58° Congresso Nazionale della Società di Gerontologia e Geriatria

Simposio SIGG-Forum in Bone & Mineral Research

Sistema immune ed osso

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Dip. di Scienze Mediche

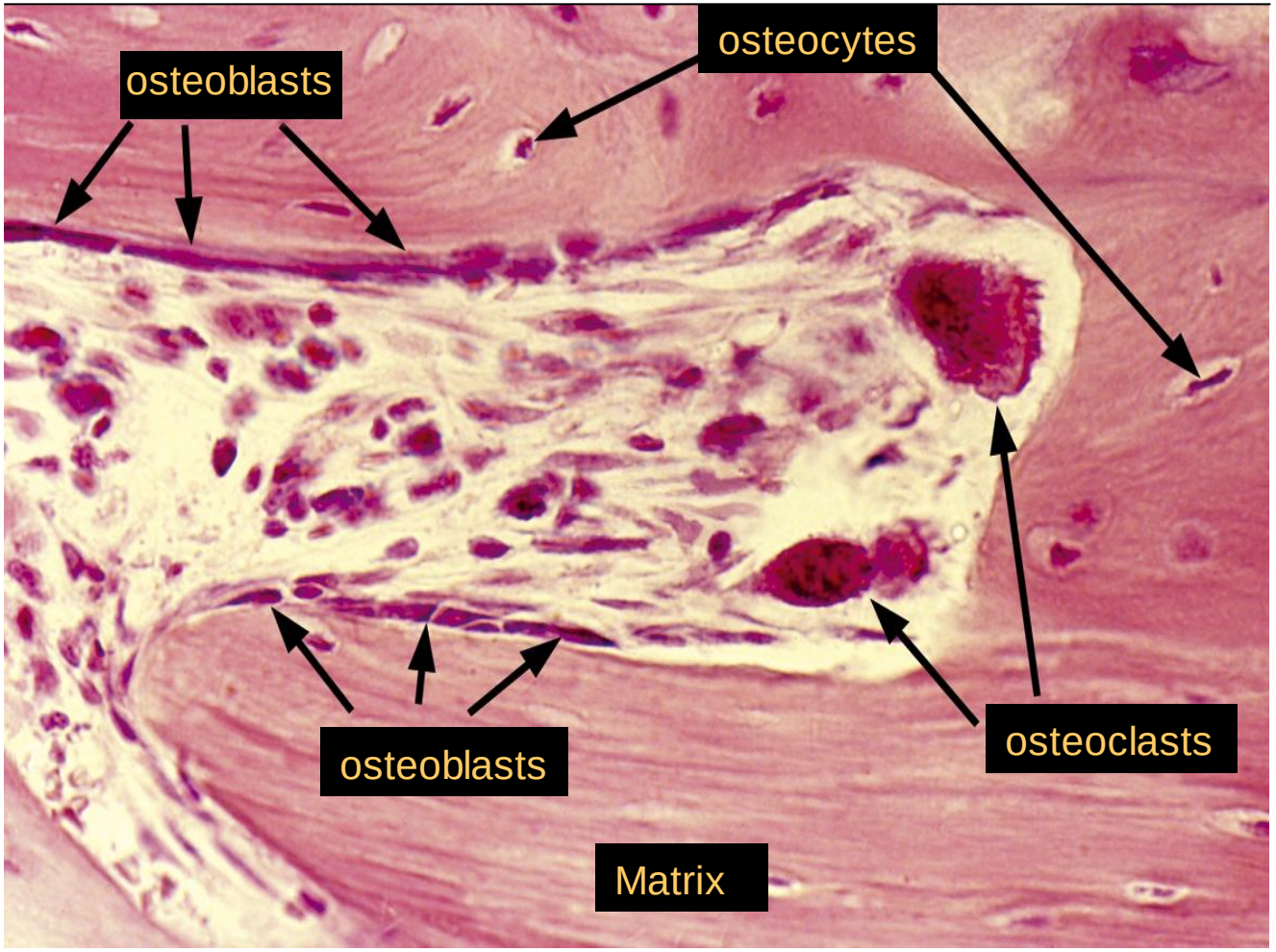
Università di Torino

Torino, 27-30 Novembre 2013

Osteoimmunology

The term osteoimmunology was coined to identify studies related to interactions between the bone, hematopoietic, and immune systems. These systems are in deep physical contact and share several common pathways.

BASIC MULTICELLULAR UNIT OF BONE

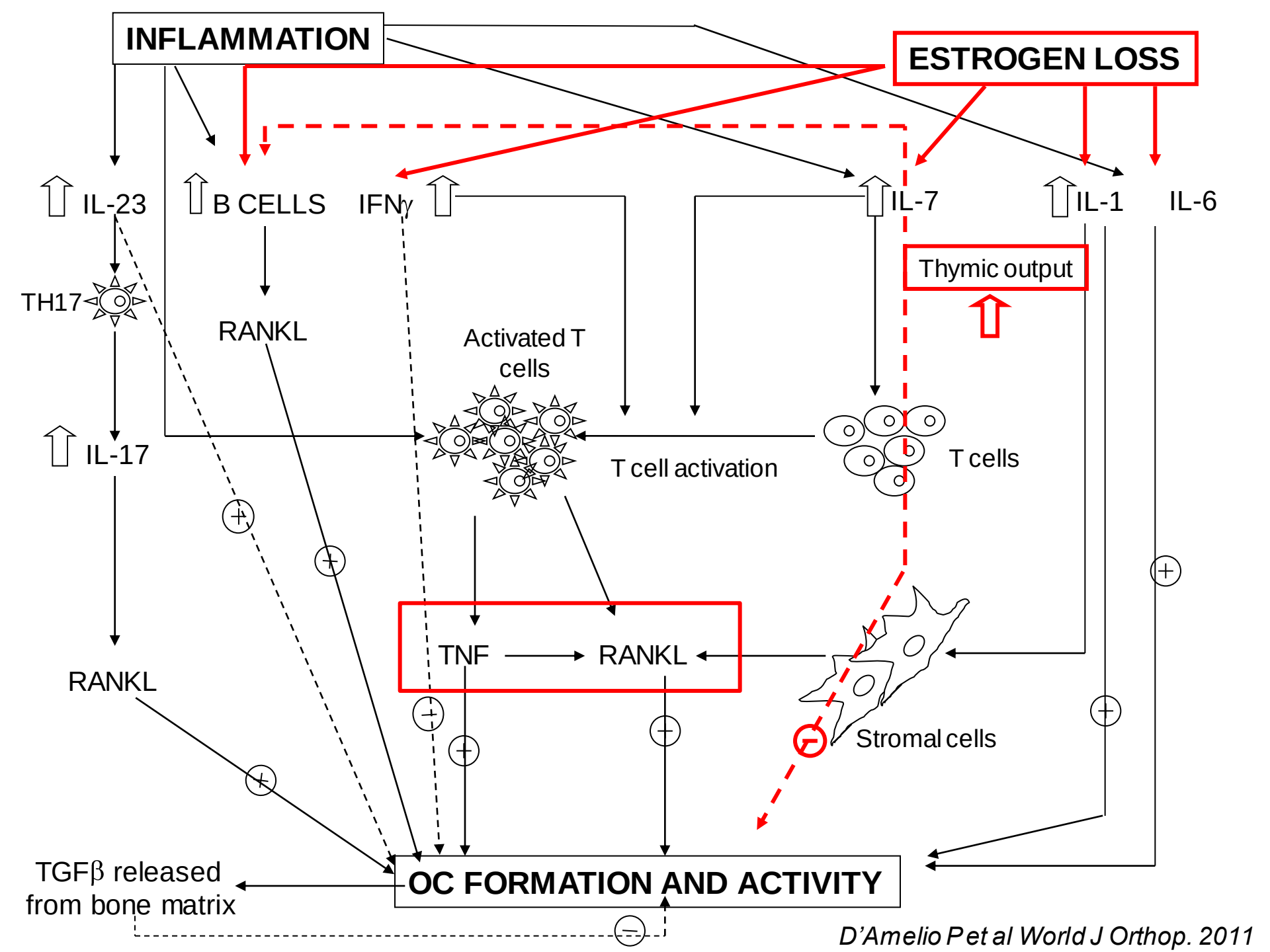


INFLAMMATION AND BONE LOSS

It is well known that diseases characterised by inflammation and activation of immune system are associated with systemic and local bone loss

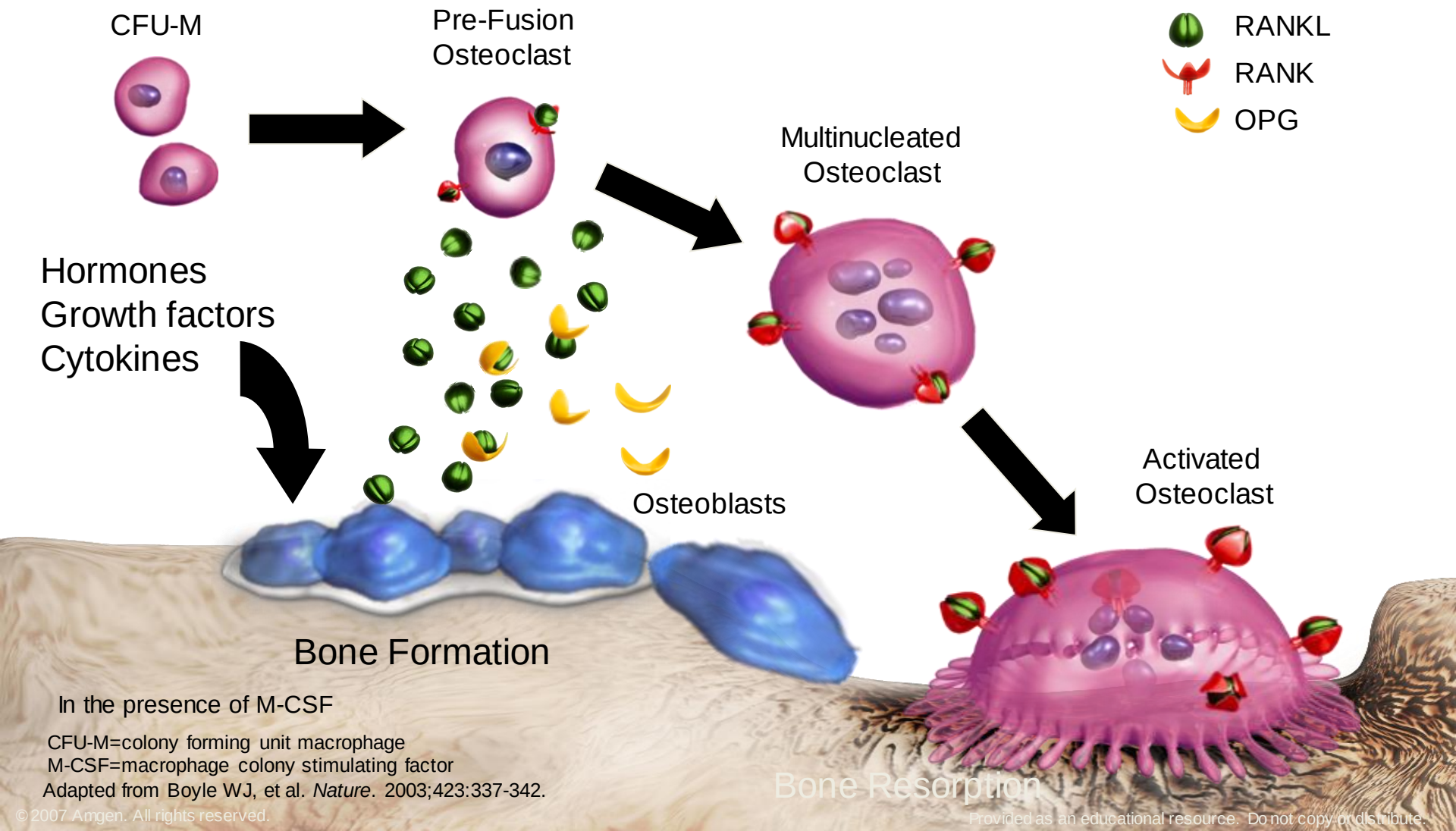
1. Osteoporosis and inflammation. Mundy GR. Nutr Rev. 2007 Dec;65(12 Pt 2):S147-51.

