UNIVERSITÀ DEGLI STUDI DI VERONA

61° CONGRESSO NAZIONALE SIGG

"Stiamo lavorando per farti invecchiare meglio"

SOCIETÀ ITALIANA
DI GERONTOLOGIA
E GERIATRIA

Chronic low grade inflammation nell'anziano

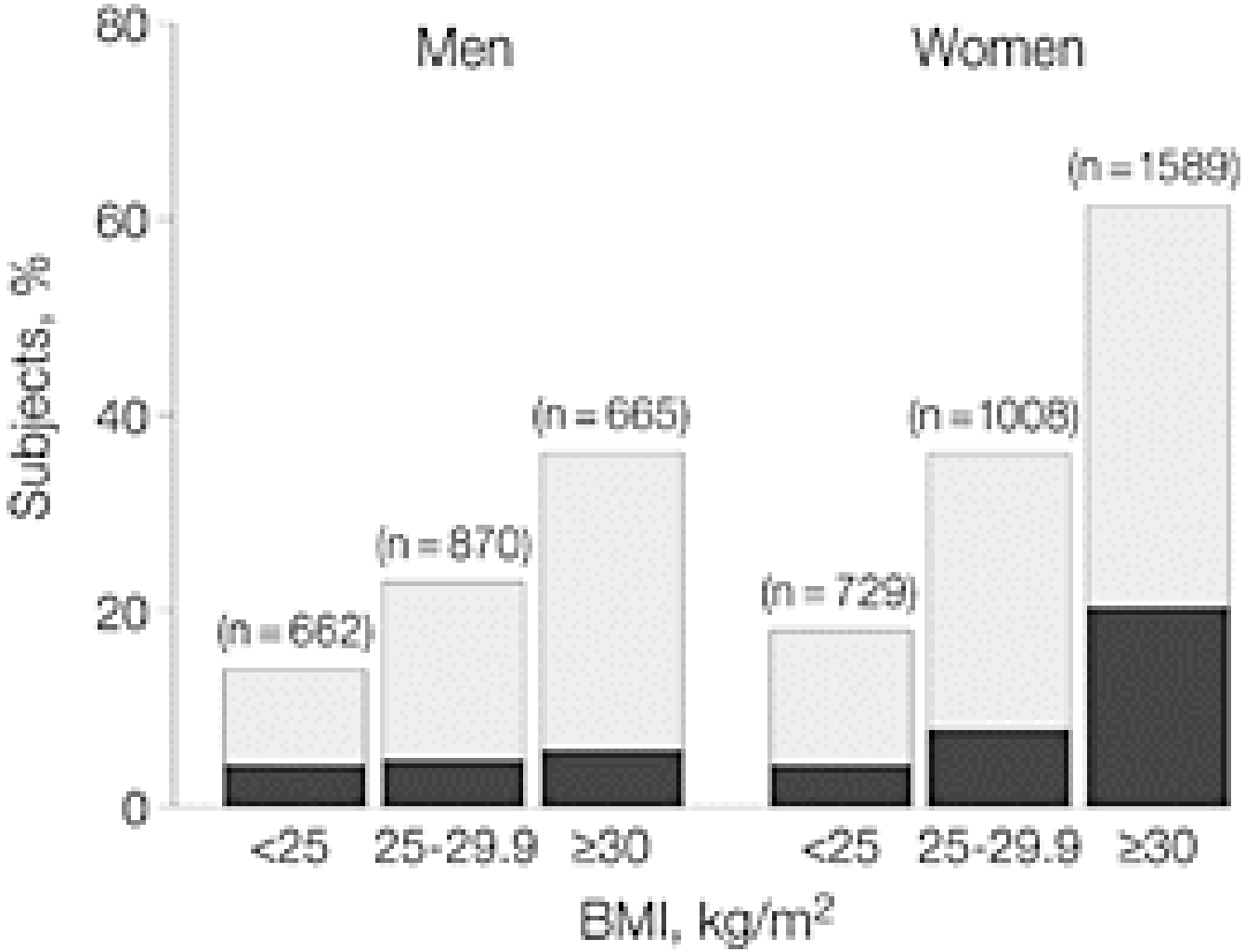
Problematiche in corso in ambito di:

Obesità

Prof Mauro Zamboni

Clinica Geriatrica-Università di Verona

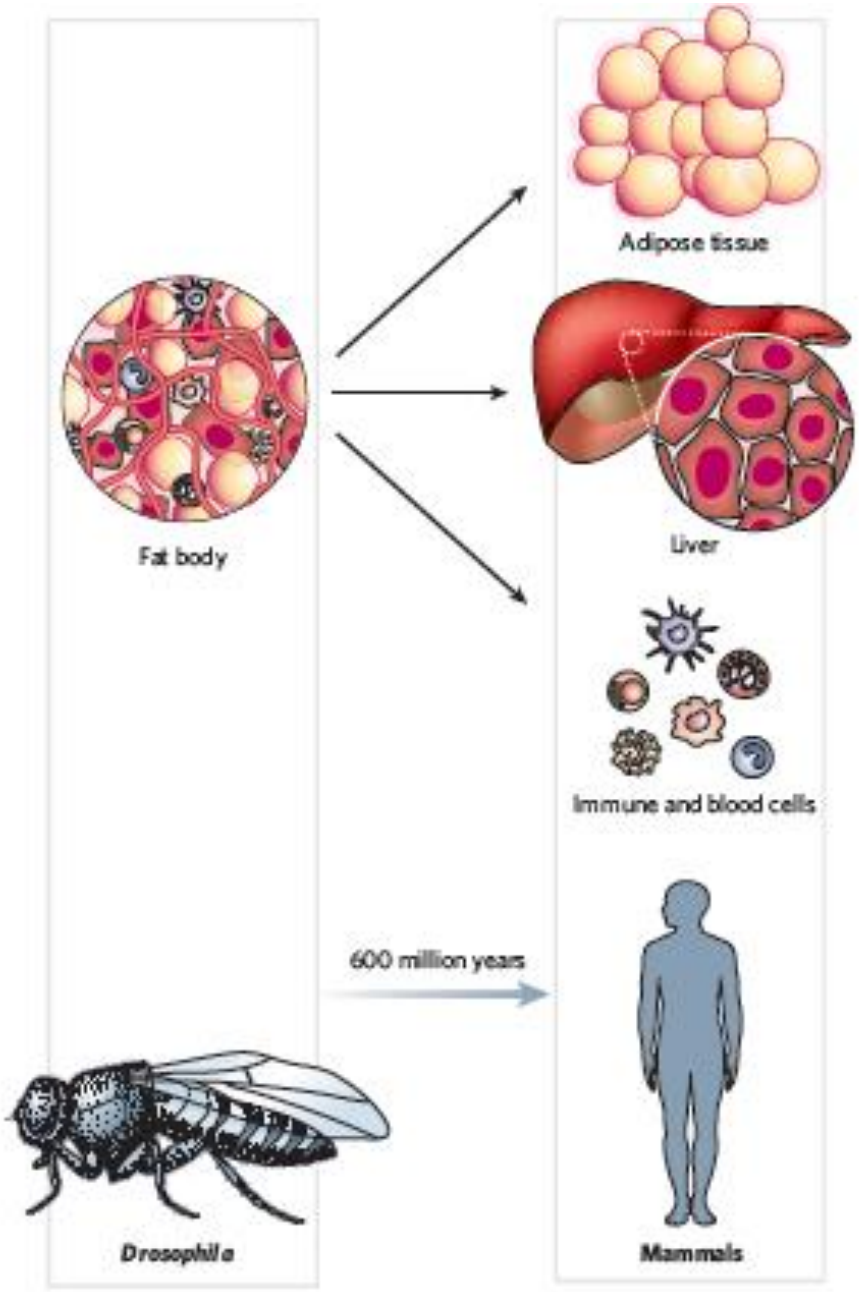
Prevalence of Elevated (>0.22 mg/dL) Serum C-Reactive Protein Concentration by BMI Category in Men and Women Aged 17 Years or Older



JAMA

Visser, M. et al. JAMA 1999

Evolution of AT, the liver and the haematopoietic system from one functional unit in Drosophila (the "fat body") into distinct organs in mammals



NATURE|Vol 444|14 December 2006|doi:101038/nature05485

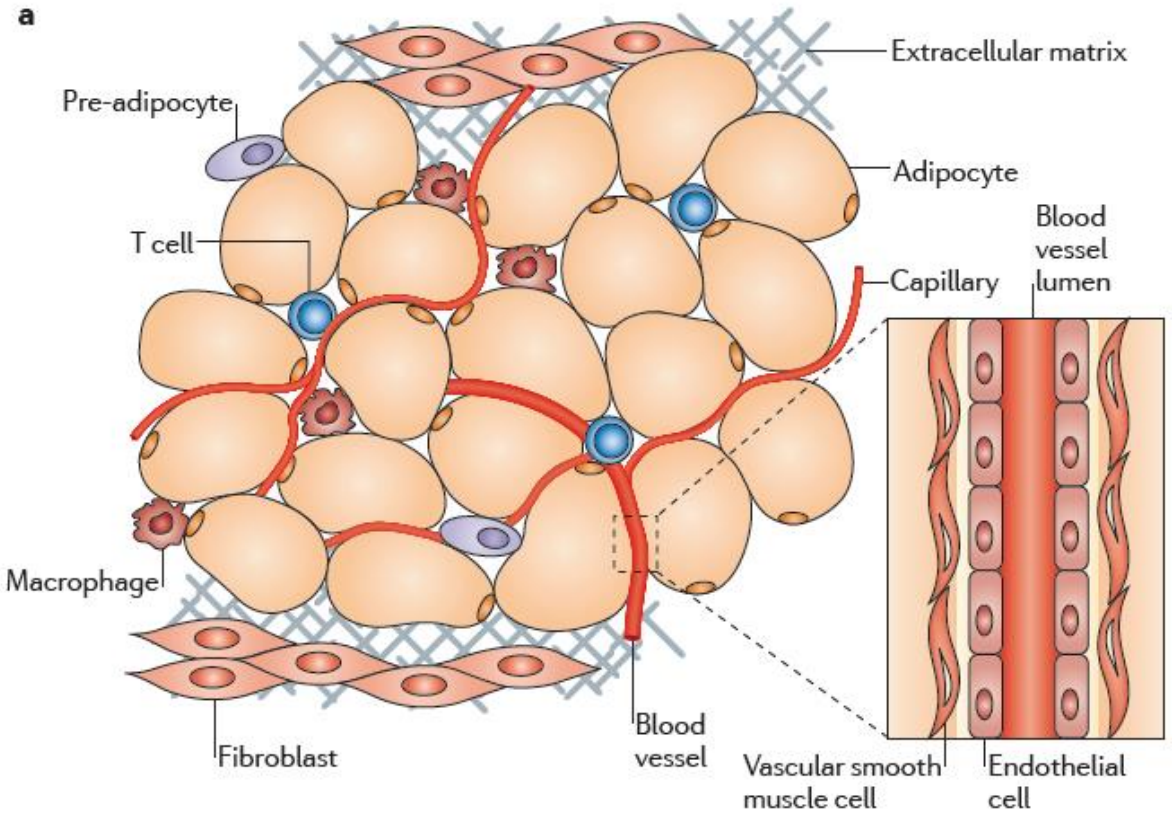
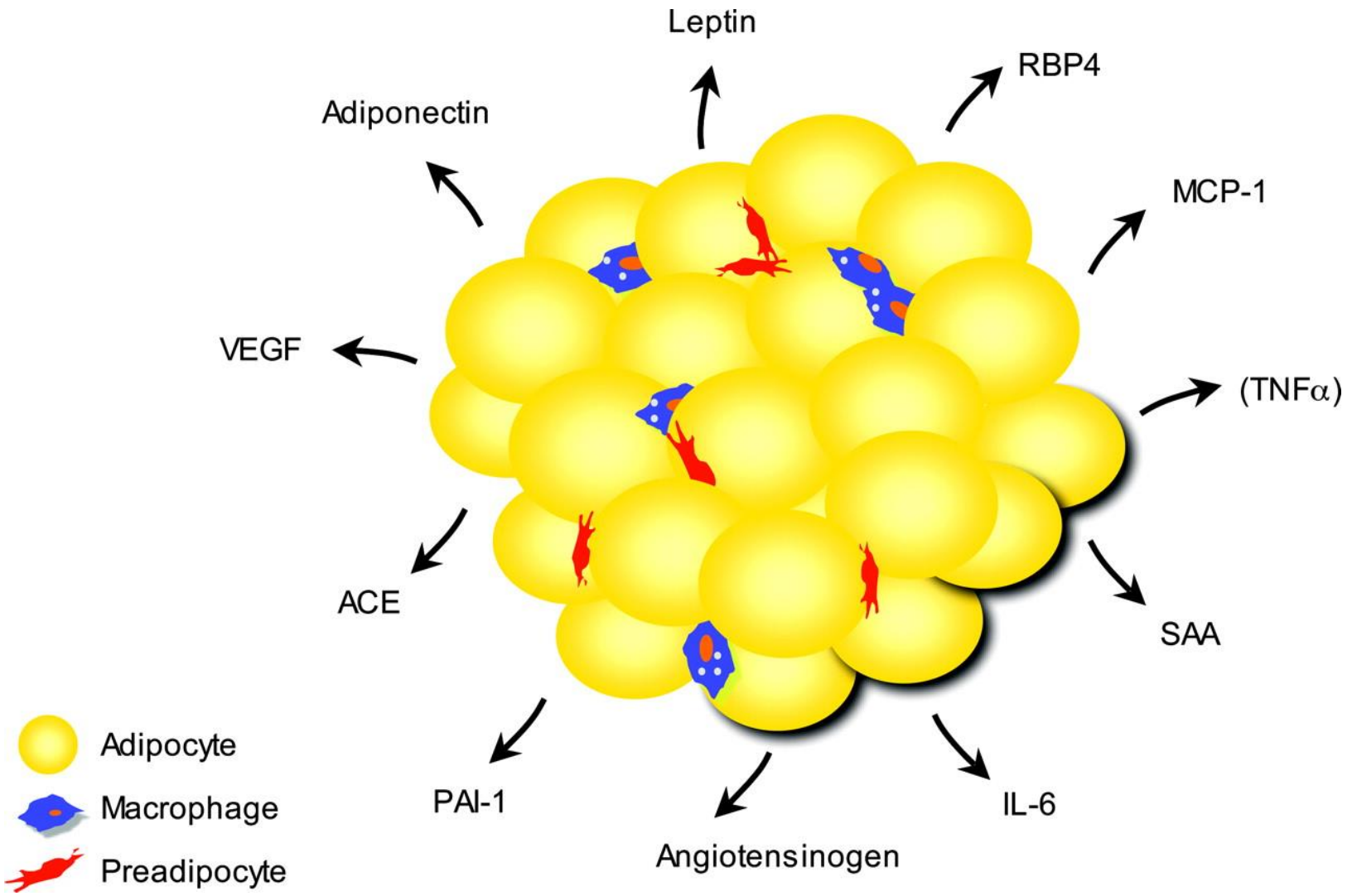


