



PLATFORM OF LABORATORIES FOR ADVANCES IN CARDIAC EXPERIENCE

ROMA

Centro Congressi
di Confindustria
Auditorium
della Tecnica

9^a Edizione

30 Settembre
1 Ottobre
2022

PREVENZIONE CARDIOVASCOLARE

**Stress ossidativo e
rischio cardiovascolare
in età pediatrica**

Martino F.



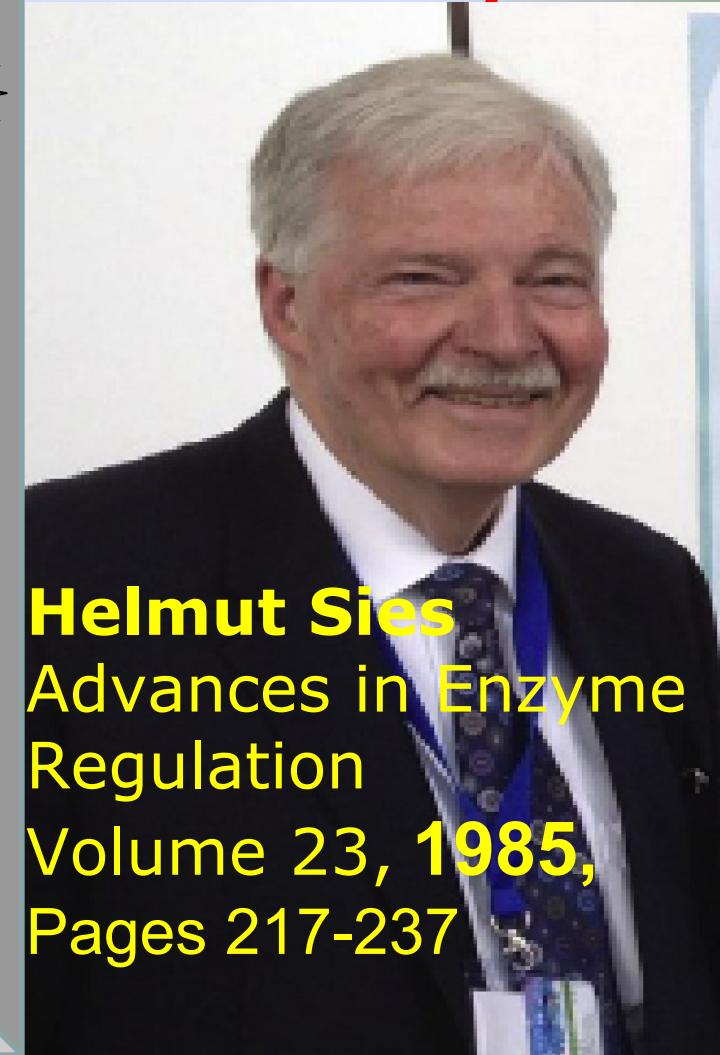
- Infiammazione
- proliferazione
- apoptosi
- Migrazione
- fibrosi

- compromissione della funzione vascolare,
- rimodellamento cardiovascolare,
- disfunzione renale,
- attivazione cellulare immunitaria
- ipertensione.

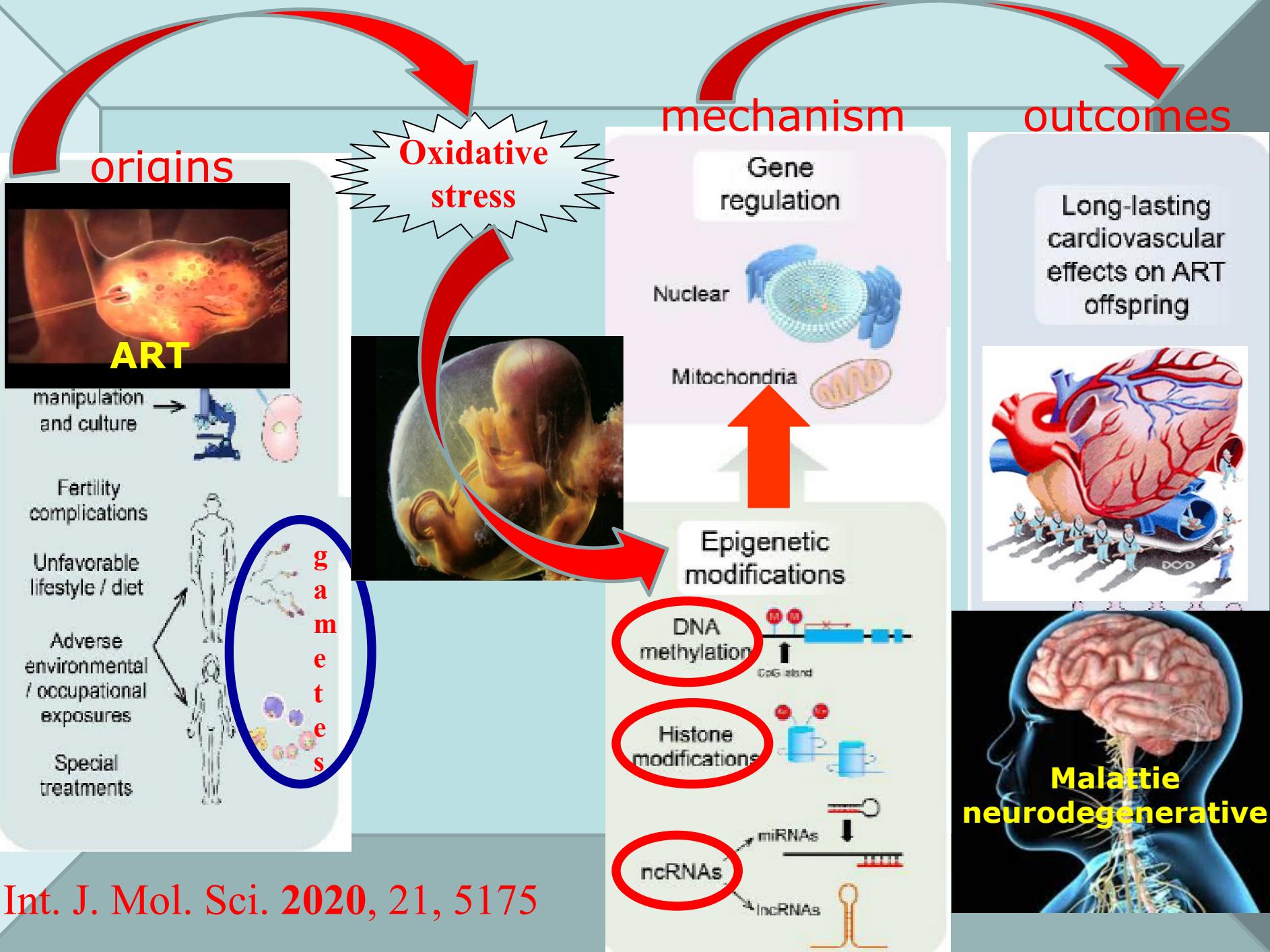
Oxidative Medicine and
Cellular Longevity
Volume 2020, Article ID 5732956

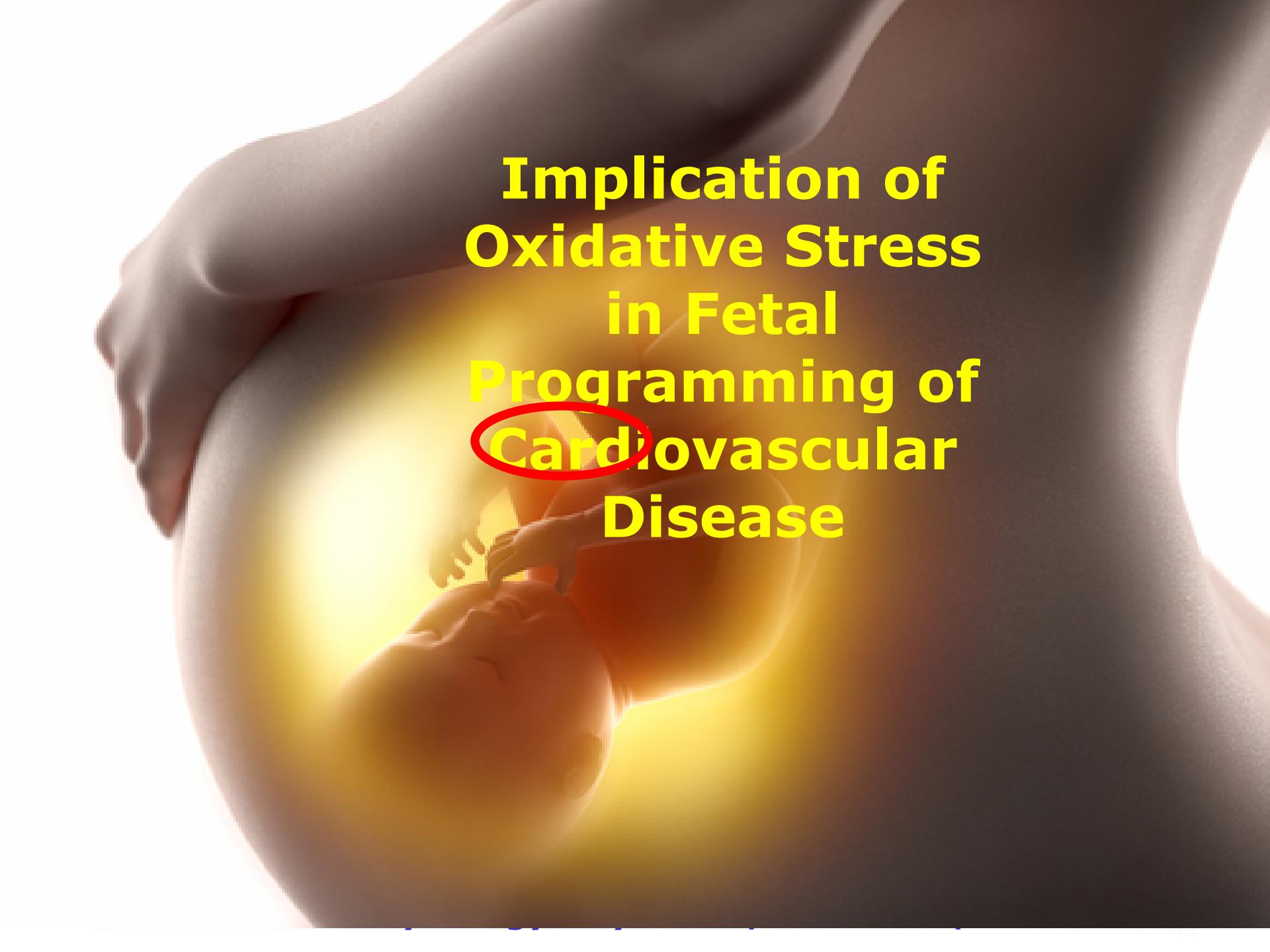


Oxidative stress (OS) is related to an excess of reactive oxygen species (ROS) and a decrease in antioxidant enzymes.



Helmut Sies
Advances in Enzyme Regulation
Volume 23, 1985,
Pages 217-237





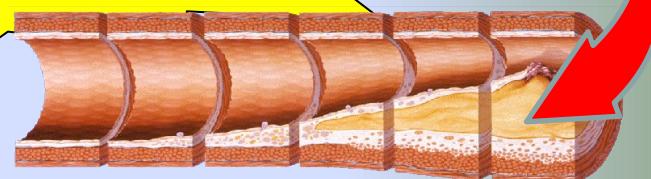
Implication of Oxidative Stress in Fetal Programming of Cardiovascular Disease

The text is displayed in a large, bold, yellow font. The word "Cardiovascular" is circled in red.

Mitochondrial Dysfunction and DNA Damage in the Context of Pathogenesis of Atherosclerosis

The effects of increased mitochondrial ROS involve endothelial dysfunction, vascular inflammation, and the accumulation of oxidized LDL in the arterial wall.

mitochondrial dysfunction may turn out to be a key link in the pathogenesis of atherosclerosis, and elevated ROS is a likely mediator of this process.