2. Lymphocyte-derived cytokines in inflammatory arthritis. Horwood N. Autoimmunity. 2008 pr;41(3):230-8.



D'Amelio P et al World J Orthop. 2011

RANK Ligand is an Essential Mediator of Osteoclast Formation, Function, and Survival



In the presence of M-CSF

CFU-M=colony forming unit macrophage
M-CSF=macrophage colony stimulating factor

Adapted from Boyle WJ, et al. *Nature*. 2003;423:337-342.

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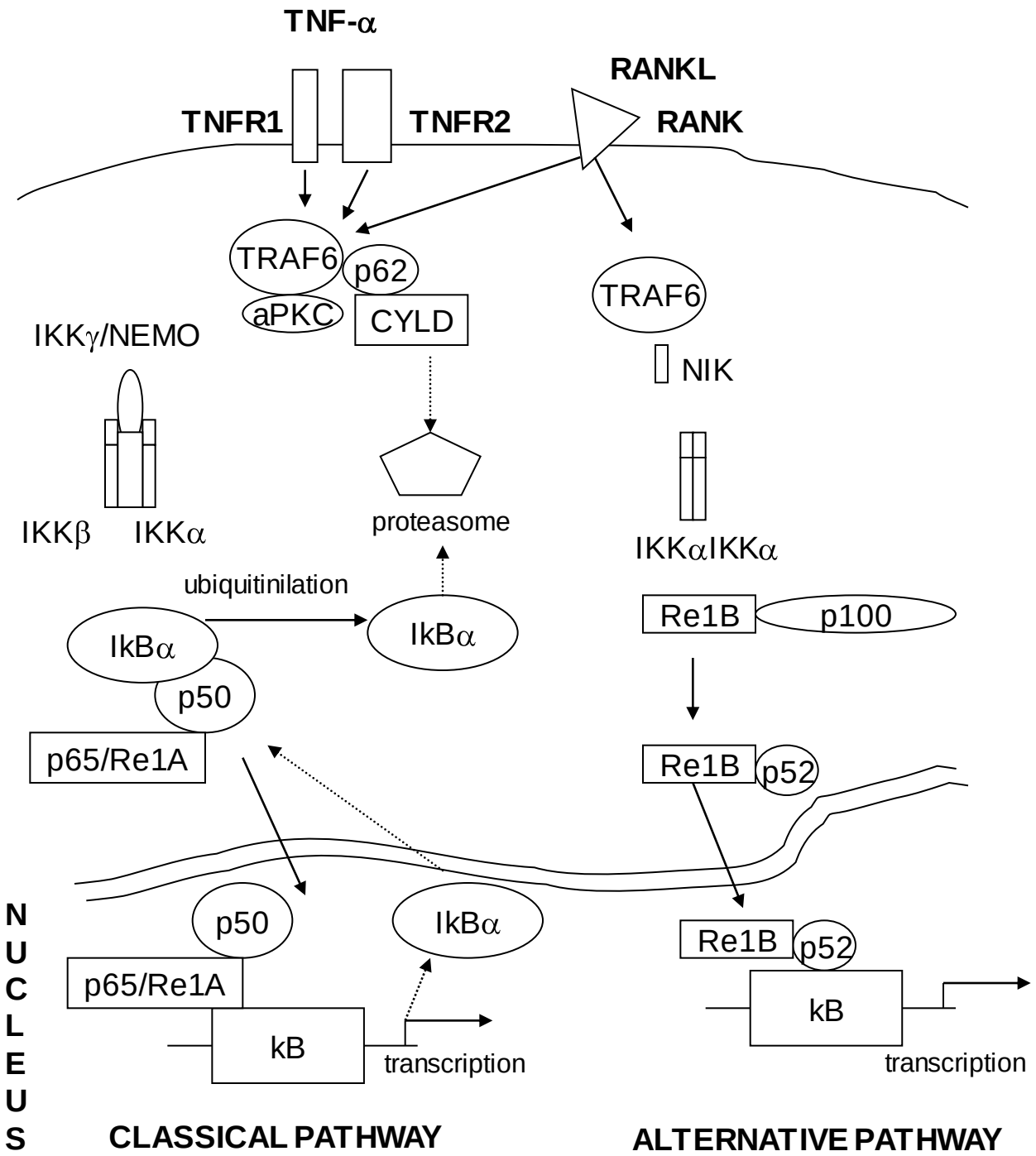
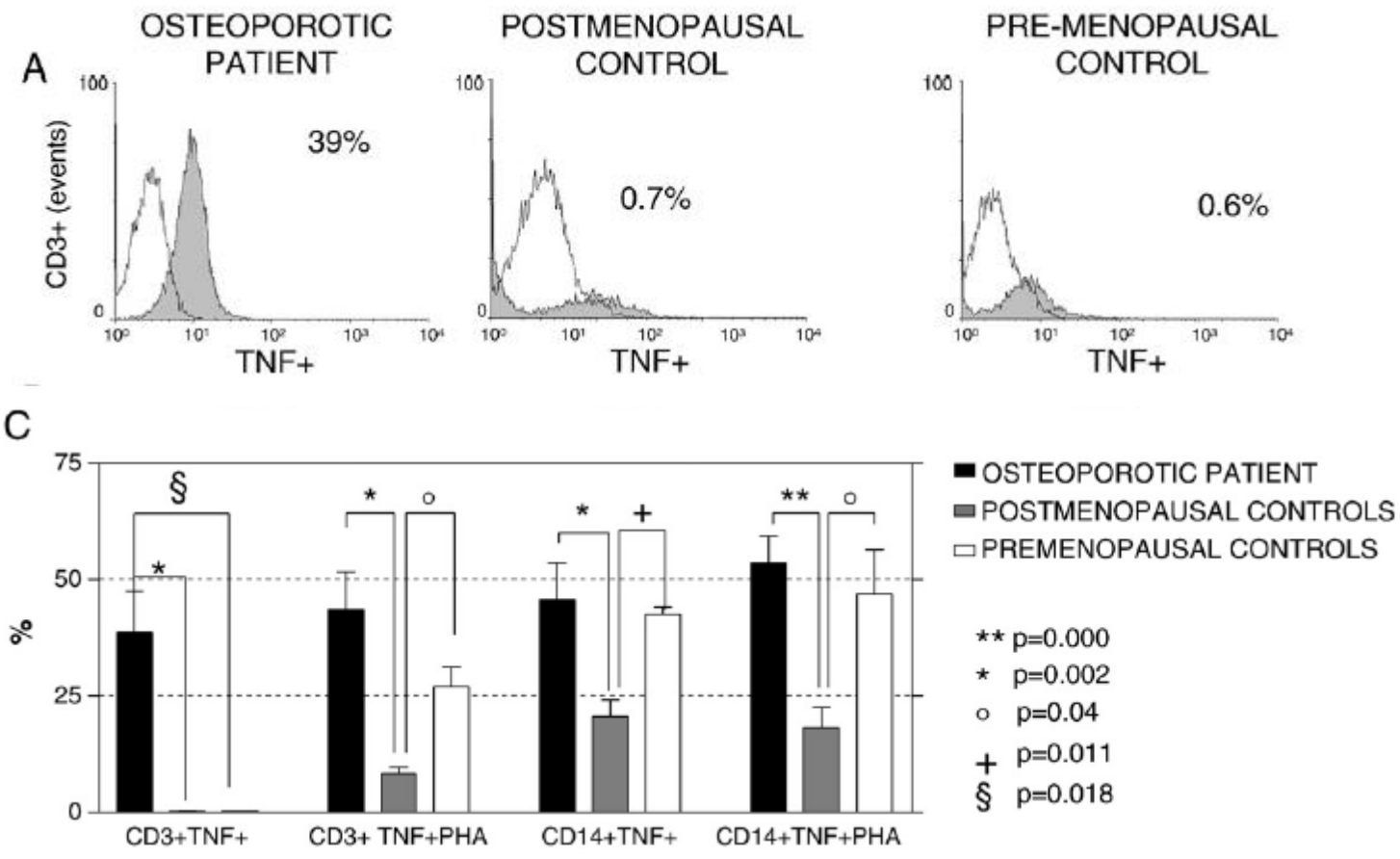


