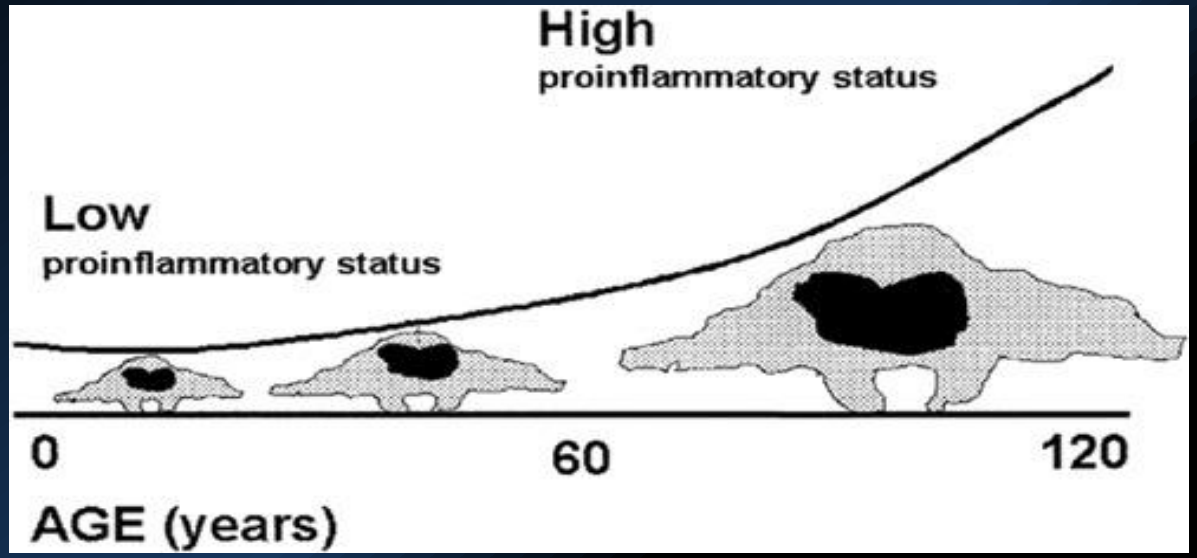
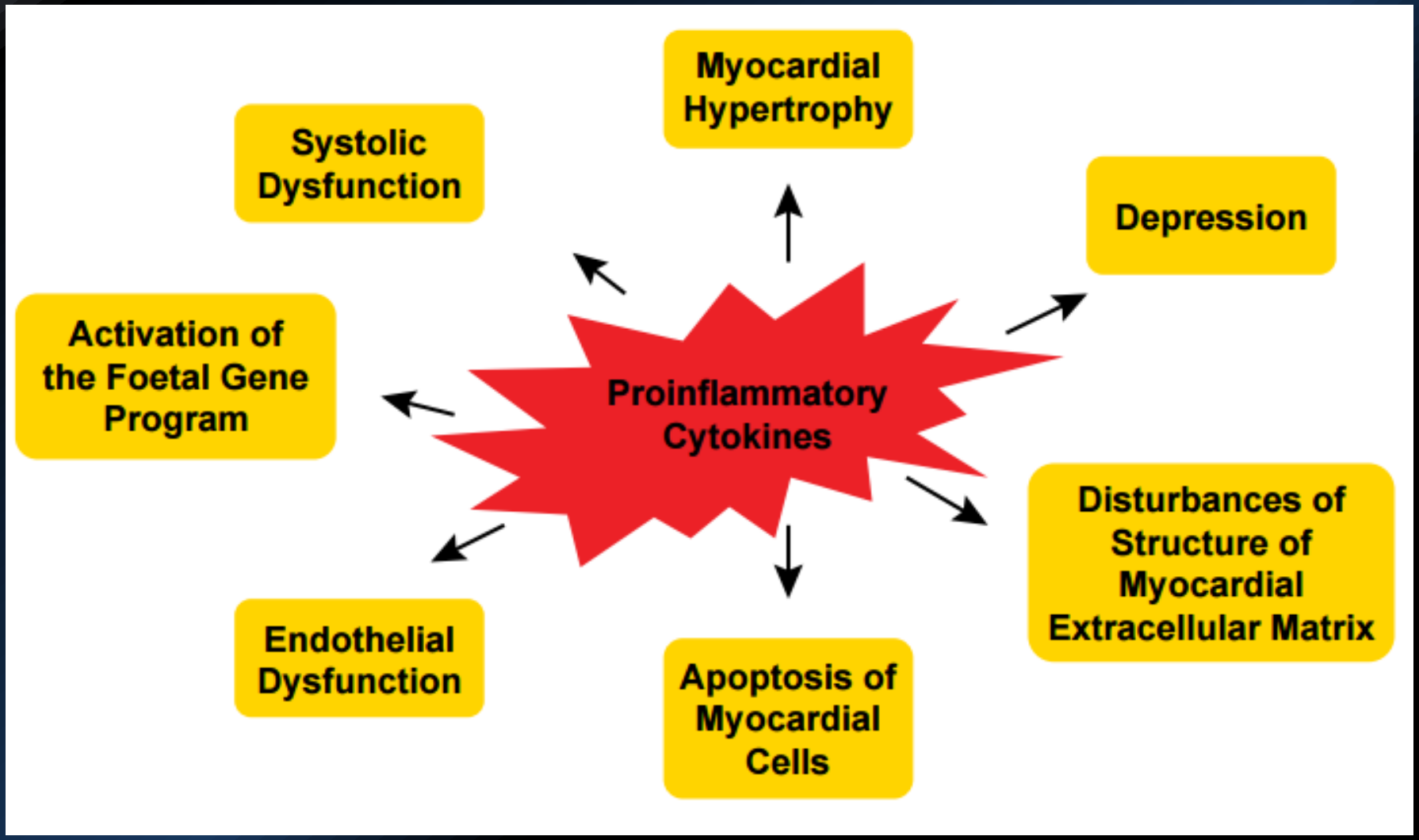
TESSUTO ADIPOSO E MALATTIE CARDIOVASCOLARI

