

## CURRICULUM VITAE

### John HISCOTT

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[www.johnhiscottlab.ca](http://www.johnhiscottlab.ca)

### PRESENT POSITIONS

2009	Associate Director, Lady Davis Institute
1996 - present	Professor Departments of Microbiology & Immunology, Medicine and Oncology, McGill University
1992 - 2008	Director, Molecular Oncology Group
1984 - present	Staff Investigator, Lady Davis Institute for Medical Research

### PREVIOUS POSITIONS HELD

1991-1996	Associate Professor Departments of Microbiology and Immunology, Medicine and Oncology, McGill University
1985 - 1990	Assistant Professor Department of Microbiology & Immunology, McGill University
1982 - 1984	Postdoctoral Fellow Institut für Molekularbiologie, Universität Zürich
1981	Postdoctoral Fellow Roche Institute for Molecular Biology, Nutley NJ

### EDUCATION

1976 - 1980	Ph.D.	Basic Medical Sciences Department of Pathology, NYU Medical Center (Supervisor: Dr. Vittorio Defendi)
1973 - 1975	M.Sc.	Cancer Research Laboratory University of Western Ontario
1969 - 1973	B.Sc. (Honours)	Bacteriology and Immunology University of Western Ontario

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### HONOURS AND AWARDS

2008	Award for Excellence in Medical Research Jewish General Hospital
2006	15 <sup>th</sup> Allan Granoff Lecturer in Virology St. Jude Children's Research Hospital
2004	Richard Klein Memorial Lecture Dept. of Microbiology, NYU Medical Center
2003	Recipient of the 2003 Milstein Award International Society for Interferon and Cytokine Research (shared with Dr. Tom Maniatis, Harvard University)
2003-2008	Senior Investigator Canadian Institutes of Health Research
1998-2003	Senior Scientist Award Medical Research Council of Canada
1999-present	Canadian Who's Who
1993 - 1998	Medical Research Council Scientist Award
1993 – 1998	Senior chercheur boursier (Merit Exceptionnel) Fonds de la Recherche en Sante du Quebec (declined)
1996, 2003	Elliott Osserman Award for Distinguished Service Israel Cancer Research Fund, New York
1990 - 1993	Senior chercheur boursier Fonds de la Recherche en Sante du Quebec
1985 - 1990	Medical Research Council of Canada Scholarship
1982 - 1983	Leukemia Society of America Post-doctoral Fellowship
1981	Hoffmann-LaRoche Postdoctoral Fellowship
1973 - 1975	Medical Research Council of Canada Studentship

### SOCIETY MEMBERSHIPS

1984 - present	American Society for Microbiology
1984 - present	International Society for Interferon & Cytokine Research
1991 - present	American Society for Cancer Research
1999 - present	International Cytokine Society
1999 – present	American Association of Immunologists

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## **RESEARCH CONTRIBUTIONS**

Throughout my scientific career, I have been interested in the pathogenic consequences of virus-cell interactions at the molecular level. During graduate studies at NYU Medical Center with Dr. Vittorio Defendi (1976-80), I examined SV40 mediated cellular transformation by temperature sensitive mutants of **SV40 large T antigen** and the structure of viral integration sites in transformed cells (published in *Cell*, *PNAS*, *J. Virol.*, and *Cold Spring Harbor Symp.*, 1979-81). At the University of Zurich with Dr. Charles Weissmann (1982-84), I investigated virus-cell interactions from a different perspective – the activation of interferon genes as a response to virus infection, utilizing the newly cloned **interferon gene family** in the first studies to describe the differential IFN gene expression after virus infection (published in *Proc. Royal Soc.* and *Nucleic Acids Res.*)

At the Lady Davis Institute/McGill University (1985-present), I initiated studies to examine the molecular basis of differential regulation of IFN gene expression. A watershed discovery was the realization that the newly identified **NF- $\kappa$ B** transcription factor was involved in regulating IFN $\beta$  but not IFN $\alpha$  gene transcription, thus providing a molecular basis for differential control of IFN genes (*Mol. Cell Biol.*, *J. Virol.*, and *J. Biol. Chem.*, 1987-1989). The fact that NF- $\kappa$ B factors regulated multiple immune response and inflammatory genes, including many cytokines, as well as the HIV LTR, prompted an investigation of the coordinate **regulation of HIV-1 and cytokine gene expression** in collaboration with my colleague Dr. Mark Wainberg. We initially described and characterized a new myelomonoblastic cell line PLB-985 chronically infected with HIV-1 and demonstrated virus dependent monocytic differentiation, aberrant cytokine gene expression, and constitutive activation of NF- $\kappa$ B/Rel, as a consequence of HIV infection, the first demonstration of NF- $\kappa$ B dysregulation during HIV infection (*J. Exp. Med.*, *J. Virol.*, *J. Immunol.*, 1990-1993). During that period, we also investigated the mechanisms by which the **human T cell leukemia virus and the Tax oncoprotein** modified the regulation of the NF- $\kappa$ B/Rel transcription factor family. (*Oncogene*, *J. Virol.*, and *Virology*, 1994-1995), including analysis of the protein-protein interactions that control the **I $\kappa$ B $\alpha$**  regulatory inhibitor (*PNAS*, *J. Virol.*, *Mol. Cell. Biol.*, 1994,1996-97). Using transdominant mutants of I $\kappa$ B, we demonstrated that I $\kappa$ B expression blocked NF- $\kappa$ B gene activation and dramatically interfered with HIV-1 multiplication, suggesting a strategy to interfere with HIV multiplication (*J. Biol. Chem.*, *J. Virol.* 1998-99).

During the past decade, the evolution of these complementary themes has included important contributions in the areas of virology, immunology and cancer biology.

1) Research from our laboratory provided major contributions to a new paradigm of IFN gene regulation, involving positive stimulatory amplification of IFN expression through the combined activities of **IRF-3 and NF- $\kappa$ B** as primary triggers of IFN production and **IRF-7** as secondary amplifier of the IFN response (*Mol. Cell. Biol.*; *PNAS*; *JBC* 1998-2000). A particularly gratifying discovery in 2002 was the identification of a critical missing link in the understanding of interferon signaling - the virus-activated kinase (VAK) activity that targets IRF-3 and IRF-7. We demonstrated for the first time that the IKK-related kinases – **IKKepsilon/TBK-1** - are components of VAK that mediate IRF-3 and IRF-7 phosphorylation and thus functionally link the NF- $\kappa$ B and IRF pathways in the development of the antiviral response (*Science*, 2003; *J. Virol.* 2004). Since that time, IRF-3 and IRF-7, as well as the IKK-related kinases, are now regarded as master regulators of type 1 IFN activation and are firmly integrated within the TLR-dependent and -independent pathways of the innate immune response to viral pathogens (*J. Immunol.* 2006; *Nature Immunol.* 2007; *Mol. Cell. Biol.* 2009; *Eur. J. Immunol.* 2009).

2) In adult T cell leukemia, the viral Tax oncogene reprograms host transcriptional signaling through its ability to interface with host signaling pathways. One such Tax-induced alteration that appears crucial to T cell leukemogenesis involves the lymphoid restricted **IRF-4** factor that is constitutively expressed in HTLV-I infected T cells. IRF-4 functions in the T cell context predominantly as a repressor of gene expression and

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modulates the expression of many transformation related gene families, including protein kinases, tumor suppressors and cell cycle proteins (J. Immunol, Oncogene, 2002). A physiological interaction was characterized between **IRF-4 and the immunophilin FKBP52**, the first demonstration of a post-translational mechanism of transcriptional control, mediated through the interaction of an immunophilin with a transcriptional protein (Immunity, 2000). The failure of conventional chemotherapy in the treatment of acute ATL prompted us to consider the use of an oncolytic virus approach to target the CD4+ CD25+ leukemic T cells. Importantly, VSV cell killing was only observed in CD4+CD25+ leukemic but not in CD4+CD25- non-leukemic cells. These findings represent the first essential information for the development of a VSV-based treatment for ATL (Oncogene 2006; J. Virol. 2008).

