



Annual Report
Division of Hematology
Department of Medicine - Jewish General Hospital
January 1 - December 31, 2015

SUMMARY

General Considerations

“Looking to the Future: a Dialogue with doctors” was the title of a seminar directed by Dr. Lawrence Rosenberg at the Gelber Center, December 2nd 2016. In this retreat, dealing mainly with the integration of the Jewish General Hospital (JGH) within the CIUSSS Centre-Ouest-de-l’Île-de-Montréal, 40 department and divisional chiefs and 13 management team members of the CIUSSS participated. Two of the longstanding, golden McGill principles have strongly been reaffirmed: i) Patients have to be treated at the right place, at the right time, by the right people, and ii) The importance of the Academic Mission of the JGH and its’ affiliation as a major McGill teaching center. These two missions have been in the center of our Hematology Division over the past years and will not change in the future, whatever adversities may emerge. On the other hand, when drastic budgetary restrictions are mandatory, doctors, nurses, laboratory technicians and administrative staff, all have to work even more intensely in order to achieve these standards. I wholeheartedly agree with the Editorial by Dr. James Martin, Chair, Department of Medicine, McGill, when he states in the March issue of *VITAL SIGNS* *“In these times where budget considerations rule we (as institutions) should not lose our humanity.”*

Decidedly, there is no good medicine without humanity. To diagnose a devastating hematological disease is for a well trained hematologist an intellectual work of sometimes only a few minutes, but to explain this to the patient, his family, to accompany him or her on the way of understanding, during the treatment, takes not only time but also a lot of energy and, most importantly, support of specially trained nurses. If one link within this chain is missing (disease, incident), and there is no money for temporary replacement, a stressful situation, mainly for the patients, will occur. Notwithstanding, all members of the Division of Hematology form one coherent team who has been able to overcome successfully such adversities and who will be able to do so in the future. Our 8 Clinical Programs (Stem Cell Transplant Program, Hematology-Oncology Clinic/Segal Cancer Center, CML Clinic, MPN Clinic, MDS Clinic, Gaucher Clinic, Anti-Coagulant Clinic, and Benign Outpatient Clinic) supported by a cutting-edge molecular hematopathology are straightforward and guarantee timely high standard patient care.

1. Clinical programs

Autologous Stem Cell Transplant Program

The Jewish General Hospital’s Hematology Autologous Stem Cell Transplant (ASCT) Program, headed by Dr. Martin Gyger, is an essential component of the McGill Bone Marrow Transplant Program. The JGH is an approved center for the performance of ASCT by an official letter from the Ministry of Health (March 23, 2007). A total of 35 autologous stem cell transplants have been performed in 2015: 22 (63%) ASCTs for multiple myeloma (MM), 6 for diffuse large B-cell lymphoma (DLBCL), 5 for Hodgkin’s lymphoma (HL), and 1 for mantle cell lymphoma (MCL). For MM patients Dr. Gyger’s algorithm for an outpatient transplant approach was strictly applied, allowing considerable cost savings. Based on this model, where 60% of the total number of transplants are for MM and performed with an outpatient transplant approach, the projected costs for a total of 42 patients per year are \$ 47,000.- less than for a total of 30 inpatient transplants. This approach, i.e. increasing significantly the number of ASCTs but in parallel lowering the total costs, was most appreciated by the JGH direction.

Hematology-Oncology Clinic/Segal Cancer Center

Despite the redirection of many patients from outside the 514 code area to hospitals located near to their place of residence, the hematology-oncology division of the Segal Cancer Center was very busy with a total of 9595 patient visits. Currently there are 21 Clinical Hematology Research Trials offering patients with aggressive disease new hope. Most trials recruit patients with multiple relapses, relapse post ASCT or primary refractory hematologic cancers. Four trials are phase I studies and 8 trials phase II studies. The trials are in the field of acute leukemia (AML, ALL), follicular lymphoma (FL), MM, DLBCL, HL, chronic lymphatic leukemia (B-CLL), Waldenstroem's macroglobulinemia (WM) and peripheral T-cell lymphoma (PTCL). Apart from the tremendous benefit for the suffering these trials are a backbone for the advancement of clinical and translational research. Moreover, in times with tough financial restrictions most of these trials offer powerful new treatments without any financial burden for the public health system and help the hospital to save money. There is a deep satisfaction for the patient and the treating physician to realize that there is again a remission for a lymphoma after the fifth relapse allowing the patient to restart his daily physical (swimming) activities.