Valentina Parisi
Università 'Federico II', Napoli

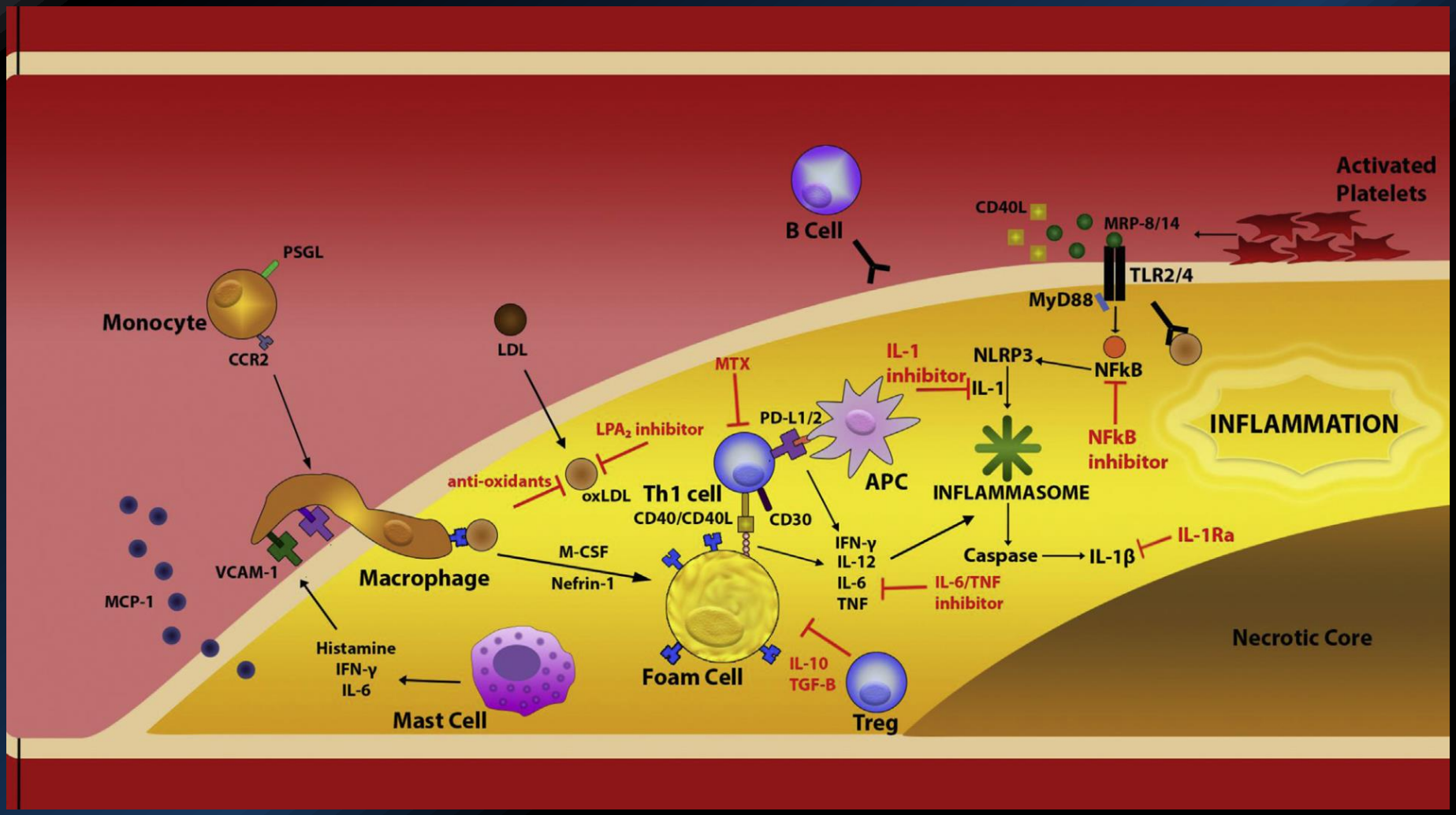
INFIAMMAZIONE CRONICA NELL'ANZIANO



INFIAMMAZIONE ED INSUFFICIENZA CARDIACA



INFIAMMAZIONE ED ATEROSCLEROSI



Khambhati, Atherosclerosis 2018

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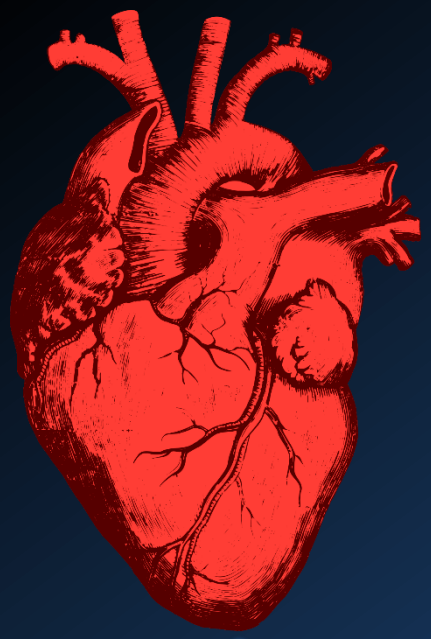
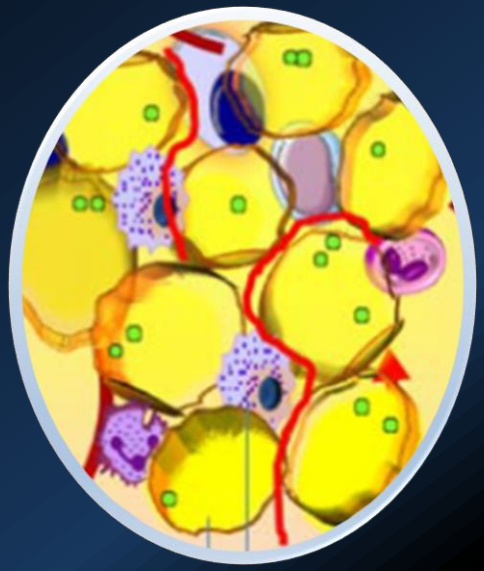
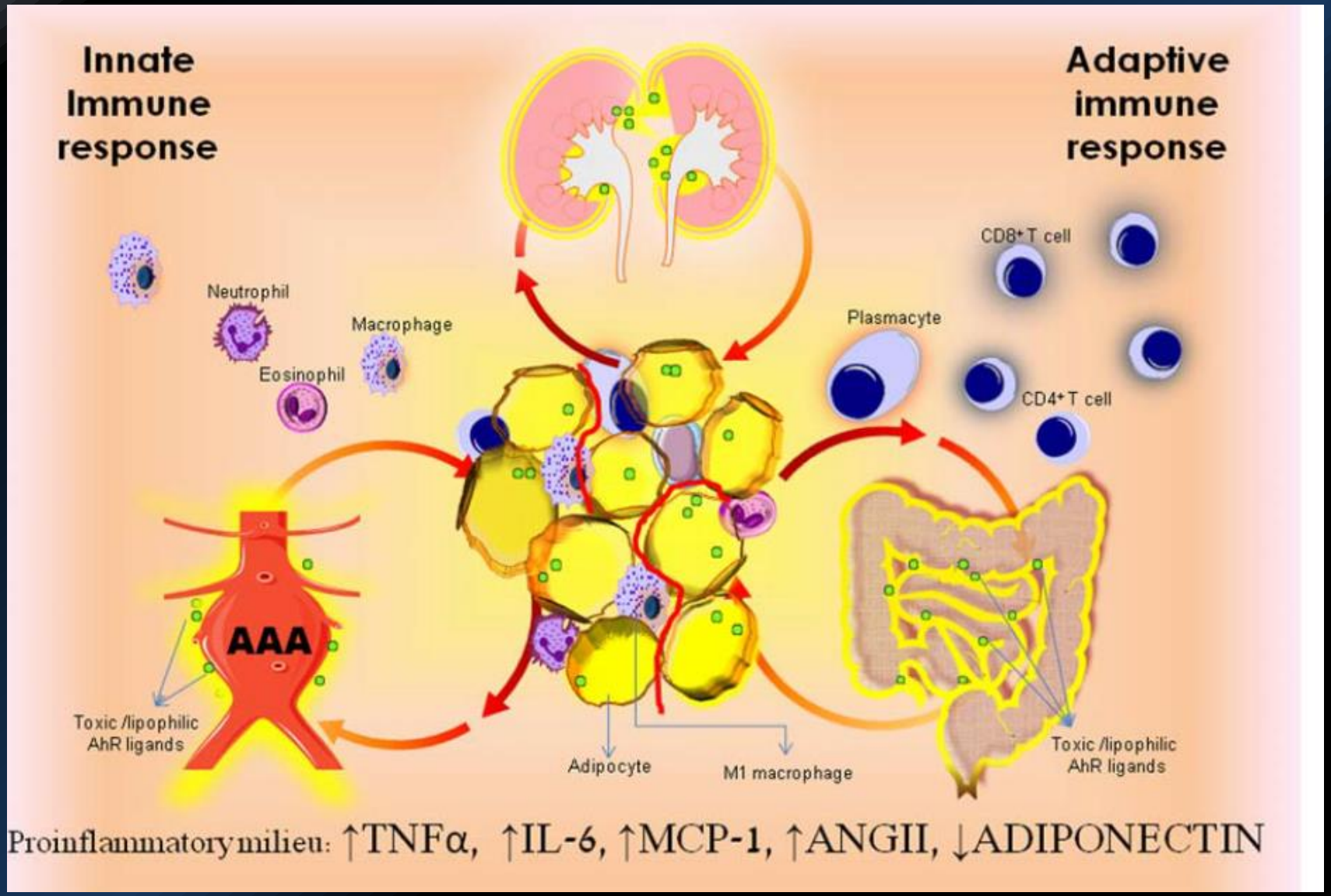