In collaboration with Drs. Raymond Cesaire and Agnes Lezin from the INSERM unit in Martinique, we have access to a unique cohort of patients with HTLV-1 associated diseases - asymptomatic carriers (AC), patients who are newly diagnosed with acute ATL, and patients diagnosed with HAM/TSP. To better understand the genetic differences between the HTLV-1- associated diseases, we examined gene expression profiles of CD4+ T cells isolated from this unique cohort of 31 patients with HTLV-1 associated diseases to identify markers of disease progression. Using a genomics approach followed by bioinformatics analysis, predictive relationships have been established that may ultimately link gene profiles to an HTLV disease outcome (Oliere et al, 2008; 2009)

3) We have studied the subtype specific differences in African, Asian and North American HIV subtypes with regard to promoter architecture and interaction with **NF- $\kappa$ B**, **Tat** and the **pTEFb** elongation complex (Virology, 2002). Functional distinctions in promoter architecture between HIV subtypes raise the possibility that regulatory divergence has occurred amongst the subtypes of HIV-1 that may explain differences in virus replication and transmission (J. Virol. 2005, 2006).

4) We have explored a novel virus-based approach to biological therapy of cancer, involving **oncolytic viruses**. During the evolution of malignancies, genetic abnormalities accumulate that, while providing the cancer cells with growth and survival advantages, compromise the normal antiviral program of transformed cells. Defects in the interferon antiviral response in transformed cells have been implicated in tumor-specific oncolysis, a strategy termed **virotherapy**. IFN-related defects allow VSV and other oncolytic viruses to replicate to high titers, uninterrupted by the host antiviral response, resulting in high virus production and virus-induced lysis (Cancer Cell 2003). With the support of the Terry Fox Foundation, a multi-center program, headed by Dr. John Bell, has been initiated to accelerate the development of candidate oncolytic virus therapeutics. Candidate viruses at all stages of development are being studied, with the goal to combine scientific and clinical expertise to foster the generation of new therapeutics and clinical approaches. This project functions in the context of the Canadian Oncolytic Virus Consortium (COVCo), a network of clinicians and scientists dedicated to developing novel oncolytic virus therapeutics.

Although virotherapy with VSV is often highly effective against a variety of cancer cells, many primary tumor cells are highly resistant to VSV oncolysis. Recently, we discovered that resistant cells may be sensitized to VSV-mediated killing by treating tumor cells with compounds that increase cell death or block the IFN response. Current projects seek to evaluate the efficiency of combination therapies in VSV-resistant cancer models using: 1) the combination of VSV and anti-apoptotic Bcl-2 inhibitors in chronic lymphocytic leukemia (Tumilasci, J. Virol. 2008); and 2) the combination of VSV and histone deacetylase inhibitors in a variety of resistant cancers (Nguyen et al, Proc. Natl. Acad. Sci. USA 2008). The general utility of HDIs as chemical switches to regulate cellular innate antiviral responses and to provide controlled growth of therapeutic viruses within malignancies may have a positive impact on the clinical implementation of oncolytic virus therapeutics by improving the spectra of oncolytic viruses as anti-cancer agents. Because of differences in mechanisms of action and toxicity, these combinations of oncolytic viruses with pro-apoptotic or anti-cancer agents may have clinical potential with greater efficiency and less toxicity than either agent alone.

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### McGILL UNIVERSITY ACADEMIC RESPONSIBILITIES

1997-present	Viral Pathogenesis and Immunity 528-466B Dept. of Microbiology and Immunology Lectures on: viral pathogenesis and evasion of the immune response; molecular biology of interferons and induction by viruses; human retroviruses; mechanism of antiviral action of interferons and other cytokines; HTLV-1 pathogenesis (Course Coordinator 1997-2000)
2002	Graduate Readings and Conference Dept. of Microbiology and Immunology Viral Evasion of the Host Immune Response (Course Coordinator)
1995-present	Fundamental Virology 324A Dept. of Microbiology and Immunology
1993	Graduate Readings and Conference -705 Dept. of Microbiology and Immunology
1985-1996	Infection and Immunity - 466B Dept. of Microbiology and Immunology
1987-2000	Physiology of Blood - 516B Dept. of Physiology
1988-1990	Fundamental Virology - 324A Dept. of Microbiology and Immunology
1989	Graduate Readings and Conference -705 Dept. of Microbiology and Immunology

### CURRENT GRADUATE STUDENTS (DEPTS. OF MICROBIOLOGY AND MEDICINE)

Mayra Solis	PhD 4 (Microbiology & Immunology) - Recipient of a CIHR Studentship
Stephanie Oliere	PhD 4 (Microbiology & Immunology) - Recipient of a FRSQ Studentship
Suzanne Paz	PhD 4 (Microbiology & Immunology) - Recipient of a FRSQ Studentship
Peyman Nakhaei	PhD 4 (Microbiology & Immunology) - Recipient of a FRSQ Studentship
Vanessa Tumilasci	PhD 4 (Experimental Medicine) - Recipient of a NSERC Studentship
Simone Leveille	PhD 2 (Microbiology & Immunology) - Recipient of a NSERC Studentship
Sara Samuel	PhD 2 (Microbiology & Immunology)

### CURRENT POST-DOCTORAL FELLOWS

Thi Lien Anh Nguyen (PhD, Universite Libre de Bruxelles) – Recipient of FRSQ Fellowship  
Meztli Arguello, (PhD, McGill University)  
Renee Douville (PhD, University of Manitoba)  
Steve Werden (PhD, University of Florida)  
Mehdi Belgnaoui (PhD, Eastern Virginia Medical Center)

### CURRENT RESEARCH ASSOCIATES

TJ Zhao, PhD	Research Associate, HCV Program
Qiang Sun PhD	Research Associate, IFN Signaling
Marie-Line Goulet	Research Assistant, Oncolytic Viruses

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### PREVIOUS GRADUATE STUDENTS

1. Steven Xanthoudakis      Ph.D. 1990  
Regulation of the Human Interferon  $\beta$  Promoter (Dean's Honours List)
2. Deborah Alper              M.Sc. 1990  
Characterization of mechanisms regulating induction of human IFN alpha and beta gene transcription.
3. Jean-Francois Leblanc      M.Sc. 1990  
Functional analysis of human interferon beta gene transcriptional regulatory elements
4. Lucie Cohen                Ph.D. 1992  
Regulation of human interferon beta gene expression: in vitro studies
5. Mario D'Addario            M.Sc. 1992  
Cytokine gene expression in human immunodeficiency virus infected myeloid cells.
6. Amir Mustafa              M.Sc. 1994  
Mutational analysis of interferon regulatory factors - IRF-1 and IRF-2.
7. Vanessa McKiel            M.Sc. 1994  
Cytokine induced alterations in human immunodeficiency virus multiplication.
8. Judith Lacoste              Ph.D. 1995  
HTLV-I Tax Interactions with the NF- $\kappa$ B/I $\kappa$ B Regulators of Transcription (Dean's Honours List)
9. Anne Roulston              Ph.D. 1995  
Regulation of NF-kappaB dependent cytokine gene expression in chronically HIV-1 infected myeloid cells.
10. Richard Bitar              M.Sc. 1995  
Retrovirus mediated transfer of NF- $\kappa$ B subunit genes modulates I $\kappa$ B $\alpha$  and IFN- $\beta$  expression.
11. Pierre Beuparlant        Ph.D. 1996  
Control of gene expression and cell growth by the NF- $\kappa$ B/I $\kappa$ B family of transcription regulators.  
(Dean's Honours List)
12. Raymond Lee              M.Sc. 1997  
Inhibition of NF- $\kappa$ B activation and HIV-1 gene expression by antioxidants.
13. Hannah Nguyen            Ph.D. 1998  
Regulation of gene expression and cell growth by transcriptional proteins of the IFN system (Honours List)
14. William Spencer          M.Sc. 1998  
Phorbol ester mediated NF- $\kappa$ B transactivation is selectively inhibited by Taxol.
15. Louisa Petropoulos        Ph.D. 1998  
Molecular interactions between HTLV-1 Tax oncoprotein and the NF- $\kappa$ B/I $\kappa$ B Transcription Regulators.

