SOCIETÀ ITALIANA
G.U.I.D.A.
PER LA GESTIONE UNIFICATA E INTERDISCIPLINARE DEL DOLORE MUSCOLO-SCHELETRICO E DELL'ALGODISTROFIA

Ruolo del tessuto adiposo nell'artrosi

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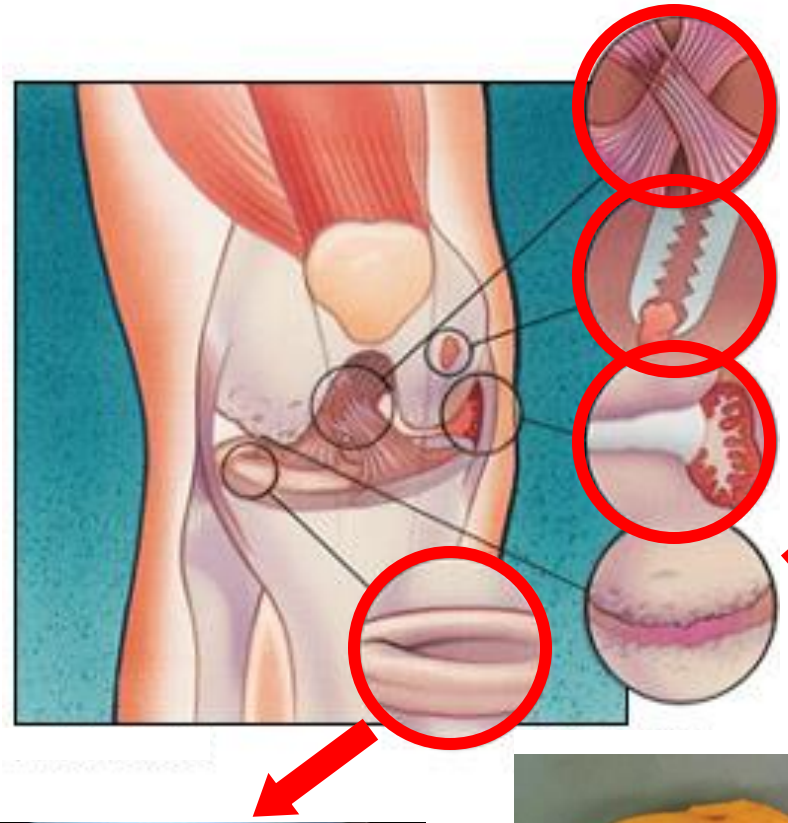
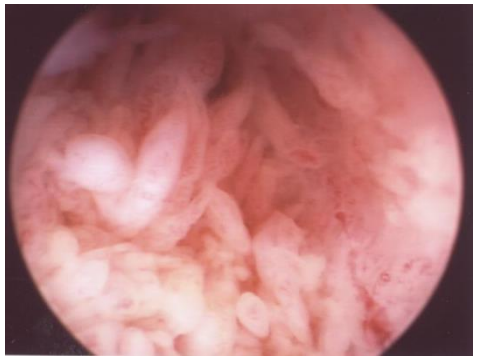
Centro Congressi Unione Industriali
TORINO 11-13 MAGGIO 2023

OA: A WHOLE JOINT DISEASE



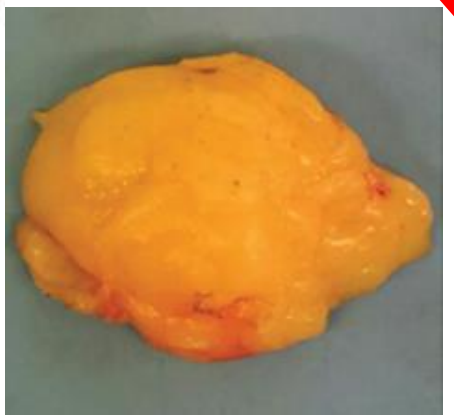
LIGAMENTS
CAPSULA

CARTILAGE



SYNOVIUM

MENISCUS



HOFFA

http://nemsi.uchc.edu/clinical_services/orthopaedic/knee/arthroscopy.html

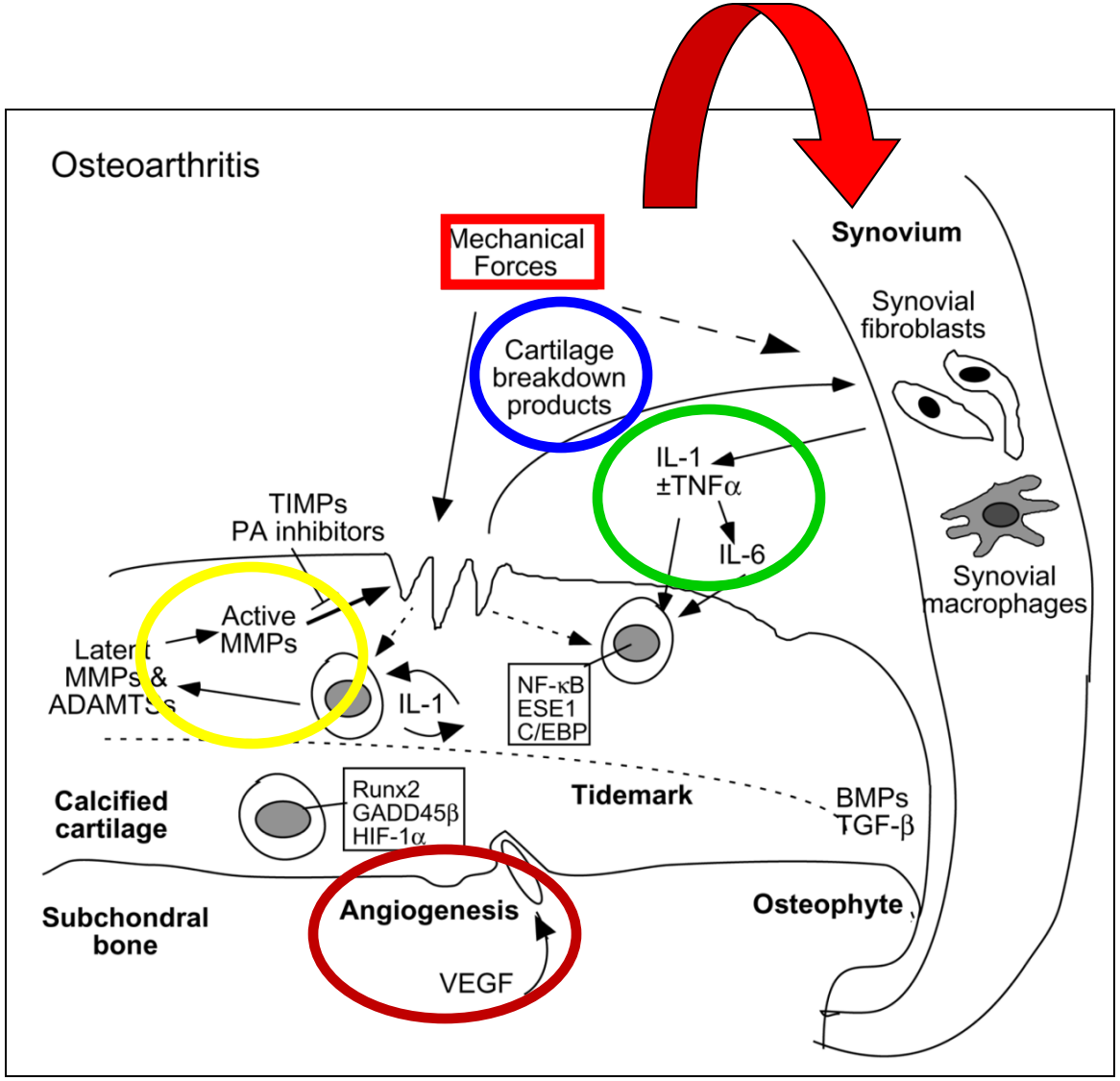
OA: IS NOT A NON INFLAMMATORY FORM

- Signs of inflammation are common
- Synovitis is common in early and late OA *(Benito 2005, Pearle 2007)*
- Synovitis is related with OA symptoms and progression
- Synovial inflammation is a factor that contributes to dysregulation of chondrocyte function, favoring an imbalance between the catabolic and anabolic activities of chondrocyte in remodeling the cartilage ECM *(Loeser 2006)*

Felson DT. Br J Sports Med. 2011

OA PATHOGENESIS

- Chondrocytes are major players in cartilage destruction
- Mechanical forces (mechanical loading) are associated with chondrocyte activation
- Chondrocyte activation may involve upregulation by cytokines released by the synovium or the chondrocytes themselves.



From MB Goldring, Arthritis Research and Therapy 2009

OA IS NOT ONE DISEASE
CLINICAL PHENOTYPES ARE BASED ON RISK FACTORS

	Post-traumatic (acute or repetitive)	Metabolic	Ageing	Genetic	Pain
Age	Young (<45 years)	Middle-aged (45–65 years)	Old (>65 years)	Variable	Variable
Main causative feature	Mechanical stress	Mechanical stress, adipokines, hyperglycaemia, oestrogen/ progesterone imbalance	AGE, chondrocyte senescence	Gene related	Inflammation, bony changes, aberrant pain perception
Main site	Knee, thumb, ankle, shoulder	Knee, hand, generalised	Hip, knee, hand	Hand, hip, spine	Hip, knee, hand
Intervention	Joint protection, joint stabilisation, prevention of falls, surgical interventions	Weight loss, glycaemia control, lipid control, hormone replacement therapy	No specific intervention, sRAGE/AGE breakers	No specific intervention, gene therapy	Pain medication, anti-inflammatory drugs

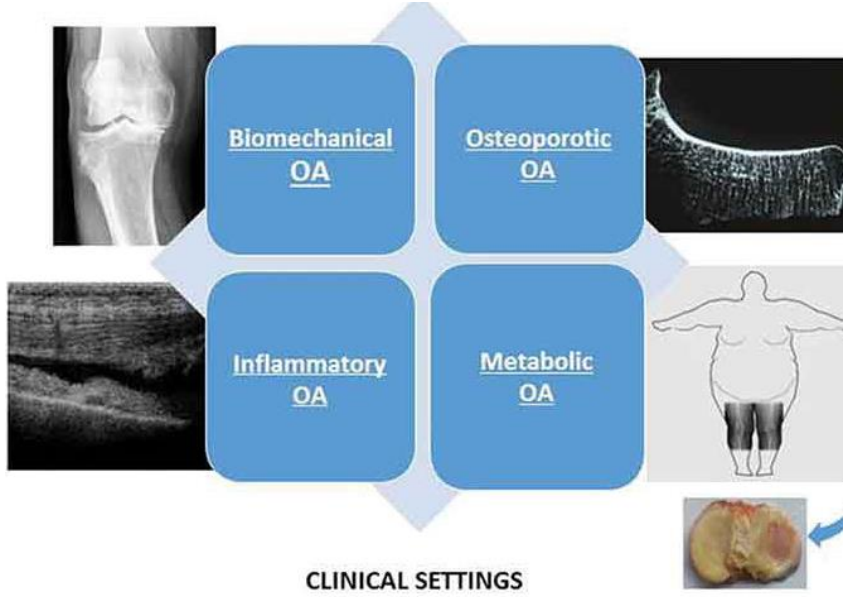
Osteoarthritis is not one disease, and might benefit from the recognition of its different phenotypes. AGE=advanced glycation endproducts. sRAGE=soluble receptor for advanced glycation endproducts.