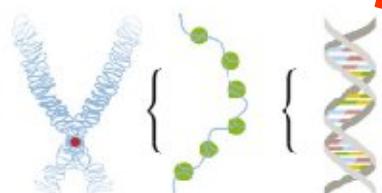
Fetal cardiovascular programming and remodeling associated to fetal growth restriction

PLACENTAL INSUFFICIENCY

- Undernutrition
- Fetal Hypoxia
- Volume/Pressure overload due to increased placenta resistance

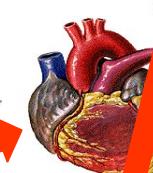
Oxidative
stress

EPIGENETIC CHANGES



- DNA methylation
- Histone modifications
- miRNA dysregulation

IUGR



CARDIOVASCULAR REMODELING

Organ level

- Change in fibre orientation
- Abnormal coronary vascular tree
- Increased vascular intima-media thickness

Tissue level

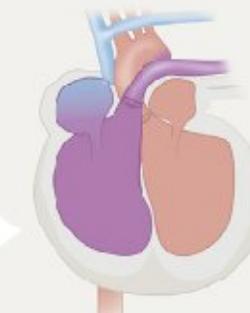
- Reduced number of cardiomyocytes
- Higher cardiomyocyte mean volume
- Diminished capillary length and number

Sub-Cellular level

- Shorter sarcomere length
- Mitochondrial rearrangement
- Change in titin and myosin isoforms

Long-term cardiovascular consequences of fetal growth restriction:

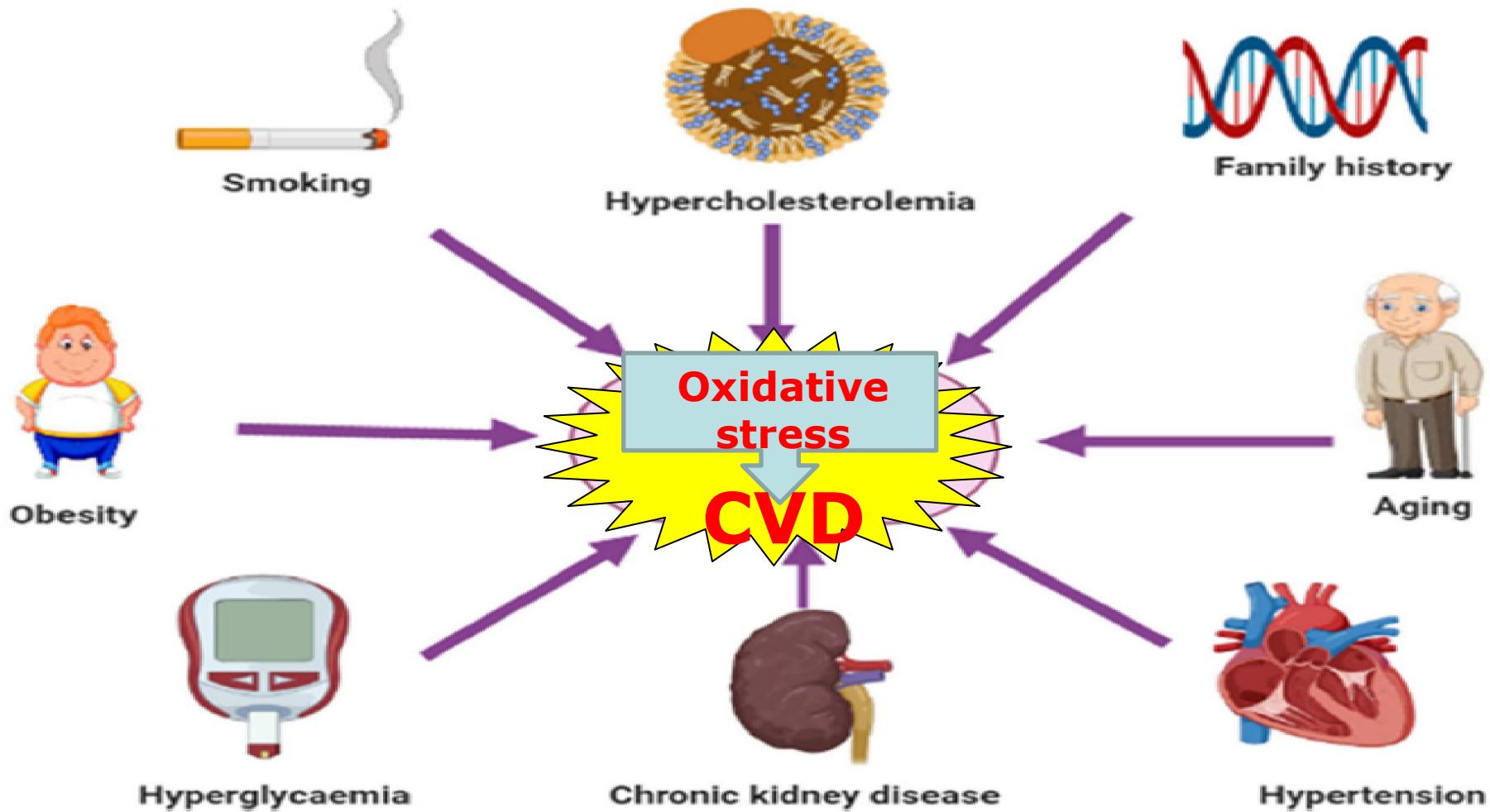
PHENOTYPES OF FETAL CARDIAC REMODELING



Am J Obstet Gynecol. 2018 Feb;218(2S):S869-S879



**Several cardiovascular risk factors,
are associated with enhanced oxidative stress,
which favors the progression of cardiovascular disease**

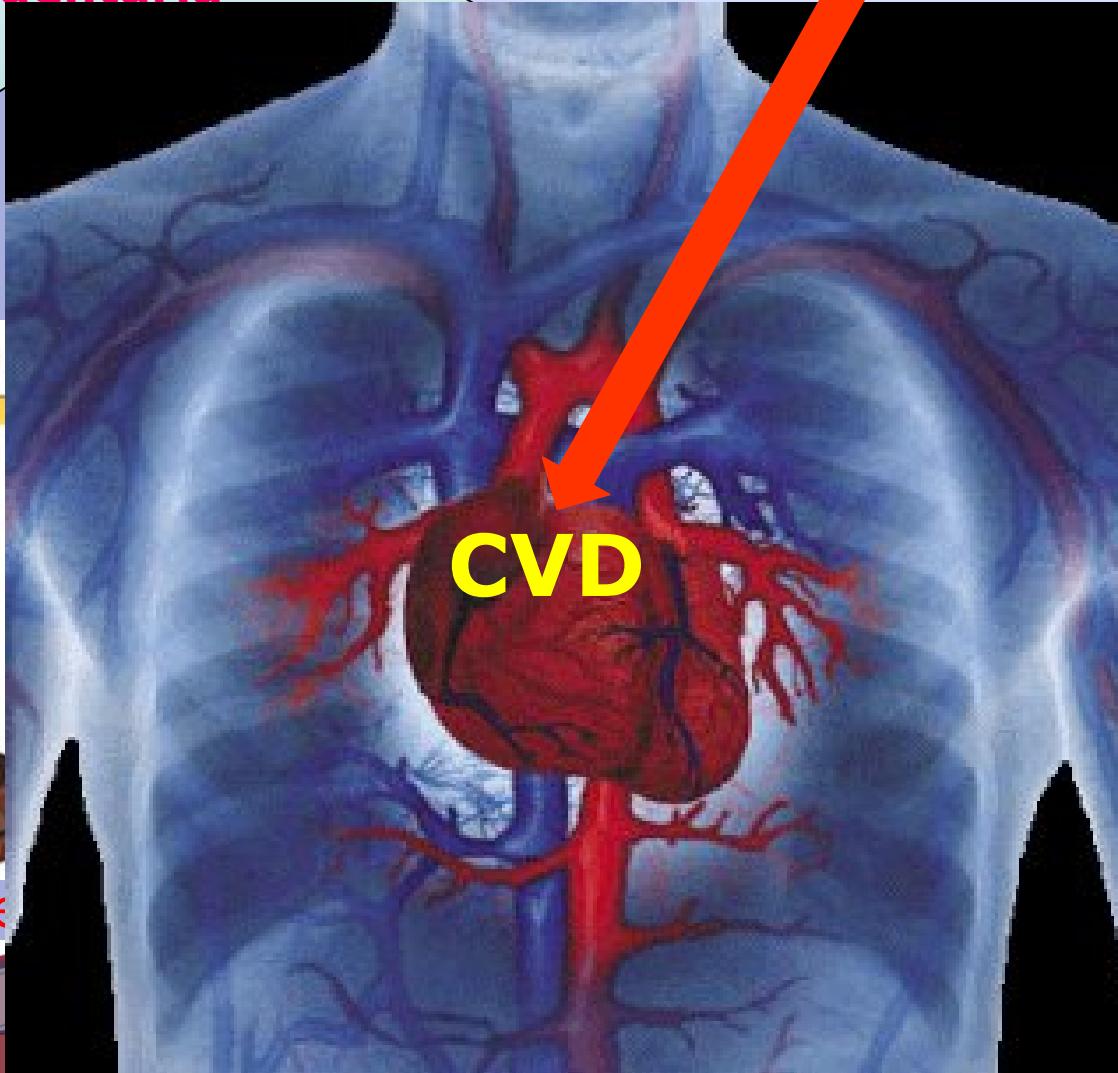


**Dislipidemie
Obesità
Ipertensione Arteriosa
Diabete
Vita sedentaria**

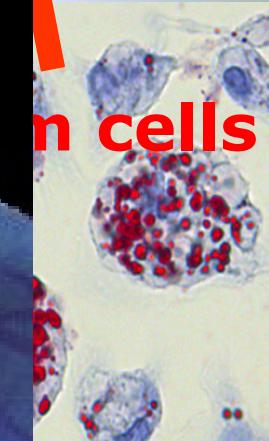
**Fumo
Alcool
Stress**



Disfunzione endothelialia



Aterosclerosi



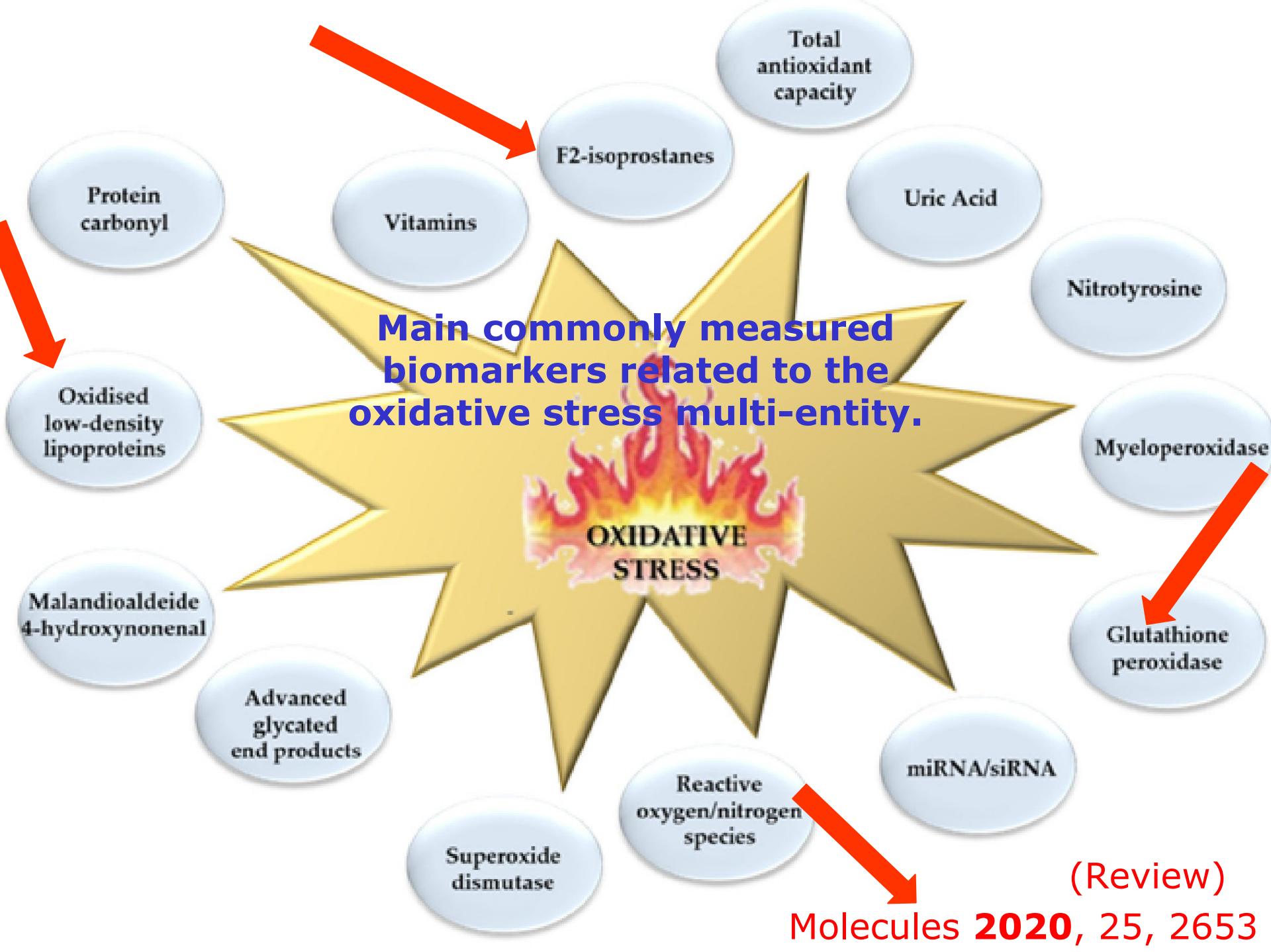


Systemic Inflammation, Oxidative Stress and Cardiovascular Health in Children and Adolescents: A Systematic Review (1228 potentially eligible pediatric articles; 160 articles were included.) (3 articles F. Martino et al.)

