



12th International Medical Postgraduate Conference  
Hradec Kralove, October 27th 2015

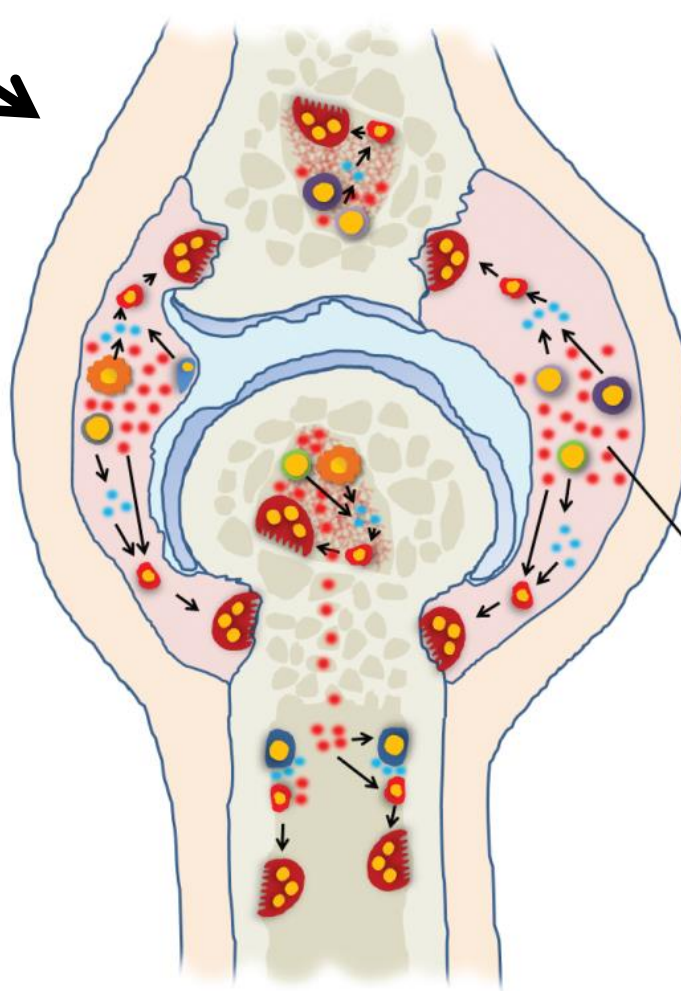
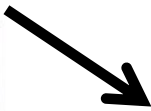
# CHEMOKINE RECEPTOR PROFILE OF OSTEOCLAST PROGENITOR CELLS IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Mentor: Prof. Danka Grčević, MD, PhD

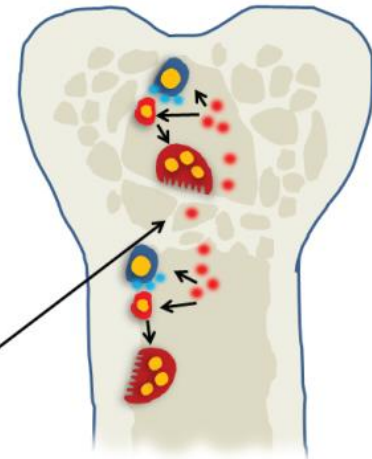
Department of Physiology and Croatian Institute for Brain Research,  
School of Medicine, University of Zagreb, Salata 3, 10 000 Zagreb, Croatia