D'Amelio P. "Modern Insights Into Disease From Molecules to Man: Cytokines" 2011

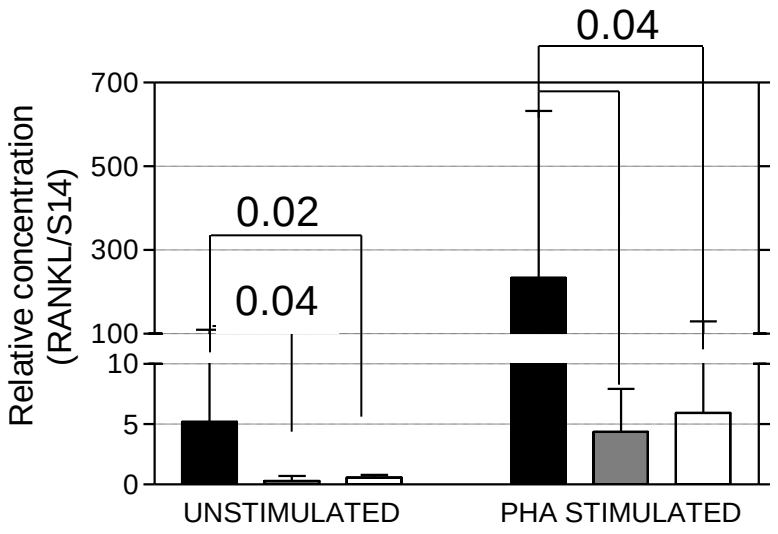
T CELLS FROM OSTEOPOROTIC PATIENTS PRODUCE MORE TNF α



D'Amelio P et al, Bone 2008

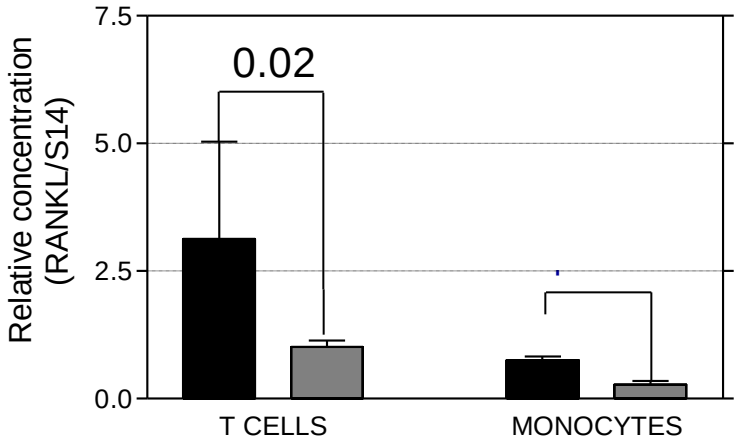
T CELLS FROM OSTEOPOROTIC PATIENTS PRODUCE MORE RANKL

Unfractioned PBMC



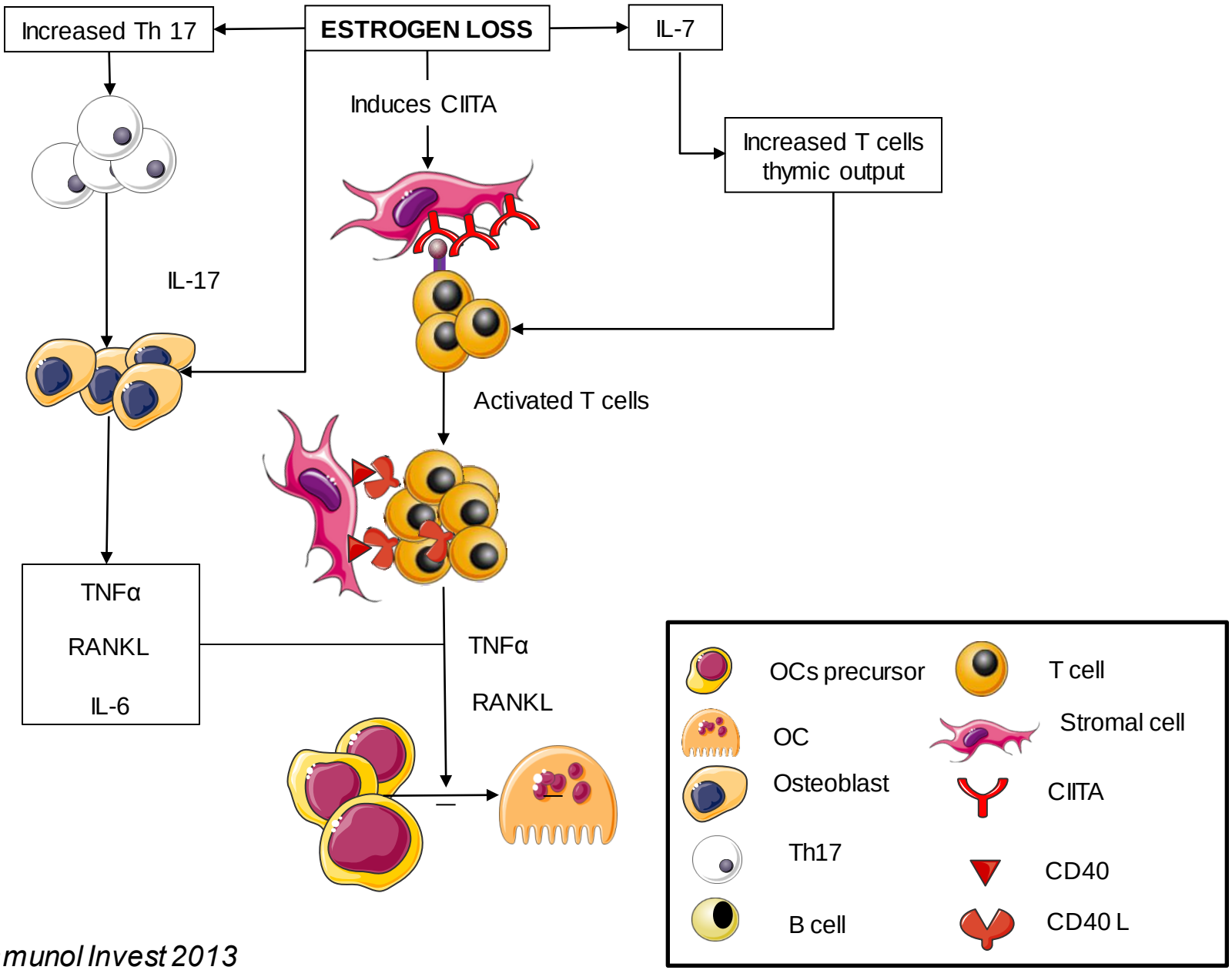
Osteoporotic patients
Post-menopausal controls
Pre-menopausal controls

