# Effetti molecolari della riabilitazione cardiaca post-scompenso in pazienti anziani: Sirt1 e catalase regolano la risposta antiossidante

*G. Corbi*[1], *V. Conti*[2], *G. Russomanno*[2], *S. Latte*[3], *V. Manzo*[2], *A. Filippelli*[2], *N. Ferrara* [3]

[1] Dpt di Medicina e Scienze della Salute, Università degli Studi del Molise

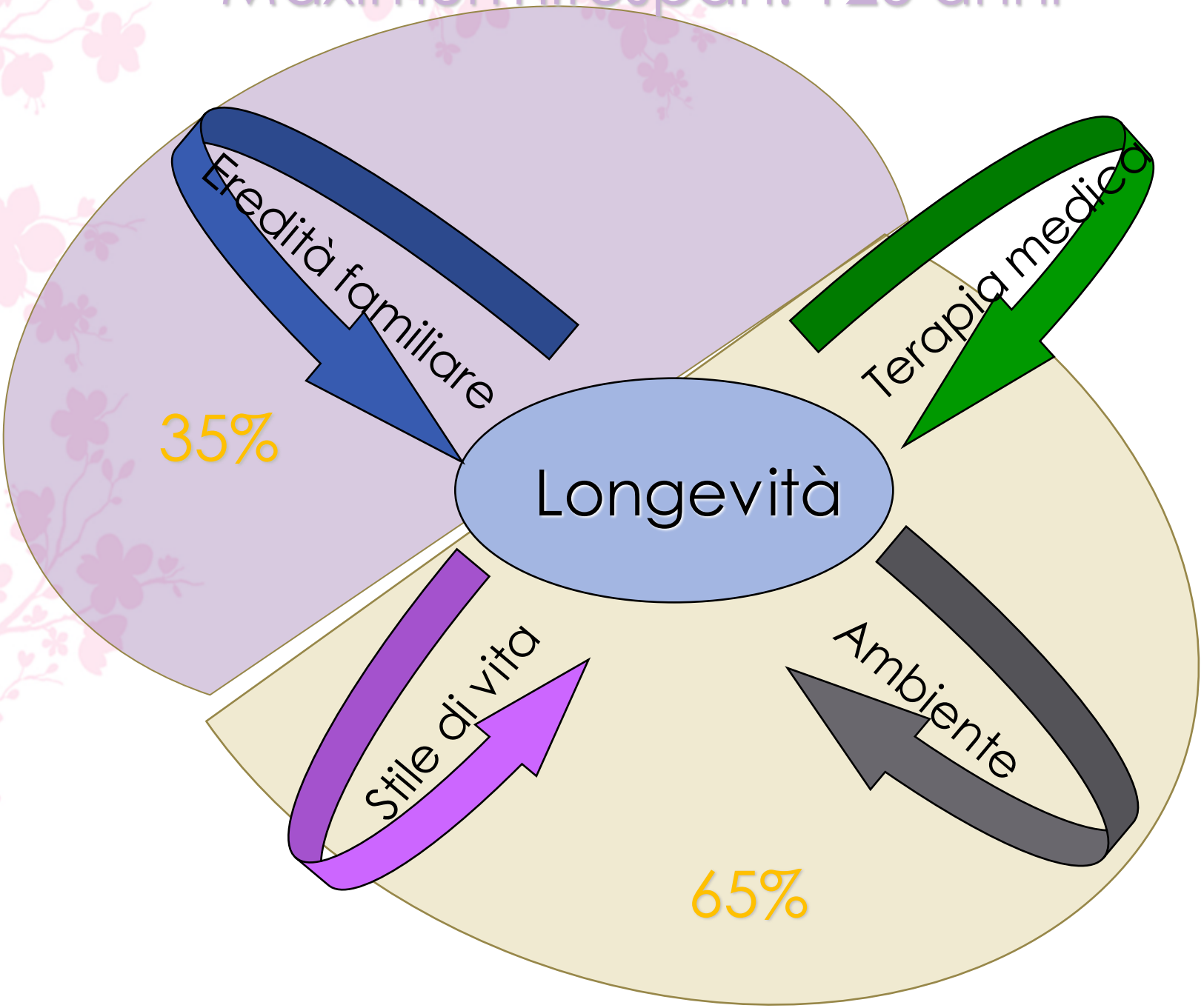
[2] Dpt di Medicina e Chirurgia, Università degli Studi di Salerno

[3] Divisione di Cardiologia, Ospedale San Gennaro dei Poveri, Napoli

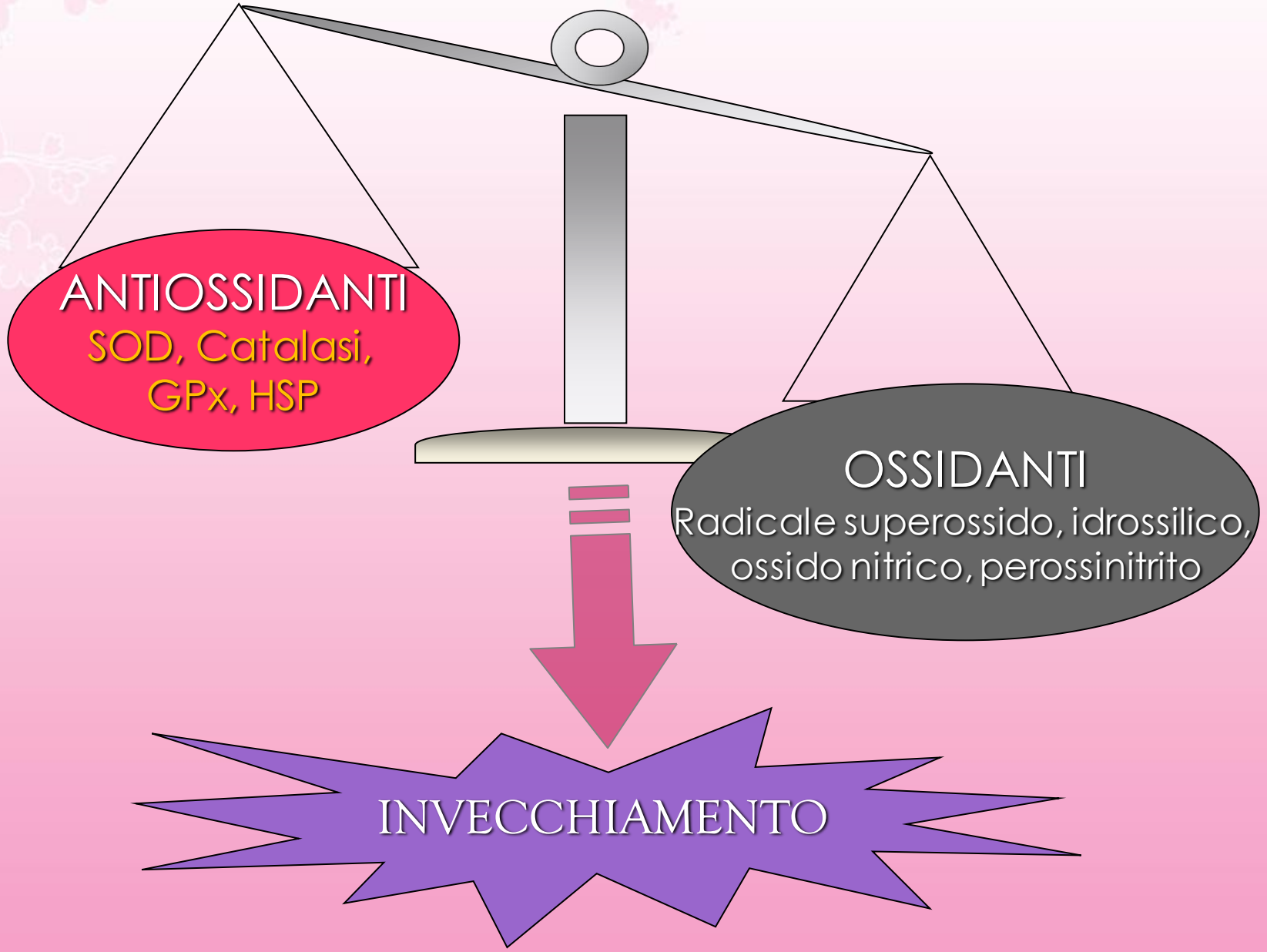
[4] Dipartimento di Scienze Mediche Traslazionali, Università "Federico II" di Napoli

© TemplatesWise.com

# Maximum lifespan: 125 anni



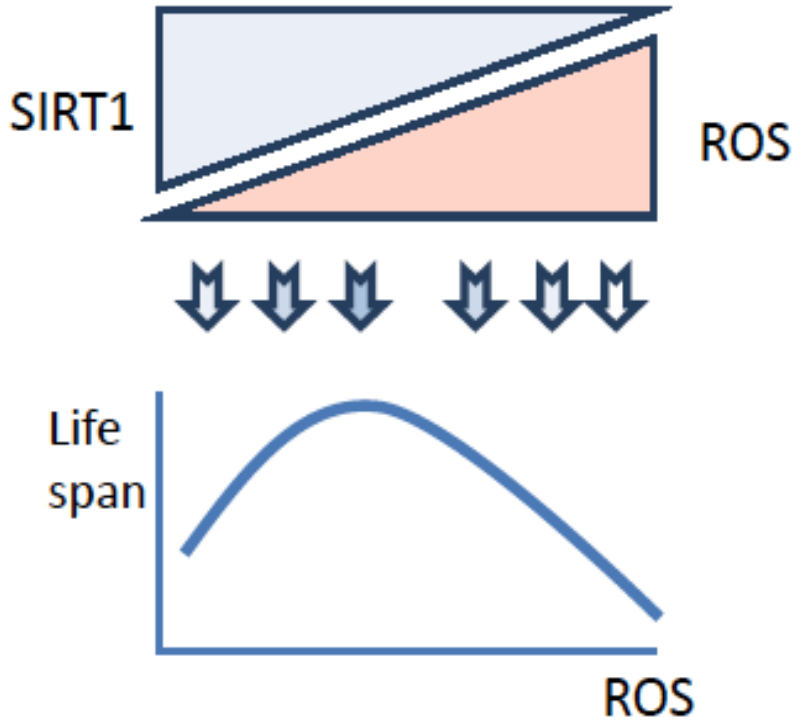
# Invecchiamento e stress ossidativo

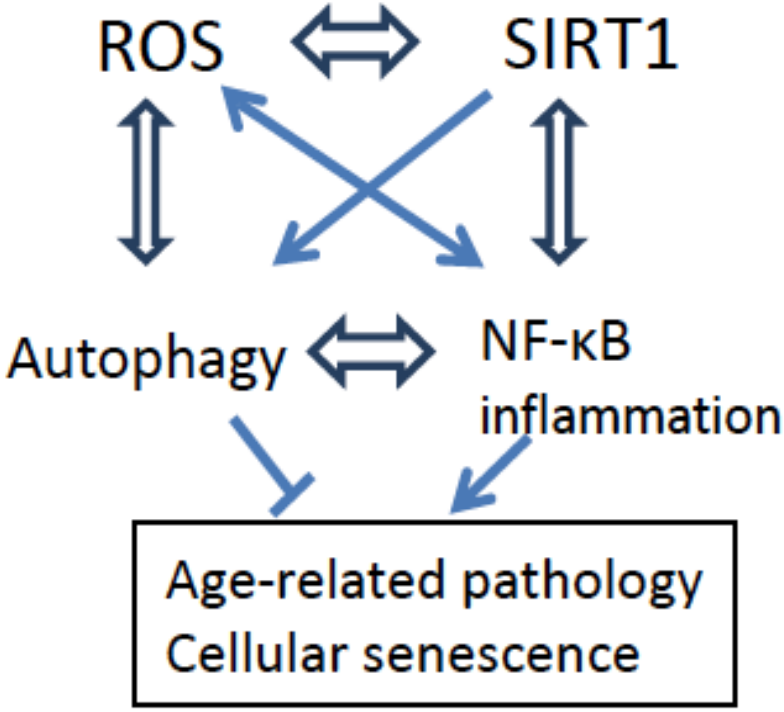


Int J Mol Sci. 2013 Feb 11;14(2):3834-59. doi: 10.3390/ijms14023834.

