

Bone Destruction in Arthritis



New Emerging Team in

Osteoclastogenesis and Osteoclast Activation in Rheumatoid Arthritis

*"Today's research towards tomorrow's prevention,
detection and management of bone loss"*

<http://www.ece.ualberta.ca/~lkurgan/OOARA/index.php?home>



1) Drs. Brum-Fernandes and Boire, Université de Sherbrooke



Patient recruitment; Clinical data acquisition and analysis; cell culture, osteoclastogenesis and bone resorption studies; distribution of cells and samples amongst team members



1) Drs. Brum-Fernandes and Boire, Université de Sherbrooke



Patient recruitment; Clinical data acquisition and analysis; cell culture, osteoclastogenesis and bone resorption studies; distribution of cells and samples amongst team members



2) Dr. Komarova, McGill University

Test components of RANKL signalling on RNA samples

1) Drs. Brum-Fernandes and Boire, Université de Sherbrooke



Patient recruitment; Clinical data acquisition and analysis; cell culture, osteoclastogenesis and bone resorption studies; distribution of cells and samples amongst team members



2) Dr. Komarova, McGill University

Test components of RANKL signalling on RNA samples



3) Manolson, Harrison University of Toronto

Test for differences in OC morphology, expression of cell surface receptors (RANK, IL-R1 and R2), and response to cytokines and cytokine agonist.

1) Drs. Brum-Fernandes and Boire, Université de Sherbrooke



Patient recruitment; Clinical data acquisition and analysis; cell culture, osteoclastogenesis and bone resorption studies; distribution of cells and samples amongst team members



2) Dr. Komarova, McGill University

Test components of RANKL signalling on RNA samples

4) Drs. Dixon and Sims, University of Western Ontario

Assess chemotactic behaviour of mature osteoclasts by time-lapse video-microscopy.



3) Manolson, Harrison University of Toronto

Test for differences in OC morphology, expression of cell surface receptors (RANK, IL-R1 and R2), and response to cytokines and cytokine agonist.

1) Drs. Brum-Fernandes and Boire, Université de Sherbrooke



Patient recruitment; Clinical data acquisition and analysis; cell culture, osteoclastogenesis and bone resorption studies; distribution of cells and samples amongst team members



2) Dr. Komarova, McGill University

Test components of RANKL signalling on RNA samples



5) Dr Kurgan , University of Alberta

Data mining analysis with the goal of identifying associations between independent variables and the identified dependent variables



4) Drs. Dixon and Sims, University of Western Ontario

Assess chemotactic behaviour of mature osteoclasts by time-lapse video-microscopy.



3) Manolson, Harrison University of Toronto

Test for differences in OC morphology, expression of cell surface receptors (RANK, IL-R1 and R2), and response to cytokines and cytokine agonist.



6) Jean Légaré, Canadian Arthritis Network, Co-Chair, Consumer Advisory Council

Responsibility:
Knowledge translation and exchange



5) Dr Kurgan , University of Alberta

Data mining analysis with the goal of identifying associations between independent variables and the identified dependent variables.



4) Drs. Dixon and Sims, University of Western Ontario

Assess chemotactic behaviour of mature osteoclasts by time-lapse video-microscopy.



UNIVERSITÉ DE SHERBROOKE



1) Drs. Brum-Fernandes and Boire, Université de Sherbrooke

Patient recruitment; Clinical data acquisition and analysis; cell culture, osteoclastogenesis and bone resorption studies; distribution of cells and samples amongst team members



2) Dr. Komarova, McGill University

Test components of RANKL signalling on RNA samples



3) Manolson, Harrison University of Toronto

Test for differences in OC morphology, expression of cell surface receptors (RANK, IL-R1 and R2), and response to cytokines and cytokine agonist.





7) Stéphane Dion, Pfizer Canada

Responsibility: Industrial partner



1) Drs. Brum-Fernandes and Boire, Université de Sherbrooke

Patient recruitment; Clinical data acquisition and analysis; cell culture, osteoclastogenesis and bone resorption studies; distribution of cells and samples amongst team members

6) Jean Légaré Canadian Arthritis Network, Co-Chair, Consumer Advisory Council

Responsibility: Knowledge translation and exchange



2) Dr. Komarova, McGill University

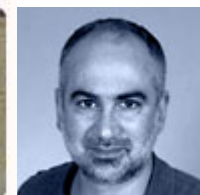
Test components of RANKL signalling on RNA samples

5) Dr Kurgan , University of Alberta

Data mining analysis with the goal of identifying associations between independent variables and the identified dependent variables.