# Rheumatoid arthritis



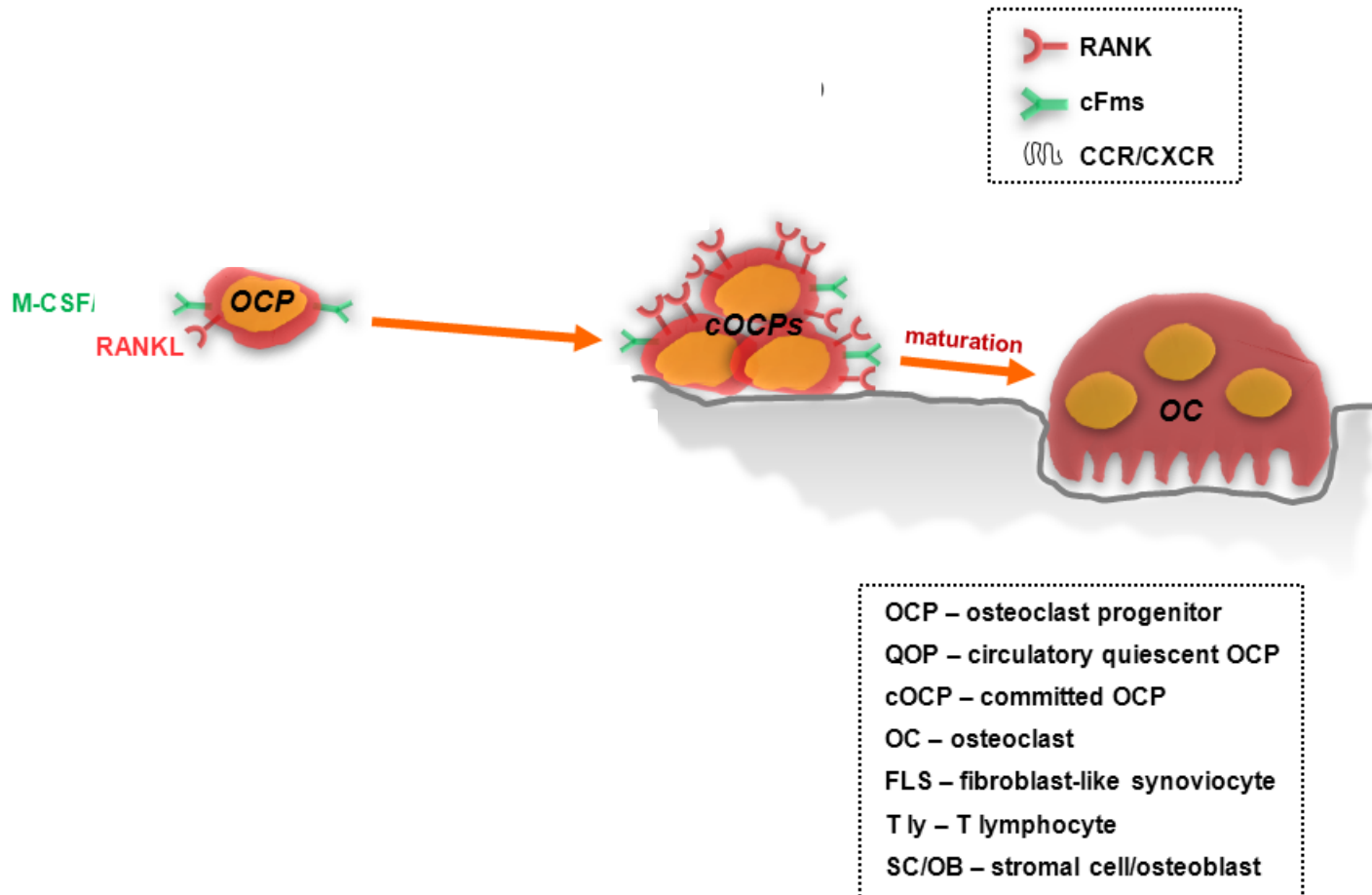
local bone loss

- osteoclast
- osteoclast progenitor
- T lymphocyte
- B lymphocyte
- plasma cell
- Th17 cell
- macrophage
- fibroblast
- osteoblast
- osteoresorptive cytokines
- RANKL

