I  HIGHLIGHTS

A) Stem Cell Transplant Program
The stem cell transplant program under Dr. Martin Gyger’s directorship continued with active accrual of patients for both the autologous and allogeneic stem cell transplant program. A total of 35 patients were transplanted in the last fiscal year. In order to strengthen the viability of a McGill University transplant program and to locate on a single site at the Royal Victoria Hospital, the division agreed to stop accrual of patients to the non-myeloablative allogeneic stem cell transplant program at the Jewish General Hospital. These transplants are to be referred to the McGill University program at the Royal Victoria Hospital site. Dr. Gyger remains an important contributor to the transplant effort at McGill and is guiding establishment of the transplant protocols and treatment guidelines for allogeneic transplantation. In addition, the Jewish General Hospital continues its strong association with the Maisonneuve-Rosemont Hospital and its large allogeneic transplant program.

B) Clinician-Scientists
The division continues to support the efforts of both Drs. Galipeau and Blostein in their active bench science laboratories. Both continue in their respective research fields with publications in excellent peer review journals. Dr. Galipeau continues in his important position in the Canadian Stem Cell Network.

C) Molecular Diagnostics Laboratory
The Jewish General Hospital Molecular Diagnostics Laboratory continues to remain as the referral hospital for molecular diagnostics for the entire McGill university network. The panel of molecular studies has now been expanded to include important new assays for chronic lymphocytic leukemia and myeloproliferative disorders. Chimerism studies for the McGill university transplant program continue to be performed at the Jewish General Hospital laboratory. The laboratory was temporarily relocated in Pavilion H during a period of laboratory renovations. In addition, the Molecular Diagnostics Laboratory is now under the jurisdiction of the Department of Pathology. Dr. Tina Haliotis is the hematopathologist responsible for the interpretation and supervision of the hematopathological molecular studies performed in the laboratory.

D) CML Clinic
This specialized clinic for the treatment of chronic myelogeneous leukemia is directed by Dr. Carlos Gambacorti, a research-scientist in the Department of Oncology whose main clinical interest is in this disease. Drs. Sarit Assouline from the Lakeshore General Hospital and Dr. Jeff Prchal from St. Mary’s Hospital assist Dr. Gambacorti in the clinic particularly when he is unavailable because of research and other commitments. This unique clinic is now following more than 35 patients with this rare disorder and has established a guideline for monitoring and treatment of all CML patients in the clinic. Additionally, Dr. Gambacorti has established a clinical research program and is the principle investigator for two studies testing novel tyrosine kinase inhibitors in patients relapsing or refractory to the conventional agents.
E) Myeloproliferative Disorder (MPD) Clinic
Dr. J. Prchal had approached the Jewish General Hospital Division of Hematology to establish an MPD clinic as part of a multinational group to develop a registry and new treatment studies for these disorders. Dr. Prchal is part of a consortium that has applied for a large NIH grant for both clinical and research studies in myeloproliferative diseases. Recently we have been informed that the grant was accepted by the NIH to commence July 1st, 2006. The establishment grant is for a total of $5 million for a period of at least 4 years. Dr. Prchal is to establish a clinic for the purpose initially of registration of all patients at the Jewish General Hospital with myeloproliferative diseases and will subsequently establish a site of novel diagnostic procedures and eventually studies on therapeutic modalities for these disorders.

F) Segal Cancer Centre
Over the last 12 months, the division has been planning for its move into the Segal Cancer Centre which initially opened at the end of January 2006. The Division of Hematology moved all of its patients with hematologic malignancies to the cancer clinics in the Segal Cancer Centre while maintaining its core facility and clinics for benign hematologic disease and thrombosis on the first floor pavilion E site. Dr. Susan Kahn and her thrombosis research nurses will move its operations into the first floor area vacated by some of the personnel moving to the 7th floor cancer centre. Drs. Caplan, Gyger, Shamy and Patenaude have their offices to the 7th floor and Dr. Jacques Galipeau has moved his office to the 4th floor of the new pavilion E to his research labs in that location.