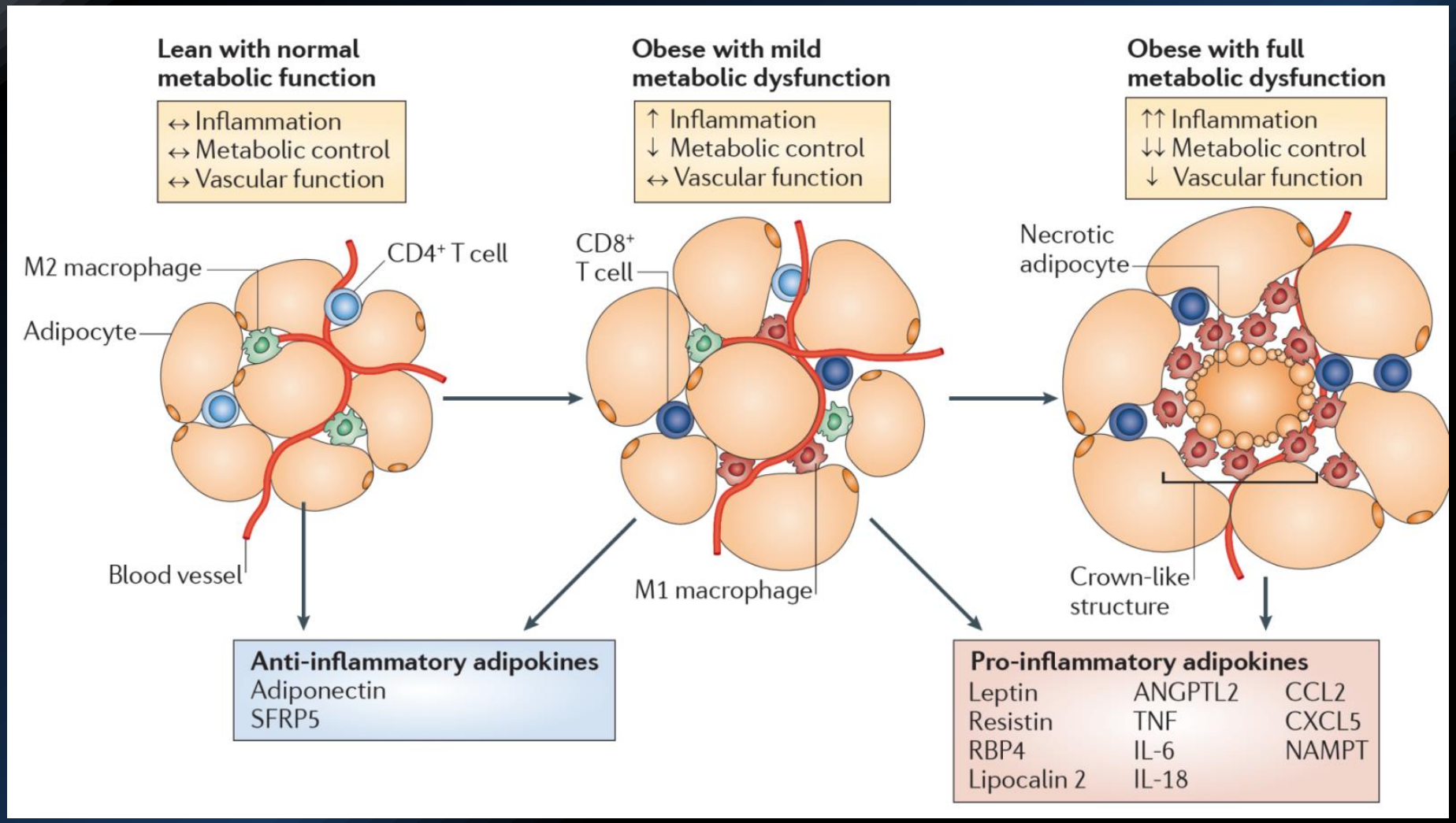
ATEROSCLEROSI

INFIAMMAZIONE E TESSUTO ADIPOSO



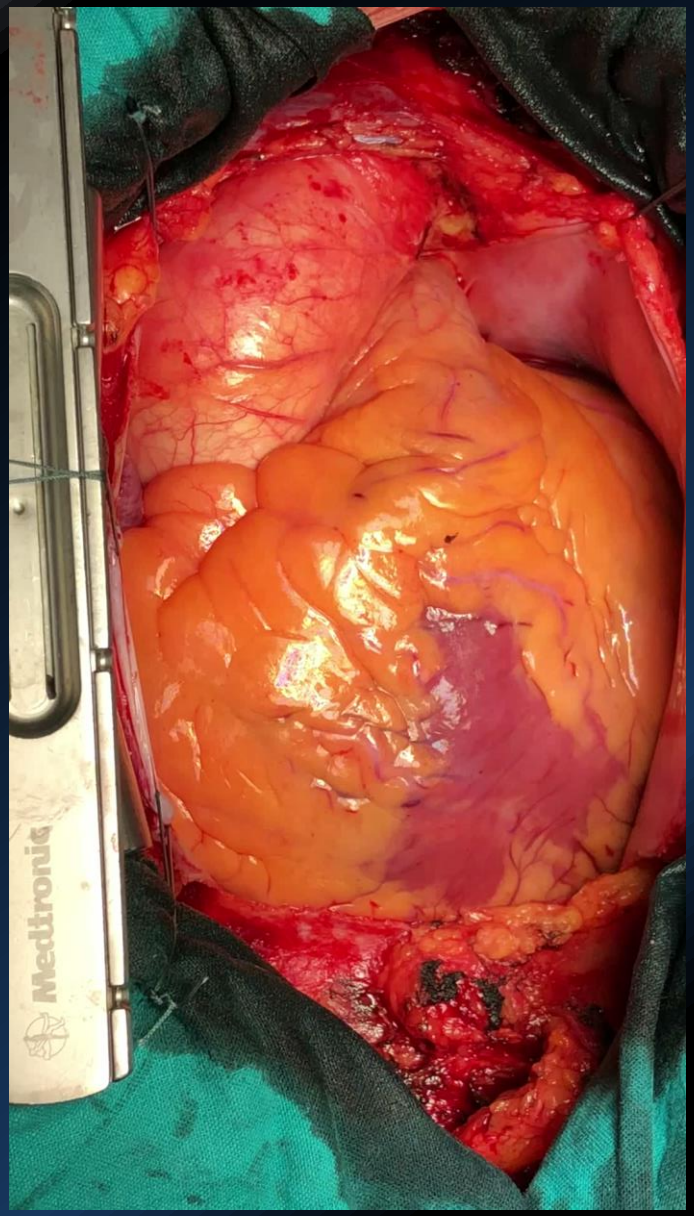
Ghigliotti G, Inflammation 2014

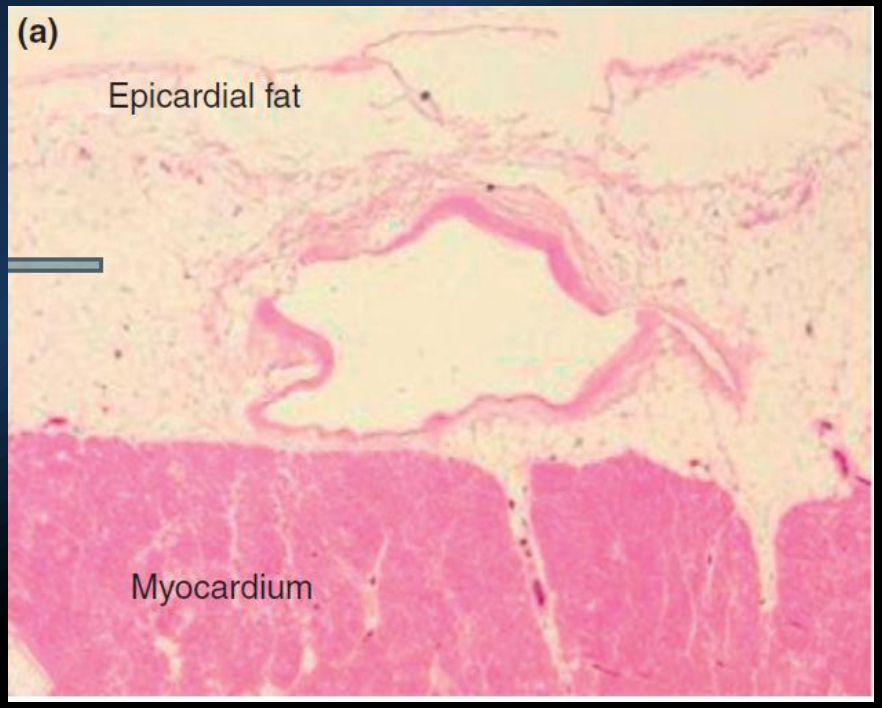
Visceral adipose tissue



Iacobellis et al. Trends in Endocrinology and Metabolism 2011

Epicardial adipose tissue





TESSUTO ADIPOSO VISCERALE

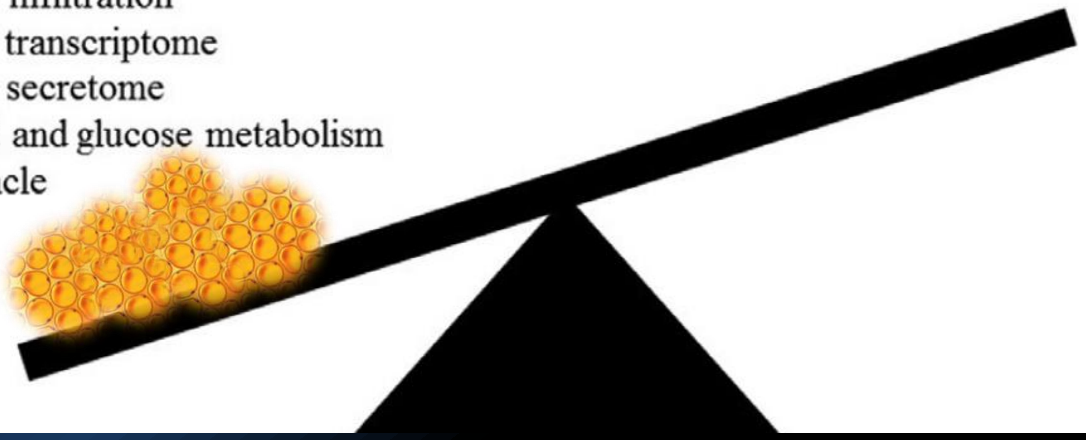
Epicardial Fat Imbalance

Overfeeding

Intrinsic inflammatory infiltrate
Highest synthesis and release of FFAs
Lower glucose uptake
High lipolysis
Intrinsic insulin resistance
Myocardial fatty infiltration
Proinflammatory transcriptome
Proinflammatory secretome
Atherogenic lipid and glucose metabolism
Mechanical obstacle

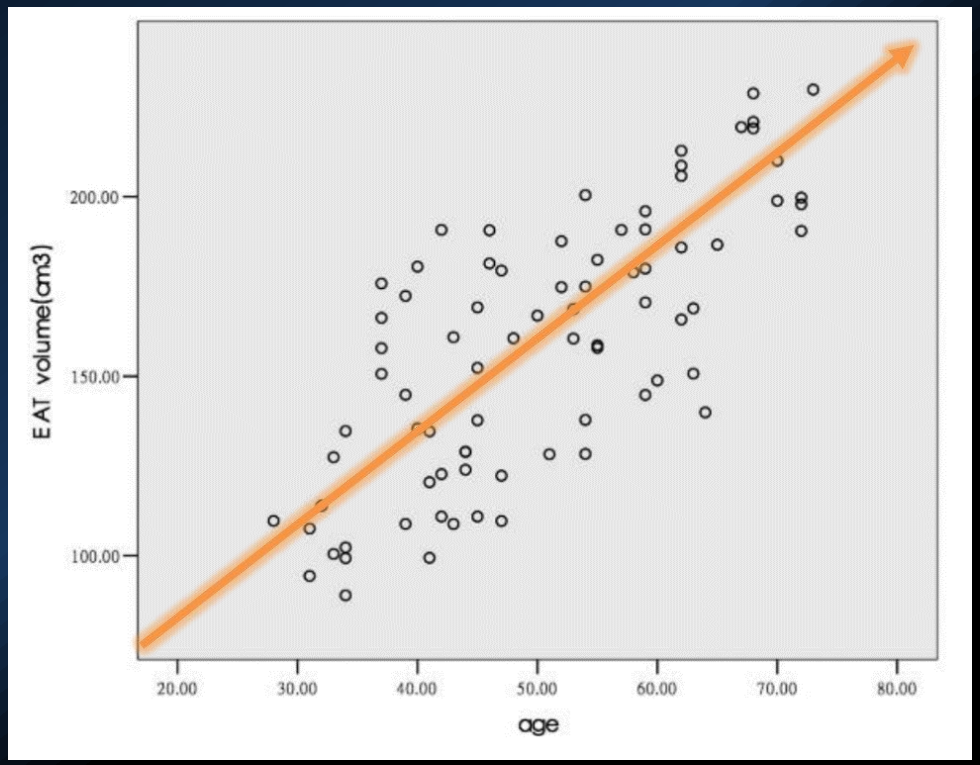
Feeding

Thermoregulation of the myocardium
FFA source for the myocardium
Buffer against FFA toxic effect
Antiinflammatory cytokines
Mechanical protection



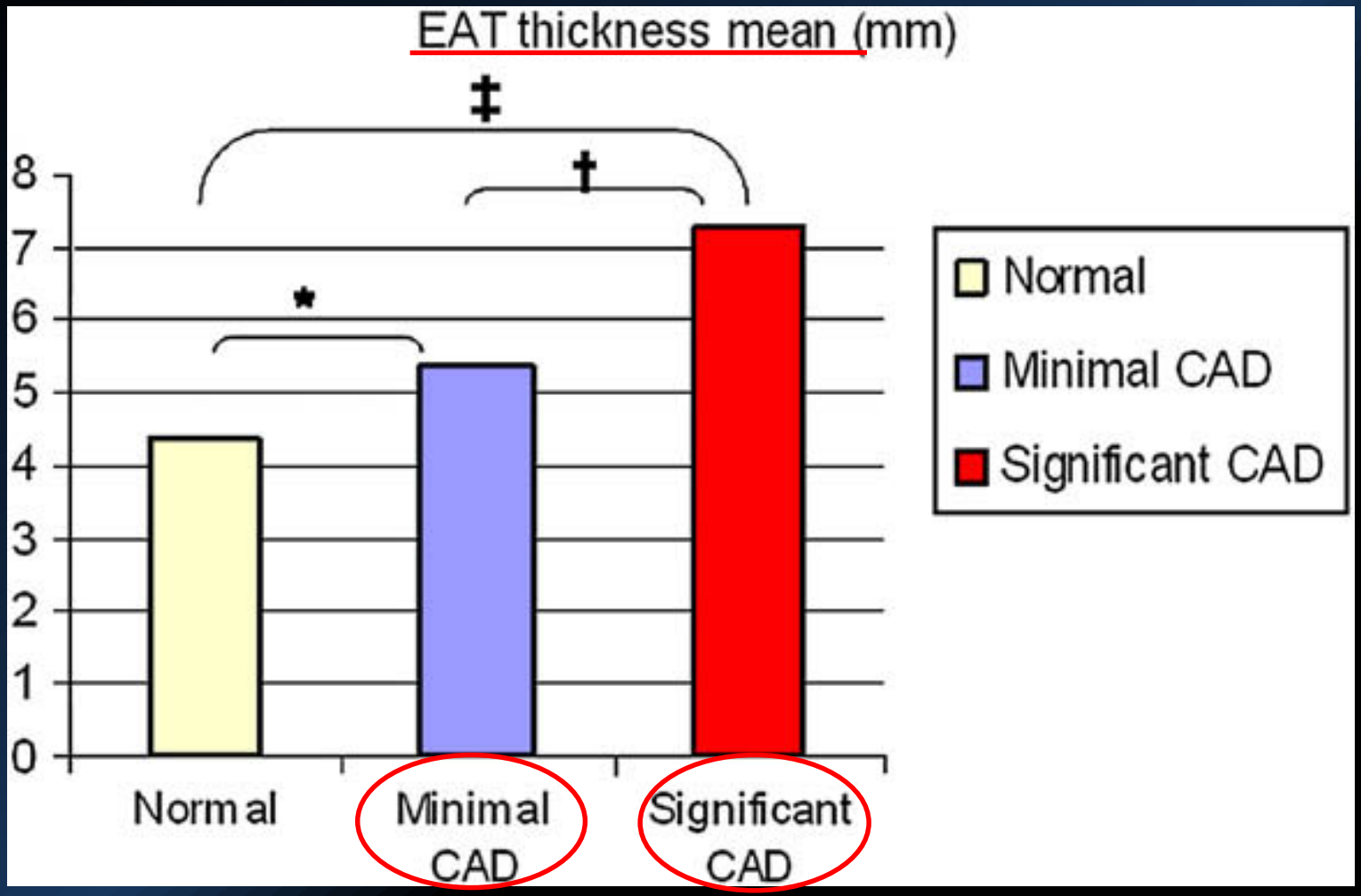
Iacobellis, Nutrition 2018

Epicardial adipose tissue and age



Nakanishi K, Circ J 2015

Epicardial adipose tissue andCAD

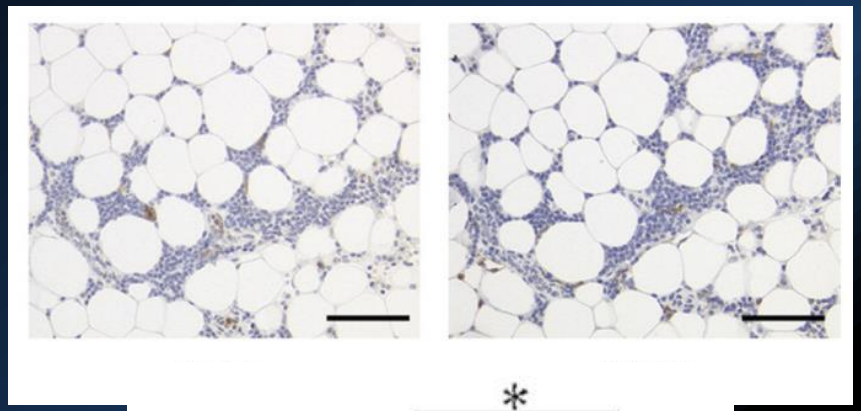


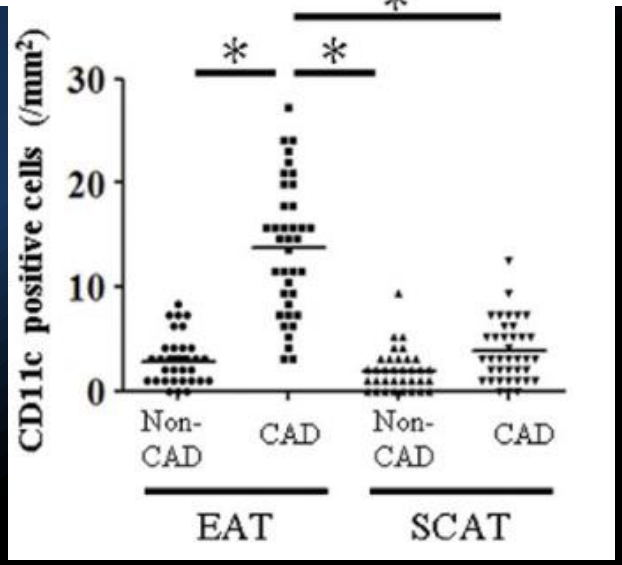
S. Eroglu, Nutrition Metabolism & Cardiovascular Diseases 2009

Epicardial adipose tissue andCAD

- In presenza di CAD aumenta l'infiltrazione macrofagica
- Polarizzazzione dei macrofagi M1/M2