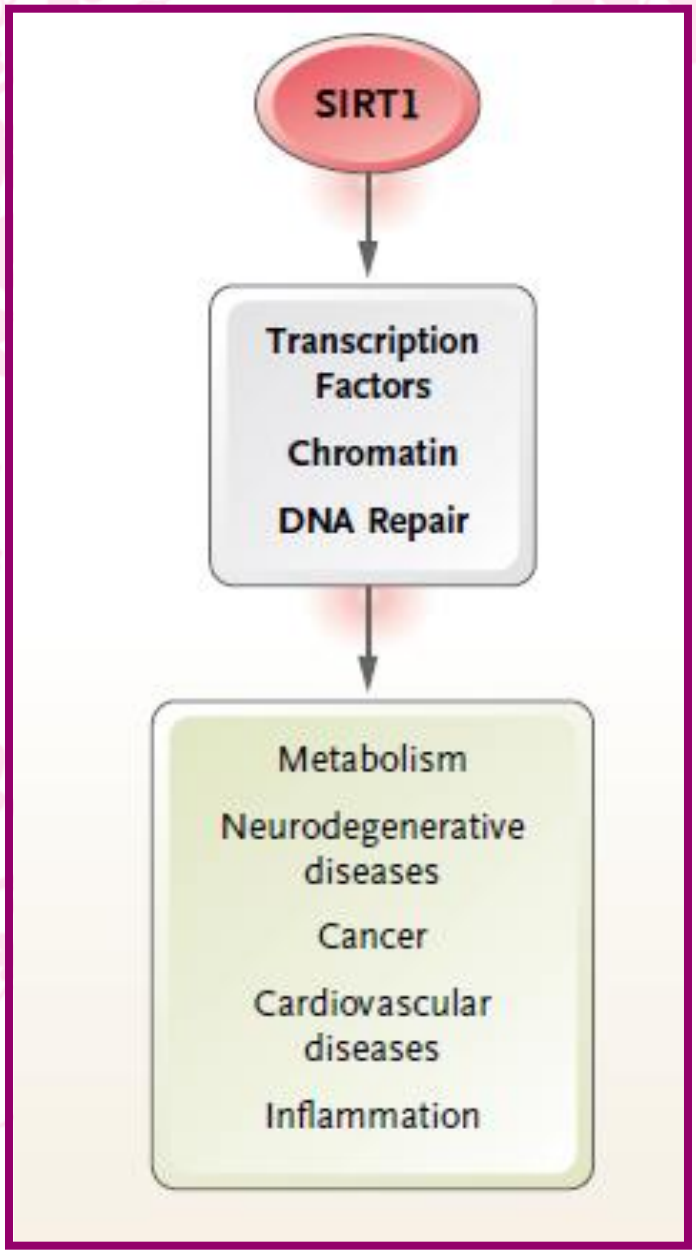
**Crosstalk between Oxidative Stress and SIRT1: Impact on the Aging Process.**

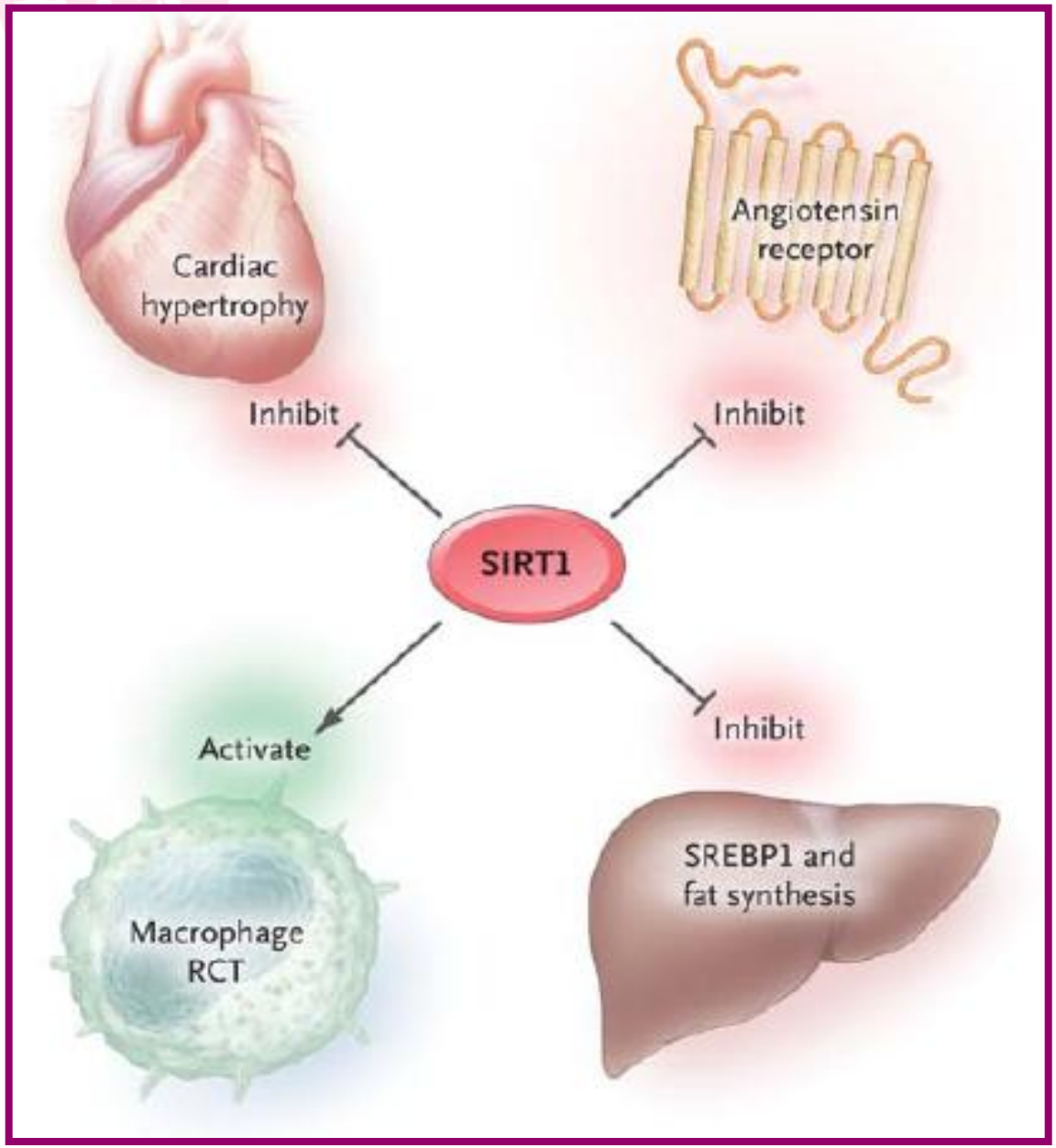
Salminen A, Kaarniranta K, Kauppinen A.



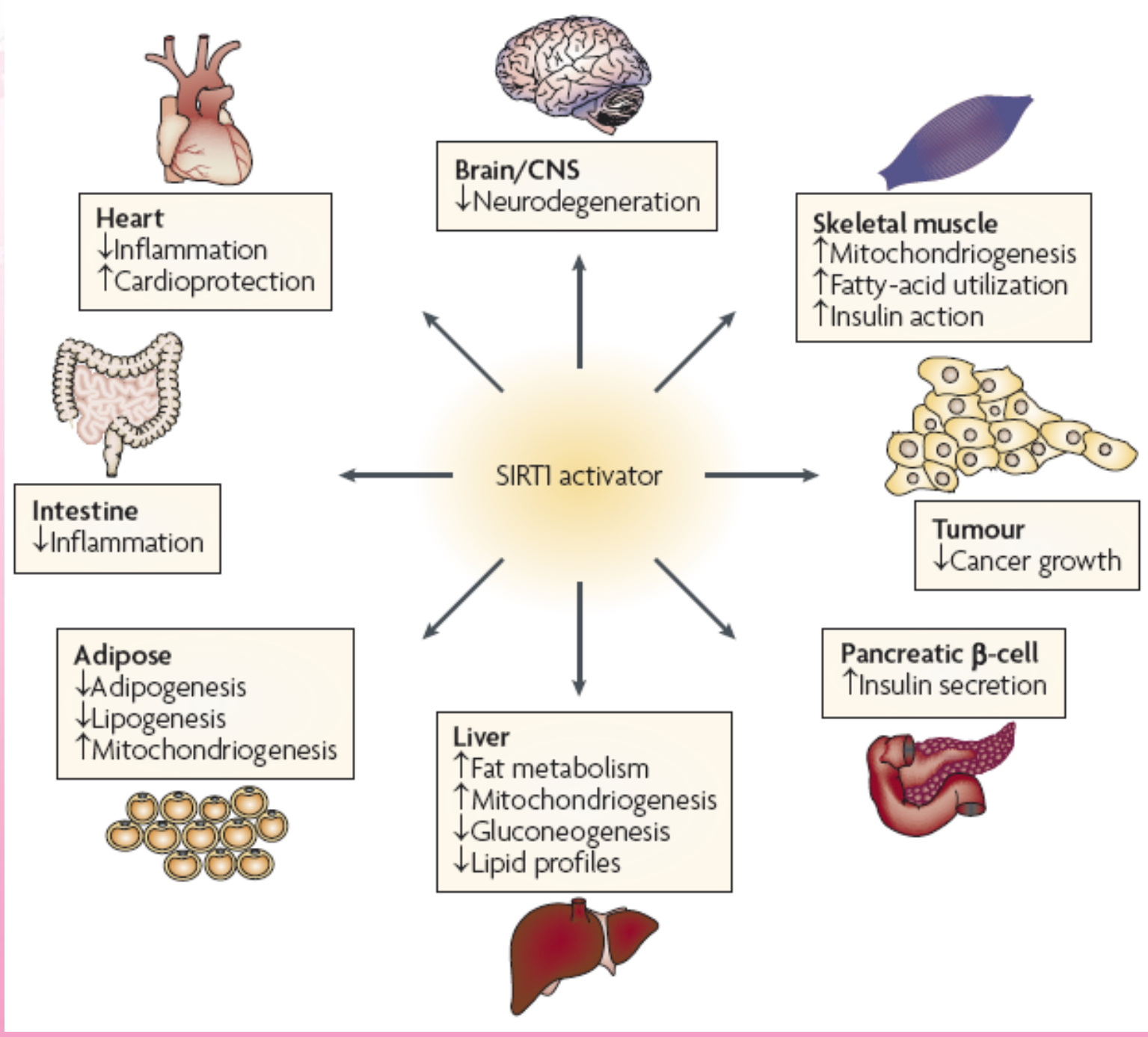



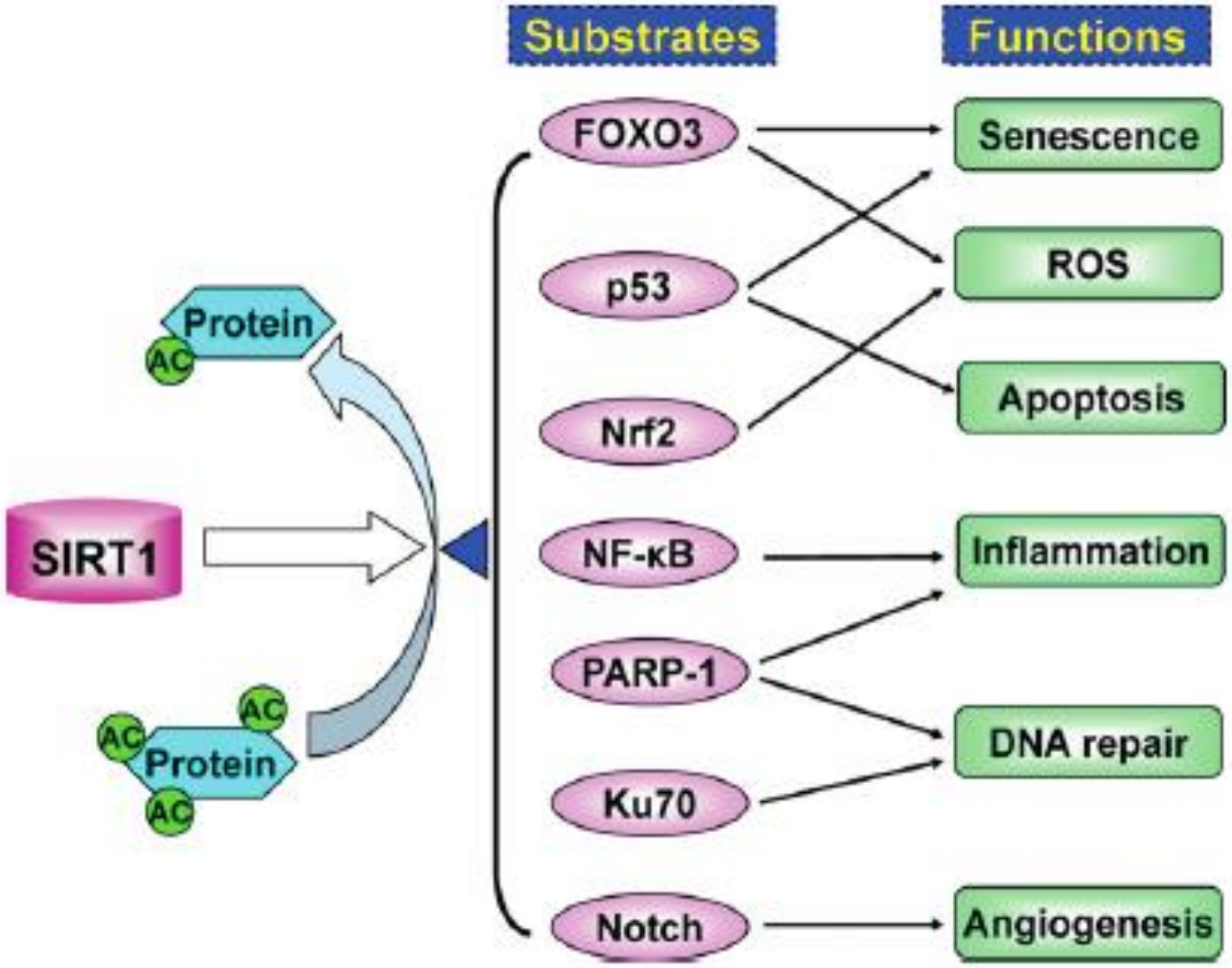

*Sirtuins as an Elixir of Longevity*




Leonard Guarente. Sirtuins, Aging, and Medicine
N Engl J Med 2011;364:2235-44.