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16. Carmela DeLuca                      Ph.D. 1999  
Molecular analysis of NF- $\kappa$ B activation in HIV-1 infected myeloid cells.
17. Christophe Heylbroeck            M.Sc. 1999  
Role of IRF-3 in cytokine gene activation.
18. Hakju Kwon                            Ph.D. 2000  
Use of mutants of I $\kappa$ B to interfere with NF- $\kappa$ B gene activation and HIV replication
19. Tudor Baetu                            MSc 2001  
Role for NF- $\kappa$ B in the regulation of TNF $\alpha$  related apoptosis inducing ligand (TRAIL) expression.
20. Yael Mamane                          PhD 2002  
Regulation of IRF-4 activity in lymphoid cells and involvement in HTLV-1 induced T cell leukemogenesis.
21. Delphine Duguay                    MSc 2004  
Characterization of the tumor suppressor activity of IRF3.
22. Sonia Sharma                          PhD 2004  
IKK Kinases control activation of interferon regulatory factor signaling (Dean's Honor List)
23. Benjamin tenOever                  PhD 2004  
Recognition of RNA virus infection leading to activation of IRF3 and IRF7.
24. Yan Desfosses                        MSc 2005  
Regulation of HIV-1 gene expression by clade specific Tat proteins
25. Jennifer Harris                        MSc 2005  
Regulation of c-Rel phosphorylation by TBK1 and IKK $\epsilon$
26. Meztli Arguello                      PhD 2006  
Disruption of the B cell transcriptional program in primary effusion lymphoma
27. Myriam Vilasco                        PhD 2008 (Institut Pasteur, Université de Paris V)  
Role de la kinase IKK $\epsilon$  lors de l'infection par le virus de l'hépatite C
28. Delphine Goubau                      MSc 2008  
Distinct roles of IRF3 and IRF7 in the activation of the anti-tumor properties of human macrophages

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### PREVIOUS POST-DOCTORAL FELLOWS

Jacqueline Lanoix, PhD	Research Scientist in Biotech
Lucia Conti, PhD	Research Scientist, Istituto Superiore di Sanita, Rome
Stephane Dionne, PhD	Research Scientist, Biotech
Rongtuan Lin, PhD	Associate Professor, McGill University
Pascale Crepieux, PhD	Charge de Recherche, CNRS Tours France
Pierre Genin, PhD	Charge de Recherche, CNRS, Paris France
Rita Crinelli, PhD	Research Scientist, Universitat de Urbino Italy
Cecile LePage, PhD	Research Scientist, Notre Dame Hospital Montreal
Laura Faggioli, PhD	Research Scientist, University of Verona
Michele Algarte, PhD	Research Scientist, Hopital Necker, Paris France
Guo-Ping Zhou, MD	Associate Professor, Shanghai China
Marco Sgarbanti, PhD	Research Scientist, Istituto Superiore di Sanita, Rome
Marc Servant, PhD	Associate Professor, Universite de Montreal
Nathalie Grandvaux PhD	Assistant Professor, Universite de Montreal
Judith Lacoste, PhD	Director of Microscopy Services, McGill University
Raphaelle Romieu, PhD	Research Associate, Lady Davis Institute

### VISITING SCIENTISTS

Raymond Cesaire, MD – INSERM Fort-de-France Martinique 2002-2003  
Agnes Lezin, PhD - INSERM Fort-de-France Martinique 2003-2004  
Guy LeMay, PhD – Université de Montreal 2006-2007

### UNDERGRADUATE HONOURS STUDENTS

1. Adele Marshall	1986-1987 Dept. of Biology
2. Charles P. Tremblay	1987-1988 Dept. of Biology
3. Arthur Kania	1989-1990 Dept. of Microbiology and Immunology
4. Alex Ho	1989-1990 Dept. of Microbiology and Immunology
5. Alison Farrell	1991-1992 Dept. of Microbiology and Immunology
6. Lily Le	1992-1993 Dept. of Microbiology and Immunology
7. James Marois	1992-1993 Dept. of Microbiology and Immunology
8. Juan Carlos Guigon	1992 Univ. of Manitoba Medical School
9. Mila Oh	1992 McGill University Medical School
10. Michelle Clark	1994 -1995 Dept. of Microbiology and Immunology
11. Alissa Scalera	1994 -1995 Dept. of Microbiology and Immunology
12. John O'Grady	1995 -1996 Dept. of Microbiology and Immunology
13. Ivan Fong	1995 -1996 Dept. of Microbiology and Immunology
14. Lindsey Teskey	1997 -1998 Dept. of Microbiology and Immunology
15. Sonia Sharma	1998-1999 Dept. of Microbiology and Immunology
16. Oana Popescu	1999-2000 Dept. of Microbiology and Immunology
17. Guillaume Martell	2000-2001 Interdepartmental Honours in Immunology
18. Douglas Hayami	2001-2002 Interdepartmental Honours in Immunology
19. Jennifer Palmer	2002-2003 Dept. of Microbiology and Immunology
20. Catherine Corriveau	2003-2004 Dept. of Microbiology and Immunology
21. Steven Gowing	2005-2006 Dept. of Microbiology and Immunology
22. Hassan Tarique	2006-2007 Dept. of Microbiology and Immunology
23. James Zhang	2007-2008 Dept. of Biology, McGill

**Ph.D. THESIS COMMITTEES, Ph.D. ADVISORY COMMITTEES, COMPREHENSIVE EXAMINATION COMMITTEES:** I have served on over seventy Ph.D. student advisory and thesis defense committees.

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## **UNIVERSITY, HOSPITAL AND INTERNATIONAL CONTRIBUTIONS**

### **DEVELOPMENT OF THE TERRY FOX MOLECULAR ONCOLOGY GROUP**

**Dr. John Hiscott** is the Director of the Molecular Oncology Group at the Lady Davis Institute, a research team involved in the study of oncogenes, signal transduction and oncogenic development at the molecular level. The group includes internationally recognized scientists. Dr. Hiscott is studying transcriptional control of cytokine and oncogene expression; he is also studying the impact of human retrovirus infection on the expression of immunoregulatory genes and signalling through the NF- $\kappa$ B/rel pathway.

**Dr. Antonis Koromilas** is examining the role of a novel tumor suppressor gene - the interferon inducible p68 kinase - PKR - in cell growth, differentiation, and tumorigenesis.

**Dr. Wilson Miller** is examining differentiation inducing agents known as retinoids and has demonstrated that the retinoic acid receptor is chromosomally translocated in acute promyelocytic leukemia. Moreover, he and others have shown that retinoic acid is able to induce striking remission in the course of this type of leukemia.

**Dr. Stéphane Richard** has isolated a new family of RNA binding proteins - p62/SAM68 - which are involved in protein-RNA trafficking to and from the nucleus.

**Dr. Rongtuan Lin** is interested in cytokine gene transcription and has been examining the virus induced phosphorylation and degradation of IRF-3 and IRF-7 transcription factor.

**Dr. Anne Gatignol** is studying the mechanisms of transactivation of the HIV LTR by the Tat protein and by host cellular proteins involved in transcriptional initiation and elongation.

**Dr. Volker Blank** was recently recruited from the Children's Hospital, Harvard Medical School in Boston and is studying transcriptional control of gene expression during erythroid differentiation and development.

All members of the Group are independently funded (CIHR, NCI, FRSQ, Cancer Research Society) and all members of the Group now have independent salary support. Extensive discussions, collaborations and interactions amongst the Members of the Group occur on a daily basis. In part due to complementary research interests and in part to the scientific enthusiasm of a newly established team, this aspect of the Molecular Oncology and Virology Group creates an atmosphere that fosters training, education, development and discovery. We fully expect to see the emergence of new research directions, and the application of those discoveries to clinical care in the areas of cancer, AIDS and chronic inflammatory diseases.