Tjaša Hertiš Petek et al. Antioxidants 2022, 11, 894

**The results indicate that
systemic inflammation and oxidative stress
influence cardiovascular health in many chronic
pediatric conditions, including hypertension,
obesity, diabetes mellitus types 1 and 2, chronic
kidney disease, hyperlipidemia and
obstructive sleep apnea.**

**Exercise and diet may diminish ROS formation and
enhance the total serum antioxidant capacity.**

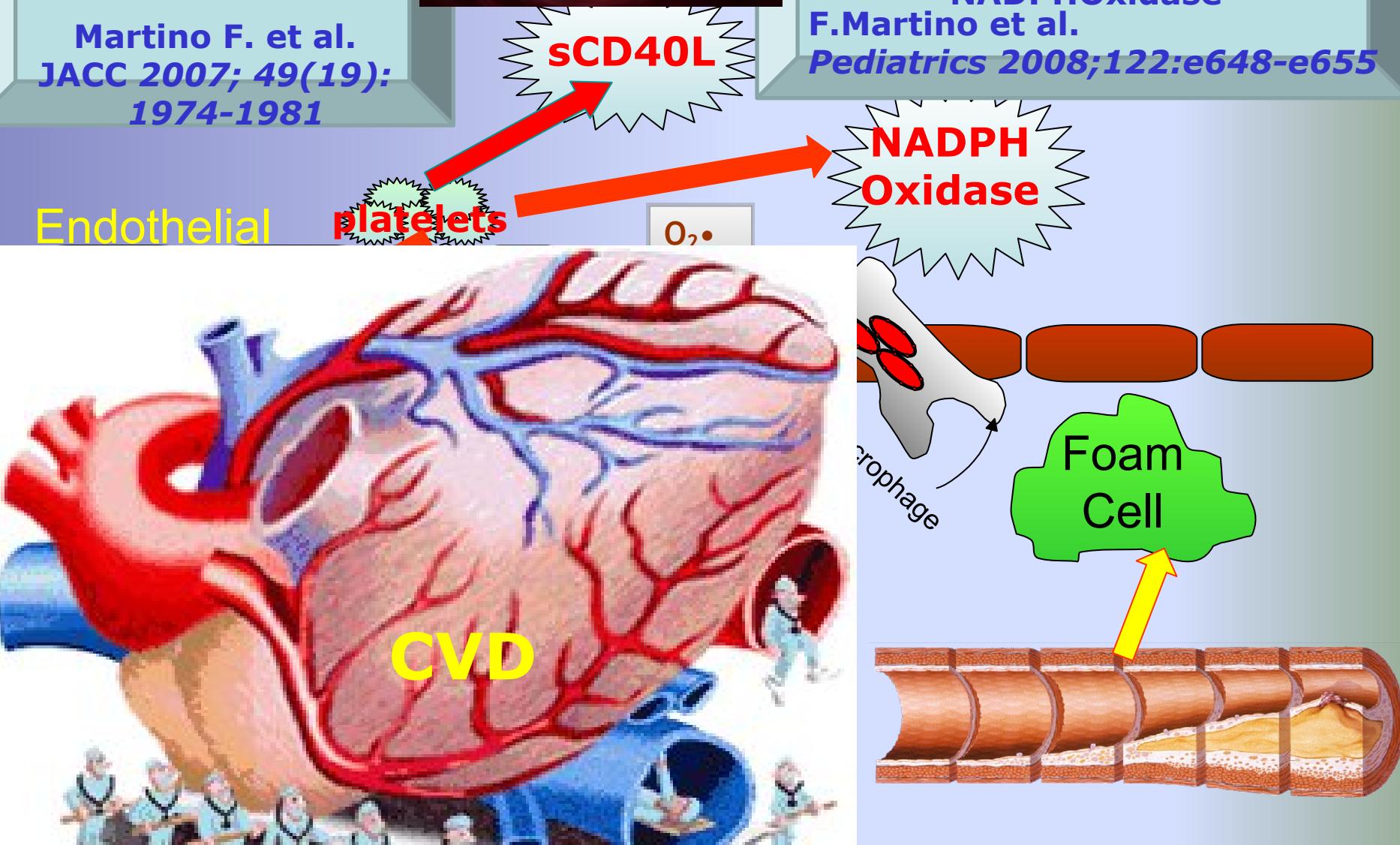


**Early Increase of
Oxidative Stress
and Soluble CD40L
in Children With
Hypercholesterolemia**

Martino F. et al.
JACC 2007; 49(19):
1974-1981

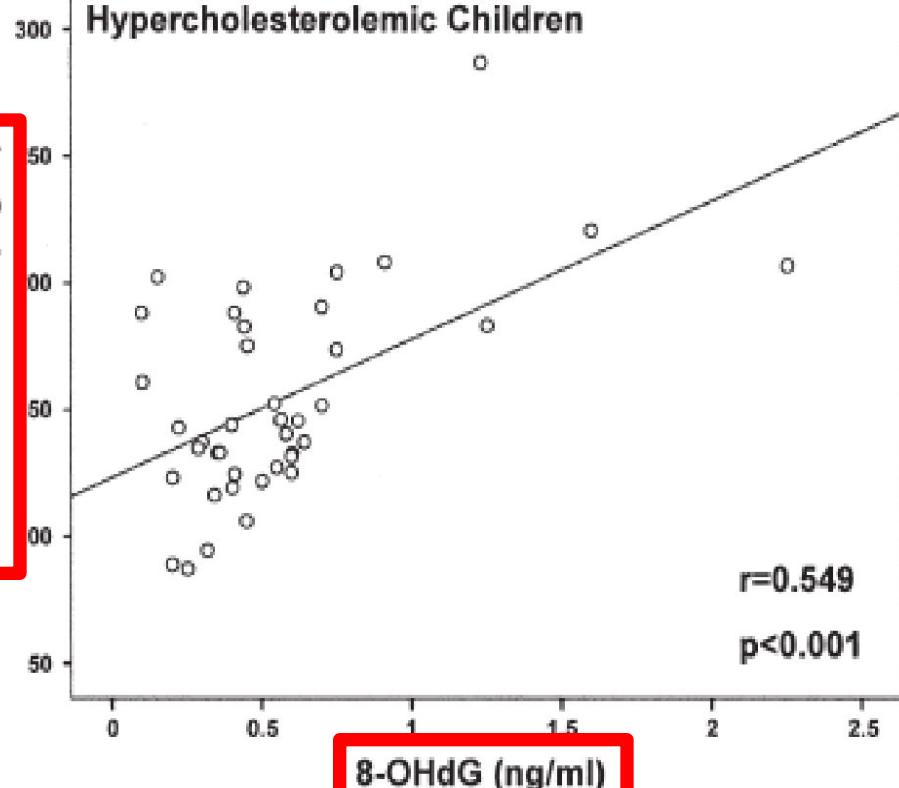


**Oxidative Stress Is Associated
With Arterial Dysfunction and
Enhanced IMT in Children With
Hypercholesterolemia:
The Potential Role of
NADPH Oxidase**
F.Martino et al.
Pediatrics 2008;122:e648-e655





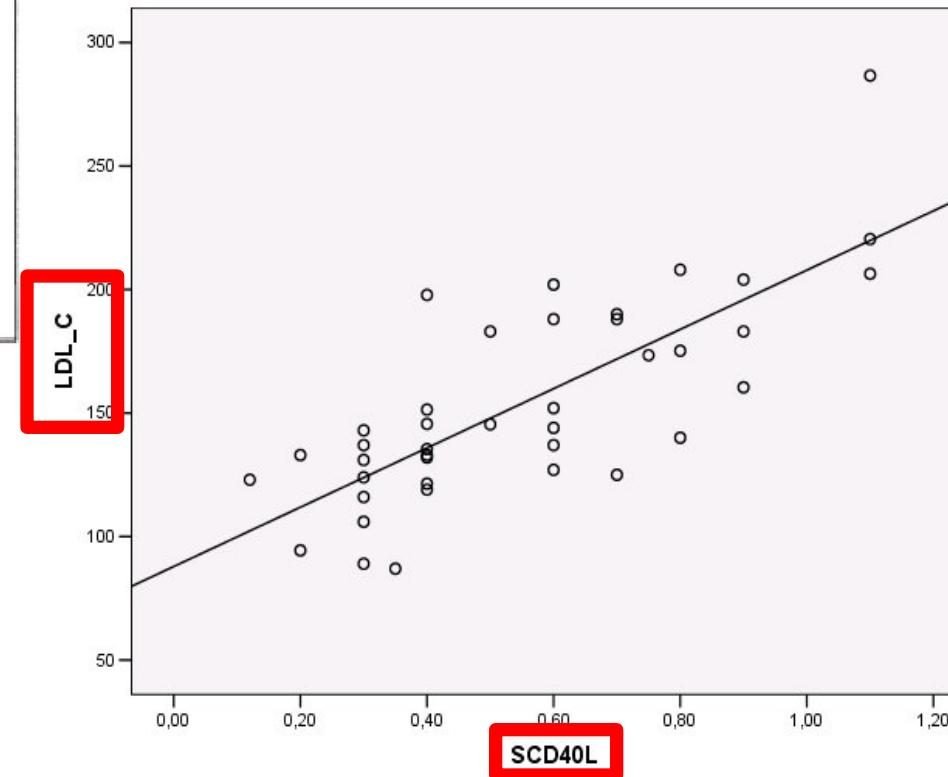
LDL Cholesterol (mg/dl)

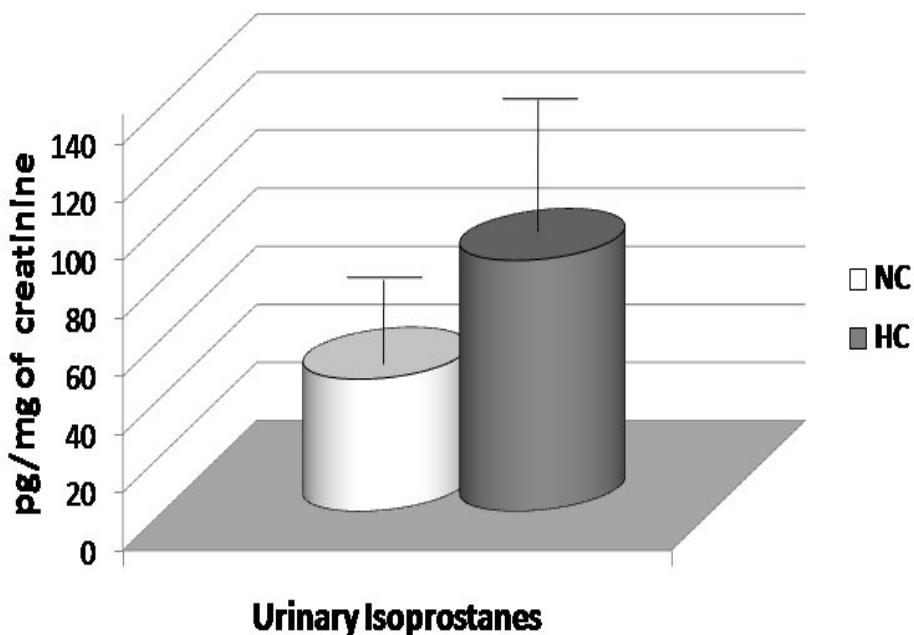
Hypercholesterolemic Children

8-OHdG (ng/ml)