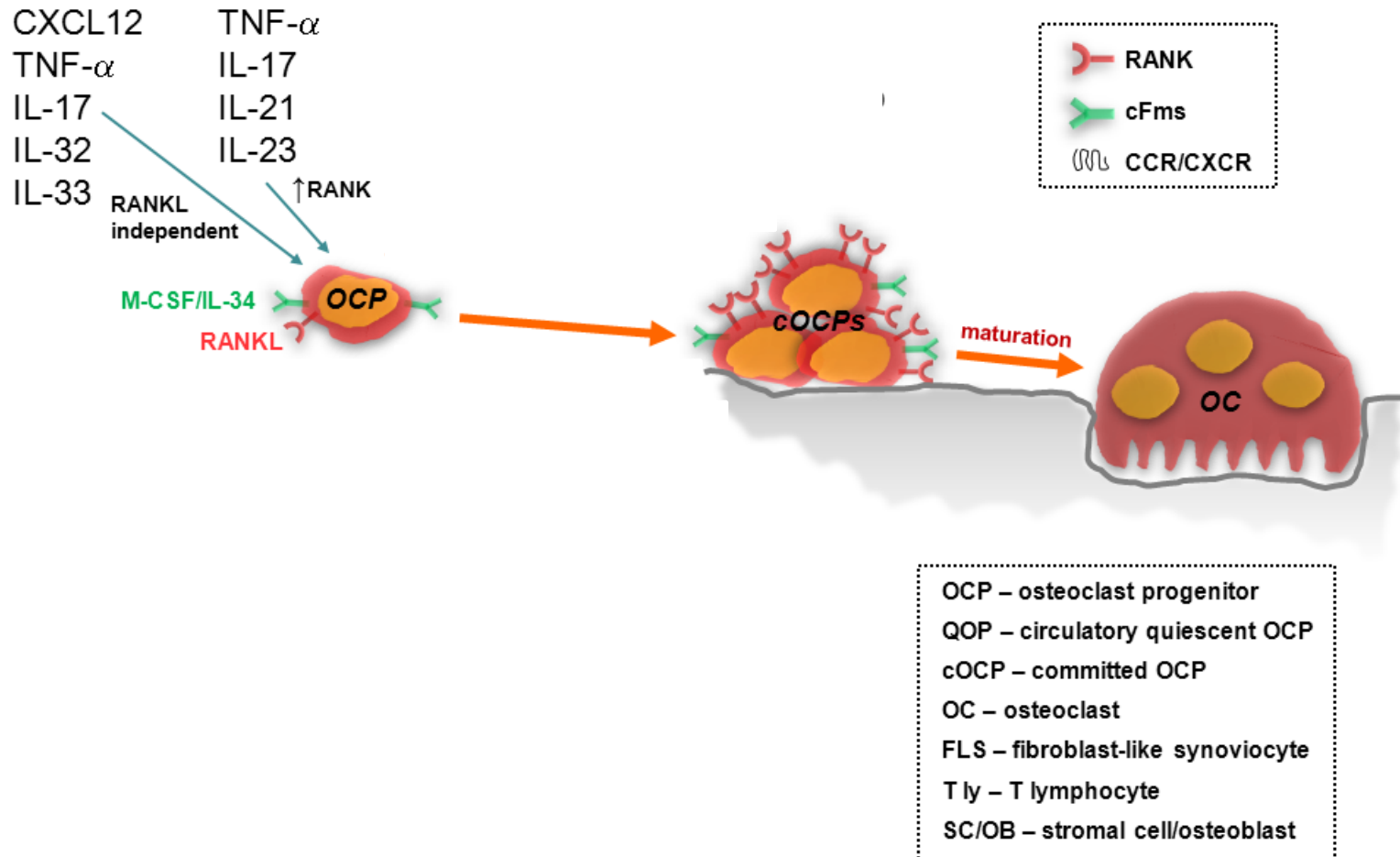


generalized bone loss

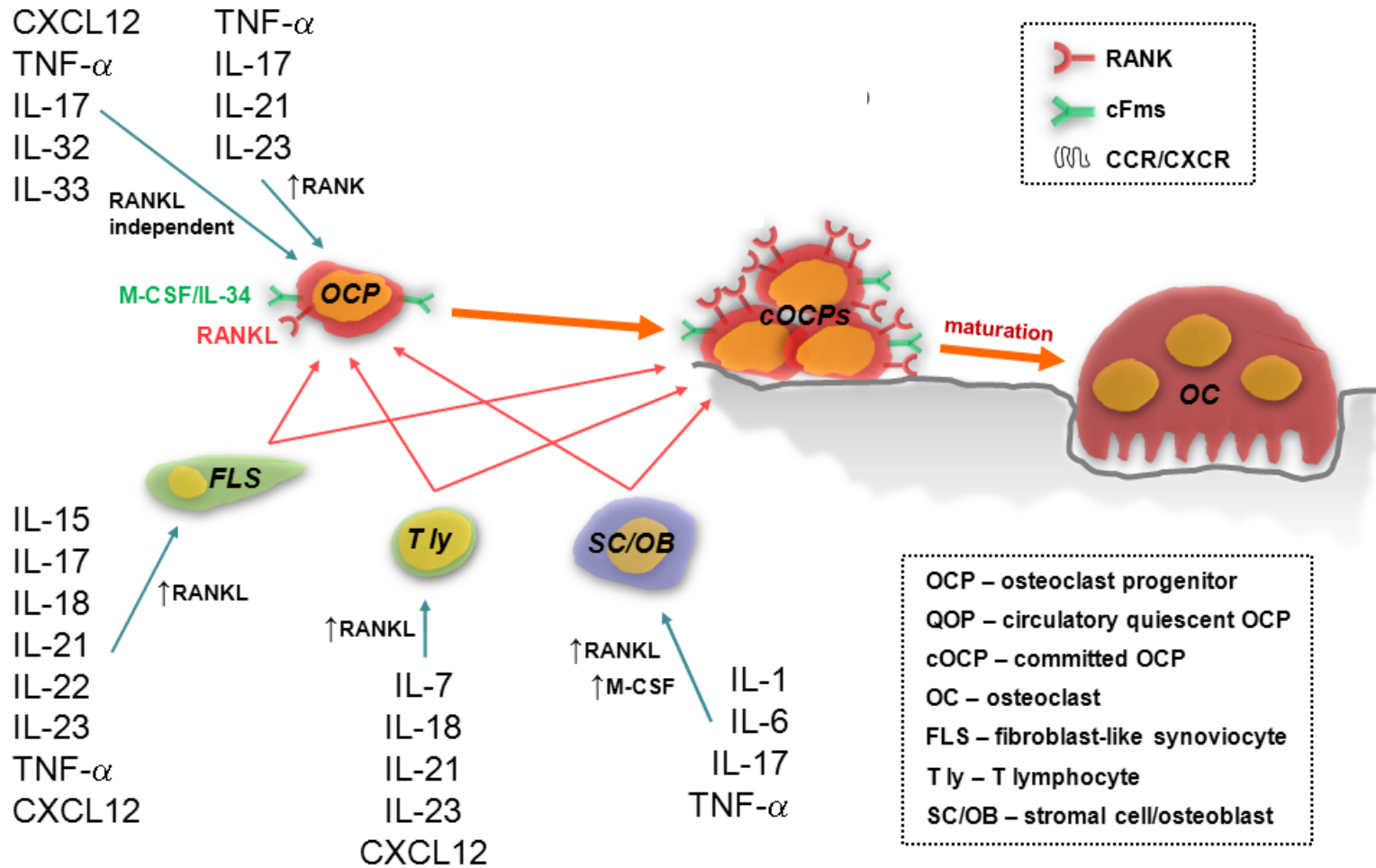
# Inflammation induced osteoclast activation



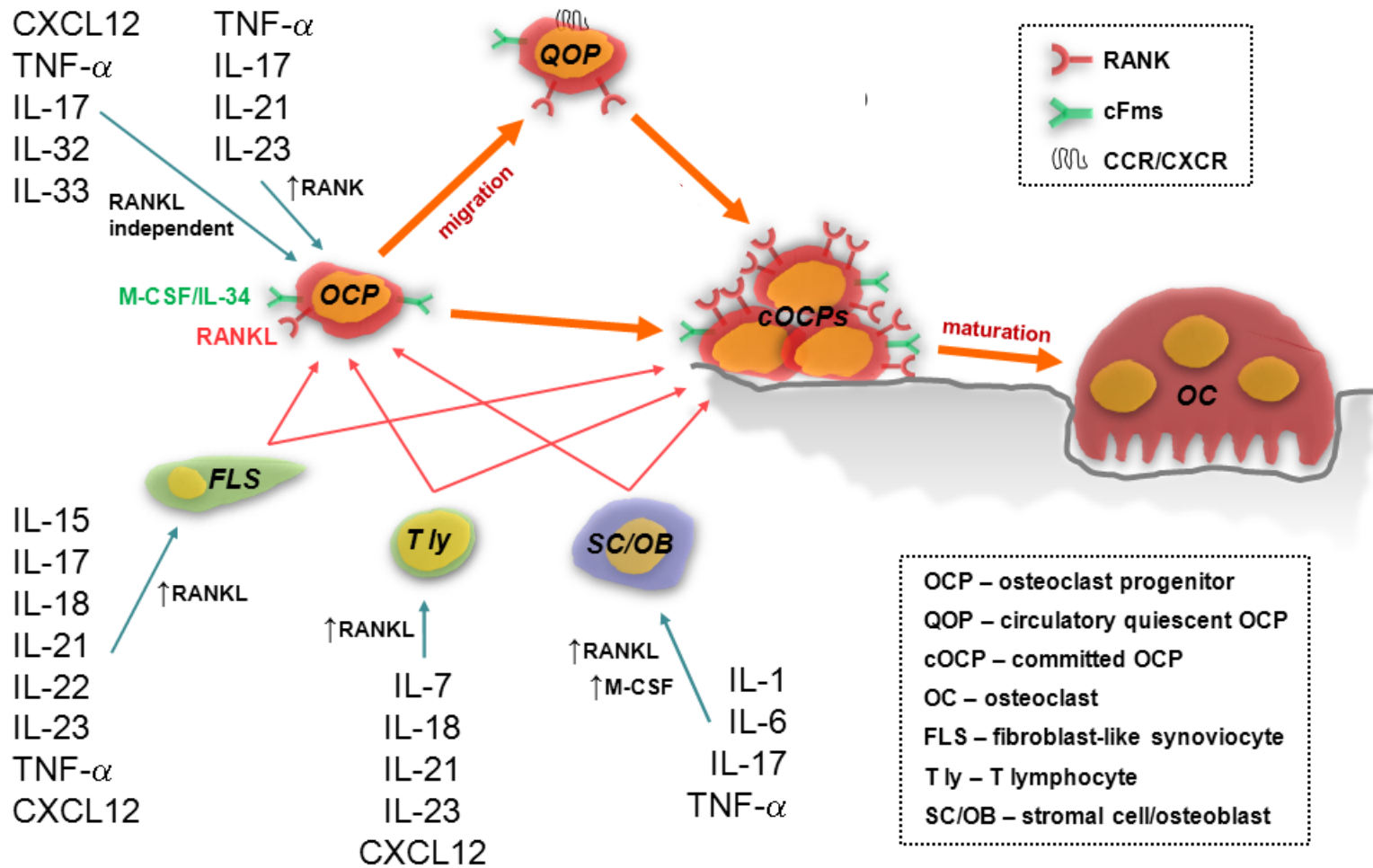
# Inflammation induced osteoclast activation



