

CURRICULUM VITAE

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EDUCATION

1995 - Ph.D. Microbiology and Immunology, University of Ottawa, Ottawa, ON
1988 - B.Sc. Honours, University of Ottawa, Ottawa, ON

APPOINTMENTS

Mar. 1, 2000 - Assistant Professor, Dept. of Medicine, University of Ottawa
1995 - 2000 Post-doctoral Fellow, MOBIX, Institute for Molecular Biology and Biotechnology, McMaster University

RESEARCH EXPERIENCE

1995 - 1999 Post-doctoral Fellowship, McMaster University
1) *The characterization of novel MyoD interacting proteins and the study of MyoD and myf-5 spatio-temporal expression in vivo through gene targeting of reporter constructs.*
2) *Cloning and characterization of a novel Ste20-related kinase involved in apoptosis and cytoskeletal reorganization.*

1990 - 1995 Graduate Student (Ph.D.), University of Ottawa

- 1) *Molecular cloning and characterization of a c-cbl related cDNA.*
 - 2) *Characterization of expression of the myotonic dystrophy kinase (DMK) gene and its role during myogenesis.*
- Thesis: "*Myotonic Dystrophy: A study of the expression of the myotonic dystrophy gene in affected tissues and cells.*"
- 1998 - 1990 Graduate Student (M.Sc.), University of Ottawa
Proto-oncogene expression and cell cycle regulation in IL-6-dependent hybridomas.
- 1988 Summer Student, University of Ottawa
Construction of retroviral vectors for gene transfer into eukaryotic cells.
- 1984 - 1988 Honours Student (B.Sc.), University of Ottawa
Thesis: "*Quantitation of c-fos mRNA in human granulocytes.*"
- 1987 Summer Student, University of Ottawa
Development of a rapid RNA extraction procedure for cultured cells.
- 1986 Summer Student, University of Ottawa
Organic synthesis and purification of natural hydrocarbons.

HONOURS AND AWARDS

- 1995 - 1998 Medical Research Council (Fellowship), McMaster University
- 1996 NSERC Doctoral Prize Nominee, University of Ottawa
- 1996 Governor General's Award Recipient, University of Ottawa
- 1992 - 1995 Medical Research Council (Ph.D. Studentship), University of Ottawa
- 1992 - 1995 U. of O. Scholarship (for MRC), University of Ottawa
- 1990 - 1992 FCAR Studentship (Ph.D.), University of Ottawa
- 1988 - 1993 Merit Entrance Scholarship, University of Ottawa
- 1988 - 1990 FCAR Studentship (M.Sc.), University of Ottawa
- 1985 - 1986 NSERC Studentship, University of Ottawa

TEACHING EXPERIENCE

Demonstrated (TA) or lectured in the following courses (University of Ottawa):

- | | |
|----------|---|
| BCH 2946 | Biochemistry |
| BCH 3126 | Physical Biochemistry |
| BCH 3946 | Metabolism |
| BCH 4106 | Molecular Biology |
| BCH 4F03 | Gene Expression (2 lecture series on the molecular control of myogenesis) |

RESEARCH INTERESTS

1) Plasticity and Cellular Remodeling

Cell survival, movement, differentiation and growth is dependent on interactions between cell surface proteins called integrins and components of the extracellular matrix. These interactions trigger the clustering of several signaling molecules on the cytoplasmic side of the cells at sites of adhesions. These activated signaling complexes then modulate the activity of various kinases and other signal transducers implicated in the control of cell shape, survival and proliferation. A number of processes such as growth cone progression, axonal guidance and tumor invasion are highly dependent on the activity of these signaling molecules.

Our laboratory has recently cloned a novel Ste20-related kinase involved in apoptosis and cytoskeletal remodeling. Overexpression of this novel kinase, termed SMAK, in a variety of cell types, induces cell death and disassembly of actin stress fibers and focal contacts. Using biochemical approaches and cell culture systems, we are currently focusing on the remodeling events and signaling pathways that are modulated by SMAK and the upstream signals that regulate its activity. Applying yeast two hybrid and in situ protein-protein interaction screens we are attempting to isolate SMAK binding proteins and substrates. In addition, gene knock-out and transgenic technology is currently being used in our laboratory to investigate the role of SMAK during embryonic development. We have already identified several oncogenes that regulate the activity of SMAK, suggesting a role for SMAK in tumorigenesis and invasiveness. Defining the pathways that regulate apoptosis and cellular remodeling will prove useful in the design of treatment against highly metastatic tumors and post-traumatic injuries such as ischemia.