II EVALUATION OF PAST ACADEMIC YEAR

Faculty
Dr. Stephen Caplan remains as Interim Director of the Division of Hematology at McGill University. Dr. Caplan was also responsible for coordinating an important document submitted to the Ministry in order to maintain the allogeneic stem cell transplant program at McGill University by moving all activities to the Royal Victoria Hospital site. Dr. Jacques Galipeau has continued to contribute significantly to the literature by publishing manuscripts on stem cell biology in both vascular and malignant disease. Dr. April Shamy continues as CTU Director of the hematology-oncology unit on 7NW and Dr. Wahbi Hammouda remains a representative to the McGill Hematology Fellowship Training program.

Dr. Sarit Assouline has joined the Jewish General Hospital Division of Hematology and is responsible for establishment of phase I and phase II studies in hematologic malignancies and for the establishment and Directorship of the new Hematology Tumor Board in the cancer centre.

Dr. Jeff Prchal has been given a cross-appointment in the division in order to establish the MPD clinic as previously described.
<table>
<thead>
<tr>
<th>Source</th>
<th>Title</th>
<th>Amount</th>
<th>Term</th>
<th>Starting date</th>
<th>Role</th>
</tr>
</thead>
<tbody>
<tr>
<td>Department of National Defence (Canada)</td>
<td>Development and Optimization of Hemostatic Peptides For Hemorrhage Control</td>
<td>$380,000</td>
<td>3 years</td>
<td>September 2005</td>
<td>Principle Investigator</td>
</tr>
<tr>
<td>Heart and Stroke Foundation of Canada</td>
<td>The role of protein domains containing gamma-carboxy-glutamic acid in vascular biology</td>
<td>$45,000</td>
<td>3 years</td>
<td>July 2003</td>
<td>Principle Investigator</td>
</tr>
<tr>
<td>Canadian Institutes for Health Research (CIHR)</td>
<td>Physiology of gas6-Axl interactions</td>
<td>$76,957</td>
<td>1 year</td>
<td>January, 2006</td>
<td>Principle Investigator</td>
</tr>
<tr>
<td>Fonds de Recherche Scientifique du Quebec</td>
<td>Gene Therapy of Hemophilia B</td>
<td>$152,717</td>
<td>3 years</td>
<td>September 2004</td>
<td>Co-investigator (PI Dr. J. Galipeau)</td>
</tr>
<tr>
<td>Canadian Institutes for Health Research (CIHR)</td>
<td>Randomized Trial of Oral Vitamin K for Warfarin-Induced Coagulaopathy</td>
<td>$600,000</td>
<td>3 years</td>
<td>March 2005</td>
<td>Co-investigator of a clinical trial</td>
</tr>
<tr>
<td>Heart and Stroke Foundation of Canada</td>
<td>Thrombophilia in Pregnancy Prophylaxis Study</td>
<td>$600,000</td>
<td>3 years</td>
<td>July 2003</td>
<td>Co-investigator of a clinical trial</td>
</tr>
<tr>
<td>Canadian Institutes for Health Research (CIHR)</td>
<td>A double blind randomized control trial of post Operative low molecular weight heparin bridging therapy versus placebo bridging therapy for patients who are at high risk for arterial thromboembolism</td>
<td>To be announced</td>
<td>3 years</td>
<td>March 2006</td>
<td>Co-investigator of a clinical trial</td>
</tr>
<tr>
<td>Canadian Institutes for Health Research (CIHR)</td>
<td>CIHR Team Grant in Venous Thromboembolism</td>
<td>To be announced</td>
<td>3 years</td>
<td>March 2006</td>
<td>Co-Investigator (PI Dr. J. Weitz)</td>
</tr>
</tbody>
</table>
### Ponka, P

| Agency | 1. CIHR  
|       | 2. CIHR  
|       | 3. CIHR  
| Type of Award | 1. Operating  
|             | 2. Operating  
|             | 3. Operating  
| Title | 1. Chelation, mobilization, and metabolism of storage iron  
|       | 2. Regulation of iron metabolism and heme synthesis in erythroid cells  
|       | 3. The effect of redox species of nitrogen monoxide on intracellular iron metabolism  
| Amount | 1. $84,000/yr  
|        | 2. $113,054/yr  
|        | 3. $97,168/yr  
| Year 1st Awarded | 1.  
|                  | 2.  
|                  | 3.  
| # of Years | 1.2001-2006  
|           | 2.2000-2005  
|           | 3.2003-2006  
| Principal Investigator | 1.Prem Ponka  
|                      | 2.Prem Ponka  
|                      | 3.Prem Ponka  

#### Title of Grant: Cancer Cell and Gene Therapy – A study of novel chimeric anti-cancer immunomodulatory transgenes and transgenic cell therapy.

