Annual Report
Division of Hematology-Oncology
April 1, 2005 – May 31, 2006

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.

CURRENT RESEARCH SUPPORT

Galipeau, J

Source	Title	Amount	Term	Starting date	Role
Department of National Defence (Canada)	Development and Optimization of Hemostatic Peptides For Hemorrhage Control	$380,000	3 years	September 2005	Principle Investigator
Heart and Stroke Foundation of Canada	The role of protein domains containing gamma-carboxy-glutamic acid in vascular biology	$45,000	3 years	July 2003	Principle Investigator
Canadian Institutes for Health Research (CIHR)	Physiology of gas6-Axl interactions	$76,957	1 year	January, 2006	Principle Investigator
Fonds de Recherche Scientifique du Qubec	Gene Therapy of Hemophilia B	$152,717	3 years	September 2004	Co-investigator (PI Dr. J. Galipeau)
Canadian Institutes for Health Research (CIHR)	Randomized Trial of Oral Vitamin K for Warfarin-Induced Coagulaopathy	$600,000	3 years	March 2005	Co-investigator of a clinical trial
Heart and Stroke Foundation of Canada	Thrombophilia in Pregnancy Prophylaxis Study	$600,000	3 years	July 2003	Co-investigator of a clinical trial
Canadian Institutes for Health Research (CIHR)	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	To be annouced	3 years	March 2006	Co-investigator of a clinical trial
Canadian Institutes for Health Research (CIHR)	CIHR Team Grant in Venous Thromboembolism	To be annouced	3 years	March 2006	Co-Investigator (PI Dr. J.Weitz)

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:

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: 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: 5hours/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: 5hours/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: 5hours/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.(5hours/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: 5hours/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: 5hours/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

i) 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)

"Kiss and Run: The Route of Iron from Endosomes to Mitochondria can Bypass the Cytosol in Hemoglobin-Producing Cells", Porphyrins and Porphyria 2005, Cape Town, South Africa, South Africa, February 27-March 3, 2005.

"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.

"Nitrogen Monoxide and Carbon Monoxide Dramatically Modulate Cellular and Molecular Iron Metabolism", Workshop on "Gaseous Signaling in Health and Disease", European Society for Clinical Investigation Meeting, Prague, Czech Republic, March 15-18, 2006.

"The Path of Iron from Plasma Transferrin to Hemoglobin in Developing Red Blood Cells", Mini-Symposium on "Metals in Blood", Centre for Blood Research, University of British Columbia, April 10-11, 2006.

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

Diaz Z, Colombo M, Mann KK, Su H, Smith KN, Bohle DS, HM Schipper, **Miller WH Jr**. Trolox selectively enhances arsenic-mediated oxidative stress and apoptosis in APL and other malignant cell lines. Blood, 105:1237-1245, 2005.

Eliopoulos N, Stagg J, Lejeune L, **Galipeau J**. Allogeneic Marrow Stromal Cells are Immune Rejected by MHC Class I and II Mismatched Recipient Mice. Blood 2005 Dec 15, 106 (13): 4057-65.

Fazi F, Travaglini L, Carotti D, Palitti F, Diverio D, Alcalay M, McNamara S, **Miller WH Jr**, Lo Coco F, Pelicci PG, Nervi C. Retinoic targets DNA-methyltransferases and histone deacetylases during APL blast differentiation in vitro and in vivo. Oncogene, 24:1820-1830, 2005.

Fillebeen C, Rivas-Estilla AM, Bisaillon M, **Ponka P**, Muckenthaler M, Hentze MW, Koromilas AE, Pantopoulos K. Iron inactivites the RNA polymerase N25B and suppresses subgenomic replication of hepatitis C virus. J Biol Chem 280: 9049-9057, 2005.

Fontaine F, Boucher H, Hernandez J, Eliopoulos N, Dunn M, MacLeod JN, **Galipeau J**, Martineau D. Long-term delivery of erythropoietin in immunocompetent dogs by an organoid composed of bone marrow stromal cells. Submitted *2005*

Gornitsky M., **Hammouda M**., Rosen H. Rehabilitation of a Hemophiliac with implants: A medical perspective and case report. J. Oral Maxillofac. Surg. 63: 592-597, 2005

Goss G, Hirte H, **Miller WH Jr**, Lorimer IA, Stewart D, Batist G, Parolin DA, Hanna P, Stafford S, Friedmann J, Walsh W, Mathews S, Douglas L, Seymour LK. A phase I study of oral ZD 1839 given daily in patients with solid tumors: IND.122, a study of the Investigational New Drug Program of the National Cancer Institute of Canada Clinical Trials Group. Invest New Drugs, 23:147-55, 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.

Kahn ,S.K., Elyssa E., Bornais, C., **Blostein, M.** Wells, P.S. Post-thrombotic syndrome, functional disability and quality of life after upper extremity deep venous thrombosis in adults. J. Thromb & Hemostasis 93:499-502, 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

hydrazone in rabbit plasma and application of this method to an in vivo study. J Sep Sci 28: 1300-1306, 2005.
Kovarikova P, Klimes J, Sterba M, Popelova O, Gersl V, **Ponka P**. HPLC determination of a novel aroylhydrazone iron chelator (o-108) in rabbit plasma and its application to a pilot pharmacokinetic study. J Chromatogr B Analyt Technol Biomed Life Sci May 2006 (E-pub ahead of print).