### **CANADIAN INSTITUTES OF HEALTH GROUP PROGRAM IN AIDS PATHOGENESIS McGILL AIDS CENTER - John Hiscott and Mark Wainberg, co-Directors**

The McGill AIDS Centre Program Grant (2002-2007) entitled "Molecular Mechanisms Regulating HIV-1 Pathogenesis" brings together the efforts of several established investigators at the Lady Davis Institute for Medical Research, McGill University in a multi-disciplinary approach to the study of the molecular mechanisms involved in HIV gene regulation, virus assembly, viral persistence/latency, emergence of drug resistance and antiviral/vaccine development. Our unified approach has brought together researchers from diverse backgrounds - molecular biology/virology, biochemistry and immunology/cell biology - with unique but overlapping perspectives to the projects. Furthermore, as a Group, we continue to benefit from the availability of a wide range of technologies, an invaluable collection of virus and cell strains available through the McGill AIDS Center, as well as biological and molecular reagents required to perform *in vivo* and *in vitro* experiments. The members of the Group have individually and collectively made major advances in the understanding of the pathogenesis of HIV-1 disease. We believe this CIHR Group has become the premier AIDS research group in Canada studying the molecular aspects of HIV-1 infection.

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Our Group in HIV-1 Pathogenesis may be subdivided into two thematically interrelated projects.

**Analysis of the mechanisms of reverse transcription and HIV assembly** with contributions of Drs. Gotte, Laughrea, Liang, Kleiman, Wainberg who study different aspects of HIV-1 reverse transcription, virus assembly and drug resistance.

**Mechanisms of viral RNA processing and Tat mediated regulation of HIV-1 expression** encompassing the research of Drs. Gatignol, Hiscott, Lin, Mouland, Wainberg who study the mechanisms of Tat transactivation, chemokine gene expression and RNA processing.

## **CANADIAN ONCOLYTIC VIRUS CONSORTIUM (supported by a NCIC Program Grant)**

The objective of this program is to create an oncolytic virus consortium devoted to the development and refinement of conditionally replicating viruses as novel treatments for cancer. Our overall hypothesis is that malignant cells, by virtue of the constellation of genes they do or do not express, can be unique niches for the growth of oncolytic viruses. As an example, we have evidence that the genetic abnormalities contributing to the malignant phenotype also compromise the innate antiviral programs of these same cells. Our goals are to understand virus:host cell interactions in a comprehensive manner, exploit this knowledge to selectively target tumour cells, and develop oncolytic viruses as therapeutics in concurrent and synergistic projects.

The consortium includes investigators from Montreal, Ottawa, London and Calgary; however we anticipate recruiting other members to our group as the program develops.

### **OTTAWA REGIONAL CANCER CENTRE:**

**Drs. Bell, Stojdl and Atkins** are studying the molecular basis of VSV induced oncolysis, the immunological determinants of responsiveness and the characterization of novel rhabdoviruses. In addition, a newly constructed GMP laboratory will permit the preparation and testing of clinical grade oncolytic viruses for phase 1 trials.

### **MCGILL UNIVERSITY AND THE MOLECULAR ONCOLOGY GROUP, MONTREAL**

**Drs. Sonenberg and Hiscott** have been long time collaborators at McGill University and share a common interest in the understanding of viral gene expression in infected cells. Dr. Sonenberg is world renowned for his work in protein translation regulation especially as it pertains to malignant transformation and virus replication. His discovery and characterization of viral IRES elements is a cornerstone of the Picorna oncolytic virus technology. Dr. Hiscott is an international leader in the field of host cell response to virus infection and has published seminal discoveries related to the host signaling pathways that respond to virus infection. He is also exploring the mechanistic basis of oncolytic virus-induced apoptosis.

### **TOM BAKER CANCER CENTRE, UNIVERSITY OF CALGARY**

**Dr. Forsyth** is a clinician scientist who has pioneered the development and application of Reovirus as an oncolytic agent in humans. Dr. Forsyth is a neuro-oncologist and principal author on many papers describing Reovirus as an oncolytic agent. He evaluates and tests oncolytic viruses as experimental therapeutics for brain tumors and is the Principle Investigator on the first human trial of Reovirus for the treatment of Malignant Gliomas.

### **CANCER RESEARCH GROUP, DALHOUSIE UNIVERSITY**

**Dr. Patrick Lee** is a world leader in the use of Reovirus as an oncolytic virus. Dr. Lee pioneered the mechanistic understanding of the basis of Reovirus oncolysis as it relates to the activated Ras oncogene pathway.

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### GRANTS PANELS and ADVISORY COMMITTEES

2009	Chair, CIHR Influenza Pandemic Response Panel
2007-2008	Chair, CIHR HIV/AIDS Emerging Team Grants Panel
2007	Virology B Study Section, National Institutes of Health
2006-2008	Virology and Viral Pathogenesis, CIHR
2006	National Cancer Institute of Canada, Virology Study Section
2005	AIDS Molecular and Cellular Biology Study Section, NIH
2003	Network Centers of Excellence Selection Committee
2003	Virology Study Section, National Institutes of Health
2003	National Institutes of Health, NCI Site Visit Cleveland Clinic Foundation Program Project
2001-2005	Virology and Viral Pathogenesis Grants Panel, CIHR
2000-2003	Israel Cancer Research Fund Grants Panel, New York, NY
2000-2002	Canada Research Chairs Program Review Committee
1999-present	Scientific Advisory Board, Israel Cancer Research Fund
1999	Dean's Search Committee, Faculty of Medicine Chair of the Dept. of Genetics, McGill University
1999-2003	Academic Advisory Committee, Jewish General Hospital
1998-2000	Scientific Officer, Virology and Viral Pathogenesis Grants Panel Canadian Institutes of Health Research
1995-1998	Biochemistry and Molecular Biology Grants Panel Medical Research Council of Canada
1995-1996	MRC/Health and Welfare Canada AIDS Research Grants Panel
1996-97	National Institutes of Health, NINDS Center for Demyelinating Diseases Baltimore, MD
1996	Scientific Officer, Health and Welfare Canada – AIDS Research Panel
1994-1996	Israel Cancer Research Fund Grants Panel, New York, NY
1993 - 1995	McGill Cancer Center Canderel Fellowship Committee
1995	MRC Group Program Site Review Committee, University of Manitoba
1993	NCIC Site Review Committee, Terry Fox Program Project Ontario Cancer Institute, Toronto Ontario
1993	National Institutes of Health, NCI Site Visit Cleveland Clinic Foundation Program Project
1993	Human Science Frontier Program Review
1991 - 1994	Cell and Molecular Biology Grants Panel, Cancer Research Society, Inc.
1991 - 1993	MRC- NHRDP AIDS Grants Panel, MRC
1991 - 1992	Chercheur-Boursier Committee, FRSQ
1991 - 1994	Faculty of Medicine Scholarship Committee, McGill University
1991	Fonds de la Recherche en Santé du Québec Chercheur Boursier Committee
1989 - 1993	NHRDP AIDS Review Committee Health and Welfare Canada
1987 - 1989	Fellowship Grants Panel Cancer Research Society, Inc

### GRANT/JOURNAL REVIEWS

2005-2010	Editor-in-Chief, Cytokine and Growth Factor Reviews
2004 - 2009	Editorial Board, Journal of Biological Chemistry
2004 - 2009	Editorial Board, Retrovirology
2002 - present	Editorial Board, Current HIV Research
1998 - 2006	Section Editor, Journal of Interferon and Cytokine Research
1995 - 2005	Editorial Board, Cytokine and Growth Factor Reviews
1993 - 2001	Associate Editor of VIROLOGY

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### AD HOC JOURNAL REVIEWS

Cell, Immunity, Nature, Science, Cancer Research, Journal of Exp. Medicine, PLoS Pathogens, Cell Host & Microbe, EMBO J, Molecular and Cellular Biology, Proc. Natl. Acad. Sci. USA, Journal of Biological Chemistry, Journal of Immunology, Journal of Clinical Investigation, Journal of Leukocyte Biology, Journal of Virology, Oncogene, Virology, European Journal of Biochemistry, Biochemistry,