**Funding Source and Program Name:** CIHR – Operating grant renewal Grant # 128733

**Dollars awarded:** $693,170 over 5 years from October 2004 to September 2009

**Name of P.I:** Jacques Galipeau  
**% effort on this grant:** 15%

**List of co-applicants:** none  
**% effort for Co-applicants:** not applicable

**Major goals of this project:** This proposal seeks to treat cancer by eliciting an anti-tumor immune response via two parallel and related pathways. Axis I: de novo expression of novel fusion cytokin and interleukin genes in pre-established cancer as part of a whole cell tumor vaccine strategy. Axis II: transgenic stromal cells therapy by implanting in tumors autologous bone marrow stroma engineered to express interleukin genes.

**% overlap with current application:** 0%

#### Title of Grant: Cardiovascular and Respiratory Stem Cell Plasticity – CARE Project

**Funding Source and Program Name:** CIHR / Regenerative Medicine and Nanomedicine – New Emerging Team (NET) Grant Program (Grant # 25523)

**Dollars awarded:** Total awarded is $300,000/year, from October 2004 to July 2009.

**Name of P.I:** Jacques Galipeau  
**% effort on this grant:** 10%

**List of co-applicants and % effort on this grant:** Aly Karsan (10%), Peter Landsorp (10%), Peter Liu (20%), Lynn Megeney (10%), Duncan Stewart (20%)

**Major goals of this project:** This proposal will assess the potential of stem cells to repair and regenerate critical organ function in three broad areas: cardiac, vascular and pulmonary. The ultimate goal is to develop novel and effective therapies while at the same time establishing innovative programs along lines of the major target organs.
Budgetary Overlap with present application: 0%

**Title of Grant:** CARENeT-SCN partnership: a focus on clinical translation of stem cells for cardiovascular regeneration  
**Funding Source and Program Name:** Stem Cell Network – Core Project Proposals 2005  
**Dollars requested:** Total awarded is $213,600 from September 1, 2005 to March 31, 2008.  
**Name of P.I.:** Jacques Galipeau  
**% effort on this grant:** 10%  
**List of co-applicants and % effort on this grant:** James Cross (10%), May Griffith (10%), Aly Karsan (10%), Bartha Knoppers (10%), Peter Liu (20%), Lynn Megeney (10%), Duncan Stewart (20%)  
**Major goals of this project:** This proposal will assess the potential of stem cells to repair and regenerate critical organ function in three broad areas: cardiac, vascular and pulmonary. The ultimate goal is to develop novel and effective therapies while at the same time establishing innovative programs along lines of the major target organs.  
**Budgetary Overlap with present application:** 0%

**Title of Grant:** Regroupement stratégique québécois pour la recherche et le développement de la thérapie cellulaire et génique pour les maladies hémovasculaires. 
**Funding Source and Program Name:** FRSQ- Subventions de recherches en médecine transfusionnelle et en hémovigilance Grant # 6089  
**Dollars awarded:** $673,205 over 3 years from May 2004 to April 2007  
**Name of P.I.:** Jacques Galipeau  
**% effort on this grant:** 15%  
**List of co-applicants and % effort on this grant:** Mark Blostein (20%), Marilyn Dunn (10%), Raymonde F. Gagnon (10%), Daniel Martineau (35%), Georges-E. Rivard (5%).  
**Major goals of this project:** The goal of this program is to develop a novel biopharmaceutical strategy for *in vivo* delivery of erythropoietin and anti-hemophilic factors, for treatment of anemia and hemophilia respectively.  
**% overlap with current application:** 0%