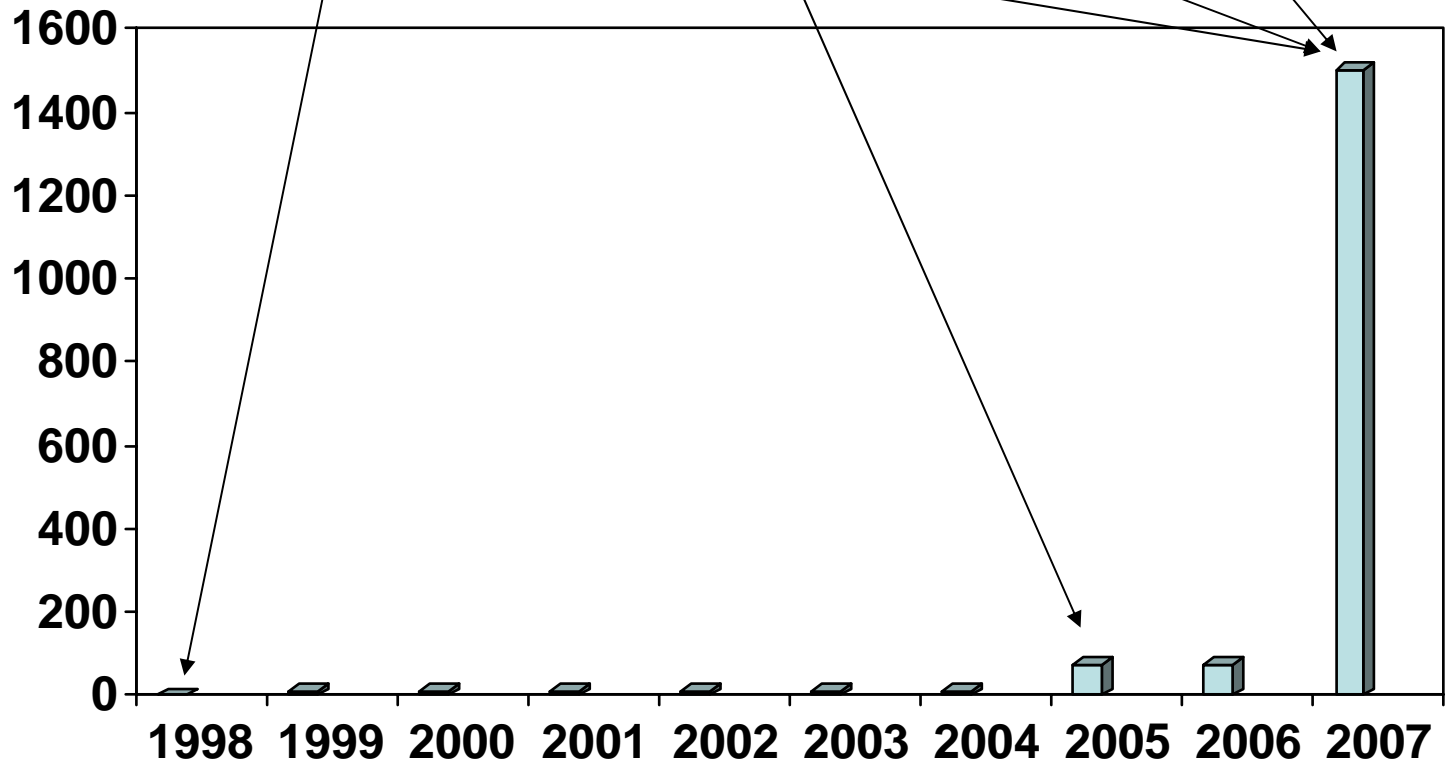
4) Drs. Dixon and Sims, University of Western Ontario

Assess chemotactic behaviour of mature osteoclasts by time-lapse video-microscopy.



