

Os & inflammation

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Conflits d'intérêts

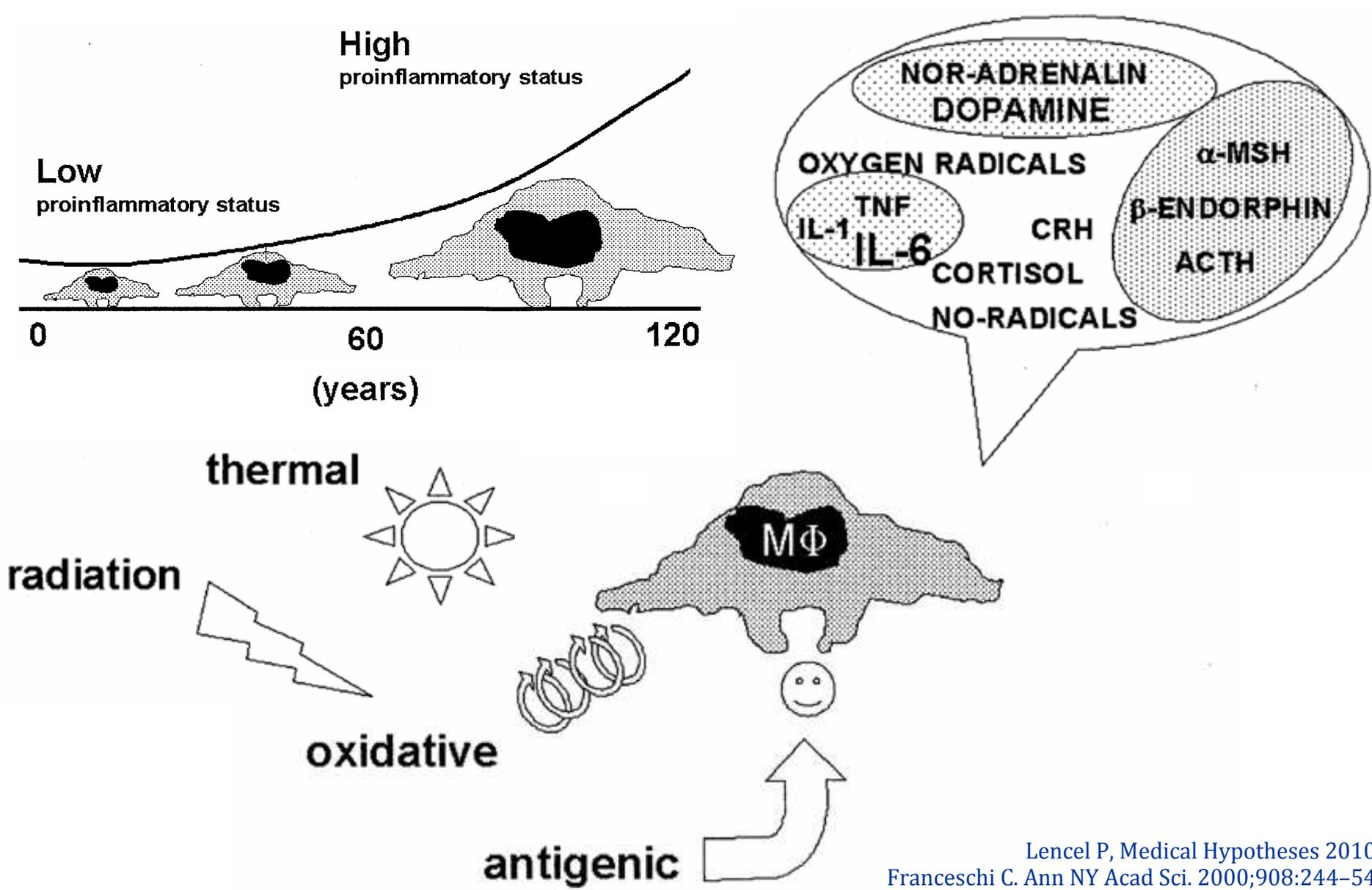
- **Interventions ponctuelles**

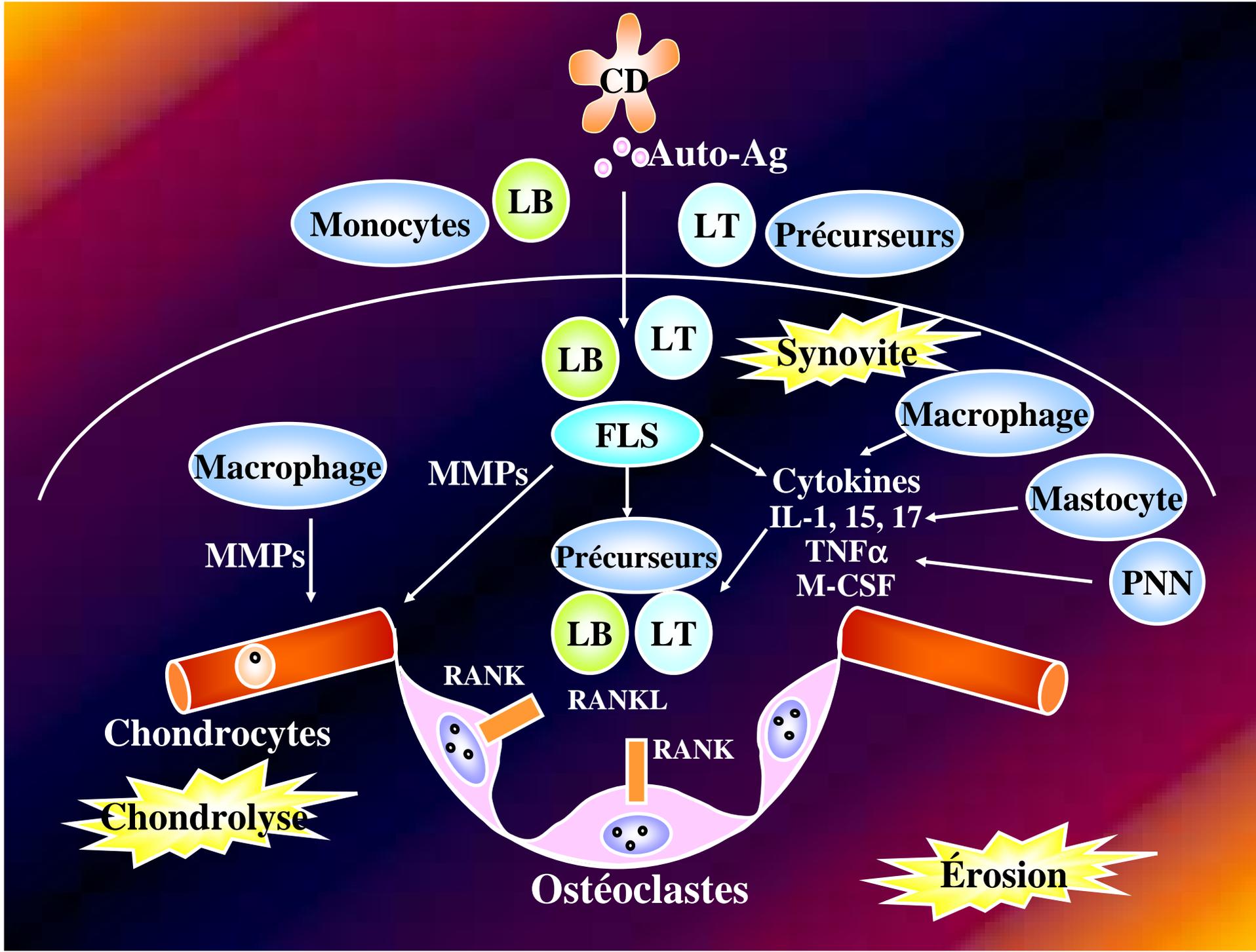
Honoraires en tant qu'expert ou orateur de Amgen, Génévrier, GSK, Lilly, Merck, Novartis, Servier

- **Intérêts indirects**

Soutien financier pour des programmes de recherche ou investigateur de Amgen, Chugai, Merck, Novartis, Pfizer, Roche, Servier, UCB, Warner-Chilcott

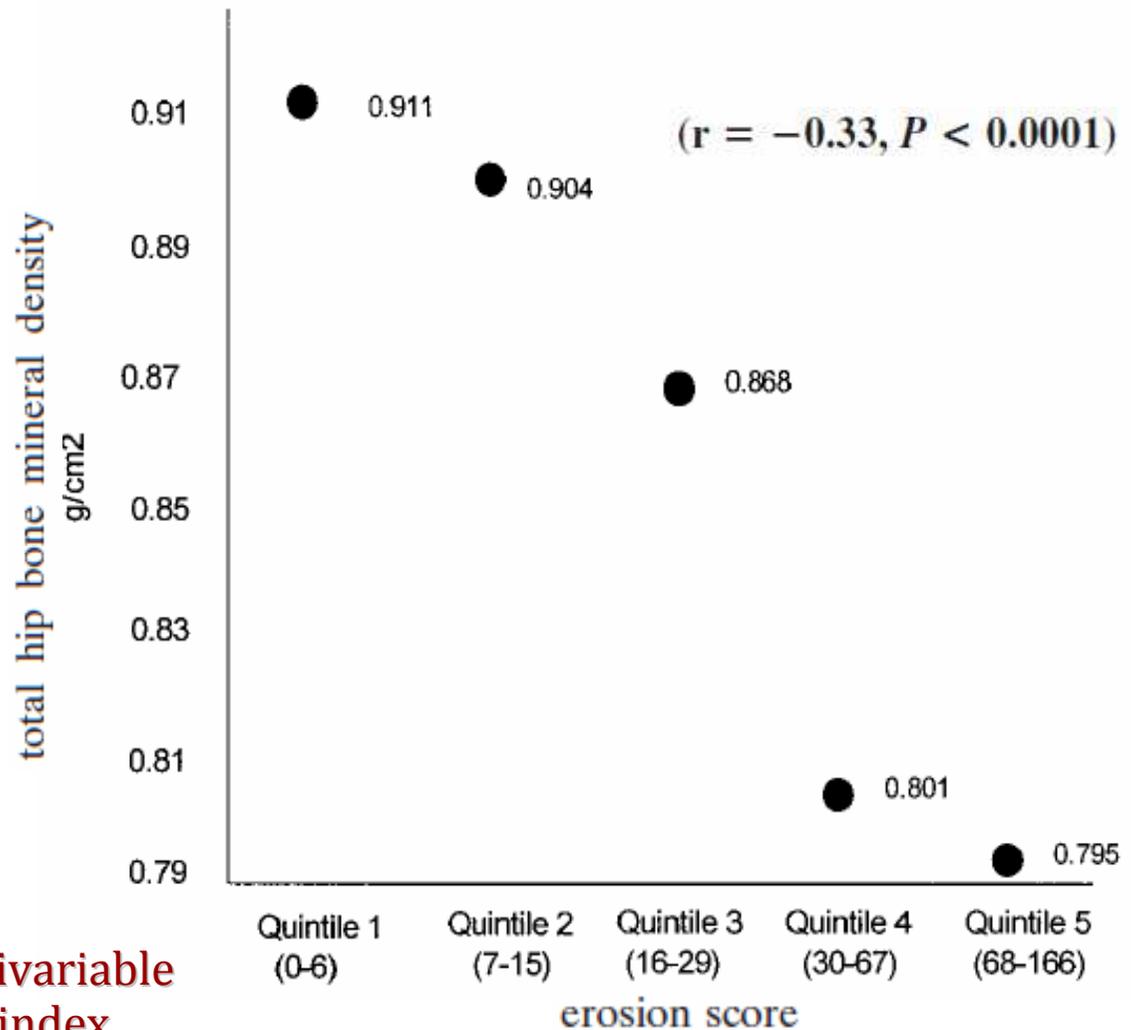
Osteoporosis, part of inflamm-aging





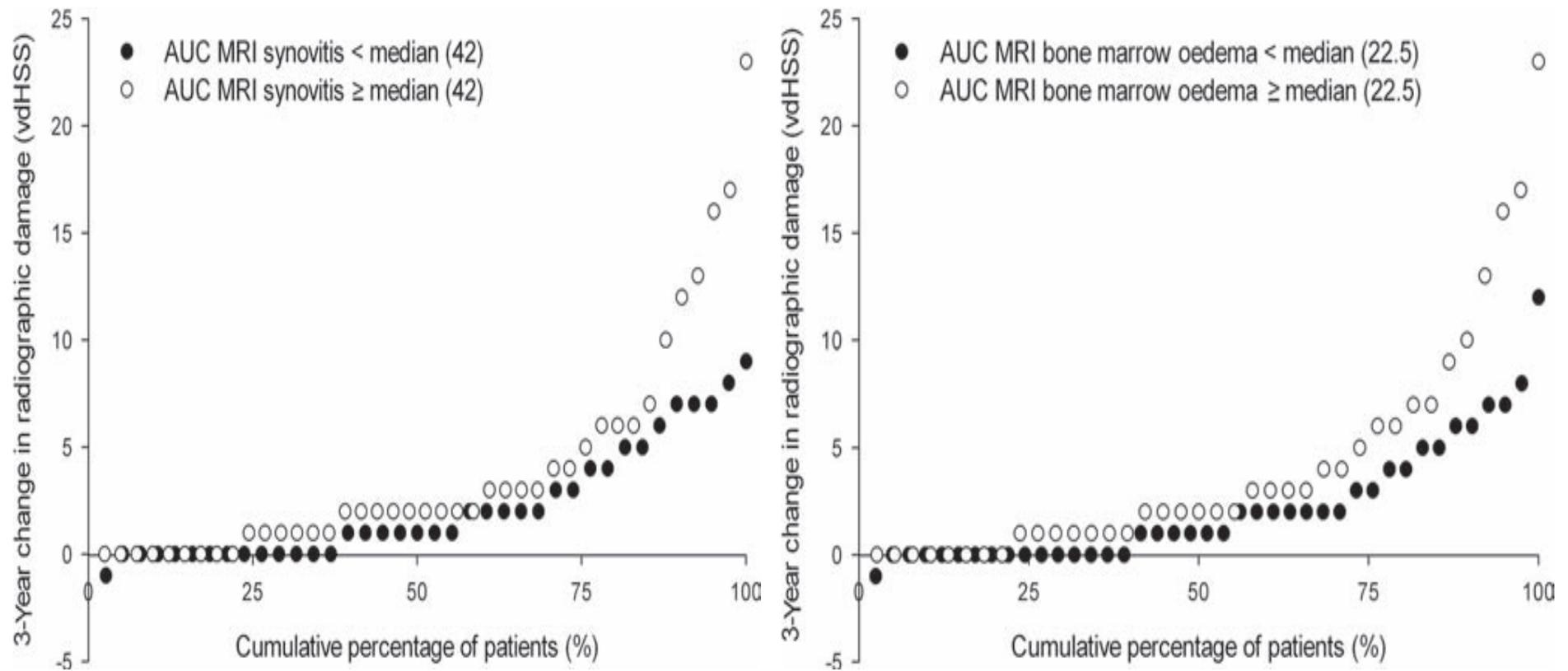
The relationship between focal erosions and generalized osteoporosis in postmenopausal women with RA