Table 1. Cellular components (%) of human adipose tissue

Mature adipocytes	50–70
Stromal 'preadipocytes'	20–40
Endothelial cells	1–10
Macrophages	1–30
Other cell types	?

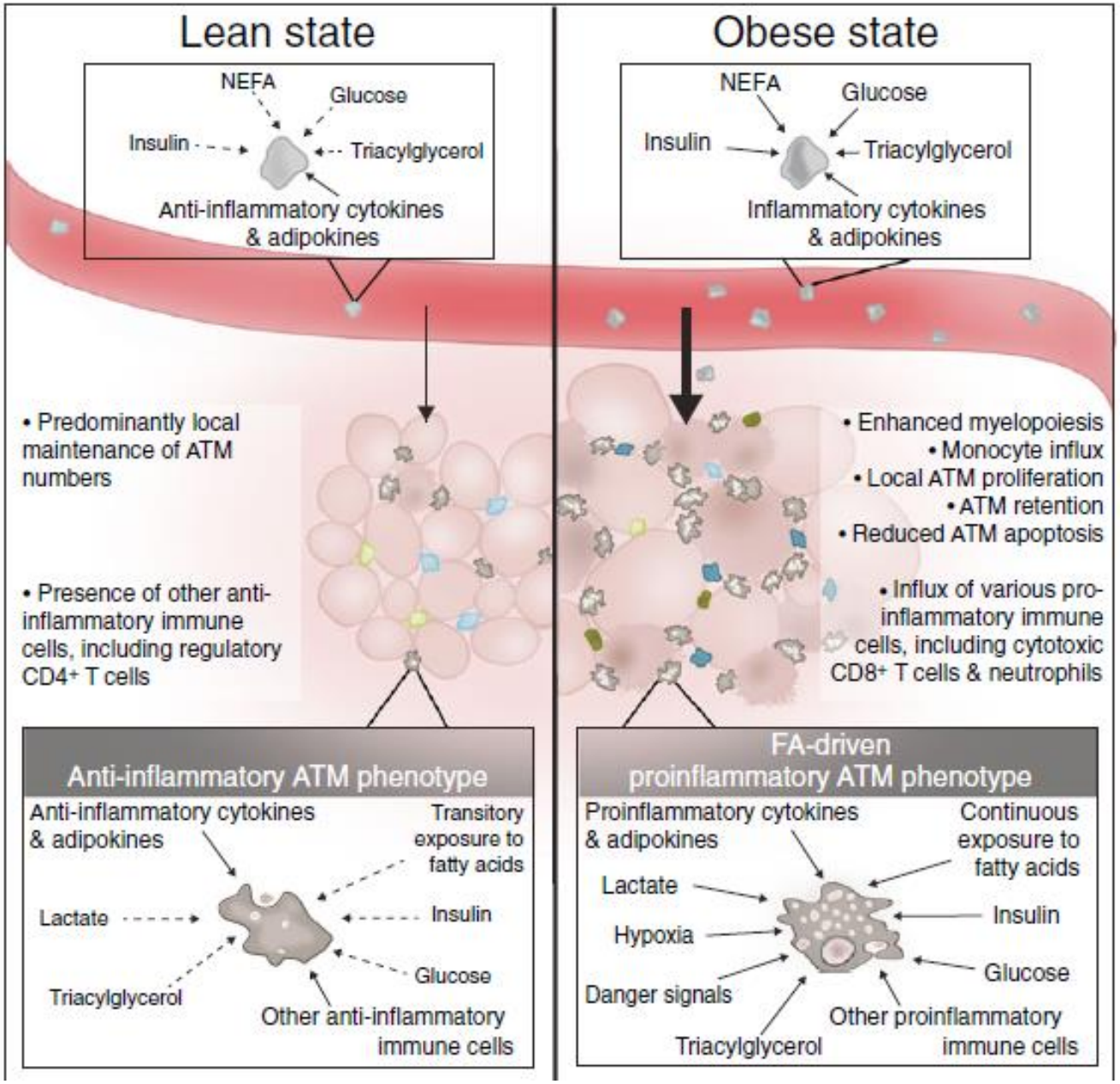
Hauner H, Proc Nat Soc 2005

adipokines released by the adipose tissue.



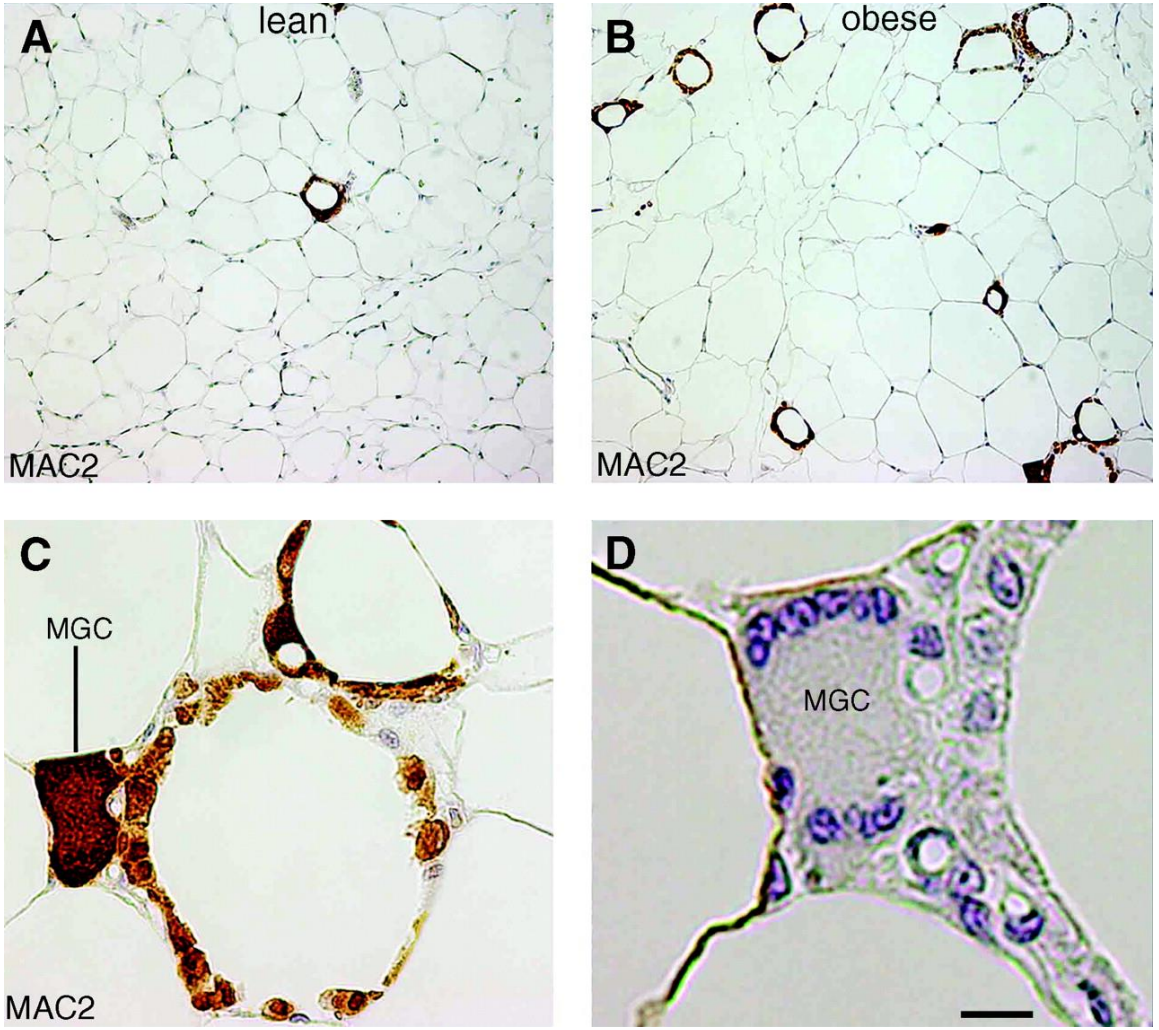
American Heart Association
Learn and Live

Gustafson B et al. 2007



Boutens l and Stienstra R, Diabetologia 2016

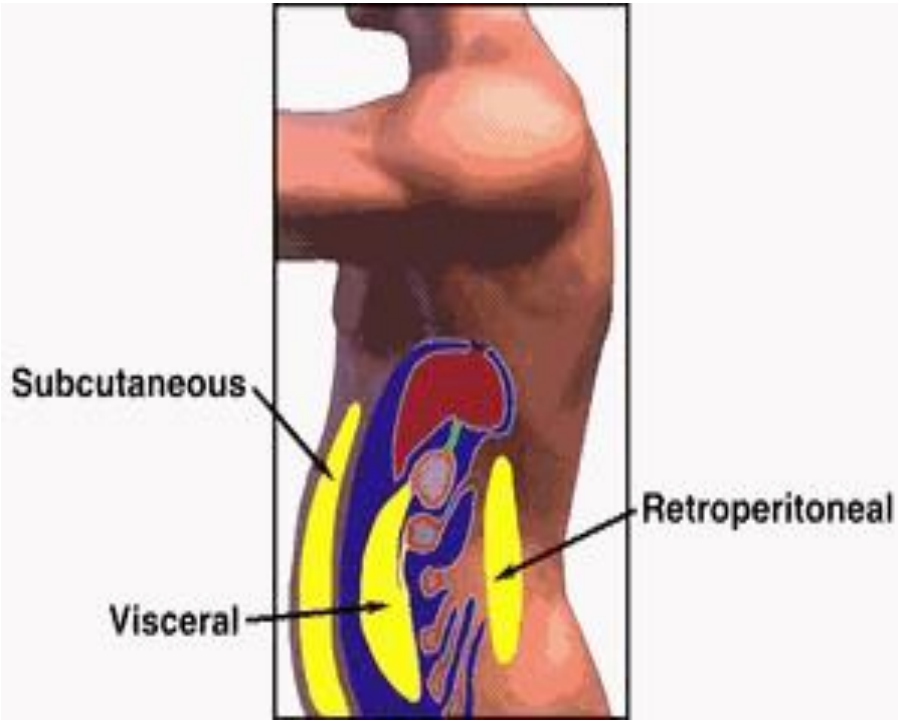
White adipose tissue (WAT) macrophages localize to crown-like structures (CLS) around individual adipocytes, which increase in frequency with obesity