Table 4: **Proposal for differentiation of clinical phenotypes of osteoarthritis**

Bijlsma JW, Berenbaum F, Lafeber FP. Lancet. 2011

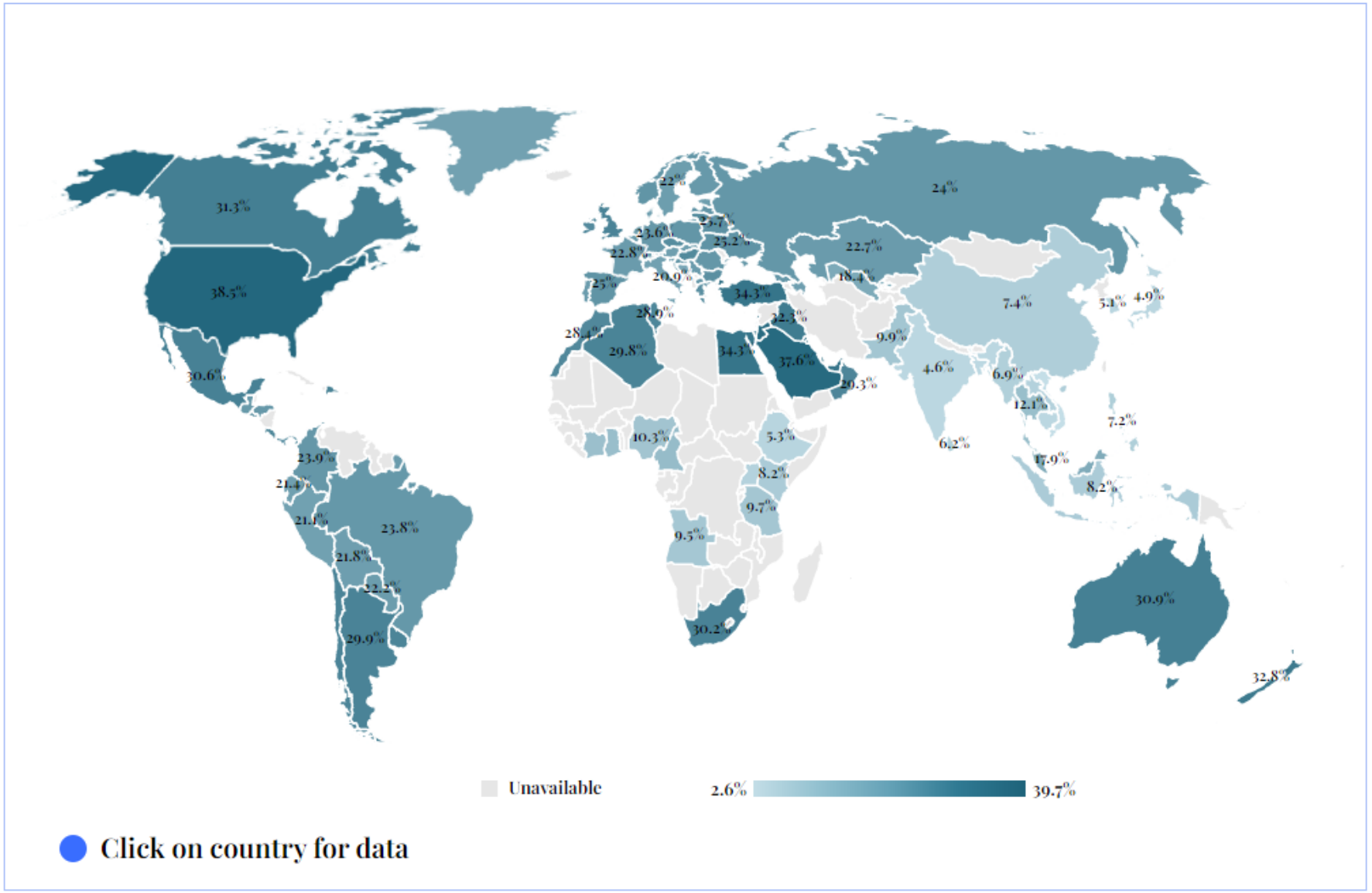
OA RISK FACTORS:

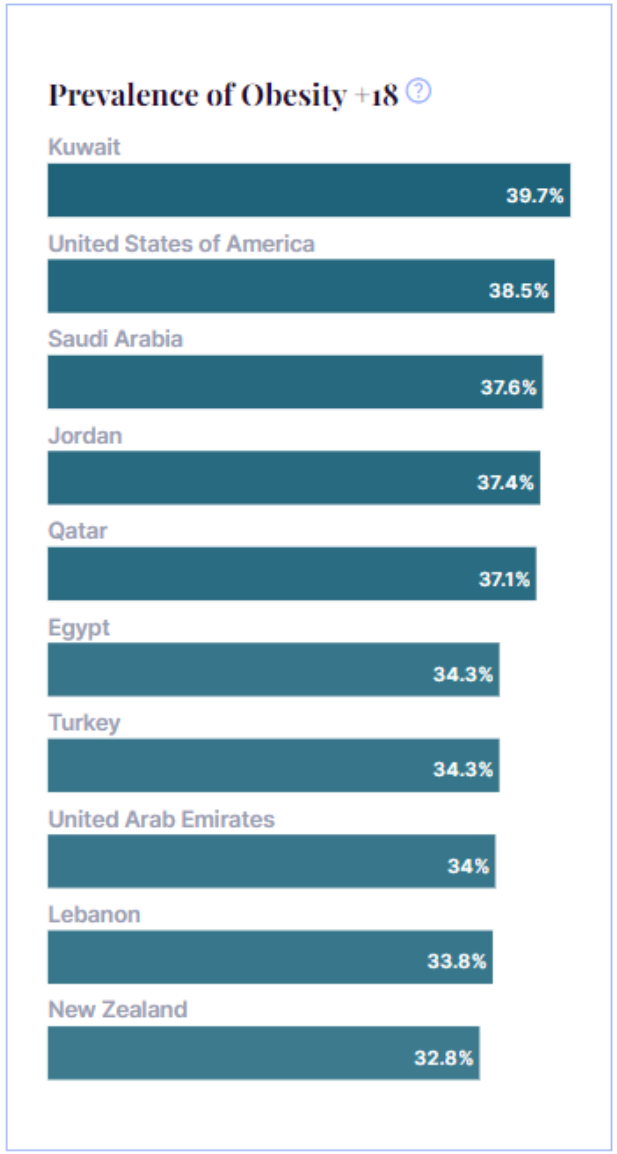
- Injury/mechanical loading
- Inflammation
- Obesity/metabolic syndrome
- Age
- Genetics



Roman-Blas, Expert Opinion on Pharmacotherapy 2016

OBESITY PREVALENCE



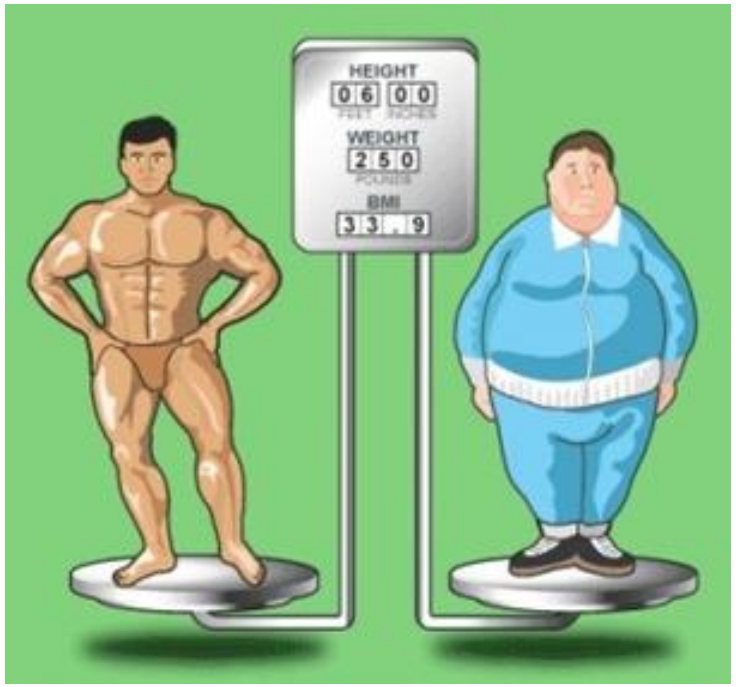


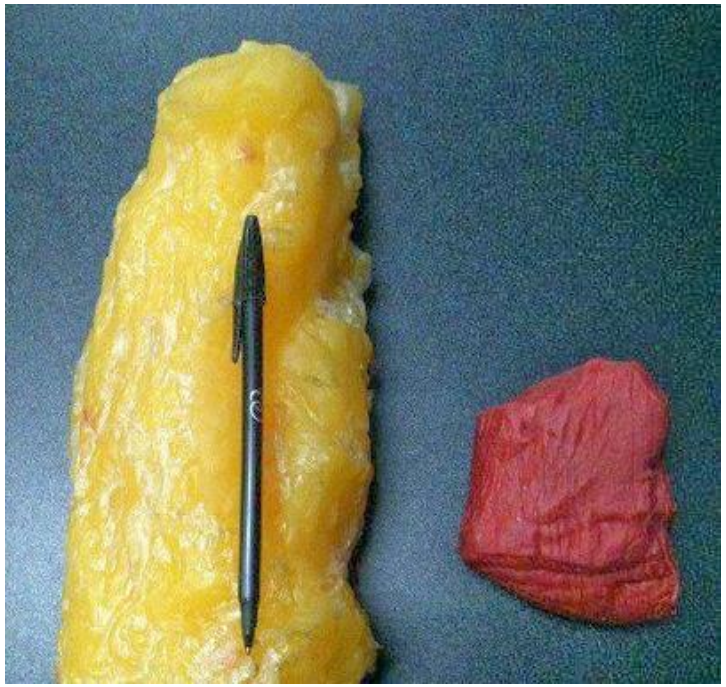
https://wisevoter.com/country-rankings/obesity-rates-by-country/

OVERWEIGHT AND OBESITY ARE DEFINED AS "ABNORMAL OR EXCESSIVE FAT ACCUMULATION THAT MAY IMPAIR HEALTH"

BMI classification	
Underweight	< 18.5
Normal range	18.5 - 24.9
Overweight	⩾ 25.0
Preobese	25.0 - 29.9
Obese	⩾ 30.0
Obese class I	30.0 - 34.9
Obese class II	35.0 - 39.9
Obese class III	⩾ 40.0