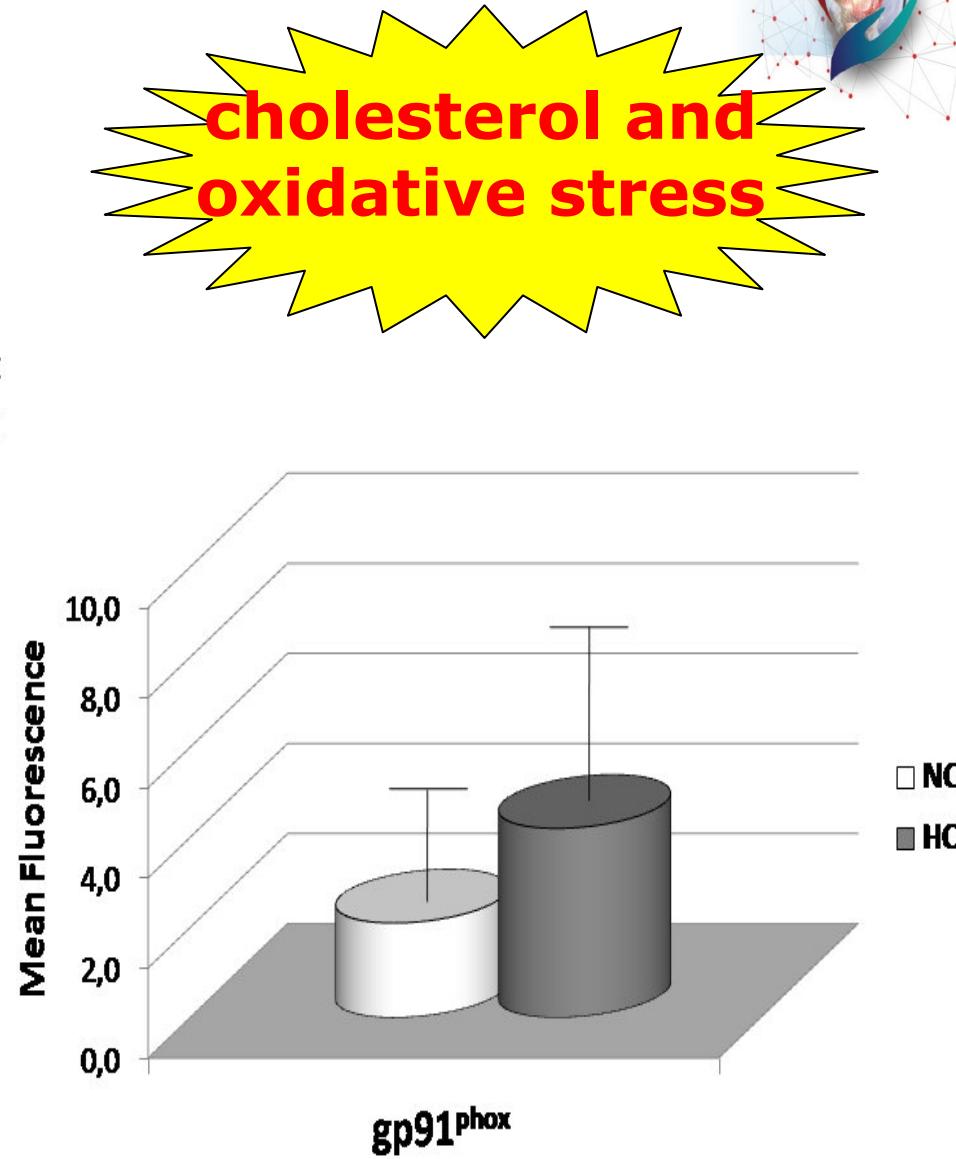
Martino F et al.
J Am Coll Cardiol
2007;49:197-81

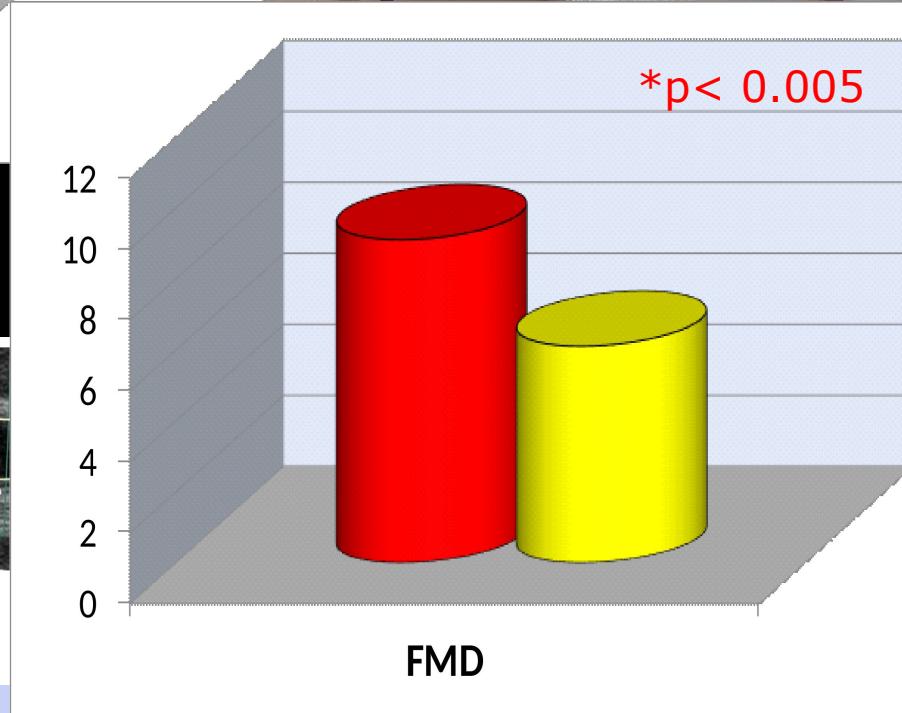
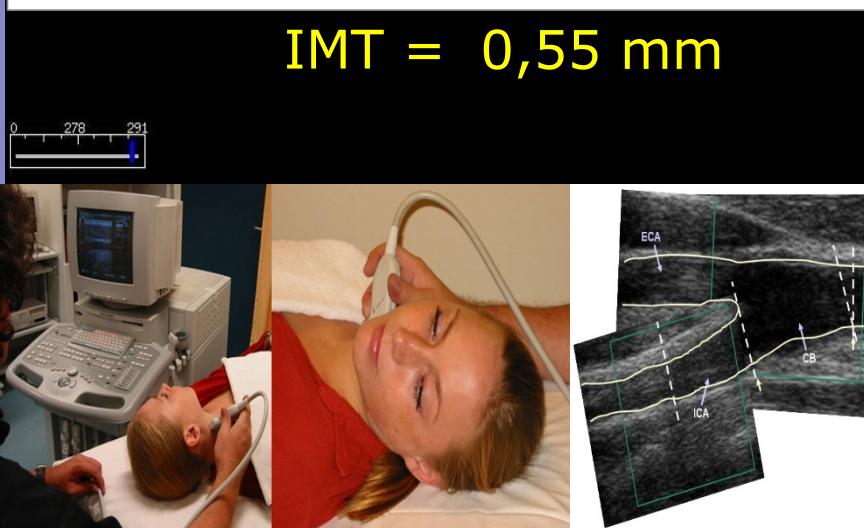
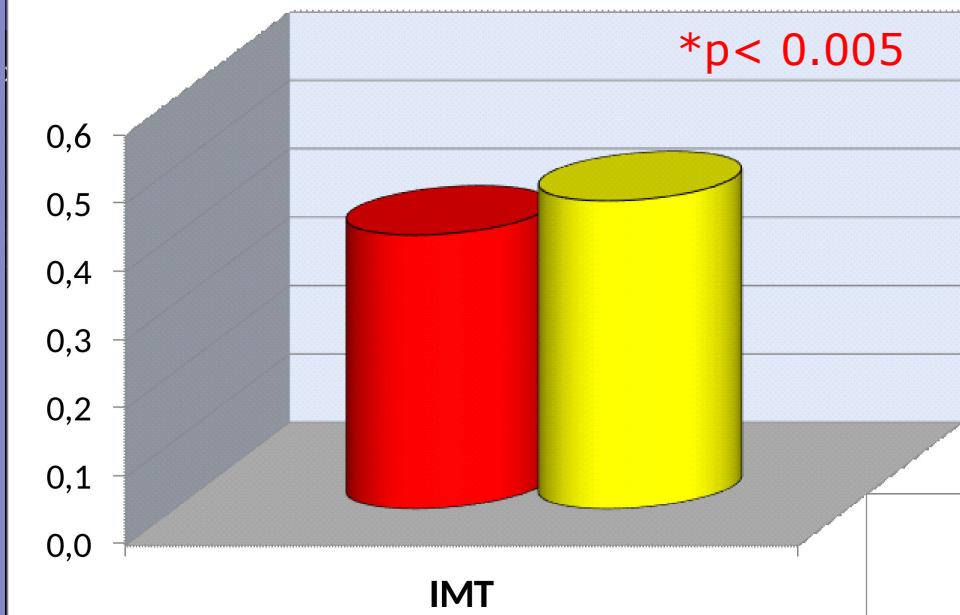
cholesterol and oxidative stress





**Martino F et al.
Pediatrics 2008;122:
198-208**





Martino F. et al.
Pediatrics 2008;122:648–655





Vascular Medicine

Hereditary Deficiency of gp91^{phox} Is Associated With Enhanced Arterial Dilatation

Results of a Multicenter Study

Francesco Violi, MD; Valerio Sanguigni, MD; Roberto Carnevale, PhD; Alessandro Plebani, MD; Paolo Rossi, MD; Andrea Finocchi, MD; Claudio Pignata, MD; Domenico De Mattia, MD; Baldassarre Martire, MD; Maria Cristina Pietrogrande, MD; Silvana Martino, MD; Eleonora Gambineri, MD; Anna Rosa Soresina, MD; Pasquale Pignatelli, MD; Francesco Martino, MD; Stefania Basili, MD; Lorenzo Loffredo, MD

Circulation. 2009;120:1616-1622.

Violi, F. et al. Circulation 2009;120:1616-1622


p<0.001

100,0
80,0
60,0
40,0
20,0
0,0

Urinary Isoprostanates


6,0
5,0
4,0
3,0
2,0
1,0
0,0

Gp91 phox

p<0.001

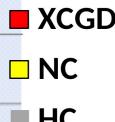


**25 patients with hereditary deficiency of gp91phox,
 25 hypercholesteolemic subjects (HC)
 and 25 normocholesterolemic patients (NC).**