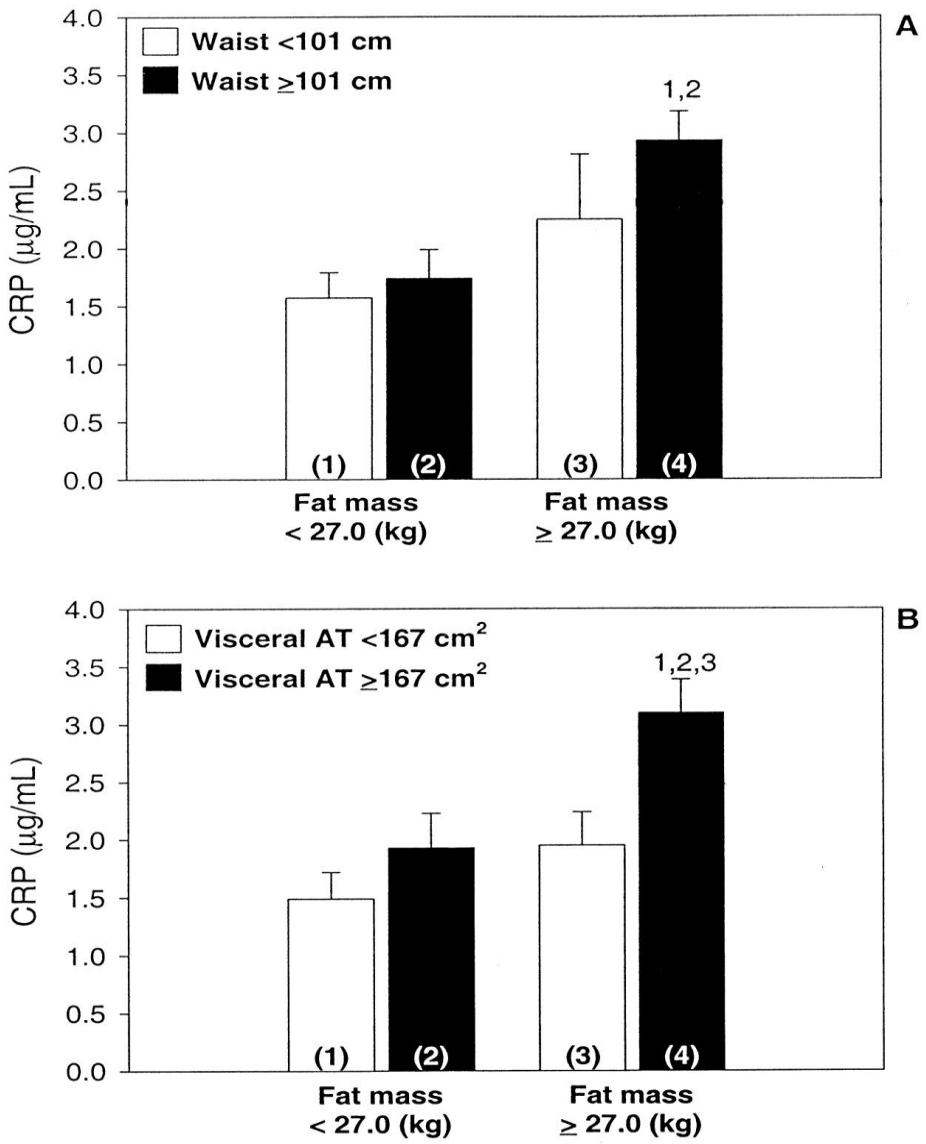
CLS form exclusively at sites of adipocyte death and scavenge the residual adipocyte lipid droplet

Cinti, S. et al. J. Lipid Res. 2005

Fenotipi di obesità e infiammazione



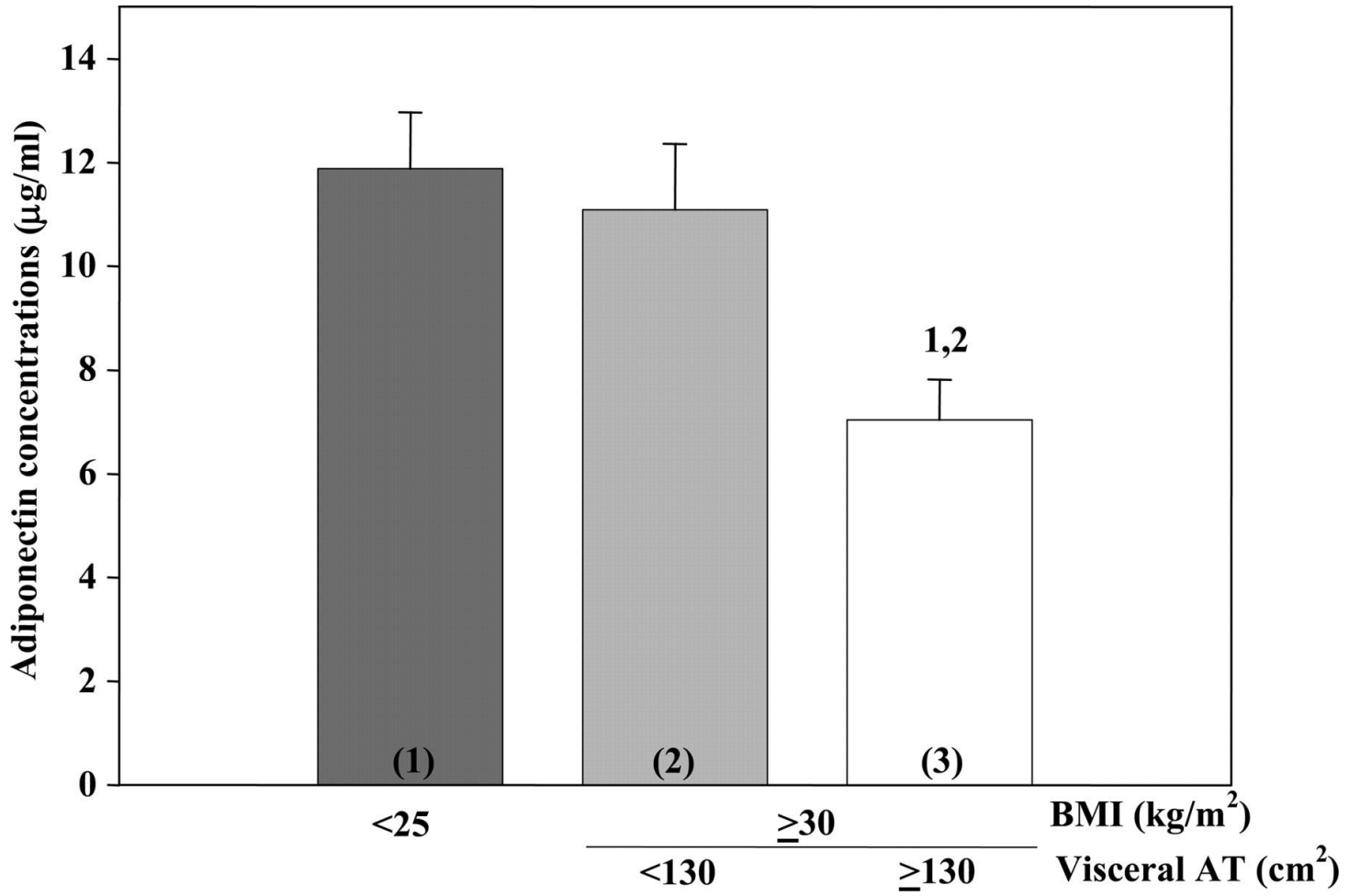
CRP concentrations according to the 50th percentile values of either waist girth (A) or visceral AT (B) and body fat mass



American Heart Association®
Learn and Live℠

Lemieux I, Arterioscler Thromb Vasc Biol, 2001

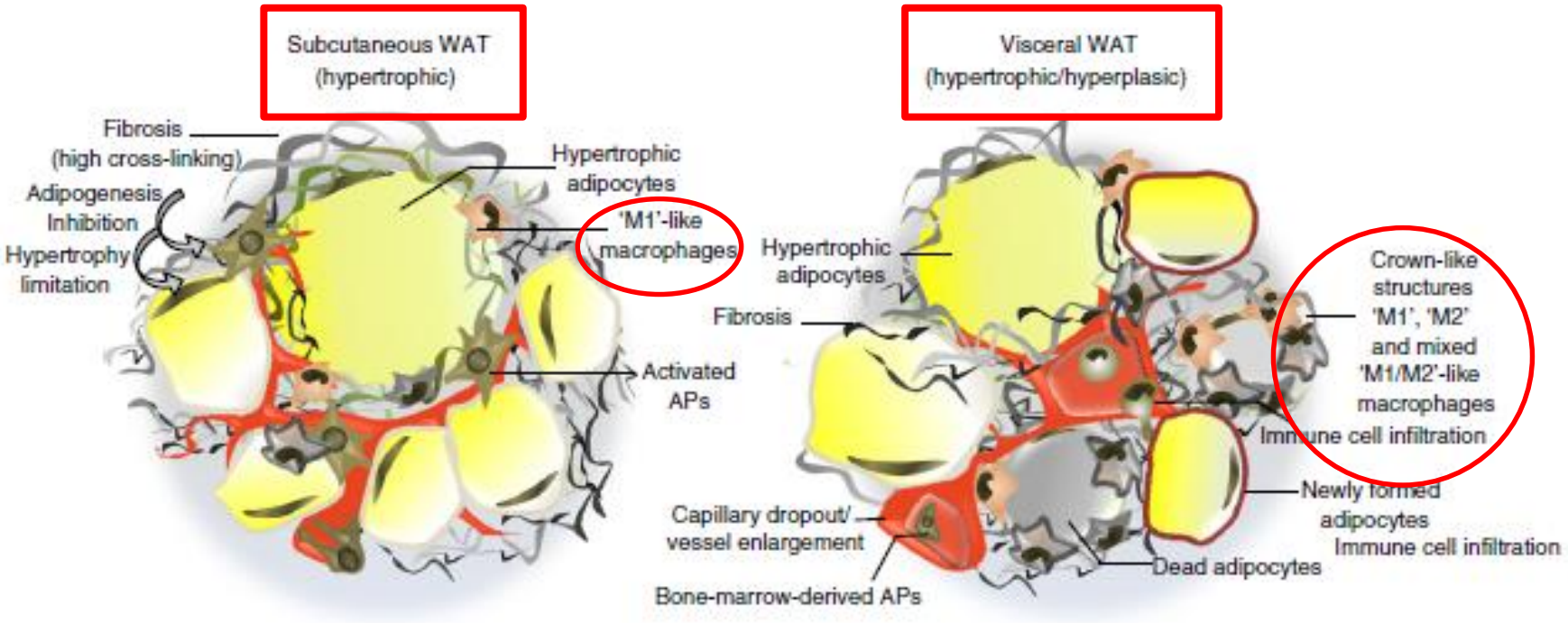
Adiponectin concentrations in 39 non-obese men (1) and in two groups of 15 obese subjects each matched for similar BMI with low (2) or high (3) visceral AT



THE JOURNAL OF CLINICAL ENDOCRINOLOGY & METABOLISM

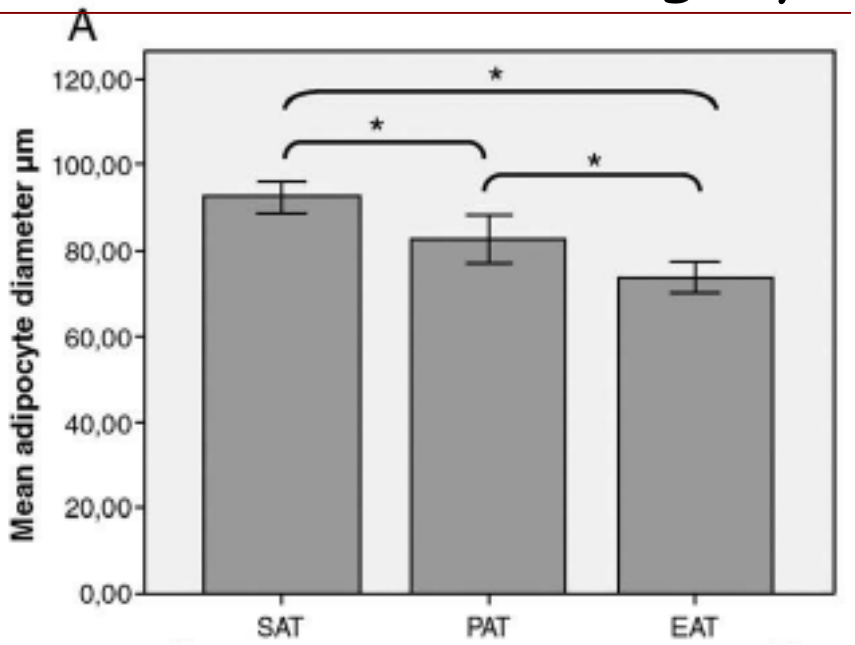
Cote, M. et al. ,2005

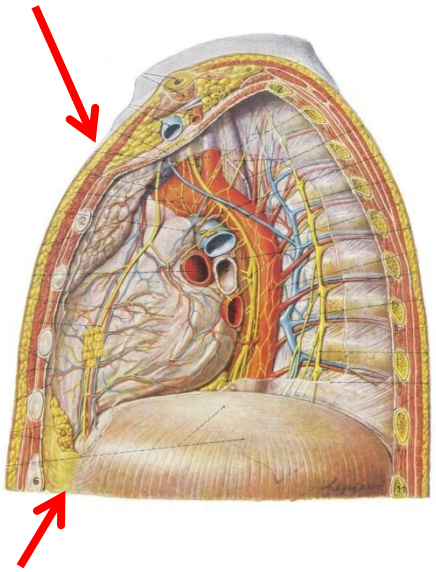
Adipose tissue plasticity: how fat depots respond differently to pathophysiological cues