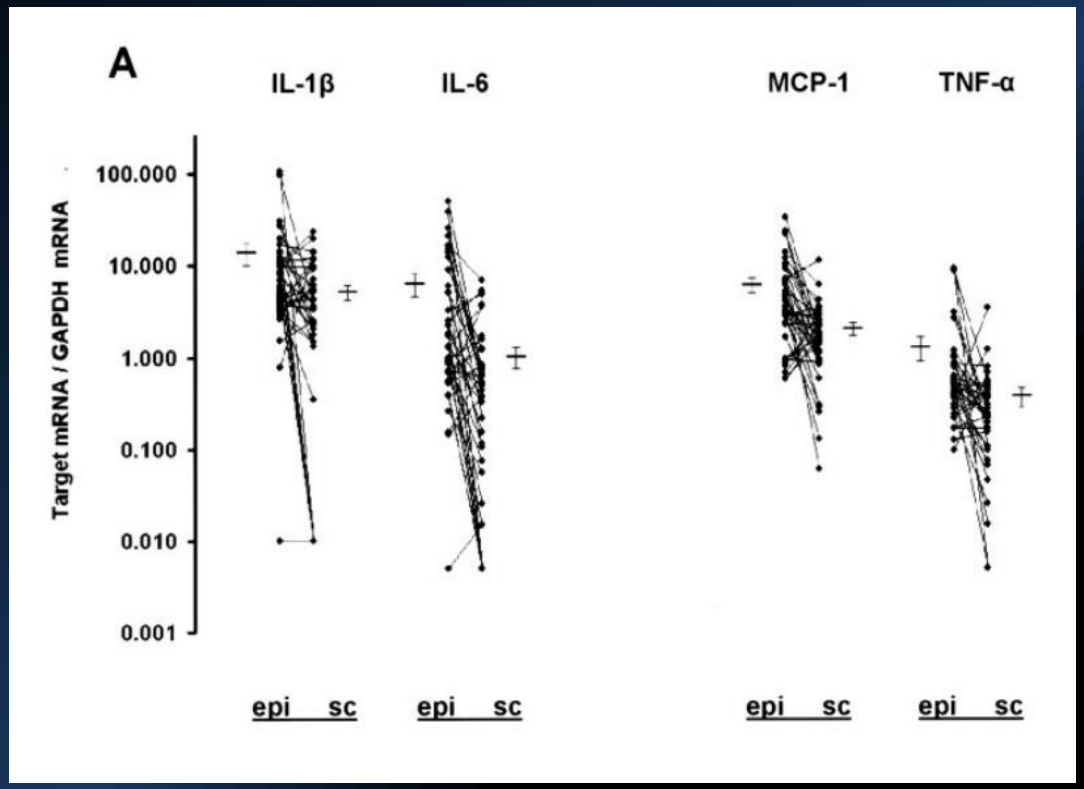
M1 M2





Hirata, JACC 2011

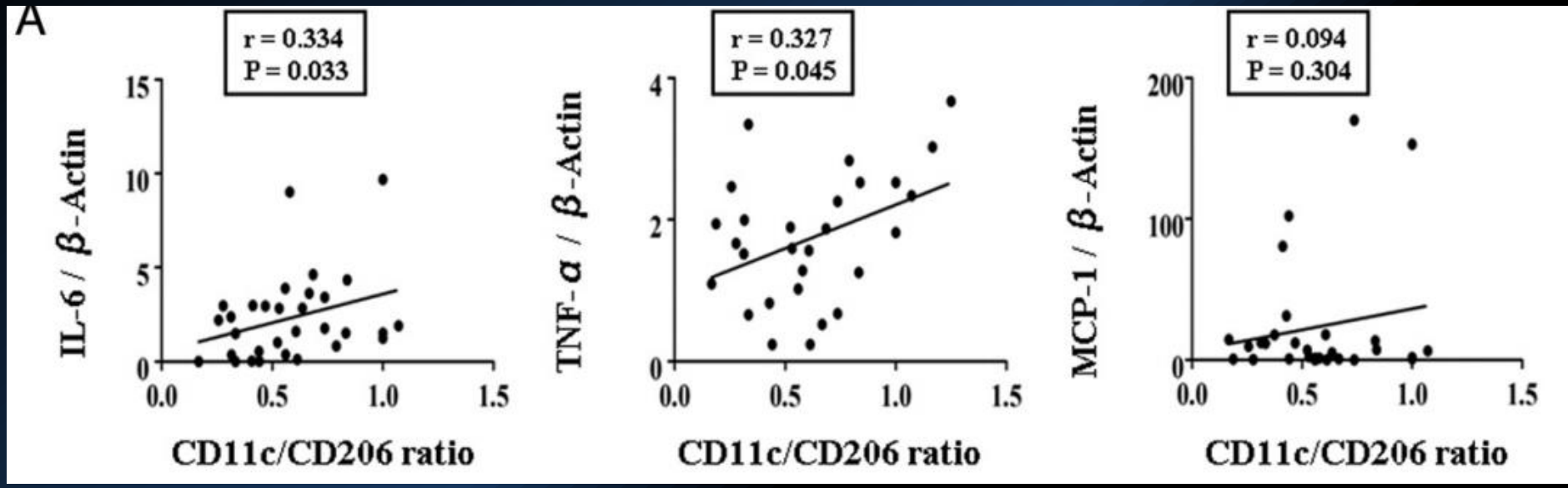
EAT is a source of inflammatory mediators in CAD pts



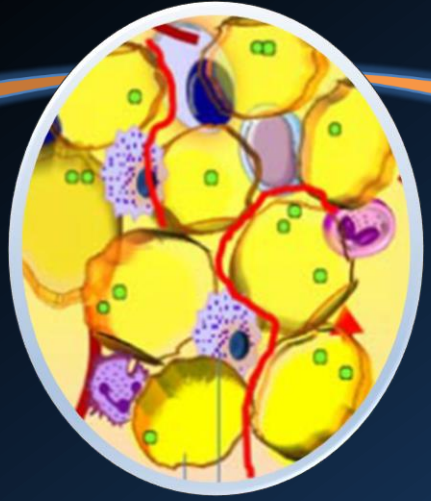
Mazurek T et al. Circulation. 2003

Epicardial adipose tissue andCAD

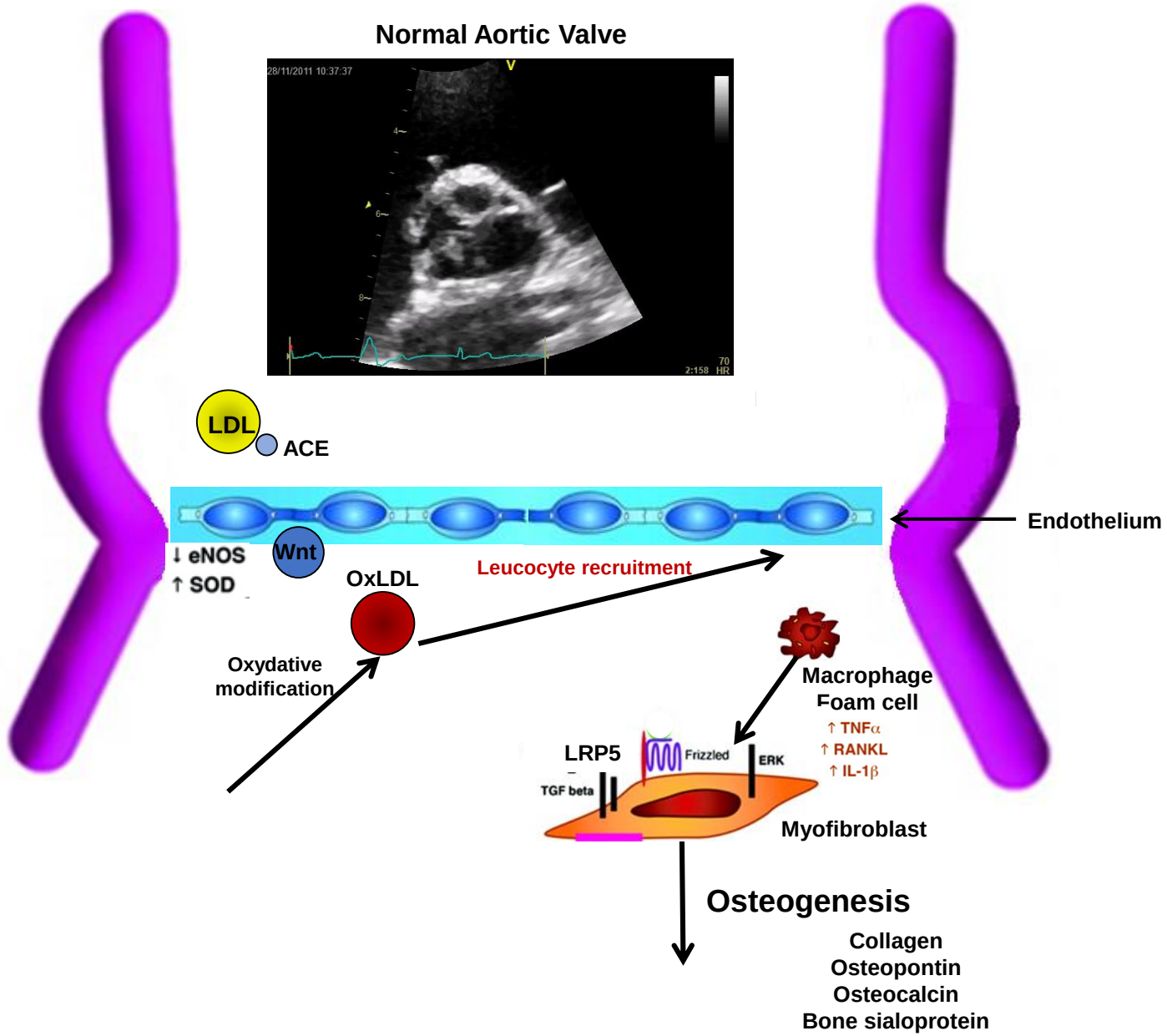
La quantità di macrfagi M1 correla con il livelli di :
IL-6; TNF-alpha; MCP-1