2) Myotonic Dystrophy

Myotonic Dystrophy (DM) is an autosomal dominant heritable disorder that affects 1 in 8000 individuals globally. DM is caused by the expansion of a polymorphic (CTG)_n repeat found in the 3' untranslated region of a serine/threonine protein kinase (DMPK). The adult onset of DM is characterized mainly by myotonia, progressive muscle wasting and cardiac conduction defects. Severe congenital cases display hypotonia, developmental defects and mental retardation. The mechanisms by which the CTG repeat expansion mediates the DM phenotype is still elusive and the normal function of the DMPK protein is still unknown. In addition, to date, there are no animal models allowing the investigation of the mechanisms underlying the pathogenesis of DM *in vivo*.

Our laboratory focuses on the biochemical characterization of DMPK using cell culture and transgenic approaches. We are investigating the signaling pathways that regulate DMPK activity as well as the characterization of DMPK signal effector proteins. In addition, our laboratory has initiated the generation of transgenic animal models for DM using the Cre-loxP recombination technology. This novel approach will allow the production of animals that can be induced to express the DM mutation in a time-

dependent and tissue-specific manner. This system will allow the investigation of the mechanisms underlying DM *in vivo* and *in vitro* using primary cultures derived from DM animals. The establishment of a DM animal model will provide a system in which potential therapies can be tested and evaluated.

RESEARCH KEYWORDS

- transgenic
- knock-out
- plasticity
- apoptosis
- cellular remodeling
- signal transduction
- cancer
- myotonic dystrophy

RESEARCH TRAINEES

Professor Sabourin is currently accepting applicants for graduate studies. Research areas of interest are outlined in the NRI RESEARCHERS section of this website as well as in this curriculum vitae.

PUBLICATIONS (PEER-REVIEWED PAPERS)

- + abstracts for publications denoted with an asterisk are found later in this homepage
1. Hawley TS, Sabourin LA, Hawley RG (1989) Comparative analysis of retroviral vector expression in mouse embryonal carcinoma cells. *Plasmid* 22: 120-131.
 2. Hawley RG, Sabourin LA, Hawley TS (1989) An improved retroviral vector for gene transfer into undifferentiated cells. *Nucl Acids Res* 17: 4001.
 3. Sabourin LA, Hawley RG (1990) Suppression of programmed death and G1 arrest in B-cell hybridomas by interleukin-6 is not accompanied by altered expression of immediate early response genes. *J Cellular Physiol* 145: 564-574.
 4. Jansen G, Mahadevan M, Amemiya C, Wormskamp N, Segers B, Hendriks W, O'Hoy K, Baird S, Sabourin L, Lennon G, Jap PL, Iles D, Coerwinkel M, Hofker M, Carrano AV, de Jong PJ, Korneluk RG, Wieringa B (1992) Characterization of the myotonic dystrophy region predicts multiple protein isoform-encoding mRNAs. *Nature Genetics* 1: 261-266.

5. Mahadevan M, Tsilfidis C, Sabourin L, Shutler G, Amemiya C, Jansen G, Neville C, Narang M, Barcelo J, O'Hoy K, Lebond S, Earle-Macdonald J, de Jong PJ, Wieringa B, Korneluk RG (1992) Myotonic dystrophy mutation: an unstable CTG repeat in the 3' untranslated region of the gene. *Science* 255: 1253-1255.
6. Mahadevan MS, Amemiya C, Jansen G, Sabourin L, Baird S, Neville CE, Wormskamp N, Segers B, Batzer M, Lamerdin J, de Jong P, Wieringa B, Korneluk RG (1993) Structure and genomic sequence of the myotonic dystrophy (DM kinase) gene. *Hum Mol Gen* 2: 299-304.
- +7. Sabourin LA, Mahadevan M, Narang M, Lee DSC, Surh LC, Korneluk RG (1993) Effect of the myotonic dystrophy (DM) mutation on mRNA levels of the DM gene. *Nature Genetics* 4: 233-238.
8. Mahadevan MS, Baird S, Bailly JE, Shutler GG, Sabourin LA, Tsilfidis C, Neville CE, Narang M, Korneluk RG (1995) Isolation of a novel G protein-coupled receptor (GPR4) localized to chromosome 19q13.3. *Genomics* 30: 84-88.
9. Waring JD, Haq R, Tamai K, Sabourin LA, Ikeda JE, Korneluk RG (1996) Investigation of myotonic dystrophy kinase isoform translocation and membrane association. *J Biol Chem* 271: 15187-15193.
- +10. Sabourin LA, Tamai K, Narang MA, Korneluk RG (1997) Over-expression of 3' untranslated region of the myotonic dystrophy kinase cDNA inhibits myoblast differentiation in vitro. *J Biol Chem* 272: 29626-29635.
11. Storbeck C, Sabourin LA, Waring JD, Korneluk RG (1998) Definition of regulatory sequence elements in the promoter region and the first intron of the myotonic dystrophy protein kinase gene. *J Biol Chem* 273: 9139-9147.
12. Sabourin LA, Girgis-Gabardo A, Seale P, Asakura A, Rudnicki MA (1999) Reduced differentiation potential of primary *MyoD*^{-/-} myogenic cells derived from adult skeletal muscle. *J Cell Biol* 144: 631-643.
- +13. Sabourin LA, Rudnicki MA (1999) Induction of apoptosis by SLK, a Ste20-related kinase. *Oncogene* 18: 7566-7575.
- +14. Sabourin LA, Seale P, Wagner J, Rudnicki MA (2000) Caspase 3 cleavage of the Ste20-related kinase SLK releases and activates an apoptosis-inducing kinase domain and an actin disassembling region. *Mol Cell Biol*. 20: 684-696.
15. Sabourin LA, Rudnicki MA (1999) The molecular control of myogenesis. *Clin Genet*. (in press)
16. Narang MA, Sabourin LA, Waring JD, Simpson J, Kryskwa E, Rajcan-Separovic D, Parry F, Jirik F, Korneluk RG (1999) Over-expression of the human myotonic dystrophy kinase gene (DMK) in transgenic mice causes a DM-like myopathy. (submitted)
17. Sabourin LA, Hirst M, Rudnicki MA, Sadowski I (1999) Identification of SNF2H as a MyoD-binding protein by reverse two hybrid: a novel system for the isolation of proteins that interact with transactivators. *Proc Natl Acad Sci USA*. (submitted)
18. Hirst M, Sabourin LA, Rudnicki MA, Sadowski I (1999) A yeast two hybrid system for characterization: an identification of proteins that interact with transactivators in vivo. *Proc Natl Acad Sci USA*. (submitted)