163 postmenopausal women with RA
Average disease duration of 13.7 years
Almost all under DMARDs
None taking osteoporosis medications
Dual x-ray absorptiometry at the hip
Hand radiography (Sharp method)



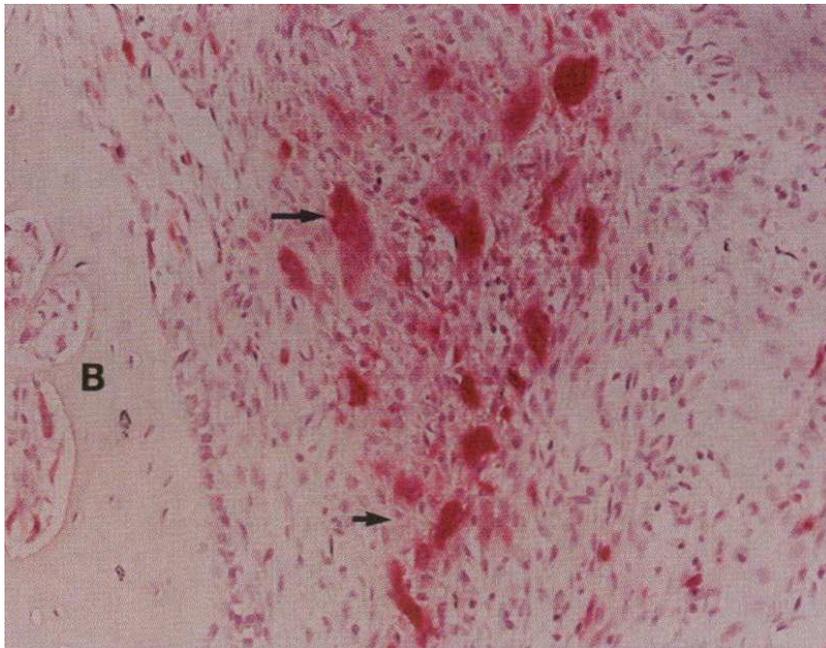
No significant association in multivariable models including age, body mass index, and cumulative oral glucocorticoid dose

Synovitis and bone marrow oedema as independent predictors of subsequent radiographic progression



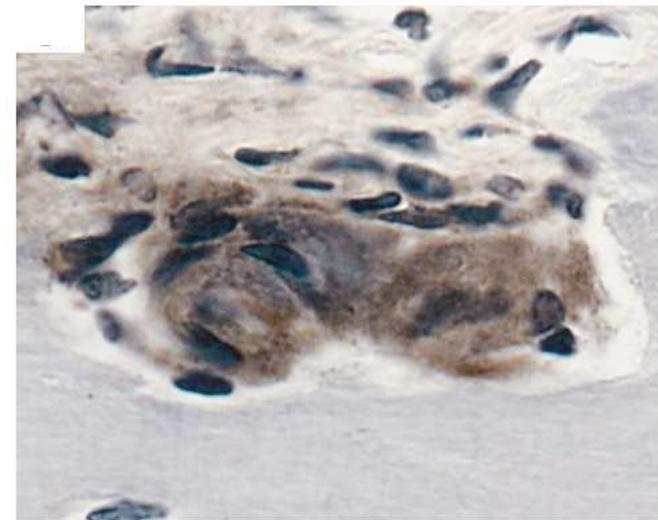
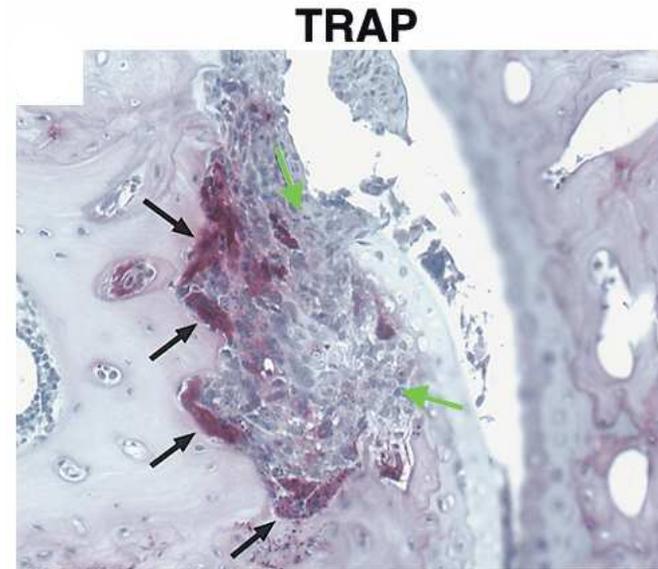
55 patients with RA with disease duration
<1 year participated in this 3-year follow-up study

Identification of cell type responsible for bone resorption in rheumatoid arthritis



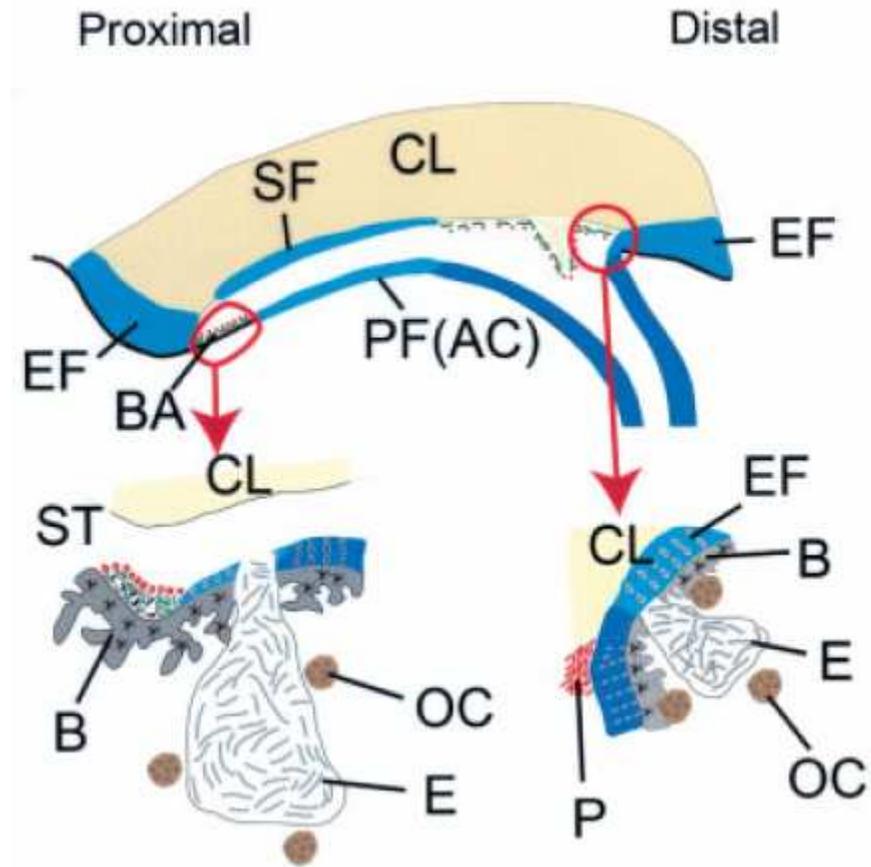
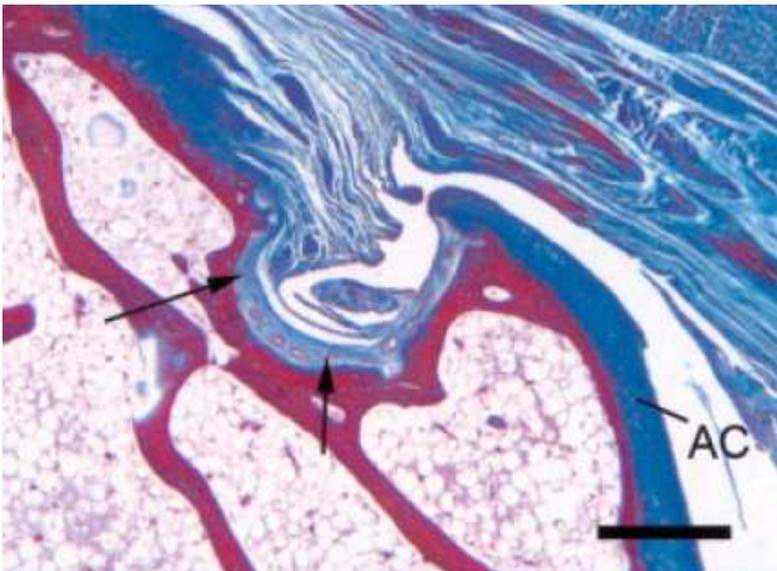
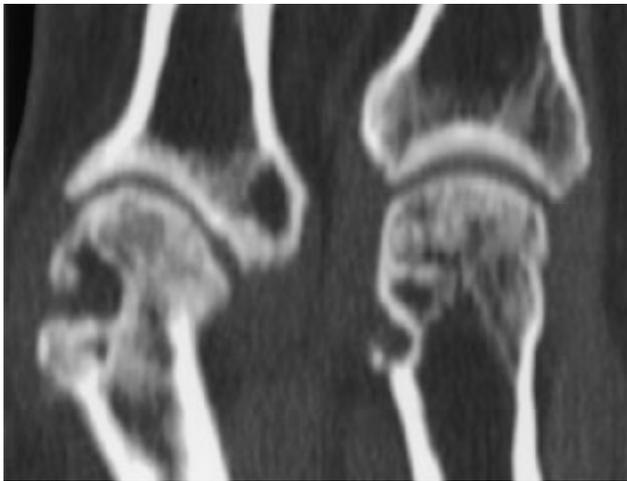
TRAP staining in joint tissue from a patient with RA
Numerous TRAP-positive MNCs (long arrow)
and MNCs (short arrow) in pannus remote from bone
B, bone. Hematoxylin counterstain. Magnification x50

Histology of a hTNFtg proximal interphalangeal
Inflammation (green arrows)
with subsequent subchondral bone erosion (black arrows)
Magnification TRAP x200; CTR x400



Calcitonin receptor

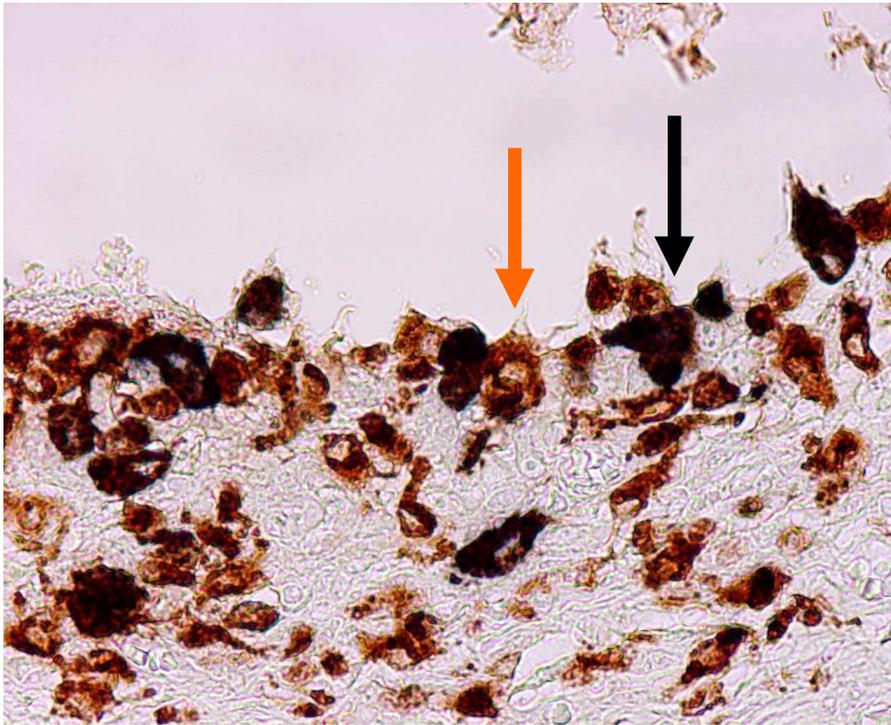
Topography of periarticular erosion formation in arthritis