### OTHER UNIVERSITY / COMMUNITY SERVICES

2007-2008	Chairman, ISICR-ICS Conference “ <b>Cytokines 2008</b> ”, Montreal Quebec
2006-present	Dept. of Medicine Tenure Committee
2004-2007	Board of Directors, International Society for Interferon and Cytokine Research
2002-2004	Treasurer, International Cytokine Society
2003	Canadian SARS Research Consortium – Scientific Advisory Committee
2003-2004	Scientific Organizer of the ISICR/ICS Conference in Puerto Rico
1998-2001	Expert Witness, Cravath, Swain and Moore, New York
1998-1999	International Patent Application - PCT/CA99/00314 “Highly Active Forms of Interferon Regulatory Factor Proteins”
1999	Presentation to the Israel Cancer Research Foundation
1997	Chairman, Basic Science Track Annual Meeting of the Canadian Assoc. for HIV Research
1997	Chairman, Interferon Gene Regulation Session Annual Meeting of the ISICR, San Diego, Cal.
1996	Chairman, Regulation of HIV Gene Expression XI International Conference on AIDS, Vancouver, BC
1995	Search Committee (2nd recruitment) Dept. of Immunology, Institut Armand Frappier
1994	Scientific Advisory Committee International Society for Oncodevelopmental Biology and Medicine
1993-present	Board of Directors, Lady Davis Institute Jewish General Hospital
1993	Search Committee, Dept. of Immunology Institut Armand Frappier
1993	Chairman, Molecular Regulatory Mechanisms Session International Association for Research on Leukemia and Related Diseases Annual Meeting, Montreal Quebec
1993	Seminar presentation to the Terry Fox Foundation
1993	Corporate Challenge Luncheon, Terry Fox Foundation
1992	Seminar presentation to the Montreal Chapter Canadian Society for the Weizmann Institute of Science

## John HISCOTT

### INVITED EXTERNAL LECTURES (1996-present)

#### 1996

"Transdominant mutants of  $\text{I}\kappa\text{B}\alpha$  interfere with HIV-1 gene expression and replication"  
XI International Conference on AIDS, Vancouver, B.C. (July 1996)

"The role of protein kinase PKR in HIV pathogenesis"  
XI International Conference on AIDS, Vancouver, B.C. (July 1996)

"Regulation of HIV-1 and Cytokine Gene Expression by the NF- $\kappa$ B/Rel Transcription Factors"  
International Workshop on HIV and Cells of the Macrophage Lineage  
Lake Como, Italy (Oct. 1996)

"Transdominant mutants of  $\text{I}\kappa\text{B}\alpha$  block activation of HIV-1 gene expression and virus replication.  
International Cytokine Society/ISICR Meeting, Geneva, Switzerland (Oct.1996)

"Chronic HIV-1 infection activates the NF- $\kappa$ B/Rel pathway via enhanced  $\text{I}\kappa\text{B}\alpha$  degradation mediated by PKR"  
International Cytokine Society/ISICR Meeting, Geneva, Switzerland (Oct.1996)

"Regulation of HIV-1 and Interferon Gene Expression by the NF- $\kappa$ B/Rel Transcription Factors"  
Universita Degli Studi di Verona, Istituto di Chimica Biologica, Verona, Italy (Oct. 1996)

"Regulation of HIV-1 and Cytokine Gene Expression by the NF- $\kappa$ B/Rel Transcription Factors"  
Pathogenesis of HIV Infection, IXth Entretiens Jacques Cartier, Ste. Adele, Quebec (Oct. 1996)

#### 1997

"Regulation of HIV-1 and cytokine gene expression by the NF- $\kappa$ B/Rel transcription factors"  
Istituto di Chimica Biologica, Universita degli Studi di Urbino (February 1997)

"Protein interactions regulating  $\text{I}\kappa\text{B}\alpha$  function during human retrovirus infection"  
Dept. of Microbiology, NYU Medical Center (March 1997)

"Regulation of cytokine gene expression by the NF- $\kappa$ B and IRF transcription factors"  
National Public Health Institute, University of Helsinki Finland (April 1997)

"Protein interactions regulating  $\text{I}\kappa\text{B}\alpha$  function during human retrovirus infection"  
Université Paris V René Descartes, Paris France (May 1997)

"Protein interactions regulating  $\text{I}\kappa\text{B}\alpha$  function during human retrovirus infection"  
Chiron Corp., Emeryville CA (June 1997)

"A role for casein kinase II in the regulation of transcription factors controlling cytokine gene activation"  
Workshop on Structural and Functional Aspects of Casein Kinase II, Grenoble France (September1997)

" Inducible expression of  $\text{I}\kappa\text{B}$  transdominant mutants interferes with HIV-1 multiplication in Jurkat T cells".  
International Society for Interferon and Cytokine Research Meeting, San Diego CA (Oct. 1997)

## **John HISCOTT**

### **1998**

"Regulation of interferon gene expression by the NF- $\kappa$ B and IRF transcription factors"  
Seron Symposium on Interferons and Lymphoproliferative Diseases, Venice, Italy (March 1998)

"Regulation of interferon gene expression by the IRF-3 transcription factor"  
Institut Curie, Paris France (March 1998)

"Control of cytokine gene expression by the IRF and NF- $\kappa$ B factors"  
Dept. of Biochemistry, McMaster University, Hamilton, Ontario (April 1998)

"Regulatory proteins of the interferon system and control of HIV-1 pathogenesis"  
Laboratory of Virology, Istituto Superiore di Sanita, Rome, Italy (May 1998)

"Coordinate regulation of cytokine and chemokine gene expression in HIV-1 infected cells"  
Faculty of Science, Universita degli Studi di Urbino, Urbino, Italy (May 1998)

"Essential role of IRF-3 in the direct activation of RANTES CC-chemokine transcription"  
International Conference on Interferons and Cytokines, Jerusalem, Israel (October 1998)

"Molecular mechanisms regulating T-cell Leukemogenesis by HTLV-1 Tax Oncoprotein"  
Faculty of Science, Universita degli Studi di Urbino, Urbino, Italy (October 1998)

"Essential role of IRF-3 in the direct activation of RANTES CC-chemokine transcription"  
San Marino Conference on Cancer and AIDS, Republic of San Marino (October 1998)

Triggering the interferon response: a structural and functional analysis of the IRF-3 transcription factor"  
Université Paris V René Descartes, Paris France (December 1998)

### **1999**

"Transcriptional control of cytokine and chemokine gene expression during human retrovirus pathogenesis"  
Robarts Research Institute, University of Western Ontario (January 1999)"

"Transcriptional control of cytokine and chemokine gene expression during human retrovirus pathogenesis"  
Dept. of Molecular Genetics and Microbiology, University of Toronto (March 1999)

"Transcriptional control of cytokine and chemokine gene expression during human retrovirus pathogenesis"  
Clinical Research Institute of Montreal (March 1999)

"Regulation of interferon gene transcription"  
Lerner Research Institute, Cleveland Clinic Foundation, Cleveland Ohio (March 1999)

"Activation of the IRF-4 transcription factor in HTLV-1 infected T cells"  
International Symposium on HIV, Leukemia and Opportunistic Infections, Marrakech, Morocco (May 1999)

"Transcriptional control of cytokine and chemokine gene expression during human retrovirus pathogenesis"  
Sylvester Comprehensive Cancer Center, University of Miami, Miami, FL (May 1999)

## **John HISCOTT**

"Transcriptional control of cytokine and gene expression during human retrovirus pathogenesis"  
Institut Curie, Paris France (July 1999)

"Novel post-translational mechanisms controlling the functional activities of the IRF family"  
International Society for Interferon and Cytokine Research, Paris, France (September 1999)

"Regulation of the IRF-4 transcription factor by the immunophilin FKBP52 in HTLV-1 infected cells"  
International Cytokine Society Annual Meeting, Hilton Head SC (December 1999)

### **2000**

"Regulation of chemokine gene expression in HTLV-1 infected cells"  
Dept. of Microbiology, NYU Medical Center, New York (February 2000)

"Activation and regulation of IRF-4 expression in HTLV-1 infected T cells"  
Molecular Biology and Pathogenesis of HTLV-1, Airlie Center, Warrington Virginia (March 2000)

"Regulation of IRF-4 function in HTLV-1 infected T cells"  
Viral Oncogenesis Symposium, AACR Meeting, San Francisco, CA (April 2000)

"Control of interferon and chemokine gene expression during viral pathogenesis"  
Dept. of Microbiology & Immunology, Hershey Medical Center, Penn State University (Sept. 2000)

