



**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):	None
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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

1. Molecular biology (cloning, PCR, site directed mutagenesis, expression vectors, gene expression, reporter vectors, gene transfection, EMSA, etc.)
2. Zymography (measure of MMP activity)
3. Confocal microscopy (GFP, RFP, etc)
4. Transgenic and KO mouse models
5. Quantitative RT-PCR
6. Western blot analysis, ELISA, etc.
7. Epigenetics (ChIP, DNA methylation, etc)
8. Fluorescent-Activated Substrate Conversion Assay (FASC)
- 9.
- 10.

Brief description (up to ½ page)

Matrix Metalloproteinases (MMP) are members of a family of extracellular enzymes involved in the degradation of extracellular matrix. The elevated levels of MMPs and most notably of MMP-9, in serum or in synovial fluids (SF) have been shown to reflect the degenerative conditions of the joints resulting from an alteration in the equilibrium between proteases and their inhibitors. As the future of therapy might have to rely more and more on selective approaches, our lab is investigating the molecular mechanisms regulating the expression MMPs. Indeed, as the number of inflammatory diseases continues to increase, understanding the role of the molecules implicated in the signalling pathways leading to the expression of this enzyme has become a priority in order to identify the therapeutic targets that will allow to selectively inhibit its expression. Our laboratory has also developed a method, the fluorescent activated substrate conversion (FASC) assay, which allows efficient and reproducible measurement of proteolytic activity by flow cytometry. We have used this method to monitor the net proteolytic activity in SF of patients suffering from joint diseases, including RA. Overall, our research program will allow us to better understand the contribution of active proteases in arthritis and to develop relevant clinical approaches against this disease.

Key publications (maximum 5 publications)

- 1.- Simard N., Boire, G., de Brum Fernandes, A., and St-Pierre Y. 2006. Heterogeneity in the contribution of MMPs in the overall net proteolytic activity in synovial fluids of patients with different forms of arthritis. *Arthritis Res Ther.* Jul 19;8(4):R125



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- 2.- Couillard, M., Demers M, Lavoie G, and St-Pierre Y. 2006. The role of DNA hypomethylation in the control of stromelysin gene expression. *Biochem Biophys Res Commun* 21;342(4):1233-9.
- 3.- Demers M, Magnaldo T, and St-Pierre Y. 2005. A novel function for galectin-7: promoting tumorigenesis by upregulating MMP-9 gene expression. *Cancer Research* Jun 15;65(12):5205-10.
- 4.- Esteve PO, Chicoine E, Robledo O, Aoudjit F, Descoteaux A, Potworowski EF, St-Pierre Y. 2002. Protein kinase c-zeta regulates transcription of the matrix metalloproteinase-9 gene induced by IL-1 and TNF-alpha in glioma cells via NF-kB. *Journal of Biological Chemistry*. Sep 20;277(38):35150-5.
- 5.- Champagne B, Tremblay P, Cantin A, and St-Pierre Y. 1998. 1998. Proteolytic cleavage of intercellular adhesion molecule-1 by human neutrophil elastase. *J Immunol* 161: 6398-6405.