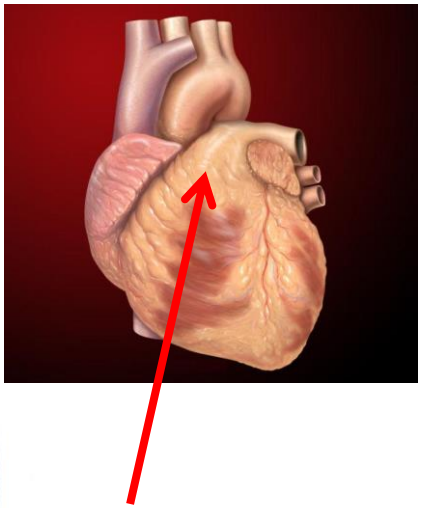


Pellegrinelli V. Diabetologia 2016

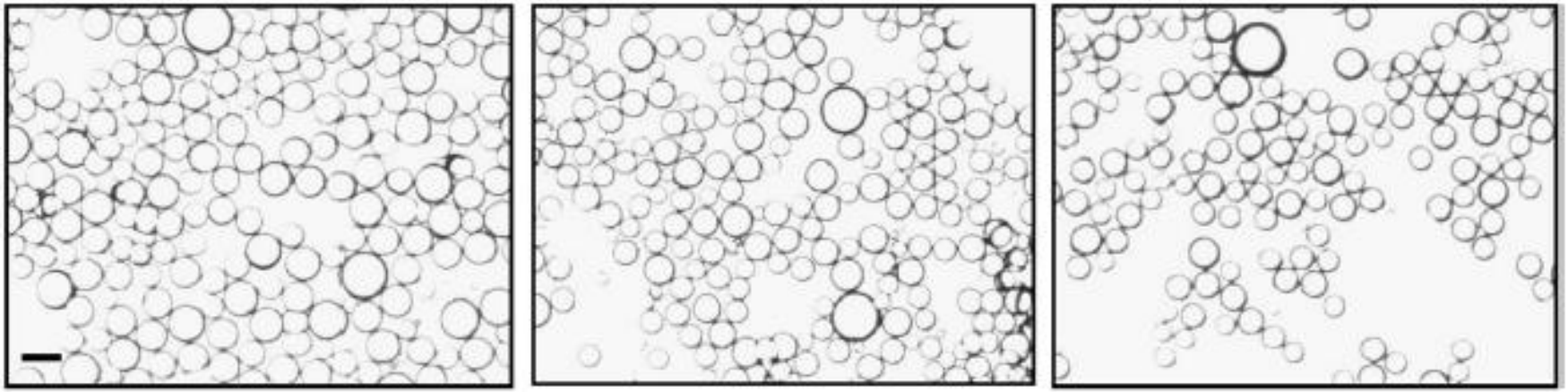
21 men undergoing elective cardiac surgery







Epicardial fat



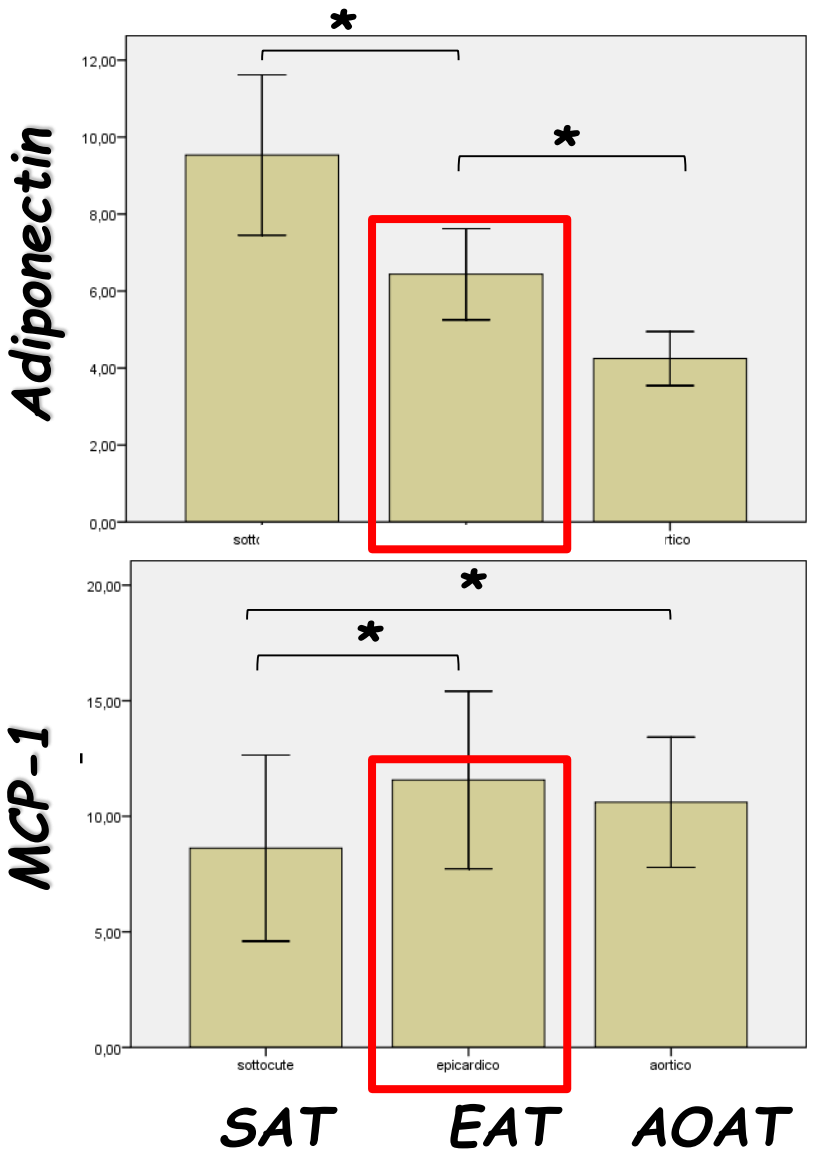
SAT

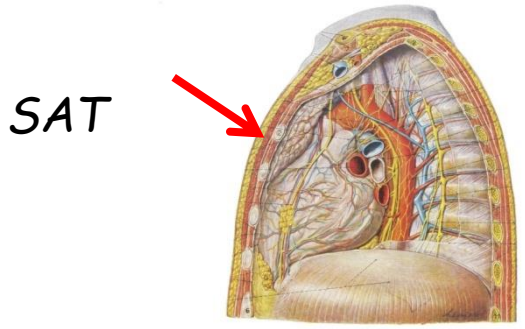
PAT

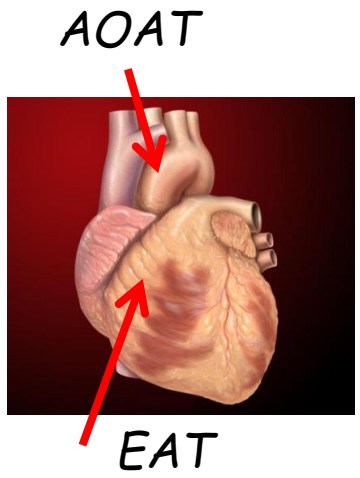
EAT

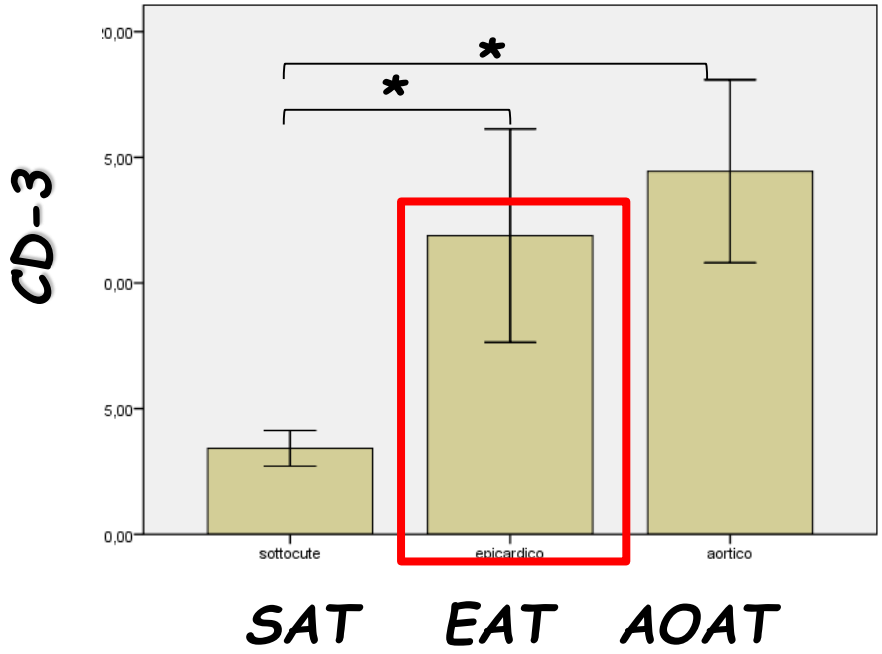
Bambace et al. Cardiovascular Pathology 2011

Gene Expression in Subcutaneous (SAT) vs Epicardial (EAT) and PeriAortic (AOAT) Adipose Tissue





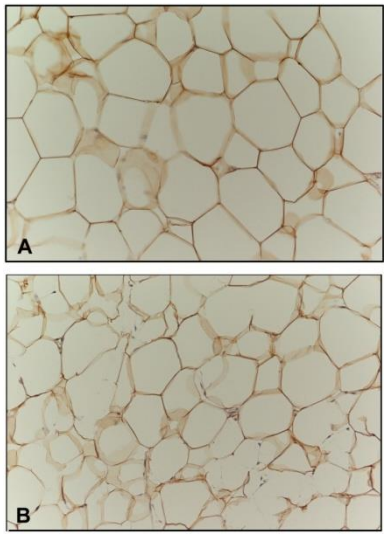




*=p<0,05

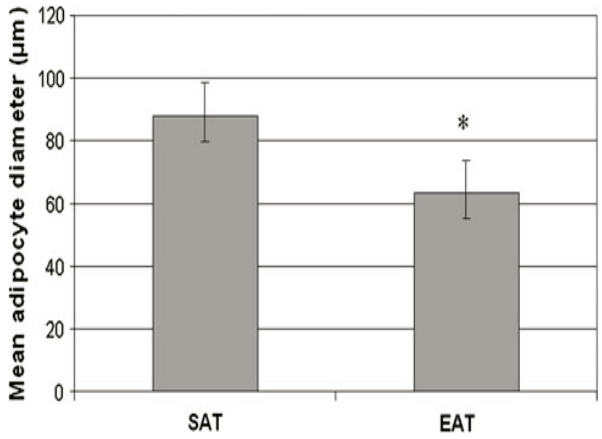
Bambace et al. Cardiovascular Pathology 2011

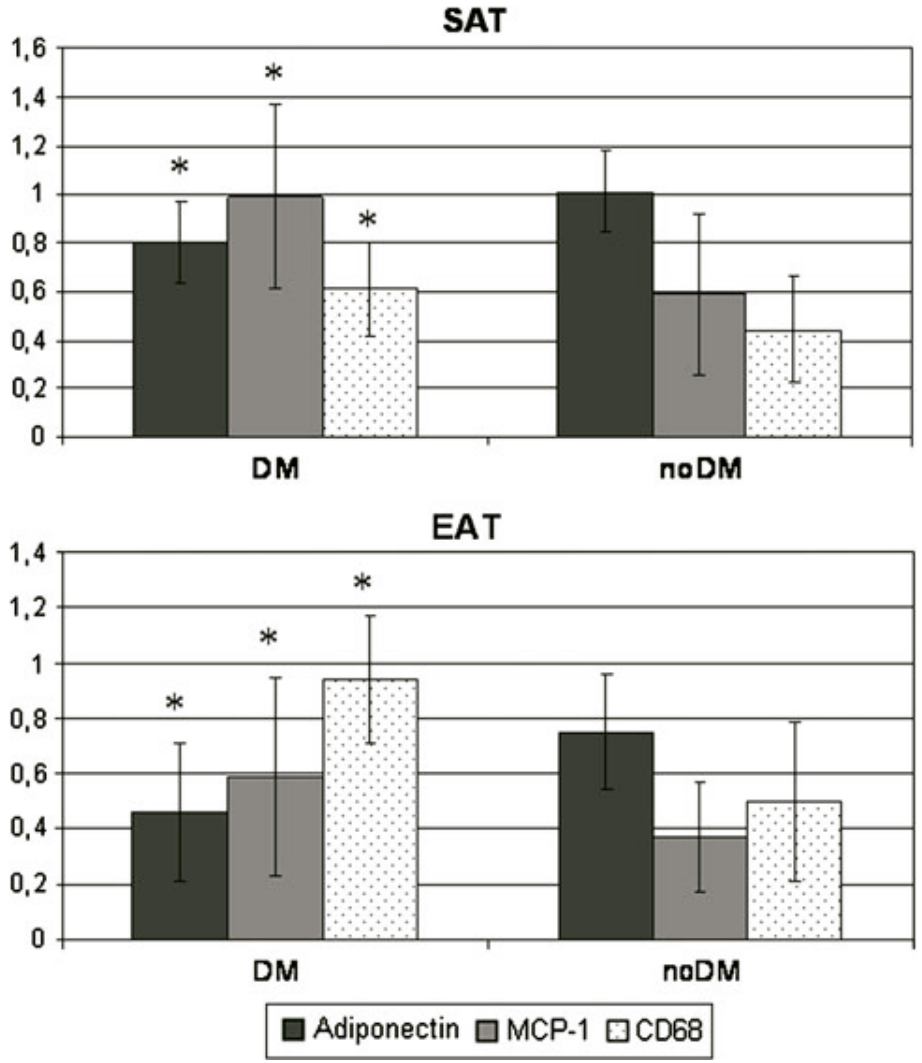
Inflammatory profile in subcutaneous (SAT) and epicardial adipose tissue (EAT) in men with and without diabetes