3) Manolson, Harrison University of Toronto

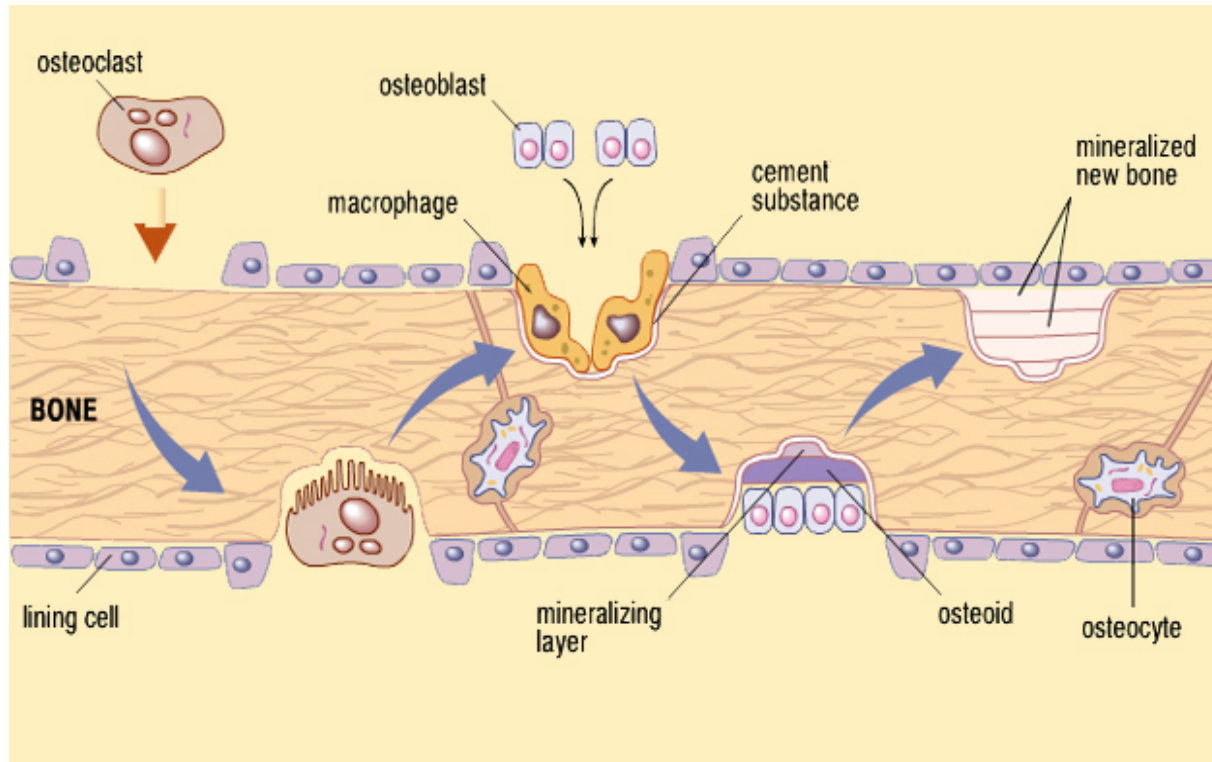
Test for differences in OC morphology, expression of cell surface receptors (RANK, IL-R1 and R2), and response to cytokines and cytokine agonist.

