



**Canadian Arthritis Network  
International Partnership Initiative**

**International Research & Training Program  
LABORATORY/CLINIC PROFILE**

**Contact information of the principal investigator**

<b>Name:</b>	Jeff Dixon
<b>Dept and Institution:</b>	CIHR Group in Skeletal Development and Remodeling The University of Western Ontario
<b>Complete mailing address:</b>	Dr. S. Jeffrey Dixon CIHR Group in Skeletal Development and Remodeling Schulich School of Medicine & Dentistry The University of Western Ontario London, Ontario, Canada N6A 5C1
<b>Phone:</b>	519-661-3769
<b>Email:</b>	jeff.dixon@schulich.uwo.ca

**Please indicate if you are member or affiliate of one or more of the following International Partnership Initiative organizations:**

- AO Foundation – Biotechnology Advisory Board, Switzerland
- Arthritis Foundation, USA
- Arthritis Research Campaign, UK
- Canadian Arthritis Network, Canada
- Japan Society for the Promotion of Science, Japan
- Nuffield Foundation Oliver Bird Rheumatism Program, UK

**International Research & Training Program Opportunity**

**Please indicate which of the following international opportunities would be available at your laboratory/clinic.**

- Training Elective Rotation
- Research Mini-sabbatical
- Industry Training Rotation



**The International Research & Training Program will be available for trainee elective rotations and investigator mini-sabbaticals that commence on or before March 31, 2009. If you have any preferences regarding the dates when you can host an international trainee or investigator, please indicate this below.**

<b>Visit Length</b> (please indicate start and end dates if known):	Flexible
---	----------

**Please provide ten key words and a brief description of the research currently being conducted in your laboratory/clinic, including descriptions of any specialized equipment, methods or technologies employed at your facility.**

**10 key words**

1. bone and cartilage
2. cell and molecular biology
3. ion transport
4. signal transduction
5. cytosolic calcium and pH
6. live-cell imaging
7. patch-clamp electrophysiology
8. receptors
9. microphysiometry
10. fluorescence spectrophotometry

**Brief description (up to ½ page)**

Our research focuses on cellular and molecular mechanisms underlying the formation and destruction of bone and cartilage. We study the function and regulation of osteoblasts (bone forming cells), chondrocytes (cartilage forming cells) and osteoclasts (bone resorbing cells). Bone loss in inflammatory and metabolic diseases arises from imbalance between the rates of bone formation and resorption. Therefore, goals are to understand the physiological regulation of these processes and to identify therapeutic agents that inhibit loss of bone and cartilage. Cell behavior is investigated using a variety of approaches, including fluorescence spectrophotometry, patch-clamp electrophysiology, microphysiometry, live-cell imaging and molecular biology. Studies are supported by the Canadian Institutes of Health Research (CIHR), The Arthritis Society (jointly with CIHR), pharmaceutical and biotech industries, and the Canadian Arthritis Network (CAN).

We are part of the CIHR Group in Skeletal Development and Remodeling ([www.cihrskeletal.ca](http://www.cihrskeletal.ca)), whose interests include the developmental biology of cartilage and bone, biomineralization, extracellular matrix, signal transduction and membrane biophysics. This interdisciplinary research group is housed within new laboratories equipped with state-of-the-art instrumentation. Experimental approaches include molecular dynamics, physical & protein chemistry, molecular & cellular biology including gene array analyses, functional genomics including genetically modified mouse models, patch-clamp electrophysiology and fluorescence imaging. The goal of our research is to develop new approaches for the prevention, diagnosis and treatment of musculoskeletal and dental diseases.

**Key publications** (maximum 5 publications)

Komarova, S.V., Pereverzev, A., Shum, J.W., Sims, S.M. and Dixon, S.J. Convergent signaling by acidosis and receptor activator of NF- $\kappa$ B ligand (RANKL) on the calcium/calcineurin/NFAT pathway in osteoclasts. *Proc. Natl. Acad. Sci. USA* 102: 2643-2648, 2005.

Korcok, J., Raimundo, L. N., Du, X., Sims, S. M. and Dixon, S. J. P2Y6 nucleotide receptors activate NF- $\kappa$ B and increase survival of osteoclasts. *J. Biol. Chem.* 280: 16909-16915, 2005.

Jones, D. H., Nakashima, T., Sanchez, O. H., Kozieradzki, I., Komarova, S. V., Sarosi, I., Morony, S., Rubin, E., Sarao, R., Hojilla, C. V., Komnenovic, V., Kong, Y. Y., Schreiber, M., Dixon, S. J., Sims, S. M., Khokha, R., Wada, T. and Penninger, J. M. Regulation of cancer cell migration and bone metastasis by RANKL. *Nature* 440: 692-696, 2006.

Roy, A.A., Nunn, C., Ming, H., Zou, M.-X., Penninger, J., Kirshenbaum, L.A., Dixon, S.J. and Chidiac, P. Up-regulation of endogenous RGS2 mediates cross-desensitization between Gs and Gq signaling in osteoblasts. *J. Biol. Chem.* 281: 32684-32693, 2006.

Panupinthu, N., Zhao, L., Possmayer, F., Ke, H.Z., Sims, S.M. and Dixon, S.J. P2X7 nucleotide receptors mediate blebbing in osteoblasts through a pathway involving lysophosphatidic acid. *J. Biol. Chem.* 282: 3403-3412, 2007.