SAT

EAT

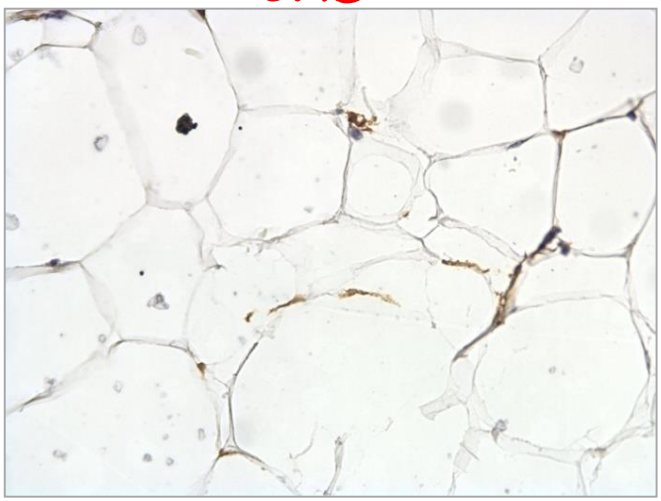




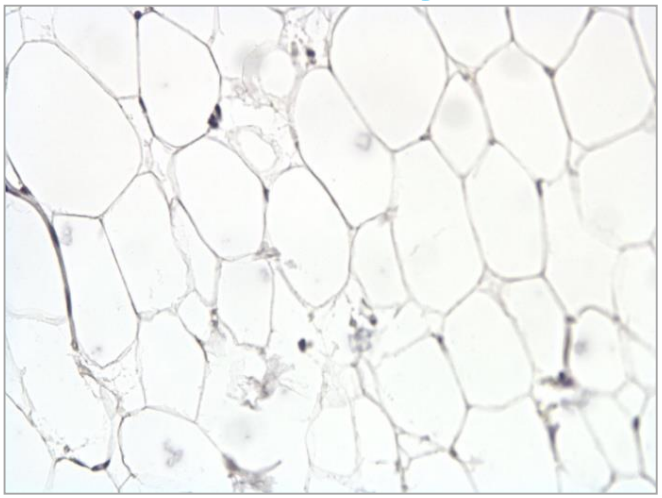
Bambace C et al et al. Heart Vessels 2013

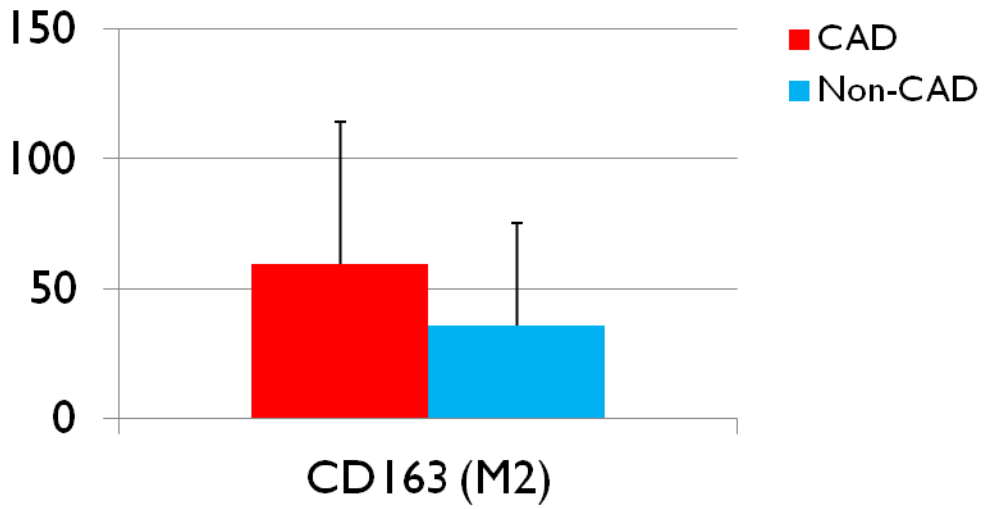
Infiltrazione macrofagica nel tessuto adiposo epicardico

CAD



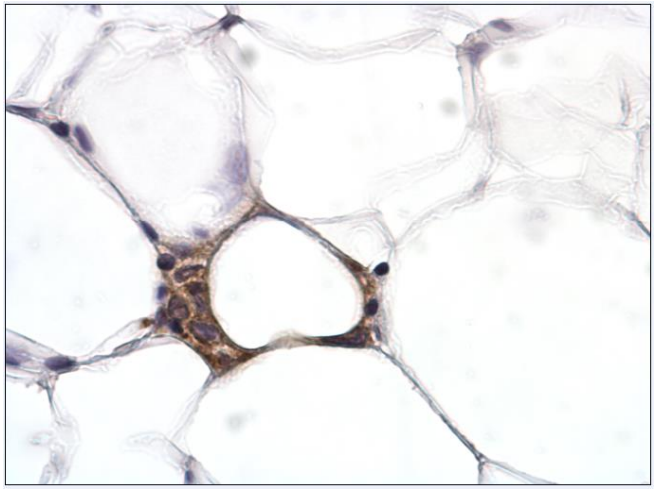
NON-CAD



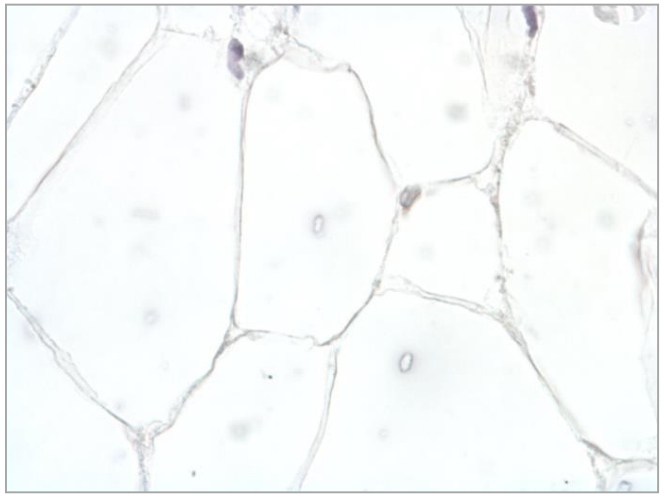


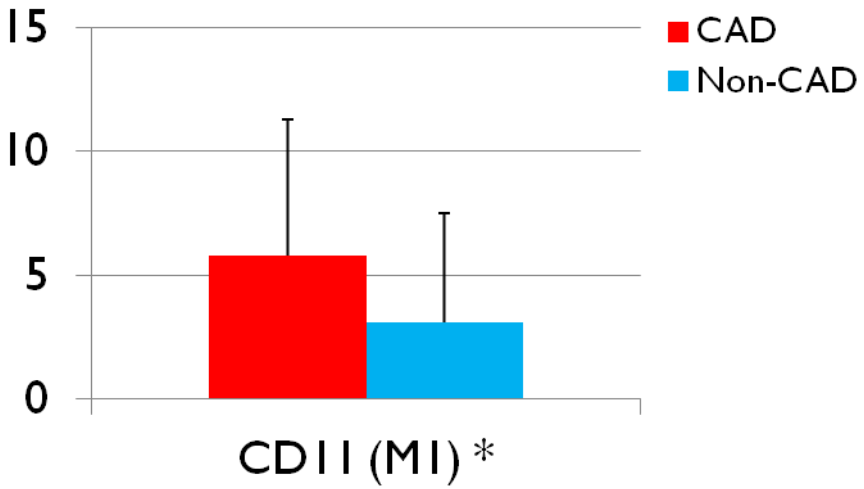
Infiltrazione macrofagica nel tessuto adiposo epicardico