15,0
12,0
9,0
6,0
3,0
0,0

FMD

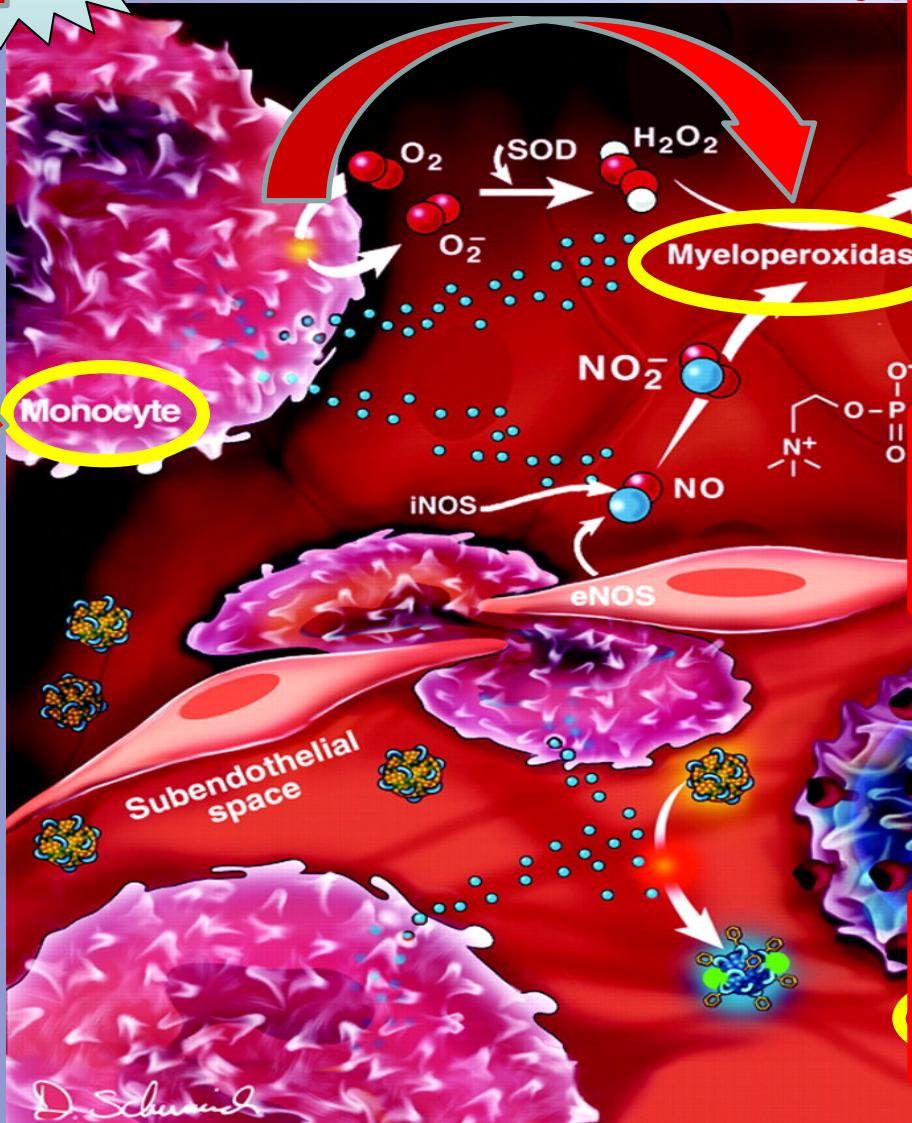
p<0.001



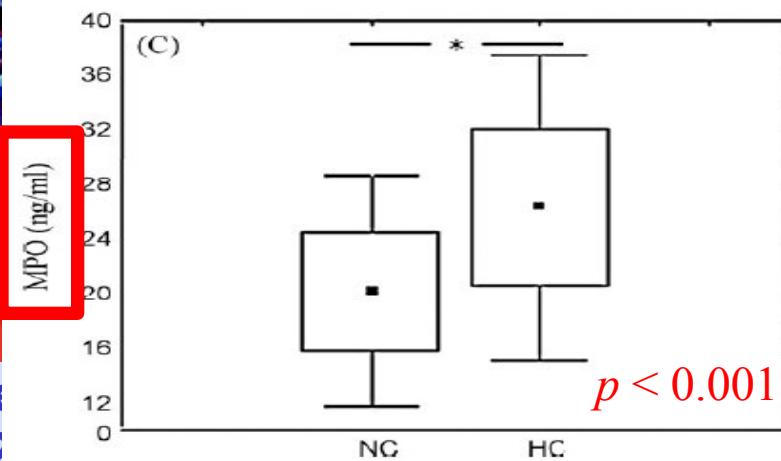
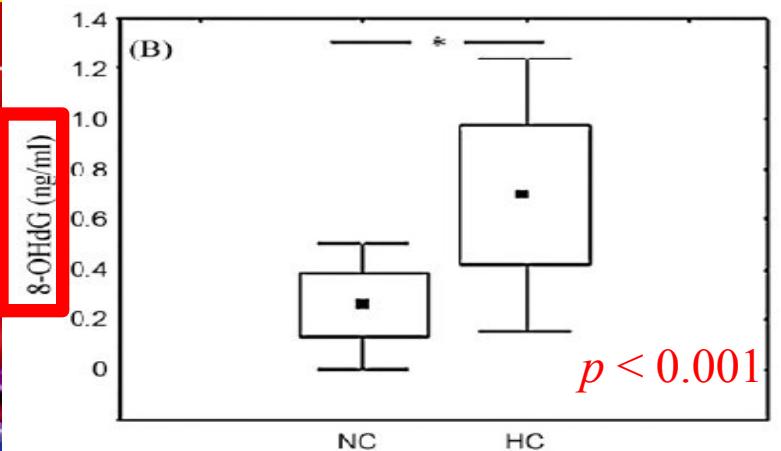
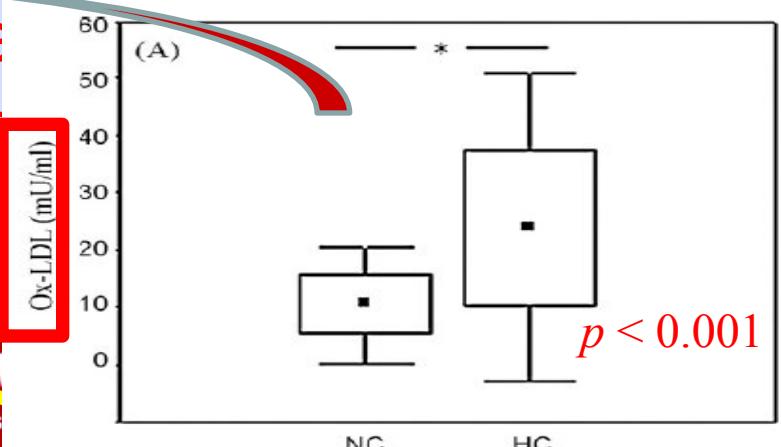
Oxidative
stress

Myeloperoxidase in children with hyper

a
c
t
i
v
a
t
i
o
n



D. Schmid
P.Pignatelli, L.Loffredo, F. Martino et al.
Atherosclerosis. 2009; 205: 239-245





Myeloperoxidase as cardiovascular risk marker in pre-pubertal preterm children?

Denise O Schoeps et al. NMCD 2019 Dec;29(12):1345-1352.

Preterm group

Control group

Myeloperoxidase ng/mL 21.1 (5.7; 120.0)
< 0.0012

8.1 (2.6; 29.6)

Myeloperoxidase/HDL-c ratio 0.39 (0.09; 2.07)
< 0.001

0.11 (0.05; 0.58)

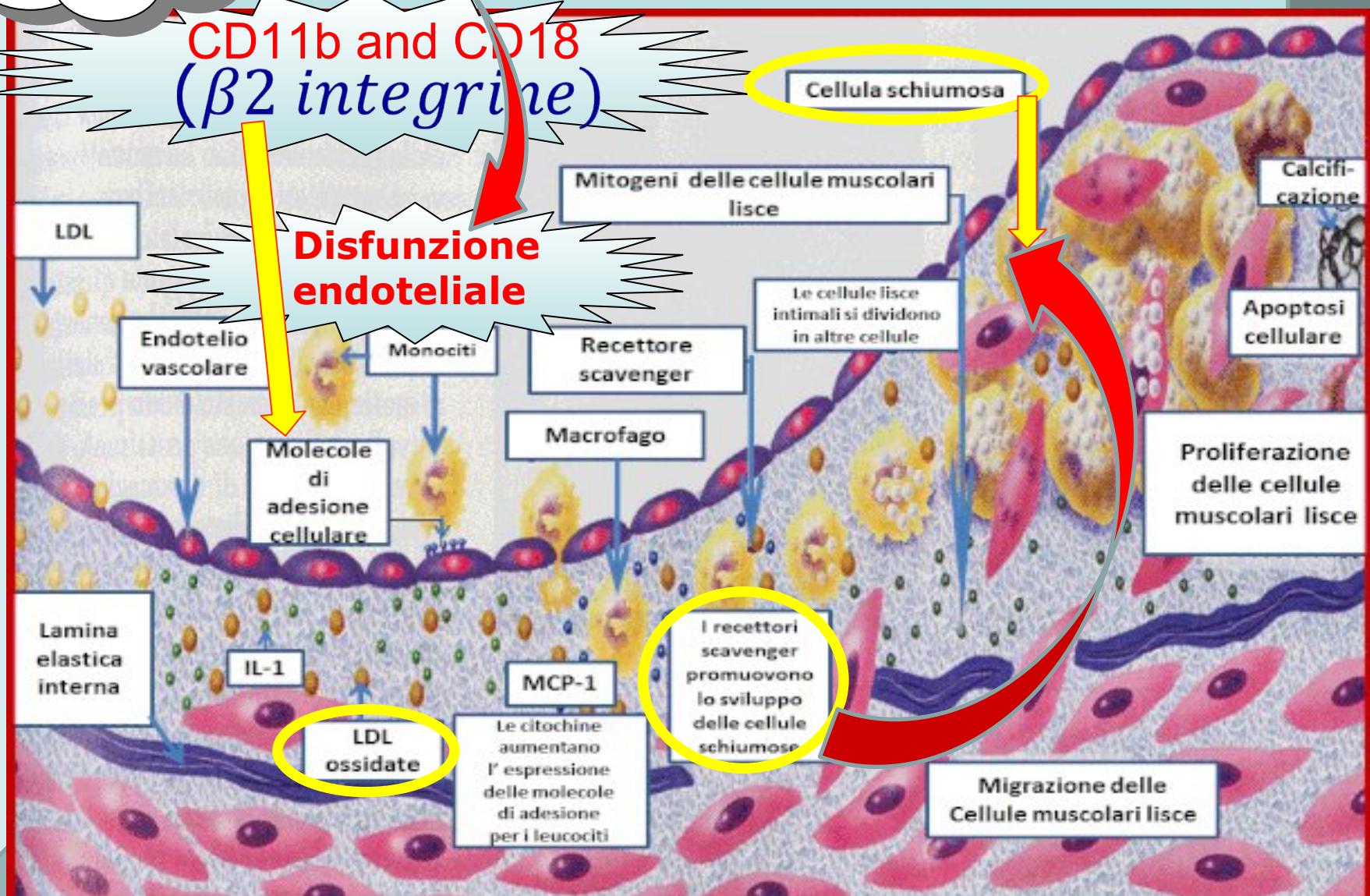
Conclusion:

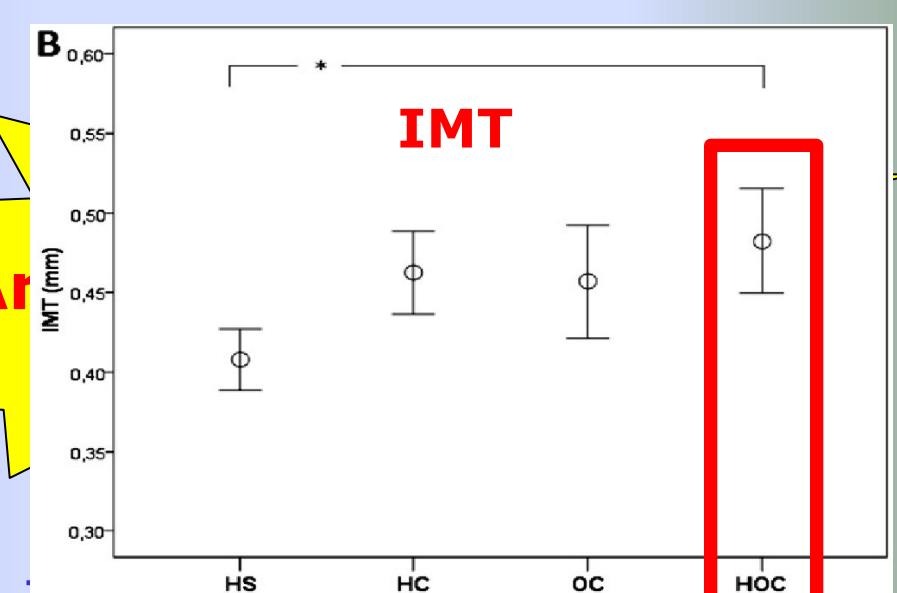
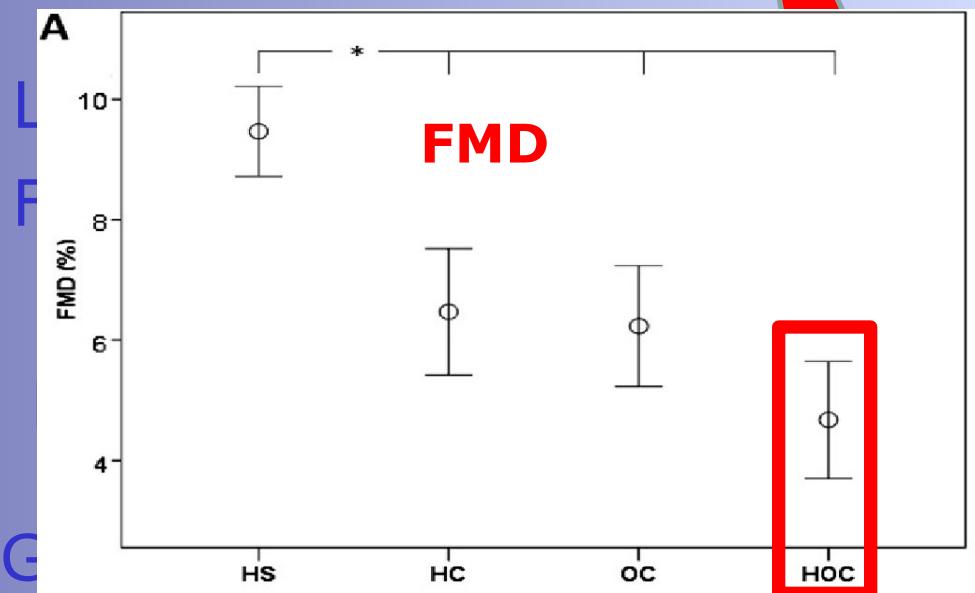
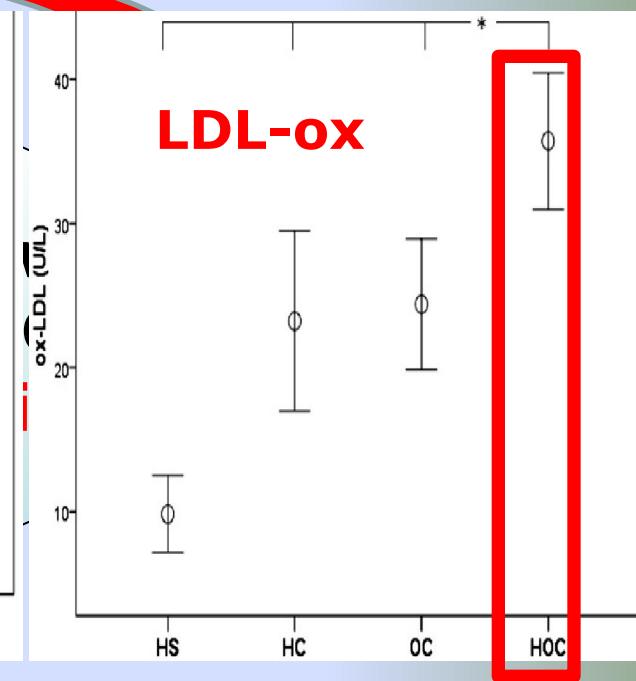
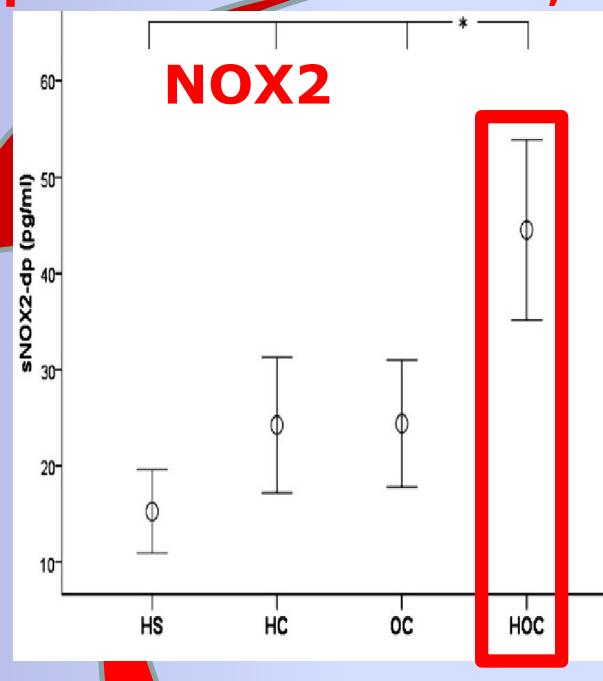
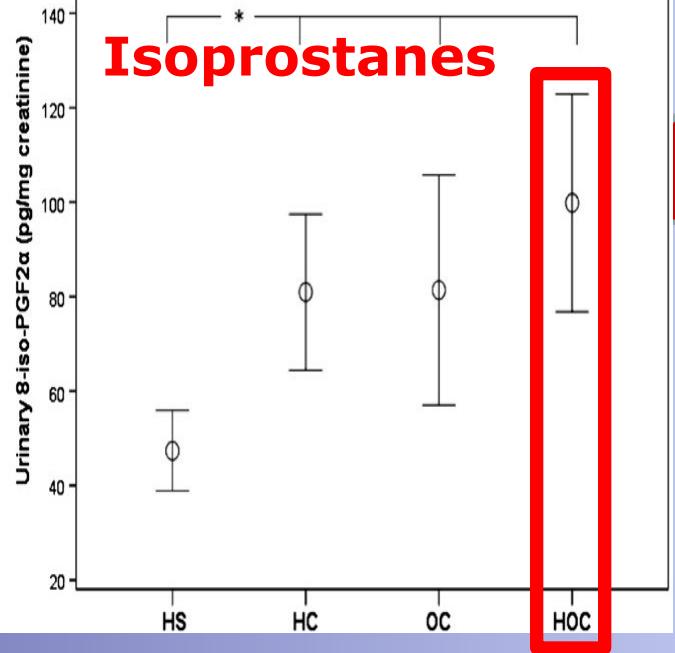
Prepubertal preterm children show high MPO concentrations and MPO/HDL-c ratio that are associated with inflammation and oxidative stress, which, in turn, may be associated with atherosclerosis.