**Title of Grant:** Genetically Modified Autologous Blood and Marrow-derived Stem Cells for the Treatment of Hemophilia A  
**Funding Source and Program Name:** Bayer Hemophilia Award Program –Special project award (Grant #: not applicable)  
**Dollars awarded:** $180,000 US over 2 years from Sept. 2004 to Sept. 2006  
**Name of P.I.:** Jacques Galipeau  
**% effort on this grant:** 10%  
**List of co-applicant:** David Lillicrap (Queen’s University)  
**% effort on this grant:** 10%  
**Major goals of this project:** The specific experimental goals are as follows:  
1. To isolate and culture two forms of adult progenitor cell populations from humans and dogs: bone marrow stromal cells and blood outgrowth endothelial progenitors.  
2. To transduce each of the adult progenitor cell populations, *ex vivo*, with a recombinant 3rd generation lentiviral vector encoding the canine B domain-deleted factor VIII cDNA.  
3. Following re-introduction of the transduced progenitor cells in either immunodeficient mice or hemophilic dogs, factor VIII transgene expression will be followed by appropriate tests of hemostasis, and the fate of the genetically modified cells will be followed.  
**% overlap with current application:** 0%

**Title of Grant:** Marrow Stromal Cells for Transgenic Cell Therapy of Hemophilia A. 
**Funding Source and Program Name:** Partnership Funds with Bayer / CIHR / Canadian Blood Services / Hema Quebec (Grant # not applicable)
**Dollars awarded:** Total awarded is up to $195,050 over 2 years from October 2004 to September 2006

**Name of P.I:** Jacques Galipeau  
**% effort on this grant:** 15%

**List of co-applicants:** David Lillicrap and  
**% effort on this grant:** 15%

**Major goals of this project:** The specific experimental goals are as follows: I. To isolate and culture two forms of adult progenitor cell populations from humans and dogs: bone marrow stromal cells and blood outgrowth endothelial progenitors. II. To transduce each of the adult progenitor cell populations, *ex vivo*, with a recombinant 3rd generation lentiviral vector encoding the canine B domain-deleted factor VIII cDNA. III. Following re-introduction of the transduced progenitor cells in either immunodeficient mice or hemophilic dogs, factor VIII transgene expression will be followed by appropriate tests of hemostasis, and the fate of the genetically modified cells will be followed.

**% overlap with current application:** 0%

**Title of Grant:** Autologous bone marrow stromal cells genetically-engineered to secrete erythropoietin for anemia therapy

**Funding Source and Program Name:** Anemia Institute for Research and Education (AIRE) Operating Grant

**Dollars awarded:** Total awarded is up to $30,000 over 2 years from October 2004 to Sept. 2006

**Name of P.I:** Jacques Galipeau  
**% effort on this grant:** 15%

**List of co-applicants:** David Lillicrap and  
**% effort on this grant:** 15%

**Major goals of this project:** The goal of this study is to determine if sustained secretion of therapeutically relevant levels of mouse Epo can occur *in vivo* in immunocompetent anemic mice from gene-modified syngeneic bone marrow stromal cells implanted subcutaneously. In a second phase, this cell and gene therapy approach will be explored in normal dogs.

**% overlap with current application:** 0%

**Title of proposal:** Transcriptional synergy between retinoic acid and tumor necrosis factor

**Funding source and program name:** Leukemia Research Fund of Canada – Operating grant (Grant # not applicable)

**Dollars awarded:** $100,000 over 2 years from July 2004-July 2006.

**Name of PI:** Dr. Wilson H. Miller Jr.  
**% effort on this grant:** 5 hours/week

**List of co-applicants:** None  
**% effort on this grant:** N/A

**Major goals of this project:** This focuses exclusively on interactions between RA and TNF in leukemia cells.

**Title of proposal:** Mechanisms of the anti-cancer actions of arsenic

**Funding source and program name:** Canadian Institute of Health Research operating grant – Operating grant (Grant# MOP-43979)

**Dollars awarded:** $589,123 over 5 years from April 2004-March 2009.

**Name of PI:** Dr. Wilson H. Miller Jr.  
**% effort on this grant:** 5 hours/week

**List of co-applicants:** None  
**% effort on this grant:** N/A

**Major goals of this project:** This project focuses on the molecular mechanisms of the anti-cancer actions of arsenic and antimony in cancer cells.