"Regulation of interferons and chemokines by NF- $\kappa$ B and IRF transcription factors"  
Lymphocyte Signal Transduction Conference, Santorini, Greece (Oct. 2000)

"Interferon and chemokine gene regulation"  
Third joint Meeting of the ICS/ISICR, Amsterdam, The Netherlands (Nov. 2000)

### **2001**

"Regulation of interferons and chemokines by NF- $\kappa$ B and IRF transcription factors"  
Signal Transduction in Normal and Cancer Cells, Banff, Alberta (March 2001)

NF-AT and NF- $\kappa$ B regulation of IRF-4 in HTLV-1 infected T lymphocytes  
Institut Curie Paris France (May 2001)

Activation of antiviral cascades by the NF- $\kappa$ B and IRF transcription factors  
University of Paris V, Paris France (May 2001)

Activation of antiviral cascades by the NF- $\kappa$ B and IRF pathways during viral infection  
Ottawa General Hospital Research Center, Ottawa, Ont. (Sept. 2001)

Activation of antiviral cascades by the NF- $\kappa$ B and IRF pathways during viral infection  
Dept. of Medical Microbiology and Immunology, University of Alberta, Edmonton, AL (October 2001)

Activation of antiviral cascades by the NF- $\kappa$ B and IRF pathways during viral infection  
Plenary Lecture, ISICR Annual Meeting, Cleveland Ohio (October 2001)

Activation of antiviral cascades by the NF- $\kappa$ B and IRF pathways during viral infection  
Dept. of Pathology, Albert Einstein College of Medicine, Bronx, New York (November 2001)

## **John HISCOTT**

Transcriptional profiling of antiviral genes stimulated by IRF-3  
Entretiens Jacques Cartier, Lyon France (December 2001)

Activation of antiviral cascades by the NF- $\kappa$ B and IRF pathways during viral infection  
Plenary Lecture, International Interferon and Cytokine Conference, Havana Cuba (December 2001)

### **2002**

“Hostile Takeovers: Viral appropriation of cytokine pathways”  
Robarts Research Institute, University of Western Ontario, London, Ontario (January 2002)

“Activation of antiviral cascades by the NF $\kappa$ B and IRF transcription factors”  
Signal Transduction Conference, Luxembourg (January 2002)

“Hostile Takeovers: Viral appropriation of cytokine pathways”  
Department of Microbiology, Mount Sinai School of Medicine, New York, NY (March 2002)

“Hostile Takeovers: Viral appropriation of cytokine pathways”  
Department of Microbiology and Immunology, University of Alberta, Edmonton, Alberta (March 2002)

“Hostile Takeovers: Viral appropriation of cytokine pathways”  
Department of Microbiology and Immunology, University of Maryland, Baltimore, MD (April 2002)

“Hostile Takeovers: Viral appropriation of cytokine pathways”  
Department of Microbiology and Immunology, University of Calgary, Calgary, Alberta (April 2002)

“Regulation of HIV LTR mediated transcription by NF- $\kappa$ B and Tat”  
Dept. of Microbiology and Immunology, University of Western Ontario (April 2002)

“Functional Genomics and Proteomics of the Immune Response”  
Genome Quebec, Montreal Quebec (May 2002)

“Tumor Suppressor and Immunomodulatory Activities of IRF Factors”  
IDM Biotech Inc., Paris France (August 2002)

“Dysregulation of NF- $\kappa$ B and IRF Pathways in HTLV-1 Leukemogenesis”  
Plenary Lecture: ISICR/ICS Conference on Interferons and Cytokines, Torino, Italy (October 2002)

“NF- $\kappa$ B and IFN Signaling Pathways and the Regulation of Innate Immunity”  
Sixth International Latin American Immunology Congress, Havana Cuba (December 2002)

### **2003**

“Multiple Signaling Pathways leading to the Activation of IRF Transcription Factors”  
Plenary Lecture, Signal Transduction and Apoptosis, Luxembourg (January 2003)

“Convergence of the NF- $\kappa$ B and IFN Signaling Pathways in the Development of Antiviral Defense”  
University of Paris V, Paris France (January 2003)

## **John HISCOTT**

“Convergence of the NF- $\kappa$ B and IFN Signaling Pathways in the Development of Antiviral Defense”  
Department of Microbiology, Mount Sinai School of Medicine, New York, NY (March 2003)

“Convergence of the NF- $\kappa$ B and IFN Signaling Pathways in the Development of Antiviral Defense”  
Dept. of Medicine, University of Massachusetts, Amherst, Mass. (April 2003)

Triggering the Interferon Antiviral Response through an IKK-related Pathway  
Laboratory of Virology Istituto Superiore di Sanita, Rome Italy (May 2003)

Triggering the Interferon Antiviral Response through an IKK-related Pathway  
Dept. of Medicine, Baylor College of Medicine, Houston Texas (June 2003)

Triggering the Interferon Antiviral Response through an IKK-related Pathway  
Dept. of Virology, Pasteur Institute, Paris France (July 2003)

Triggering the Interferon Antiviral Response through an IKK-related Pathway  
Institute of Biochemistry and Molecular Medicine  
Universite Libre de Bruxelles, Gosselies, Belgium (July 2003)

“Convergence of the NF- $\kappa$ B and IFN Signaling Pathways in the Development of Antiviral Defense”  
International Cytokine Conference, Dublin Ireland (September 2003)

“NF- $\kappa$ B and IFN Signaling Pathways and the Regulation of Innate Immunity”  
International Immunology Congress, Lima Peru (October 2003)

Triggering the Interferon Antiviral Response through an IKK-related Pathway  
ISICR Annual Conference, Cairns Australia (October 2003)

The Role of NF- $\kappa$ B in Viral Oncogenesis  
International Biotechnology Conference, Havana Cuba (November 2003)

The Potential Use of Oncolytic Viruses in Cancer Therapy  
International Biotechnology Conference, Havana Cuba (November 2003)

Oncolytic VSV, IFN Signaling and Experimental Cancer Therapeutics  
Carl Icahn Institute of Gene Therapy and Molecular Medicine,  
Mt. Sinai School of Medicine, New York (December 2003)

## **2004**

Triggering the Interferon Antiviral Response through an IKK-related Pathway  
Istituto Superiore di Sanita, Rome Italy (February 2004)

Oncolytic VSV, IFN Signaling and Experimental Cancer Therapeutics  
American Association for Immunology, FASEB Meeting, Washington DC (April 2004)

Toll-like Receptors, IFN signaling and Development of Antiviral Immunity  
Biogen Research Conference, Manchester, Vermont (May 2004)

The Interferon Antiviral Response: From Invasion to Evasion  
American Society for Microbiology, New Orleans, LA (May 2004)

## **John HISCOTT**

Signaling the Host Antiviral Response to Virus Infection  
13th International Symposium on Molecular Biology of Macrophages, Osaka, Japan (July 2004)

Triggering the Interferon Antiviral Response through an IKK-related Pathway  
University of Oregon, Portland Oregon (November 2004)

Triggering the Interferon Antiviral Response through an IKK-related Pathway  
ASM Conference on Signaling Mechanisms in Virus infection, Savannah, Georgia (December 2004)

### **2005**

Triggering the Interferon Antiviral Response through an IKK-related Pathway  
Rockefeller University, New York (April 2005)

Triggering the Interferon Antiviral Response through an IKK-related Pathway  
McMaster University, Hamilton Ontario (April 2005)

Triggering the Interferon Antiviral Response through an IKK-related Pathway  
Virus and Cell interactions, Gordon Research Conference, Lucca, Italy (May 2005)

Oncolytic Virus Therapy for Cancer  
Istituto Superiore di Sanita, Rome Italy (May 2005)

Oncolytic Virus activity in HTLV-1 induced leukemogenesis  
International Retrovirology Conference, Montego Bay Jamaica (June 2005)

Triggering the Interferon Antiviral Response through an IKK-related Pathway  
IDM Biotech, Paris France (July 2005)

Triggering the Interferon Antiviral Response: Implications for Viral Oncolytic Therapies  
Emerging Strategies in Molecular Medicine and Biotechnology  
Crete, Greece (September 2005)

