

Annual Report
Division of Hematology
Department of Medicine - Jewish General Hospital
January 1 - December 31, 2012

SUMMARY

1. Clinical programs, research and publications

Stem Cell Transplant Program

The Jewish General Hospital's hematology stem cell transplant program continues to remain a strong component of the McGill bone marrow transplant program. The Jewish General Hospital performed 45 autologous stem cell transplants in 2012, the largest number per year since its inception in 1993. The main focus of this activity has been in multiple myeloma, Hodgkin's, non-Hodgkin's lymphoma and acute leukemia and has contributed significantly to increased survival of patients with these malignant diseases. Dr. Martin Gyger continues to provide leadership for efforts in this area and maintains close collaboration with our MUHC partners and with colleagues at Hôpital Maisonneuve Rosemont. The Jewish General Hospital continues to perform its activity with official designation from the Ministry of Health as an approved center for the performance of autologous stem cell transplants. In addition, the Molecular Diagnostics Laboratory at the JGH supports the allogeneic transplant program at the MUHC, by providing molecular assays for chimerism post-transplant.

The division now has two Infirmière-Pivots (IPOs) which have significantly contributed to the improvement in supportive therapy, psychological support and communication with families. Our senior IPO, Chantal Cloutier, has also played a pivotal role in establishing links with other institutions and with local CLSCs and has been extremely active nationally in nursing oncology educational programs.

Molecular Diagnostics Laboratory

The Jewish General Hospital remains as the referral hospital for molecular diagnostics for the entire McGill hematology university network. New molecular studies have been initiated for chronic lymphocytic leukemia, myeloproliferative disorders, lymphoma and acute leukemia. Our molecular laboratory serves as the sole laboratory engaged in teaching of molecular diagnostics to hematology fellows. A major expansion and relocation to Pavilion E is anticipated to be completed in mid-2013.

CML Clinic

Dr. Sarit Assouline has continued as Director of the CML clinic which now follows close to 100 patients with this rare disorder, the largest single clinic for this disease in Quebec. Dr. Jaroslav Prchal, from St. Mary's Hospital, and Dr. Shireen Sirhan are also active participants in the clinic and help provide the highly specialized care to these patients, offering innovative clinical trials for patients with relapsed and refractory disease.

Myeloproliferative disorder - MPD clinic

The MPD clinic has now been in operation for 4 years supported by a substantial contribution from a donor to support the activities of the MPD clinic. The clinic has now registered more than

100 patients to the MPD registry and has been extremely active in clinical trial accrual for both myelofibrosis and polycythemia vera.

Dr. J Prchal is a member of a large international consortium which has successfully applied to the National Cancer Institute in the United States for funding for research and clinical trials in myeloproliferative disorders. His contribution and members in the consortium is an essential part of the development of this specialized clinic which will provide not only highly specialized care to patients with polycythemia vera, essential thrombocythemia and myelofibrosis but also offer participation in innovative clinical trials.

Gaucher Clinic

Dr. Sarit Assouline is responsible for the treatment of adult patients with Gaucher disease for the province of Quebec, an activity for which the Jewish General Hospital has been mandated for the last 15 years.

Dr. Sarit Assouline, a previous recipient of an FRSQ Chercheur Boursier Clinicienne, is Director of Clinical Research in Hematology-Oncology as well as Associate Director of the Clinical Research Unit. She continues to be an active member of the hematology-oncology group at NCIC and has brought to the hospital a number of innovative phase I and phase II clinical trails through the Clinical Research Unit at the Jewish General Hospital. She oversees the on ongoing clinical trials in leukemia and lymphoma. She is also conducting 2 investigator initiated trials with strong translational component. She generated 9 abstracts at American Society of Hematology annual conference in December 2012 including 2 oral presentations and 7 posters. In terms of publications, she published 2 articles on clinical trials, one in *Blood* and one in *Leukemia and Lymphoma*.