**Title of proposal:** Mechanisms of response and resistance to transcriptional therapies in acute promyelocytic leukaemia

**Funding source and program name:** Canadian Institute of Health Research-Operating grant (Grant# MOP-108600)

**Dollars awarded:** $611,050 over 5 years from April 2003-March 2008.
Name of PI: **Dr. Wilson H. Miller Jr.**  
**% effort on this grant:** 5 hours/week  
**List of co-applicants:** None  
**% effort on this grant:** N/A  
**Major goals of this project:** This project focuses exclusively on retinoids and their actions in RA-sensitive and resistant APL cells. Both cell lines and cells from APL patients are used to investigate genetic changes that mediate retinoid resistance.

**Title of proposal:** CIHR Training Program  
**Funding source and program name:** Canadian Institute of Health Research-Strategic Training Program for MCETC (Grant # not applicable)  
**Dollars awarded:** $1,455,000 over 6 years from April 2002-March 2008.

Name of PI: Dr. G. Batist  
**% effort on this grant:** N/A  
**List of co-applicants and % effort on this grant:** W. Miller Jr.(5 hours/week); M. Alaoui-Jamali; J. Galipeau; C. Rancourt; S. Mader; J. White; R. Beliveau; M. Caruso; N. Nalbantoglu  
**Major goals of this project:** None- Salary support for students of MCETC.

**Title of proposal:** Modulation of multidrug resistance by rexinoids: Role of SXR and its target genes  
**Funding source and program name:** The Cancer Research Society-Operating Grant (Grant # not applicable)  
**Dollars awarded:** $120,000 over 2 years from September 2005-August 2007

Name of PI: **Dr. Wilson H. Miller Jr.**  
**% effort on this grant:** 5 hours/week  
**List of co-applicants:** None  
**% effort on this grant:** N/A  
**Major goals of this project:** This project focuses the mechanisms of regulation of SXR target genes by rexinoids in breast cancer cells.

**Title of Grant:** Regulation of SXR activation by rexinoids-role in drug resistance  
**Funding source and program name:** Susan G. Komen Breast Cancer Foundation- Grant # BCTR72606  
**Dollars awarded:** $242,765 over 2 years May 2006-April 2008

Name of PI: **Dr. Wilson H. Miller Jr.**  
**% effort on this grant:** 5 hours/week  
**List of co-applicants:** None  
**% effort on this grant:** N/A  
**Major goals of this project:** This project focuses the mechanisms of regulation of SXR target genes by rexinoids in breast cancer cells.

**SERVICE TO ACADEMIC COMMUNITY:**

**Ponka, P**

1) **Committee Participation**
   - Departmental: GSAAC
   - Faculty: Graduate Student Advisor (LDI) Department of Medicine
   - University: MAUT Council, Member
   - Jewish General Hospital: Academic Advisory Committee
   - Major research granting councils: CIHR, NIH
   - Editorial boards of peer-reviewed journals: Biochemical Journal, Editorial Advisory Panel, Member; Redox Reports; Journal of Trace Elements in Experimental Medicine
   - Conference program committees: Subcommittee on Iron and Heme – American Society of Hematology; BioIron 2005, Chairman (my involvement in organization of this Congress started in the fall of 2003)
ii) **Grant Panels:** CIHR (Pharmaceutical Sciences), NIH (Hematole II Study Section)

iii) **Professional Organizations**
- American Society for Hematology
- American Society for Biochemistry & Molecular Biology
- European Iron Club
- Canadian Physiological Society
- International Society of Experimental Hematology
- Canadian Society for Clinical Investigation
- Nitric Oxide Society
- International Society of Hematology

iv) **Invited Talks and Conference Presentations (2005-2006)**


“Iron: Our Friend and Foe”, the Third International Symposium on Natural Antioxidants – Molecular Mechanism and Health Effects (ISNA) and a Meeting of the Society for Free Radical Research (SFRR Asia), Shanghai, China, June 24-29, 2005 (presented by Dr. Guanjung Nie, my Postdoctoral Fellow).