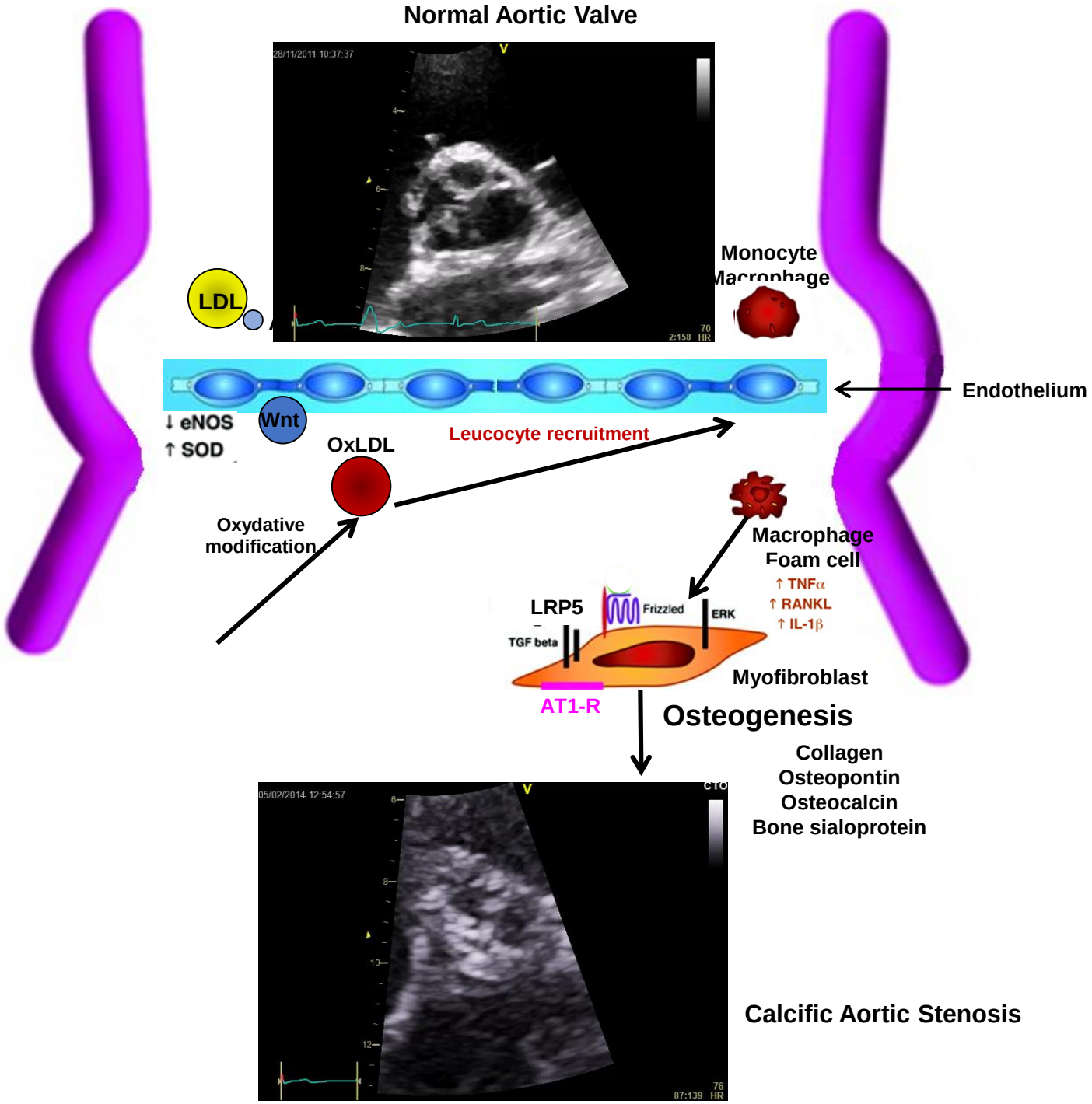


Hirata, JACC 2011

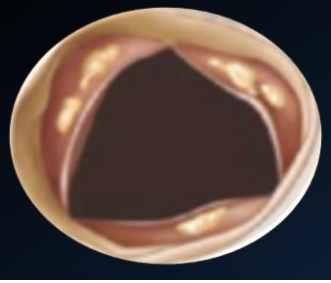


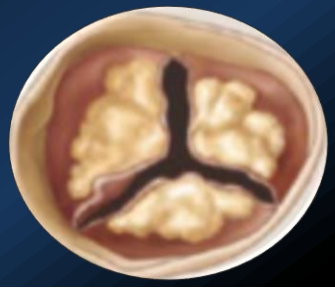
RILASCIO CITOKINE INFIAMMATORIE


Normal Aortic Valve
28/11/2011 10:37:37
LDL
ACE
Endothelium
↓ eNOS
↑ SOD
Wnt
OxLDL
Leucocyte recruitment
Oxydative modification
Macrophage
Foam cell
↑ TNFα
↑ RANKL
↑ IL-1β
LRP5
Frizzled
ERK
TGF beta
Myofibroblast
Osteogenesis
Collagen
Osteopontin
Osteocalcin
Bone sialoprotein


Normal Aortic Valve
LDL
Monocyte
Macrophage
Endothelium
↓ eNOS
↑ SOD
Wnt
OxLDL
Leucocyte recruitment
Oxydative modification
Macrophage
Foam cell
↑ TNFα
↑ RANKL
↑ IL-1β
LRP5
Frizzled
ERK
TGF beta
Myofibroblast
AT1-R
Osteogenesis
Collagen
Osteopontin
Osteocalcin
Bone sialoprotein
Calcific Aortic Stenosis

INFIAMMAZIONE E STENOSI AORTICA

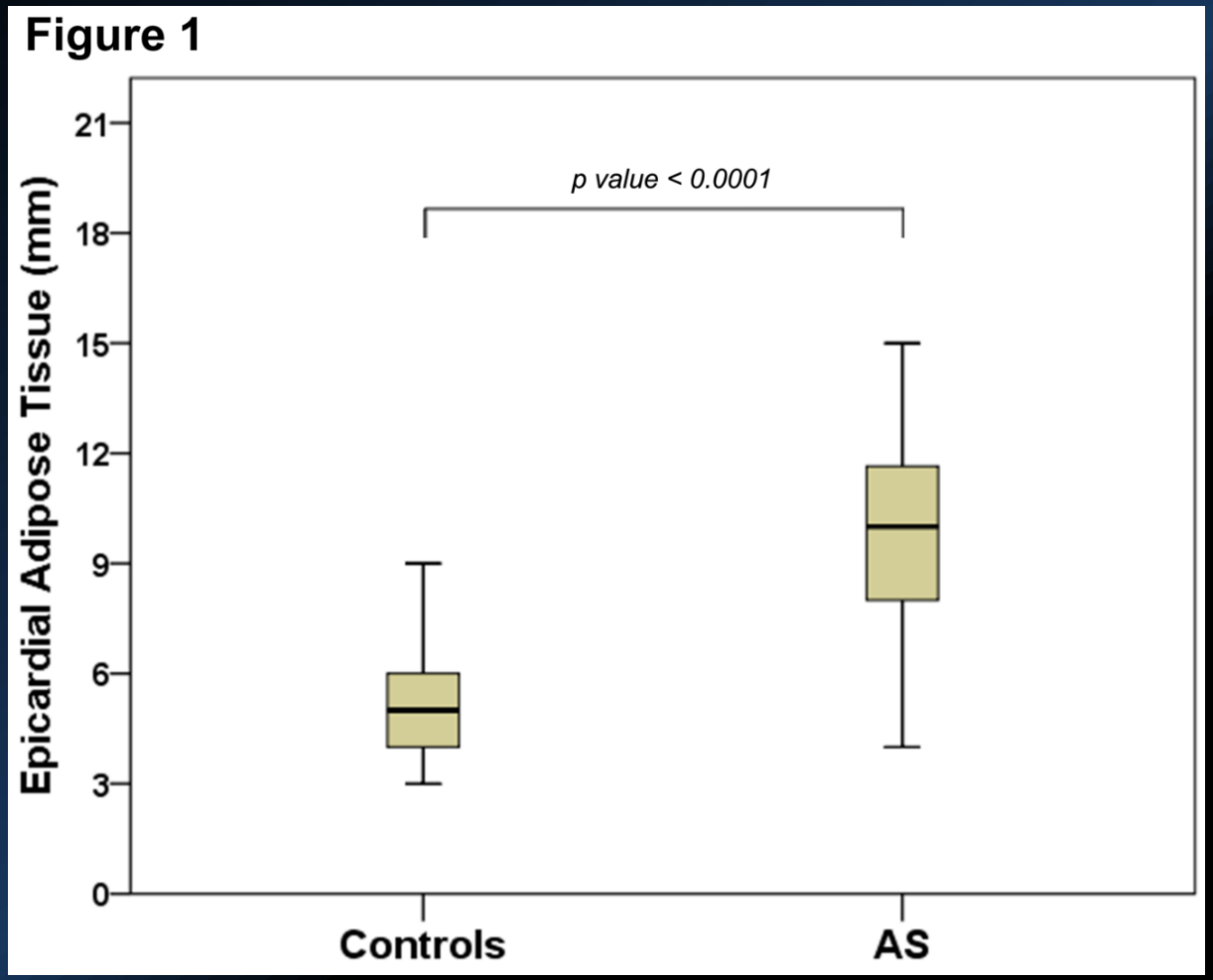


NORMAL
INFLAMMATION
FIBROSIS
CALCIFICATION

MECHANICAL STRESS
LDL
ENDOTHELIAL DAMAGE
T-Cells
MonMonocytes
ENDOTHELIUM
LIPID DEPOSITION + INFLAMMATION
FIBROSA
MACROPHAGES ES
OXIDIZED LDL
Ca^{2+}
T-Cells
Type I and III collagen
MMP TIMP
FIBROSIS
MMP TIMP
Angioneogenesis
Hemorrhage
BONE FORMATION
Remodeling
CALCIFICATION
Alk P
Osteocalcin
BMP 2
Angiotensin II
TGF-β, TNF-α, IL-1β
FIBROBLASTS
MYOFIBROBLASTS
OPG / RANK / RANK L
RUNX 2 / cbfal 1
Wnt3-Lrp5-b catenin
TNF-α
OSTEOBLASTS
Myxoid fibrous degeneration
VENTRICULARIS
Elastin

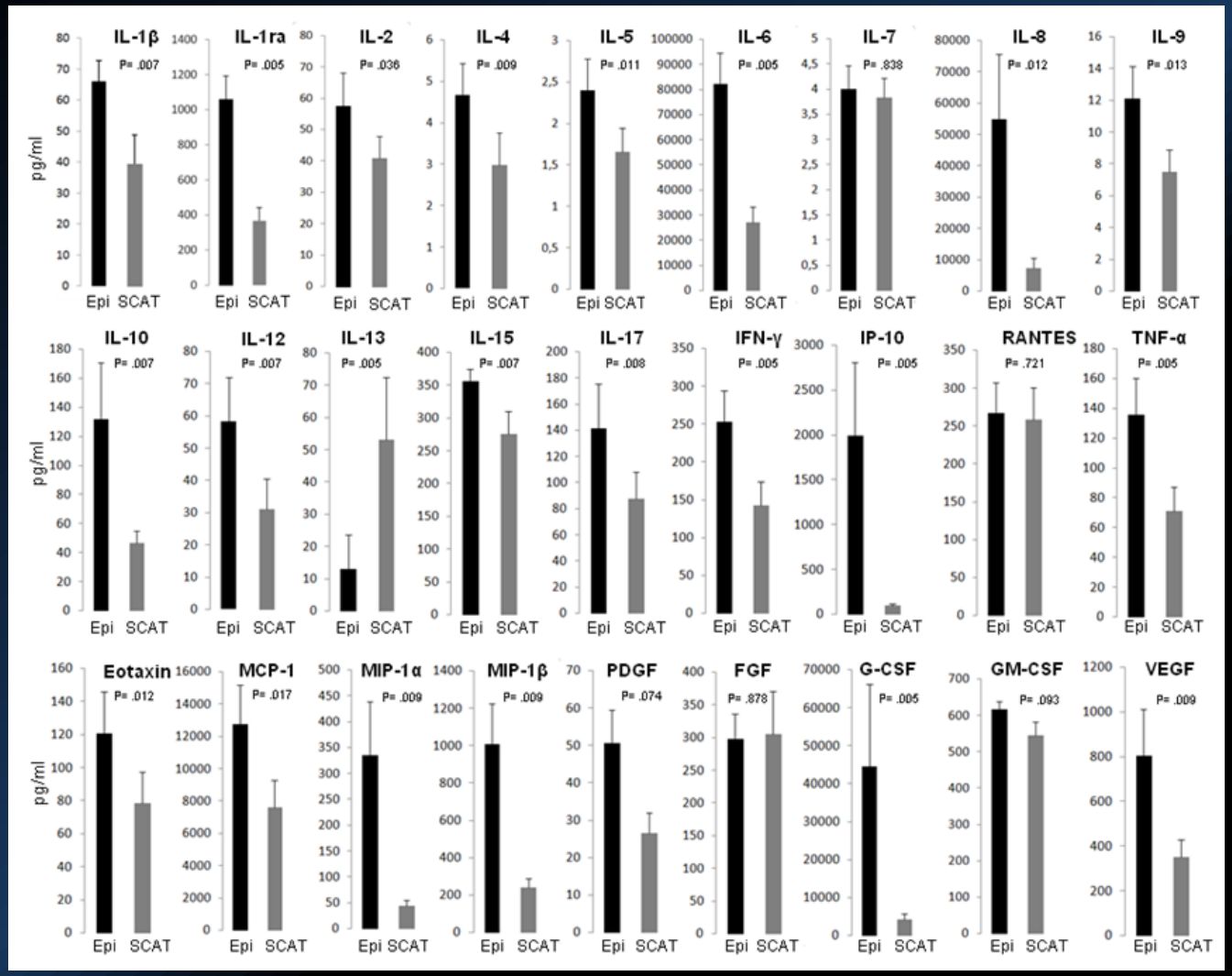
Dweck MR, JACC 2012

Epicardial adipose tissue is increased in pts with calcific aortic stenosis



Parisi V et al, Int J Cardiol 2015

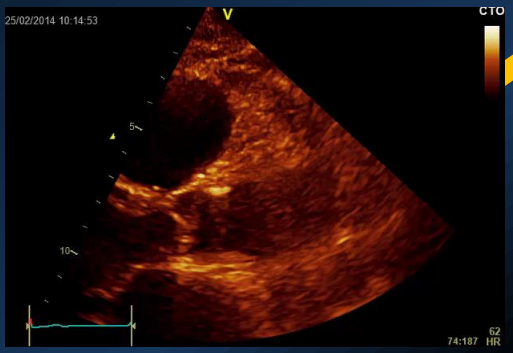
Epicardial adipose tissue is increased in pts with calcific aortic stenosis