CAD



NON-CAD

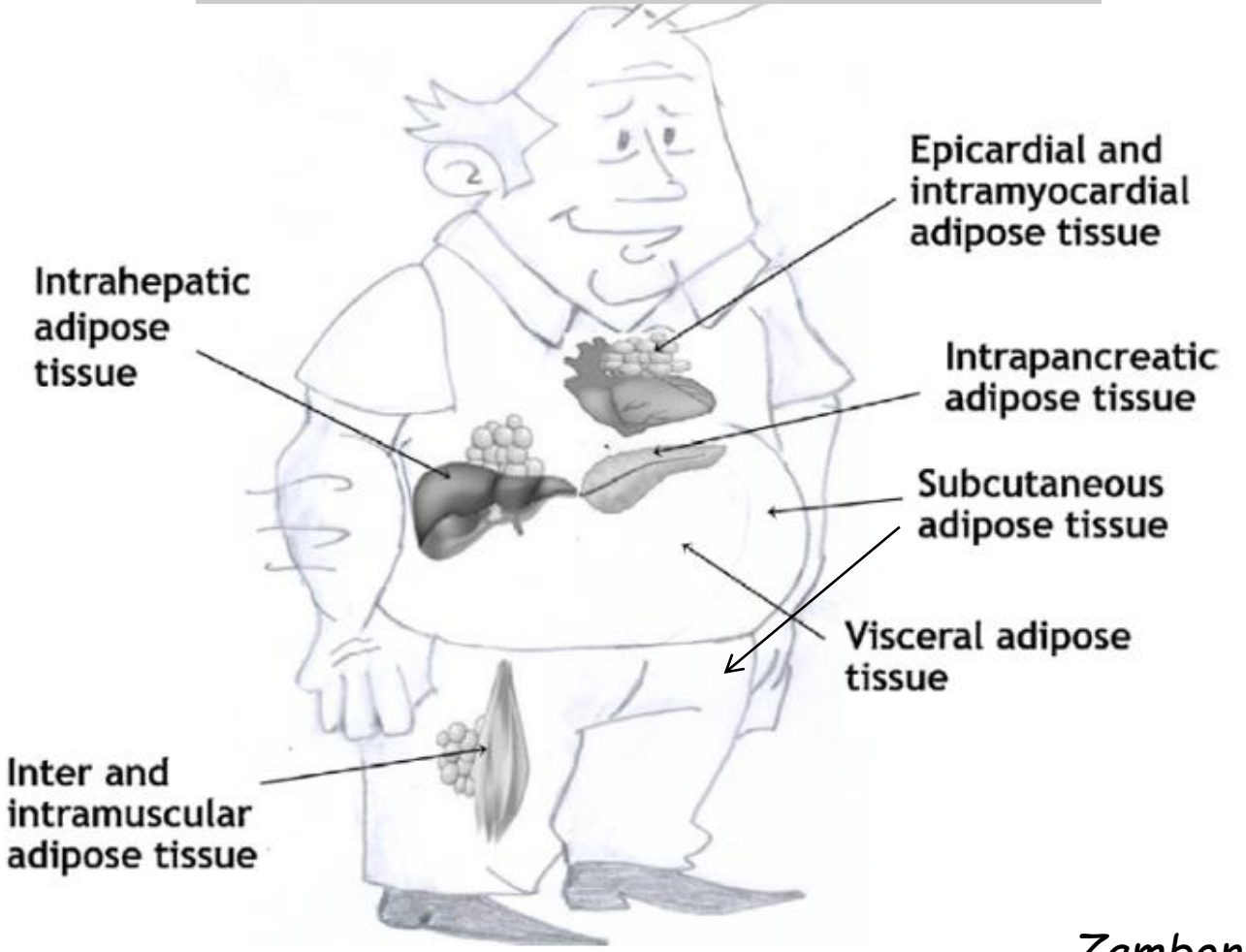


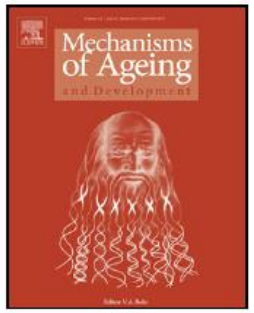


*p<0.05

Adipaging-1

Body fat re-distribution



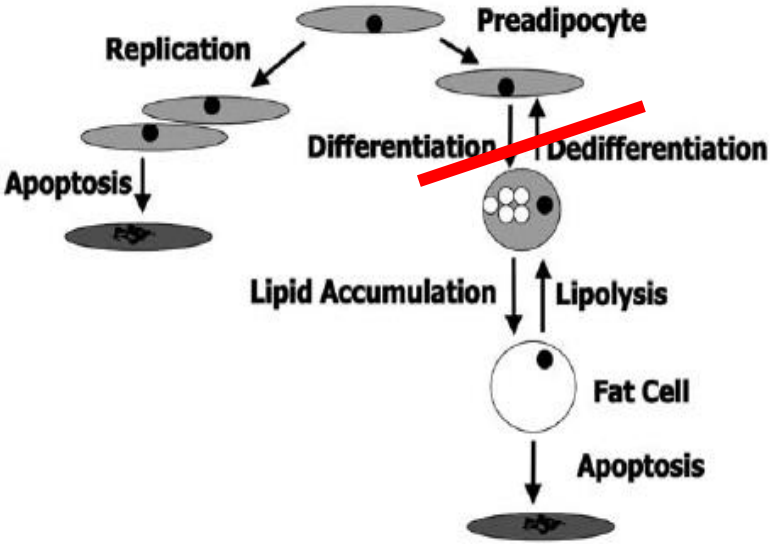


Zamboni et al, 2014

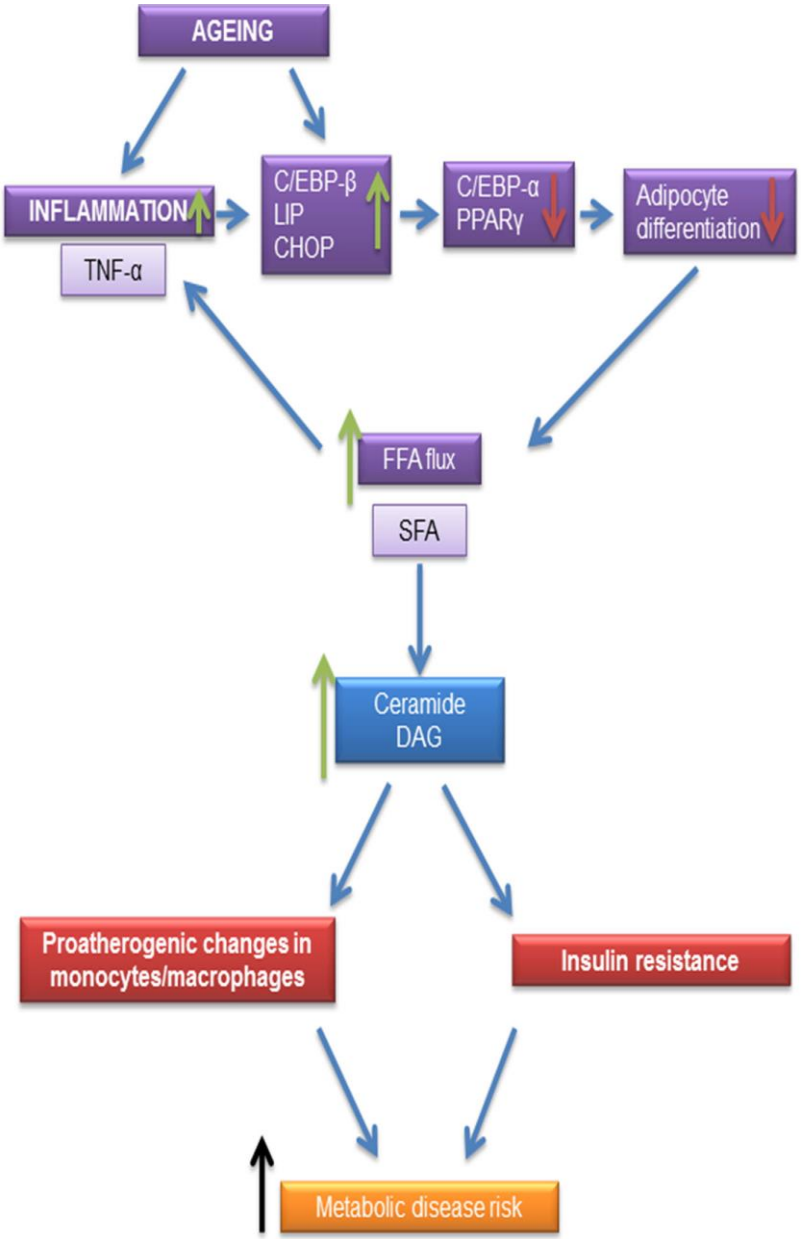
SAT loss and aging

The capacity of preadipocytes to become fully functional adipocytes declines with aging……"
"… since preadipocytes normally defend against lipotossicity by becoming fat cell that sequester fatty acids…"

Kirkland et al, 2002
Kirkland et al 2007
Sepe et al 2010



Biogerontology (2015) 16:235–248

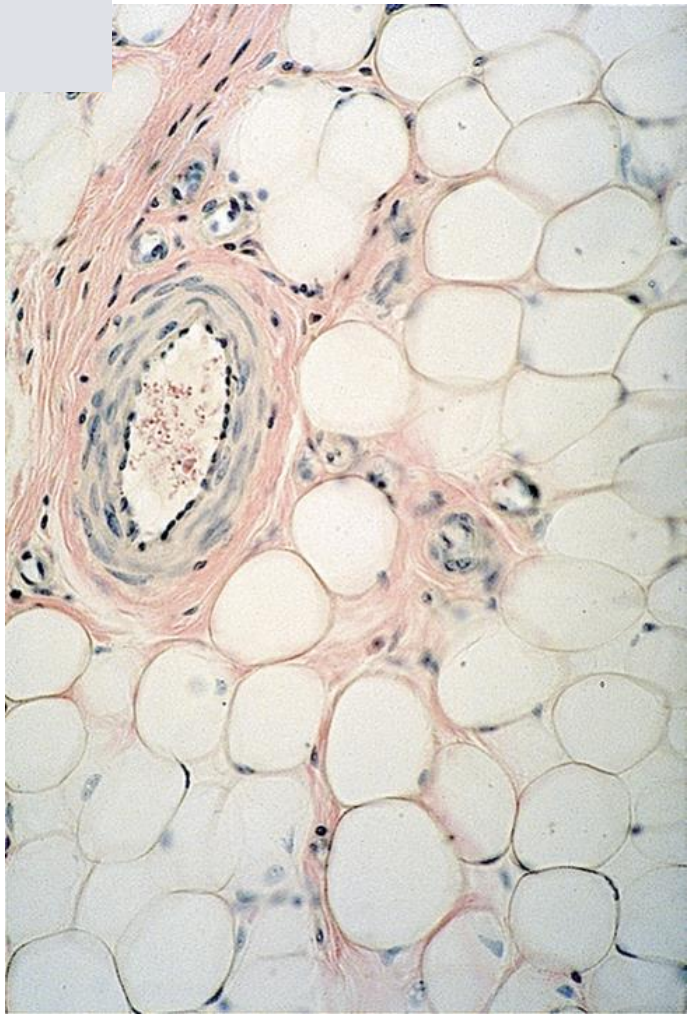


Adipaging-2

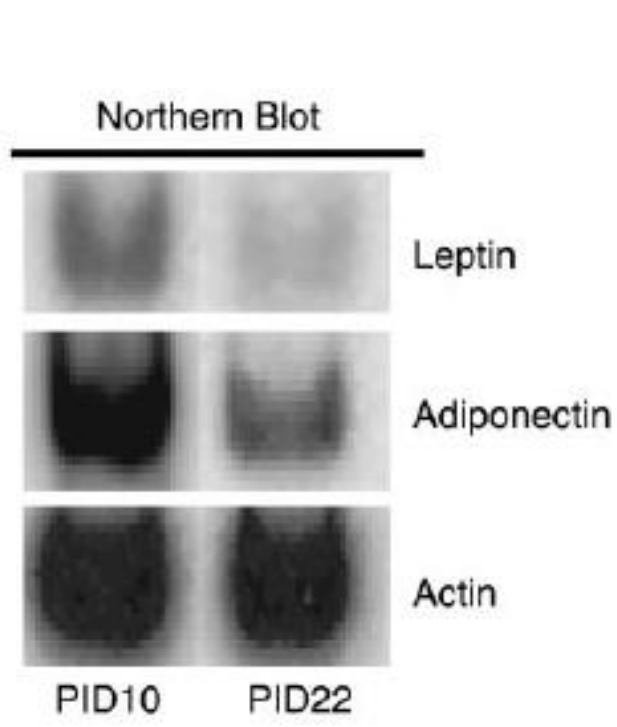
Shift infiammatorio

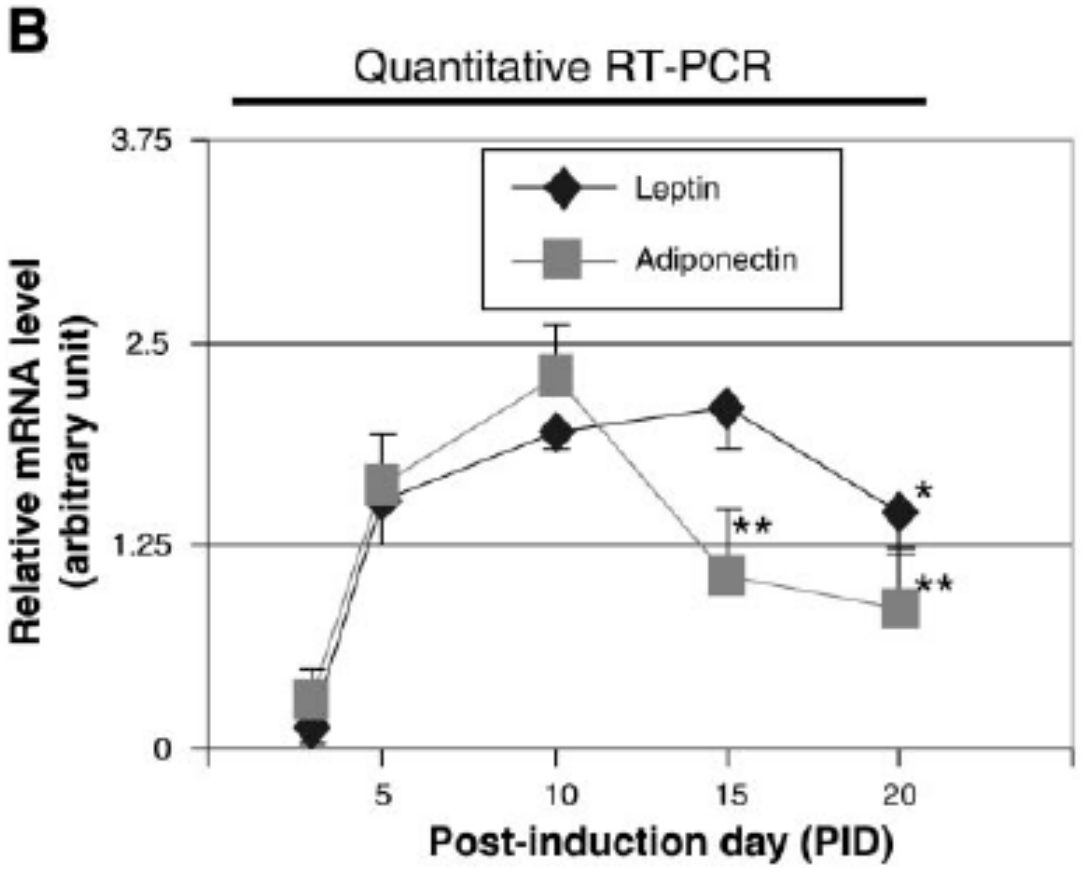
adipociti

macrofagi e linfociti



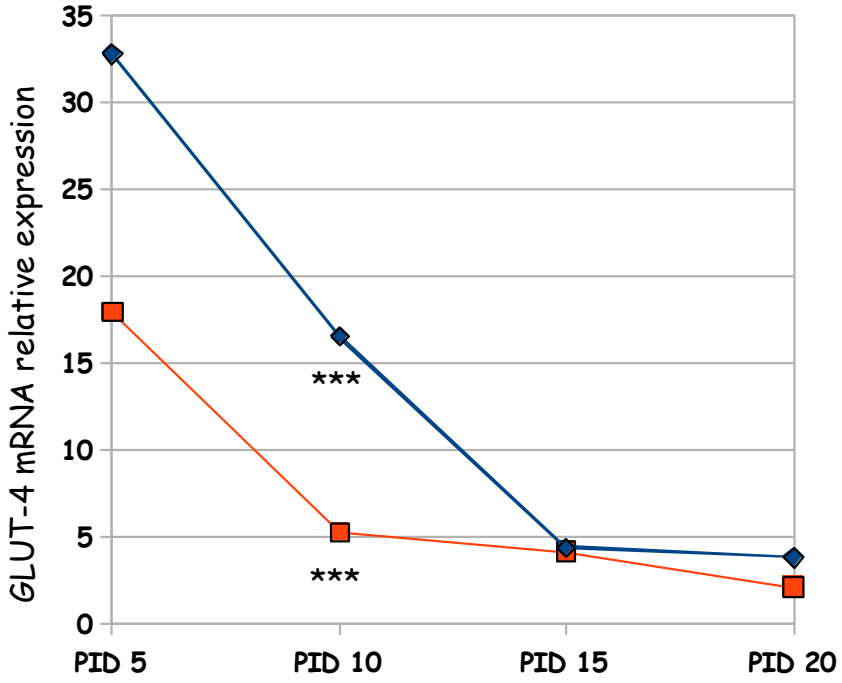
Adipocyte aging is associated with a reduction in gene expression of the secretory proteins adiponectin and leptin

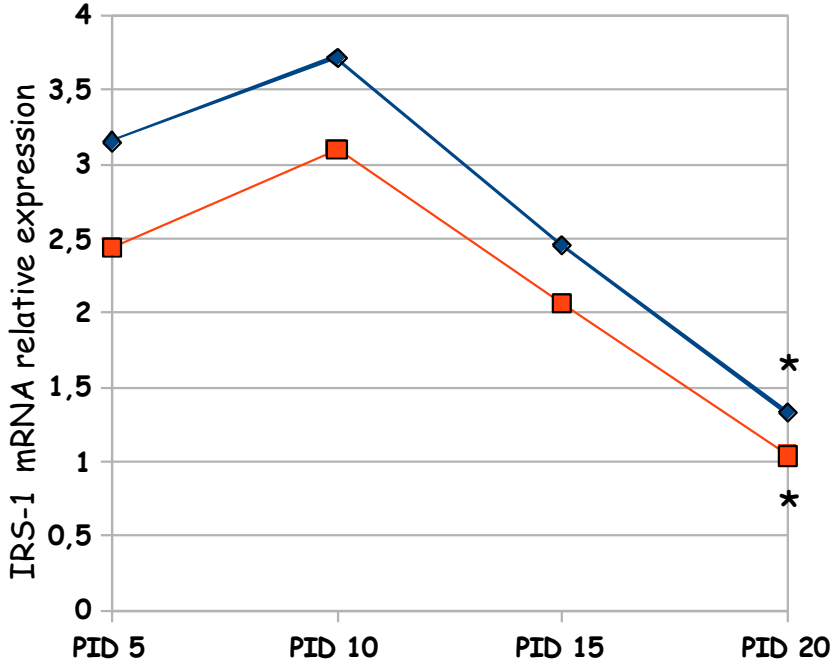




Zhu et al, Am J Physiol Endocrinol Metab 2004

effects of adipocyte aging on GLUT4 and IRS-1 gene expression of 3T3-L1 adipocytes





LPS +
LPS -

Data are presented as means ± SD.