# Inflammation induced osteoclast activation

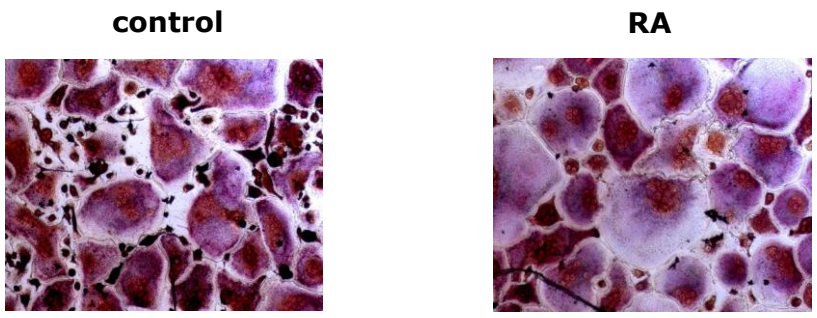
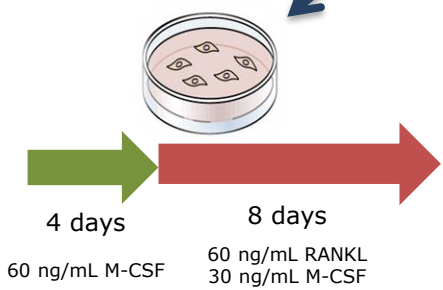
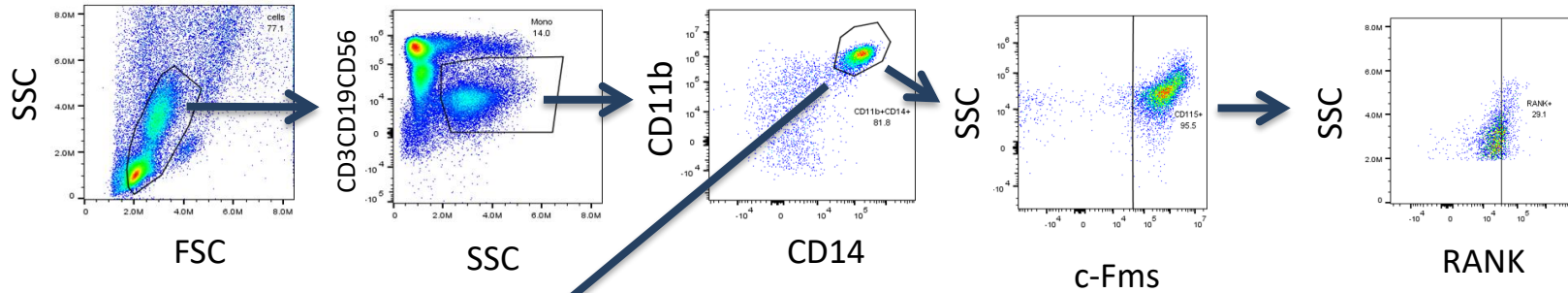


# Inflammation induced osteoclast activation



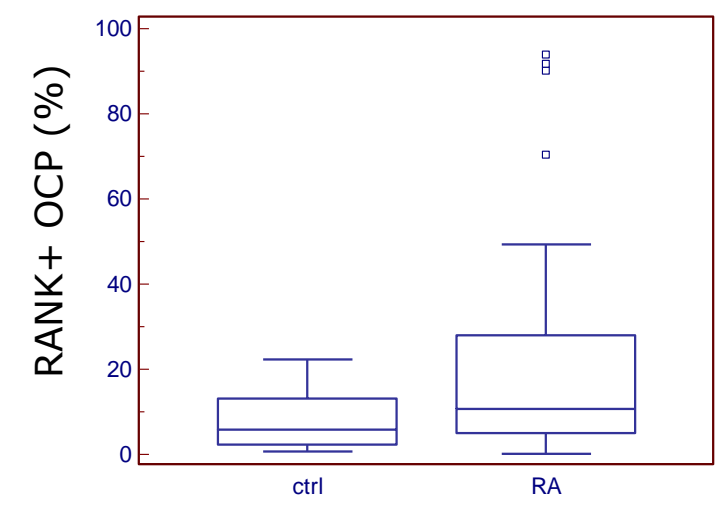
*Sucur A, Katavic V, Kelava T, Jajic Z, Kovacic N, Grcevic D. Induction of osteoclast progenitors in inflammatory conditions: key to bone destruction in arthritis. Int Orthop 2014*