http://www.who.int/features/factfiles/obesity/facts/en/



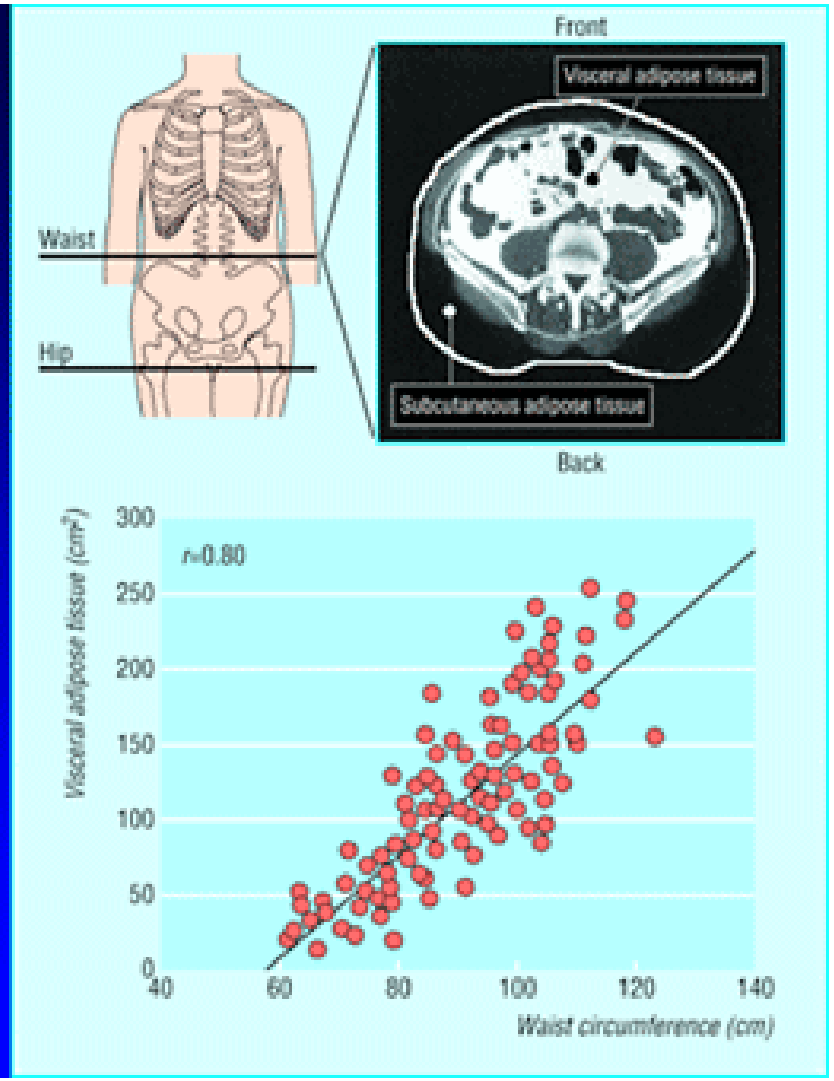


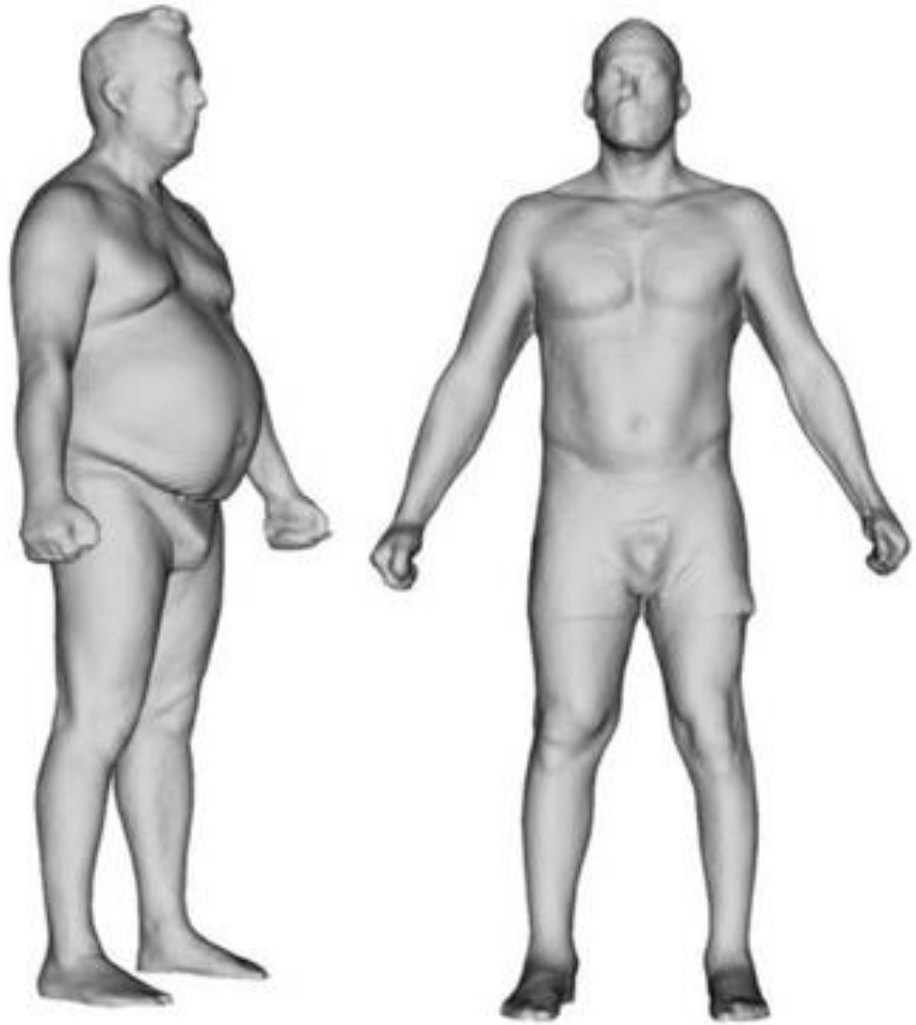
http://serlulite.blogspot.it/2014_01_01_archive.html

OBESITY ASSESSMENT

Visceral adipose tissue can be estimated by waist measurement

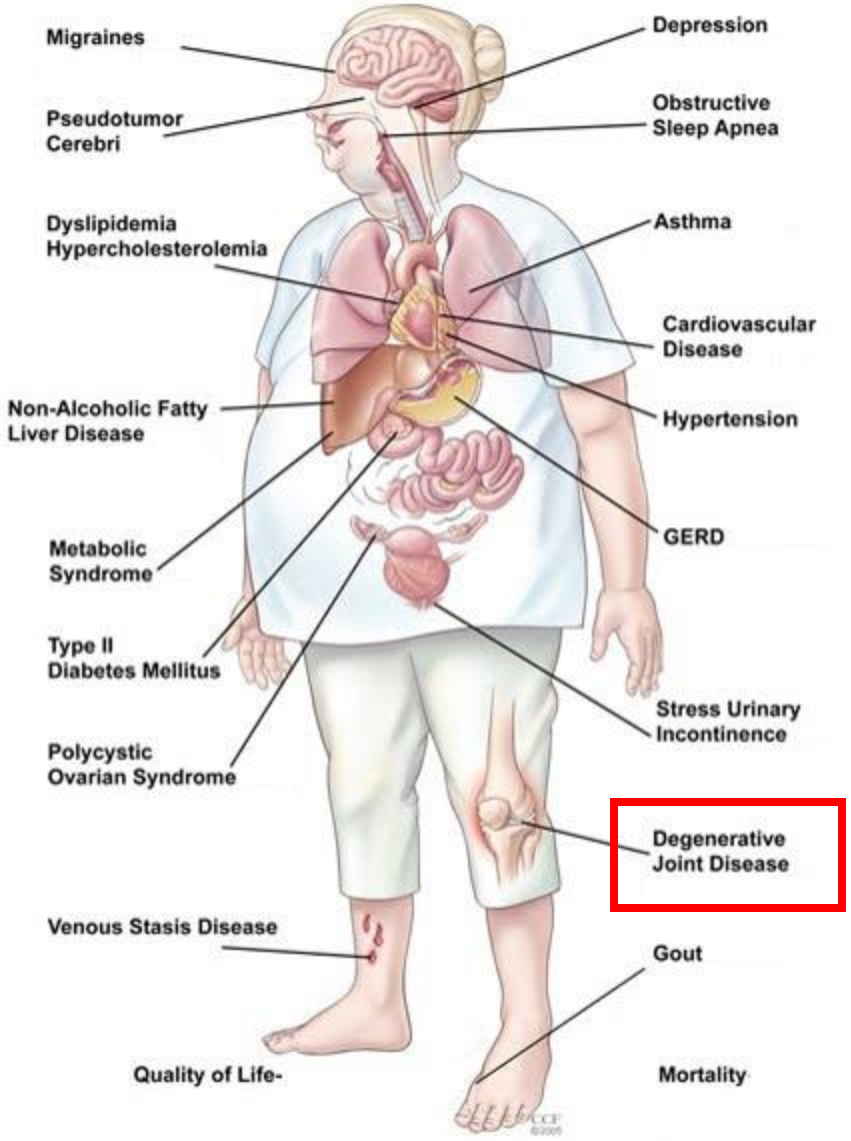
Pouliot MC et al.;
Am J Cardiol 1994;73:460





Minetto MA, J. Pers. Med. 2022

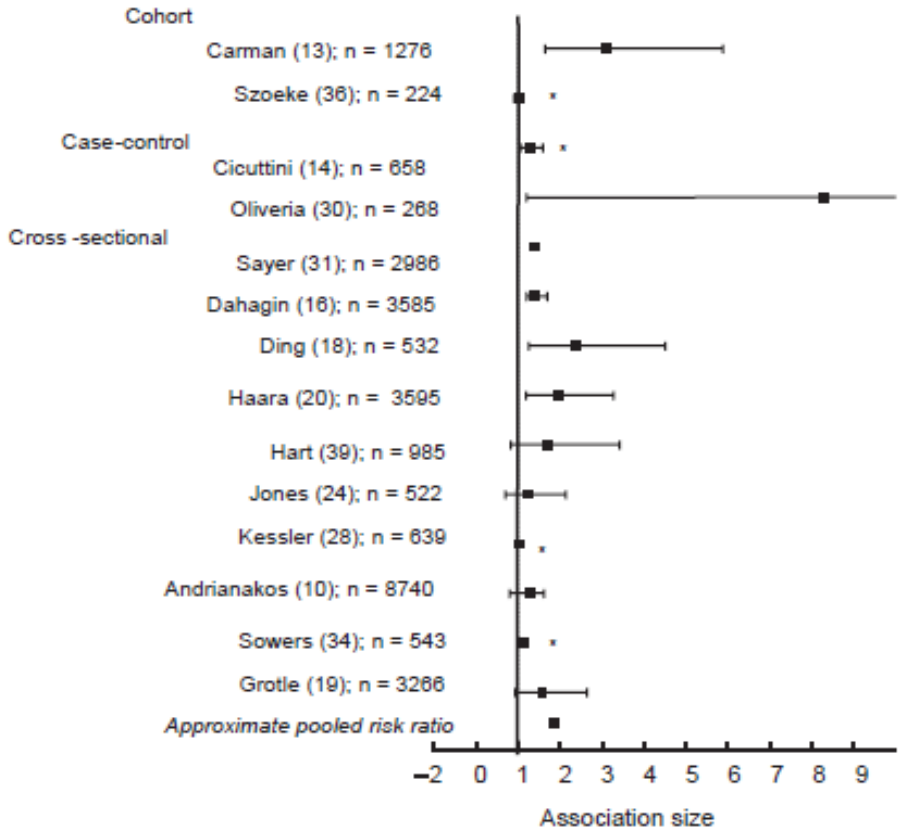
OBESITY COMORBILITIES



Modified from http://www.jawadmd.com/health-benefits/

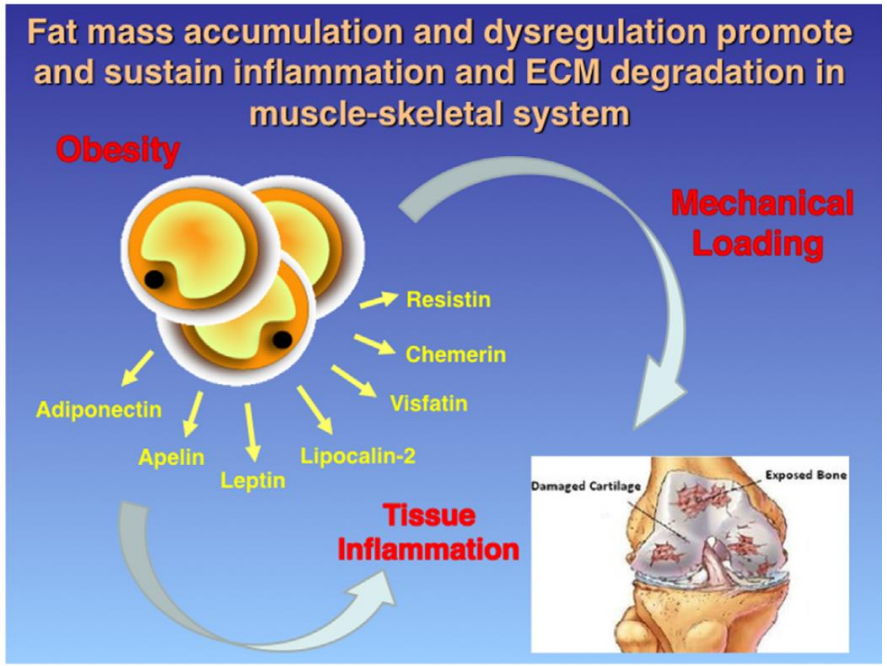
Association between weight or body mass index and hand osteoarthritis: a systematic review

