
EARLY vs LATE in LIFE



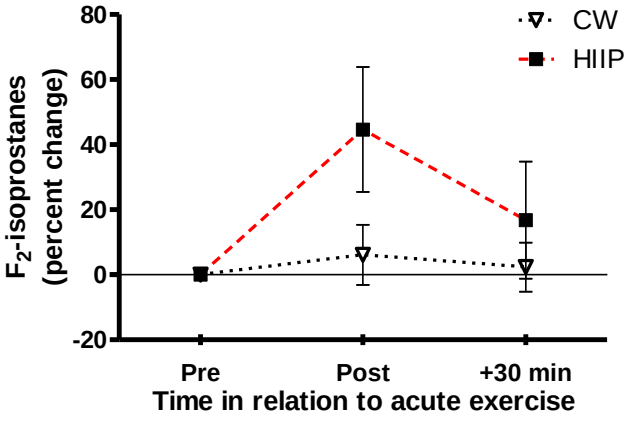
CONSTANT (CW)

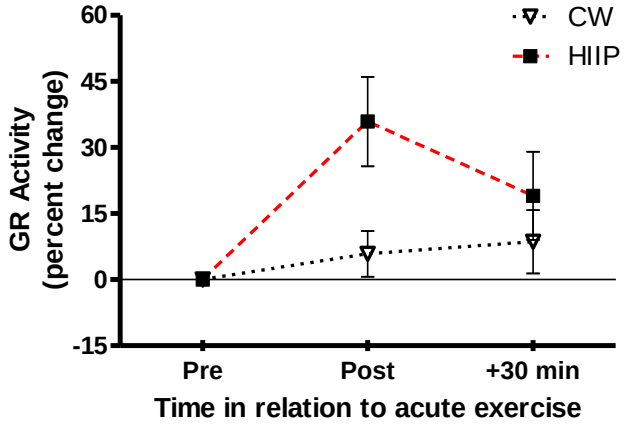
INTERVAL (HIIP)

Cellular Redox Balance



Difference in magnitude of redox response and cell signaling ??

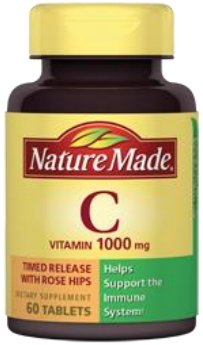


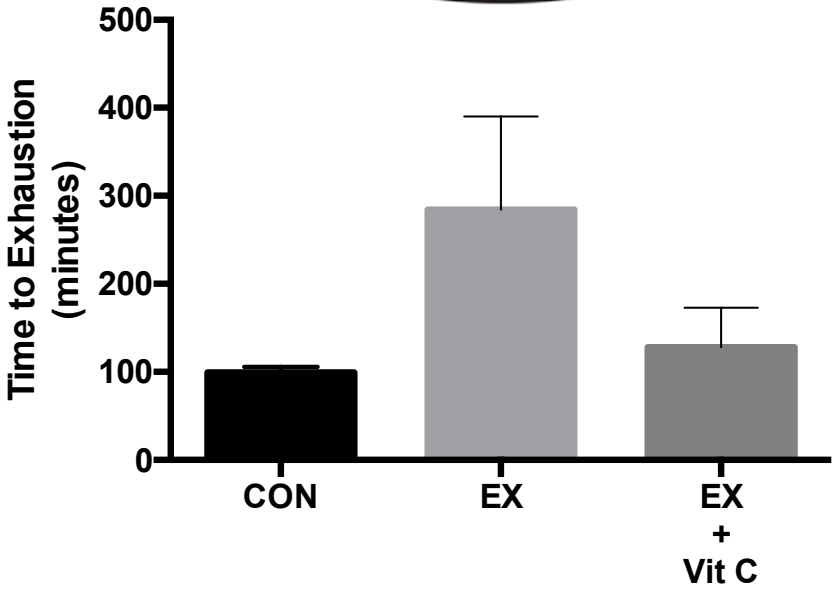


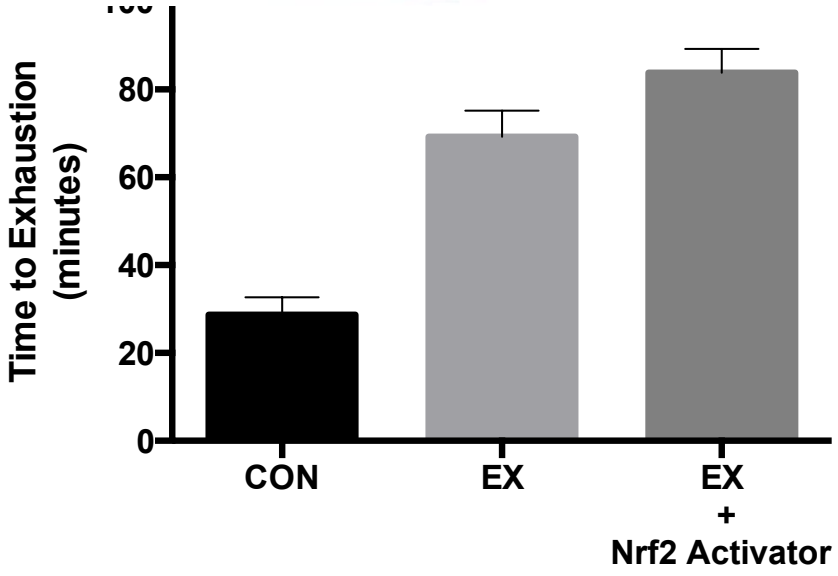
Sex differences/Estrogen

Translation to Function

Exercise and Phytonutrients = synergistic effect ??







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