Dr. Mark Blostein has contributed significantly, in past years, to the area of protein biochemistry of factor IX coagulation protein and also has been an integral part of the clinical trials effort of the Thrombosis Group at the Jewish General Hospital. As current associate Chief of the Division of Hematology, he has published 7 papers, including three major works from his laboratory that were published in *Blood*, *The Journal of Thrombosis and Hemostasis* and *Journal of Trauma*, also including a major clinical paper on Octaplex use at the Jewish General Hospital in *Transfusion*. He is also a co-investigator on a Canadian Heart and Stroke Foundation funded clinical trial examining an optimal strategy for peri-operative management of dabigatran and printed the third edition of Anticoagulation Guidelines. The Dean of Medicine, David Eidelman, personally congratulated Dr. Blostein on his work as director of the Clinical Investigator Program

Dr. Nathalie Johnson, after completing a PhD program at the University of British Columbia, was awarded an FRSQ Chercheur Boursier Clinicienne for her research program in the molecular hemato-pathology of malignant lymphoma. In 2012, she authored a manuscript in the *Journal of Clinical Oncology* that investigated the prognostic effect of MYC and BCL2 protein expression in diffuse large B cell lymphoma (DLBCL). She also co-first authored two additional manuscripts, demonstrating that BCL2 is the most mutated gene in diffuse large B cell lymphoma, and that these mutations are associated with high protein expression and therapeutic resistance in a subset of patients. The second manuscript identified a novel biomarker that could be identified by flow cytometry in lymphoma. A high side scatter profile was associated with more aggressive disease

in diffuse large B cell lymphoma and this marker was identifiable using conventional flow cytometry panels for immunophenotyping lymphomas that are currently used in most flow cytometry laboratories.

2. Teaching and learning:

All doctors in the Division of Hematology participate in teaching activities, whether through consult service (Hematology and Thrombosis), clinics, Introduction to Internal Medicine Senior Physician Rounds or Clinical Teaching Unit on 7NW.

Dr. Sarit Assouline continues to be involved as an Osler fellow, now in its 4th year. She was supervisor to a Hematology Fellow during their longitudinal clinical rotation and has ongoing research projects with 2 hematology residents as well as 2 internal medicine residents. She submitted an abstract to ASCO (American Society of Clinical Oncology).

Dr. Mark Blostein taught Approach to Anticoagulation throughout the year to undergraduate students and Bridging to Postgraduate medical students in February. He had one student who was granted an oral presentation at the Annual American Society of Hematology annual meeting and his third graduate student in his laboratory obtained his PhD from the department of Physiology.

Dr. Nathalie Johnson supervised a research trainee from the British Columbia Institute of Technology. She was a CME guest speaker at JGH rounds family medicine for 60 family doctors in March and gave 2 lectures to the Hematology Fellows; Approach to Aggressive Lymphomas in July and Approach to the Management of Hodgkin Lymphoma in August. She also participated in the Graduate teaching in February and November, Hereditary cancers: Genetic predisposition to lymphomas and Genetics of Lymphoma, respectively.

3. Involvement in the community:

Dr. Sarit Assouline was an invited lecturer for Weizmann institute lecture series. She was also invited to speak to the Leukemia and Lymphoma society about clinical trials during a weekend retreat in June 2012. She participated in INESSS to review drugs for reimbursement in CML.

Dr. April Shamy, as a founding member of the Canadian Myelodysplastic Syndrome consortium, organized the Canadian Conference Myelodysplastic Syndrome September 2012 which included speakers from across Canada, the United States and abroad.

Dr. Mark Blostein has been a Member, for the third year in row, of the Doctoral Research Awards A (DRA) and Canada Graduate Scholarships Master's Awards A (CGA) committees at CIHR

Dr. Nathalie Johnson is the representative hematologist for the McGill Adolescent and Young Adult Oncology Team that also comprises of oncologists, exercise therapists, a nurse, a psychologist, a social worker, a pharmacist, a physiotherapist and an occupational therapist. In November 2012, the McGill AYA team was honored with an award highlighting our extraordinary contribution to improving the cancer experience for adolescent and young adults by the VOBOS (Venturing out beyond Cancer) Foundation, a support program dedicated to helping adolescents and young adults with cancer.

4. Partnerships:

The division has expanded its out-reach program by establishing corridors de service with the Lakeshore General Hospital, St. Mary's Hospital, Jean Talon Hospital and more recently the Verdun and Brome-Missisquoi-Perkins Hospitals.