Heart
↓Inflammation
↑Cardioprotection
Brain/CNS
↓Neurodegeneration
Skeletal muscle
↑Mitochondriogenesis
↑Fatty-acid utilization
↑Insulin action
Intestine
↓Inflammation
SIRT1 activator
Tumour
↓Cancer growth
Adipose
↓Adipogenesis
↓Lipogenesis
↑Mitochondriogenesis
Liver
↑Fat metabolism
↑Mitochondriogenesis
↓Gluconeogenesis
↓Lipid profiles
Pancreatic β-cell
↑Insulin secretion


Substrates
Functions
FOXO3
p53
Nrf2
NF-κB
PARP-1
Ku70
Notch
Senescence
ROS
Apoptosis
Inflammation
DNA repair
Angiogenesis
SIRT1
Protein
AC
Protein
AC
AC
AC

Available online at www.sciencedirect.com
ScienceDirect
Experimental Gerontology 41 (2006) 764–770
Experimental Gerontology
www.elsevier.com/locate/expgero

# Exercise training affects age-induced changes in SOD and heat shock protein expression in rat heart

In summary, by increasing Hsp27 and Hs70 levels, prolonged exercise partially counterbalanced the heart age-related effects in the antioxidant system without altering peroxidation levels. These findings suggest that the beneficial effects on aged-related cardiovascular changes could be connected to the "anti-oxidant" effects of prolonged exercise training.

*Department of Health Sciences, University of Molise and S. Maugeri Foundation, Scientific Institute of Telese Terme, Telese Terme 82037, Italy*

REJUVENATION RESEARCH
Volume 10, Number 4, 2007
© Mary Ann Liebert, Inc.
DOI: 10.1089/rej.2007.0576

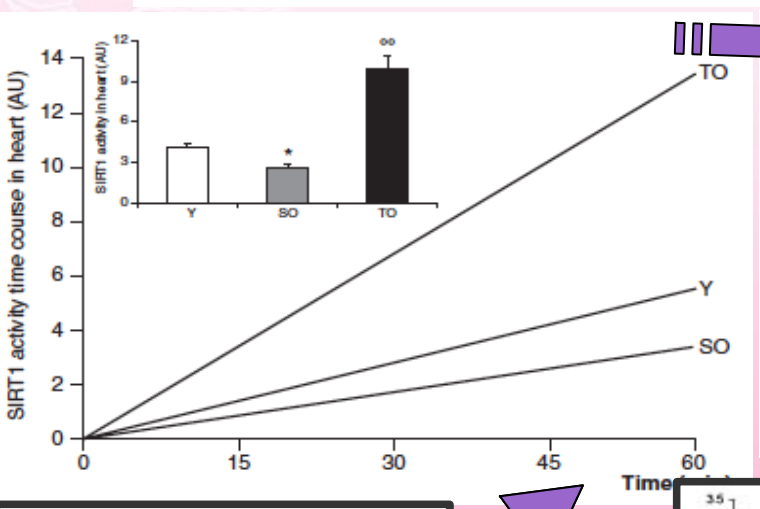
# Exercise Training Promotes SIRT1 Activity in Aged Rats

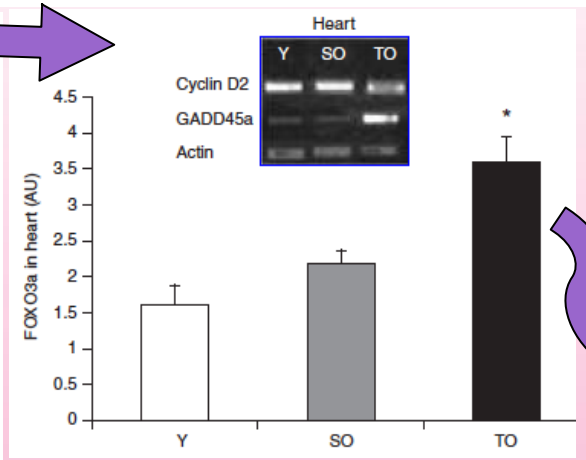
Nicola Ferrara,[1,2*] Barbara Rinaldi,[3*] Graziamaria, Corbi,[1,2] Valeria Conti,[3] Paola Stiuso,[4] Silvia Boccuti,[3] Giuseppe Rengo,[2] Francesco Rossi,[3] and Amelia Filippelli [3]

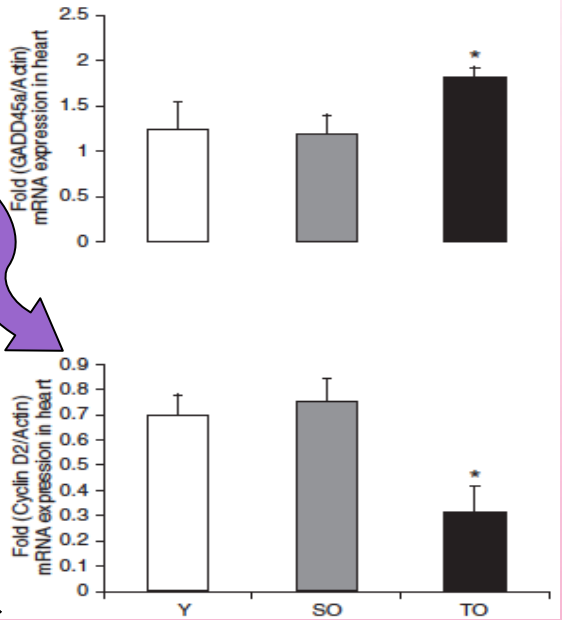
REJUVENATION RESEARCH
Volume 11, Number 1, 2008
© Mary Ann Liebert, Inc.
DOI: 10.1089/rej.2007.0576

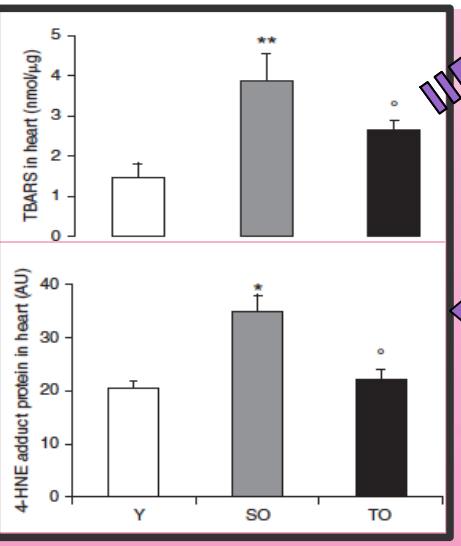
# Exercise Training Promotes SIRT1 Activity in Aged Rats

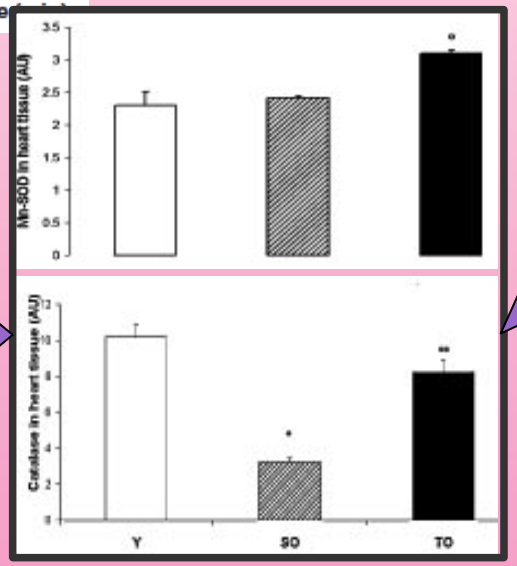
Nicola Ferrara,[1,2*] Barbara Rinaldi,[3*] Graziamaria, Corbi,[1,2] Valeria Conti,[3] Paola Stiuso,[4] Silvia Boccuti,[3] Giuseppe Rengo,[2] Francesco Rossi,[3] and Amelia Filippelli [3]



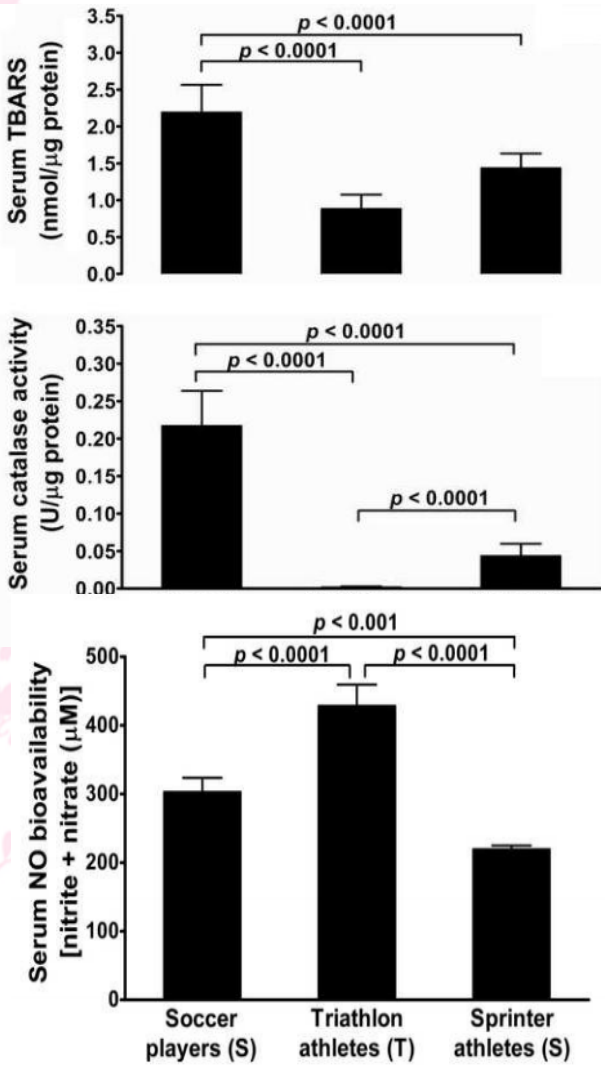



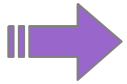

***Conclusions:*** an 8-week training period was able to increase antioxidant defenses by SIRT1 activity.

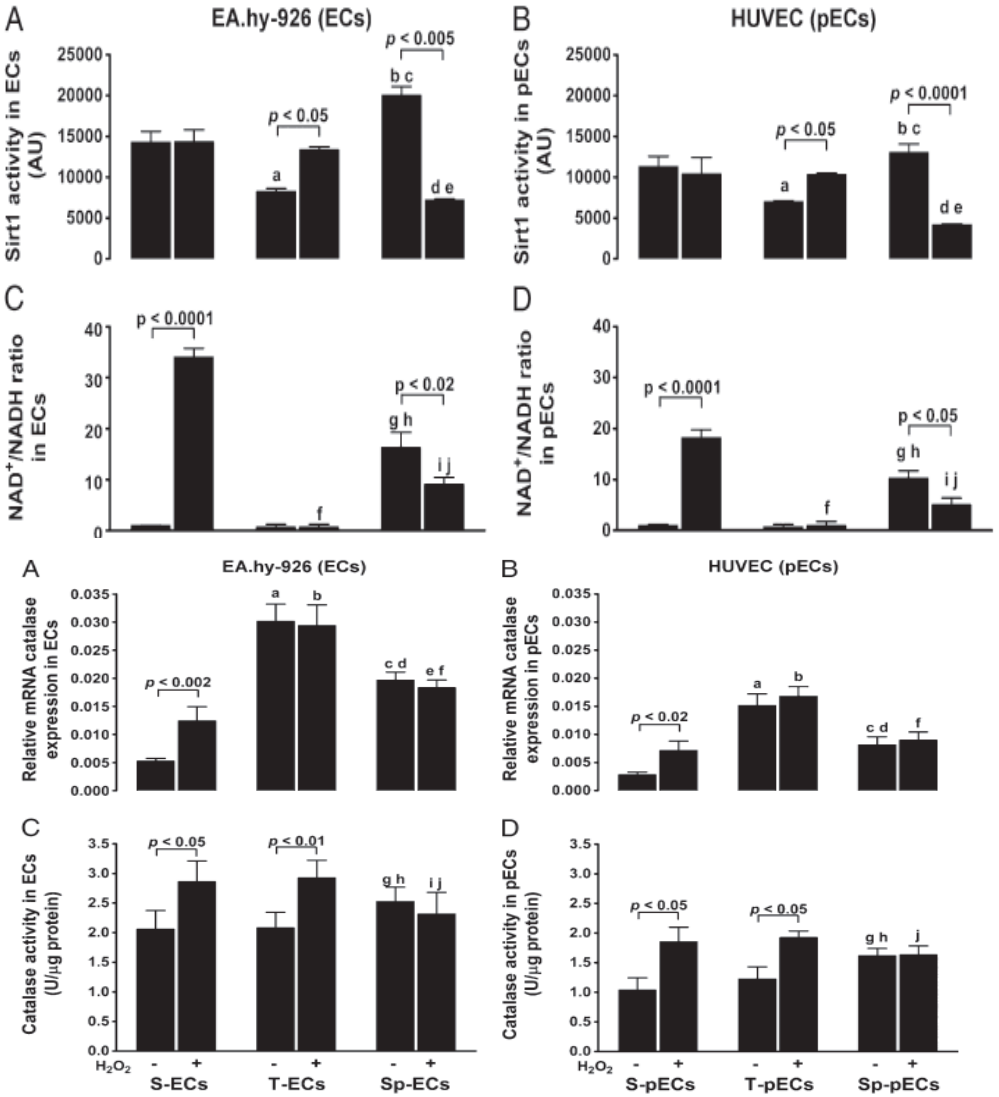
Med Sci Sports Exerc. 2012 Jan;44(1):39-49. doi: 10.1249/MSS.0b013e318227f69c.