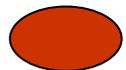
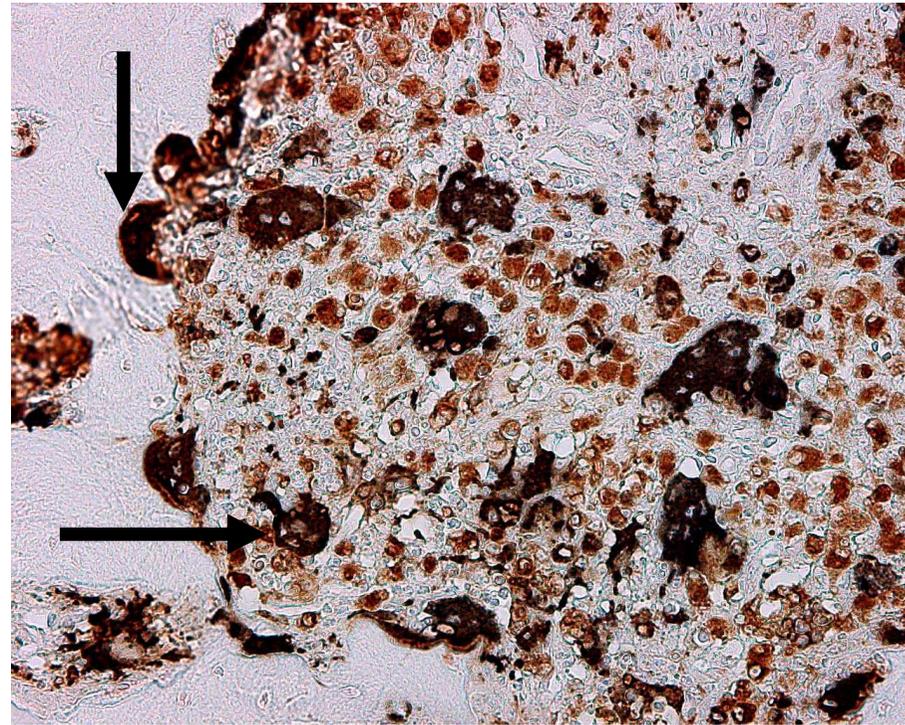
An enlarged view of the erosion in a, at a site immediately adjacent to the articular cartilage (AC) of the proximal phalanx. A synovial membrane with a thick underlying layer of connective tissue (arrows) lines the bone surface. Bar=500 um

Early osteoclast formation and bone resorption in synovitis of adjuvant-induced arthritis

Day 2



Day 5



macrophages



osteoclast precursors



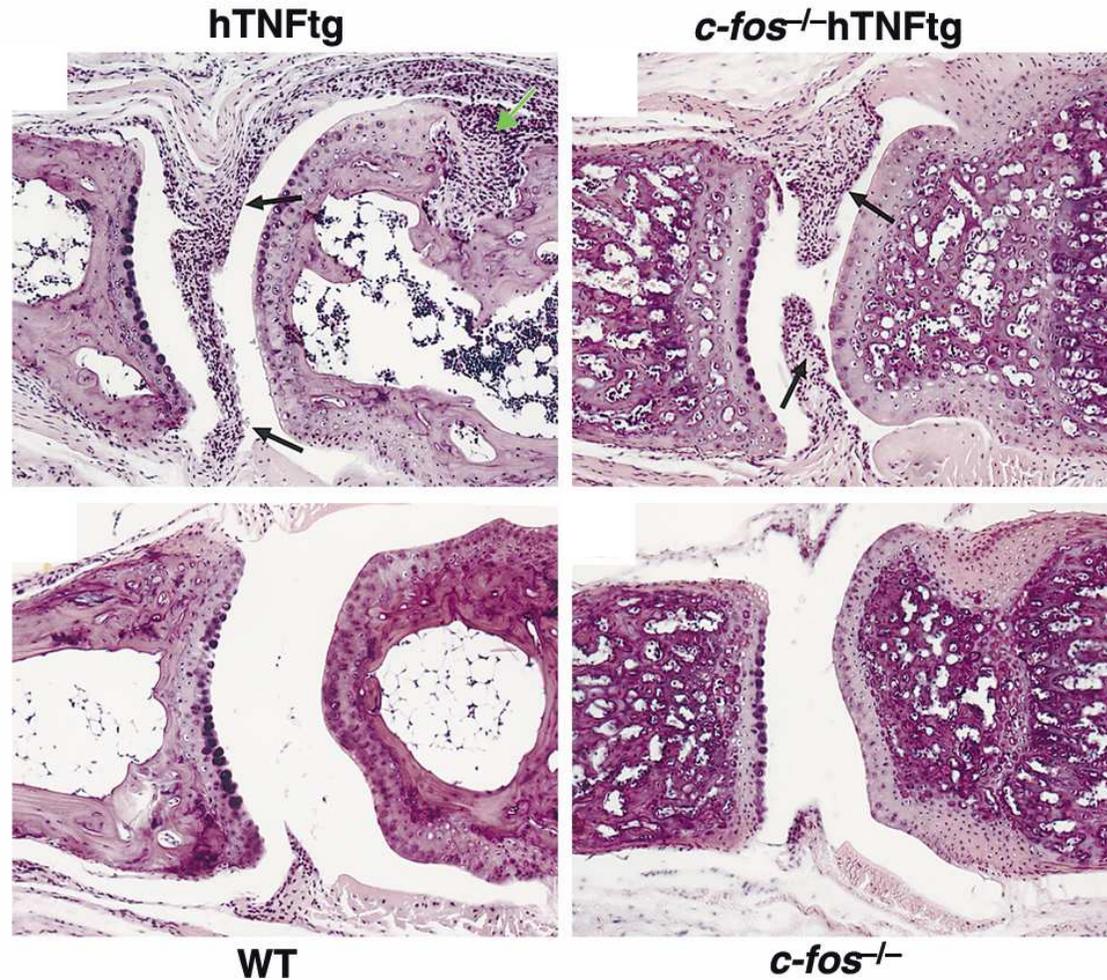
unpolarized osteoclasts



polarized osteoclasts

Osteoclasts are essential for inflammatory joint destruction

H&E stained sections of mouse digital joints

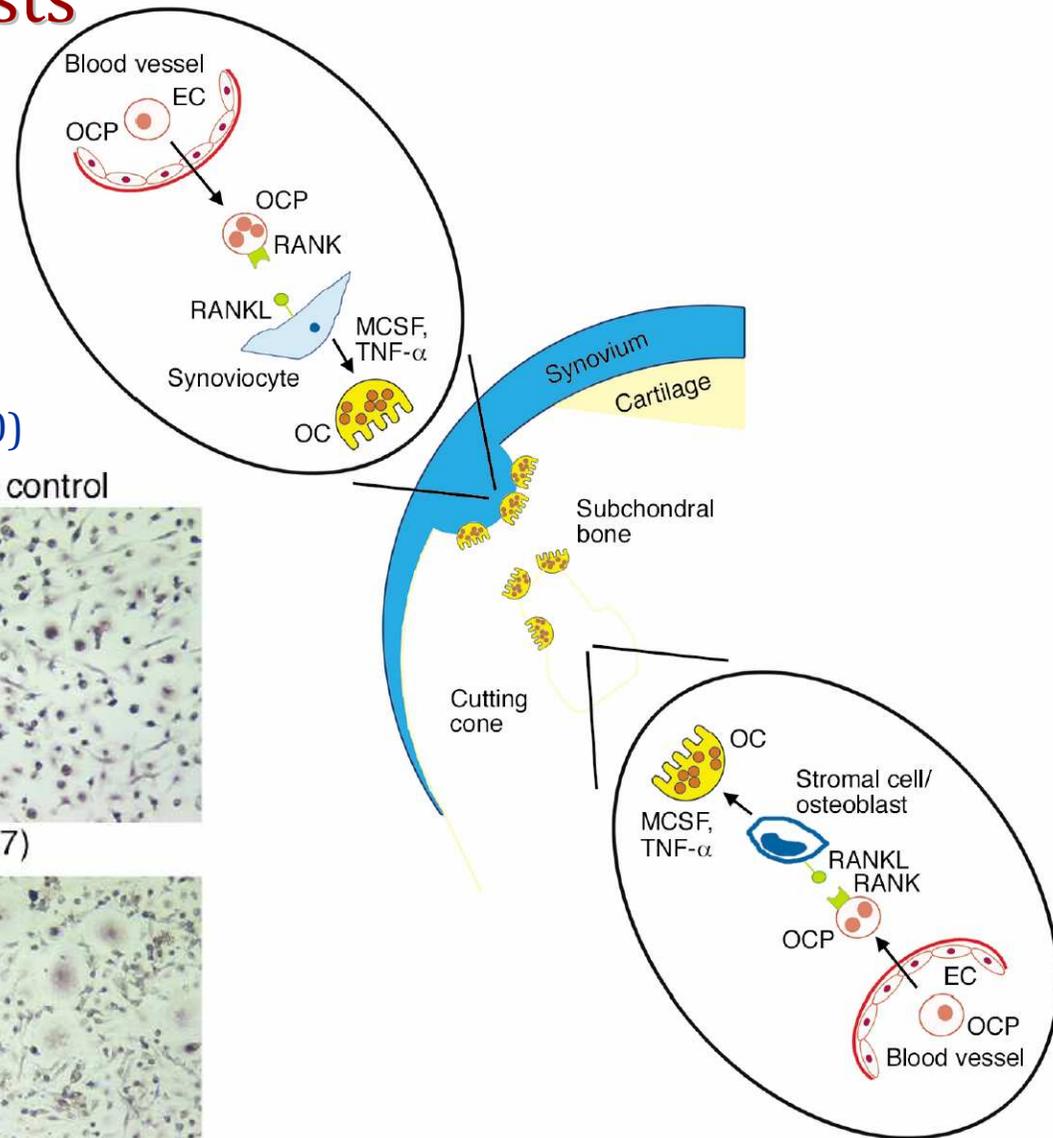
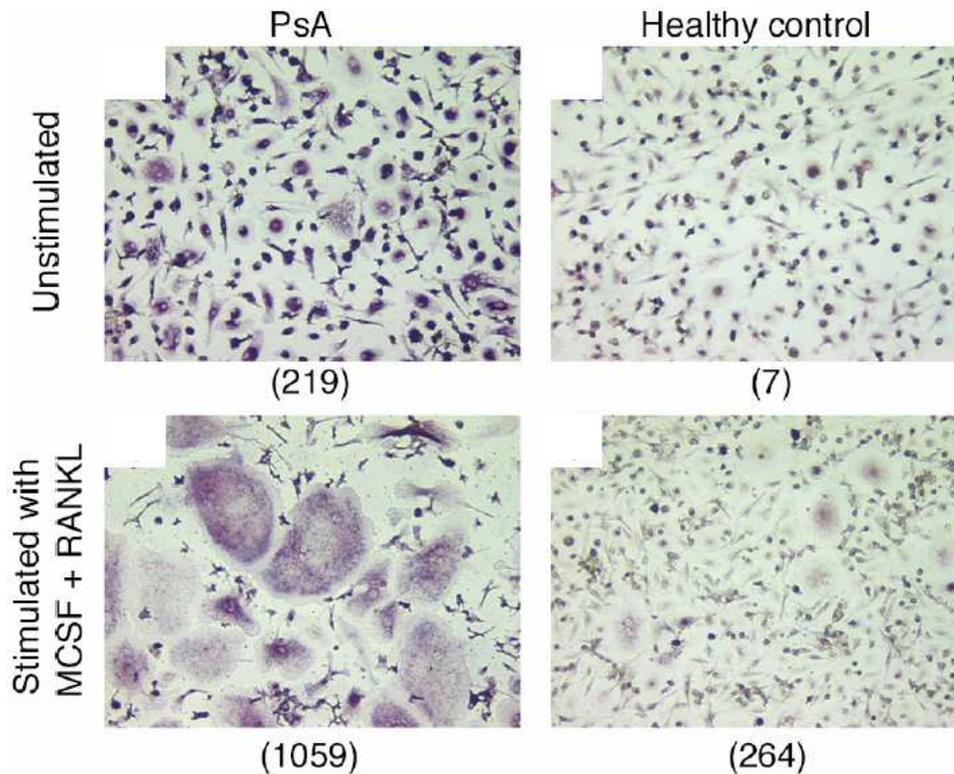


Inflammatory tissue (black arrows) and erosion (green arrow)
Magnification $\times 50$