Dr. Sarit Assouline is part of GQR LMC, Quebec consortium for CML, head of research. She is also newly appointed Investigational New Drug representative for McGill and for hematology to the NCIC-CTG IND.

Dr. Stephen Caplan is a funding member of the Canadian consortium, mandated to offer expertise in diagnosis and treatment of PNH (Paroxysmal Nocturnal Hemoglobinuria).

5. Milestones: new hires, promotions, and retirements:

In 2012, there has been the largest number of patients enrolled in clinical trials for leukemia and lymphoma, for a total of 53 patients making about one per week.

Dr. Mark Blostein was instrumental in redesigning the benign hematology area while accommodating needed space for the department of Medical Biochemistry.

There have been no changes in staffing.

Dr. Mark Blostein was appointed Associate Chief for the Division of Hematology.

Dr. Stephen Caplan was appointed Associate Director of Clinical Operations for the Segal Cancer Center.

6. Honours, awards, and prizes: None reported

7. Fundraising: None

SECTION I - DIVISION STATUS UPDATE

1. Mission and objectives of the Division

Recruitment for future years will continue to focus on the addition of clinician-scientists including those engaged in clinical research or in basic science research. A continued major focus for the next year will be to attempt to recruit an academic physician to take on the leadership role of the division to replace the current director of hematology who has been in the position since 1997. A meeting was recently held with the interim Chairman of Medicine to discuss the possibility of a simultaneous search for a Director of the McGill Division of Hematology with the hope that this director will be physically situated at the Jewish General Hospital and become its hospital division director.

The principle goals for the future will be to recruit young physicians with academic ambition and appropriate training to accomplish their goals. This requires identification early on of residents during their training, assisting them in finding the best academic programs to further their goals, and providing an attractive environment to which they could be recruited and flourish as clinical or laboratory researchers. The success of clinician-scientists hinges on planning to ensure mentoring by senior physicians or scientists, protected time for research and a strong financial base to support their research activities.

2. A nominative list of academic staff, their academic rank

Dr. Sarit Assouline	Assistant Professor	Active
Dr. Mark Blostein	Associate Professor	Active
Dr. Stephen Caplan	Associate Professor	Active
Dr. Chantal Cassis	Faculty Lecturer	Active
Dr. Martin Gyger	Full Professor	Active
Dr. Nathalie Johnson	Assistant professor, tenure track	Active
Dr. Francois Patenaude	Assistant professor	Active
Dr. Jaroslav Prchal	Associate Professor	Active
Dr. Arthur Rosenberg	Associate Professor	Active
Dr. April Shamy	Assistant Professor	Active
Dr. Shireen Sirhan	Faculty Lecturer	Active

SECTION II - GRANTS, PUBLICATIONS, AND SERVICE OUTSIDE OF MCGILL

1. Grants and awards received

Dr. Sarit Assouline

2012-2013	Co-applicant with Dr. Wilson Miller on CIHR grant; \$150,000 for 4 years Applied in 2012 but received in 2013
2010-13/10	Co-investigator on LLS US TRP grant with Katherine Borden; \$200,000/year for 3 years
2010-2014	Fonds de Recherche en Santé du Québec (FRSQ), chercheur clinicien boursier Junior 1

Dr. Mark Blostein

- 2011 Co-investigator of a clinical trial 5%, National Institutes of Health; Amount TBD; 4 years; Bridging Anticoagulation in Patients who Require Temporary Interruption of Warfarin Therapy for an Elective Invasive Procedure or Surgery, (BRIDGE) Trial
- 2012 Co-investigator of a clinical trial 5%, Heart and Stroke Foundation of Canada; \$140,000; 3 years; A prospective cohort study on the safety of interruption of dabigatran therapy for invasive procedures
- 2009 Principal Investigator 100%, Heart and Stroke Foundation of Canada; \$45,000; 3 years; Role of ga6 in Vascular Biology
- 2006 Co-investigator of a clinical trial 5%, Canadian Institutes for Health Research (CIHR); \$600,000, 3 years, Thrombophilia in Pregnancy Prophylaxis Study