Inhibition of RIG-I dependent signaling to the IFN response by Hepatitis C Protease NS3/4A  
International Conference on Hepatitis C, Montreal Canada (October 2005)

Signaling pathways leading to the activation of the interferon antiviral response  
Vanderbilt University (October 2005)

Signaling pathways leading to the activation of the interferon antiviral response  
Hospital for Special Surgery, Cornell Medical School (December 2005)

Signaling pathways leading to the activation of the interferon antiviral response  
University of Aarhus, Denmark (December 2005)

Signaling pathways leading to the activation of the interferon antiviral response  
ImmunoDesign Molecules (IDM) Inc. Paris (December 2005)

### **2006**

Signaling pathways leading to the activation of the interferon antiviral response  
Keystone Symposium on Pathogen-Host Standoff, Keystone, Colorado (January 2006)

## **John HISCOTT**

Signaling pathways leading to the activation of the interferon antiviral response  
Cell Signaling World 2006, Luxembourg (January 2006)

TLR-dependent and –independent pathways leading to the interferon antiviral response  
Toll 2006, Salvador, Brazil (March 2006)

TLR-dependent and –independent signaling to the interferon antiviral response: lessons in evasion from Hepatitis C virus  
St. Jude Children’s Research Hospital, Memphis, Tenn. (April 2006)

TLR-dependent and –independent signaling to the interferon antiviral response  
American Association for Immunology, Boston, Mass (May 2006) – Invited Speaker

TLR-dependent and –independent signaling to the interferon antiviral response: lessons in evasion from Hepatitis C virus  
Pfizer Global Research, Sandwich Kent England (May 2006)

Recruitment of an interferon signaling complex to the mitochondrial membrane  
International Society for Interferon and Cytokine Research, Vienna Austria (August 2006)

Innate immune response to virus infection  
Entretiens Jacques Cartier, Lyon France (December 2006) – Plenary Speaker

Innate immune response to virus infection  
Microbiology & Molecular Genetics, Harvard Medical School (December 2006)

## **2007**

Signaling to the antiviral response: cross-talk between apoptosis and the innate response  
Rutgers University, Piscataway, NJ (March 2007)

The innate immune response to virus infection: lessons in evasion from hepatitis C virus  
Faculty of Pharmacy, Université de Montreal (March 2007)

Signaling to the antiviral response: cross-talk between apoptosis and the innate response  
Innate Immunity Workshop, McGill University (April 2007)

The innate immune response to virus infection: cross-talk between antiviral and apoptotic signaling  
Dept. of Cellular and Molecular Medicine, University of Ottawa (June 2007)

The NEMO/IKKgamma adapter bridges the NF- $\kappa$ B and IRF pathways during RIG-I signaling  
ISICR Conference Oxford, UK (September 2007)

## **2008**

The innate immune response to virus infection: lessons in evasion from hepatitis C virus  
Institut Pasteur, Paris France (January 2008)

Innate Immunity to Virus infection: implications for oncolytic virus therapy  
Université Paris V, Rene Descartes, Paris France (January 2008)

The innate immune response to virus infection  
Meakins-Christie Laboratories, McGill University (January 2008)

## **John HISCOTT**

Molecular interactions regulating the RIG-I signaling pathway  
Dept, of Molecular Biology, University of Texas, Dallas Texas (February 2008)

Molecular interactions regulating the RIG-I signaling pathway  
Dept, of Microbiology, Queens University, Kingston Ontario (March 2008)

Molecular interactions regulating the RIG-I signaling pathway  
American Assoc. for Immunologists, San Diego CA (April 2008)

Evasion of the Innate Immune Response by Hepatitis C Virus  
International HCV Conference, Varadero Cuba (April 2008)

Molecular interactions regulating the RIG-I signaling pathway  
Host Pathogens Interactions, Munster Germany (June 2008) – Invited Speaker

Chemical targeting of the innate immune response by HDAC inhibitors renders  
refractory cancers sensitive to viral oncolysis  
Cleveland Clinic, Cleveland Ohio (June 2008)

Molecular interactions regulating the RIG-I signaling pathway  
Nagano Memorial Conference, Sapporo Japan (July 2008) – Keystone Symposium Speaker

Molecular interactions regulating the RIG-I signaling pathway  
Entretiens Jacques Cartier, Montreal Que (October 2008) – Plenary Speaker

Manipulation of the innate immune response to enhance oncolytic virotherapy  
Fox Chase Cancer Center, Philadelphia PA (November 2008)

Regulation of the RIG-I response to virus infection by the ubiquitination pathway  
Autumn Immunology Conference, Chicago Ill. (November 2008) – Plenary Sepaker

Regulation of the RIG-I response to virus infection by the ubiquitination pathway  
Greenberger Cancer Center, University of North Carolina (December 2008)

## **2009**

The innate immune response to RNA virus infection  
Université Paris-Descartes, Paris France (February 2009)

The innate immune response to RNA virus infection  
Dept. of Virology, Erasmus University, Rotterdam The Netherlands (February 2009)

Manipulating the immune response to augment oncolytic virotherapy  
Vaccine & Gene Therapy Institute, Oregon Health Sciences University, Portland OR (March 2009)

Manipulating the immune response to augment oncolytic virotherapy  
5<sup>th</sup> Oncolytic Virus Conference, Banff AB (March 2009) – Keynote Speaker

Manipulating the immune response to augment oncolytic virotherapy  
Institut Armand Frappier, Laval Que. (March 2009)

Ubiquitin-mediated Regulation of the RIG-I-MAVS Antiviral Pathway  
Stem Cell Group, Universitat Konstanz, Konstanz Germany (August 2009)

**John HISCOTT**

Manipulating the immune response to augment oncolytic virotherapy  
Temple University, Philadelphia PA (September 2009)

Ubiquitin-mediated Regulation of the RIG-I-MAVS Antiviral Pathway  
16<sup>th</sup> Conference on Hepatitis C Virus, Nice France (October 2009)

Sensing and Responding to Hepatitis C Virus Infection through RIG-I like Receptors  
CIGB Biotechnology Conference, Havana Cuba (November 2009) – Plenary Speaker

Manipulating the Innate Immune Response to Augment Oncolytic Virus Therapies  
CIGB Biotechnology Conference, Havana Cuba (November 2009) – Plenary Speaker

Molecular interactions regulating the RIG-I dependent antiviral immune response  
EMBO Conference on Pathogen-Host interactions La Colle sur Loup, France (June 2010) – Plenary Speaker.