Outside-in and inside-out bone invasion of circulating precursors of osteoclasts

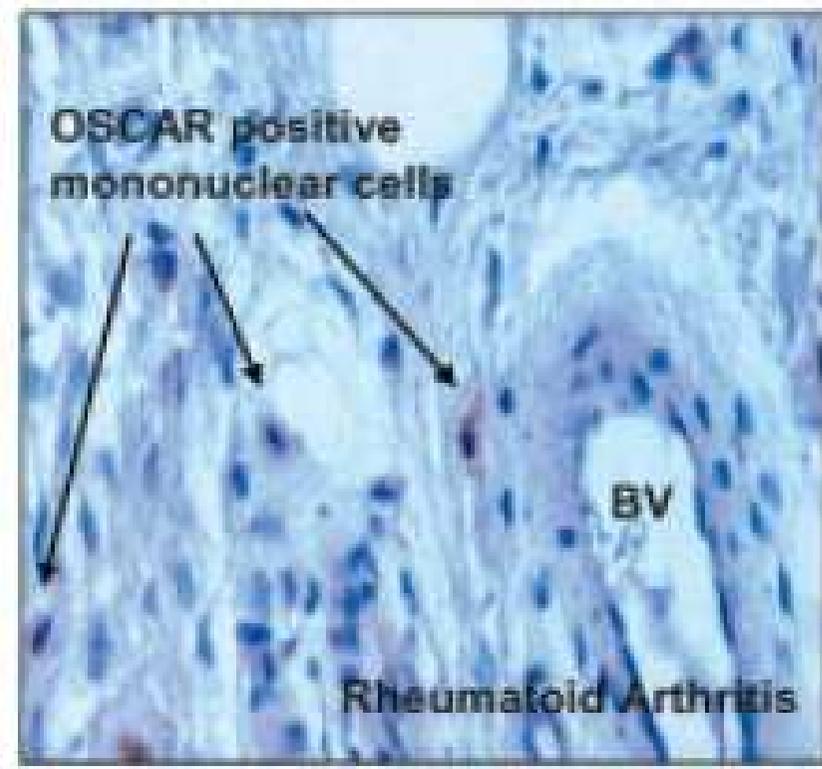
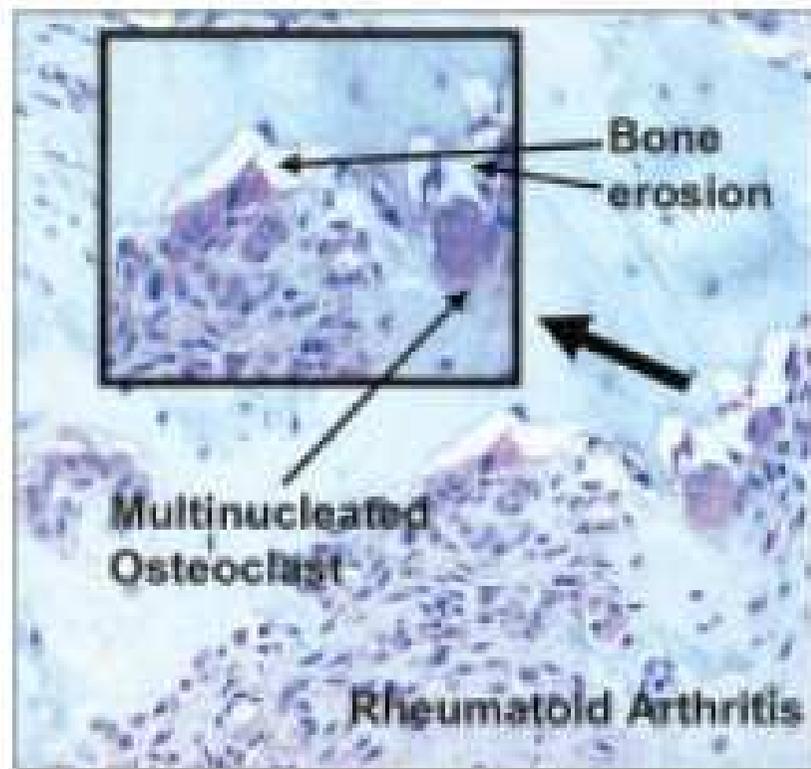
OCPs in PBMCs

PsA patients and healthy controls cells cultured for 14 days and stained for TRAP (magnification x10)



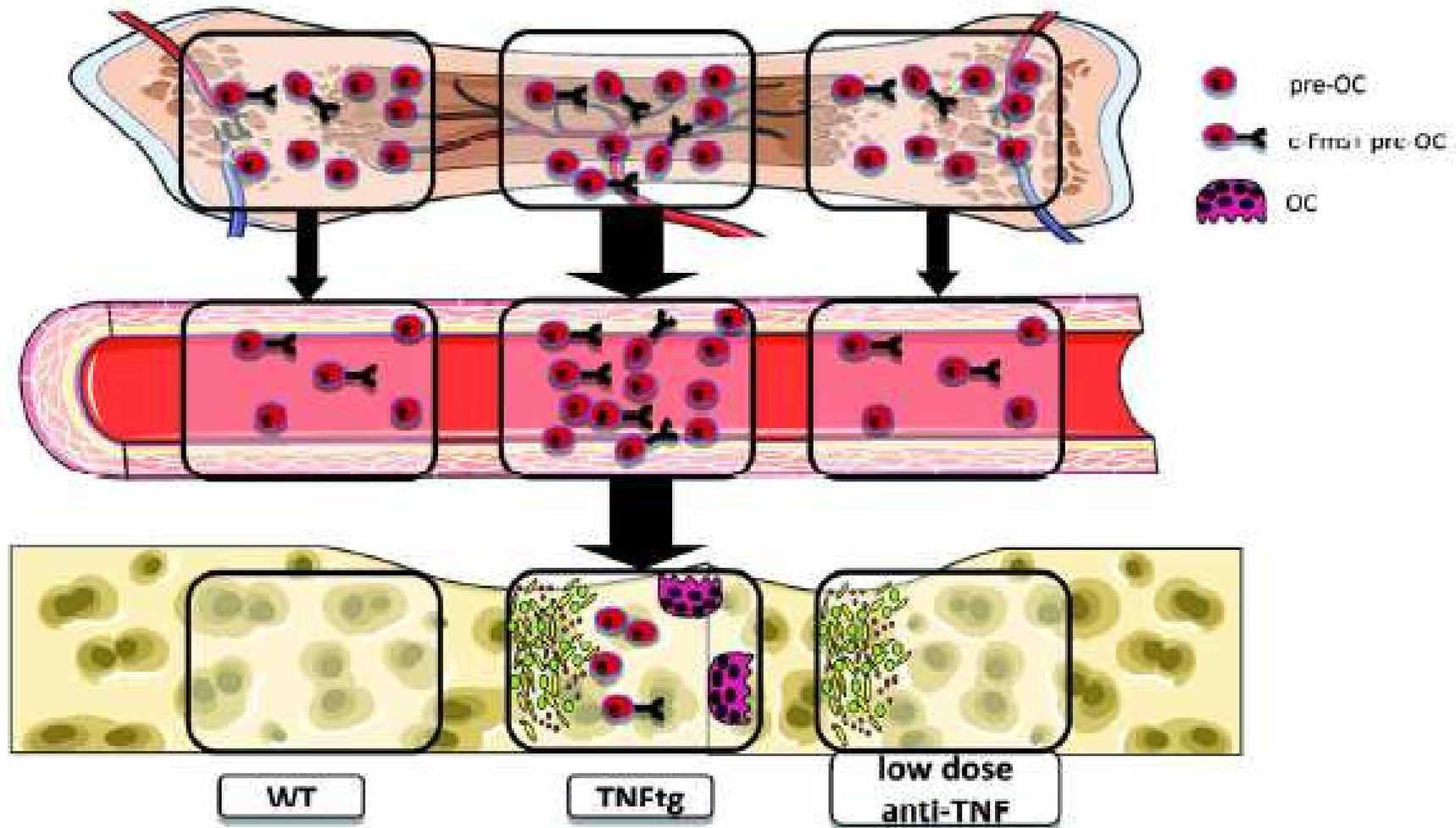
Expression of osteoclast-associated receptor (OSCAR) by mononuclear cells of patients with RA

Immunoblotting of synovial tissue extracts from patients with RA and labeling with an antibody against human OSCAR



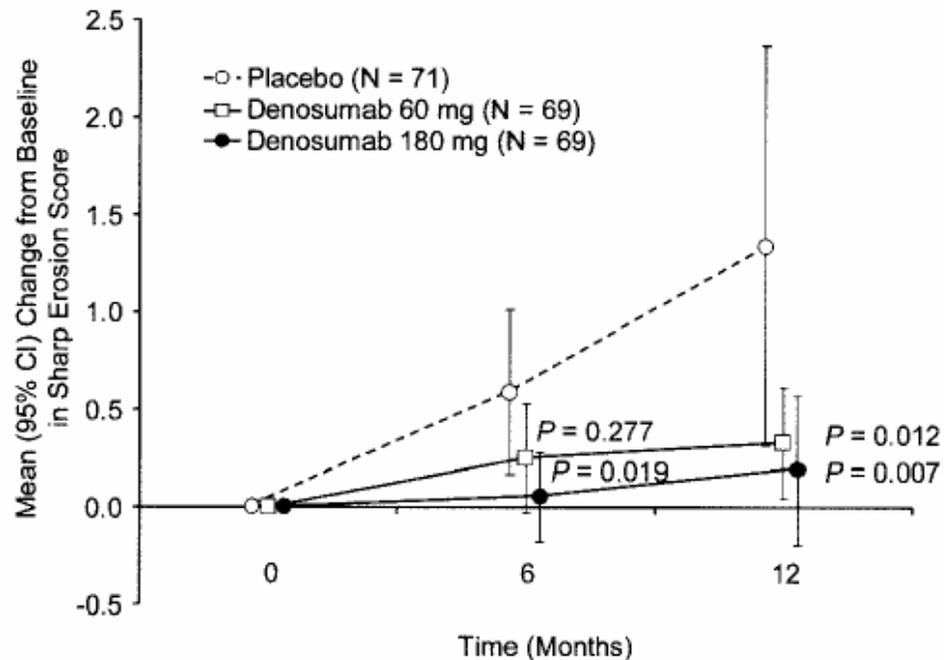
Enhanced expression of OSCAR in circulating monocytes influenced by inflammatory disease activity

Anti-TNF blockade of osteoclastogenesis independent of effects on synovial inflammation

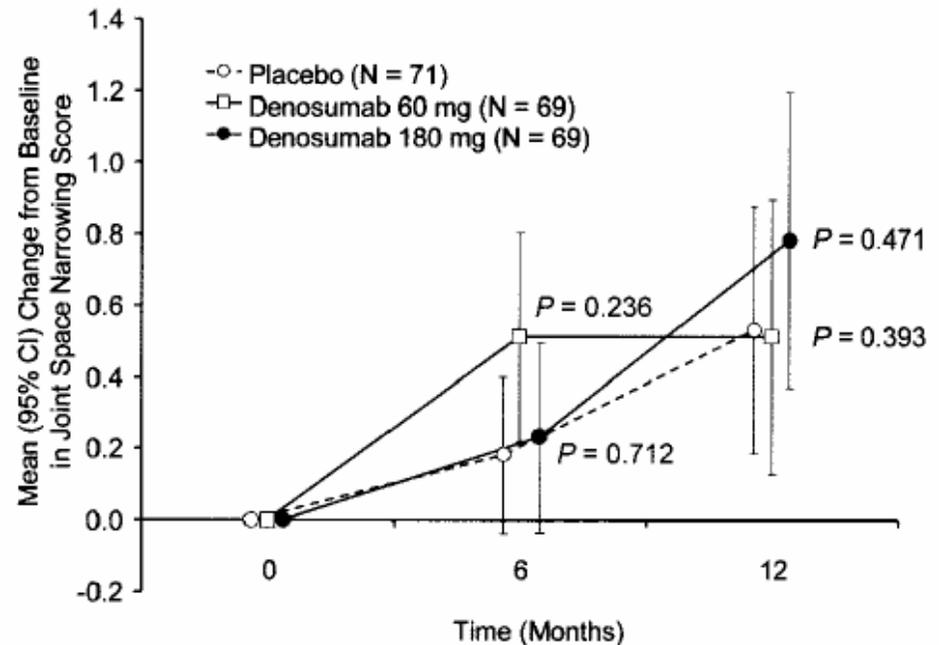


Denosumab treatment effects on structural damage in rheumatoid arthritis

Modified Sharp erosion score



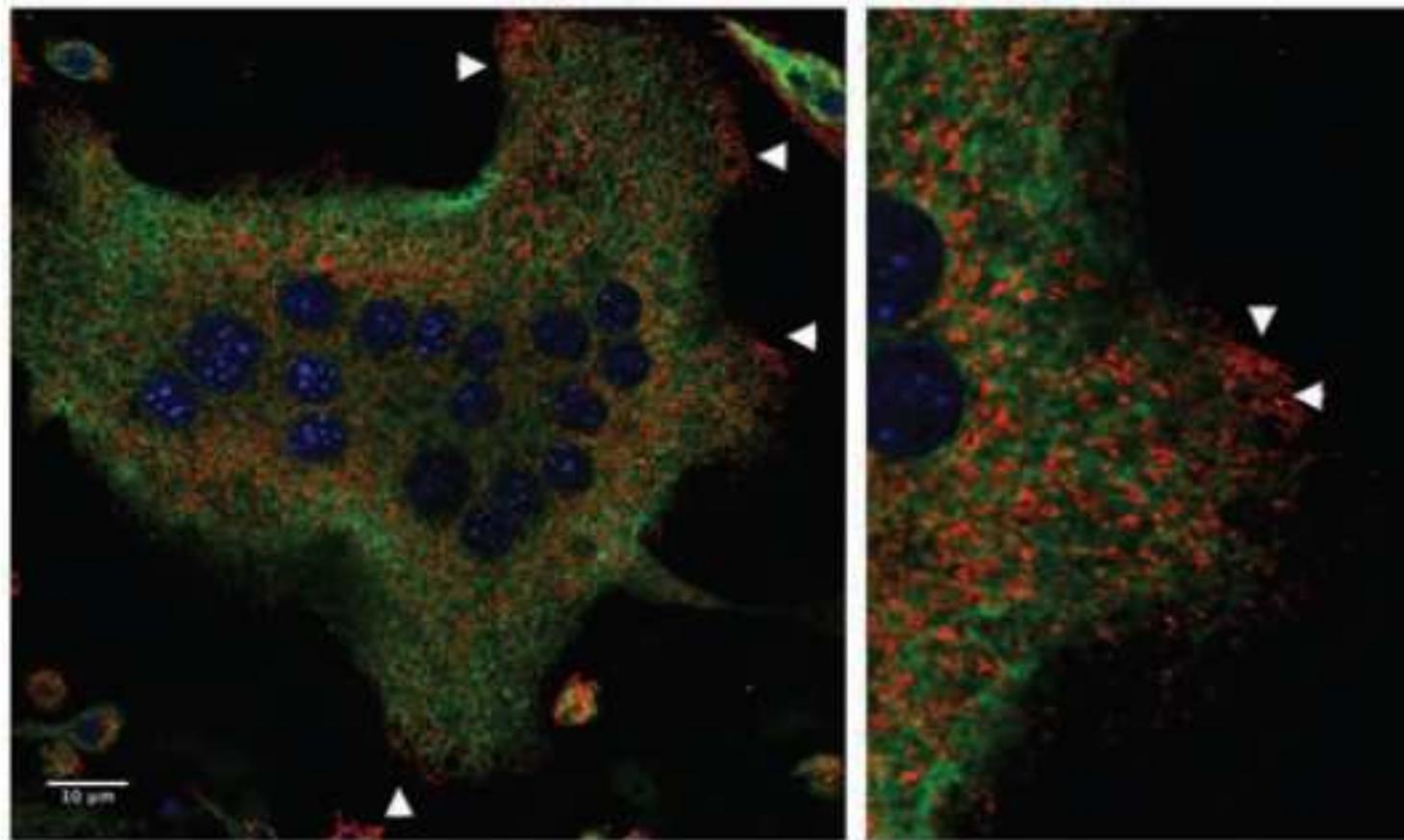
Joint space narrowing score



Double-blind randomized study in RA patients receiving subcutaneous placebo (n=75), denosumab 60 mg (n=71) or denosumab 180 mg (n=72) injections every 6 months for 12 months