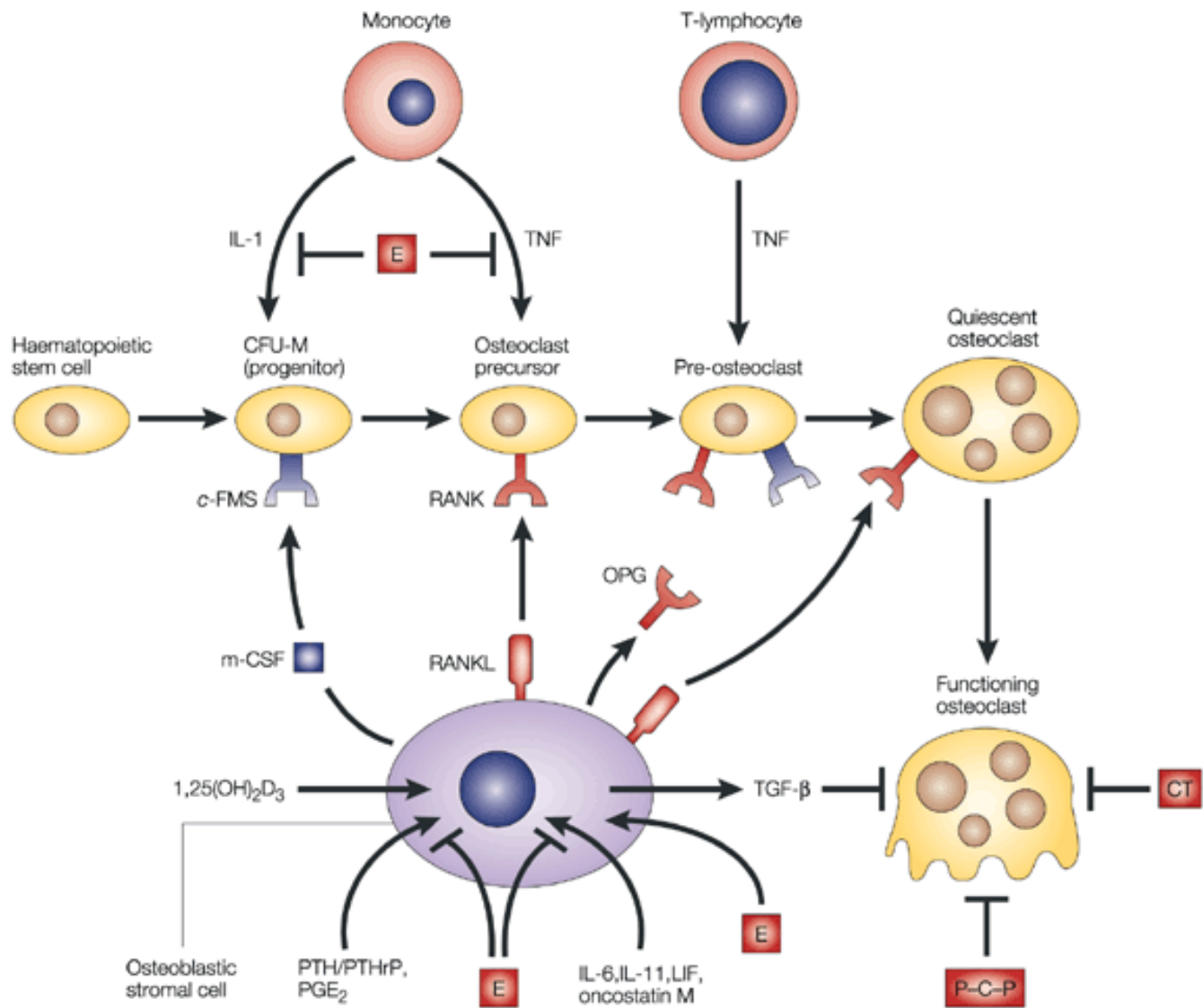


Objectives

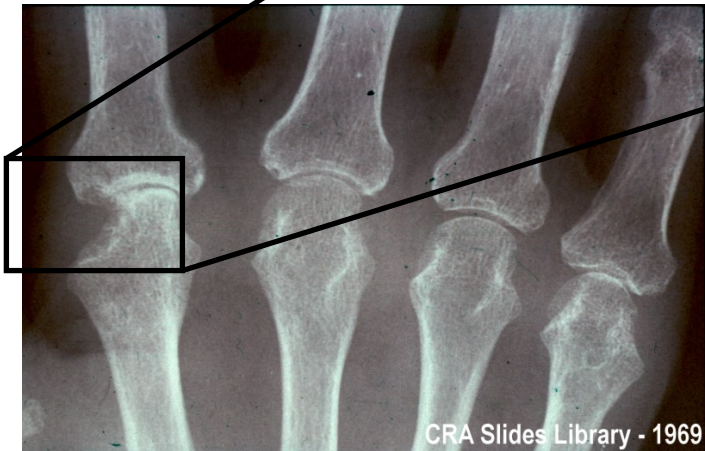
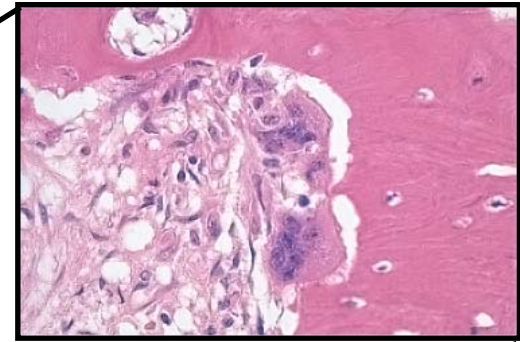
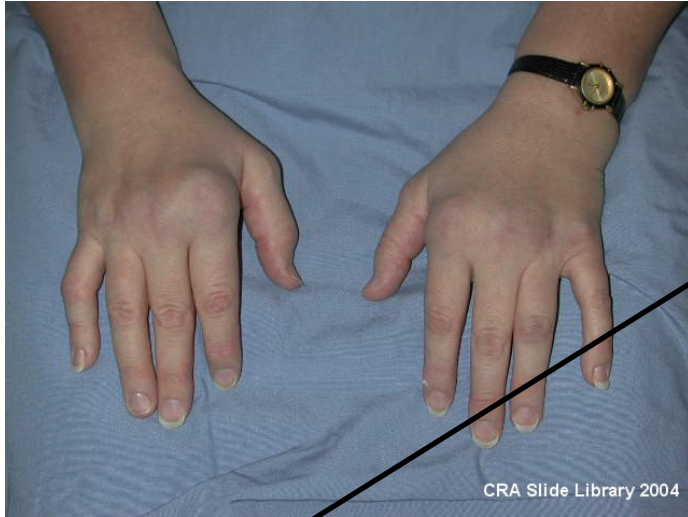
- To understand:
 - the importance of bone-resorbing cells (osteoclasts) for joint destruction in arthritis
 - How the study of these cells may contribute to the diagnosis and treatment of arthritis