Erlangga Yusuf,[1] Rob G Nelissen,[2] Andreea Ioan-Facsinay,[1] Vedrana Stojanovic-Susulic,[3] Jeroen DeGroot,[4] Gerjo van Osch,[5] Saskia Middeldorp,[6] Tom W J Huizinga,[1] Margreet Kloppenburg[1]

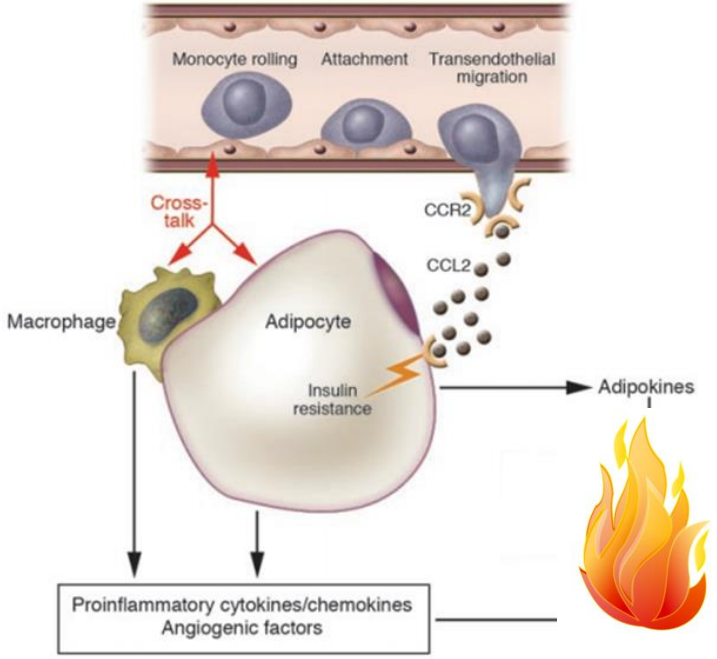


Yusuf E, Ann Rheum Dis. 2010

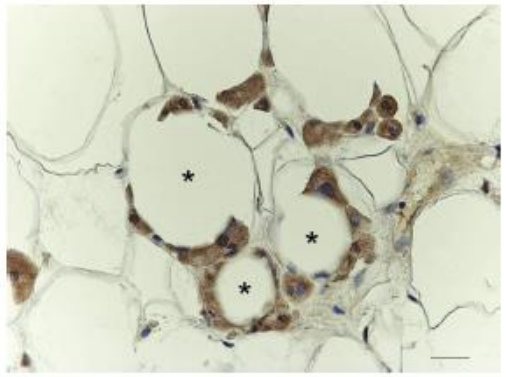
ADIPOSE TISSUE AS ENDOCRINE ORGAN



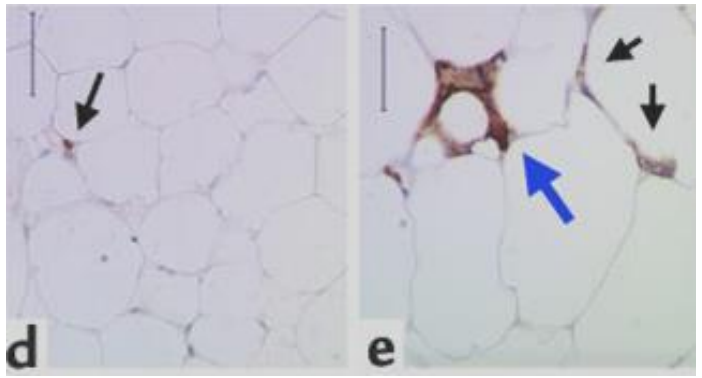
Francisco V. J Orthop Res. 2017



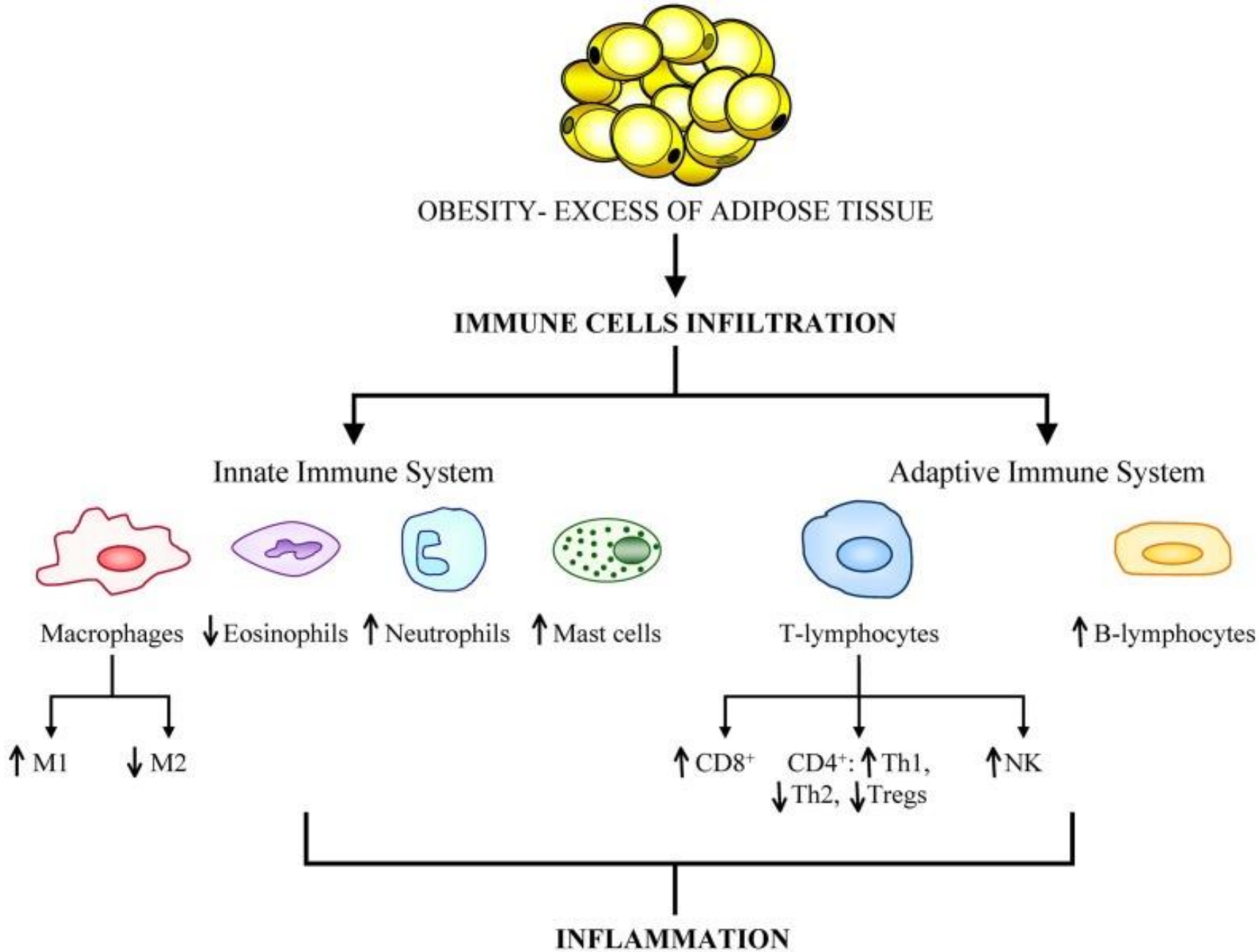
Neels J, The Journal of Clinical Investigation 2006



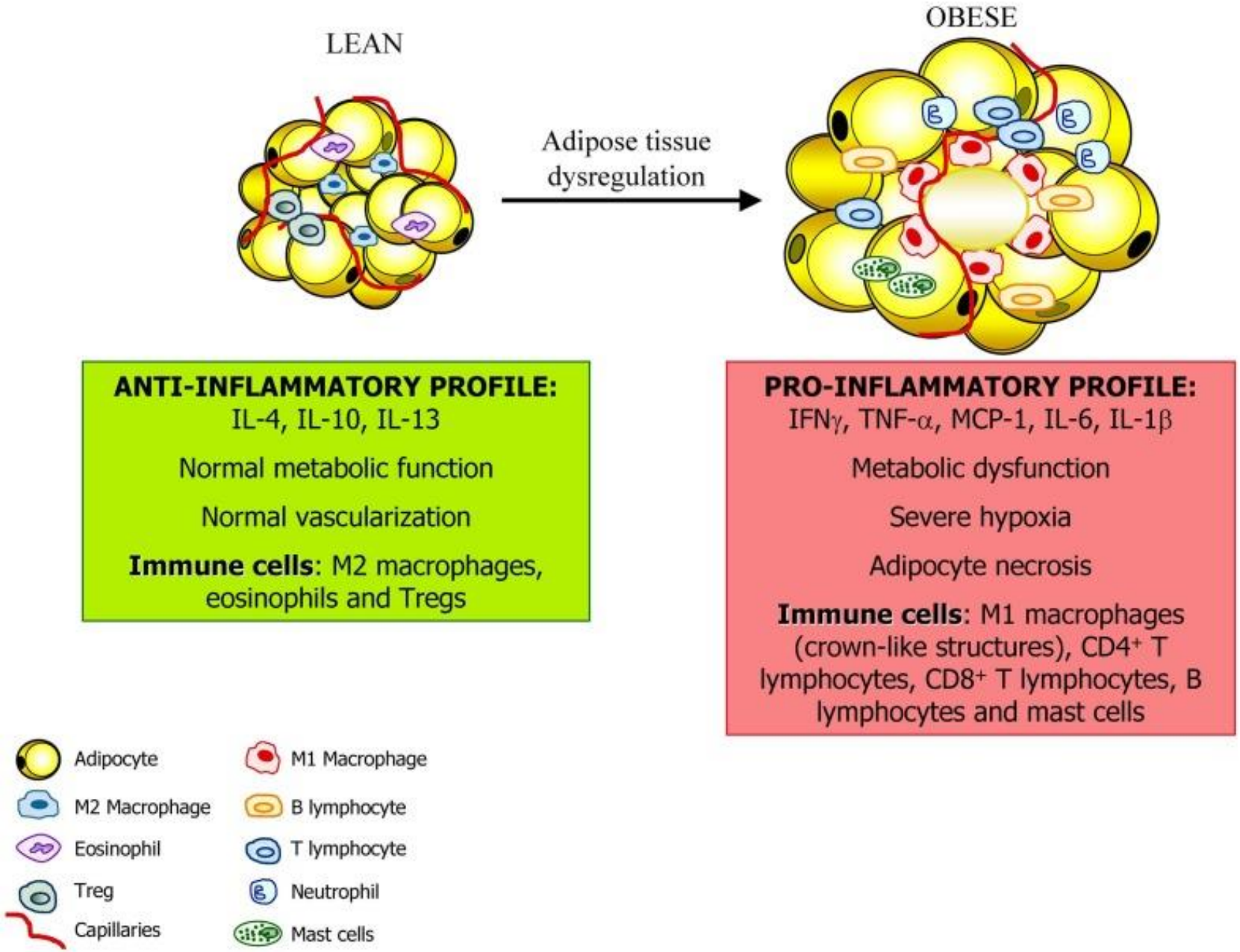
Cinti S, Am J Physiol Endocrinol Metab 2009



