

Annual Report
Division of Hematology
Department of Medicine - Jewish General Hospital
January 1 - December 31, 2013

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 40 autologous stem cell transplants in 2013, one of the largest number per year since the inception of the program 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.

Segal Cancer Center

The hematology-oncology division of the Segal Cancer Center 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 the 6th floor of Pavilion E has been completed and the laboratory has now moved into state of the art facilities in the Cancer Center.

CML Clinic

Dr. Sarit Assouline has continued as Director of the CML clinic which now follows more than 100 patients with this rare disorder, one of the largest single clinic for this disease in Quebec. Dr. Jaroslav Prchal is an active participant in this clinic.

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.

Bridging Anticoagulation Service

Dr. Mark Blostein has established a peri-operative anticoagulation management service for all patients on oral anticoagulants who require an invasive procedure at the Jewish General Hospital. Approximately 350 patients per year are managed by this service

Gaucher Clinic

Dr. Sarit Assouline is responsible for the treatment of adult patients with Gaucher's disease for the province of Quebec, an activity for which the Jewish General Hospital has been mandated for the last 16 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 is now the hematology representative and the McGill representative to the Investigational New Drug group of the 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 8 abstracts at American Society of Hematology annual conference in December 2013 including 2 oral presentations and 6 posters. She publishes regularly in the domain of clinical drug development in leukemia and lymphoma.

Dr. Mark Blostein has contributed significantly, in past years, to the area of the basic science of venous thromboembolism. His laboratory is funded by the Heart and Stroke Foundation of Canada. In addition, he 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, published in *Transfusion*, on Octaplex use at the Jewish General Hospital. He is a co-investigator on four major peer review nationally funded clinical trials examining optimal strategies for the peri-operative management of anticoagulants. 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 and a CRC award (declined) for her research program in the molecular hemato-pathology of malignant lymphoma. In 2013, she

significantly increased her teaching activities within the department of experimental medicine by giving 5 lectures in 4 classes and providing supervision to 2 master's student in her laboratory. She was successful in obtaining a CIHR operating grant, published 5 manuscripts and was invited to give 5 oral presentations in 2013.

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 is involved in the morphology teaching of hematology fellows. She also lectures at medicine and oncology teaching rounds. She participates in senior physician rounds has ongoing research projects with 2 hematology residents as well as 2 internal medicine residents

Dr. Mark Blostein taught Approach to Anticoagulation throughout the year to undergraduate students and Bridging Anticoagulation to Postgraduate residents and fellows. In addition, he teaches Coumadin management in the Anticoagulation to all trainees rotating through the Thrombosis elective at the Jewish General Hospital. He has two graduate students in the Department of Physiology and a post-doctoral fellow in the Department of Experimental Medicine. He pioneered an iPhone app for house staff regarding Anticoagulation and is a program director for the Clinical Investigator Program. He is also member of the Royal College of Physicians and Surgeons advisory committee for the Clinical Investigator Program.

Dr. Nathalie Johnson has been actively involved in teaching students at the undergraduate, graduate and post-graduate levels at McGill. In addition to the clinical teaching mentioned above, she supervises two graduate students in her laboratory who are enrolled in their Master's degree in the department of experimental medicine (Maryam Bayat and Stephanie Totten) and one undergraduate student in the summer of 2013 (Guila Wasserlauf). She has given lectures for 4 graduate level classes in experimental medicine in 2013: EXMD 635, 2 lectures of 2 hours each, EXMD614, 2 hours, EXMD 607, 2 hours, EXMD 516-616, 2 hours. She was responsible for teaching flow cytometry to the hematology fellows (nine lectures, 1 hour each). She also supervised 2 research projects performed by hematology fellows Bader Al-Rawahi and Sabina Rusu.

3. Involvement in the community:

Dr. Sarit Assouline has participated in INESSS to review drugs for reimbursement in lymphoma. She has also reviewed manuscripts for Blood and Leukemia and Lymphoma.

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 actively involved in scholarly activities in the research community. She reviewed manuscripts for various journals including Leukemia, Blood and the British Journal of Hematology. She is the director the provincial lymphoma tissue banking activities of the Banque de Cellules Leucemiques du Quebec, which has consented over 900 patients since its initiation in 2011. She reviews applications for fellowships and studentships for the Postgraduate Awards Committee at McGill (PGAC). She is also the hematology representative on the Medical Oncology Training Program Committee which meets 4 times/year.

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 PNH Network, mandated to offer expertise in diagnosis and treatment of PNH (Paroxysmal Nocturnal Hemoglobinuria).

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

A Search and Selection Committee for the position of Director of the Division of Hematology, under the chairmanship of Dr. Peter Small, was convened to choose a successor in 2013.