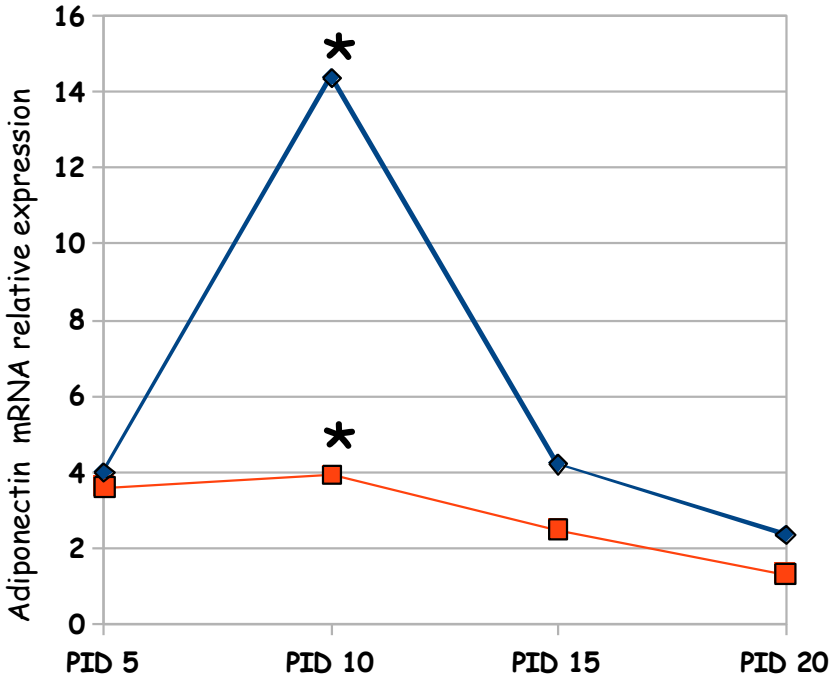
*= p < 0.05
** = p < 0.01
*** = p < 0.001

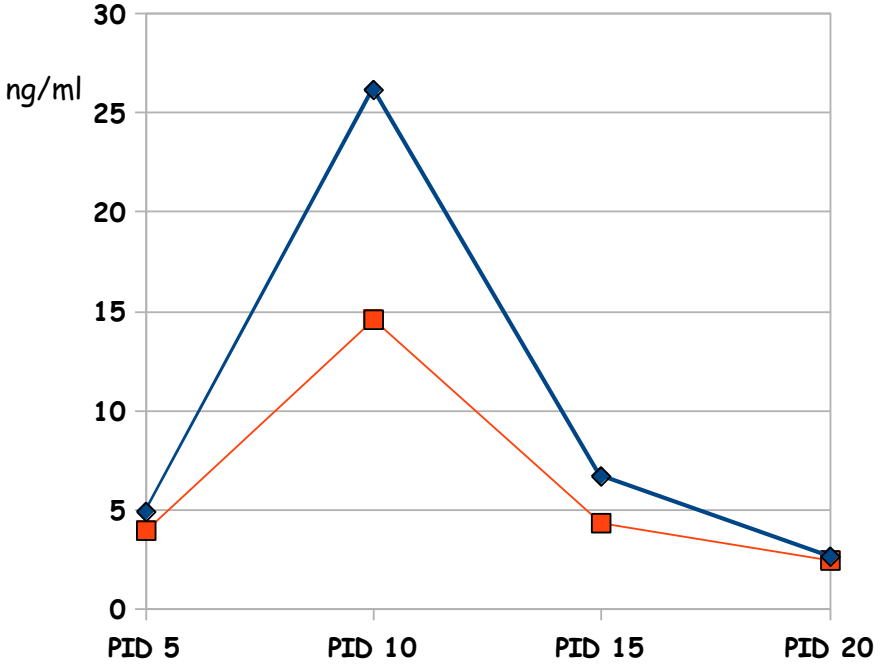
(comparison between unstimulated and LPS treated adipocytes)

LPS +
LPS -

Zoico et al, Biogerontology 2010

effects of adipocyte aging on Adiponectin gene expression and protein secretion of 3T3-L1 adipocytes





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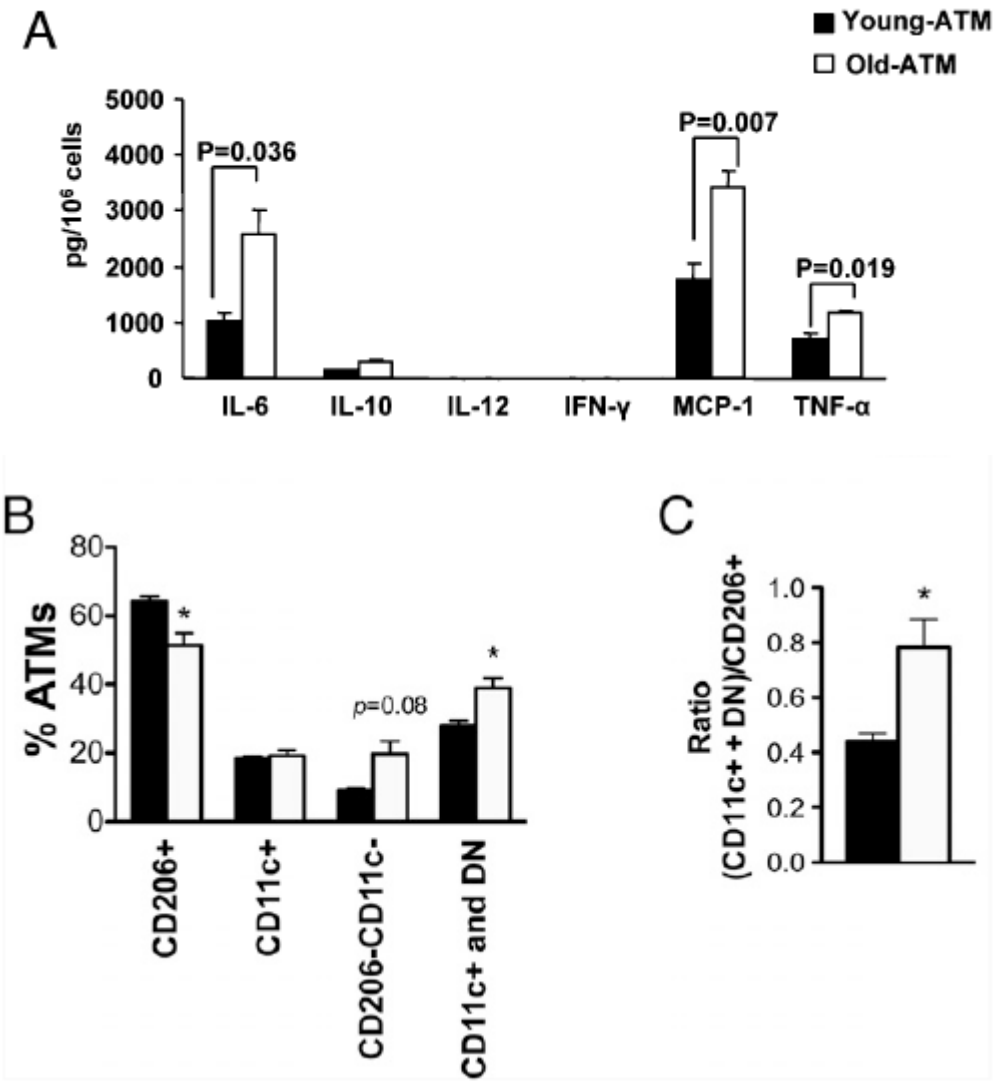
Zoico et al, Biogerontology 2010

Aging Is Associated with an Increase in T Cells and Inflammatory Macrophages in Visceral Adipose Tissue

The Journal of Immunology



profile of ATMs in old fat

shifts toward a proinflammatory environment

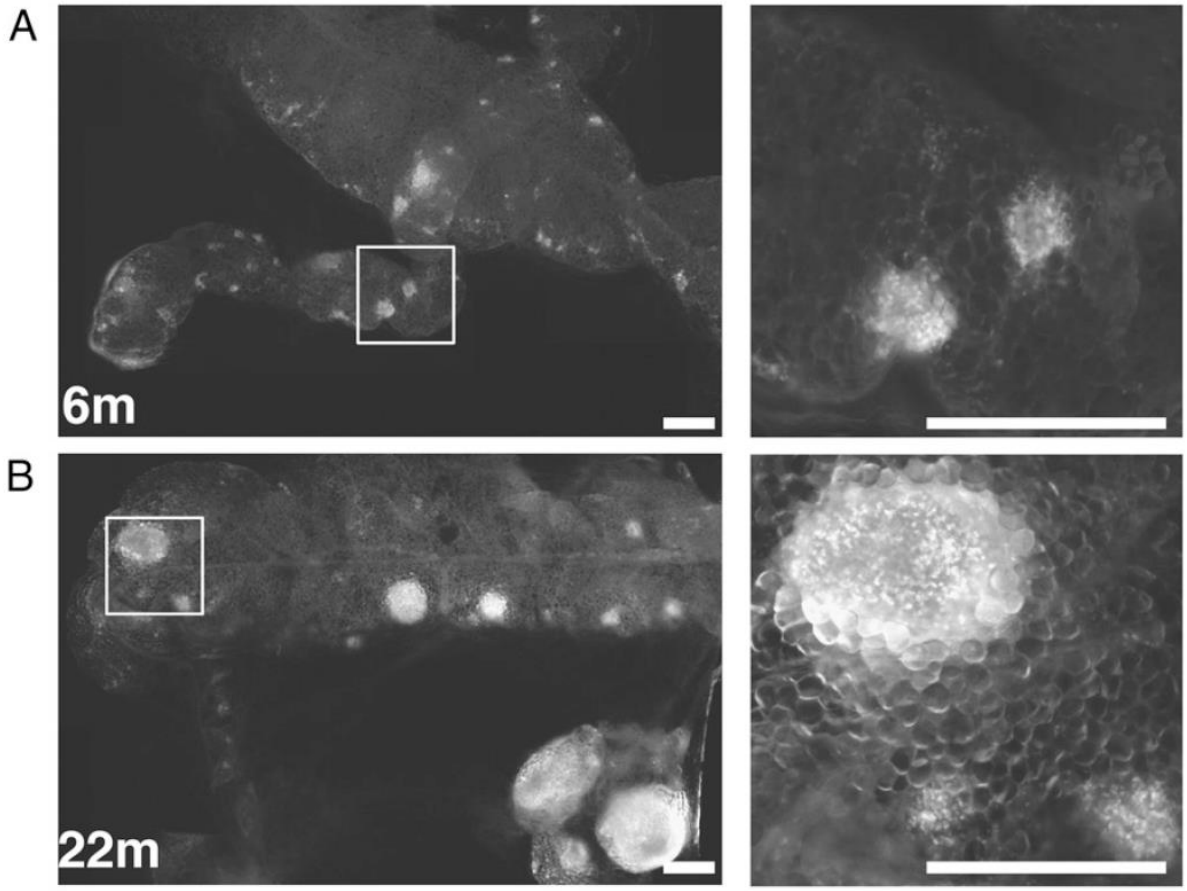
↓

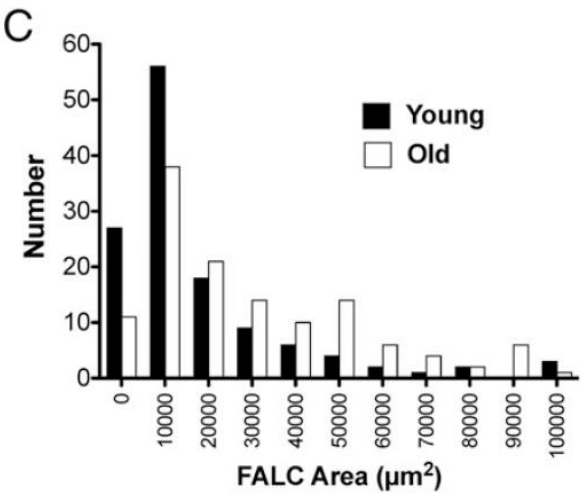
decrease in resident M2 ATMs.