MacKenzie M, Hirte H, Goss G, Maroun J, Goel R, Major P, **Miller WH Jr,** Panasci L, Lorimer I, Batist G, Mattews S, Douglas L, Seymour L. A Phase II trial of ZD1839 (Iressa) 750 mg per day, an oral epidermal growth factor receptor-tyrosine kinase inhibitor, in patients with metastatic colorectal cancer. Investigational New Drugs, 23:165-170, 2005.

Mann KK, Padovani AMS, Guo Qi, Colosimo AL, Lee HY, Kurie JM, **Miller WH Jr**. Arsenic trioxide inhibits nuclear receptor function via JNK-mediated RXR phosphorylation. J Clin Invest, 115: 2924 - 2933, 2005.

Mims MP, Guan Y, Pospisilova D, Priwitzerova M, Indrak K, **Ponka P**, Divoky V, Prchal JT. Identification of a human mutation of DMT1 in a patient with microcytic anemia and iron overload. Blood 105: 1337-1342, 2005.

Mouralian C, Buss JL, Stranix B, Chin J, **Ponka P**. Mobilization of iron from cells by hydroxyquinoline-based chelators. Biochem. Pharmacol 71: 214-222, 2005.

Napier I, **Ponka P**, Richardson DR. Iron trafficking in the mitochondrion: Novel pathways revealed by disease. Blood 105: 1867-1874, 2005.

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).

Pathak B, Bruchim I, Brisson M.L, **Hammouda W,** Bloom C, Gotlieb W.H. Granulocytic sarcoma presenting as tumors of the cervix. Gynecologic Oncology 98: 493-497, 2005

Perri SR, Nalbantoglu J, Annabi B, Koty Z, Lejeune L, François M, Di Falco MR, Béliveau R, **Galipeau J**. Plasminogen Kringle 5-engineered glioma cells block migration of tumor-associated macrophages and suppress tumor vascularization and progression. Cancer Research 2005 65: 8359-8365.

Ponka P, Eaton J. Iron. In: Handbook of Toxicology of Metals, Third Ed. (G Nordberg, B Fowler, M Nordberg, L Fridberg, eds.), Elsevier (in press).

Priwitzerova M, Nie G, Sheftel AD, Pospisilova D, Divoky V, **Ponka P.** Functional consequences of the human DMT1 (SLC11A2) mutation on protein expression and iron uptake. Blood 106: 3985-3987, 2005 (Epub August 2005).

Sharma K, Lejeune L, Copland I, Eliopoulous E, Lachapelle K, **Galipeau J**. CD34 Expression by Murine Marrow Stromal Cells and Angiogenesis. Submitted *2005*.

Simunek T, Klimtova I, Kaplanova J, Sterba M, Mazurova Y, Adamcova M, Hrdina R, Gersl V, **Ponka P**. Study of Daunorubicin cardiotoxicity prevention with pyridoxal isonicotinoyl hydrazone in rabbits. Pharmacol Res 51: 223-231, 2005.

Simunek T, Boer C, Bouwman RA, Vlasblom R, Versteilen AM, Streba M, Gersl V, Hrdina R, **Ponka P**, de Lange JJ, Paulus WJ, Musters RJ. SIH-a novel lipophilic iron chelator-protects H9c2 cardiomyoblasts from oxidative stress-induced mitochondrial injury and cell death. J Mol Cell Cardiol 39: 345-354, 2005.

Stagg J, Pommey S, Eliopoulos N, **Galipeau J**. Interferon-γ-Stimulated Marrow Stromal Cells: A New Type of Non-Hematopoietic Antigen Presenting Cell. Blood. 2006 Mar 15;107:2570-2577.

Sterba M, Popelova O, Mazurova Y, Adamcova M, Gersl V, **Ponka P**. Safety and tolerability of repeated administration of pyridoxal 2-chlorobenzoyl hydrazone in rabbits. Human and Experimental Toxicology 24: 581-589, 2005.

Watts RN, Hawkins C, **Ponka P**, Richardson DR. Nitrogen monoxide (NO)- mediated iron release from cells is linked to NO-induced glutathione efflux via multidrug resistance-associated protein 1. Proc Natl Acad Sci USA. 103: 7670-7675, 2006.

Zhang A-S, Sheftel AD, **Ponka P.** Intracellular kinetics of iron in reticulocytes: evidence for endosome involvement in iron targeting to mitochondria. Blood 105: 368-375, 2005.

Zhang AS, Sheftel AD, **Ponka P**. The anemia of "Haemoglobin deficit" (hbd/hbd) mice is caused by a defect in transferrin cycling. Exp Hematol 34: 593-598, 2006.

III OBJECTIVES AND PRIORITIES

i) <u>Recruitment</u>

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) <u>Segal Cancer Centre</u>

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