Parisi V et al, Int J Cardiol 2015

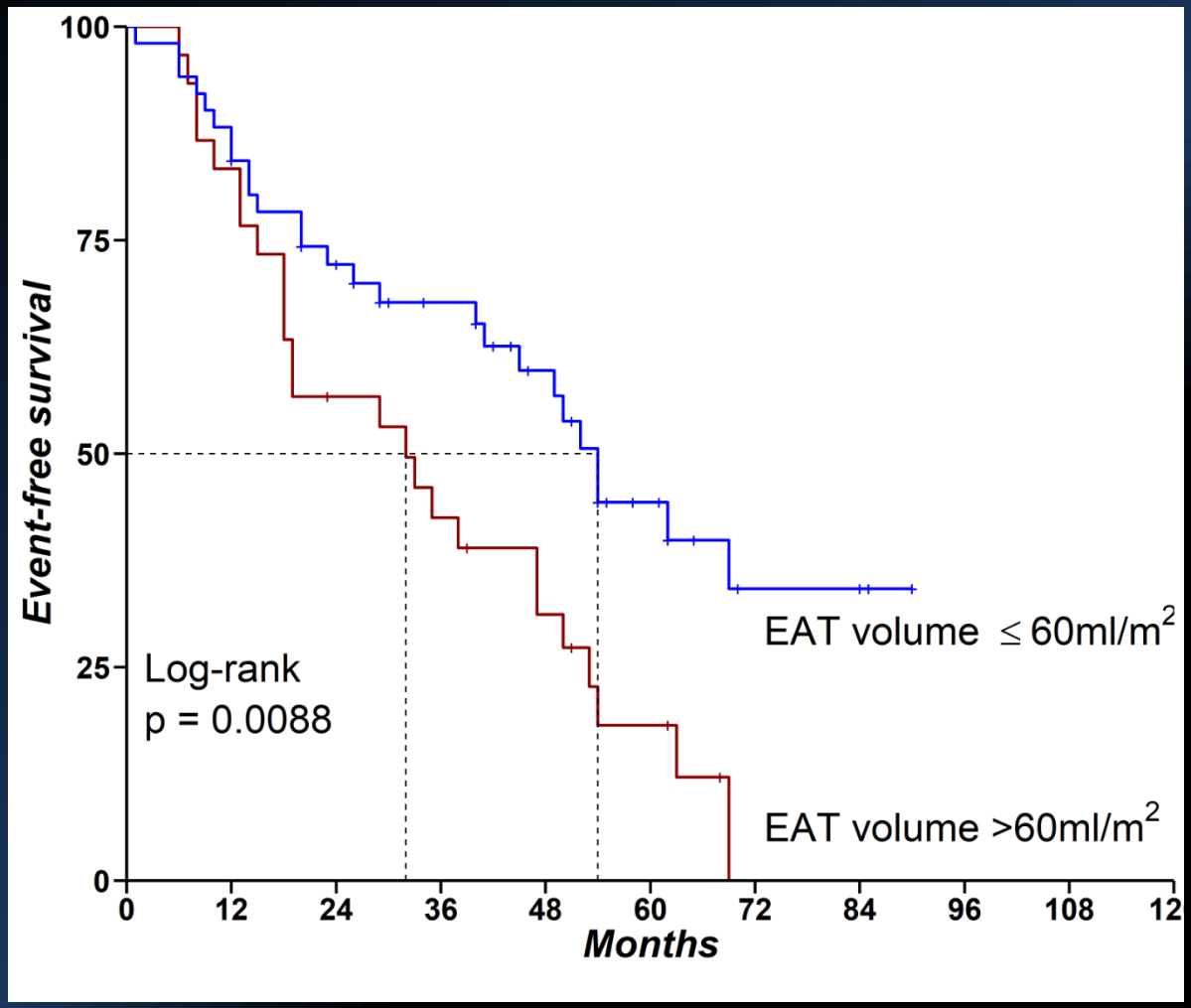
Correlazione tra spessore EAT e secrezione di mediatori infiammatori

	Epicardial fat	
	Spearman	p value
PDGF	.728*	.017
IL-1β	.887**	.001
IL-1ra	.936**	.000
IL-2	.790*	.020
IL-4	.801**	.005
IL-5	.954**	.000
IL-6	.691*	[illegible]
IL-7	.991**	.000
IL-8	.837**	.010
IL-9	.911**	.000
IL-10	.960**	.000
IL-12	.63[illegible]	.048
IL-13	.110	.762
IL-15	.538	.108
IL-17	.838**	.002
Eotaxin	.850**	.007
FGF basic	.917**	.000
G-CSF	.813**	.004
GM-CSF	.275	.441
IFN-[illegible]	.813**	.004
I[illegible]10	.881**	.001
MCP-1	.711*	.048
MIP-1α	.813**	.004
MIP-1β	.869**	.001
RANTES	.575	.082
TNF-α	.869**	.001
VEGF	.569	.086



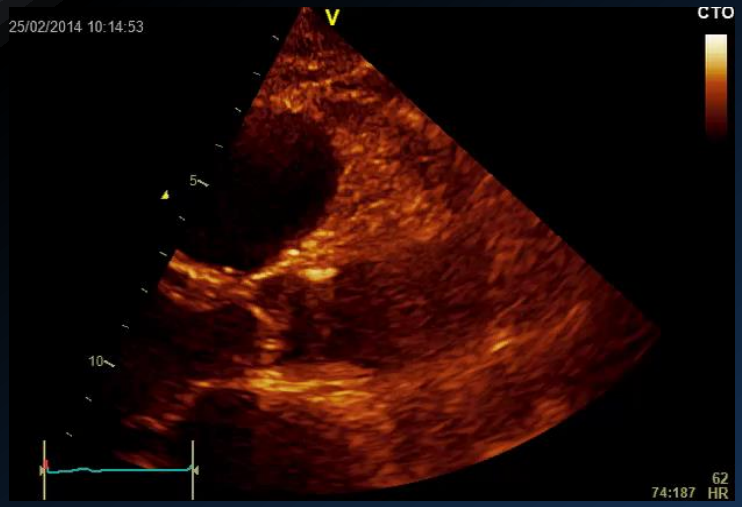
Parisi V et al, Int J Cardiol 2015

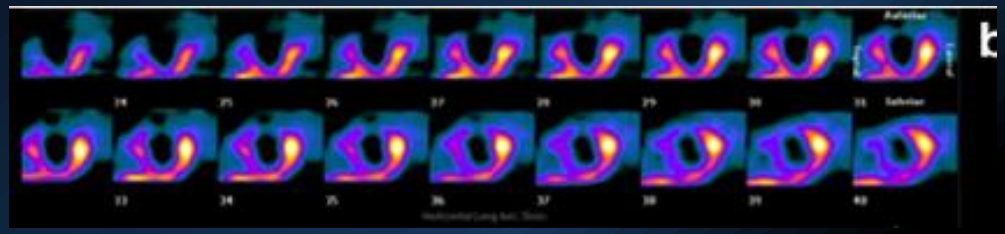
EAT and outcome in aortic stenosis AVR-survival