Dr. Hans Knecht , Professor of Medicine at the University of Sherbrooke and a member of the hematology division at CHUS was selected to replace Dr. Stephen Caplan, effective April 1,2014. Dr. Knecht has also been appointed by the Chairman of the Department of Medicine to become the University Division Director.

Dr. Chantal Cassis has been appointed Program Director of the McGill University Teaching Program effective July 1, 2013.

6. Honours, awards, and prizes: None reported

7. Fundraising:

Dr. Johnson was involved in a major fundraising event, a show called Ain't Misbehaving, organized by Mr. Sandler and the JGH foundation, where proceeds of the event were donated for lymphoma research and the lymphoma tissue bank at the JGH. This successful event took place on September 29th 2013 and raised over \$100,000.

SECTION I - DIVISION STATUS UPDATE

1. Mission and objectives of the Division.

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.

An important phase of the coming year will be the change in leadership of the division and the importance of ensuring a seamless transition ,maintaining the high quality of the clinical, teaching and research programs of the division. The outgoing director will attempt to communicate important aspects of the function and personnel in the division so as to facilitate the effective functioning of the new leader in an environment as yet unfamiliar to the new director. Communications between Drs. Caplan and Knecht have already taken place to make the transition smooth without disruption of the excellent programs already in place.

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

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
- 2013 May RK Smiley Research Grant by the Canadian Hematology Society; \$10,000
The role of *FAS* mutations in chemotherapy-resistant lymphomas
- 2013-2017 CIHR; PI; \$449,166.00
Overcoming therapeutic resistance in lymphoma
- 2013-2018 CIHR; co-PI; (PI Dr. Ryan Morin); \$612,720 total but \$22,500 for my work
Investigating the mutations driving non Hodgkin lymphomas and developing plasma-based assays for tumour detection and monitoring.

2. Scholarly works published in the 2013 calendar year:

Dr. Sarit Assouline

--Shawi M, Chu TW, Martinez-Marignac V, Yu Y, Gryaznov SM, Johnston JB, Lees-Miller SP, **Assouline SE**, **Autexier C**, Aloyz R. Telomerase contributes to fludarabine resistance in primary human leukemic lymphocytes. PLoS One. 2013 Jul 29;8(7):e70428. doi: 10.1371/journal.pone.0070428. Print 2013.

--O'Brien S, Schiller G, Lister J, Damon L, Goldberg S, Aulitzky W, Ben-Yehuda D, Stock W, Coutre S, Douer D, Heffner LT, Larson M, Seiter K, Smith S, **Assouline S**, Kuriakose P, Maness L, Nagler A, Rowe J, Schaich M, Shpilberg O, Yee K, Schmieder G, Silverman JA, Thomas D, Deitcher SR, Kantarjian H. High-dose vincristine sulfate liposome injection for advanced, relapsed, and refractory adult Philadelphia chromosome-negative acute lymphoblastic leukemia. *J Clin Oncol*. 2013 Feb 20;31(6):676-83. doi: 10.1200/JCO.2012.46.2309. Epub 2012 Nov 19.

--Palumbo MO, Kavan P, Miller WH Jr, Panasci L, **Assouline S**, **Johnson N**, Cohen V, Patenaude F, Pollak M, Jagoe RT, Batist G. Systemic cancer therapy: achievements and challenges that lie ahead. *Front Pharmacol*. 2013 May 7;4:57. doi: 10.3389/fphar.2013.00057. eCollection 2013.

--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*. 2013 Apr;54(4):760-6. doi: 10.3109/10428194.2012.737917. Epub 2012 Nov 15.

Dr. Mark Blostein

--Mfoumou E., Tripette J., **Blostein M.**, Cloutier G., Time-dependent hardening of blood clots quantitatively measured *in vivo* with shear wave ultrasound imaging in a rabbit model of venous thrombosis, *Thrombosis Research*, 133: 265-271, 2014.

--Laurance S. Aghourian MN, Jiva Lila Z, Lemarié CA, **Blostein MD**. Gas6-induced tissue factor expression in endothelial cells is mediated through caveolin-1-enriched microdomains. *J. Thromb & Hemostasis*, 2014, *in press*.

--Cartman G, **Blostein M**, Eisenberg MJ. Correlation between CHADS2 score and anticoagulant use in atrial fibrillation: Results of a mini-survey. *Exp Clin Cardiol*. 2013 Spring;18(2):101-3.

--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*, 2013 Jul;53(7):1451-8.

--Wu J, Lemarié CA, Barralet J, **Blostein MD**. Amphiphilic peptide-loaded nanofibrous calcium phosphate microspheres promote hemostasis *in vivo*. *Acta Biomater*. 2013 Nov;9(11):9194-200.