# Number, surface markers and potential of osteoclast progenitors



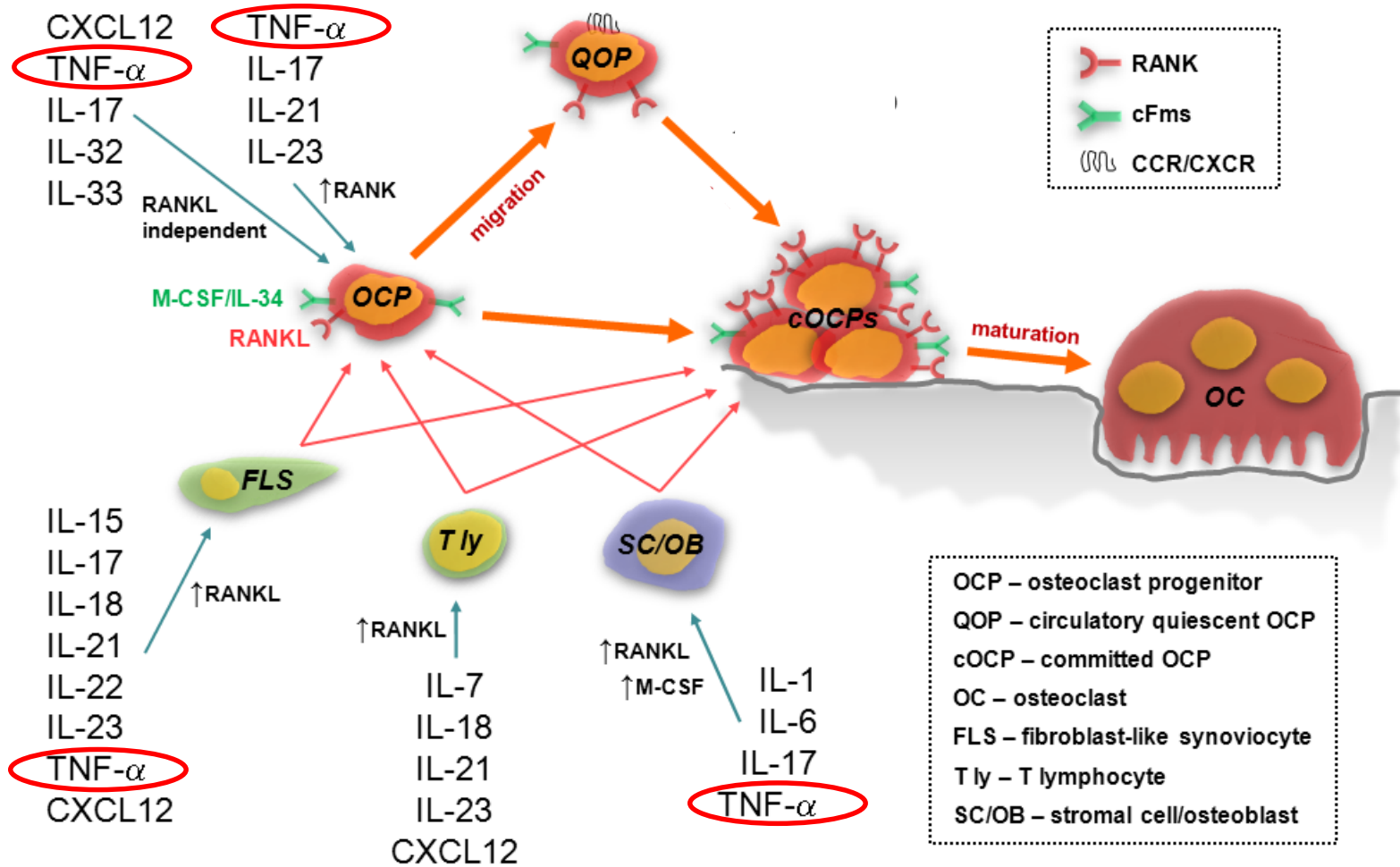
p = 0.7970

p = 0.0314



number of osteoclasts per well [median (IQR)]

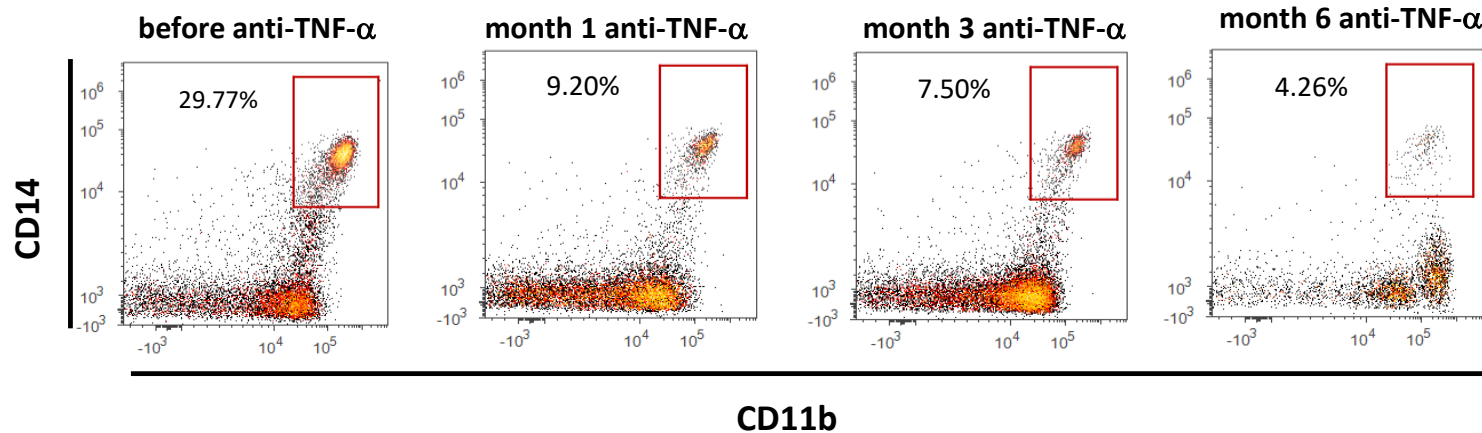
# Inflammation induced osteoclast activation