ACPA recognize citrullinated vimentin on surfaces of osteoclast precursors

Laser scanning microscopy of 2-mm osteoclast sections



Green, vimentin staining Red, MCV-ACPA staining for citrullinated vimentin Blue, DAPI staining for the nucleus

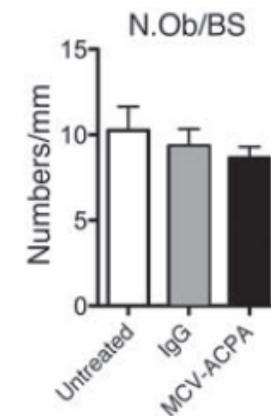
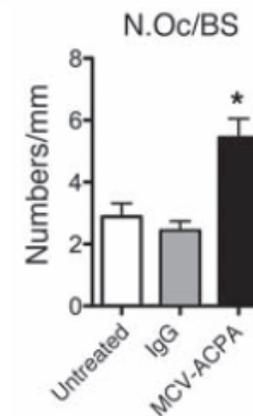
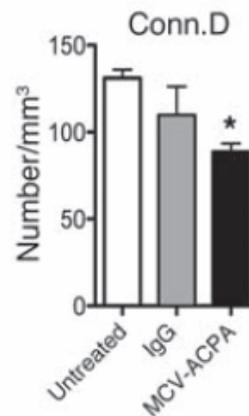
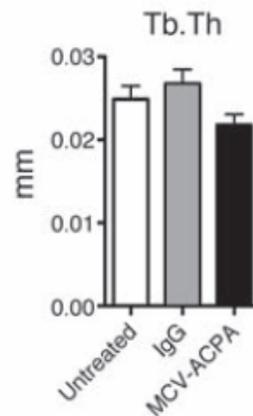
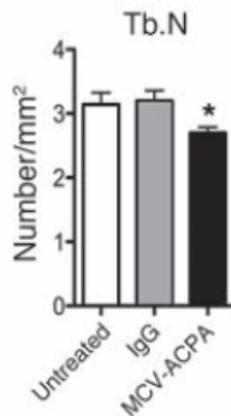
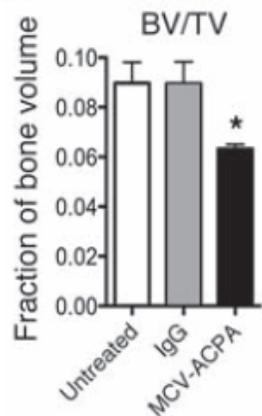
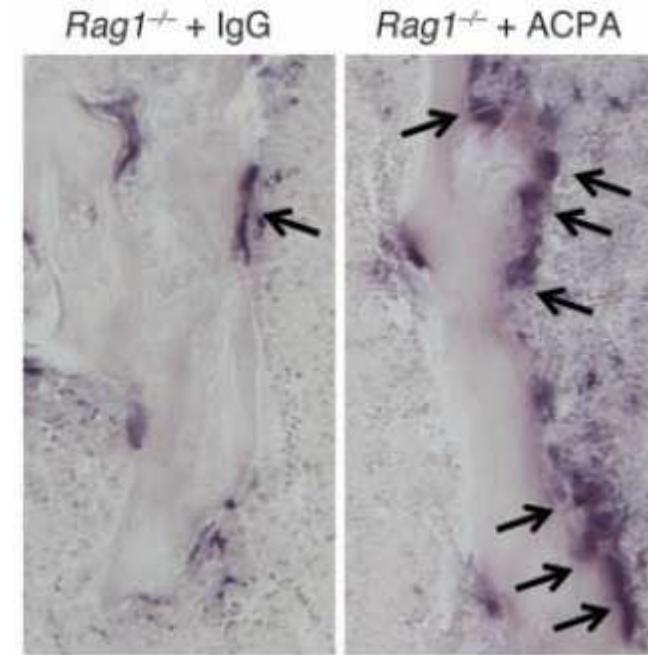
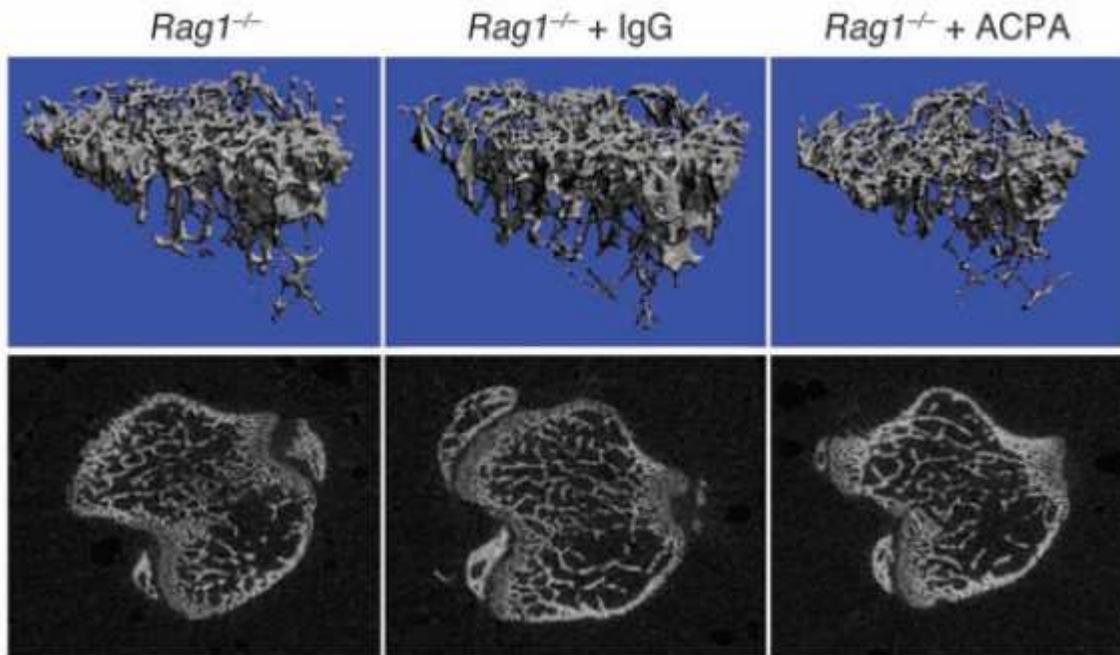
Arrowheads indicate surface staining for citrullinated vimentin

Scalebars=100 μm

MCV-ACPAs induce bone loss in vivo in a mouse model

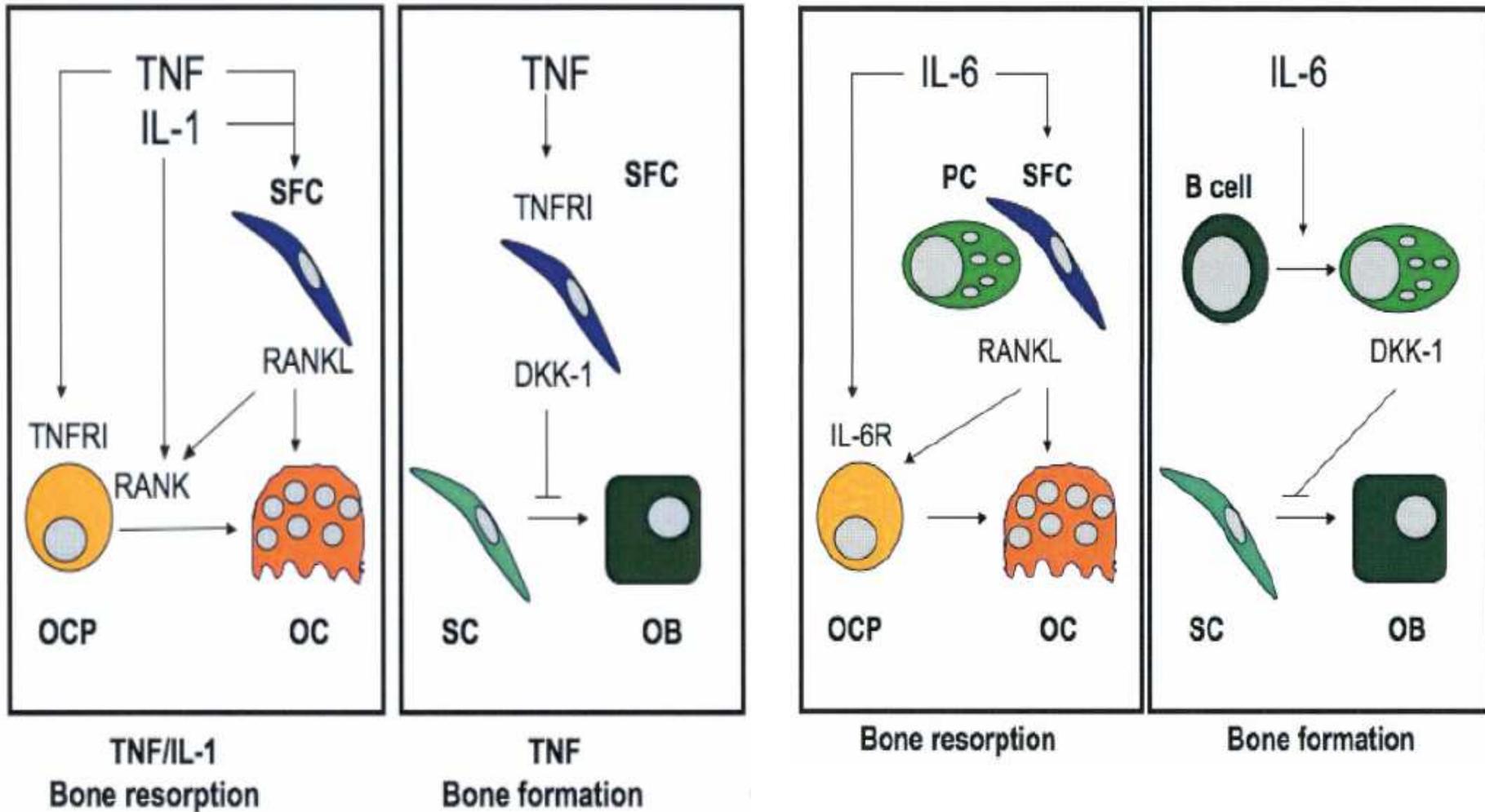
3D μ CT images of the tibial metaphysis after 4 weeks