Dr. Nathalie Johnson

- 2011-2015 FRSQ- Junior 1 research grant; PI; \$33,708 total
The biology of lymphomas in adolescents and young adults
- 2010-2013 Cole foundation transitional award; PI; \$50,000/year x 3 years
The biology of lymphomas in adolescents and young adults
- 2010-2013 Start-up funding from the Lady Davis Institute; PI; \$100,000/year x 3 years
- 2012/13 Canada Foundation for Innovation; PI; \$250,000
Targeting apoptotic pathways in lymphoma
- 2012 Hoffmann La Roche Limited; PI; \$29,250.00
Overcoming therapeutic resistance in lymphoma, funds to support tumour banking
- 2012-2013 The Jewish General Hospital Foundation; PI; \$150,000
Support for lymphoma tissue banking at the JGH (BCLQ)
- 2011-2013 Hoffmann-la Roche Limited, A Phase III, Multicenter, Open-Label, Randomized Trial Comparing the Efficacy of Ga101 (R05072759) in Combination with CHOP (G-CHOP) versus Rituximab and CHOP (R-CHOP) in Previously Untreated Patients with CD20-Positive Diffuse Large B-Cell Lymphoma (DLBCL); PI at McGill; \$102,000
- 2011-2015 Fonds de Recherche en Santé du Québec (FRSQ), chercheur clinicien boursier Junior 1

2. Scholarly works published in the 2012 calendar year:

Dr. Sarit Assouline

- Macdonald DA, **Assouline SE**, Brandwein J, Kamel-Reid S, Eisenhauer EA, Couban S, Caplan S, Foo A, Walsh W, Leber B. A phase I/II study of sorafenib in combination with low dose cytarabine in elderly patients with acute myeloid leukemia or high-risk myelodysplastic syndrome from the National Cancer Institute of Canada Clinical Trials Group: trial IND.186. *Leuk Lymphoma*. 2012 Nov 15.
- Sehn LH, **Assouline SE**, Stewart DA, Mangel J, Gascoyne RD, Fine G, Frances-Lasserre S, Carlile DJ, Crump M. A phase 1 study of obinutuzumab induction followed by 2 years of maintenance in patients with relapsed CD20-positive B-cell malignancies. *Blood*. 2012 May 31; 119(22):5118-25.

Dr. Mark Blostein

- Robins RS, Lemarié CA, Aghourian MN, Jianqiu Wu J, **Blostein MD**. Vascular gas6 contributes to thrombogenesis and promotes tissue factor upregulation following vessel injury in mice. *Blood*, *in press*, 2012.
- Varga C, Al-Touri S, Papadoukakis S, Caplan S, SR Kahn, **Blostein MD**. The Effectiveness and Safety of Fixed Low Dose Prothrombin Complex Concentrates in Patients Requiring Urgent Reversal of Warfarin. *Transfusion*, *in press*, 2012
- Kahn SR, Springmann V, Schulman S, Martineau J, Stewart JA, Komari N, McLeod A, Strulovitch C, **Blostein M**, Faucher JP, Gamble G, Gordon W, Kagoma PK, Miron MJ, Laverdière D, Game M, Mills A. Patterns of management and adherence to venous thromboembolism (VTE) treatment guidelines in a national prospective cohort study of VTE management in the Canadian outpatient setting: The Recovery Study. *Thromb Haemost*. 2012 Jul 10;108
- Laurence S, Lemarie CA, **Blostein, MD**. Growth arrest-specific gene (gas6) and vascular hemostasis. *Advances in Nutrition*, 2012 Mar 1;3(2):196-203.
- Aghourian M, Lemarié CA, **Blostein MD**. In Vivo Monitoring Of Venous Thrombosis In Mice. *Journal of Thrombosis and Hemostasis*, 10 :447-52, 2012.
- Peng HT, **Blostein MD**, Shek PN Characterization of In Vitro Hemostatic Peptide Effects by Thromboelastography. *Clin Appl Thromb Hemost*. 18 :27-34,2012
- Charbonneau S, Lemarié CA, Peng HT, Ganopolsky JG, Shek PN, and **Blostein MD**. Surface-attached Amphipathic Peptides Reduce Hemorrhage *J Trauma*, 72(1):136-42, 2012.
- Nishida K, Chiba K, Iwasaki YK, Katsouras G, Shi YF, **Blostein MD**, Khairy P, Guerra PG, Dubuc M, Tardif JC, Tanguay JF, Nattel S. Atrial fibrillation-associated remodeling does not promote atrial thrombus formation in canine models. *Circ Arrhythm Electrophysiol*. 2012 Dec 1;5(6):1168-75
- Easton JD, Lopes RD, Bahit MC, Wojdyla DM, Granger CB, Wallentin L, Alings M, Goto S, Lewis BS, Rosenqvist M, Hanna M, Mohan P, Alexander JH, Diener HC; ARISTOTLE Committees and Investigators * (local site investigator: **Blostein, M**. Apixaban compared with warfarin in patients with atrial fibrillation and previous stroke or transient ischaemic attack: a subgroup analysis of the ARISTOTLE trial. *Lancet Neurol*. 2012 Jun; 11(6):503-11.