Fractioned PBMC



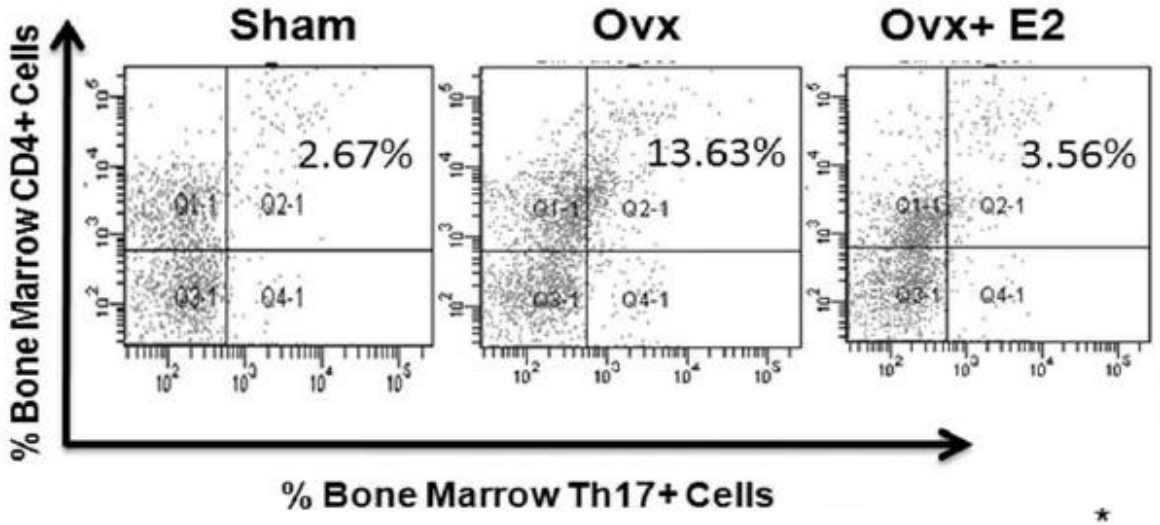
D'Amelio P et al, Bone 2008

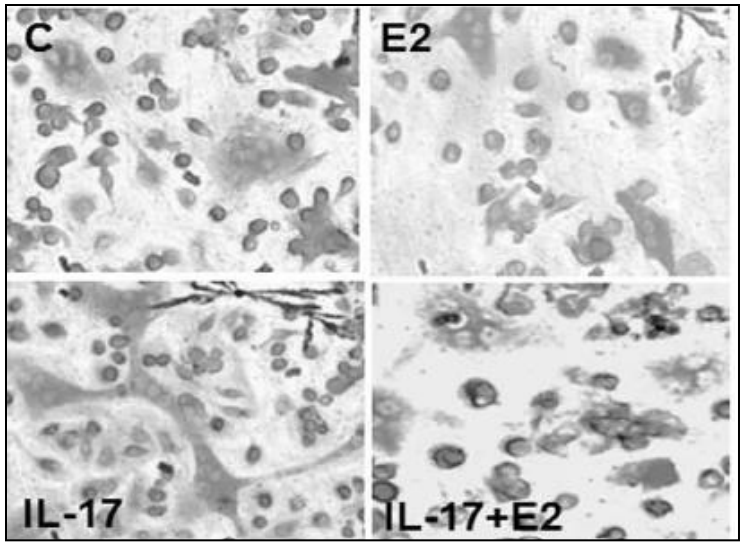
ESTROGEN LOSS AND T CELLS

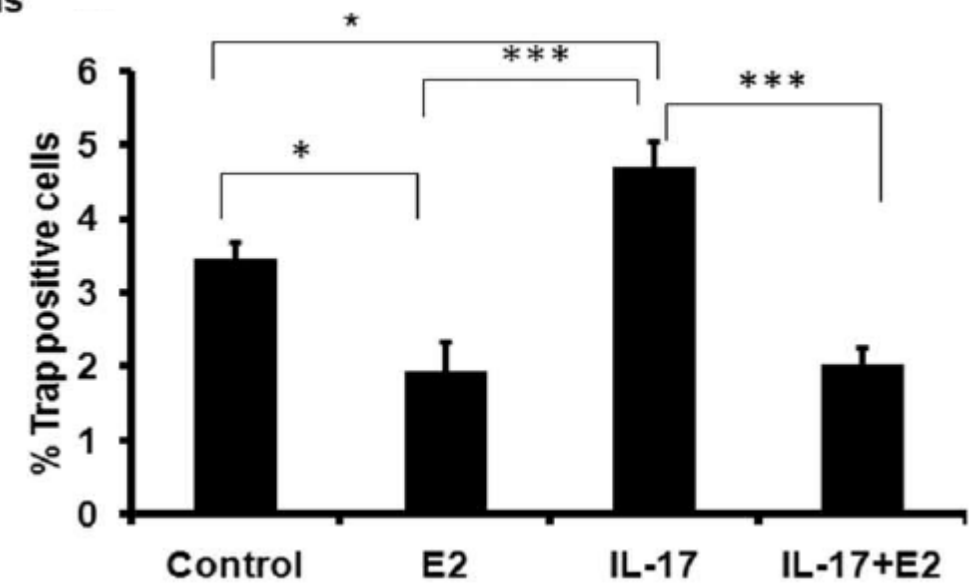


P. D'Amelio. Immunol Invest 2013

Ovx induces the production of IL-17 secreting Th17 cells

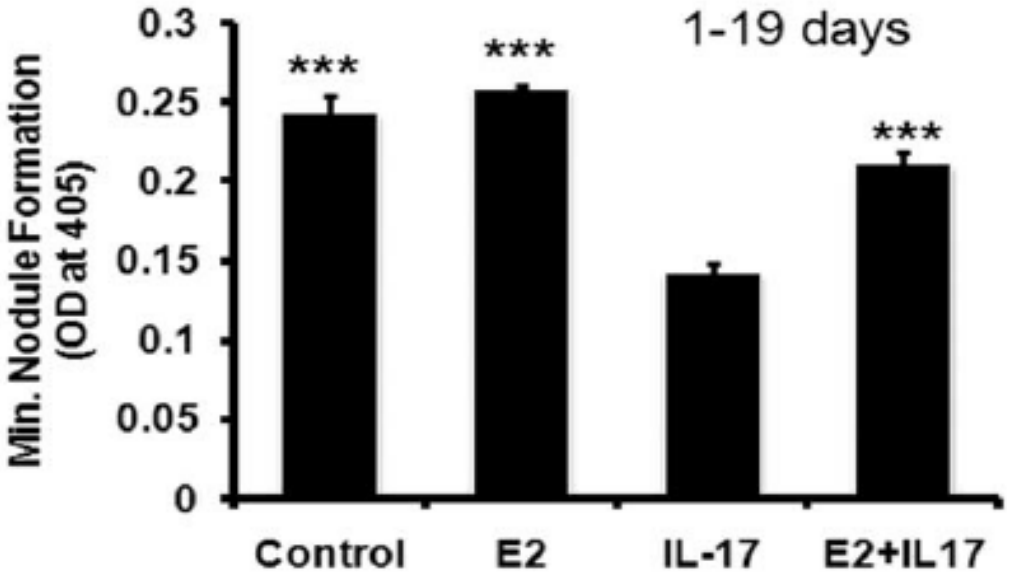


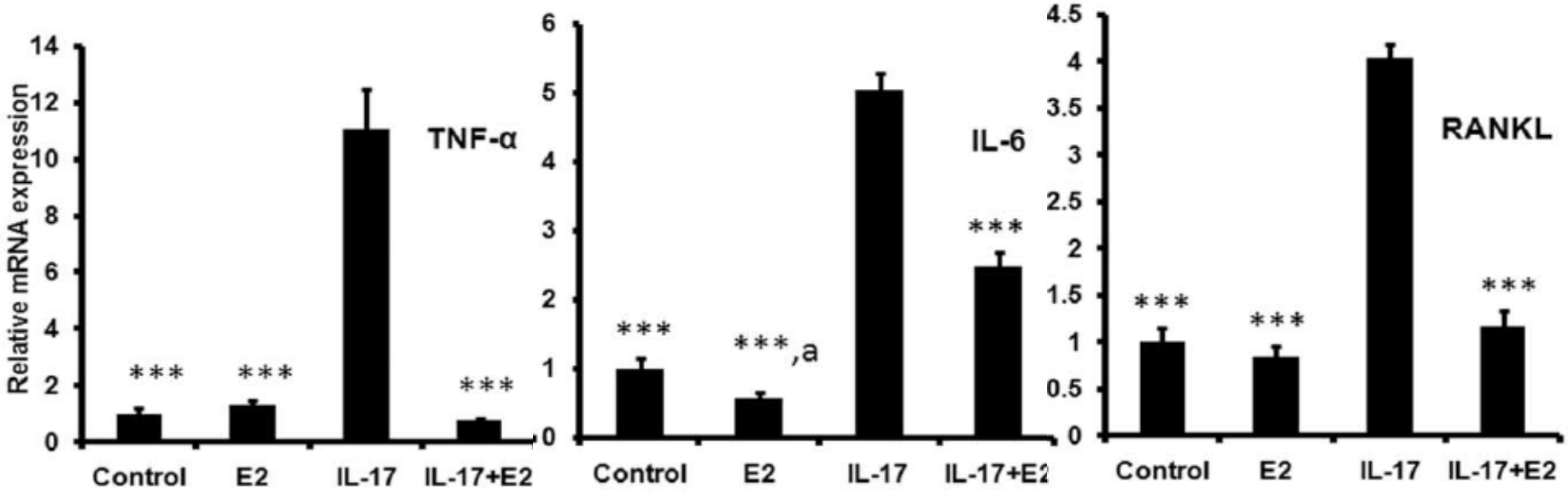




Tyagi AM et al Plos One 2012

IL-17 and osteoblasts





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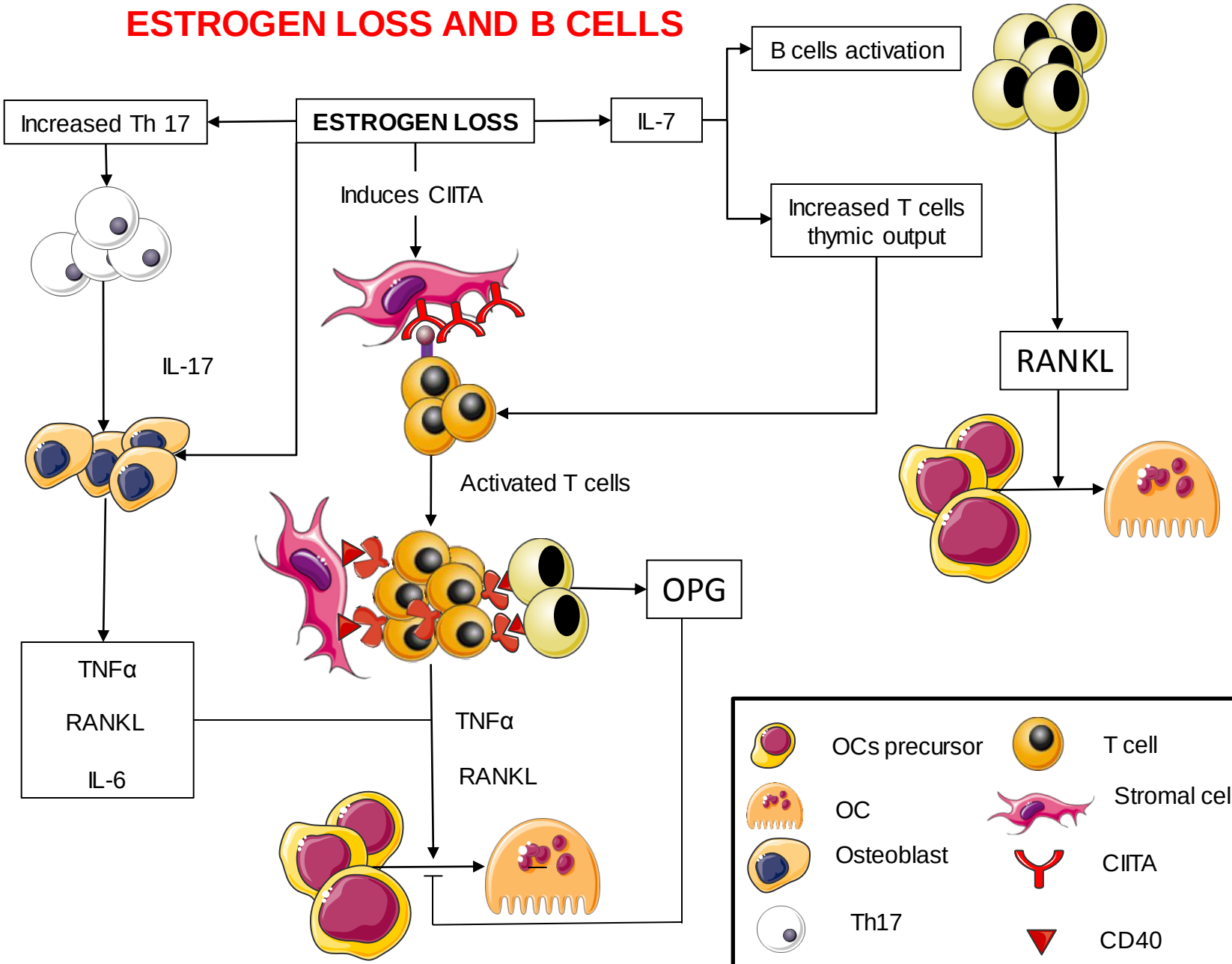
ESTROGEN LOSS AND B CELLS