children with
hypercholesterolemia

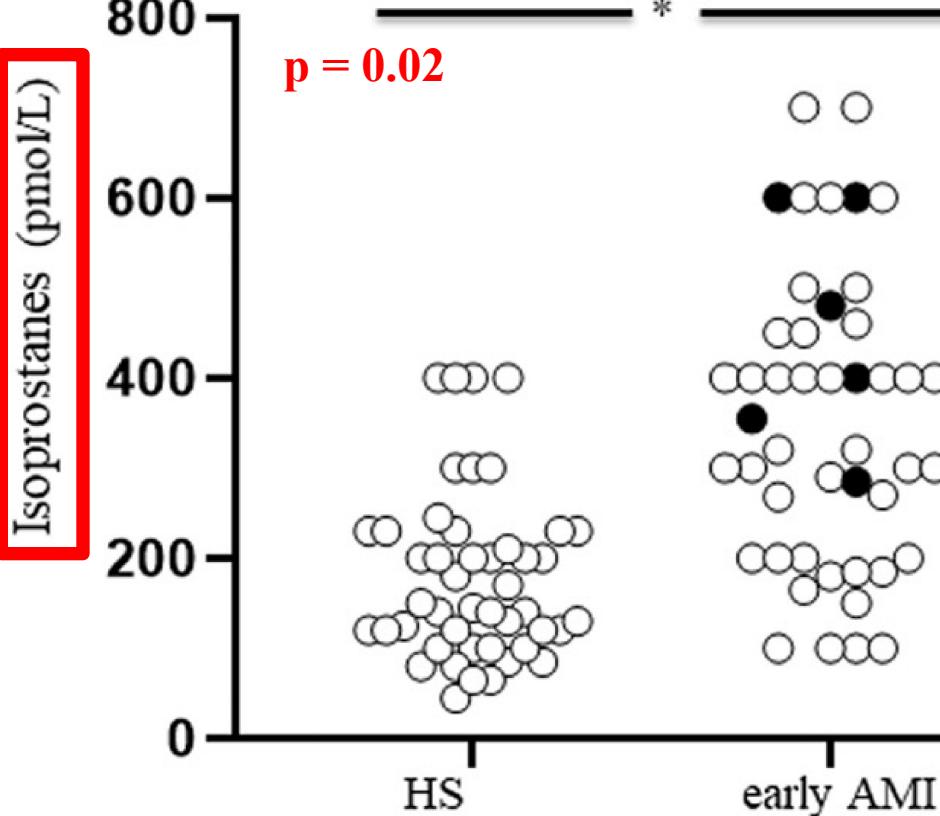
Stress

ossidativo

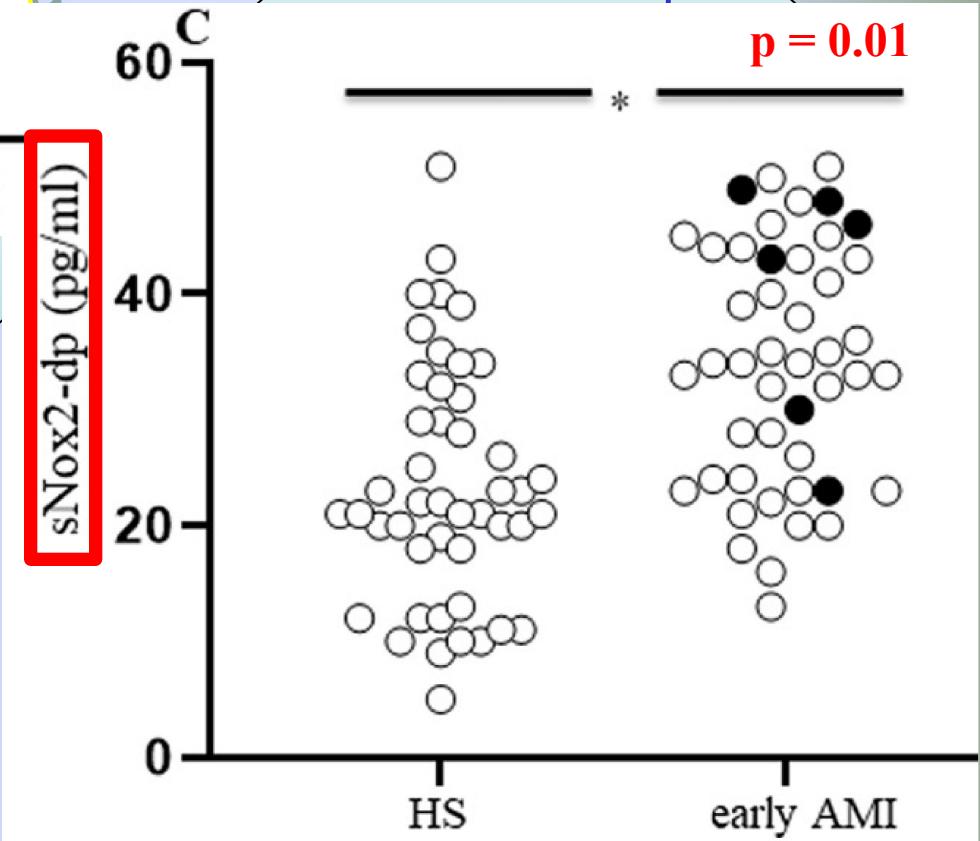


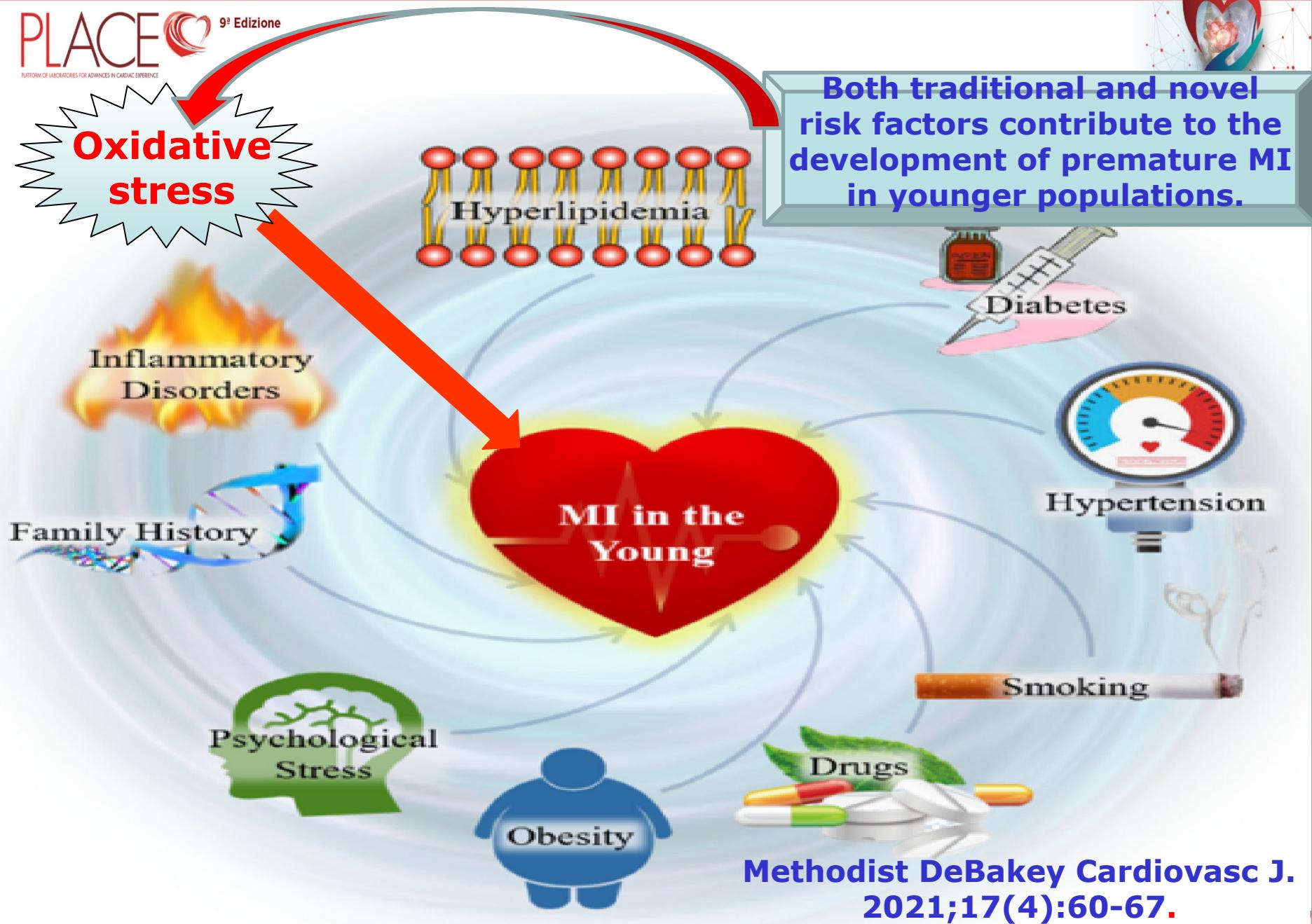


and Arterial Dysfunction



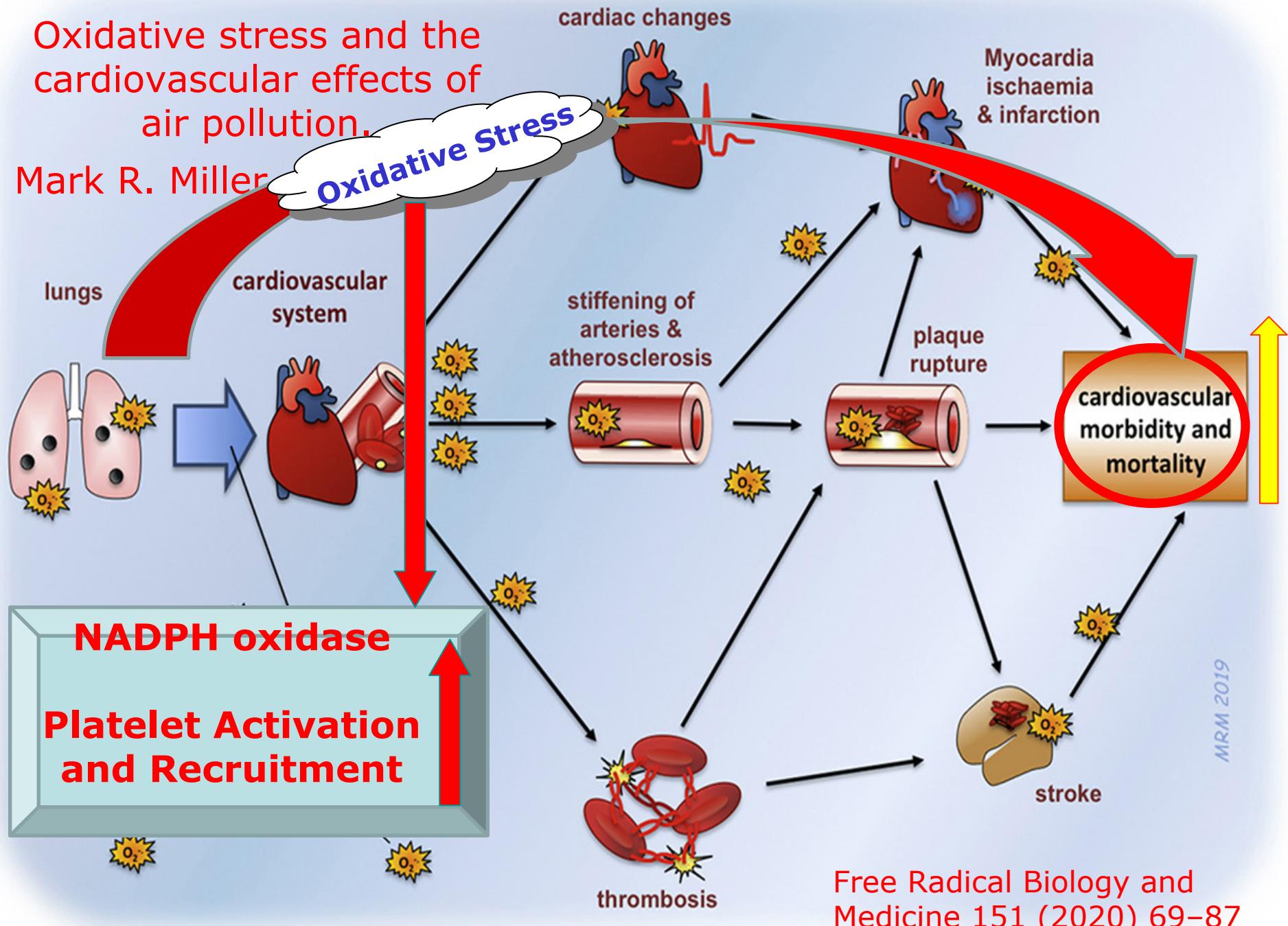
In conclusion, our study shows that NOX-2 activation is a key determinant of oxidative stress and platelet activation in offspring of patients with premature myocardial infarction.





Oxidative stress and the cardiovascular effects of air pollution.

Mark R. Miller



L. Loffredo,**F. Martino** et al. **Passive Smoking Exacerbates Nicotinamide-Adenine Dinucleotide Phosphate Oxidase Isoform 2-Induced Oxidative Stress and Arterial Dysfunction in Children with Persistent Allergic Rhinitis.** **J Pediatr 2018; 202: 252-257,**

ROMA 30 Settembre - 1 Ottobre 2022 Centro Congressi di Confindustria Auditorium della Tecnica



**Conclusion
NOX2 is activated
in children with
persistent allergic rhinitis
and passive smoke exposure
exacerbates this effect.**

**We further demonstrate an association
between higher sNOX2-dp and
oxidative stress
and endothelial dysfunction.**

A

sNOX2-dp (pg/ml)

C

NO bioavailability (μM)

SPEGNI LA SIGARETTA, PROTEGGI IL TUO BAMBINO!



FUMO DI “PRIMA MANO”

Fumo inalato direttamente
da un fumatore.

FUMO DI “SECONDA MANO”

Fumo inalato da chi è vicino
ad un fumatore.

FUMO DI “TERZA MANO”

Rischi del fumo di fumo su bambini e neonati che inquinano
rispettivamente anche la seguenti spese.



www.associazionefilosigaretta.it

Role of NADPH oxidase-2 and oxidative stress in
children exposed to passive smoking

L. Loffredo et al. Thorax 2018;73:986–988.

Adverse health effects in children induced by second-hand smoke and prenatal tobacco smoke exposure.

Int. J. Environ. Res.
Public Health
2020, 17, 3212;



Atherosclerosis

Sudden infant death syndrome

Cardiovascular diseases

Coronary heart disease



Cognitive impairment

Inflammatory diseases

Respiratory diseases

Chronic diseases

Oral diseases

Metabolic diseases

Cancer

disease

pregnancy
condition

inflammation
England
development

I MicroRNA, che contengono circa 22 nucleotidi endogeni, regolano molti processi biologici, tra cui quelli che sono coinvolti in danni cardiaci causati da stress ossidativo (infarto miocardico, ipertrofia, ischemia/riperfusione, insufficienza cardiaca).

Branislav Kura et al. Int. J. Mol. Sci. 2020, 21, 358;

Lo stress ossidativo può alterare il livello di espressione di molti miRNA.

**Environmental Science and Pollution Research.
Publish online: 08 May 2021**

The Role of MicroRNAs in Hyperlipidemia: From Pathogenesis to Therapeutical Application

Review Article

Hindawi

Mediators of Inflammation

Volume 2022,

Article ID 3101900, 10 pages

F. Martino,...F. Barillà...
and A. Magenta

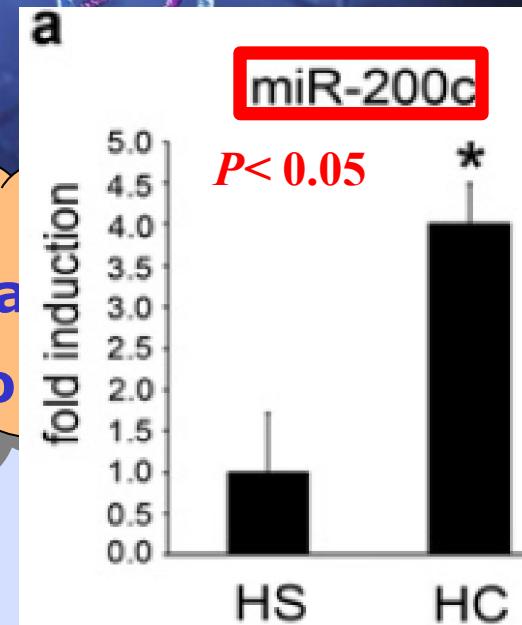
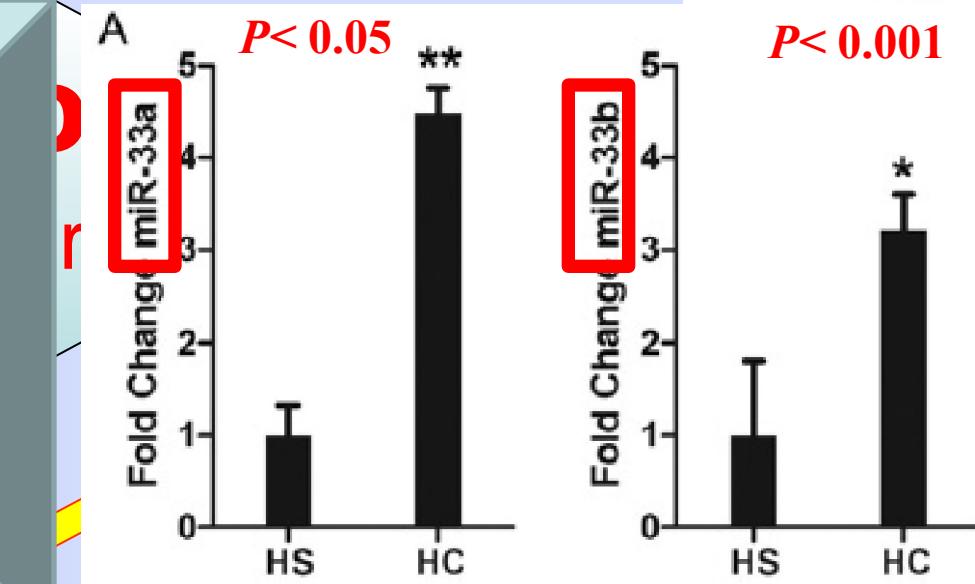
2017

Clinical Science

2017 Sep 8;131(18):2397-2408

microRNA 200c

M.D'Agostino,F.Martino,
...F.Barillà...and A.Magenta

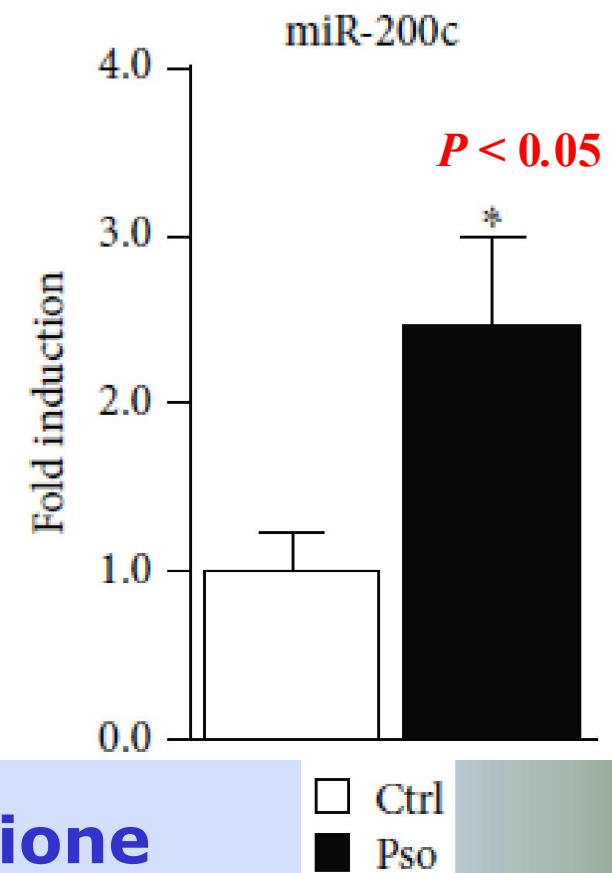




The Oxidative Stress-Induced miR-200c Is Upregulated in Psoriasis and Correlates with Disease Severity and Determinants of Cardiovascular Risk

Conclusioni

**La sovraregolazione del
miRNA 200c potrebbe svolgere
un ruolo importante nell'infiammazione
e nell'incremento dello stress ossidativo,
aumentando il rischio di eventi CV avversi
(ipertrofia cardiaca, disfunzione diastolica,
stiffness arteriosa) nei pazienti psoriasici.**



A.Magenta ,.....F. Martino, et al.