Weisberg SP, J Clin Invest 2003

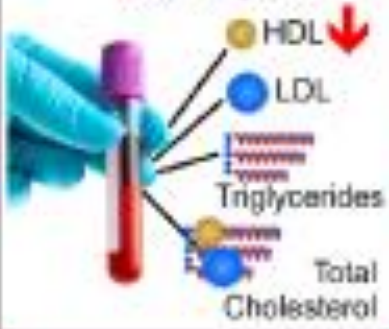
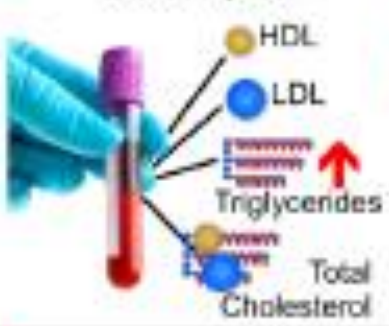


Catalan V, Front Physiol 2013



Catalan V, Front Physiol 2013

METABOLIC SYNDROME (MetS)

	Large Waistline	Low Blood HDL Cholesterol	High Blood Triglycerides	High Fasting Blood Sugar	High Blood Pressure
	>102 cm >88 cm	<40 mg/dL <50 mg/dL	≥150 mg/dL or medication	≥100 mg/dL or medication	≥130/85 mm Hg or medication
					
♀	96.6%	61.1%	84.0%	50.7%	49.0%
♂	88.0%	57.5%	86.6%	57.4%	47.8%

Ronald J, Journal of Orthopaedic Research Month 2016

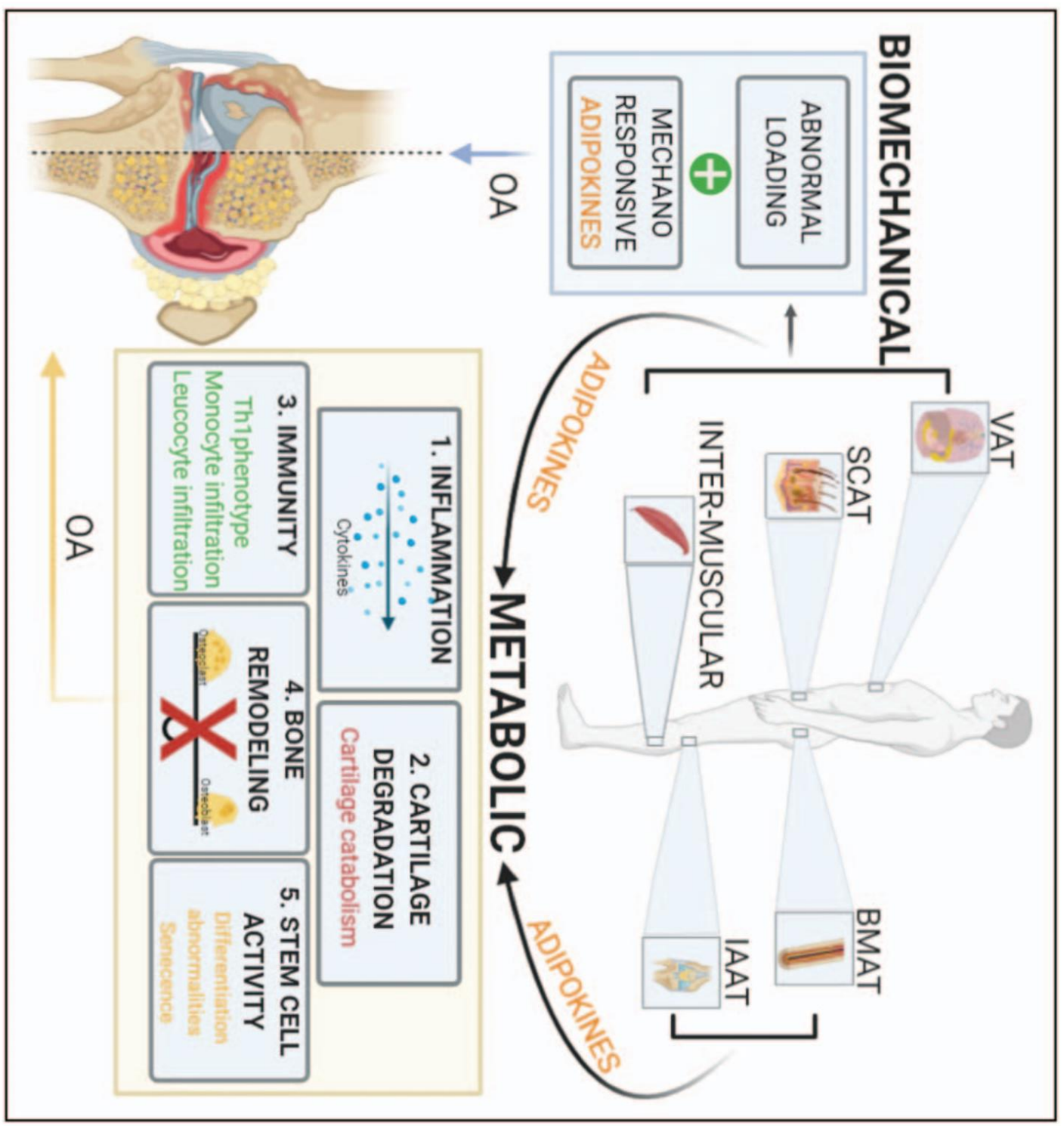
OA AND METABOLIC SYNDROME (MetS)

- MetS is an independent risk factor for OA *(Barenbaum 2009)*
- 59% of OA patients had MetS compared to 23% in the general population *(Puenpatum 2009)*
- Obese patients with MetS have an increased risk of incidence and severity of knee OA *(Hoeven TA 2013)*
- The presence of MetS is also associated with hand OA *(Tomi A-L 2016, Visser AW 2015)*
- The accumulation of MetS components is associated with OA incidence and severity, and with TKR, independently of BMI *(Yoshimura N 2012, Monira Hussain S 2014)*

CURRENT OPINION

Role of adipose tissues in osteoarthritis

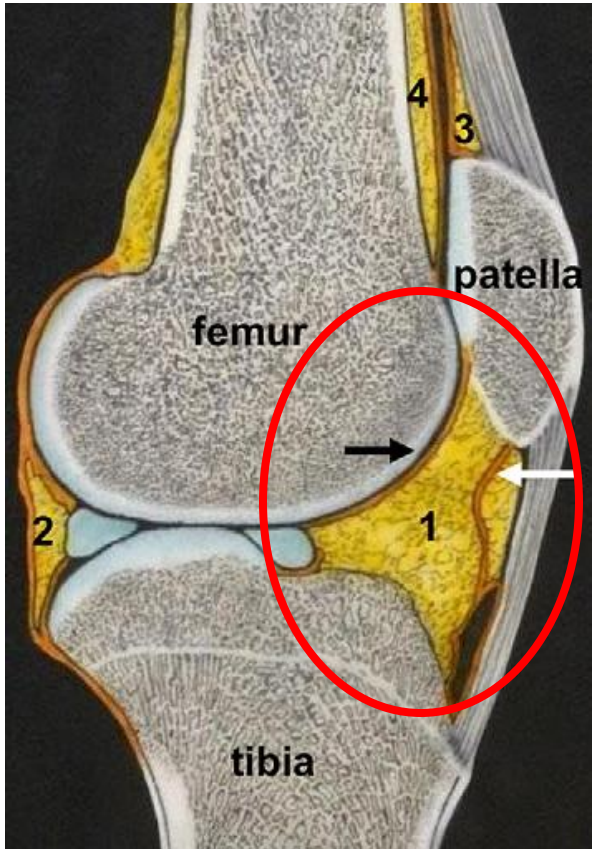
Natalia Zapata-Linares[a], *Florent Eymard*[b,c], *Francis Berenbaum*[a,d], *and Xavier Houard*[a]



REVIEW

An emerging player in knee osteoarthritis: the infrapatellar fat pad

Ioan-Facsinay A, Arthritis Res Ther. 2013



- Intracapsular and extrasynovial
- Innerved and vascularized

- Distribution of lubricant
- Biomechanical function

S. Clockaerts yz. Osteoarthritis Cartilage 2010

HOFFA'S GROUP PADOVA UNIVERSITY

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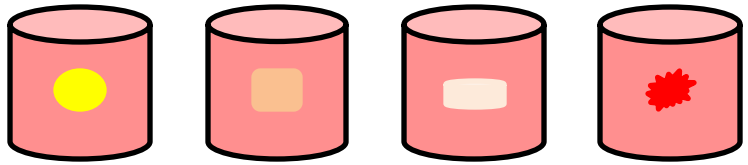
Orthopedics and
Orthopedic
Oncology

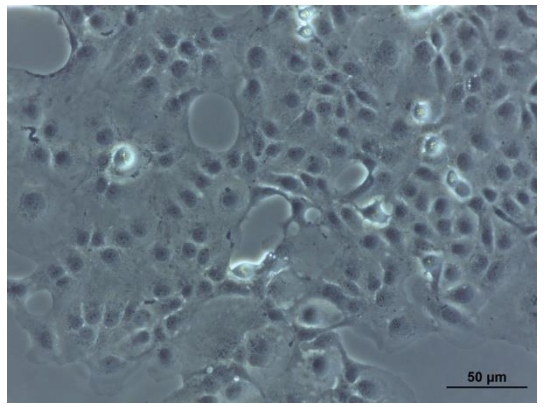
Elisa Belluzzi
Orthopedics and
Orthopedic
Oncology

Prof. Chiara Giulia Fontanella
Department of Industrial
Engineering

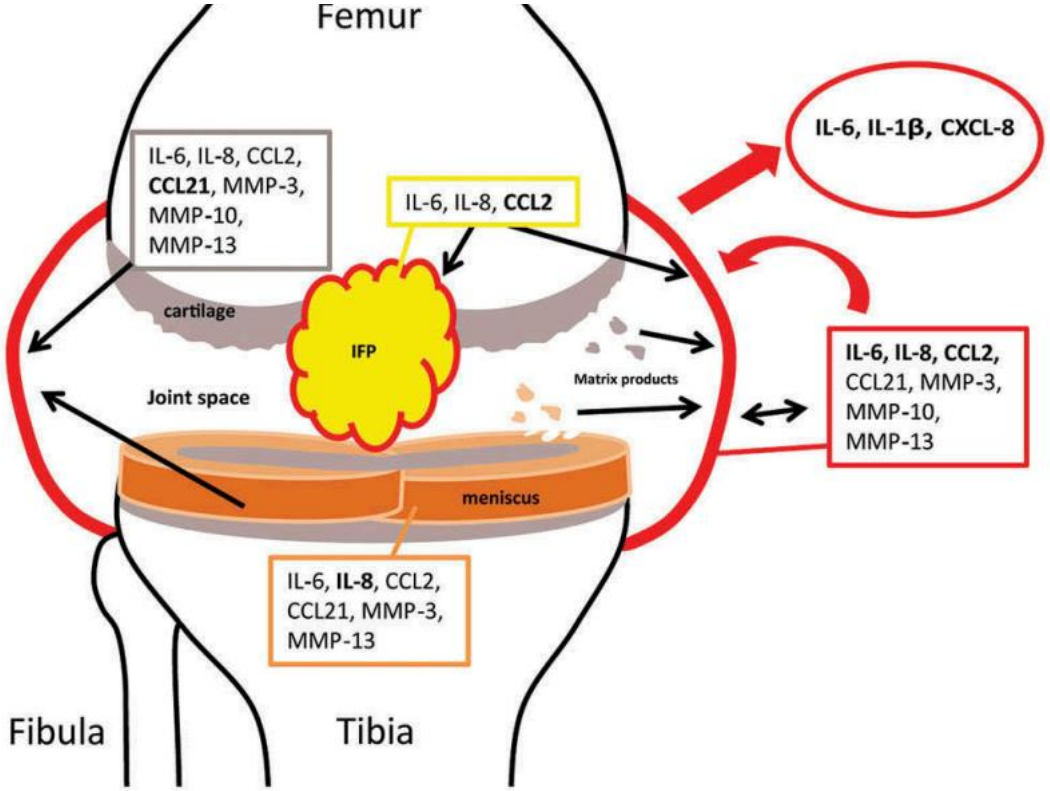
Conditioned media from human osteoarthritic synovium induces inflammation in a synoviocyte cell line