# Tendency of anti-TNF therapy to lower osteoclast progenitor number

percentage of osteoclast progenitor cells in lymphoid marker negative population (CD3<sup>-</sup>CD19<sup>-</sup>CD56<sup>-</sup>)



## Anti-TNF therapy only temporarily suppresses osteoclastogenic potential

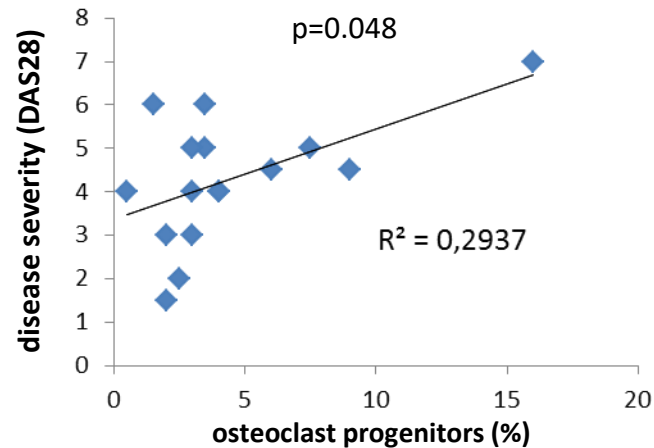
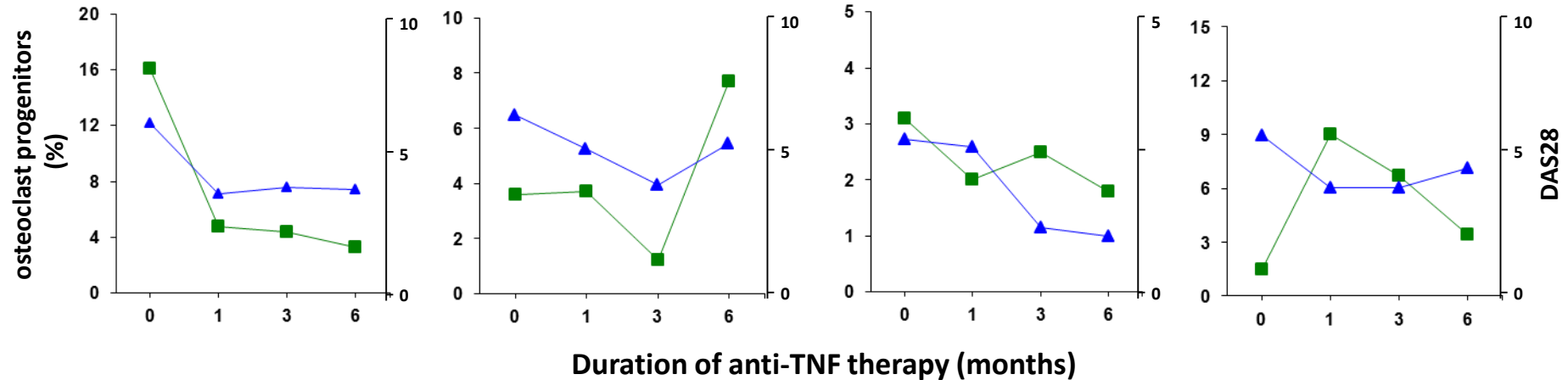
before anti-TNF	1st month	3rd month	6th month
320 $\pm$ 55	49 $\pm$ 8	275 $\pm$ 47	384 $\pm$ 56