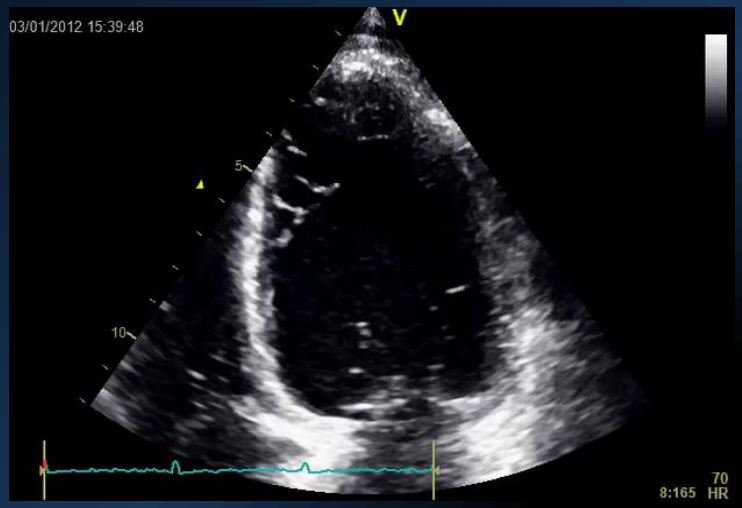


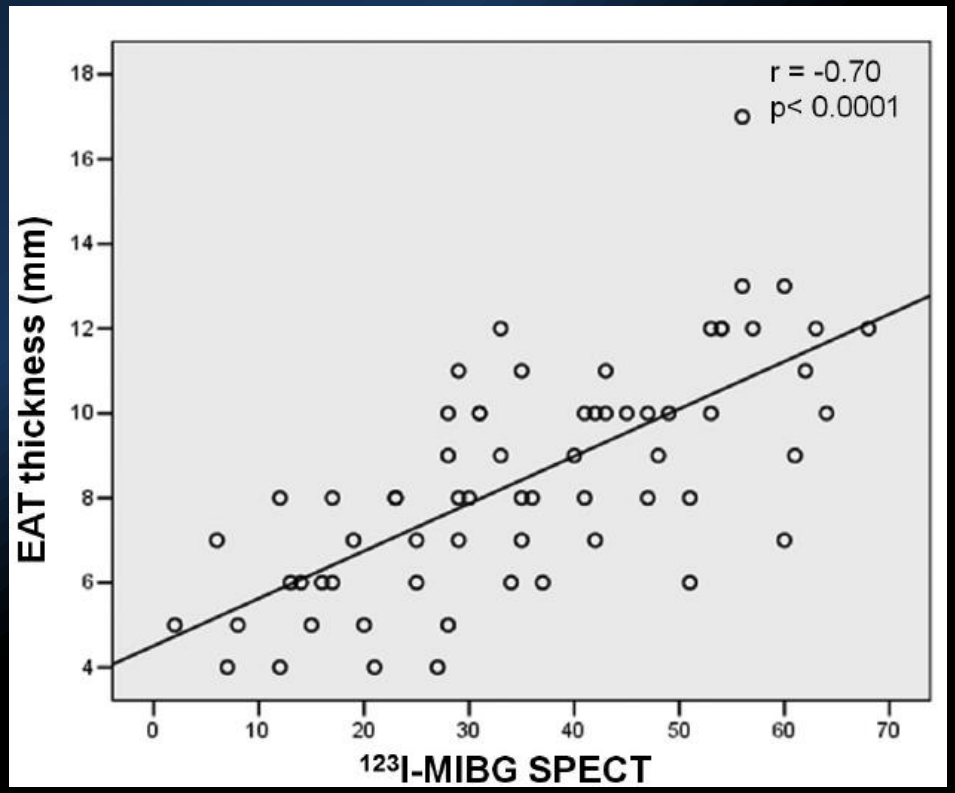
Davin L..Parisi V. et al. JACC CI 2018

EAT – sistema adrenegico nello scompenso



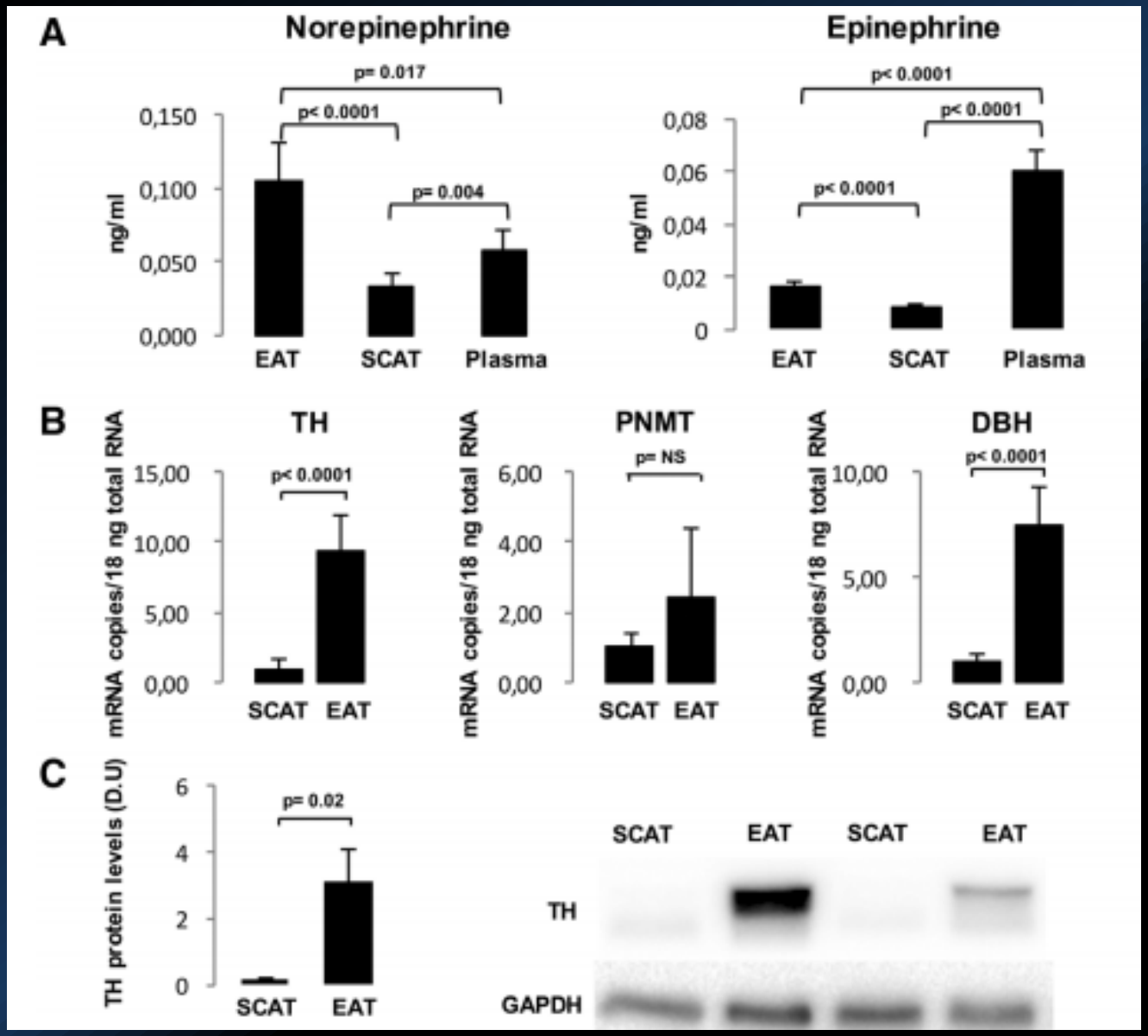






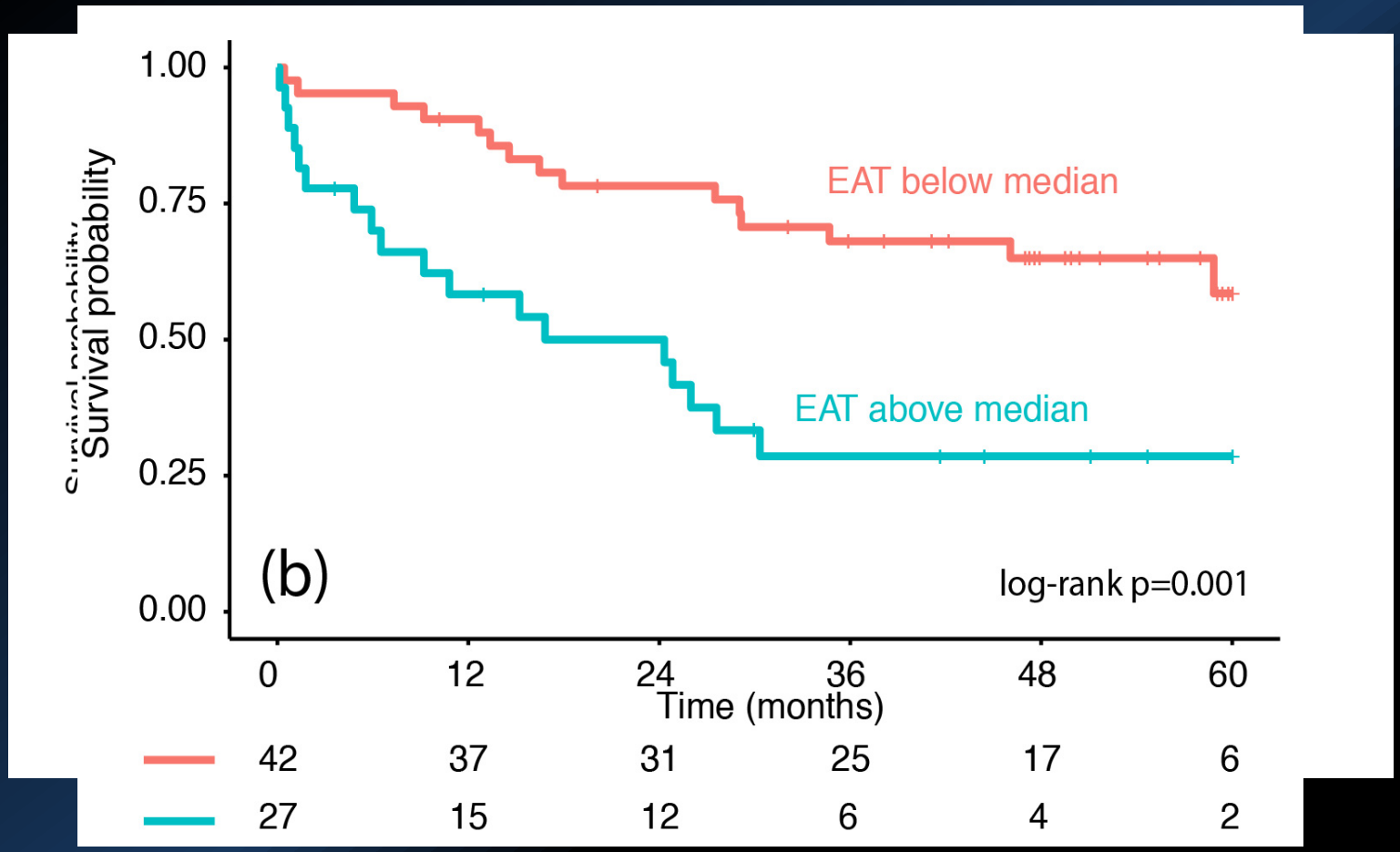
Parisi V et al, Circ Res 2016

EAT – sistema adrenegico nello scompenso

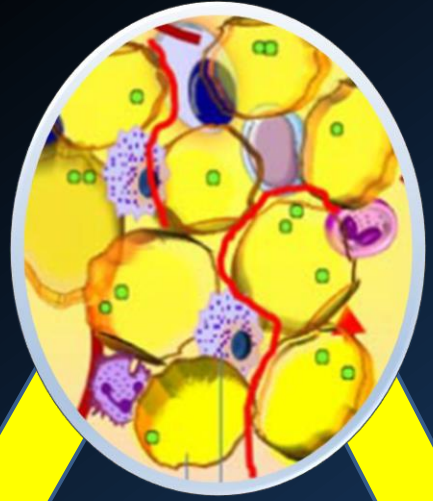


Parisi V et al, Circ Res 2016

EAT and outcome in heart failure



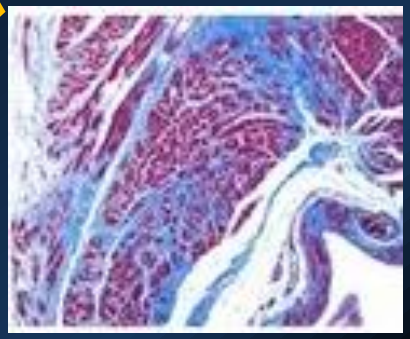
Parisi V et al, unpublished data



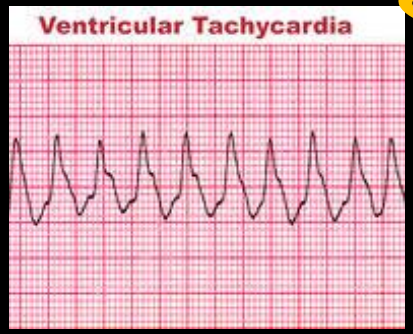
Rilascio citokine infiammatorie e pro-fibrotiche