Oxidative Medicine and Cellular Longevity Volume 2019, Article ID 8061901, 12 pages

CONCLUSIONI

Individuazione e
trattamento
precoce
dei fattori di rischio

CV



età
gestazionale



Riduzione
dello stress
ossidativo

FUTURE

Prevenzione
delle Malattie
cardiovascolari





Review

Should We Be Screening for Ischaemic Heart Disease Earlier in Childhood?

Pier Paolo Bassareo, Stephen T. O'Brien, Esme Dunne, Sophie Duignan, Eliana Martino, Francesco Martino and Colin J. McMahon

Children 2022, 9, 982

Conclusioni:.....negli ultimi anni sono state sviluppate strategie per identificare le persone a maggior rischio di ischemia cardiaca e infarto miocardico, correlati ad aterosclerosi, e trattarle in termini di prevenzione primaria.

La mancanza,però, di dati solidi sulla sua efficacia è ancora un punto debole e nel prossimo futuro saranno necessarie molte più ricerche nel campo.

Oxidative Stress in Cardiovascular Diseases: Still a Therapeutic Target?



Nutrients 2019, 11, 2090

Probiotics

Mediterranean diet

Dietary or supplementary antioxidants

Vitamins C and E

Mitochondria targeted

N- acetylcysteine

Polyunsaturated fatty acids

**Dietary and supplementary antioxidants
for decreasing cardiovascular risk**



- Mediterranean Diet
- Polyphenols
 - PUFAs
 - MUFAs
 - Fiber
 - Minerals
 - Vitamins



Mediterranean Diet and Cardiovascular Disease Prevention: What Do We Know?

↓ Oxidation

↓ Inflammation

↓ Body weight

↓ Blood pressure

↓ Fasting glucose

↑ SCFA

↓ LDL

↓ TMAO

Potential mechanisms implicated in CVD prevention

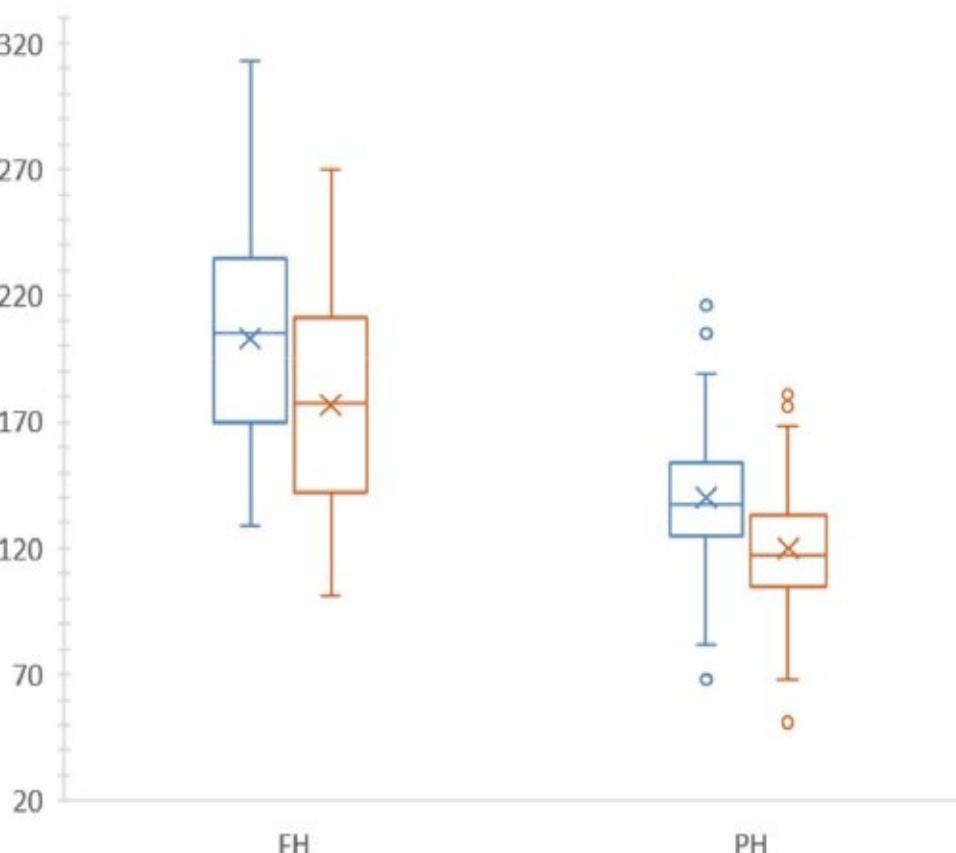
Jordi Salas Salvadó et al.
Progress in Cardiovascular Diseases 61 (2018) 62–67

LDL-C levels (mg/dL)

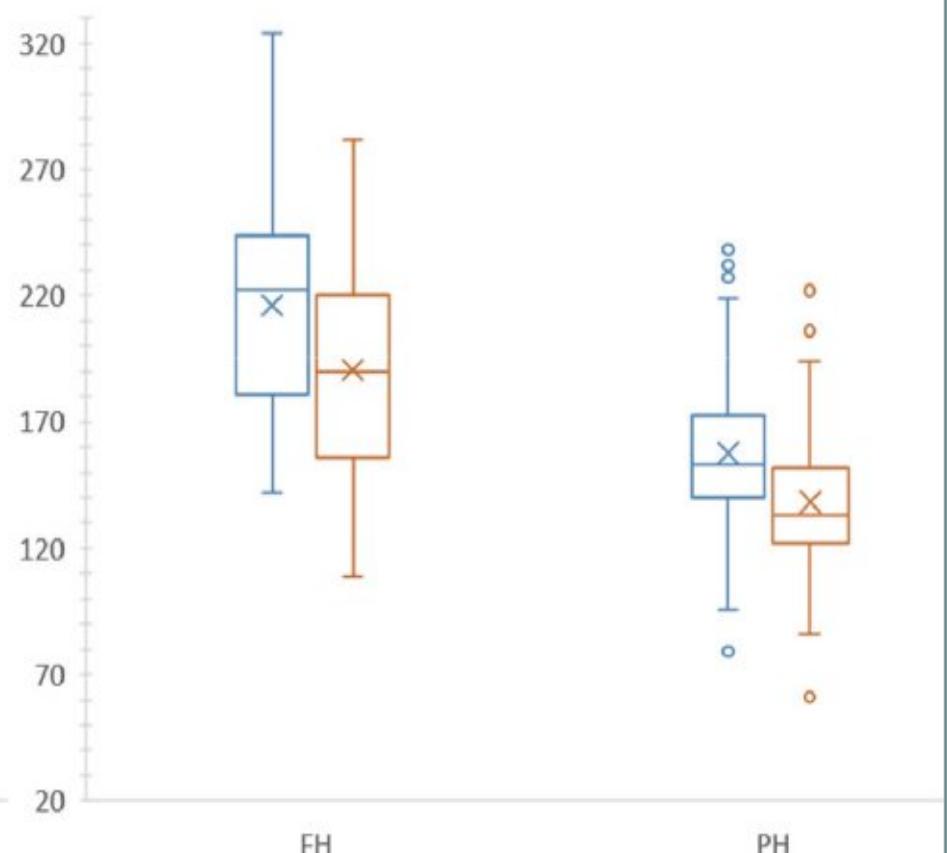
non HDL-C levels (mg/dL)

□ Baseline □ at 6 months

□ Baseline □ at 6 months

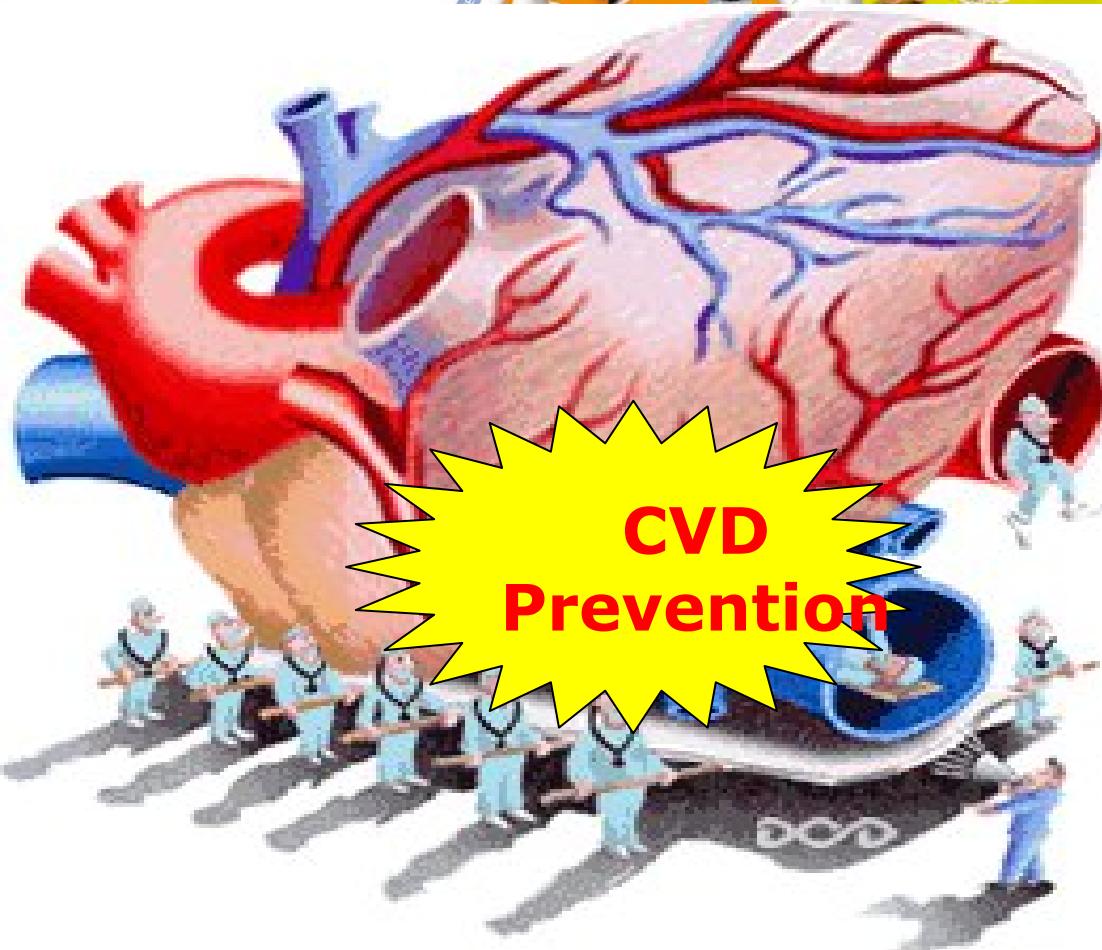


(A)

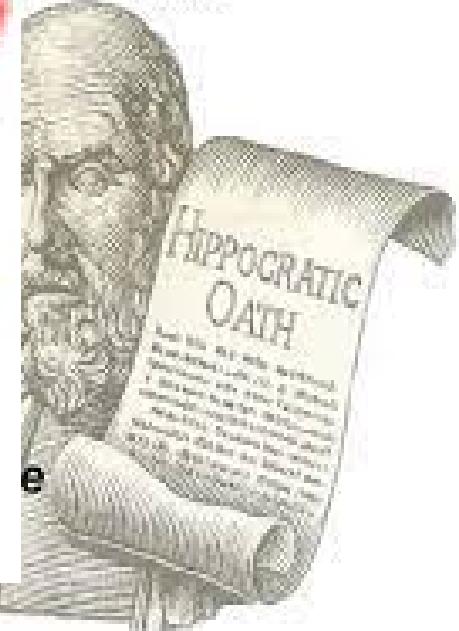


(B)

**LDL-C (A), non-HDL-C (B) Box-plot at baseline (blue)
and at 6 months follow-up (orange)
in familial hypercholesterolemia (FH)
and polygenic hypercholesterolemia (PH) in the ResponderGroup.**



di fornire





»Il balcone delle Calabrie«
Ferdinando II di Borbone



**Grazie per
l'attenzione!!!**

**un tramonto d'estate a
San Nicola Da Crissa (VV)**