Dr. Stephen Caplan

- Varga C, Al-Touri S, Papadoukakis S, **Caplan S**, SR Kahn, Blostein MD. The Effectiveness and Safety of Fixed Low Dose Prothrombin Complex Concentrates in Patients Requiring Urgent Reversal of Warfarin. *Transfusion*, Oct 15. 1537-2995.
- Macdonald DA, Assouline SE, Brandwein J, Kamel-Reid S, Eisenhauer EA, Couban S, **Caplan S**, Foo A, Walsh W, Leber B. A phase I/II study of sorafenib in combination with low dose cytarabine in elderly patients with acute myeloid leukemia or high-risk myelodysplastic syndrome from the National Cancer Institute of Canada Clinical Trials Group: trial IND.186. *Leuk Lymphoma*. 2012 Nov 15.

Dr. Nathalie Johnson

- Singh RR, Ben-Neriah S, **Johnson NA**, Connors JM, Gascoyne RD, Horsman DE. Identification of a novel non-immunoglobulin/MYC translocation t(8;12)(q24;p12) involving the LRMP gene in a primary B-cell lymphoma. A case report. *Leuk Res*. 2012 Jan;36(1):e22-4.

--Schuetz JM, **Johnson NA***, Morin RD, Scott DW, Tan K, Ben-Nierah S, Boyle M, Slack GW, Marra MA, Connors JM, Brooks-Wilson AR and Gascoyne RD. BCL2 mutations in diffuse large B-cell lymphoma. *Leukemia*. 2012 Jun;26(6):1383-90. * **contributed equally as first authors**

--Bashashati A, * **Johnson NA***, Khodabakhshi AH, Whiteside MD, Zare H, Scott DW, Lo K, Gottardo R, Brinkman FSL, Connors JM, Slack JW, Gascoyne RD, Weng AP, Brinkman RR. B-cells with high side scatter parameter by flow cytometry correlate with inferior survival in diffuse large B cell lymphoma. *Am J Clin Pathol*. 2012 May;137(5):805-14. * **contributed equally as first authors**

--**Johnson NA***, Slack JW*, Savage KJ, Connors JM, Ben-Neriah S, Rogic S, Scott DW, Tan KL, Steidl C, Horsman DH, Sehn LH, Chan WC, Iqbal J, Meyer P, Lenz G, Wright G, Rimsza LM, Valentino C, Brunhoeber P, Grogan TM, Braziel RM, Cook JR, Tubbs RR, Weisenburger DD, Campo E, Rosenwald A, Ott G, Delabie J, Jaffe ES, Staudt LM and Gascoyne RD. Concurrent expression of MYC and BCL2 in R-CHOP treated diffuse large B cell lymphoma. *J Clin Oncol*. 2012 Oct 1;30(28):3452-9. Epub 2012 Jul 30.

--Valentino C, Kendrick S, **Johnson NA**, Gascoyne R, Chan WC, Weisenburger D, Braziel R, Cook JR, Tubbs R, Campo E, Rosenwald A, Ott G, Delabie J, Jaffe E, Zhang W, Brunhoeber P, Nitta H, Grogan T, Rimsza L. Colorimetric in-situ hybridization identifies MYC gene signal clusters correlating with increased copy number, mRNA, and protein in diffuse large B-cell lymphoma. *Am J Clin Pathol*. 2013 Feb;139(2):242-54.