--Tagalakis V, Tamim H, **Blostein M**, Hanley JA, Kahn SR. Risk of prostate cancer death in long-term users of warfarin: a population-based case-control study. *Cancer Causes Control*. 2013 Jun;24(6):1079-85.

--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*, 121:692-699, 2013 with accompanying editorial on p.571-572.

Dr. Stephen Caplan

--Varga C, Al-Touri S, Papadoukakis S, **Caplan S**, Kahn S, Blostein M. The effectiveness and safety of fixed low-dose prothrombin complex concentrates in patients requiring urgent reversal of warfarin. *Transfusion*. 2013, 53(7):1451-8

Dr. Nathalie Johnson

--Nielsen TH, **Johnson NA**, Garnier N, Kwan S, Yao L, Cocolakis E, Hébert J, Morgan RA, Paquet E, Callahan KP, Jordan CT, Assouline S, Miller WH, Mann KK. Monitoring response and resistance to the novel arsenical darinaarsin in an AML patient. *Front Pharmacol.* 2013;4:9. Epub 2013 Feb 12

--Palumbo MO, Kavan P, Miller WH Jr, Panasci L, Assouline S, **Johnson N**, Cohen V, Patenaude F, Pollak M, Jagoe RT, Batist G. Systemic cancer therapy: achievements and challenges that lie ahead. *Front Pharmacol.* 2013 May 7;4:57.

--Morin RD, Mungall K, Pleasance E, Mungall AJ, Goya R, Huff R, Scott DW, Ding J, Roth A, Chiu R, Corbett RD, Chan FC, Mendez-Lago M, Trinh DL, Bolger-Munro M, Taylor G, Hadj Khodabakhshi A, Ben-Neriah S, Pon J, Meissner B, Woolcock B, Farnoud N, Rogic S, Lim E, **Johnson NA**, Shah S, Jones S, Steidl C, Holt R, Birol I, Moore R, Connors JM, Gascoyne RD, Marra MA. Mutational and structural analysis of diffuse large B-cell lymphoma using whole genome sequencing. *Blood.* 2013 Aug 15;122(7):1256-65, Epub May 22.

--Varga C, Holcroft C, Kezouh A, Bucatel S, **Johnson N**, Petrogiannas-Halioitis T, Assouline S. Comparison of outcomes among patients aged 80 and over and younger patients with diffuse large B cell lymphoma: a population based study. *Leuk Lymphoma.* 2013 Epub Jul 5.

--Chambwe N, Kormaksson M, Geng H, De S, Michor F, **Johnson NA**, Morin R, Scott DW, Godley LA, Gascoyne RD, Melnick A, Campagne F, Shaknovich R. Variability in DNA methylation defines novel epigenetic subgroups of DLBCL associated with different clinical outcomes. Accepted *Blood* December 22nd 2013.

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

Dr. Nathalie Johnson

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

19/10/2013 Colloque sur le lymphoma et le myeloma multiple, du Groupe d'étude en Oncologie du Quebec. ~100 clinicians, 30 minutes; MYC lymphomas, single hit/double hit

06/11/2013 Canadian Cancer Research Conference 2013
FAS mutations cause therapeutic resistance in lymphomas, ~200 scientists

Invited Lectures, Talks, Presentations

10/5/2013 Cole Foundation Research Celebration day, ~100 scientists in Quebec, 15 minutes
Aggressive lymphomas in young adults

19/11/2013 Cancer Care Manitoba, Winnipeg, department of medical oncology and hematology grand rounds, ~50 clinicians and scientists, 1 hour
Curing Lymphoma One Genome at a Time

26/11/2013 2013-2014 Goodman Cancer Research Centre lecture series entitled Cancer: A Disease of a Thousand Faces. 250 people, lay audience; 20 minutes
The best lymphoma therapies in 2013.

Community Outreach (public lectures, media interviews etc)

15/2/2013 The Lymphoma Research Foundation Leaflet Winter 2013 edition,
Profile on my research and lymphoma tissue banking in Quebec

24/10/2013 Interviews on TVA and Global news about limited access to novel therapies in Quebec for a patient with treatment refractory lymphoma (Samantha Poulin)

Thesis committees

8/4/2013 Linda Peltier, Department of Medicine, PhD thesis defense external examiner
29/5/2013 Nicolas Garnier, Department of Medicine, PhD thesis defense external examiner
28/6/2013 Mr. Edgar Pinedo Carpi, Department of Medicine, PhD thesis defense committee
18/9/2013 Tanvir Faisal, Department of Mechanical Engineering, PhD thesis defense
pro-dean
16/10/2013 Lili Li, Department of Human Genetics, PhD thesis defense external examiner

Respectfully submitted,

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