“Recent Advances in Iron Metabolism”, Baylor College of Medicine, Houston, Texas, November 2, 2005.

“Why Grasse is Greene or Why our Blood is Red . . .”, Department of Pediatrics and Adolescent Medicine, Charles University Faculty of Medicine, Prague, November 8, 2005.

“Iron: Our Friend and Foe”, the Third Joint Meeting of the Society of Free Radical Research of Australasia and Japan, Griffith University Gold Coast Campus, QSL, Australia, December 2-6, 2005.


PEER REVIEWED PUBLICATIONS (PAST TWELVE MONTHS)

Diaz Z, Assaraf MI, **Miller WH Jr**, and Schipper HM. Astroglial cytoprotection by erythropoietin preconditioning: implications for ischemic and degenerative CNS disorders. Journal of Neurochemistry, 93:392-402, 2005


Hasanbasic, I., Rajotte, **Blostein W.** The role of gamma-carboxylation in the anti-apoptotic effect of gas6 in endothelium. J. Thromb & Hemostasis, 3: 2790-7, 2005

Jaalouk DE, Crosato M, Brodt P, **Galipeau J**. Inhibition of Histone Deacetylation in Retroviral Packaging Cell Lines Markedly Improves the Production of Self-Inactivating Retroviral Vectors. Submitted 2005


Kovarikova P, Klimes J, Sterba M, Popelova O, Mokry M, Gersl V, **Ponka P**. Development of high-performance liquid chromatographic determination of salicylaldehyde isonicotinoyl


Nie G, Sheftel AD, Kim SF, Ponka P. Overexpression of mitochondrial ferritin causes cytosolic iron starvation and changes cellular iron homeostasis. This article was accompanied by Editorial Commentary by Chitambar CR: Cellular iron metabolism; Mitochondria in the spotlight. Blood 105, 1844-1845, 2005.

Nie G, Chen G, Sheftel AD, Pantopoulos K, Ponka P. In vivo tumor growth is inhibited by cytosolic iron deprivation caused by the expression of mitochondrial ferritin (Blood, in press).


III OBJECTIVES AND PRIORITIES

i) Recruitment

Potential recruitment for 2008-2009 include Dr. Natalie Johnson who is currently receiving specialized training in molecular hematopathology in Vancouver under the Directorship of Randy Gascoyne and is simultaneously enrolled in the master’s program at the University of British Columbia.

Recruitment of a transfusion medicine specialist remains a priority as this is one area which requires new specialized expertise and is a fertile area for clinical research.

One of the difficulties in recruitment is related to the complex bureaucratic structure imposed in Quebec for the recruitment of specialists. Also recruitment quotas include physicians specialized in hematology and medical oncology making it necessary to coordinate recruitment between hematology and medical oncology. The lack of a combined hematology oncology division makes this process more difficult particular since oncology at the Jewish General Hospital has departmental status and includes both medical and surgical oncologists. It is hoped that over the
years the rigid structure at the governmental level and the unique structure of oncology at the Jewish General Hospital will change so that recruitment will be facilitated.

ii) Segal Cancer Centre

The resolution of space deficiencies including lack of adequate numbers of examining rooms and waiting room areas has now been resolved with the creation of the Segal Cancer Centre on the 7th and 8th floors of pavilion E. The necessity of dividing clinics into benign and malignant, however, has created logistical problems both in terms of human resources and medical records. However, it should be noted that the ultra modern facilities of the Segal Cancer Centre will be enormously beneficial to both patients and staff and has now created the necessary environment for patients to receive the highest quality of cancer treatment which the Jewish General Hospital strives to deliver.

The first floor pavilion E area for benign hematologic disease and thrombosis will be reconfigured in order to accommodate the personnel associated with the Thrombosis Clinic. Drs. Blostein and Hammouda continue to contribute in very meaningful ways to both the clinical and research component of the thrombosis service. Dr. Kahn also plans to establish a thrombosis consultation service which will include some members of the hematology division and will also offer elective rotations to hematology, pulmonary and other specialty fellow programs and an exposure to investigation and treatment of thrombotic disease for medical residents.

Respectfully submitted,

S. Caplan, MD