



**Canadian Arthritis Network
International Partnership Initiative**

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

Contact information of the principal investigator

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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.

Visit Length (please indicate start and end dates if known):	
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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

<ol style="list-style-type: none">1. Biomineralization2. Hydroxyapatite3. Calcium oxalate4. Osteopontin5. Confocal microscopy6. Autotitration7. Molecular dynamics8. Peptide synthesis9. Site-directed mutagenesis10. Mass spectrometry
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Brief description (up to ½ page)

<p>My research program is directed at understanding how extracellular-matrix proteins regulate physiological and pathological forms of biomineralization. Currently we are studying the phosphoprotein osteopontin (OPN), which is a potent inhibitor of both calcium oxalate, the principal mineral phase of kidney stones, and hydroxyapatite, the mineral phase found in bone, atherosclerotic plaque and calcified cartilage. Using scanning confocal microscopy, we showed that fluorescence-labelled OPN adsorbs preferentially to edges of calcium oxalate crystals, causing them to develop a “dumbbell” morphology (ref. 1). By mass spectrometry, we identified 29 sites of phosphorylation in the rat bone isoform of OPN, although only about a third of these are modified in the average protein molecule (ref. 2). Subsequently, we synthesized peptides corresponding to highly phosphorylated OPN sequences and showed that these differ in ability to inhibit hydroxyapatite crystal formation (ref. 3). Another OPN phosphopeptide adsorbs specifically to {100} faces of calcium oxalate crystals and inhibits growth perpendicular to these faces. Using molecular dynamics, we found that, although phosphate groups are required for strong adsorption of peptides to the {100} face, it is carboxylate groups of aspartic and glutamic acid that form the closest contacts with calcium ions of the crystal (unpublished). In future studies, we plan to use the above-mentioned techniques to develop potent and specific inhibitors of hydroxyapatite and calcium oxalate crystal formation that can be used in the prevention of atherosclerosis, crystal arthropathies and kidney stone disease.</p>
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Key publications (maximum 5 publications)

A. Taller, B. Grohe, K.A. Rogers, H.A. Goldberg and G.K. Hunter. Specific adsorption of osteopontin and synthetic polypeptides to calcium oxalate crystals. *Biophysical Journal* (in press).

M. Keykhosravani, A. Doherty-Kirby, C.J. Zhang, H.A. Goldberg, G.K. Hunter and G. Lajoie. Comprehensive identification of posttranslational modifications of rat bone osteopontin by mass spectrometry. *Biochemistry* **44**, 6990-7003 (2005).

D.A. Pampena, K.A. Robertson, O. Litvinova, G. Lajoie, H.A. Goldberg and G.K. Hunter: Inhibition of hydroxyapatite formation by osteopontin phosphopeptides. *Biochemical Journal* **378**, 1083-1087 (2004).

B. Grohe, K.A. Rogers, H.A. Goldberg and G.K. Hunter: Crystallization kinetics of calcium oxalate hydrates studied by scanning confocal interference microscopy. *Journal of Crystal Growth* **295**, 148-157 (2006).