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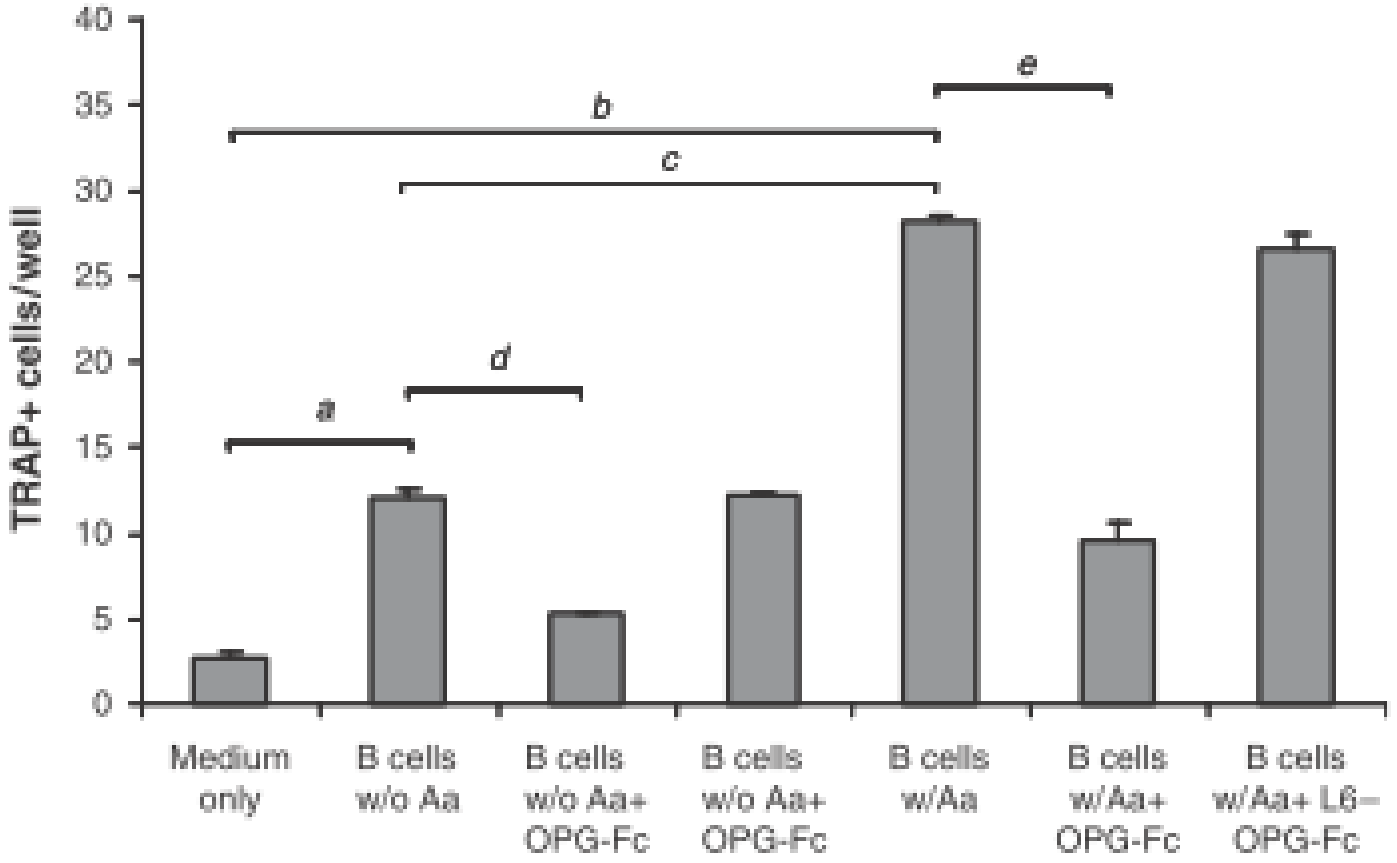
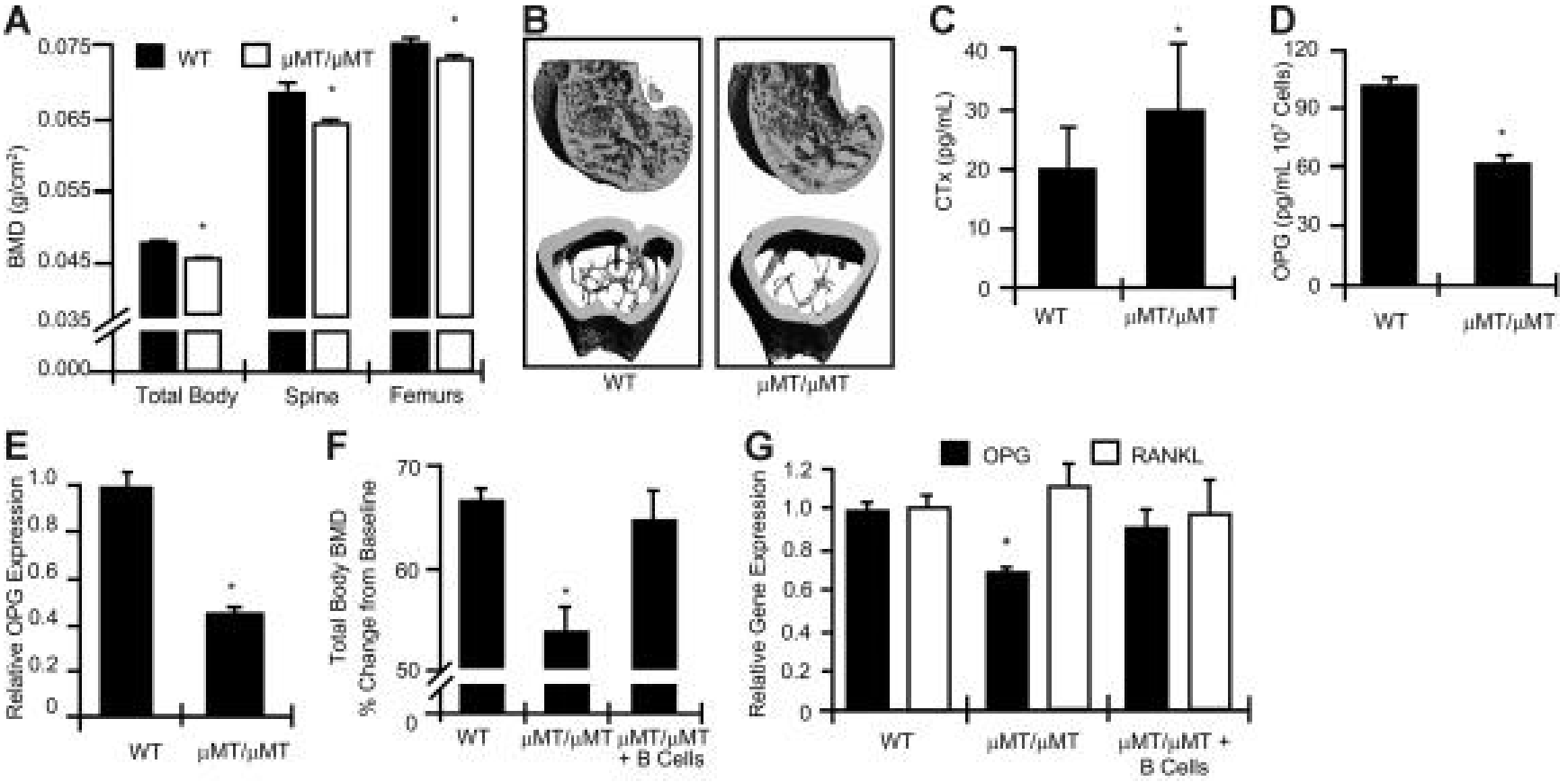
Activated B cells increase osteoclatogenesis



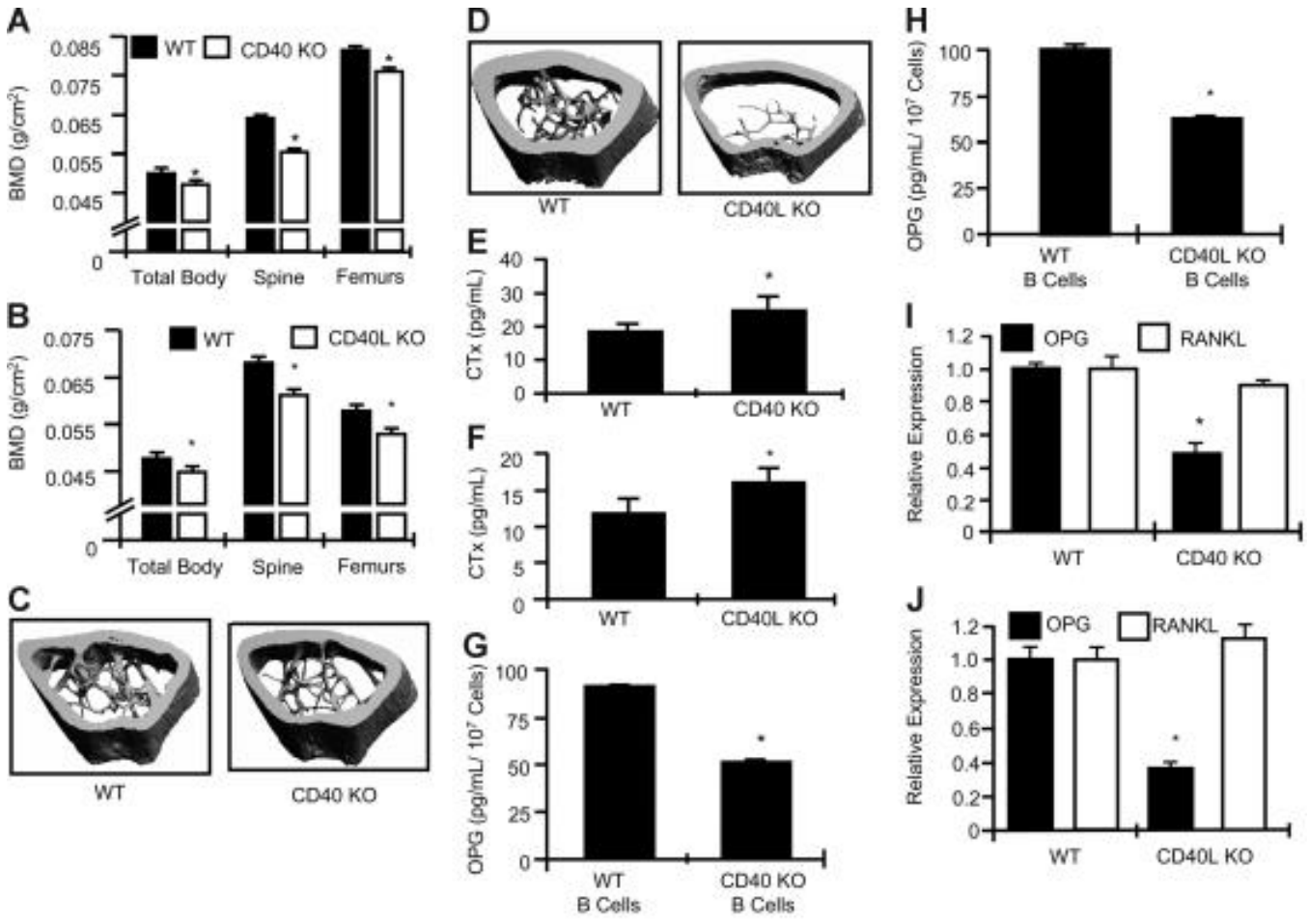
Han X et al Oral Microbiology Immunology 2009

B-cell KO mice display decreased baseline BMD and increase bone resorption, concurrent with decreased BM OPG concentrations