Bone - an ever renewing tissue

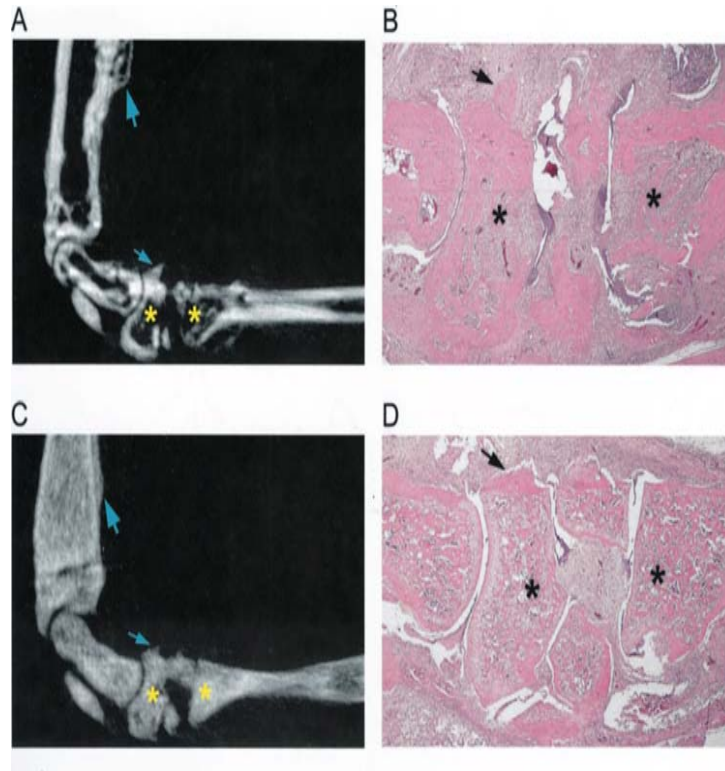




Osteoclasts and Rheumatoid Arthritis



Bone erosion in RANKL knockout mice with experimental arthritis



Pettit et al, AJP 159: 1689-99,2001

Inhibition of bone erosion in humans with RA

- Anti-RANKL antibodies
- Bisphosphonates

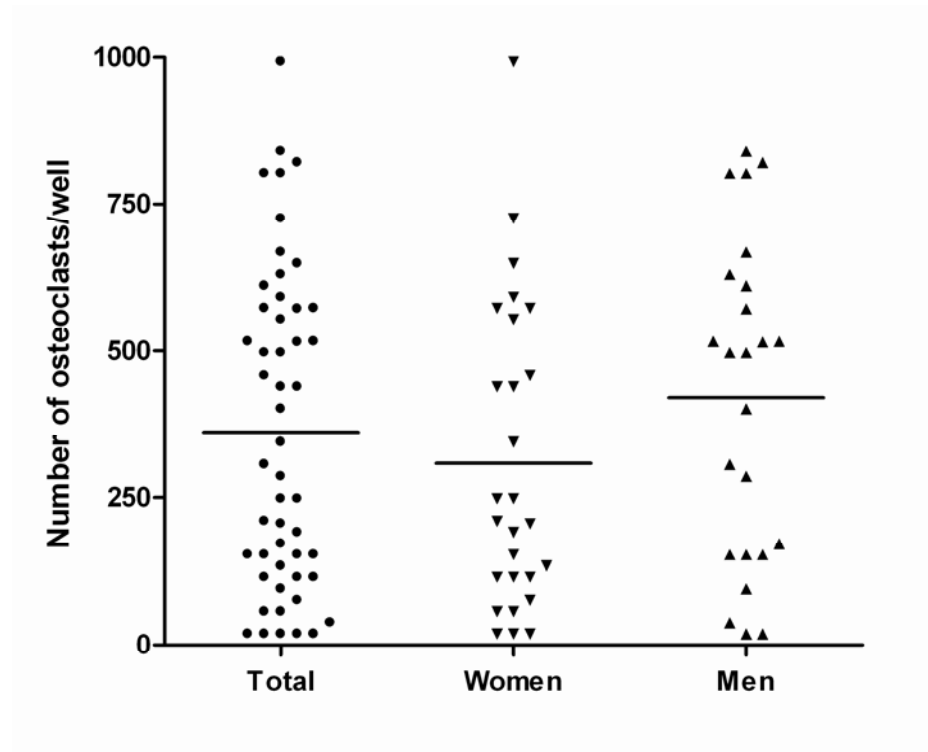
Osteoclasts and Osteoarthritis



- Subchondral bone remodeling
- Osteoblast phenotype
- Increased bone resorption in rapidly progressing OA



Capacity to generate Osteoclasts in a population of normal blood donors



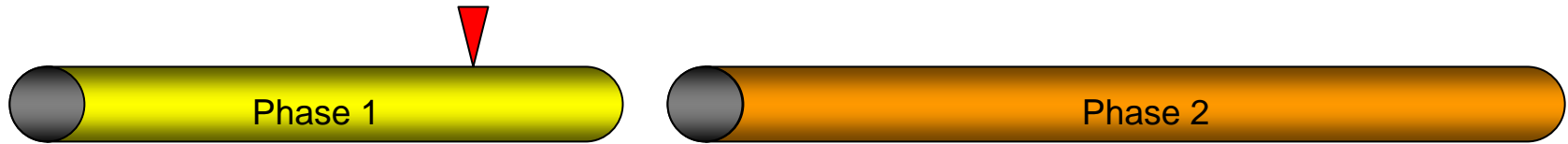
Working hypothesis

- Would the capacity to generate osteoclasts from the peripheral blood be related to the presence or severity of Rheumatoid Arthritis and Osteoarthritis?

Relevance to people with arthritis

- Identification of a subpopulation of patients more at risk of developing severe disease
- Identification of new pharmacologic targets for the treatment of RA and OA