Hoffa Meniscus cartilage synovium

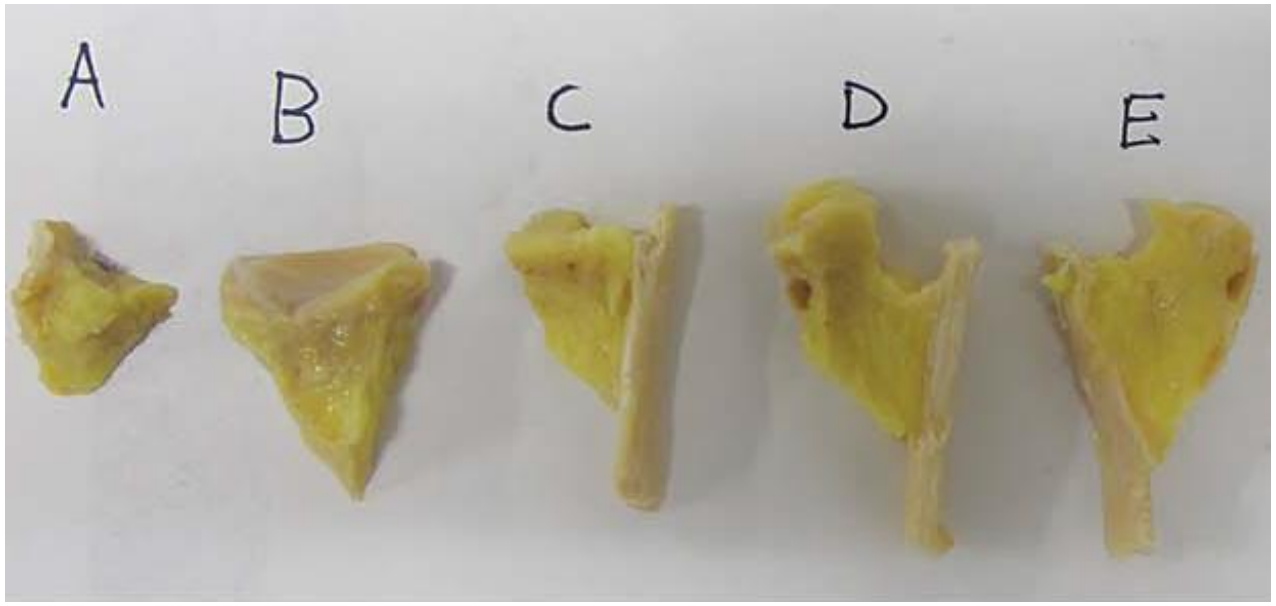


synoviocytes cell line K4IM

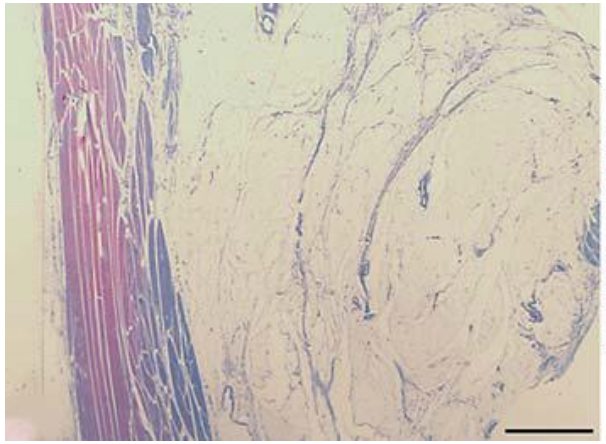


Haas C. et al, 1996

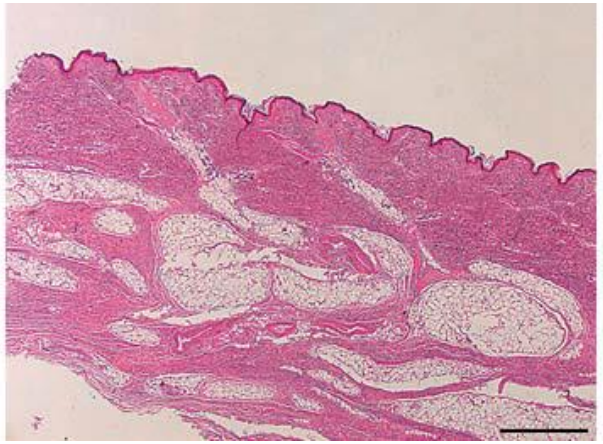
Belluzzi E, Ramonda R, Favero M, Connective Tissue Research 2018