Rimodellamento adrenergico secrezione catecolamine

Substrato

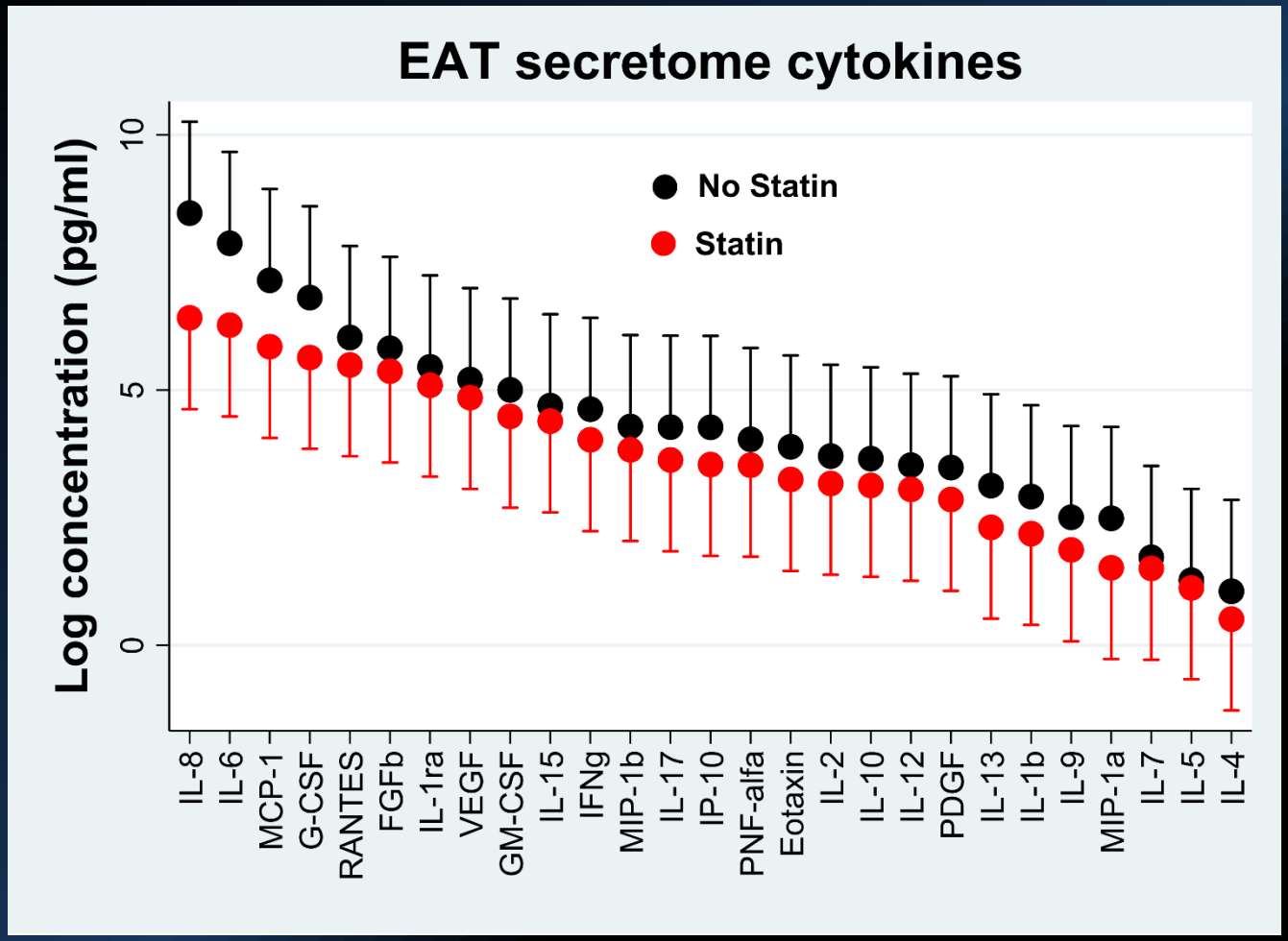


Trigger



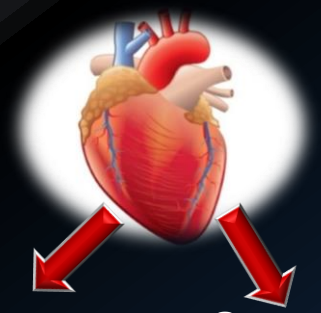
ARITMIE

Statin therapy on EAT inflammatory profile



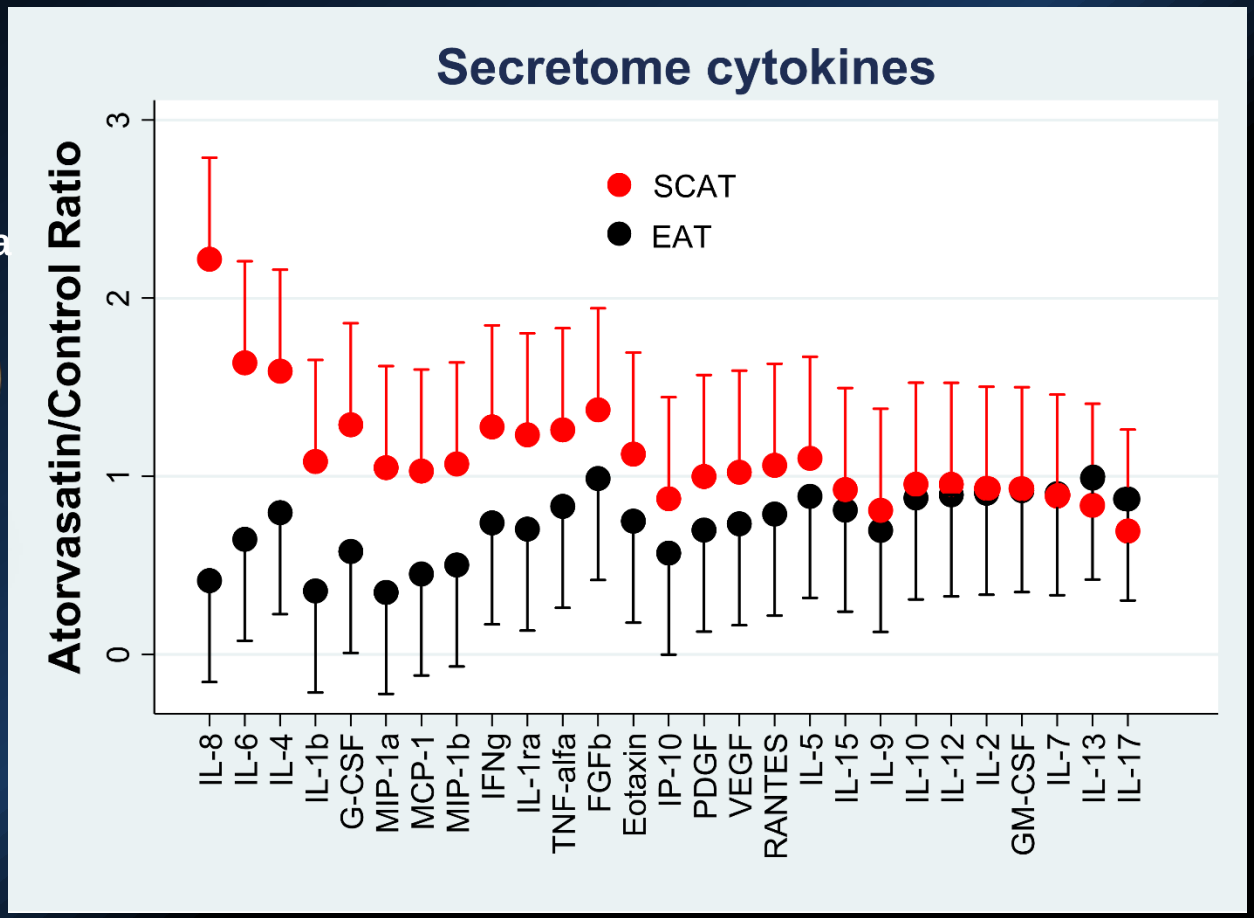
Parisi V. et al. Int J Cardiol 2018

In vitro effects of atorvastatinon on EAT inflammatory profile



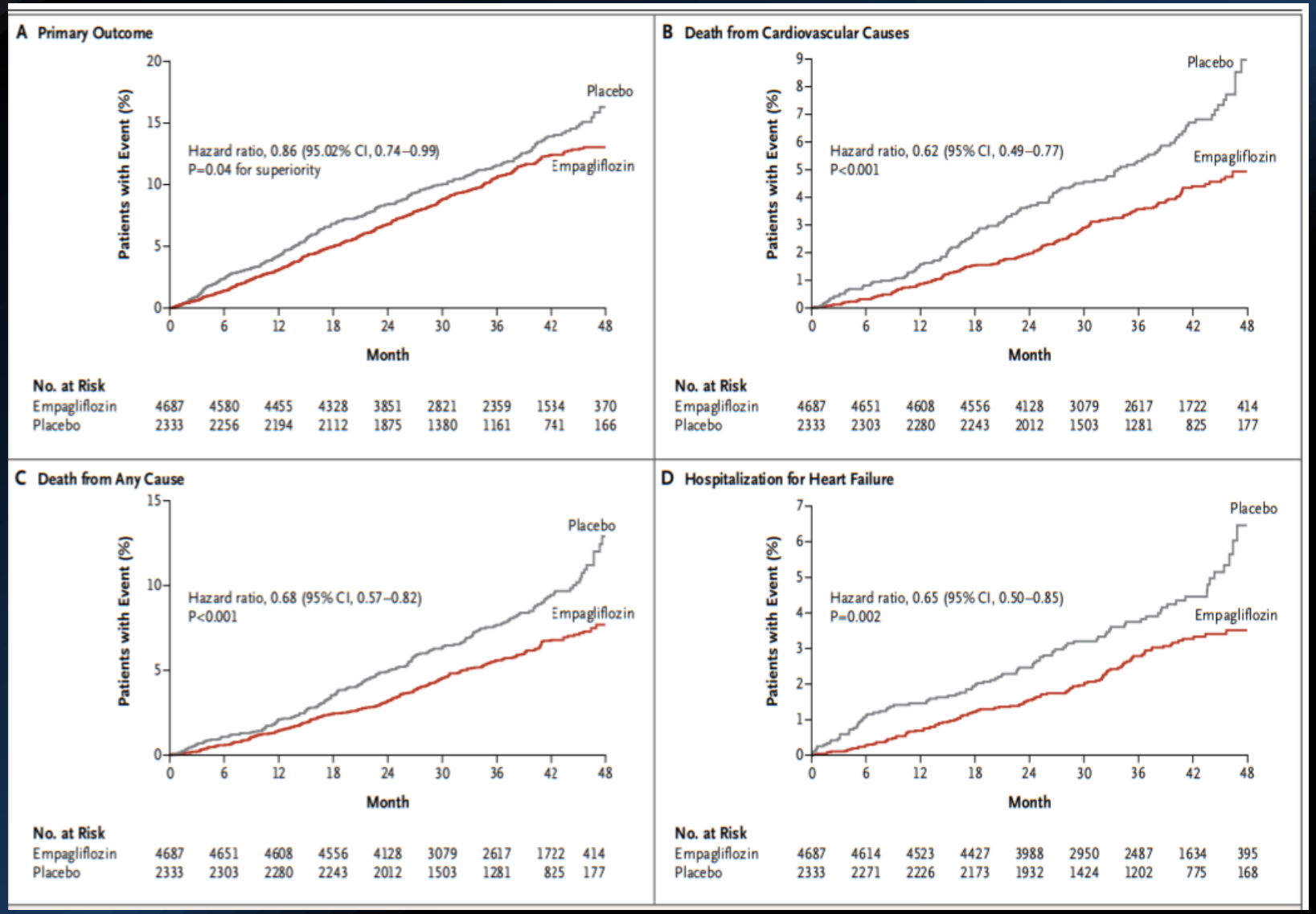
Secretoma di controllo

Secretoma + atorvastatina



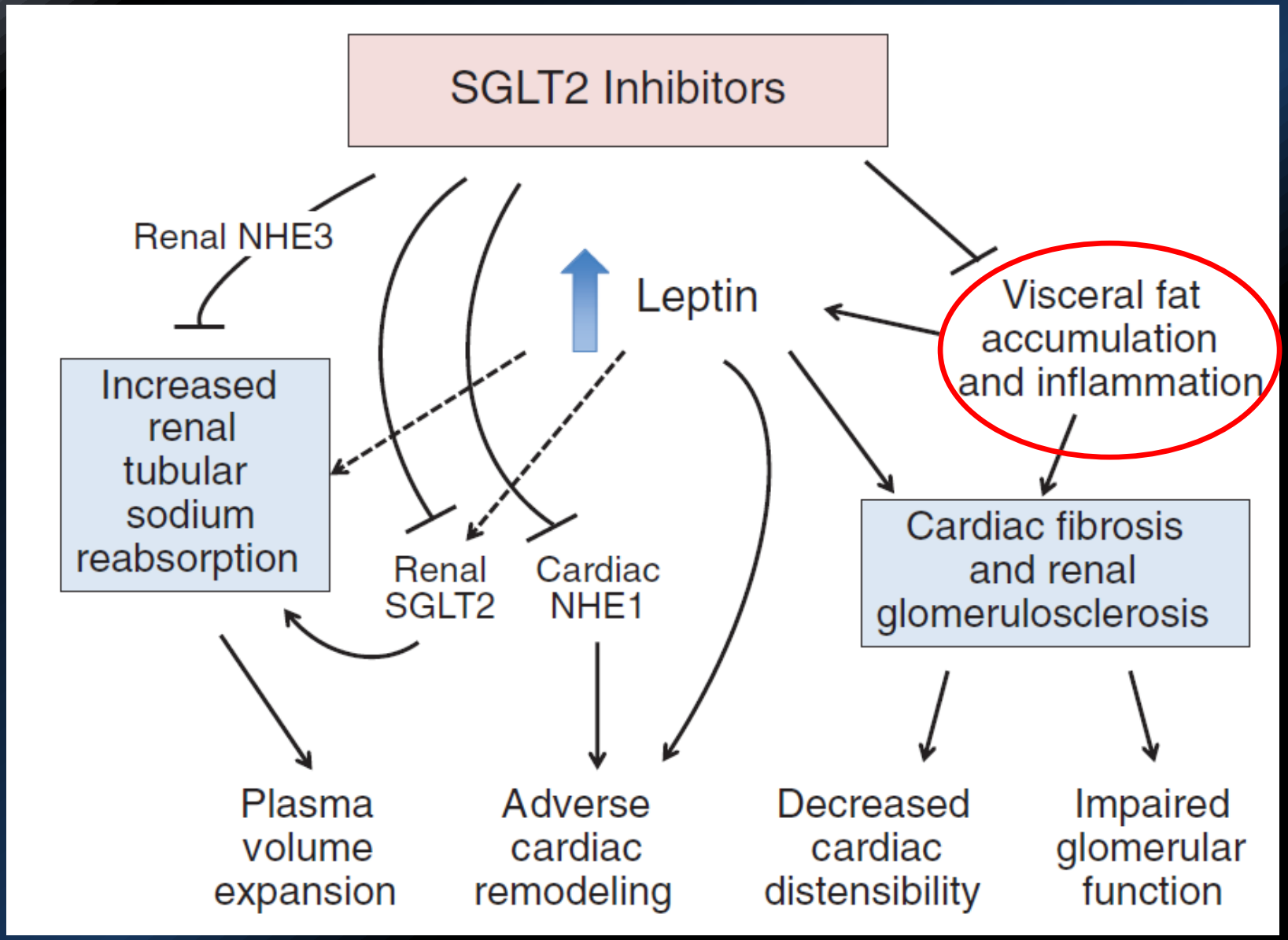
Parisi V. et al. Int J Cardiol 2018

Empagliflozin, Cardiovascular Outcomes, and Mortality in Type 2 Diabetes (EMPAREG trial)



N Engl J Med 2015

SGLT2 E TESSUTO ADIPOSO



Packer M. Diabetes Obese Metab 2018

Take Home Message

- Il tessuto adiposo viscerale è fonte di mediatori infiammatori e proaterogenici correlati a patologia cardiaca

- Il tessuto adiposo epicardico può essere considerato un marker di rischio cardiovascolare, l'aumento del suo spessore corrisponde a più alti livelli di citokine secrete

- L'aumento del grasso epicardico sembra essere associato associato a peggiore outcome nelle patologie cardiovascolari

- Tessuto adiposo epicardico potenziale nuovo target terapeutico


THANK
YOU :)