# Oxidative stress effects on endothelial cells treated with different athletes' sera.

Conti V, Corbi G, Russomanno G, Simeon V, Ferrara N, Filippelli W, Limongelli F, Canonico R, Grasso C, Stiuso P, Dicitore A, Filippelli A.





Med Sci Sports Exerc. 2012 Jan;44(1):39-49. doi: 10.1249/MSS.0b013e318227f69c.

# Oxidative stress effects on endothelial cells treated with different athletes' sera.

Conti V, Corbi G, Russomanno G, Simeon V, Ferrara N, Filippelli W, Limongelli F, Canonico R, Grasso C, Stiuso P, Dicitore A, Filippelli A.

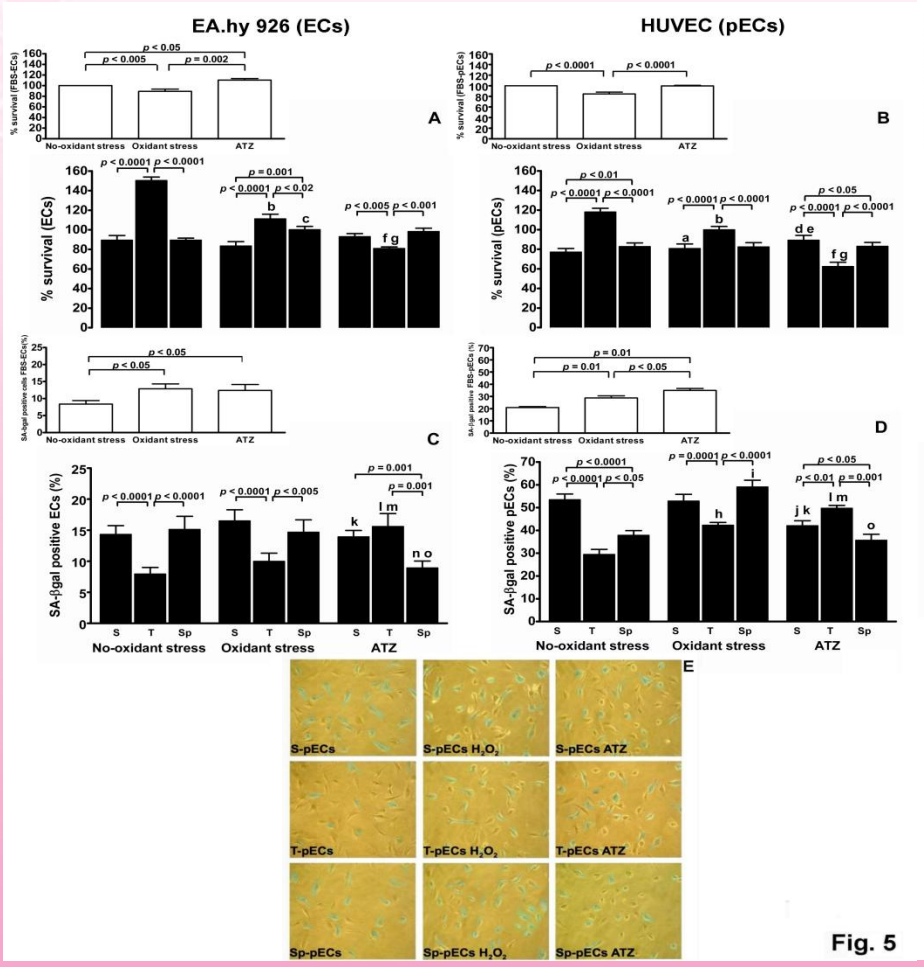
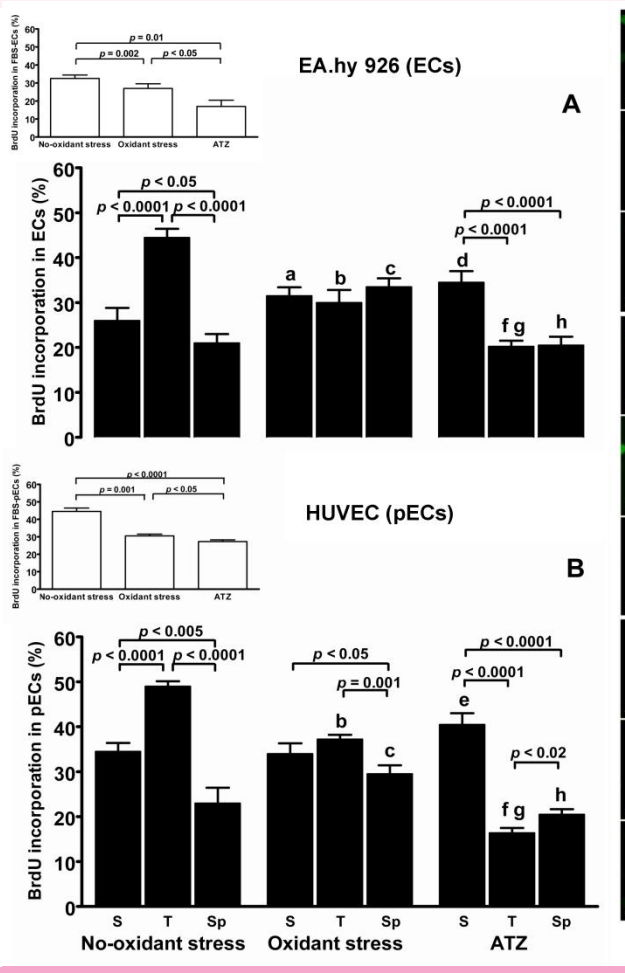



Fig. 5



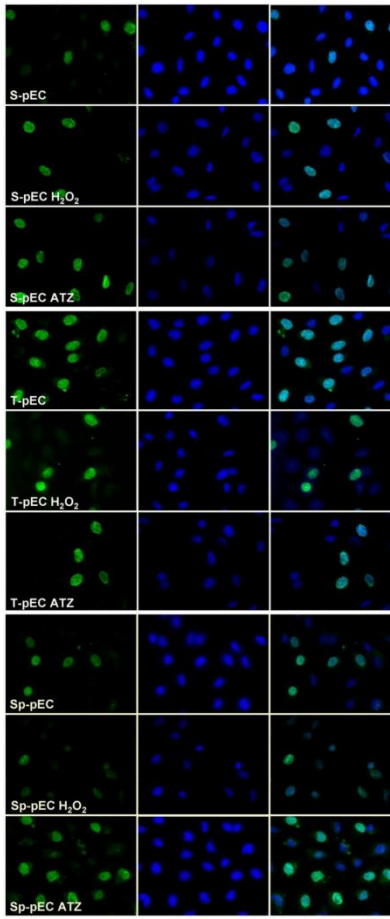




Fig.

Rejuvenation Res. 2008 Feb;11(1):139-50.

## Exercise training promotes SIRT1 activity in aged rats.

Ferrara N, Rinaldi B, Corbi G, Conti V, Stiuso P, Boccuti S, Rengo G, Rossi F, Filippelli A.

Med Sci Sports Exerc. 2012 Jan;44(1):39-49. doi: 10.1249/MSS.0b013e318227f69c.

## Oxidative stress effects on endothelial cells treated with different athletes' sera.

Conti V, Corbi G, Russomanno G, Simeon V, Ferrara N, Filippelli W, Limongelli F, Canonico R, Grasso C, Stiuso P, Dicitore A, Filippelli A.

Med Sci Sports Exerc. 2013 Apr;45(4):644-53. doi: 10.1249/MSS.0b013e318279fb59.

## Aerobic training workload affects human endothelial cells redox homeostasis.

Conti V, Russomanno G, Corbi G, Guerra G, Grasso C, Filippelli W, Paribello V, Ferrara N, Filippelli A.

# Rappresentazione del decadimento funzionale nella vecchiaia derivata dallo schema proposto dall'OMS

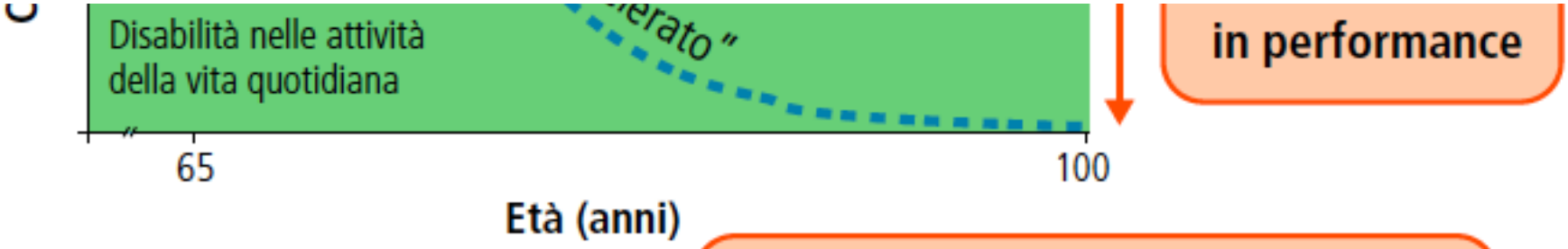
Mantenimento dell'indipendenza

J Geriatr Cardiol. 2012 Mar;9(1):68-75. doi: 10.3724/SP.J.1263.2012.00068.

**Cardiac rehabilitation and exercise therapy in the elderly: Should we invest in the aged?**

Menezes AR, Lavie CJ, Milani RV, Arena RA, Church TS.

Department of Cardiovascular Diseases, John Ochsner Heart and Vascular Institute Ochsner Clinical School, The University of Queensland School of Medicine, 1514, Jefferson Highway, New Orleans, LA 70121, USA.




in performance

Riabilitazione
Miglioramento della qualità di vita

European Heart Journal (2003) 24, 2161–2163

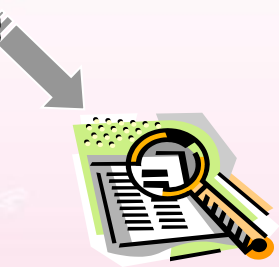
Editorial

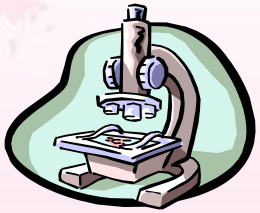
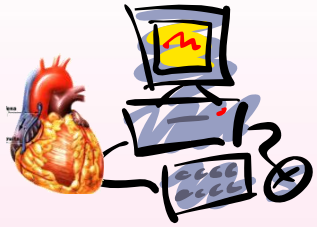
# Oxidative stress in heart failure

## More than just damage

David J. Grieve, Ajay M. Shah*

Popolazione in studio: 50 pazienti over 60 con scompenso cardiaco post-ischemico, sottoposti a Riabilitazione cardiaca di 8 settimane



Variabili demografico-antropometriche

Comorbilità e fattori di rischio

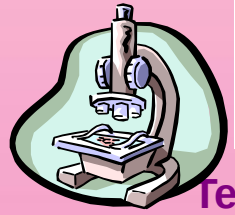
Variabili ematochimiche

Variabili ecocardiografiche

Test ergospirometrico

dopo 8 settimane

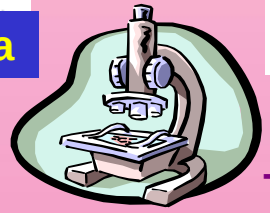
5 giorni/settimana per 30 min + ginnastica respiratoria
+ educazione sanitaria per ~ 4 settimane.