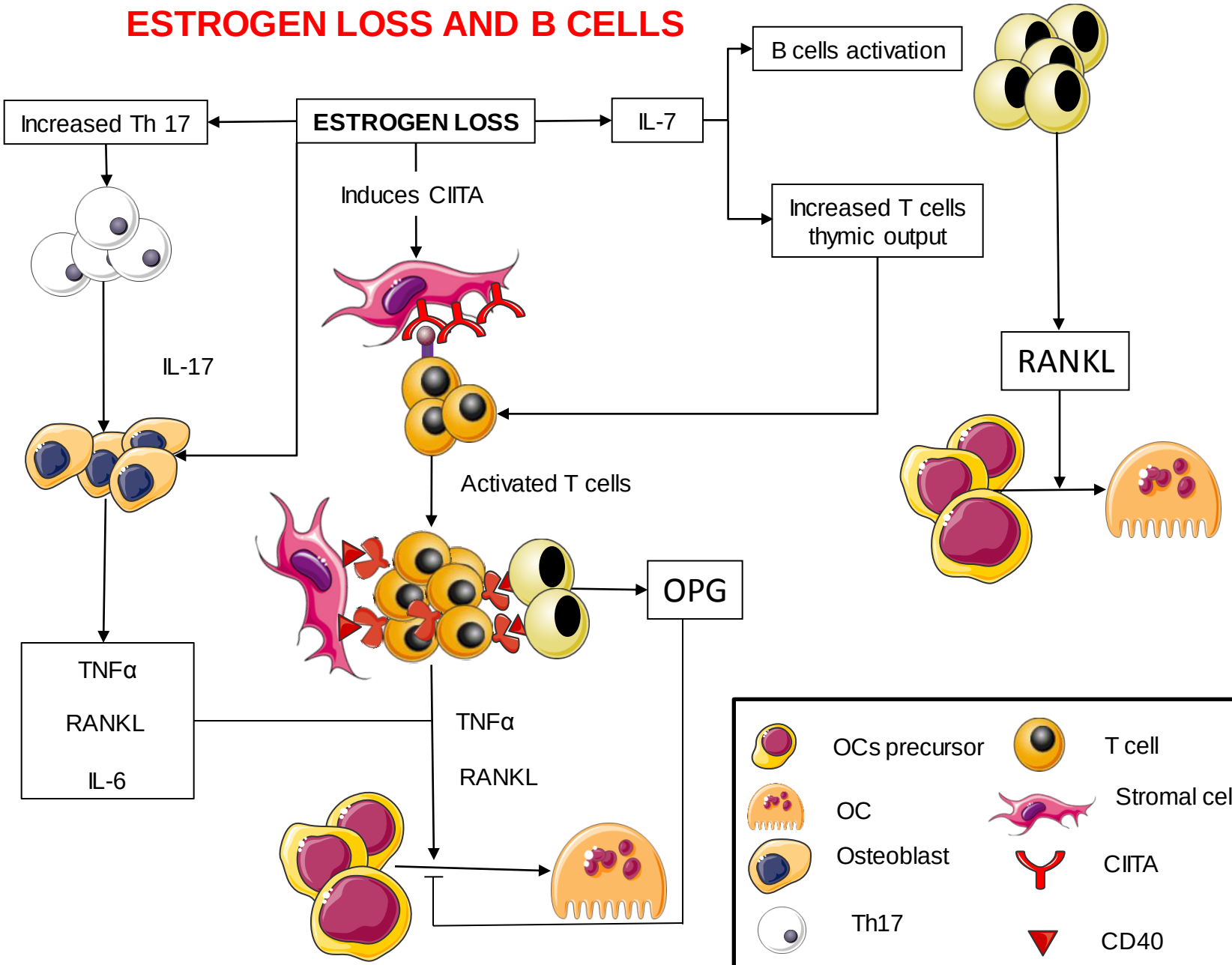
Li Y et al. Blood 2007

CD40 KO mice and CD40L KO mice display decreased B-cell OPG production.



Li Y et al. Blood 2007

ESTROGEN LOSS AND B CELLS

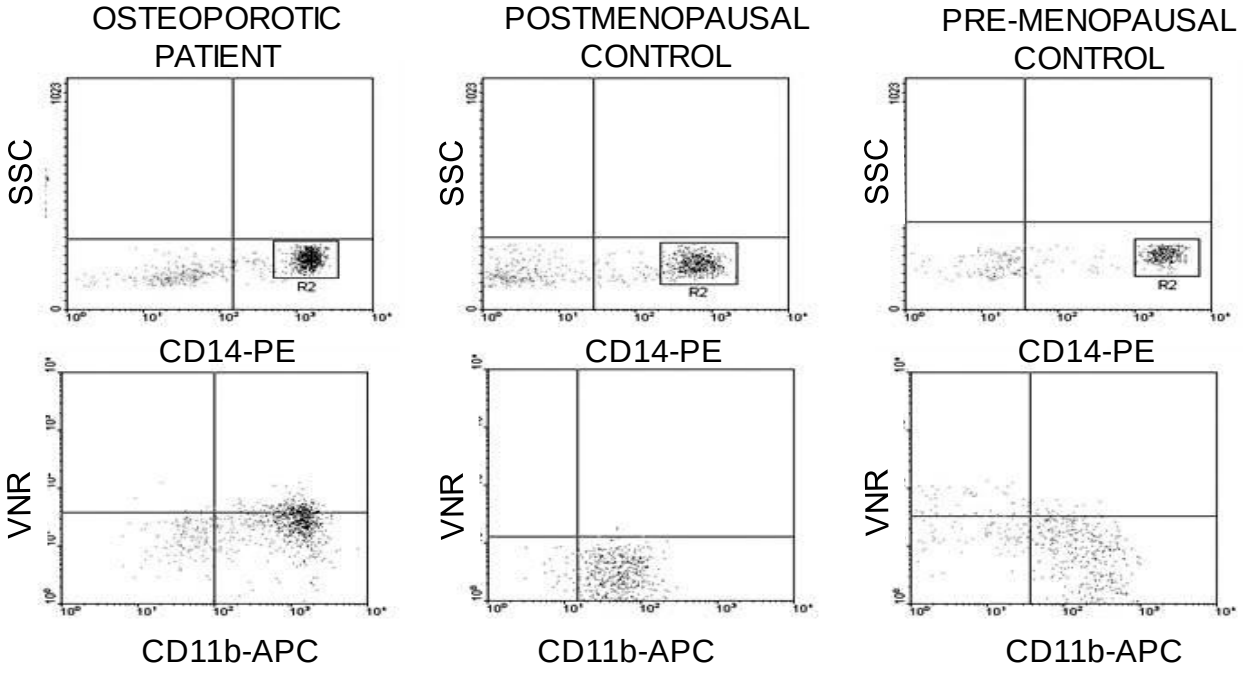


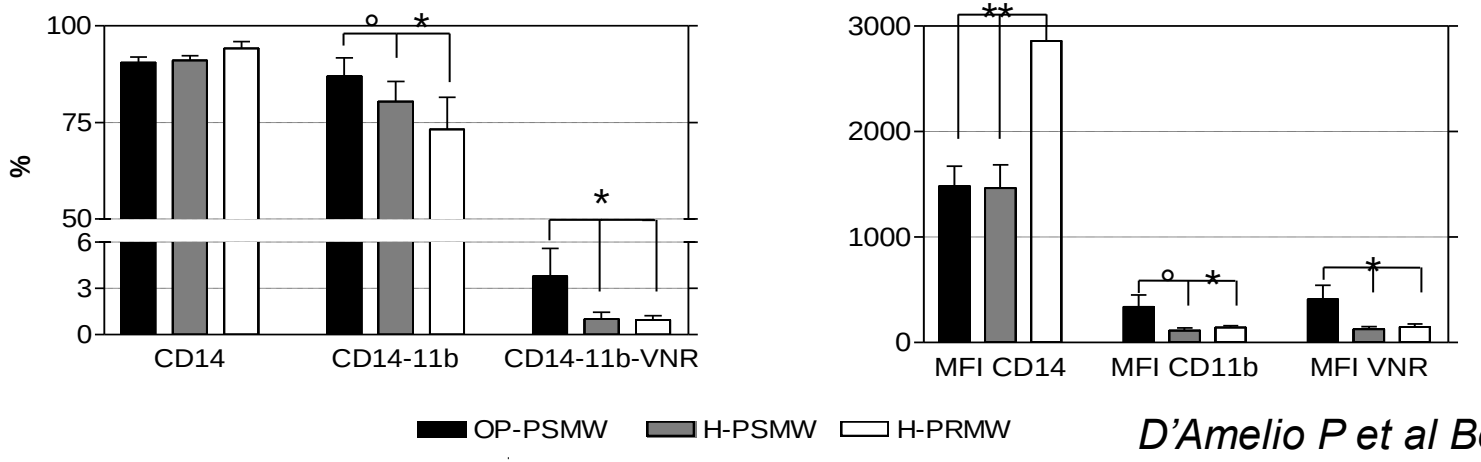
P. D'Amelio. Immunol Invest 2013

OSTEOCLASTS AT THE CROSS ROAD BETWEEN IMMUNE SYSTEM AND BONE

- OC precursors circulate within the monocityc fraction of PBMC
- Most osteoclastogenic cytokines also regulate macrophages or dendritic cells which share with OC their bone marrow precursors during development
- OC precursors derives from a specific sub-population in inflammatory conditions (CD16+)
- Deep interaction between T cells and OC