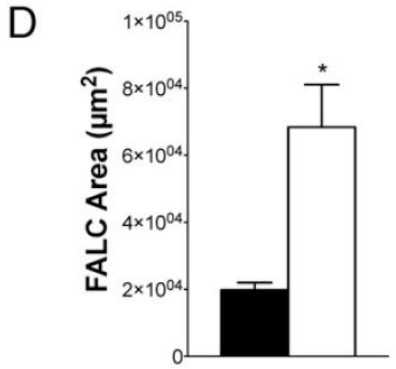
Lumeng CN et al, J Immunology 2012

Aging Is Associated with an Increase in T Cells and Inflammatory Macrophages in Visceral Adipose Tissue

The Journal of Immunology







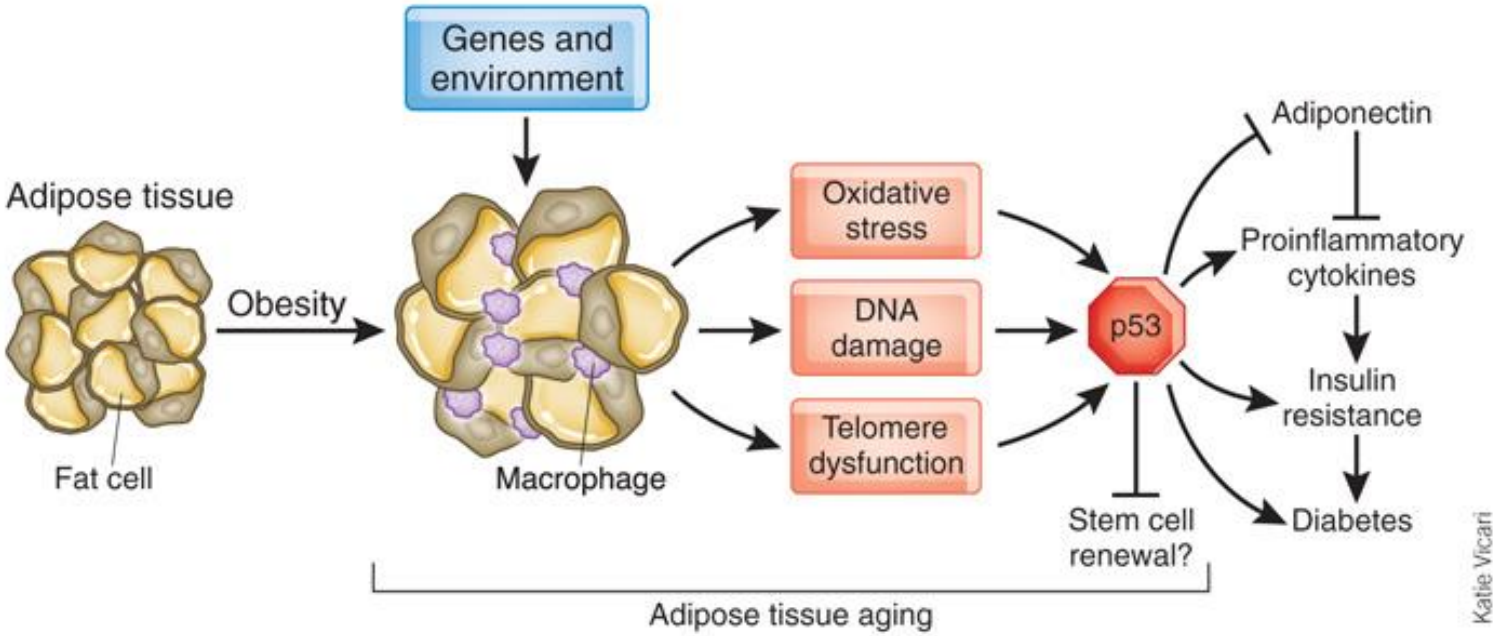
a profound and unexpected expansion of adipose tissue T cells in visceral fat with aging …

Lumeng CN et al, J Immunology 2012

Connecting obesity, aging and diabetes

Rexford S Ahima

VOLUME 15 | NUMBER 9 | SEPTEMBER 2009 NATURE MEDICINE



Con l' invecchiamento

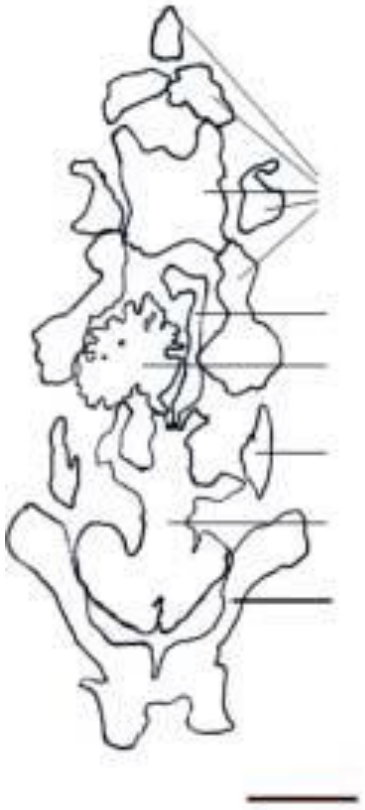
1- aumenta la quantità di TA e si modifica la sua distribuzione

2- si osservano aspetti disfunzionali sia degli adipociti che dei preadipociti

3-il TA presenta un aumentato profilo infiammatorio con incremento di M1 e Linfociti

La disfunzionalità età-correlata del TA potrebbe essere uno dei fattori responsabili del inflamm-aging

The multidepot organization of the adipose organ in mammals consisting in subcutaneous and visceral depots

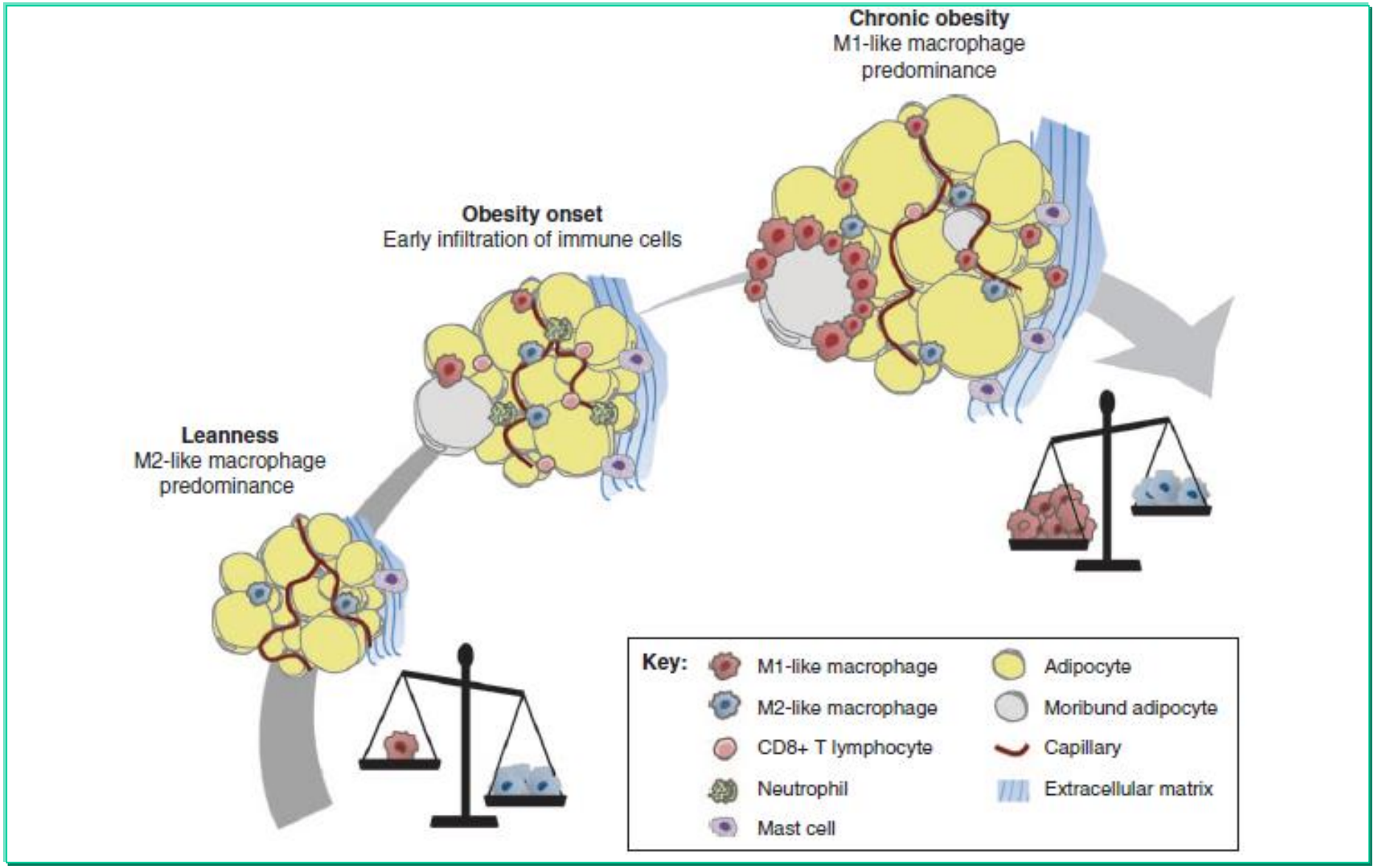


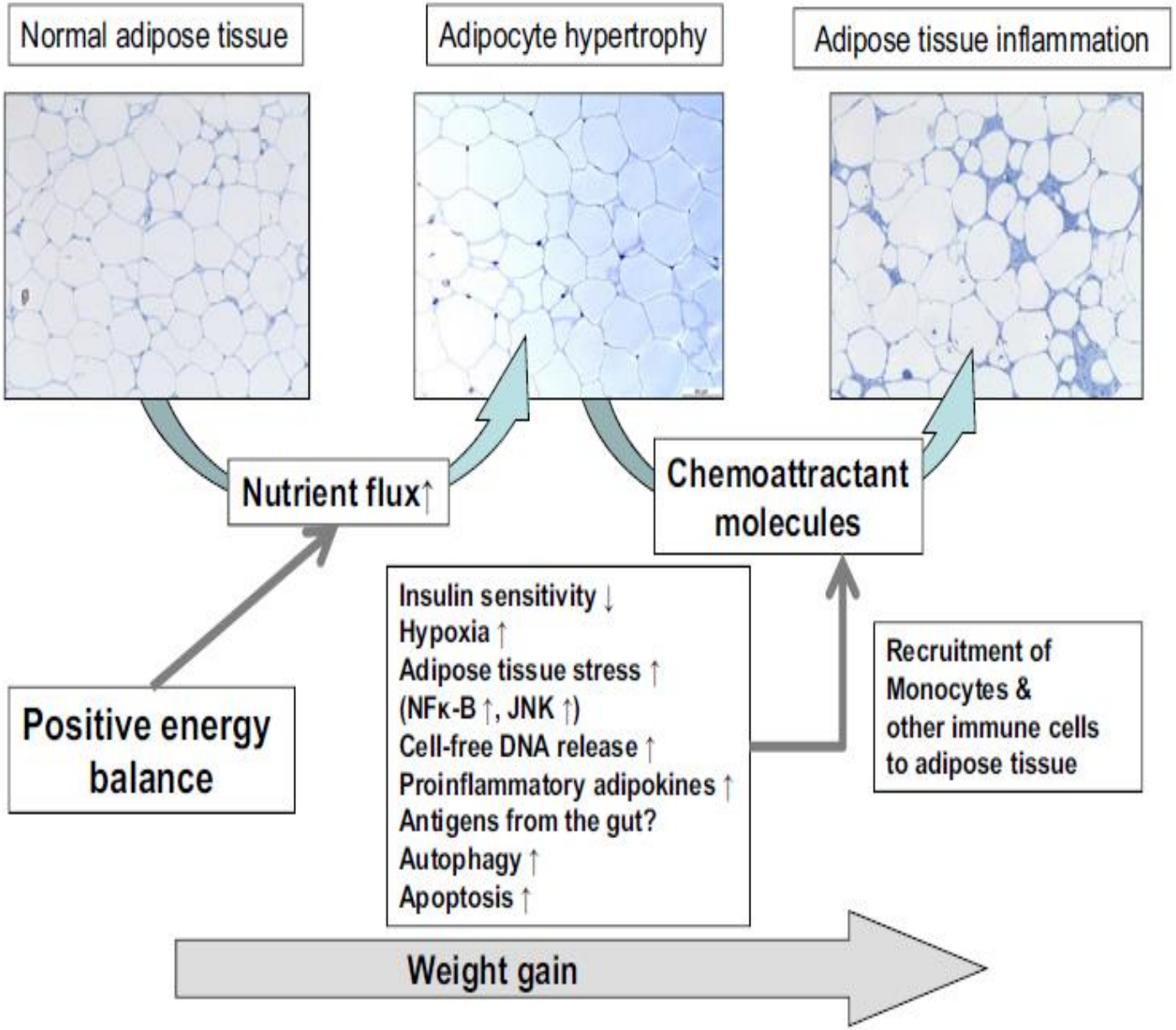
Thermoneutrality (28° for 10 days)

Cold acclimatation (6° for 10 days)

Cinti S et al, Eur J Endocrinol 2014

Polarizzazione macrofagica nel tessuto adiposo



Dalmas E., Trends in Immunology, 2011

Blüher M. Clin Sci 2016 ;130(18):1603-14