Test ergospirometrico

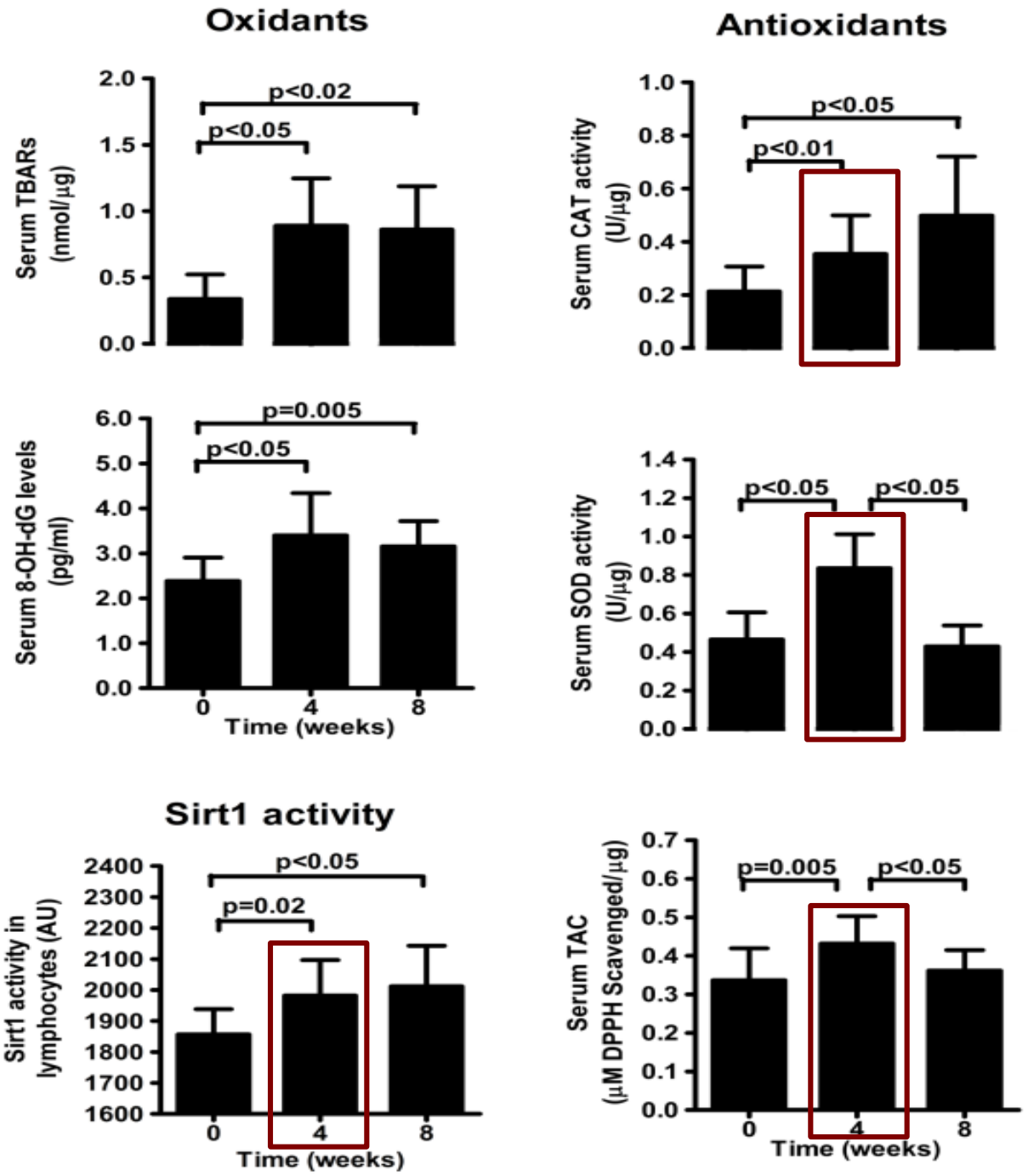
Variabili ematochimiche

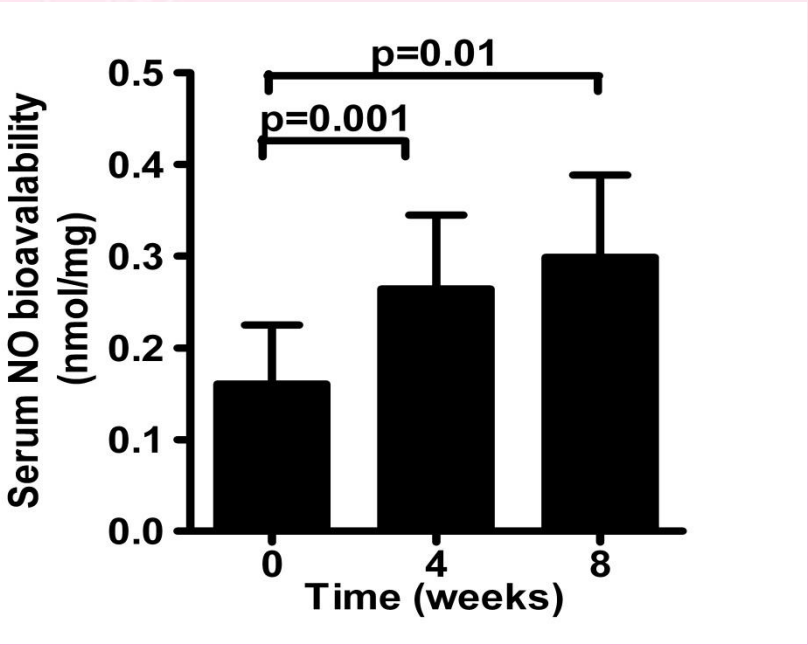
Terapia

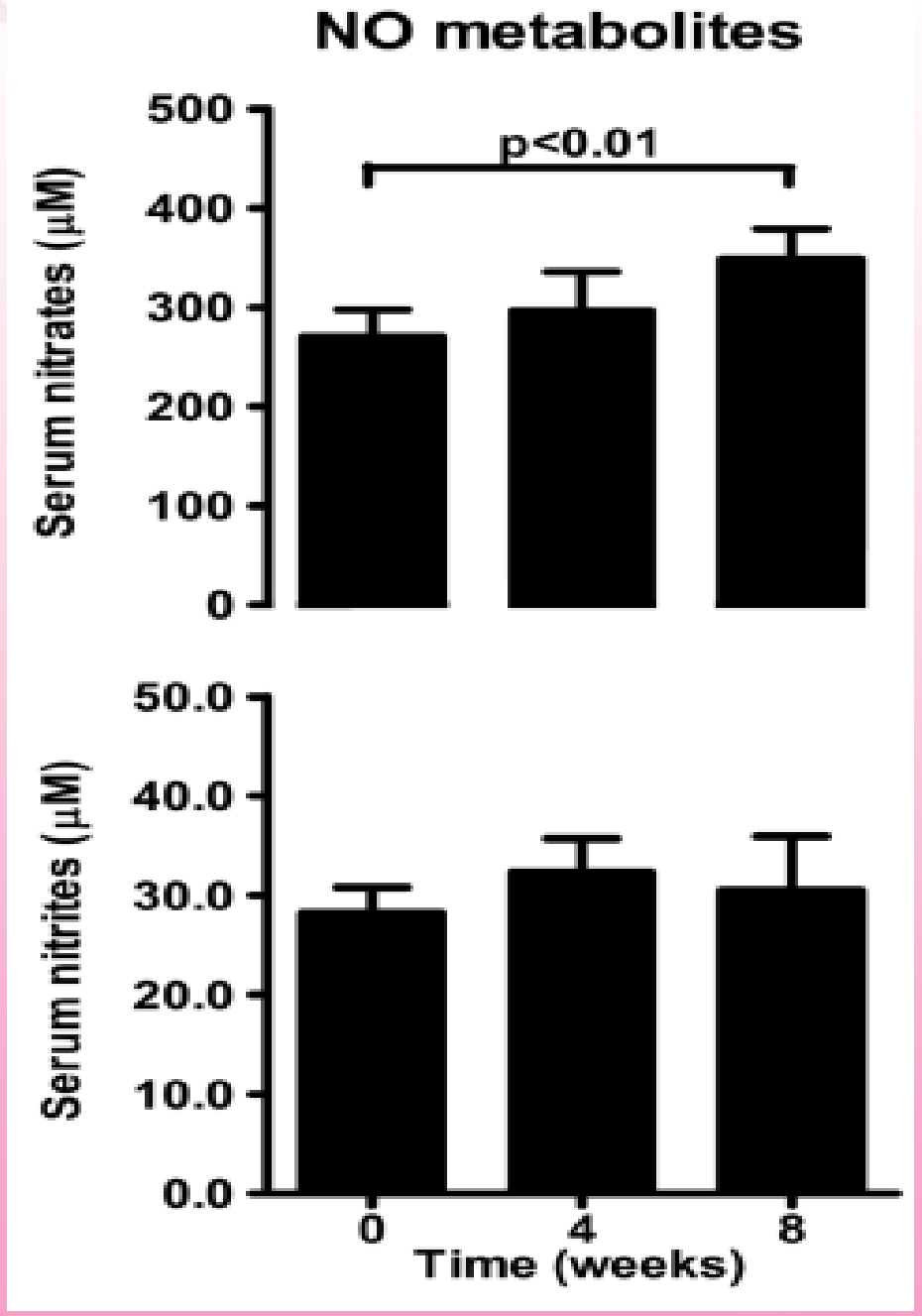


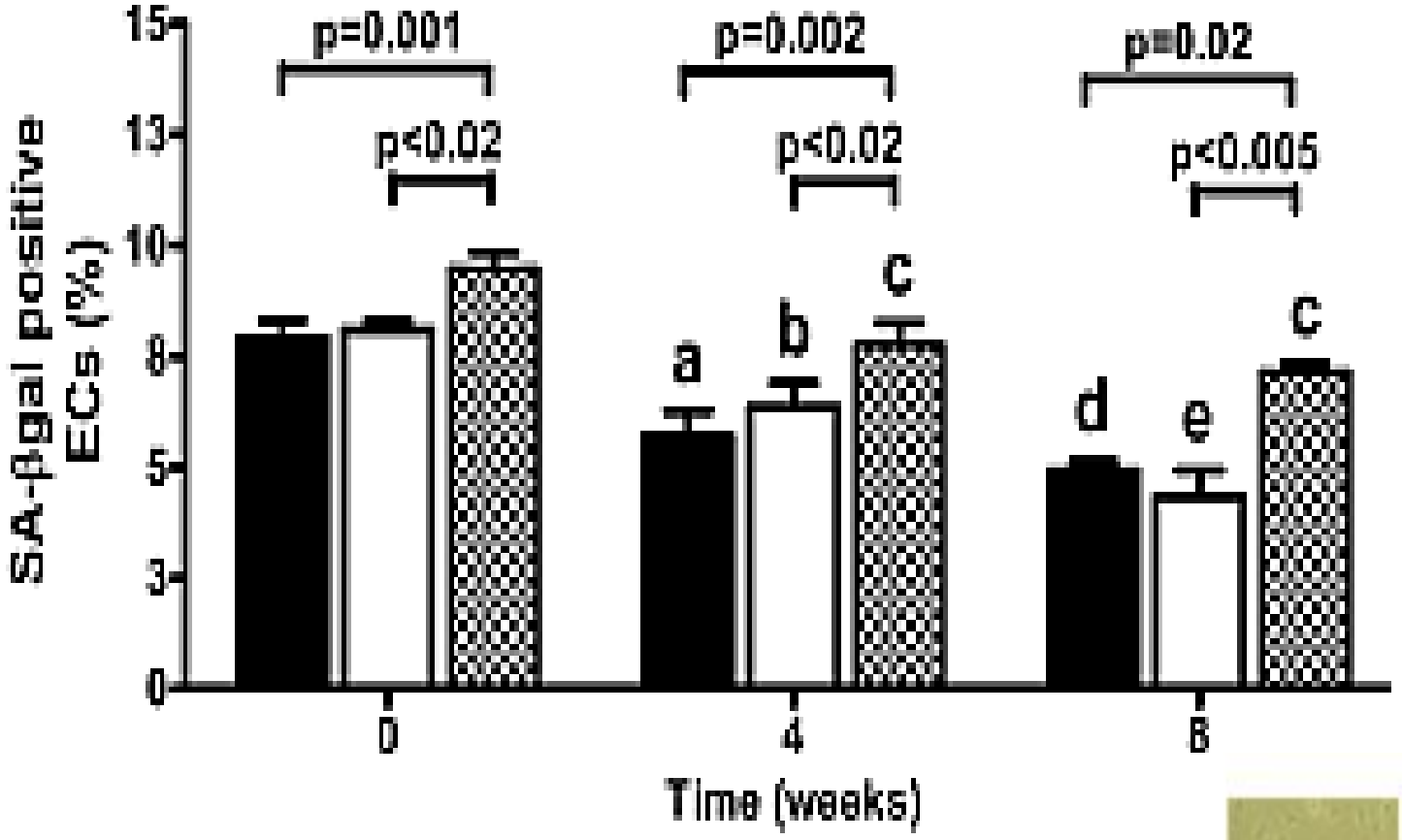
Test ergospirometrico

Variabili ematochimiche

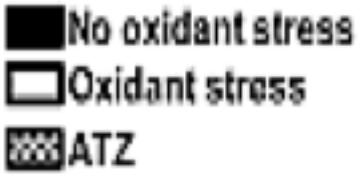

Oxidants
Serum TBARs (nmol/μg)
2.0
1.5
1.0
0.5
0.0
p<0.02
p<0.05
Serum 8-OH-dG levels (pg/ml)
6.0
5.0
4.0
3.0
2.0
1.0
0.0
p=0.005
p<0.05
0
4
8
Time (weeks)
Antioxidants
Serum CAT activity (U/μg)
1.0
0.8
0.6
0.4
0.2
0.0
p<0.05
p<0.01
Serum SOD activity (U/μg)
1.4
1.2
1.0
0.8
0.6
0.4
0.2
0.0
p<0.05
p<0.05
Sirt1 activity
Sirt1 activity in lymphocytes (AU)
2400
2300
2200
2100
2000
1900
1800
1700
1600
p<0.05
p=0.02
0
4
8
Time (weeks)
Serum TAC (μM DPPH Scavenged/μg)
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0.0
p=0.005
p<0.05
0
4
8
Time (weeks)