OCs precursors are increased in PBMCs from osteoporotic women





D'Amelio P et al Bone 2008

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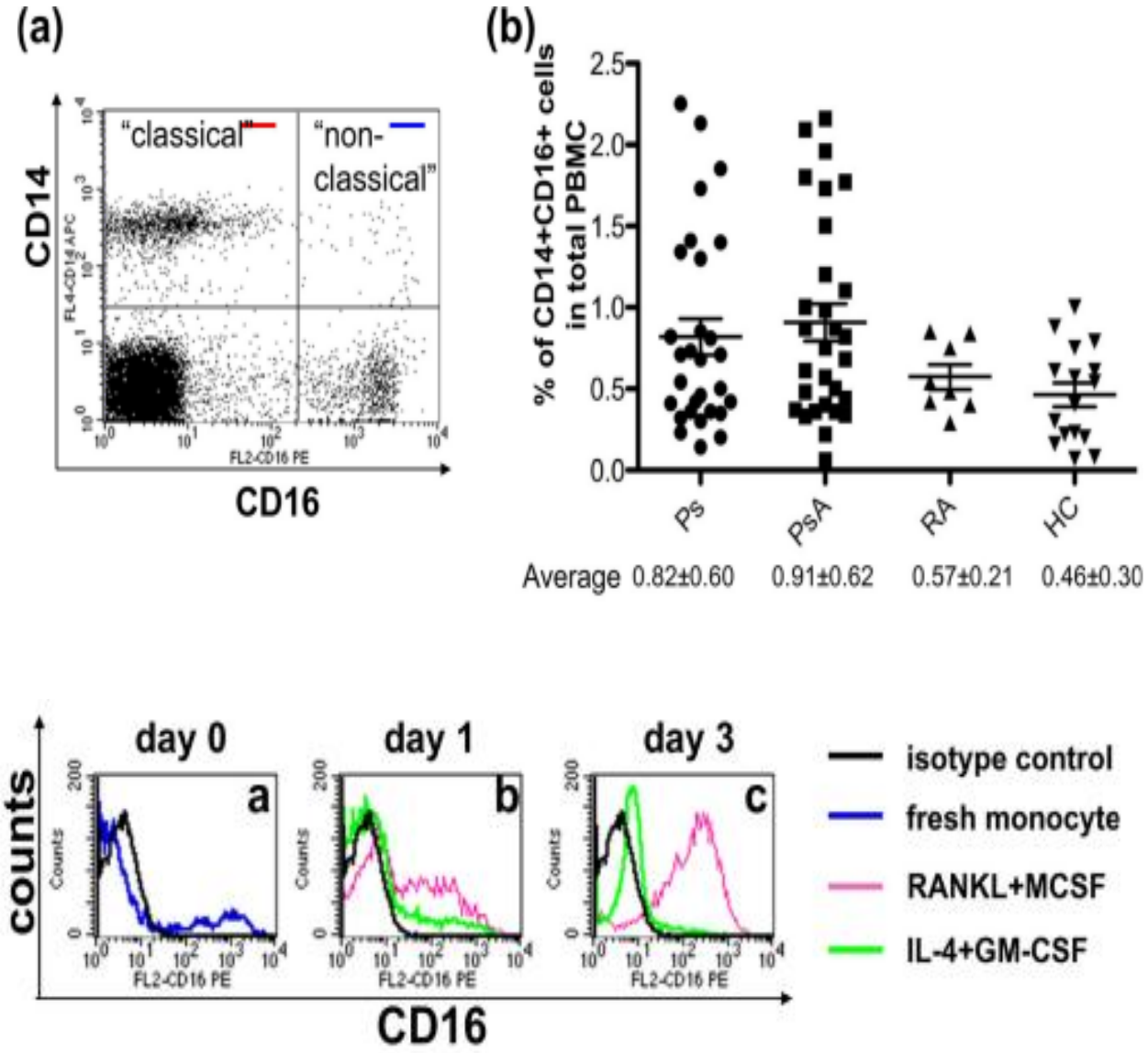
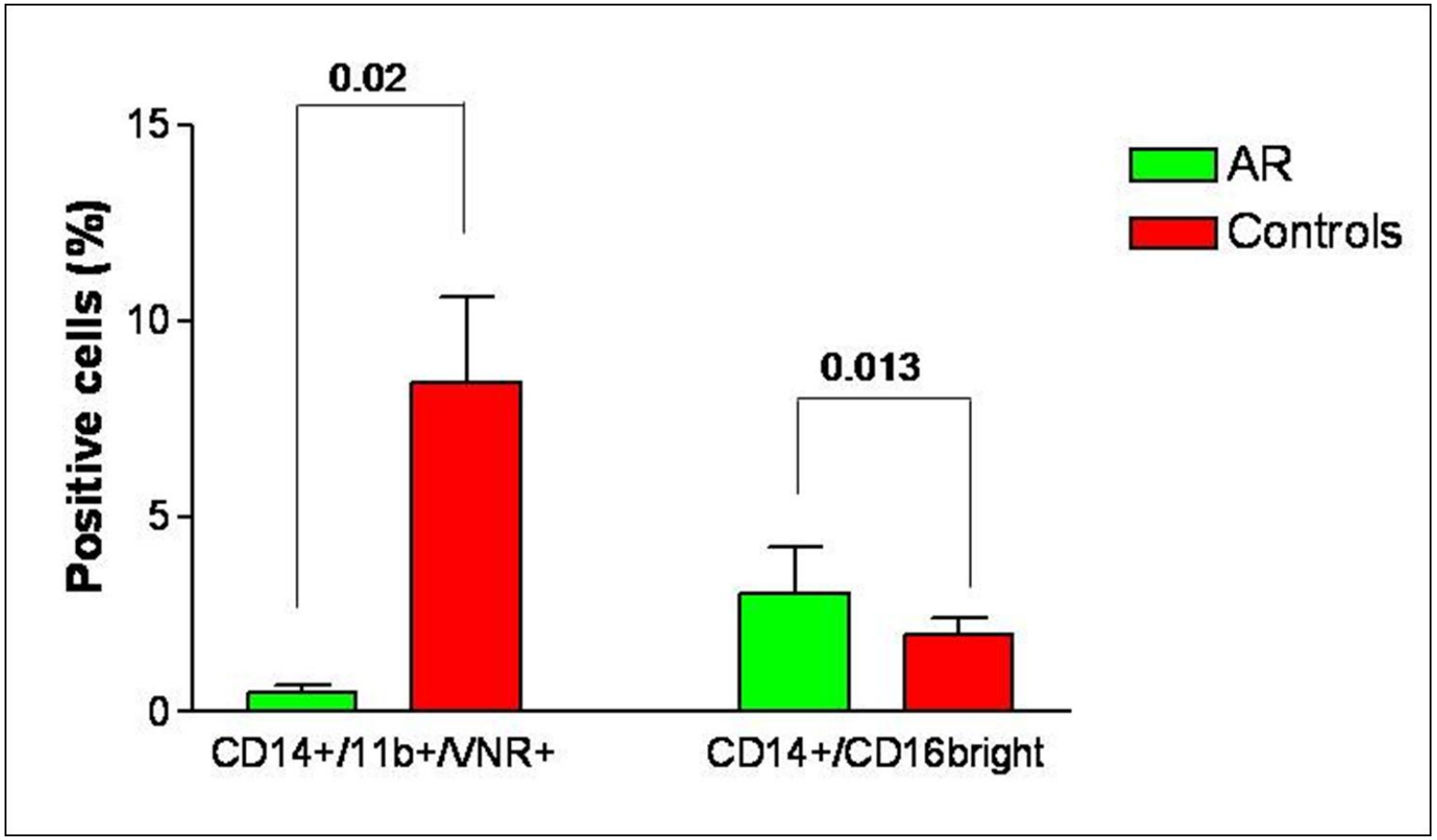


Chiu et al. Arthritis Research & Therapy 2010

CD16+ MONOCYTES ARE INCREASED IN RA PATIENTS



D'Amelio P et al ASMBR 2012

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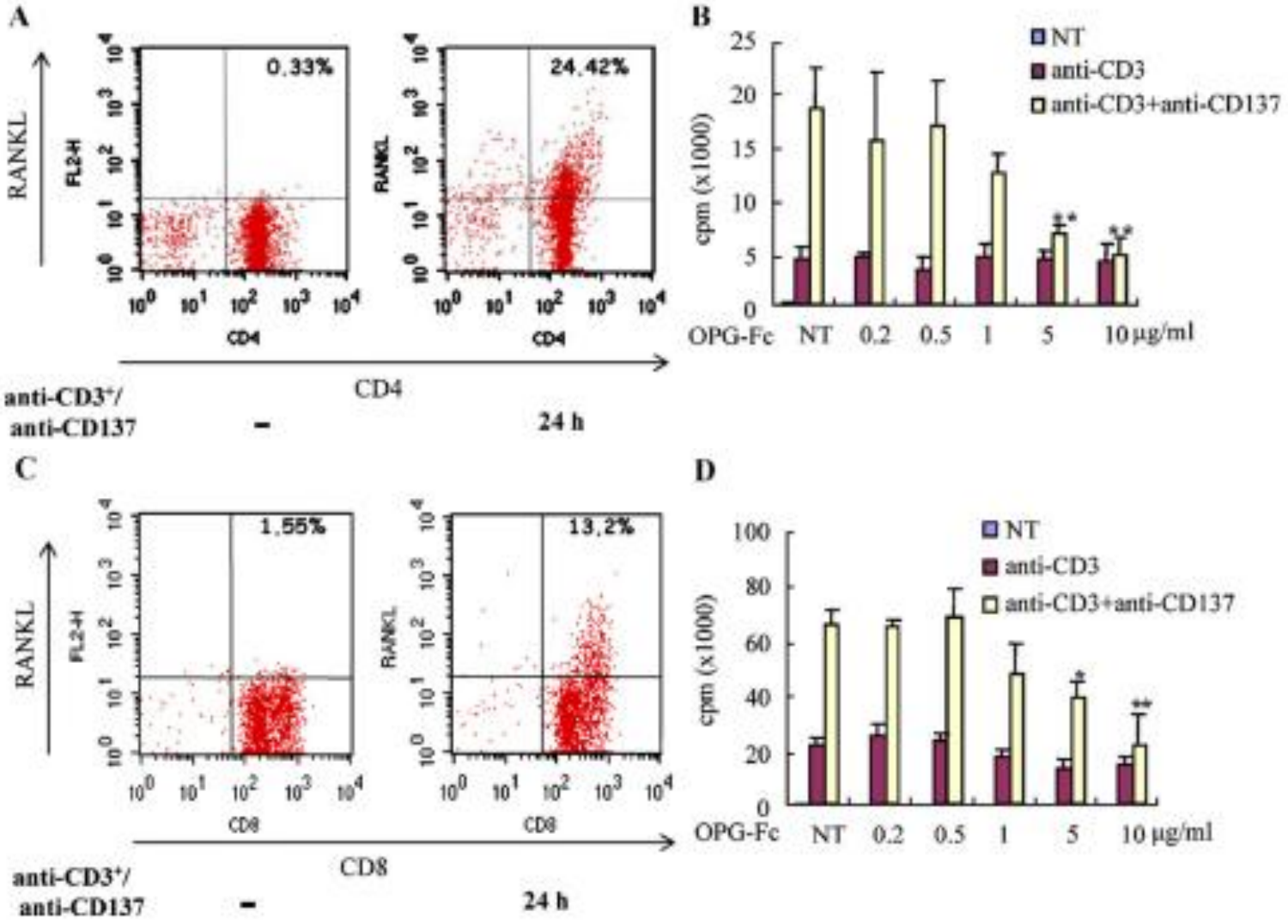
T CELLS AND OSTEOCLASTS: RECIPROCAL INTERACTION

- T cells produces inflammatory cytokines as TNFα and RANKL able to induce OC formation and activity.