TRAP staining

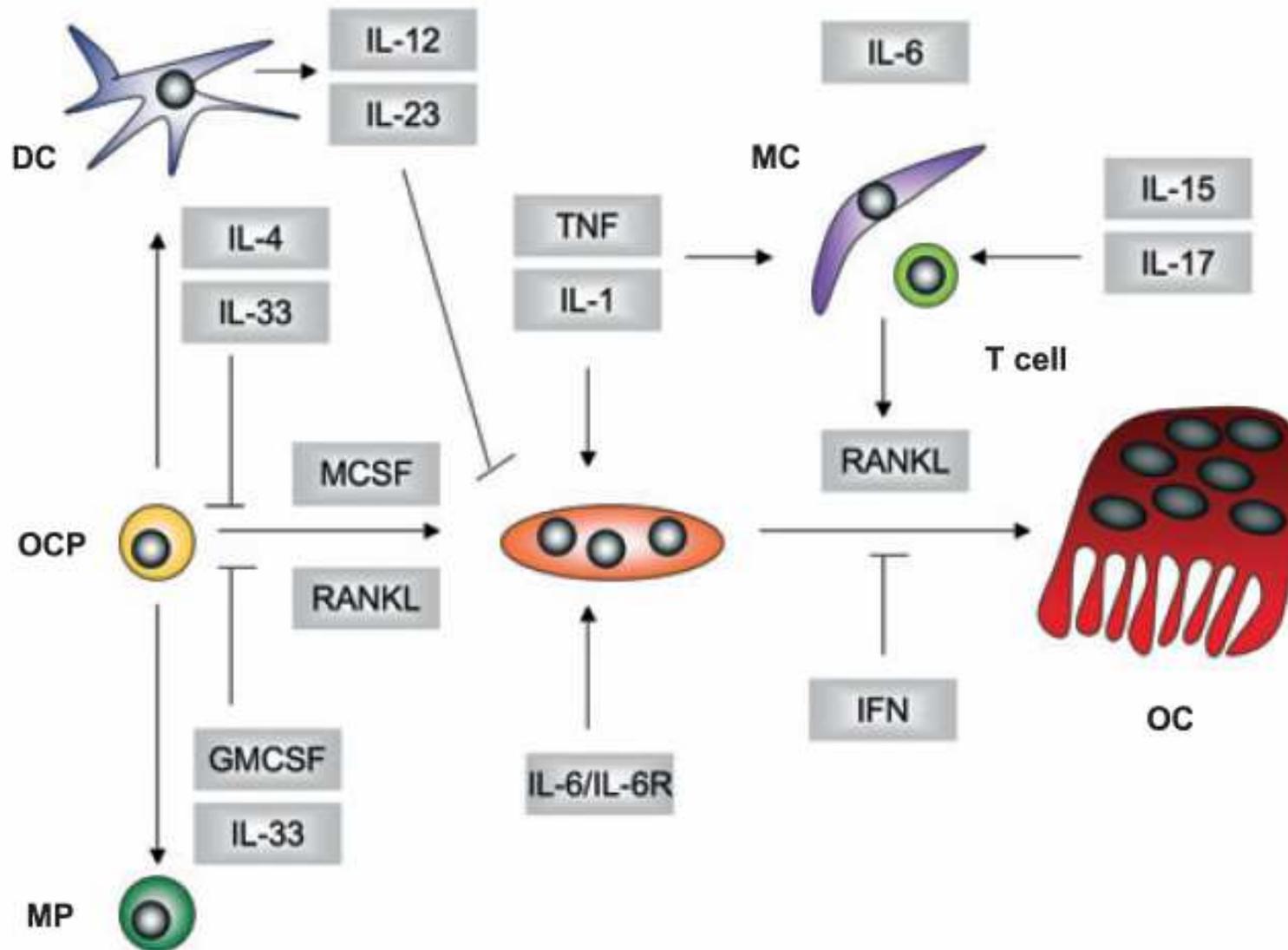


*P<0.05

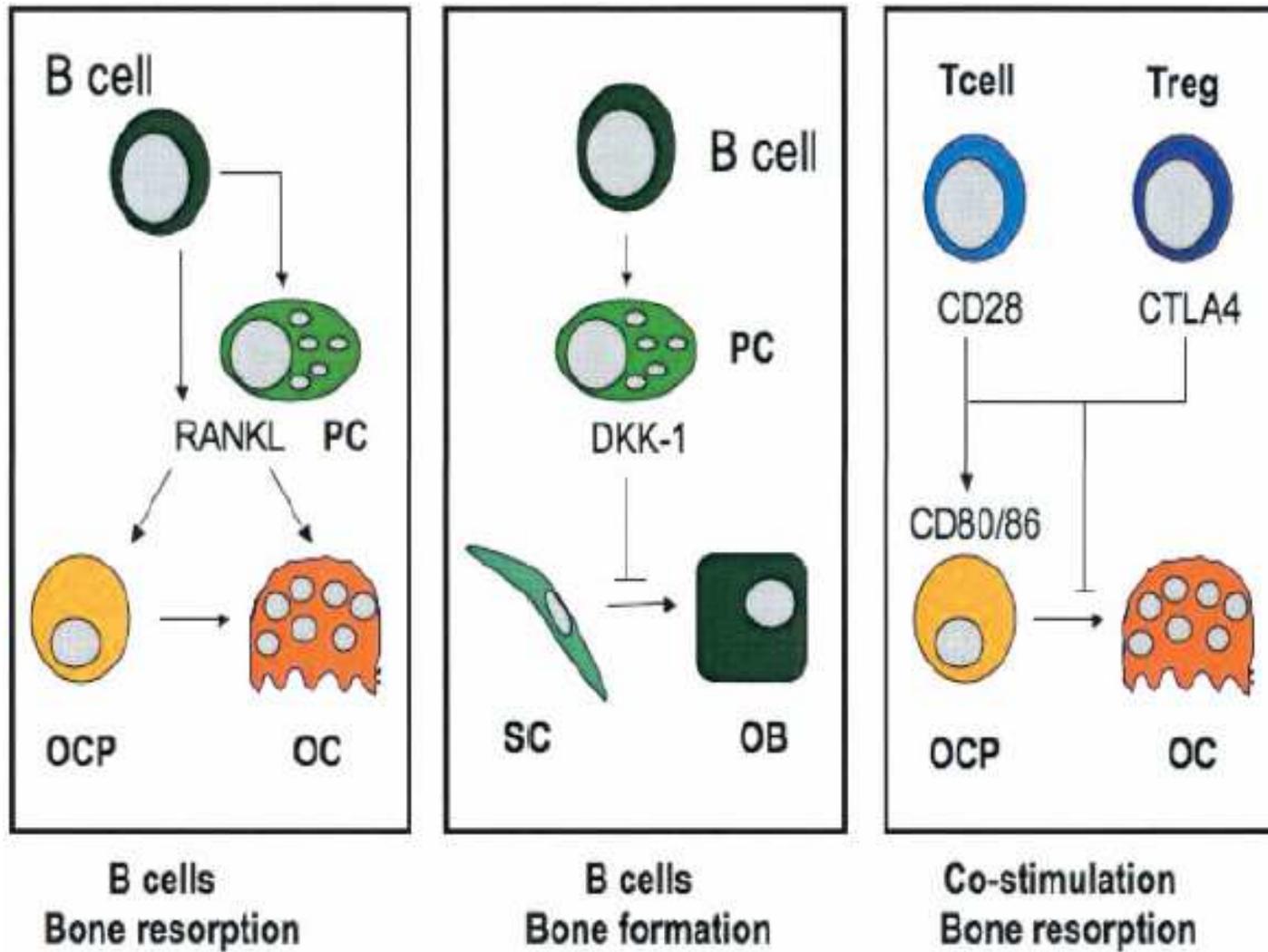
Pro-inflammatory cytokines on bone resorption and formation balance



Effects of pro- and anti-inflammatory cytokines on bone resorption



The roles of B cells and T cells co-stimulation in bone



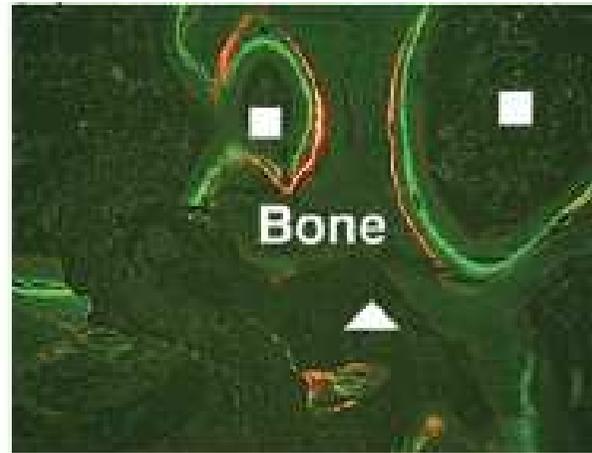
Compromised osteoblast functions in arthritis

Arthritic mice

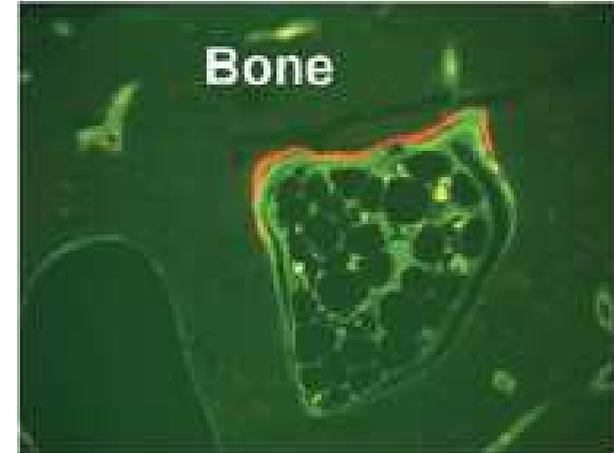
Non-arthritic mouse



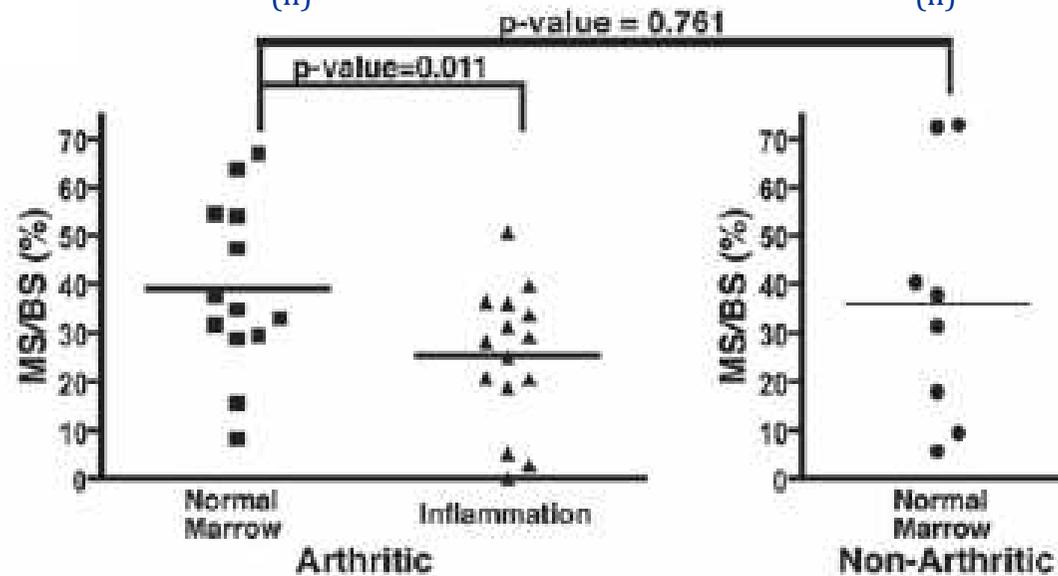
(i)



(ii)



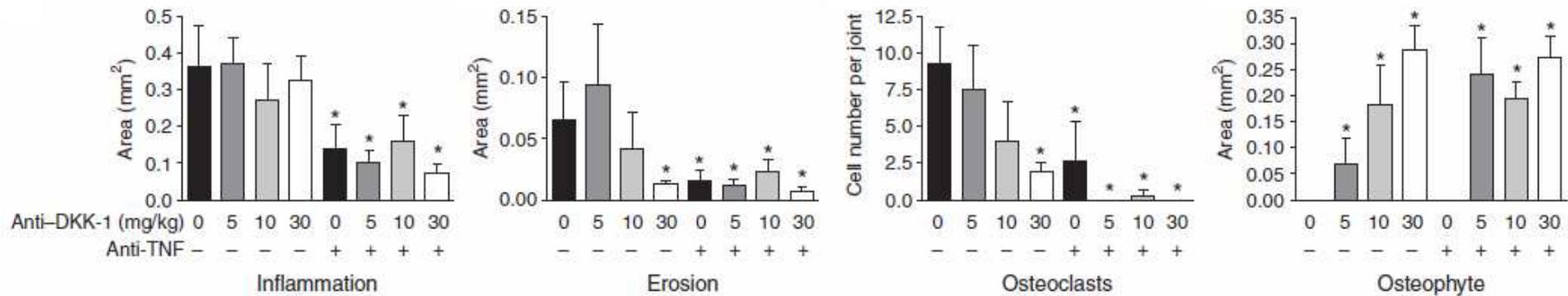
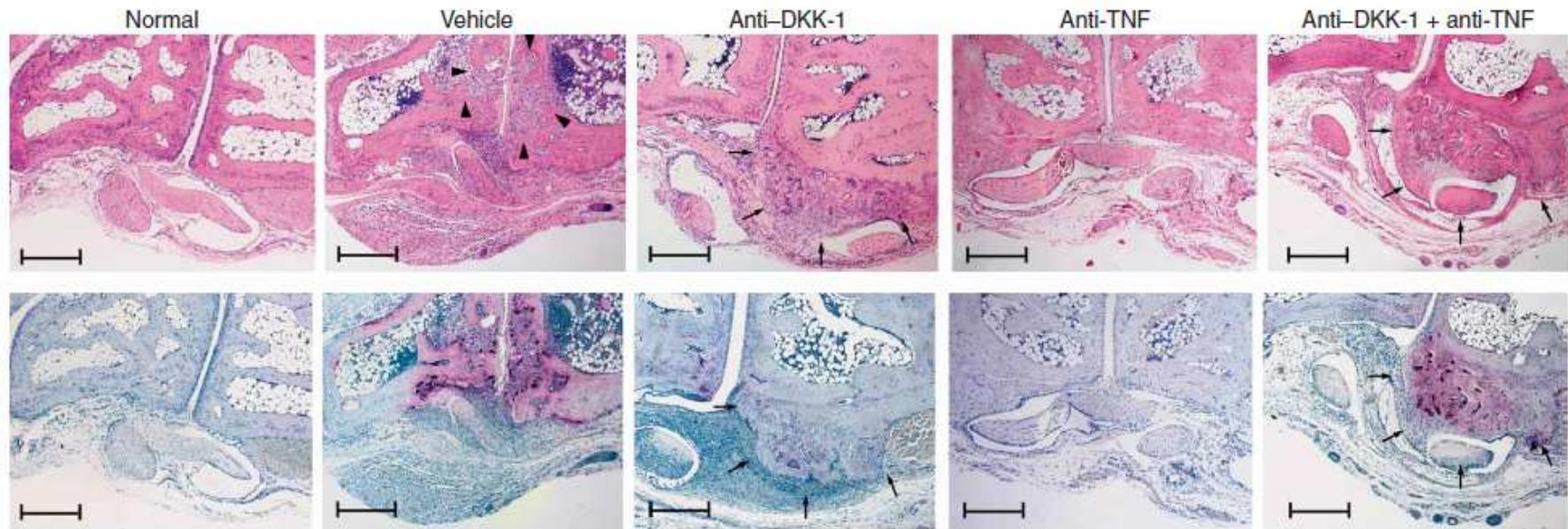
(ii)