number of osteoclasts per well

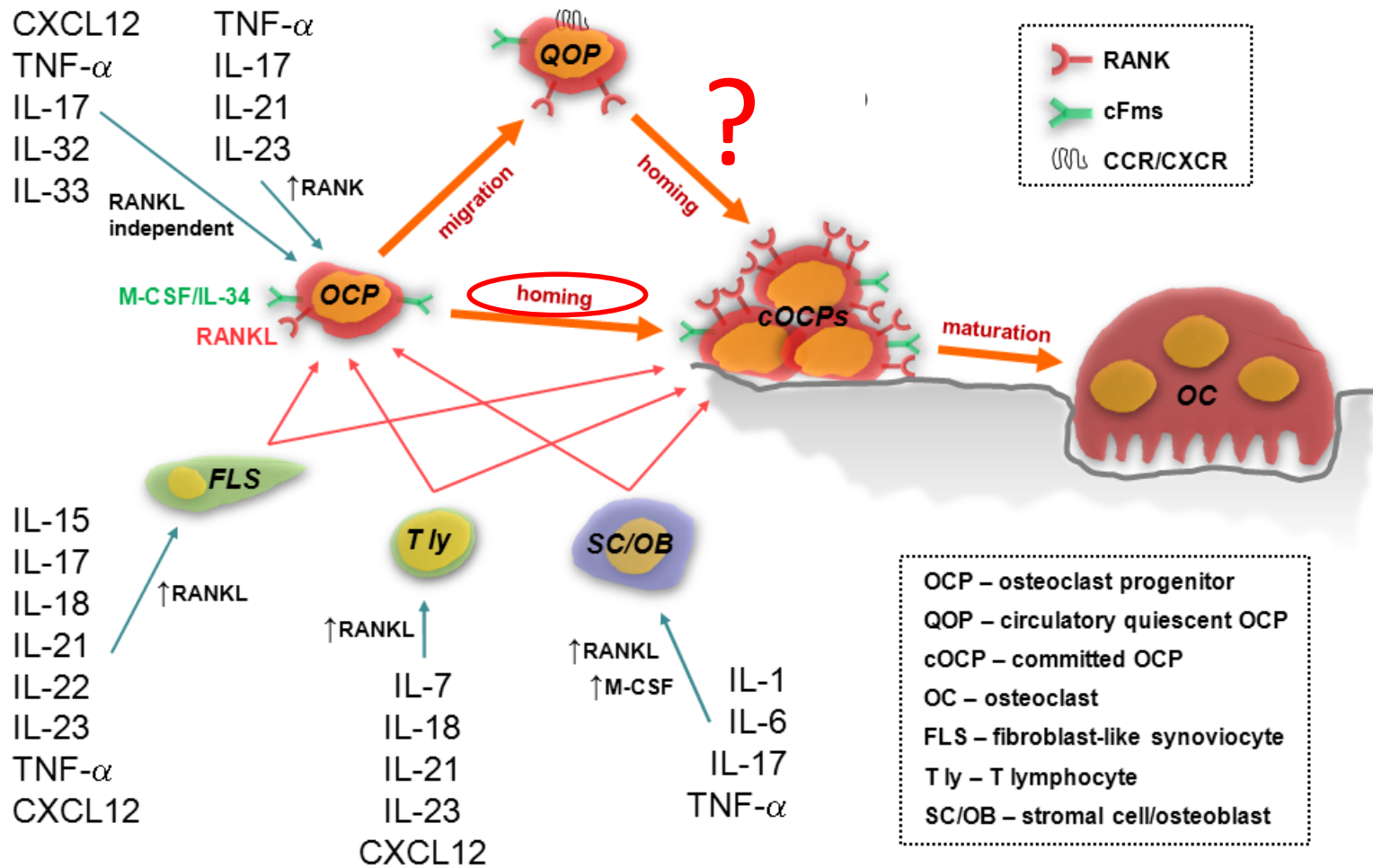
# Correlation of disease severity with the number of osteoclast progenitors

▲ disease severity (DAS28)

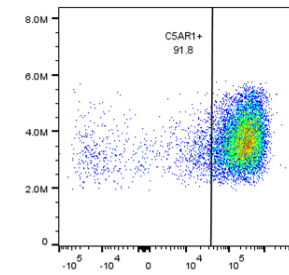
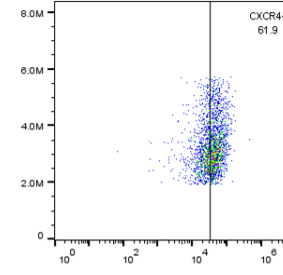
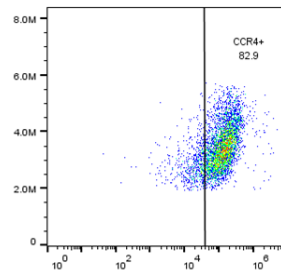
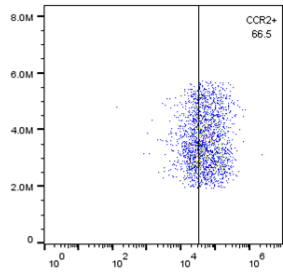
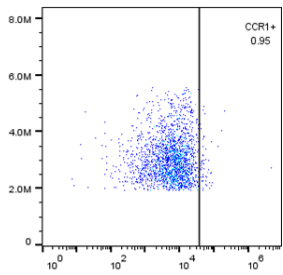
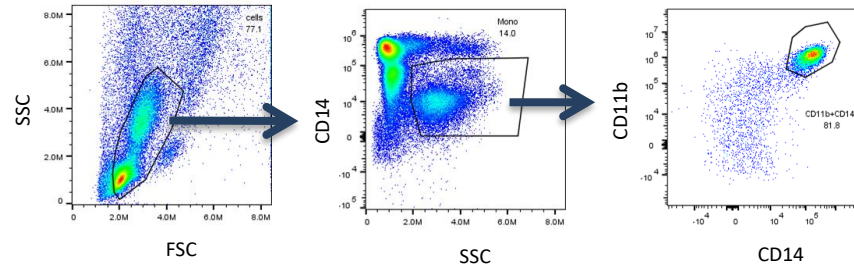
■ percentage of peripheral osteoclast progenitors



# Regulation of osteoclast progenitor trafficking



# Osteoclast progenitors express chemokine receptors



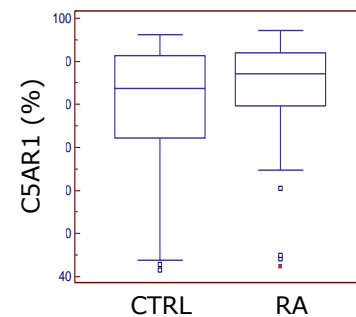
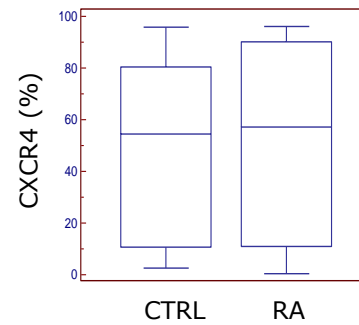
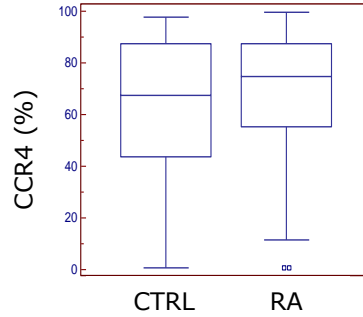
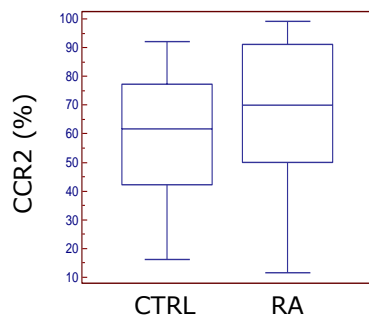
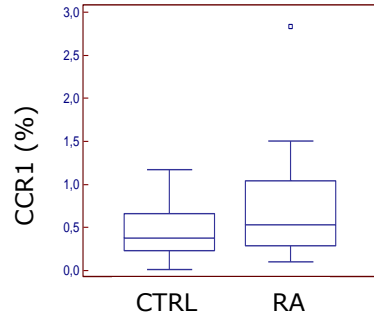
$p = 0.2601$