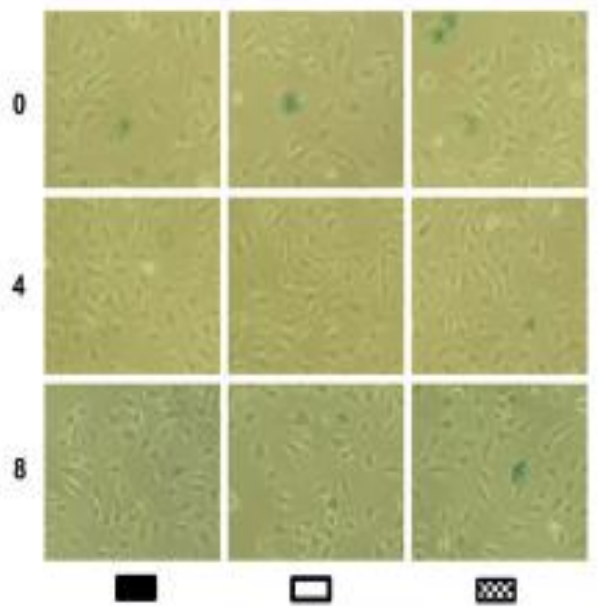

p=0.01
p=0.001
Serum NO bioavalability (nmol/mg)
0.5
0.4
0.3
0.2
0.1
0.0
0
4
8
Time (weeks)


NO metabolites
p<0.01
Serum nitrates (μM)
500
400
300
200
100
0
Serum nitrites (μM)
50.0
40.0
30.0
20.0
10.0
0.0
0
4
8
Time (weeks)

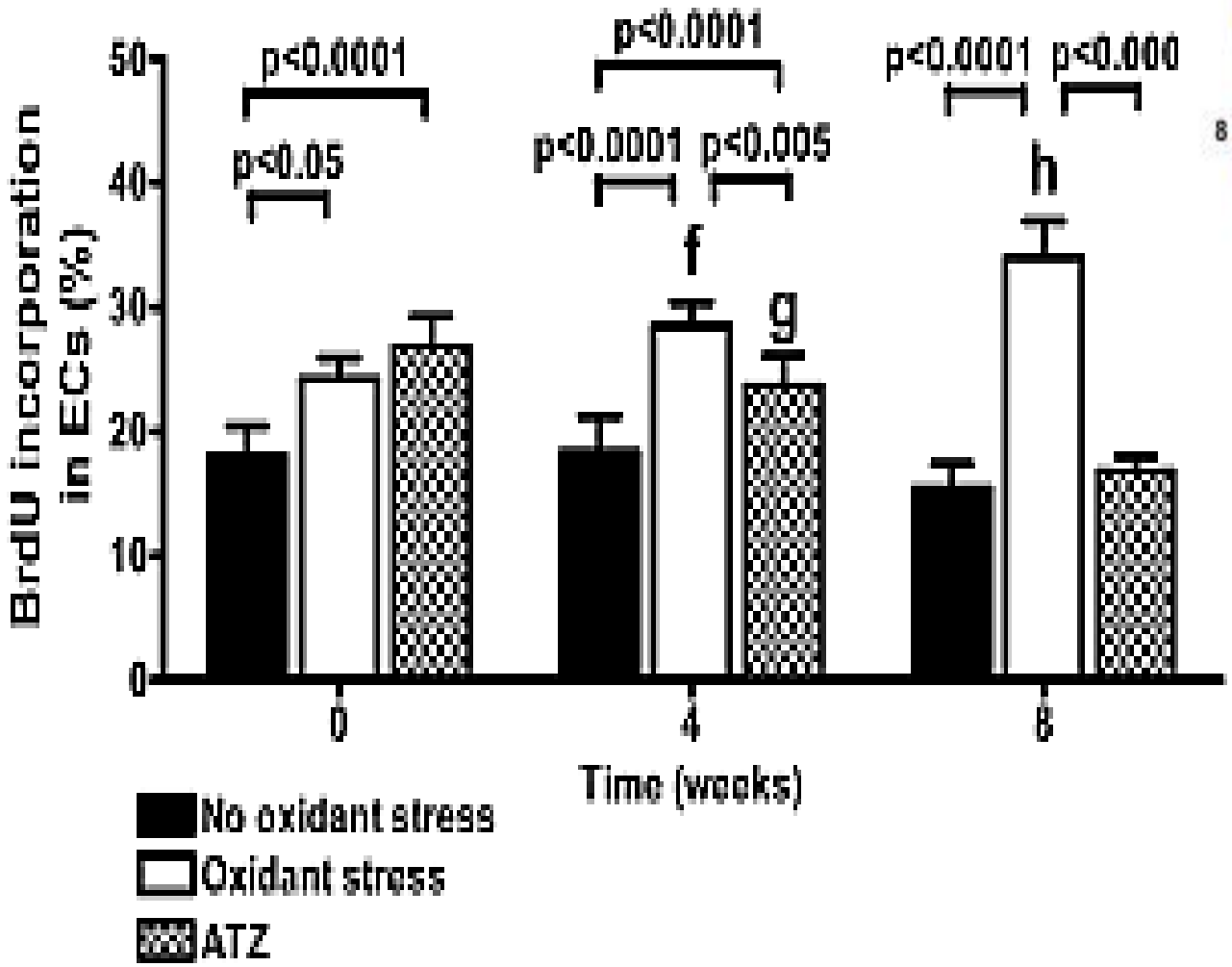


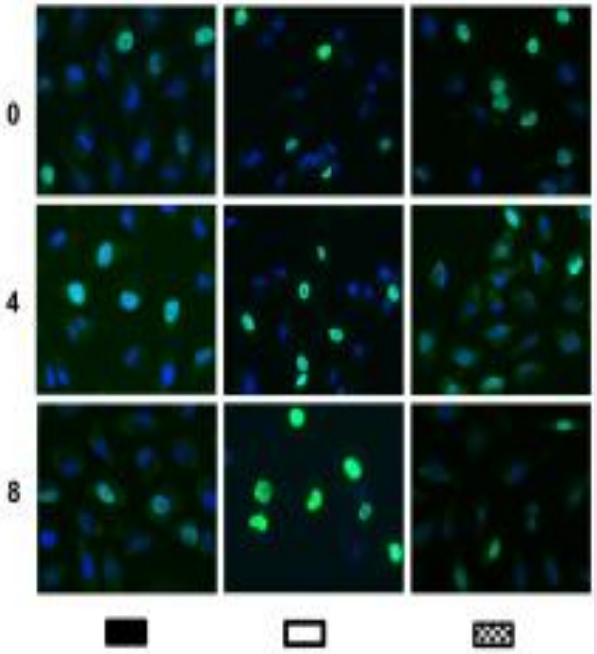

Effetti della RC sulla senescenza di cellule endoteliali trattate con il siero dei pazienti in assenza e presenza di stress e dopo trattamento con ATZ

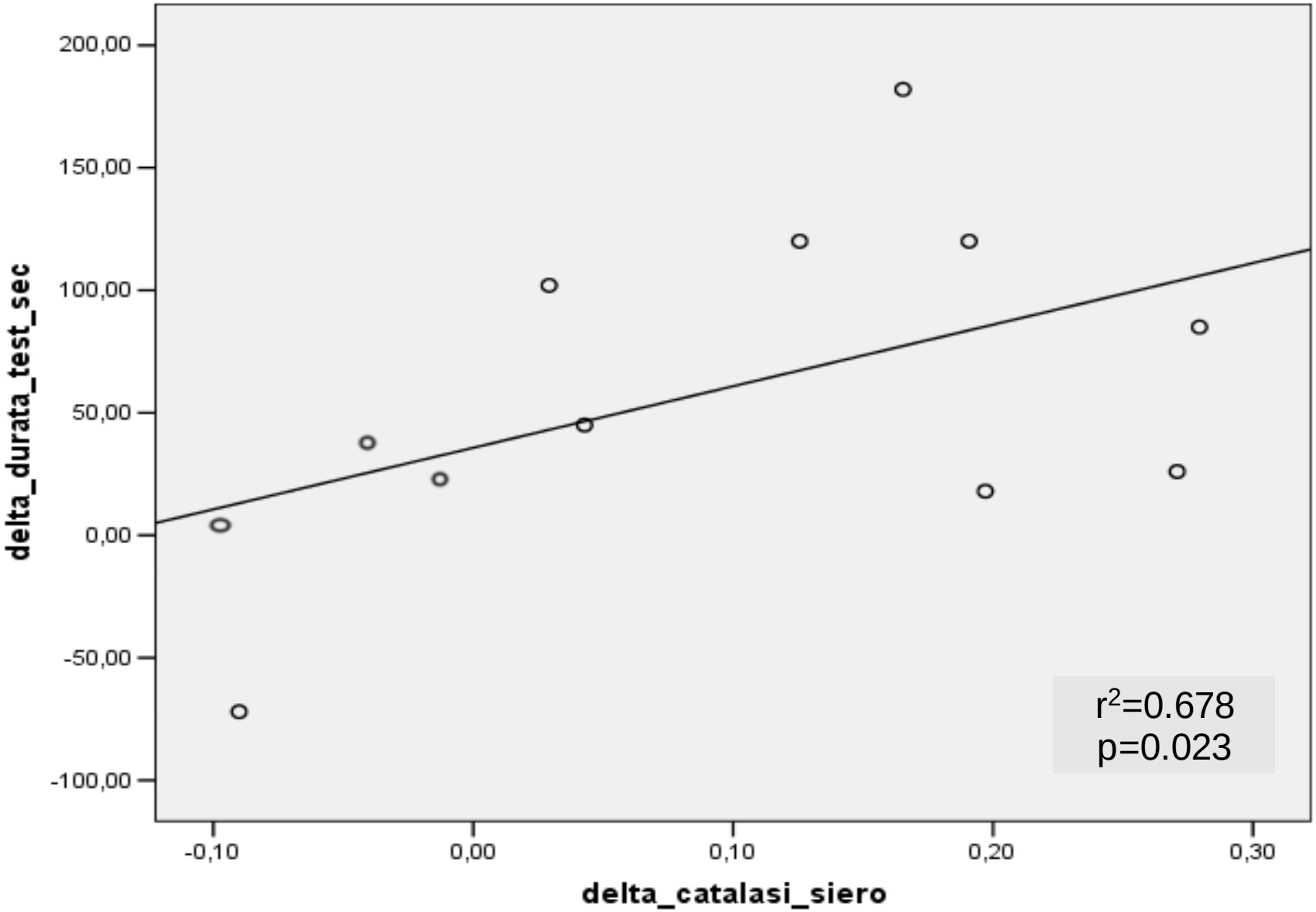


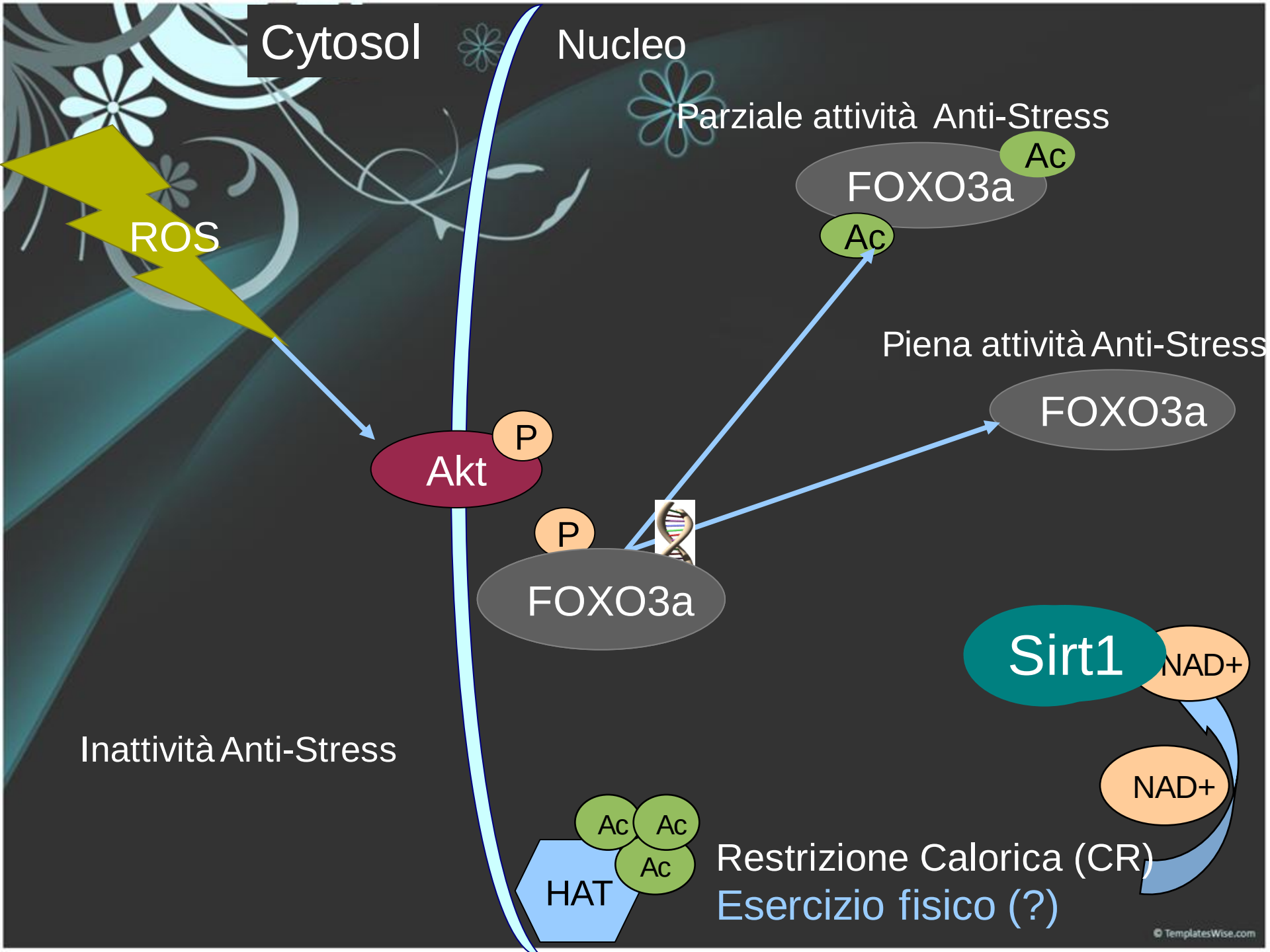
Effetti della RC sulla proliferazione di cellule endoteliali trattate con il siero dei pazienti in assenza e presenza di stress e dopo trattamento con ATZ