Photomicrographs of alizarin and calcein labeling in non- or arthritic navicular bone
 Triangles, inflammation; Squares, normal marrow - Magnification (i)x100, (ii)x200

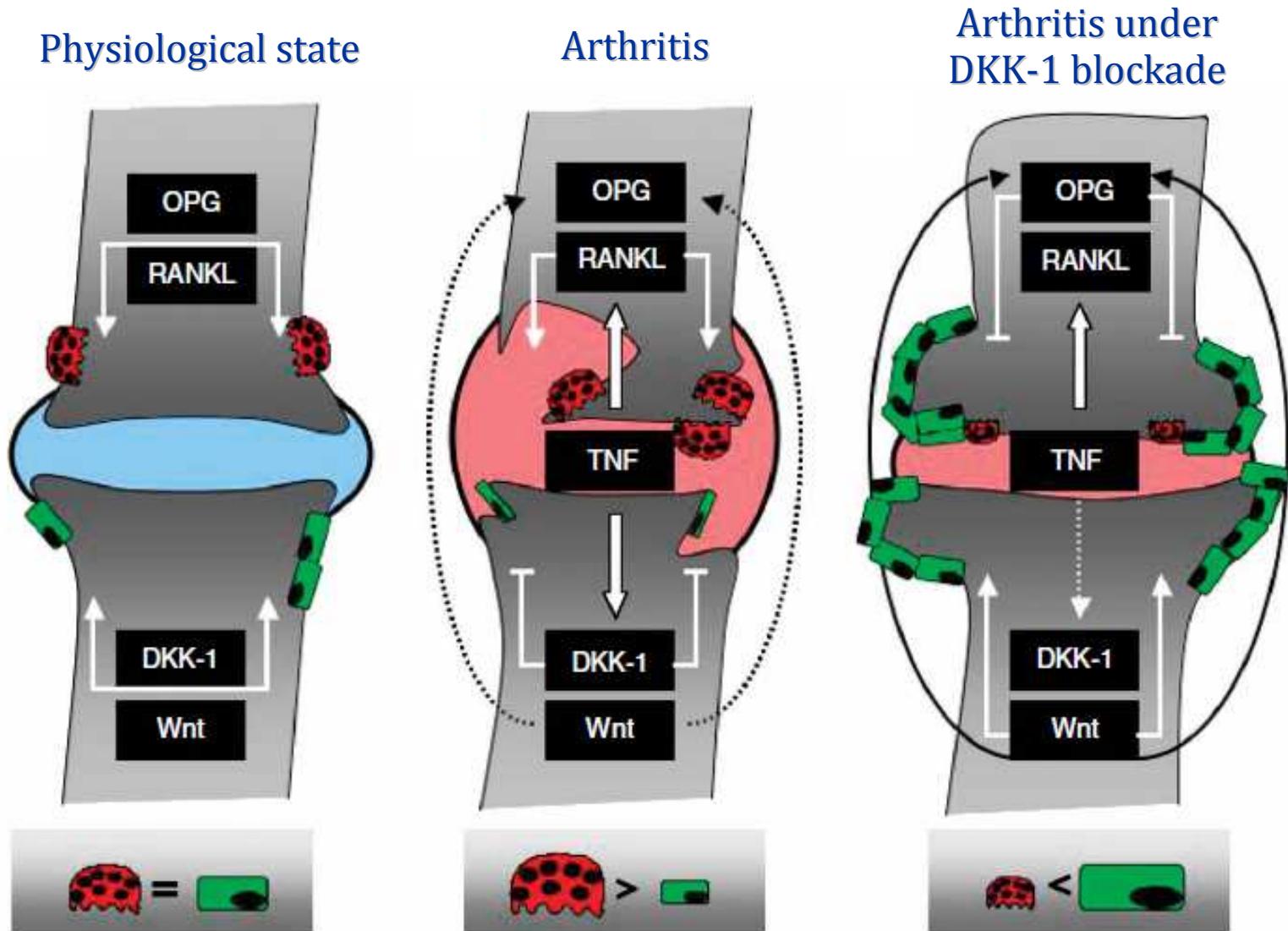
Walsch NC. J Bone Miner Res. 2009;24:1572-85

Dickkopf-1 master regulator of joint remodeling



Microphotographs of H&E-stained tissue sections of tarsal joint in wild-type mice and hTNFtg mice treated with vehicle, anti-DKK-1 antibody (30mg/kg), anti-TNF antibody (10 mg/kg) or a combination at week 10 (*p<0.05)

DKK-1 critical for joint bone balance

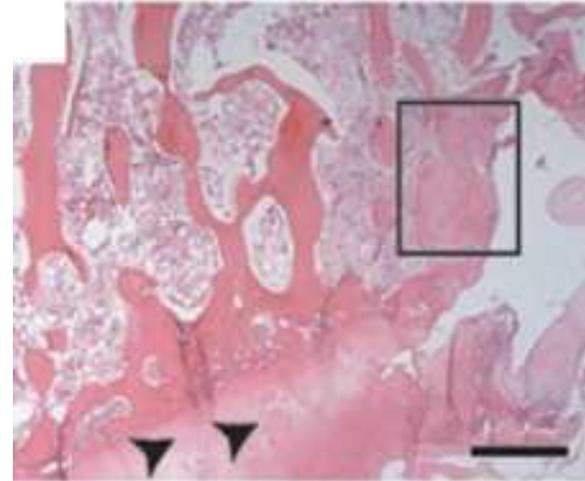


Activated BMP signaling in human enthesitis

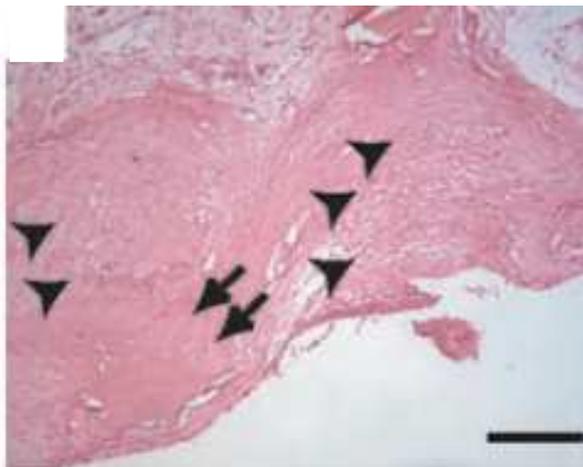
Achille enthesitis X-rays



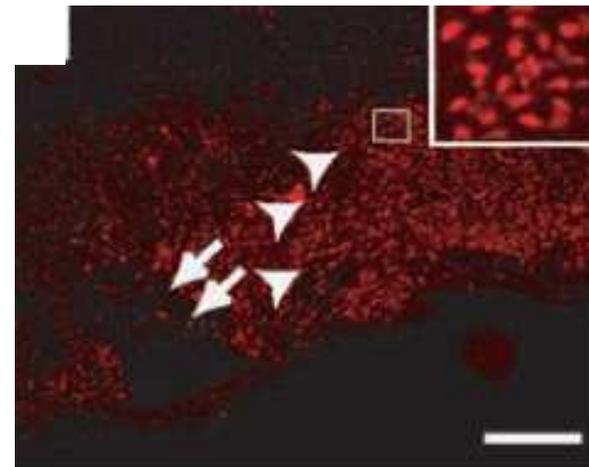
H&E stained enthesial biopsy



Detail of box area

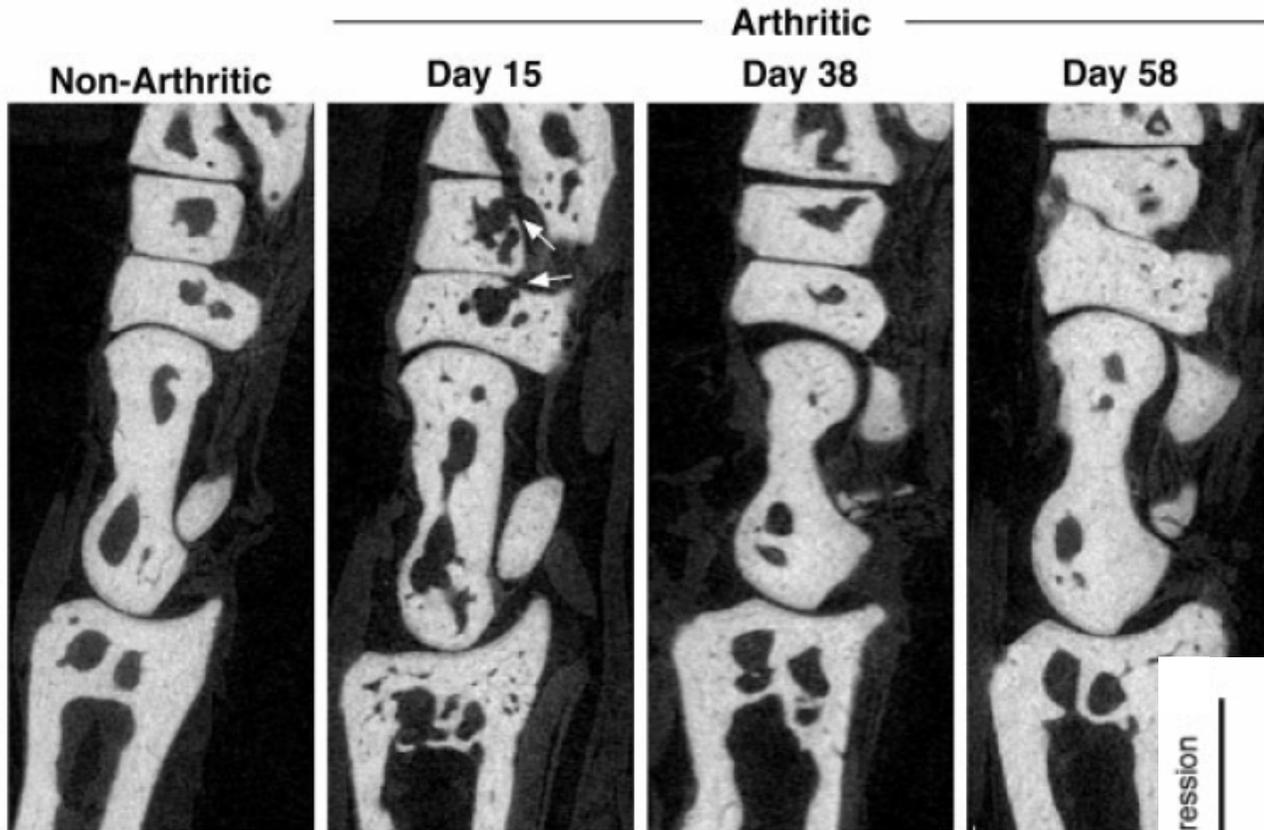


Immunofluorescent staining for phosphorylated-smad1/5/8



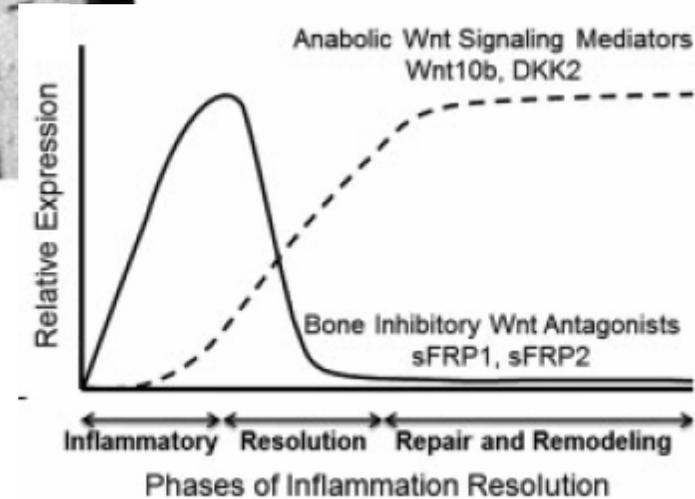
Arrowheads, proliferation - Arrows, cartilage formation