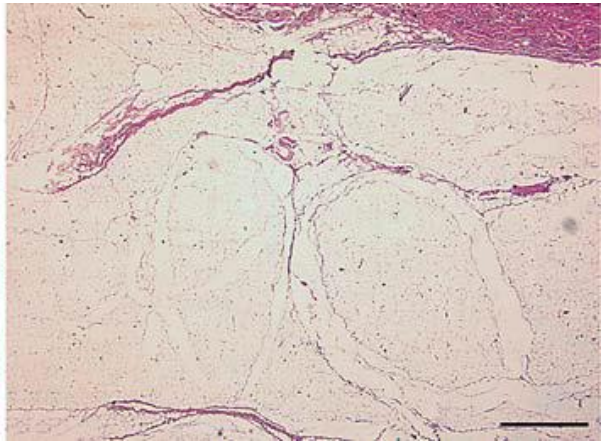
IFP



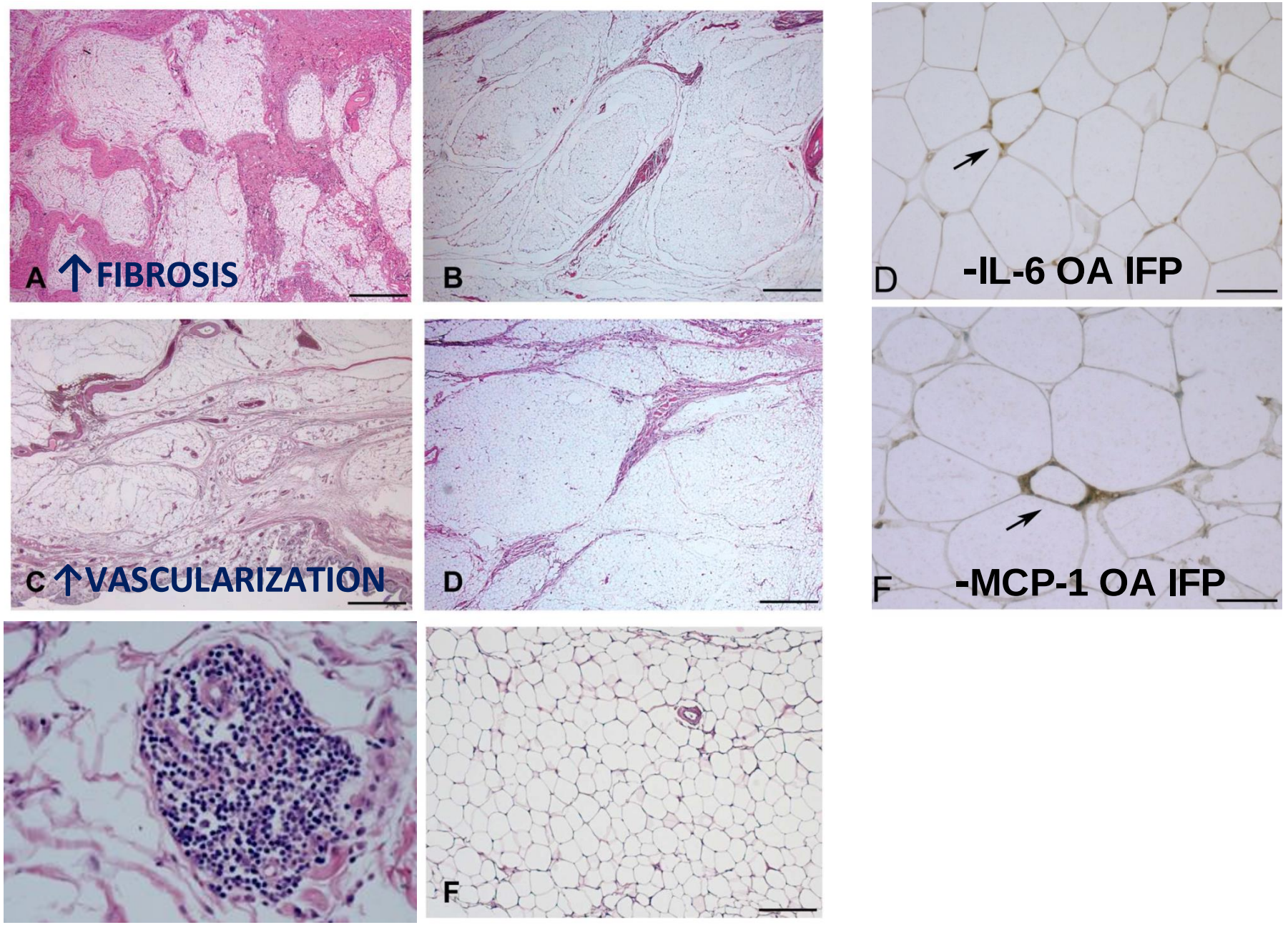
SUBCUTANEOUS



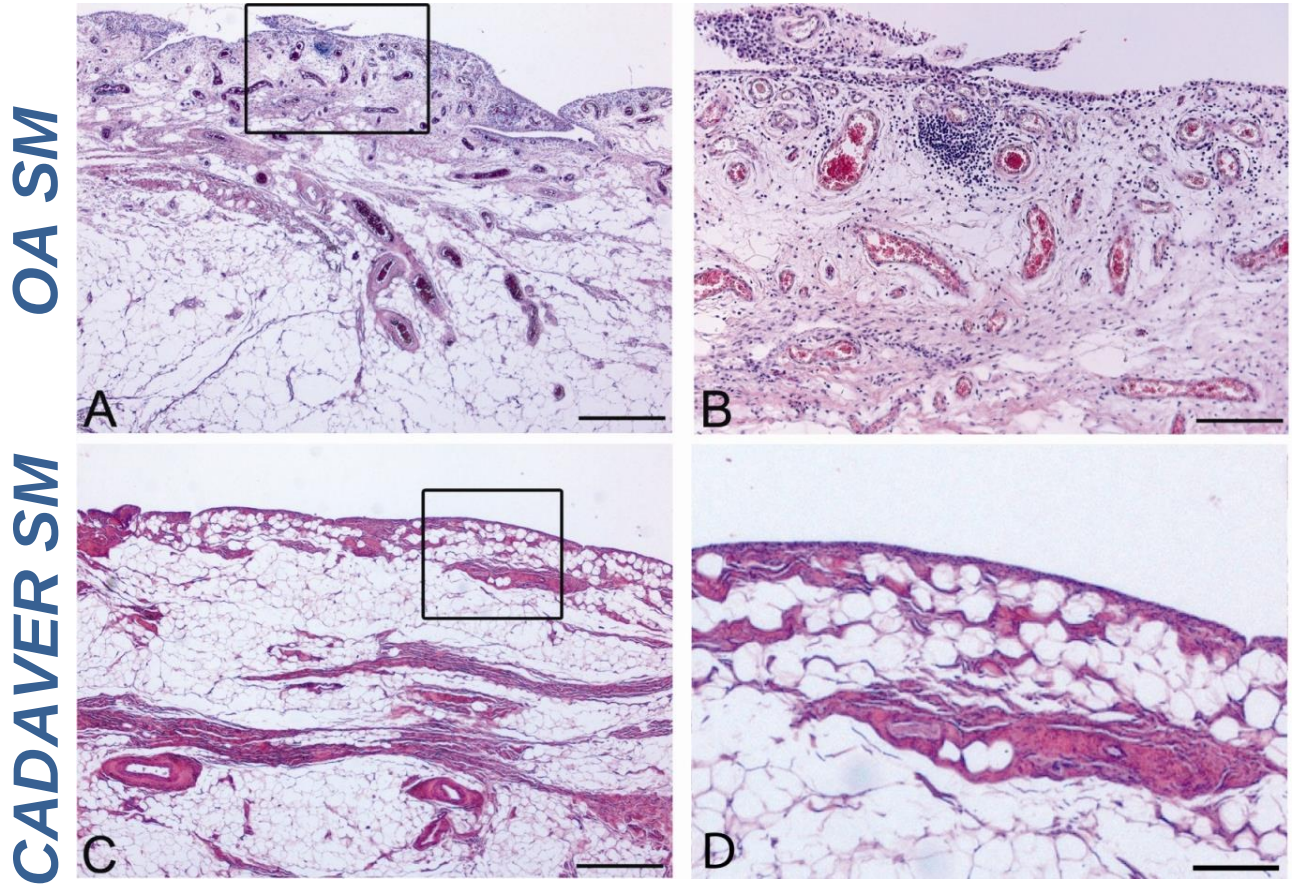
ABDOMEN



Macchi V, Rossato M, Cells Tissues Organs. 2016



Favero M, Ramonda R, Rossato M, Macchi V, et al. Rheumatology (Oxford). 2017



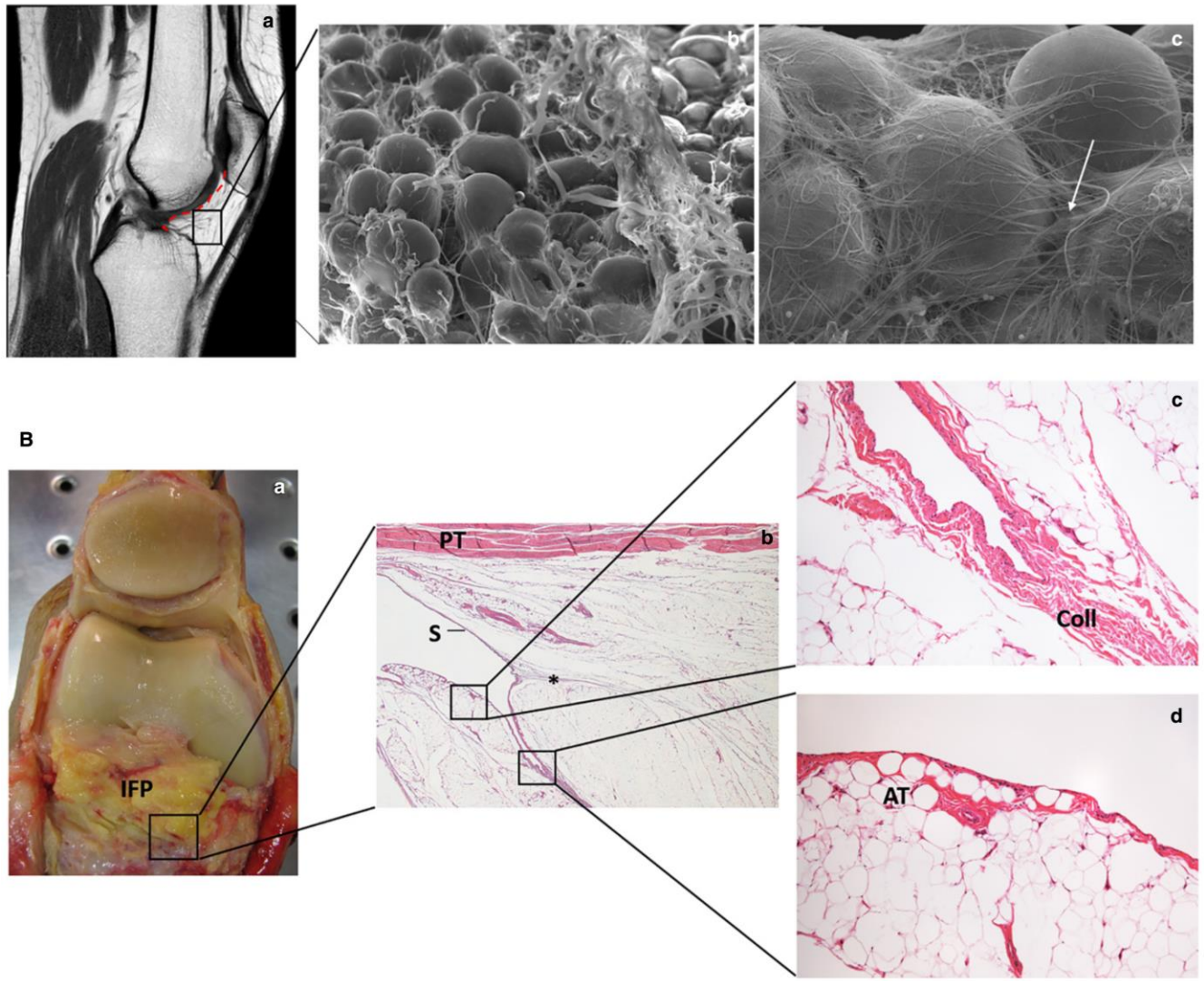
Favero M, Ramonda R, Rossato M et al. Rheumatology (Oxford). 2017

↑MONONUCLEAR CELL INFILTRATION,
↑VASCULARIZATION, ↑ FIBROSIS

- Knee OA synovitis may also depend on the release of inflammatory factors by the IFP, located at the posterior surface of synovium (*Eymard 2014, Distel 2009)*

The infrapatellar fat pad and the synovial membrane: an anatomo-functional unit

Veronica Macchi,[1] Elena Stocco,[1] Carla Stecco,[1] Elisa Belluzzi,[2,3] Marta Favero,[3] Andrea Porzionato[1] and Raffaele De Caro[1]



MOAKS SCORE

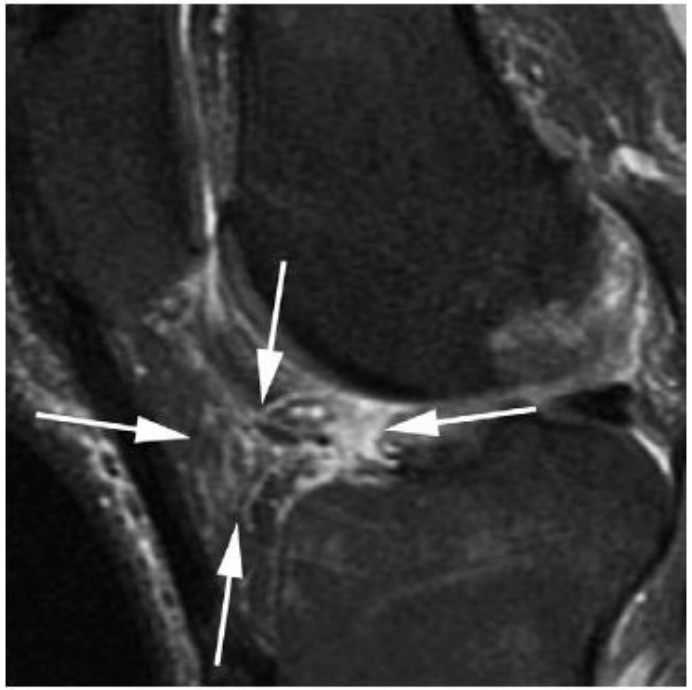
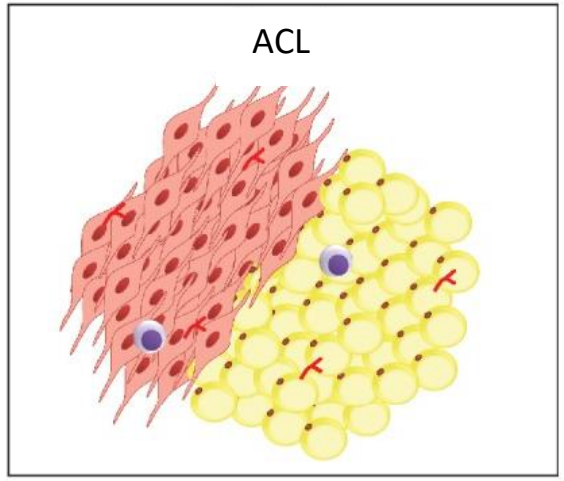
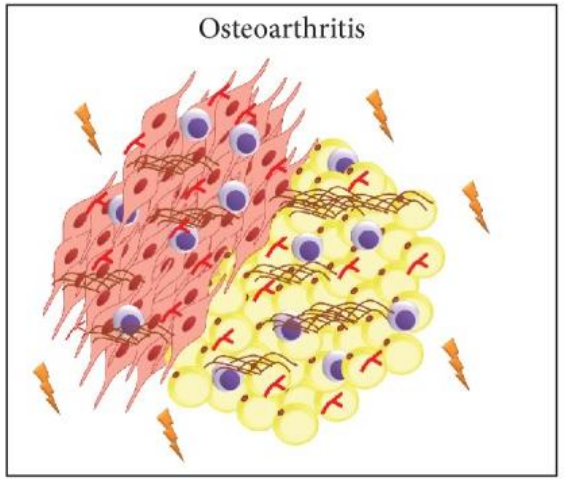


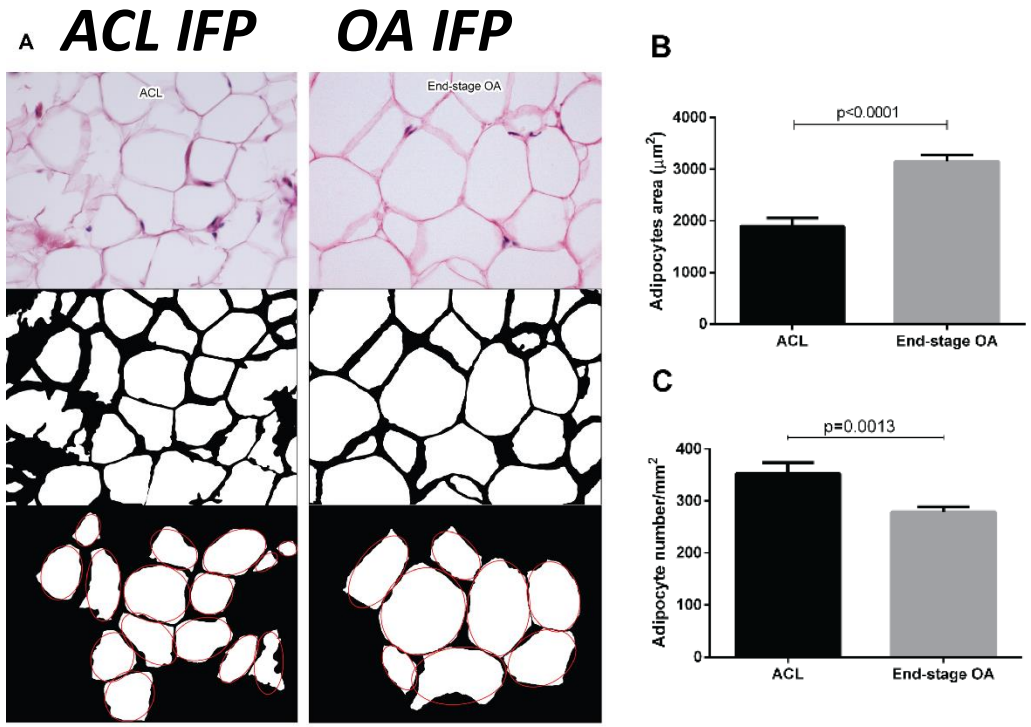
Fig. 8. Hoffa-synovitis. Sagittal T2w image shows grade 2 hyperintense signal changes in Hoffa's fat pad consistent with Hoffa-synovitis.