- T cells are upregulated by estrogen deficiency

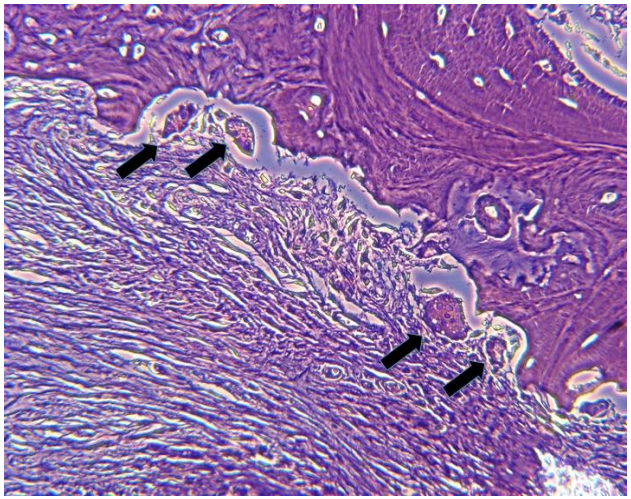
- OCs modulates T cells activity

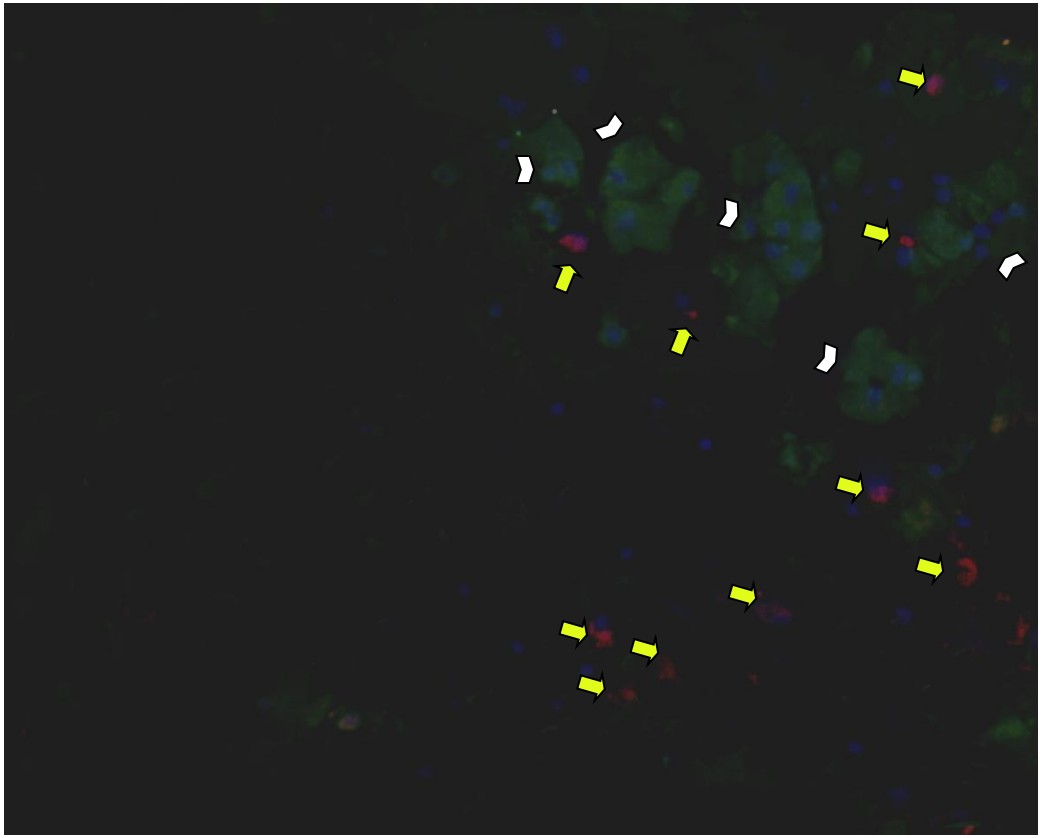
Ligation of RANKL decreases CD4+ or CD8+ T cell proliferation



R. Senthilkumar, H.-W. Lee / Immunobiology 2009

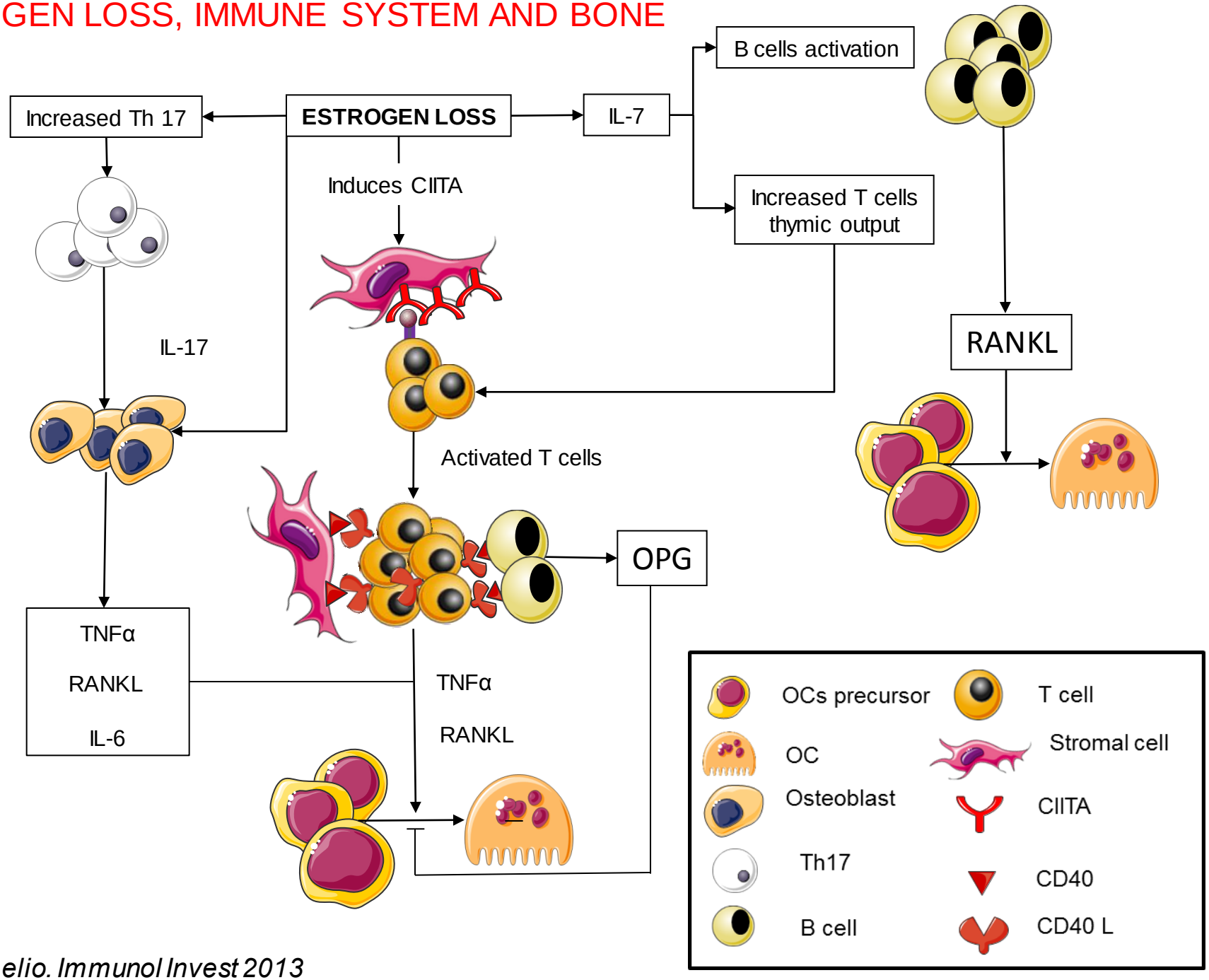
OCs closely interacts with T cells in periprosthetic osteolysis



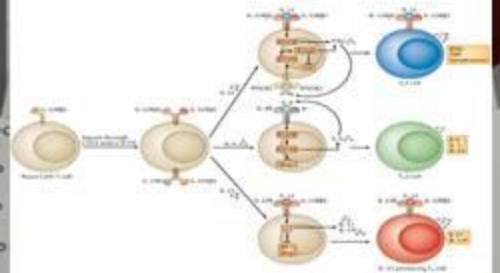
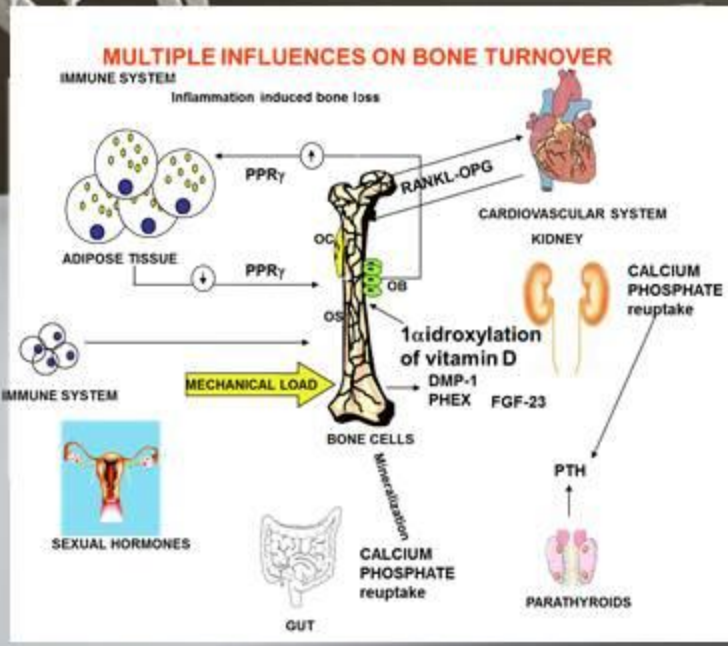


Roato I et al Biomatherial 2010

ESTROGEN LOSS, IMMUNE SYSTEM AND BONE



P. D'Amelio. Immunol Invest 2013

....T cells or not T cells...

Immune system