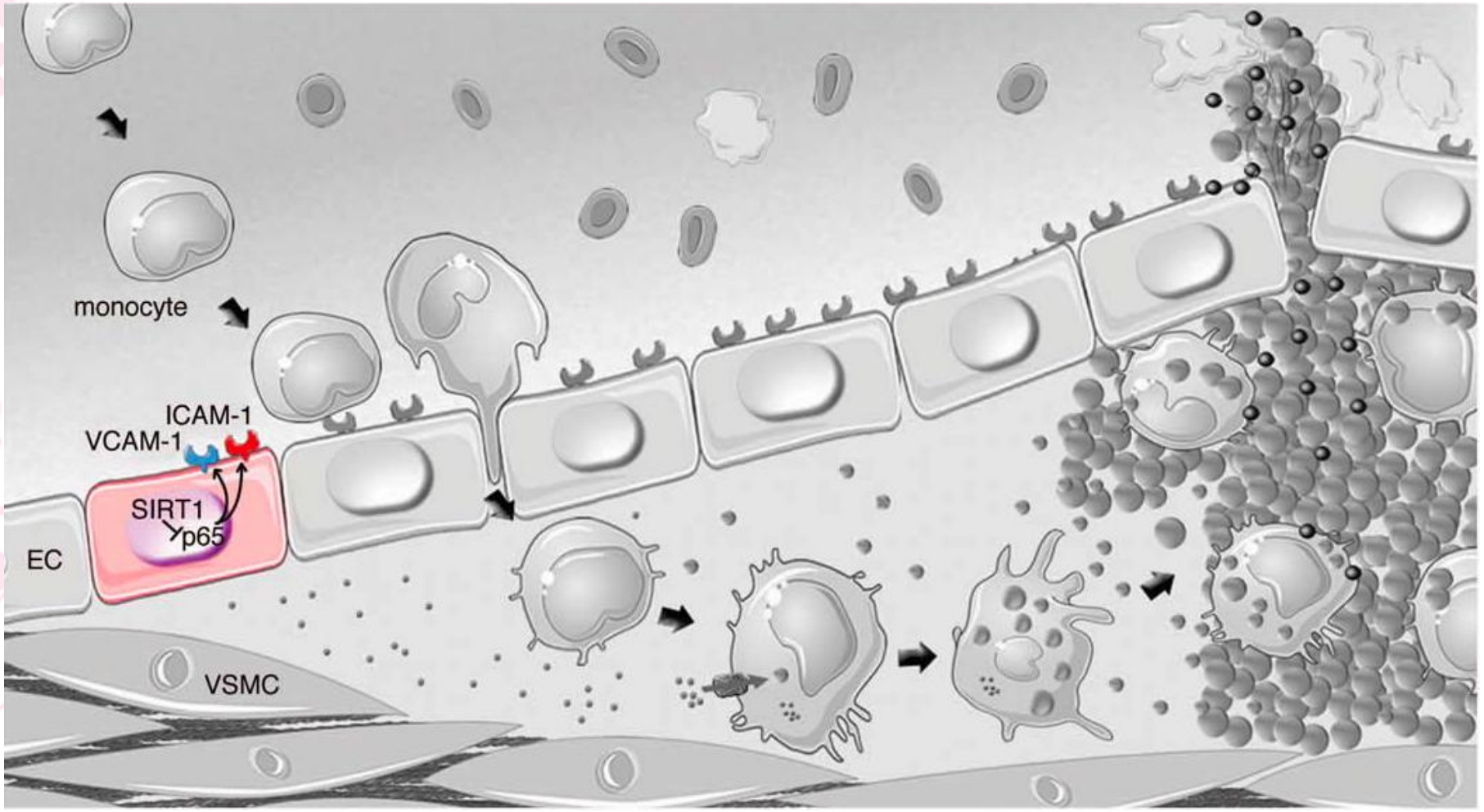

Stress test duration (min) 8'07" ±1'43" p<0.0001 p<0.0001


Cytosol
Nucleo
Parziale attività Anti-Stress
Ac
FOXO3a
Ac
ROS
Piena attività Anti-Stress
FOXO3a
P
Akt
P
FOXO3a
Sirt1
NAD+
NAD+
Inattività Anti-Stress
Ac
Ac
Ac
HAT
Restrizione Calorica (CR)
Esercizio fisico (?)
© TemplatesWise.com

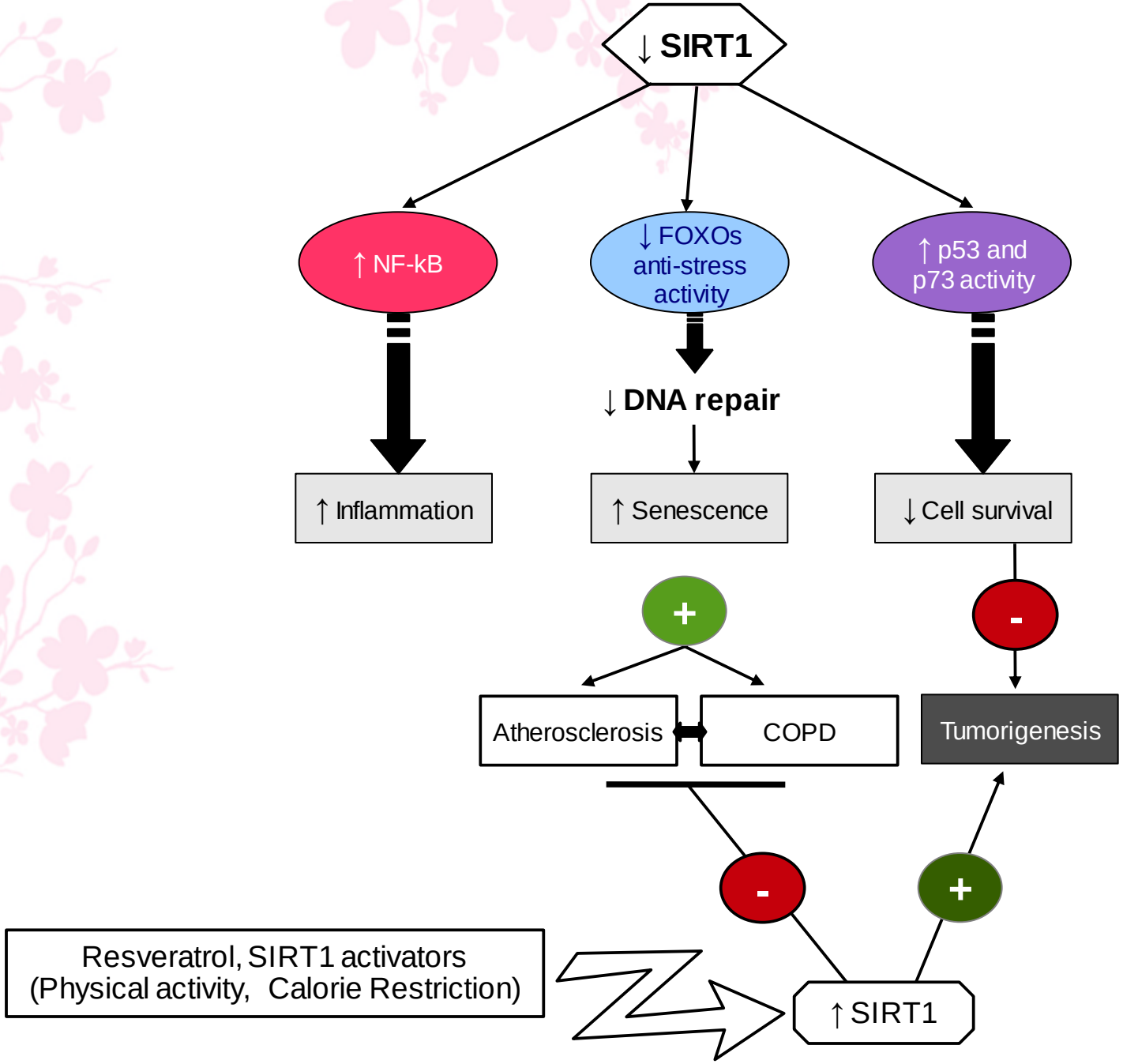
Cell Cycle 10:4, 640-647; February 15, 2011; © 2011 Landes Bioscience