$p = 0.0991$

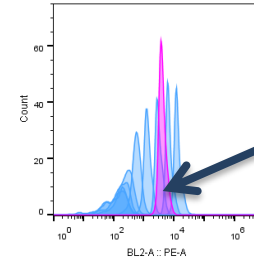
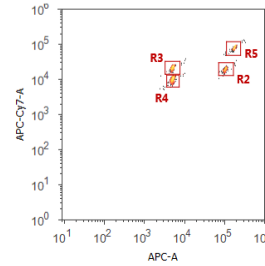
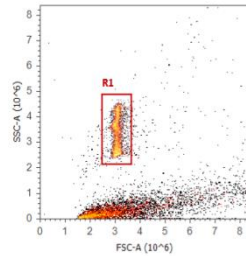
$p = 0.3531$

$p = 0.4158$

$p = 0.4358$

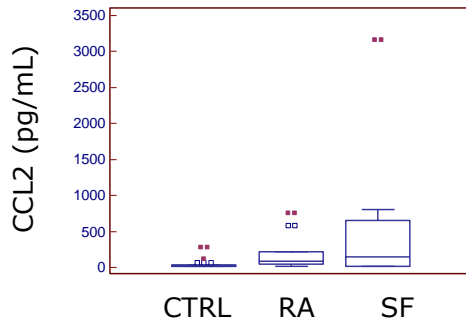


# Increased chemokine concentrations and an indication of a blood-joint gradient

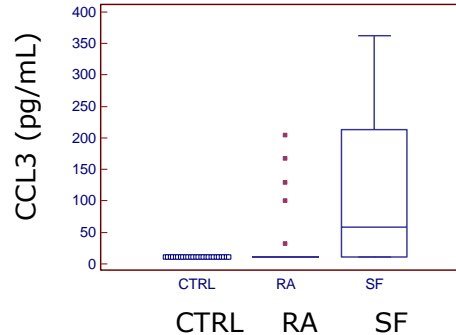


calculate concentrations of unknown samples based on MFI of standard set

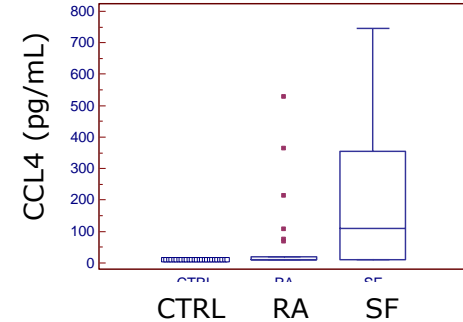
p (RA vs CTRL) < 0.001  
p (SF vs RA) = 0.0875



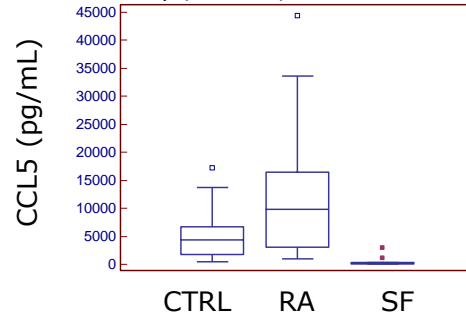
p (RA vs CTRL) = 0.0958  
p (SF vs RA) = 0.1803



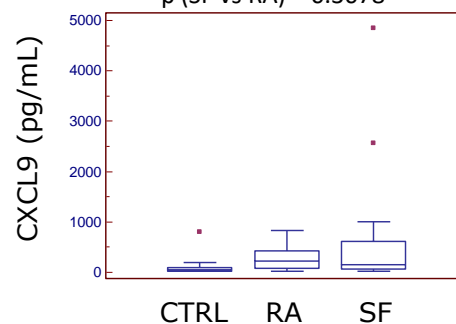
p (RA vs CTRL) = 0.0958  
p (SF vs RA) = 0.0111



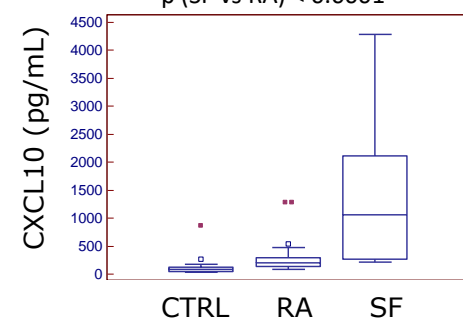
p (RA vs CTRL) = 0.1429  
p (SF vs RA) < 0.0001



p (RA vs CTRL) = 0.0007  
p (SF vs RA) = 0.3078



p (RA vs CTRL) < 0.0001  
p (SF vs RA) < 0.0001



# Conclusions

- lower number of osteoclast progenitor cells (OCP) correlated with lower disease severity (DAS28)
- anti-TNF treatment only temporarily suppressed osteoclastogenic potential
  - possible reason for weak long term effectiveness of anti-TNF therapy on bone pathology
- OCPs express several chemokine receptors and there are increased levels of several chemokine ligands in rheumatoid arthritis serum and synovial fluid with an indication of a blood-joint gradient
  - possible chemotactic mechanism of migration to affected joints
- **asociation of peripheral blood osteoclast progenitor cells with pathogenesis of rheumatoid arthritis**

# Acknowledgements



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