INVITED PRESENTATIONS AND PARTICIPATION AT SCIENTIFIC MEETINGS

Poster Presentations:

- 02/90 First Winternational Cell Cycle Symposium, Ste-Foy, QC; Suppression of programmed death and G₁ arrest in B-cell hybridomas by interleukin-6 is not accompanied by altered expression of immediate early response genes.
- 11/92 Am. Soc. of Human Genetics, 42nd Ann Mtg, San Francisco, CA; Myotonic dystrophy: transcriptional repression of the DM kinase gene in affected individuals is not an immediate effect of CTG trinucleotide expansion.
- 06/93 Genetics Soc. of Canada, Manoir du Lac Delage, QC; Investigation of the role of the myotonic dystrophy kinase (DMK) in the differentiation of cultured myoblasts.
- 09/93 Am. Soc. of Human Genetics, 43rd Ann Mtg, New Orleans; Investigation of the role of the myotonic dystrophy kinase (DMK) in the differentiation of cultured myoblasts.
- 01/94 Muscular Dystrophy Assoc (USA), Tucson, AZ; Over-expression of the myotonic dystrophy kinase (DMK) inhibits muscle terminal differentiation.
- 04/94 Molecular Biology of Muscle Development, Keystone Symposia, Snowbird; Over-expression of the myotonic dystrophy kinase (DMK) inhibits muscle terminal differentiation.
- 10/94 Am Soc of Human Genetics, 44th Ann Mtg, Montreal, QC; Effect of the myotonic dystrophy kinase on the terminal differentiation of myoblasts in culture.
- 10/95 Am Soc of Human Genetics, 45th Ann Mtg, Minneapolis; Over-expression of the myotonic dystrophy kinase (DMK) 3' untranslated region inhibits terminal differentiation of myoblasts in vitro.
- 04/97 Molecular Biology of Muscle Development, Keystone Symposia, Snowmass; Molecular cloning of MyoD-interacting proteins using two hybrid screens.
- 03/98 Signalling in Normal and Cancer Cells, 4th Conference, Banff, AB; SLK1, a novel mammalian protein kinase related to STE20.
- 09/99 EMBO Workshop: The Biology of Muscle Development, Irsee, Germany; Identification of SNF2H as a MyoD-binding protein by reverse two hybrid: a novel system for the isolation of proteins that interact with transactivators.

Presentations:

- 06/93 Genetics Soc of Canada, Manoir du Lac Delage, QC; Investigation of the role of the myotonic dystrophy kinase (DMK).
- 10/94 Am Soc of Human Genetics, 44th Ann Mtg, Montreal, QC, Plenary Session; Effect of the myotonic dystrophy kinase on the terminal differentiation of myoblasts in culture.
- 10/95 Am Soc of Human Genetics, 45th Ann Mtg, Minneapolis, Myotonic Dystrophy Workshop; Over-expression of the myotonic dystrophy kinase (DMK) 3' untranslated region inhibits terminal differentiation of myoblasts in vitro.

Updated Apr. 18, 2000