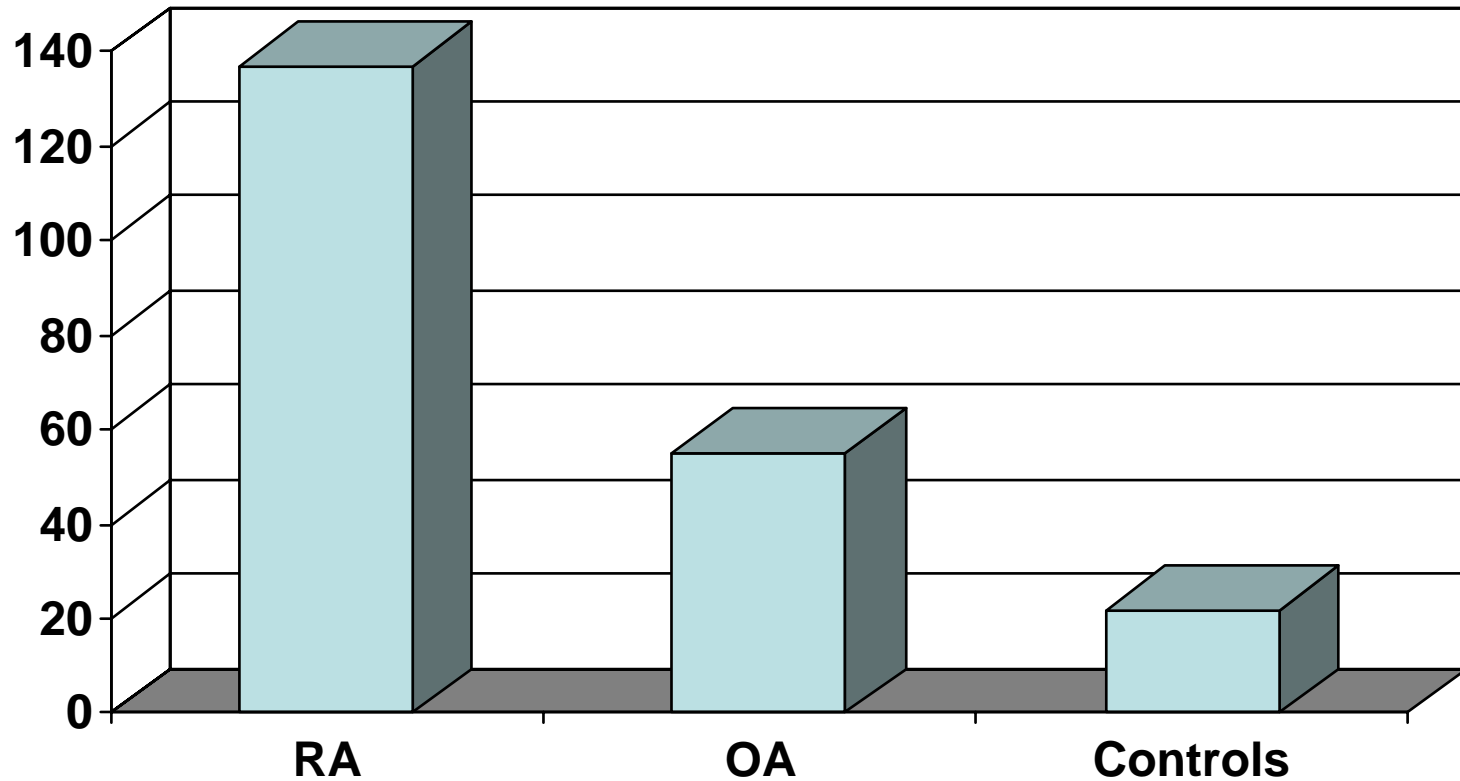
Study design



- 2 years
- Transversal
- 3 cohorts:
 - RA (140)
 - OA (140)
 - Controls (50)
- Clinical evaluation
- Radiologic evaluation
- Osteoclastogenesis
- Osteoclast characteristics

- 3 years
- Prospective
- 2 cohorts:
 - RA
 - OA
- Clinical evaluation
- Radiologic evaluation
- Osteoclastogenesis
- Osteoclast characteristics

Recruitment as of September 27, 2007



Preliminary results

- Poster Marianne Durand et al.
- Poster Svetlana Komarova et al.
- Poster Lukasz Kurgan et al.

Conclusions

- Osteoclasts participate in joint destruction in RA
- Osteoclasts may participate in OA
- A better understanding of these cells in RA and OA may lead to
 - Development of markers of aggressive disease
 - New therapeutic approaches



PANLAR 2008

PANLAR 2008
Guatemala, Guatemala
August 13-16, 2008

<http://panlar2008.agreuma.org>

<http://www.agreuma.org>



Questions ?