--Khodabakhshi AH, Morin RD, Fejes AP, Mungall AJ, Mungall KL, Bolger-Munro M, **Johnson NA**, Connors JM, Gascoyne RD, Marra MA, Birol I, Jones SJM. Recurrent targets of aberrant somatic hypermutation in lymphoma. *Oncotarget*. 2012 Nov;3(11):1308-19.

Abstract: **Nathalie A. Johnson**, Denis Gaucher, Hawley Rigsby, Ryan Morin, Tesa Severson, Andrew J. Mungall, Yongjun Zhao, Jacqueline E. Schein, Merrill Boyle, Bruce Woolcock, Richard Moore, Robert Holt, Joseph M. Connors, Steven Jones, Martin Hirst, Marco A Marra and Randy D. Gascoyne. *FAS* Mutations are Associated with Therapeutic Resistance in Follicular Lymphoma. Accepted as a poster at the American Society of Hematology meeting in Dec 2012.

3. Academic and community engagement service outside of McGill by individual members of the unit

Dr. Nathalie Johnson

External Committees and Boards

- Director of the Lymphoma tissue banking activities of the “Banque de Cellules Leucémiques du Québec” (BCLQ) : Initiated and directed the expansion of the existing BCLQ to include lymphoma tissue located at the Jewish General Hospital
- National Lymphoma tumour bank committee: The Lymphoma-axis of the BCLQ is the only Quebec representative on the committee to harmonize lymphoma banking activities in Canada provincial tumour banks meet once a year in March at the Canadian Conference on Lymphoproliferative disorders
- Fonds de Recherche en santé du Québec (FRSQ): Banque de tumeurs au Québec:Lymphoma representative at the annual meeting Sept 10th 2012

Scientific Reviews (grant panels, editorial boards, journal reviews) - Ad hoc reviews for peer reviewed journals

-Hematologica, Nature Reviews Oncology, Leukemia and Lymphoma, New England Journal of Medicine, Experimental Hematology

Grant Reviews

02/2012 Cancecare Manitoba Foundation Research Operating grants

Invited Presentations and Workshops - Invited lectures to national and international conferences

15/03/2012 3rd Quebec Conference on Therapeutic Resistance 200 physicians and scientists
Overcoming Therapeutic Resistance in Lymphoma

Invited Lectures, Talks, Presentations

06/06/2012 Hôpital Maisonneuve Rosemont clinical rounds, ~20 hematologists, 1 hour
Oncogene addiction in lymphoma

25/9/2012 Hôpital Enfant Jesus Clinical Hematology Rounds, ~20 hematologists, 1 hour
Role of MYC and BCL2 in DLBCL

25/9/2012 Hotel Dieu de Québec Clinical Hematology Rounds, ~20 hematologists, 1 hour
Role of MYC and BCL2 in DLBCL

07/11/2012 Hôpital Charles Lemoyne Clinical Heme-Oncology Rounds, ~20 oncologists, 1 hour,
Therapeutic resistance to R-CHOP in diffuse large B cell lymphoma

Community Outreach (public lectures, media interviews etc)

12/11/2012 Symposium Lymphome Action, given to ~200 people supporting the Lymphoma
Research Foundation (health advocates, nurses, physicians, patients), 20 minutes:
Biobanque de lymphomes: une mine d'or pour les chercheurs du Québec

Other contributions

18/05/2012 Lady Davis Institute Retreat: Judge for best poster competition

2012 Canadian Institute for Health Research (CIHR) Synapse Youth Mentorship
Initiative Program: mentoring a high school student Alara Ulker, meeting with her
2 hours

Personal and professional development

Nov 4-6, 2011 New CIHR investigator meeting in Mont-Gabriel

March 2012 Leadership Development workshop at faculty of McGill

SECTION III - CONFIDENTIAL INFORMATION

1. Consulting activities: None reported

Respectfully submitted,

Stephen N. Caplan, MD, FRCPC
Director, Division of Hematology