# Protective roles of SIRT1 in atherosclerosis

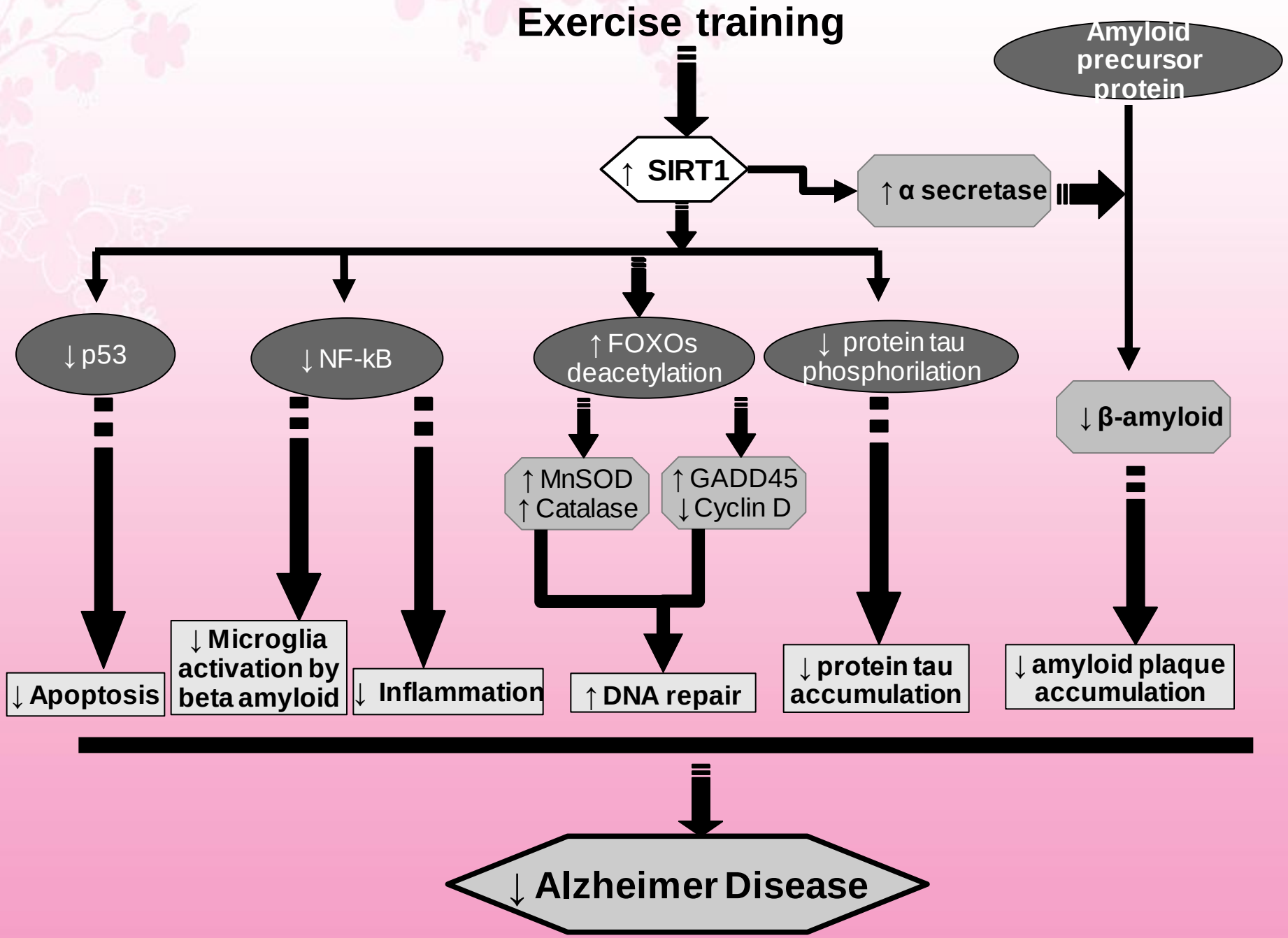
Sokrates Stein and Christian M. Matter

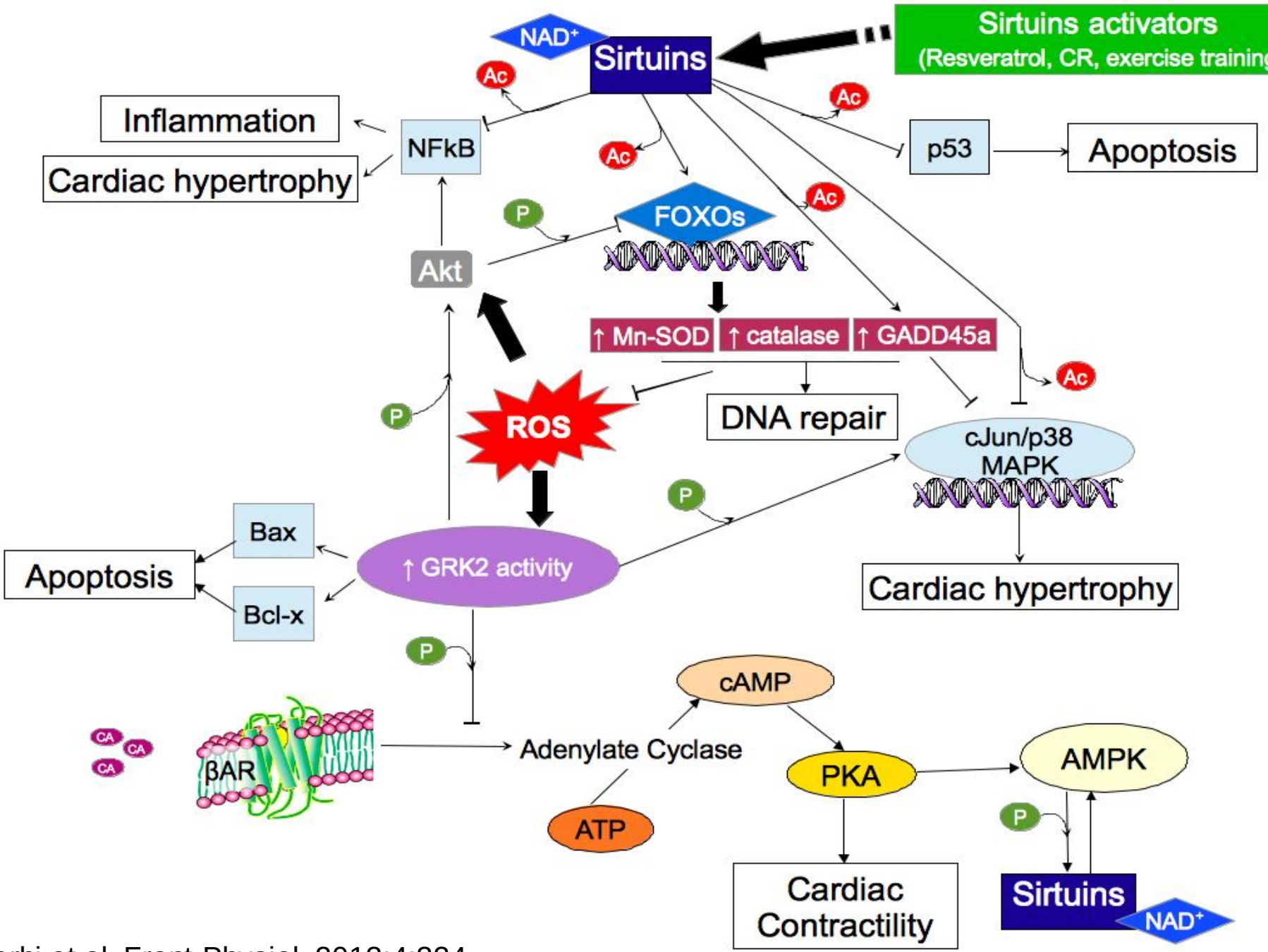



*Cell Cycle 2011;10(4): 640-647*




Corbi et al. Int J Mol Sci. 2013;14(6):12696-713.


Exercise training
Amyloid precursor protein
↑ SIRT1
↑ α secretase
↓ p53
↓ NF-kB
↑ FOXOs deacetylation
↓ protein tau phosphorilation
↓ β-amyloid
↑ MnSOD
↑ Catalase
↑ GADD45
↓ Cyclin D
↓ Apoptosis
↓ Microglia activation by beta amyloid
↓ Inflammation
↑ DNA repair
↓ protein tau accumulation
↓ amyloid plaque accumulation
↓ Alzheimer Disease

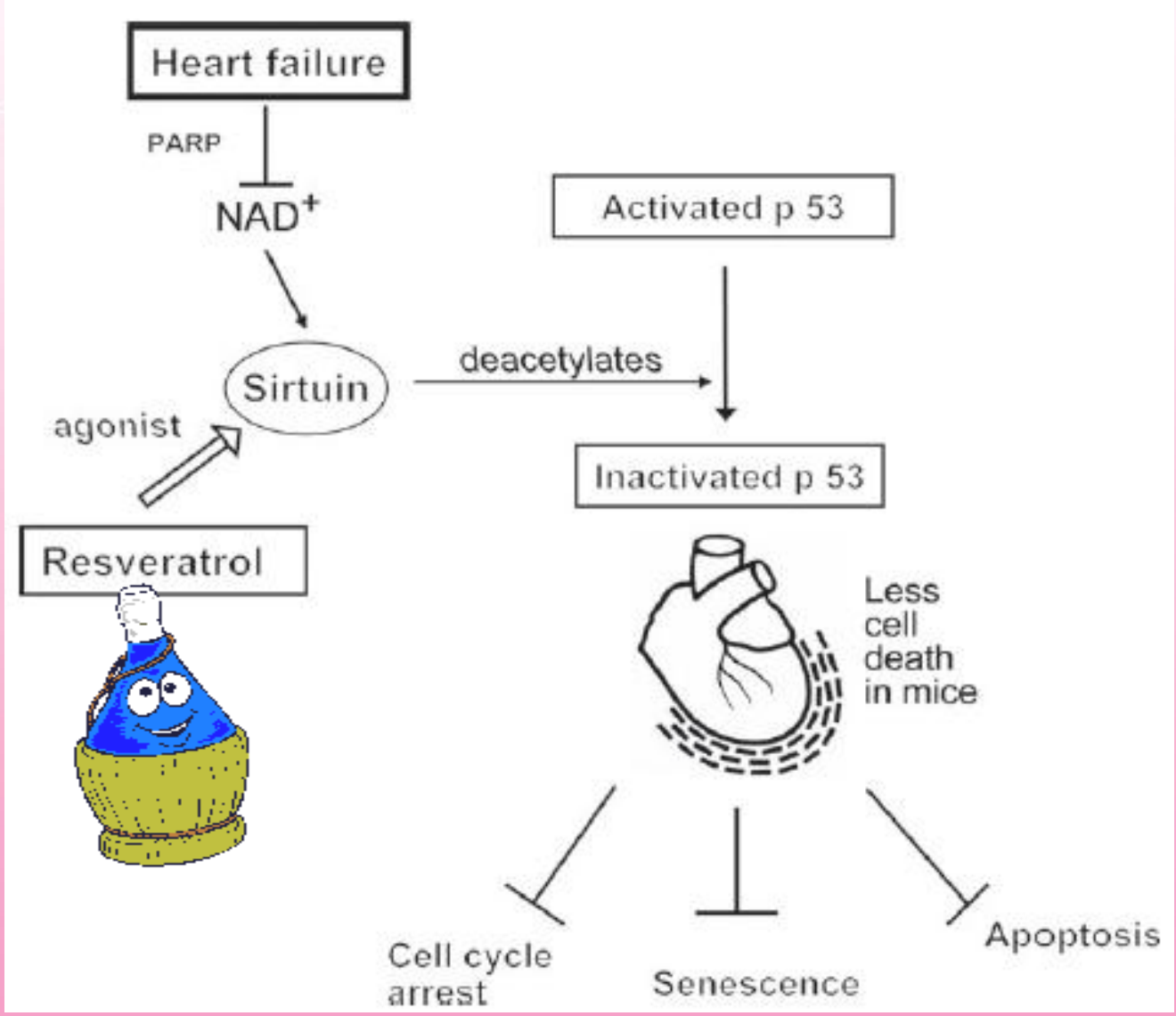



Corbi et al. Front Physiol. 2013;4:324.

Eur Heart J. 2007 Jul;28(14):1683-93. Epub 2007 Jun 7.

# The red wine hypothesis: from concepts to protective signalling molecules.

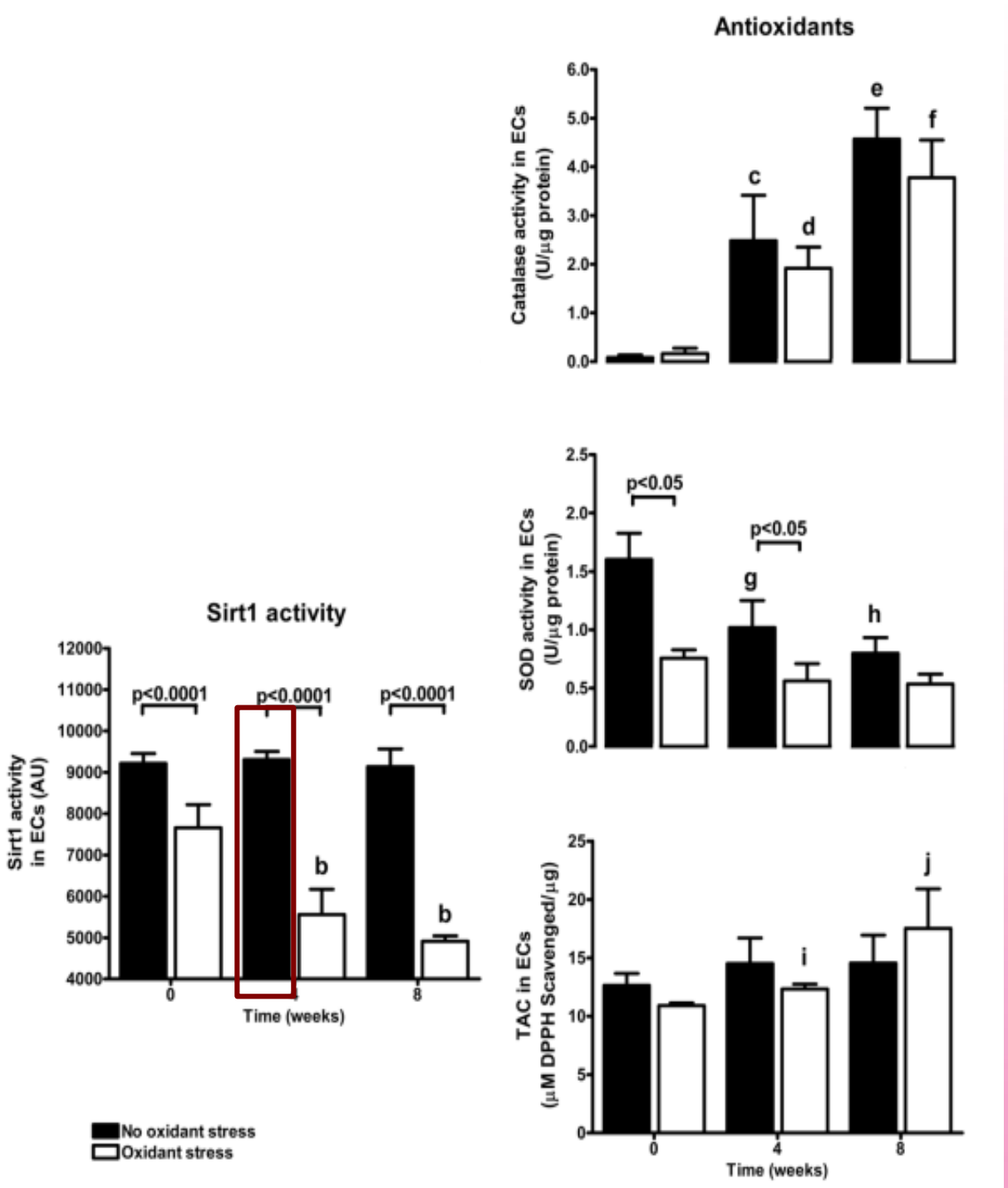
Opie LH, Lecour S.



*If I knew I was going to live this long, I would have taken better care of myself*

*James Hubert Blake*

*Grazie per l'attenzione*


Antioxidants
Catalase activity in ECs (U/μg protein)
6.0
5.0
4.0
3.0
2.0
1.0
0.0
c
d
e
f
SOD activity in ECs (U/μg protein)
2.5
2.0
1.5
1.0
0.5
0.0
p<0.05
p<0.05
g
h
TAC in ECs (μM DPPH Scavenged/μg)
25
20
15
10
5
0
i
j
0
4
8
Time (weeks)
Sirt1 activity
Sirt1 activity in ECs (AU)
12000
11000
10000
9000
8000
7000
6000
5000
4000
p<0.0001
p<0.0001
p<0.0001
b
b
0
8
Time (weeks)
No oxidant stress
Oxidant stress