Bone formation resumes after arthritis resolution

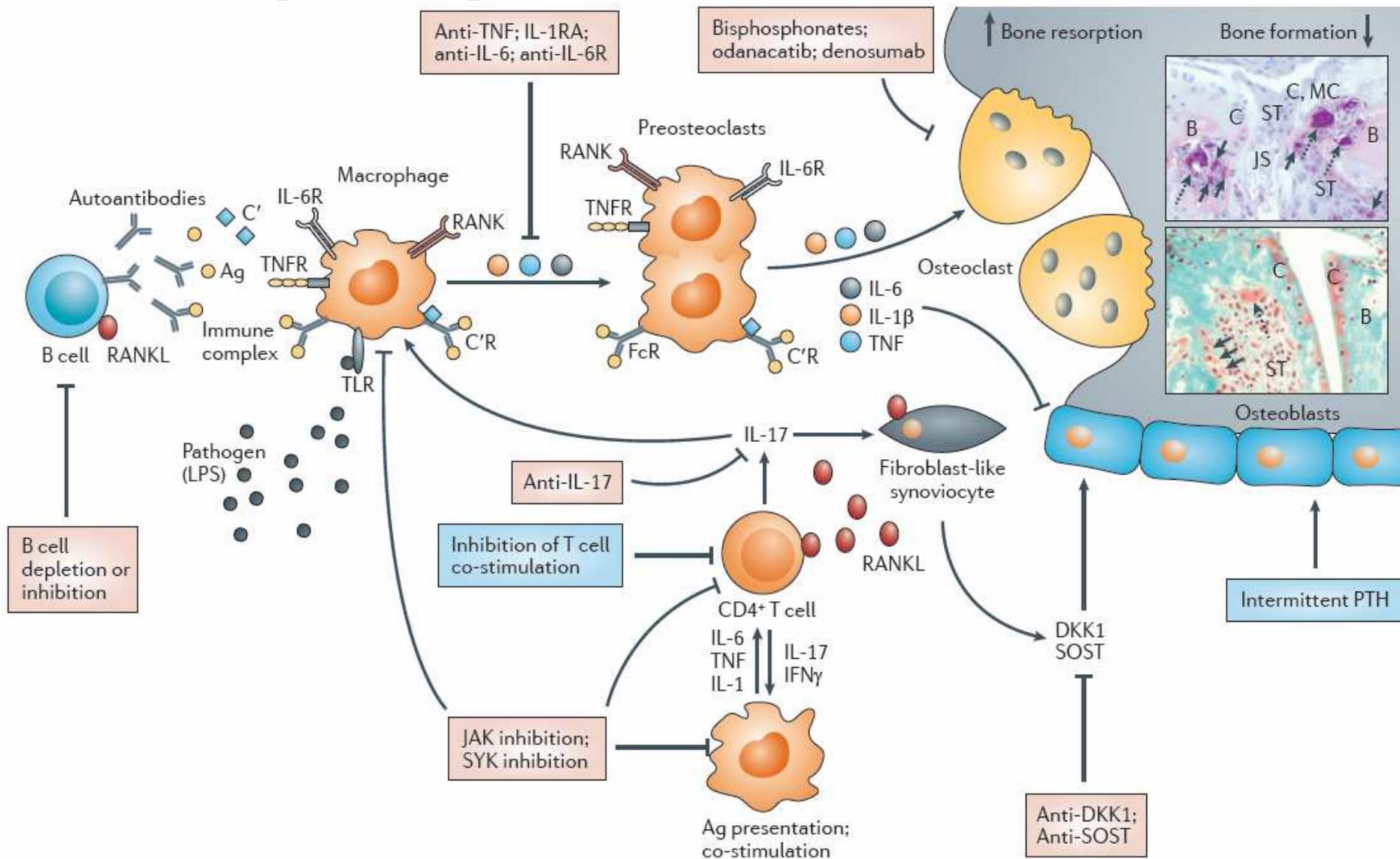


Sagittal images of the ankle and midfoot bones

Synovial mRNA expression

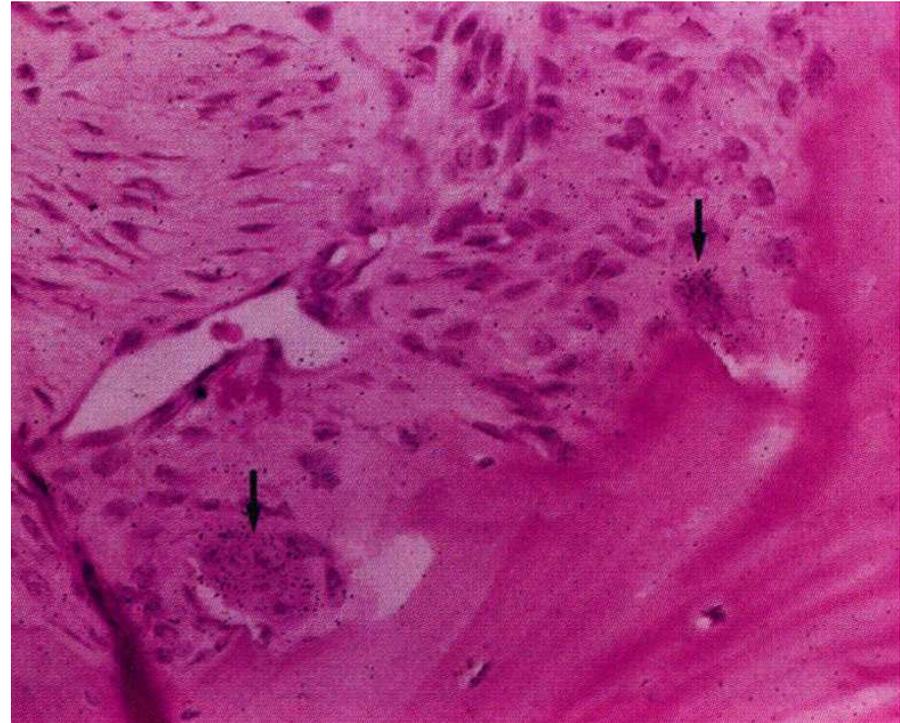
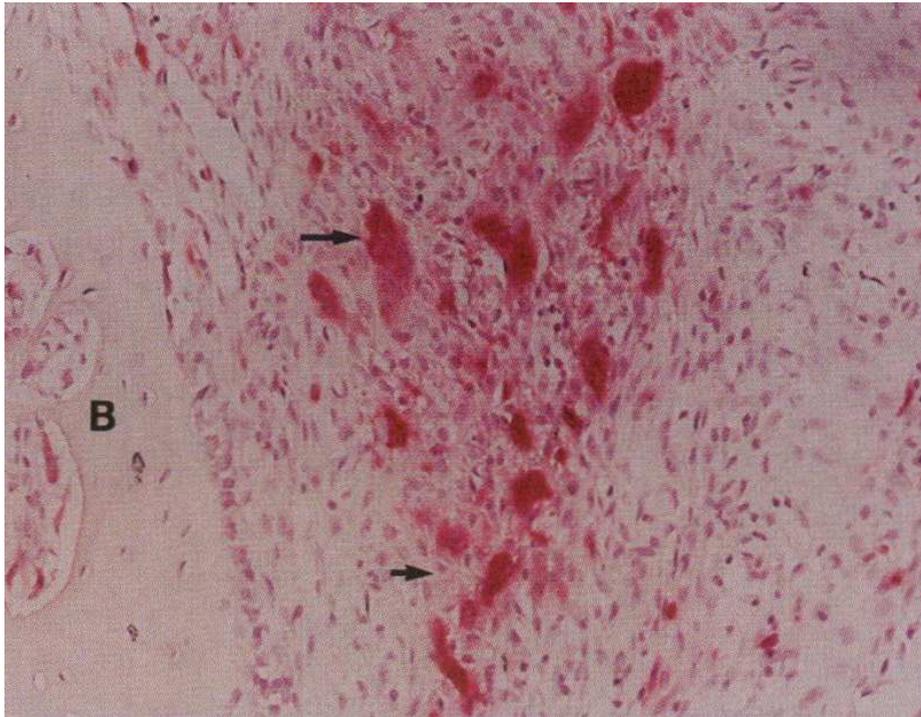


Local and systemic bone events in chronic inflammation and therapeutic options



Back up

Identification of Cell Types Responsible for Bone Resorption in Rheumatoid Arthritis



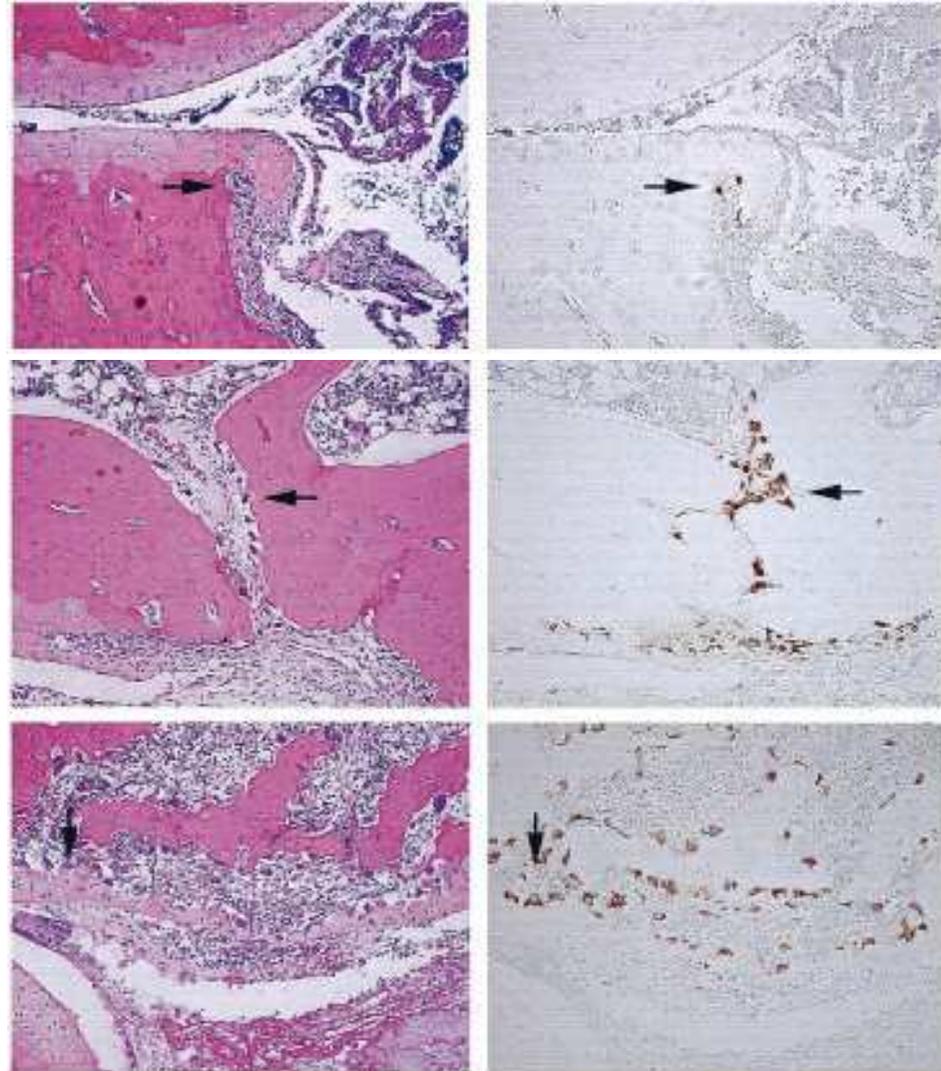
Left) TRAP staining in joint tissue from a patient with polyarticular disease. Numerous TRAP-positive MNCs (long arrow) and mononuclear cells (short arrow) in pannus remote from bone. B, bone. Hematoxylin counterstain; magnification, X50.

Right) A high-power view of MNCs on bone surface (arrows) is shown. Black grains designate cells expressing mRNA for CTR. H&E counterstain; magnification, X 100.

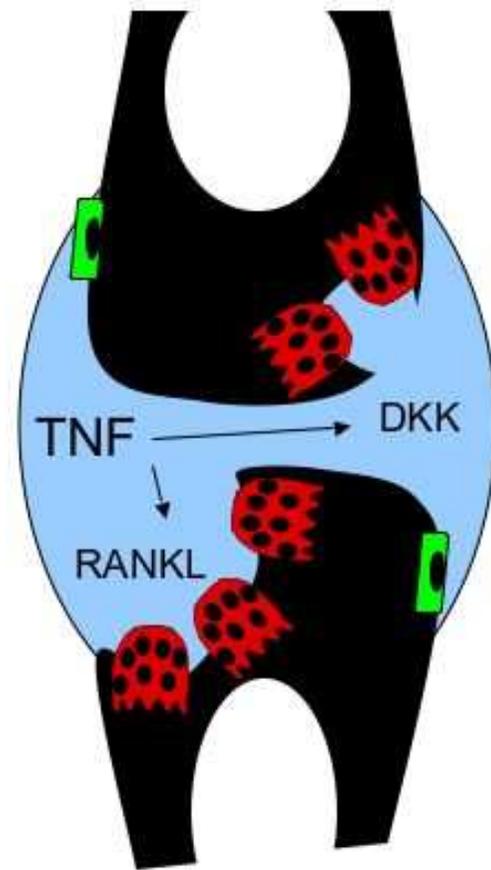
Sites of early osteoclast formation and bone resorption in adjuvant-induced arthritis

On the day of disease onset (day 0), osteoclast formation (arrow) can be seen in a subchondral bone channel next to the joint margin (A and B)

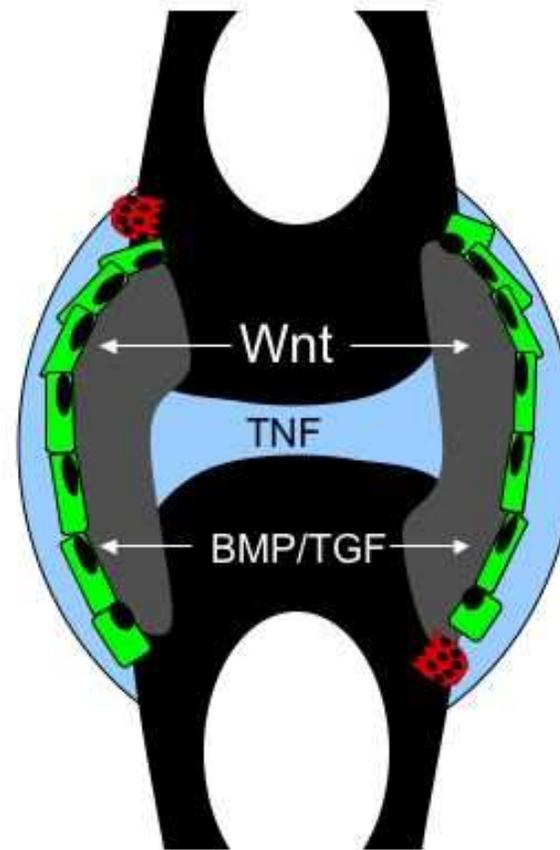
On day 5 after disease onset, the subchondral bone channel is filled with numerous osteoclasts (arrow) (E and F), the surfaces of subchondral bone (G and H) and trabecular bone are undergoing extensive resorption by osteoclasts (arrow). Original magnification x40



Structural remodeling of joints in human disease



„RA-like“



„SpA-like“