## John HISCOTT

### PUBLICATIONS

1. Cheevers WP, **Hiscott JB**: DNA synthesis in polyoma virus infection. II. Relationship between viral DNA replication and initiation of cellular DNA replicons. *J. Mol. Biol.* 78: 237-241, 1974.
2. **Hiscott JB**, Defendi V: Simian virus 40 gene A regulation of cellular DNA synthesis. In permissive cells. *J. Virol* 30: 590-599, 1978.
3. **Hiscott JB**, Defendi V: Viral and cellular control of the SV40 transformed phenotype. *Cold Spring Harbor Symp Quant Biol* 44: 343-352, 1979.
4. **Hiscott JB**, Murphy D, Defendi V: Amplification and rearrangement of integrated SV40 DNA sequences accompany the selection of anchorage independent transformed mouse cells. *Cell* 22: 535-543, 1980.
5. **Hiscott JB**, Defendi V: Simian virus 40 gene A regulation of cellular DNA synthesis. II. In nonpermissive cells. *J Virol* 37: 802-811, 1981.
6. **Hiscott JB**, Murphy D, Defendi V: Instability of integrated viral DNA in mouse cells transformed by simian virus 40. *Proc Natl Acad Sci USA* 78:1736-1740, 1981.
7. Pestka S, Maeda S, Levy M, Chang N, **Hiscott JB**, McCandliss E, Stein S, Moschera J, Staehelin T: The human interferons: the proteins and their expression in bacteria. In: *Recombinant DNA* (Baxter JD, Ed), 3rd Cleveland Symposium, pp. 51-73, Academic Press, New York 1982.
8. **Hiscott JB**, Cantell K, Weissmann C: Differential expression of human interferon genes. *Nucl Acids Res* 12: 3727-3746, 1984.
9. **Hiscott JB**, Ryals J, Dierks P, Hofmann V, Weissmann C: Expression of human alpha interferon genes. *Phil Trans Roy Soc London* 307:217-226, 1985.
10. **Hiscott JB**, Cantell K, Hofmann V, Weissmann C: Differential expression of human interferon genes. In: *Mechanisms of Viral Immune Suppression* (Gilmore N, Wainberg MA, Eds), pp. 215-225, Alan R. Liss, New York, 1985.
11. Xanthoudakis S, **Hiscott J**: Identification of a nuclear DNA binding protein associated with the interferon- $\beta$  upstream regulatory region. *J Biol Chem* 262: 8298-8302, 1987.
12. Xanthoudakis S, Alper D, **Hiscott J**: Transient expression of the beta interferon promoter in human cells. *Mol Cell Biol* 7: 3830-3835, 1987.
13. Marshall A, Alper D, **Hiscott, J**: Modulation of nuclear proto-oncogene expression and cellular growth in myeloid leukemic cells by human interferon alpha. *J Cell Phys* 135: 324-331, 1988.
14. **Hiscott J**, Wong A, Alper D, Xanthoudakis S: *Trans*-activation of type 1 interferon promoters by simian virus 40 T antigen. *Mol Cell Biol* 8: 3397-3405, 1988.
15. Xanthoudakis S, **Hiscott J**: Modulation of interferon gene transcription by positive and negative cellular factors. *Biochem Biophys Res Comm* 154: 1338-1344, 1988.
16. Xanthoudakis S, Cohen L, **Hiscott J**: Multiple protein-DNA interactions within the interferon- $\beta$  regulatory element. *J Biol Chem* 264: 1139-1145, 1989.

## John HISCOTT

17. **Hiscott J**, Alper D, Cohen L, Leblanc JF, Sportza L, Wong A, Xanthoudakis S: Induction of human interferon gene expression is associated with a nuclear factor that interacts with the NF- $\kappa$ B site of the human immunodeficiency virus enhancer. *J Virol* 63: 2557-2566, 1989.
18. Xanthoudakis S, **Hiscott J**: Cross-linking of distinct proteins to the PRDII domain of the interferon  $\beta$  promoter. *Biochem Biophys Res Comm* 167: 1086-1093, 1990.
19. Leblanc JF, Cohen L, Rodrigues M, **Hiscott J**: Synergism between distinct enhancer domains in viral induction of the human interferon  $\beta$  gene. *Mol Cell Biol* 10: 3987-3993, 1990.
20. Lacoste J, D'Addario M, Roulston A, Wainberg MA, **Hiscott J**: Cell specific differences in activation of NF- $\kappa$ B regulatory elements of human immunodeficiency virus and beta interferon by tumor necrosis factor. *J Virol* 64: 4726-4734, 1990.
21. Dubreuil M, Sportza L, D'Addario M, Lacoste J, Rooke R, Wainberg M, **Hiscott J**: Inhibition of HIV-1 multiplication by interferon and azidothymidine treatment. *Virology* 179: 388-394, 1990.
22. D'Addario M, Roulston A, Wainberg MA, **Hiscott J**: Coordinate enhancement of cytokine gene expression in human immunodeficiency virus infected promonocytic cells. *J Virol* 64:6080-6089, 1990.
23. Eymard D, Dascal A, **Hiscott J**, Gioseffini S, Stevenson J, Portnoy J, Mendelson J: Non-beta-lactamase-producing penicillin-resistant *Enterococcus faecium* in a clinical setting. *Can J Infect Dis* 1: 73-76, 1990.
24. Tremblay M, Numazaki K, Li X, Gornitsky M, **Hiscott J**, Wainberg MA: Resistance to infection by HIV-1 of peripheral blood mononuclear cells from HIV-1 infected individuals is probably mediated by neutralizing antibodies. *J Immunol* 145: 2896-2901, 1990.
25. Geleziunas R, Bour S, Boulerice F, **Hiscott J**, Wainberg MA: Diminution of CD4 surface protein but not CD4 mRNA levels in monocytic cells infected by HIV-1. *AIDS* 5: 29-33, 1991.
26. Gosselin J, Menezes J, D'Addario M, **Hiscott J**, Flamand L, Lamoureux G, Oth D: Epstein Barr virus infection inhibits tumor necrosis factor transcription in monocytes. *Eur J Immunology* 21: 203-208, 1991.
27. Geleziunas R, McQuillan A, Malapetsa A, Hutchinson M, Kopriva D, Wainberg M, **Hiscott J**, Panasci L: Increased DNA synthesis and repair enzyme expression in lymphocytes from chronic lymphocytic leukemia patients. *J Nat Cancer Inst* 83: 557-564, 1991.
28. Cohen L, Lacoste J, Parniak MA, Daigneault L, Skup D, **Hiscott J**: Stimulation of interferon- $\beta$  gene transcription by purified NF- $\kappa$ B and a novel TH protein. *Cell Growth and Differentiation* 2: 323-333, 1991.
29. Lacoste J, Cohen L, **Hiscott J**: NF- $\kappa$ B activity in T cells stably expressing the Tax gene of human T cell lymphotropic virus type 1. *Virology* 184: 553-562, 1991.
30. Flamand L, Gosselin J, D'Addario M, **Hiscott J**, Ablashi D, Gallo RC, Menezes J: Human herpes virus 6 (HHV-6) induces IL-1 $\beta$  and TNF- $\alpha$  but not IL-6 in peripheral blood mononuclear cell cultures. *J. Virol.* 65: 5105-5110, 1991.

## John HISCOTT

31. Haggarty A, Camato R, Paterno G, Cohen L, **Hiscott J**, Skup D: A developmentally regulated octamer binding activity in embryonal carcinoma cells which represses interferon  $\beta$  expression. *Cell Growth and Differentiation*: 503-510, 1991.
32. Alper D, **Hiscott J**: The simian virus 40 enhancer activates the interferon alpha promoter in human fibroblasts. *Life Sci. Adv. (Virol)*. 10: 1-12, 1991.
33. Leblanc JF, **Hiscott J**: Differential response of human interferon  $\beta$  promoter elements to *trans*-activation by HSV VP16 and IRF-1. *Virology* 186: 760-763, 1992.
34. Boulerice F, Geleziunas R, Bour S, Li H, D'Addario M, Roulston A, **Hiscott J**, Wainberg MA: Differential susceptibilities of U937 cell clones to infection by HIV-1. *J. Virol.* 66: 1183-1187, 1992.
35. D'Addario M, Wainberg MA, **Hiscott J**: Activation of cytokine genes in HIV-1 infected myelomonoblastic cells by phorbol ester and tumor necrosis factor. *J. Immunology* 148: 1222-1229, 1992.
36. Roulston A, D'Addario M, Boulerice F, Caplan S, Wainberg MA, **Hiscott J**: Induction of monocytic differentiation and NF- $\kappa$ B activity by HIV-1 infection of human myelomonoblastic cells. *J. Exp. Med.* 175: 751-763, 1992.
37. Cohen L, **Hiscott J**: Heterodimerization and transcriptional activation *in vitro* by NF- $\kappa$ B subunits. *J. Cell. Phys.* 152: 10-18, 1992.
38. Gosselin J, Flamand L, D'Addario M, **Hiscott J**, Menezes J: Infection of peripheral blood mononuclear cells by herpes simplex and Epstein-Barr viruses: differential induction of interleukin 1 and tumor necrosis factor. *J. Clin. Invest.* 89:1849-1856, 1992.
39. Flamand L, Gosselin L, D'Addario M, **Hiscott J**, Ablashi D, Menezes J: Modulatory effects of EBV, HSV and HHV-6 viral infections on cytokine expression. *J. Immunol.* 149:181-187, 1992.
40. Roberts NJ, **Hiscott J**, Signs DJ: The limited role of the human interferon system in response to respiratory syncytial virus challenge: analysis and comparison to influenza virus challenge. *Microbial Path.* 12:409-414, 1992.
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