OA IFP VS ACL RUPTURE IFP

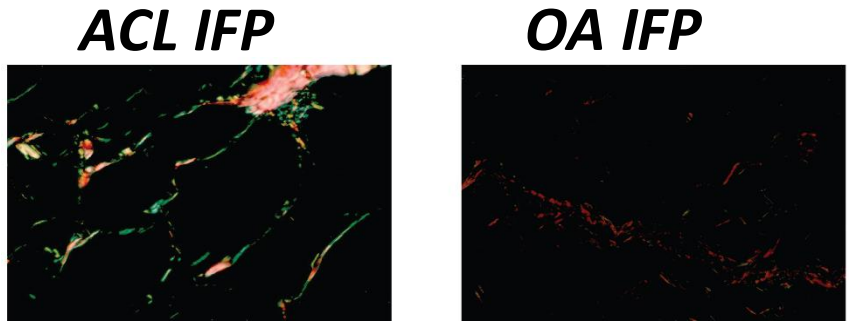




Belluzzi E, Ramonda R, Favero M, Macchi V. Biomed Res Int. 2019

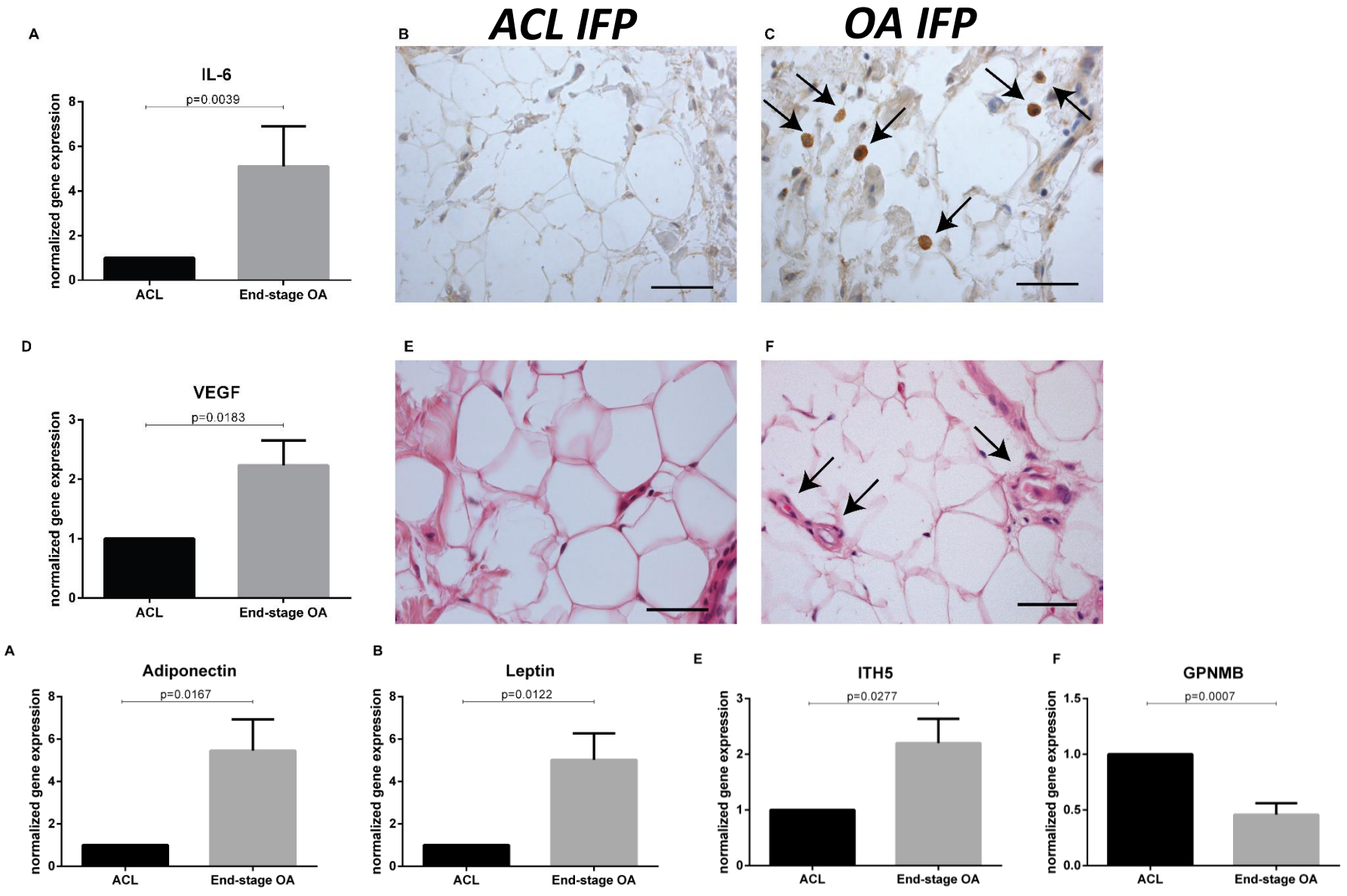


Belluzzi E, Ramonda R, Rossato M, Favero M, submitted



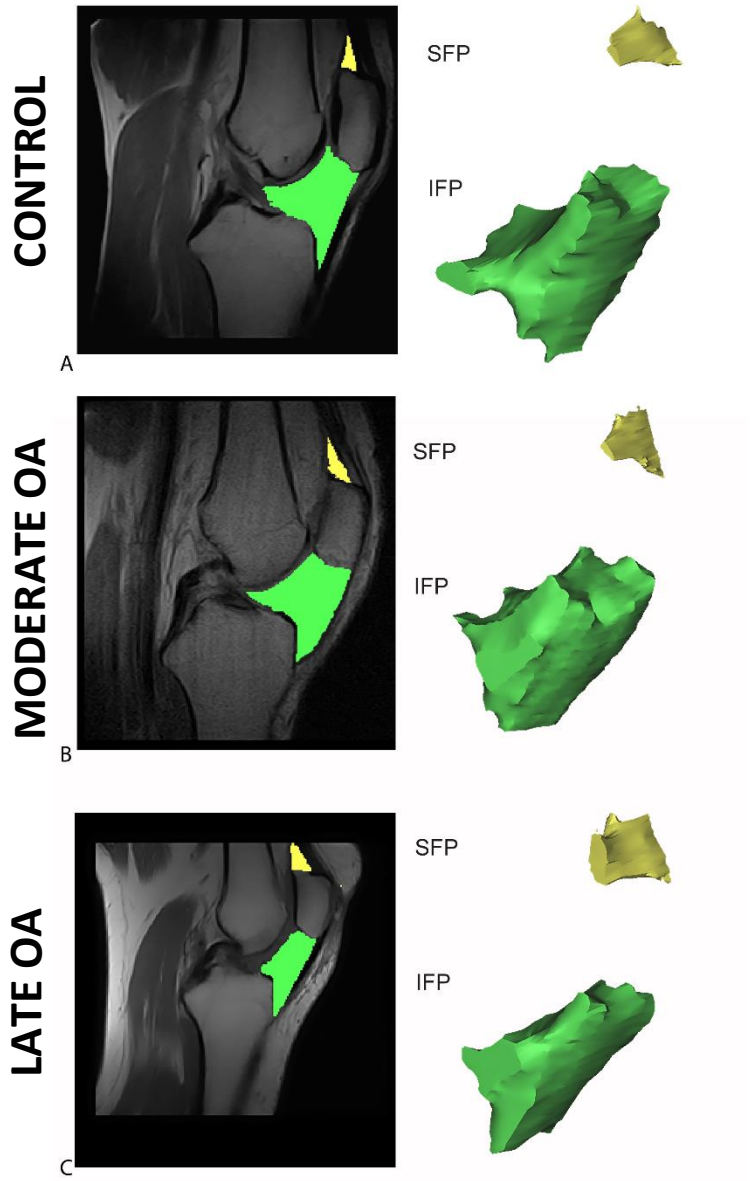
↑ COL I and III in ACL IFP

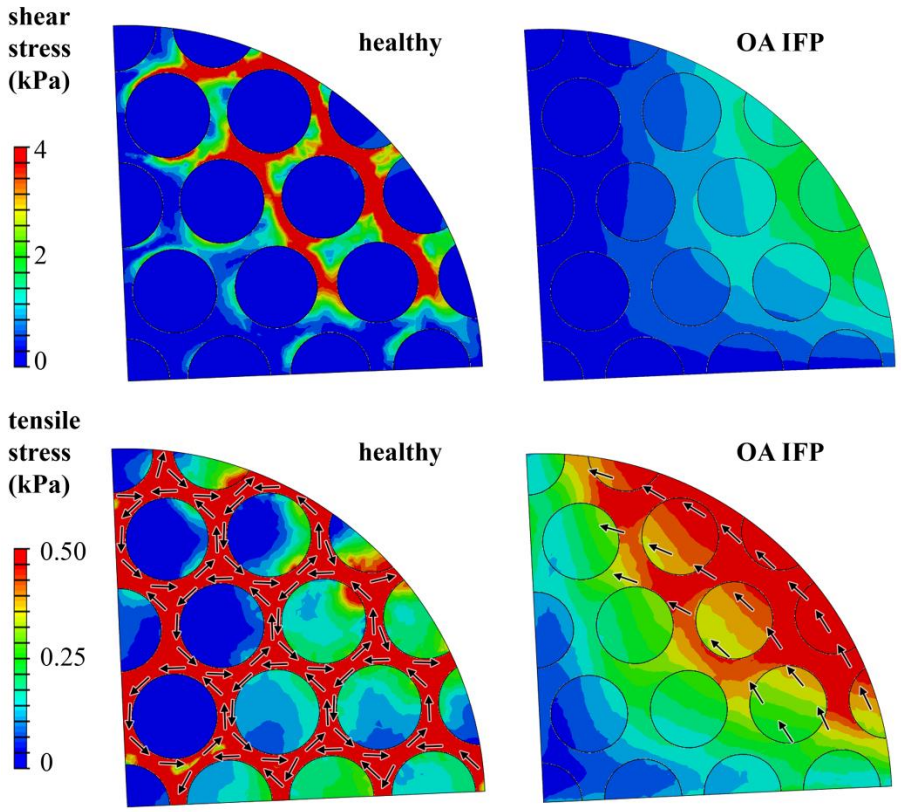
OA IFP VS ACL RUPTURE IFP



Belluzzi E, Ramonda R, Rossato M, Favero M, Rheumatology submitted

IFP IN MODERATE AND LATE OA





Fontanella, Macchi V, Favero M, Australas Phys Eng Sci Med. 2018

Fontanella CG, Ramonda R, Rossato M, Macchi V, Favero M et al. Ann Anat. 2019

CONCLUSIONS

- Obesity is a risk factor for osteoarthritis development related to low-grade systemic inflammation other than joint overloading.
- Adipose tissue, which act as endocrine organ, produce adipokines (leptin, adiponectin, ect) which can directly initiate the abnormalities in the joint.
- Metabolic syndrome is an indipendent risk factor for osteoarthritis and accumulation of MetS components is associated with OA incidence, OA severity and TKR
- Infrapatellar fat pad seems to have a role in the pathogenesis of osteoarthritis producing adipocytokines.
- Infrapatellar fat pad and adjacent synovial membrane of OA patients showed increased mononuclear cell infiltration, vascularization and fibrosis compared to controls.