CML Clinic

The CML clinic has been started in 2004 and since then an exemplary follow-up of the patients has been documented. The patients are seen either by Dr. Sarit Assouline, Head of the Clinic, or Dr. Jaroslav Prchal. Both MDs are assisted 2 days a week by a CML nurse who has frequent contact with patients during clinic visits and is available for telephone calls. This is primordial in a disease where compliance and proper patient monitoring ensure good outcomes for now more than a decade. The CML Clinic at the JGH is integrated in the Groupe Québécois sur la recherche en leucémie myéloïde chronique (GQR-LMC) and strictly adheres to their guidelines developed in 2013 and based on the European Leukemia Net (ELN) guidelines. The CML Clinic is very active in clinical research and the latest results have been presented in June 2015 at the 20th EHA Congress in Vienna. Concise up-to-date treatment guidelines have been drawn up by Dr. Sarit Assouline in October 2015.

Myeloproliferative Neoplasia (MPN) Clinic

Since its' start in 2010 the MPN clinic, co-directed by Drs. Jaroslav Prchal and Shireen Sirhan, has increased its' accrual of patients by >90%. Currently the clinic offers three clinical trials with JAK inhibitors (Ruxolitinib, Momelotinib) for patients with primary myelofibrosis or secondary myelofibrosis post polycythemia vera or post essential thrombocythemia. The MPN Clinic, -like the CML Clinic-, offers an ideal teaching environment for Hematology-, Radiation-Oncology-, and Oncology Fellows.

Myelodysplastic Syndrome Clinic (MDS) Clinic

This nationally recognized teaching program is in its third year and is run by Dr. April Shamy. MDS is mainly a disease of the elderly and thus, due to demographic changes (the life expectancy is still increasing) an ever increasing accrual of patients is predictable. To guarantee also in the future optimal patient management additional nursing support would be very much appreciated. Again, the MDS Clinic offers excellent clinical training opportunities to hematology residents and interested medical students.

Gaucher Clinic

For the past 18 years, this specialized program has been mandated by the government of Québec and includes >30 patients with this rare storage disease. The increase in patients corresponds to

the transfer of pediatric patients from Hôpital Sainte-Justine when they reach adulthood. Dr. Sarit Assouline is responsible for the treatment of these adult patients. The highly specialized treatment program for patients with Gaucher's disease includes established relationships with designated specialists, a research nurse, and a pharmacist for assistance with the dispensation of medication with its side effects, as well as a Gaucher's disease website in order to ensure optimal patient care.

Anticoagulation Clinic

The anticoagulation clinic is organized and supervised by the director, Dr. Mark Blostein. The clinic is staffed by all the hematologists and offers an ideal opportunity to hematology fellows and housestaff to learn how to manage coumadin. This concerns many patients with atrial fibrillation as well as patients with venous thromboembolic disease and mechanical heart valves. However, with new oral anticoagulants (NOACs) entering the market, expertise in the management of these drugs has become an additional role of the anticoagulation clinic. Another most important mandate of the clinic is the perioperative management of anticoagulation for surgical procedures, endoscopies, dental extractions, and other invasive procedures. The close vicinity to the hematology laboratory guarantees a short turnaround time for coagulation tests in life threatening bleeding situations where quick clinical decisions are mandatory. Thus, the coagulation laboratory and the AC Clinic have to remain in the same place in order to deliver optimal patient care. This clinic represents a cornerstone in the optimal functioning of many surgical and medical services of the Jewish General Hospital. This issue has to be considered in the planning phase of *Optilab*. The anticoagulation clinic is an integral part of the nationally and internationally recognized Centre for Thrombosis and Anticoagulation Care (headed by Dr. Susan Kahn) and collaborates with VECTOR, a consortium of Thrombosis/Anticoagulation Researchers across Eastern Canada. This year Dr. Kahn has been nominated Principal Investigator of a 5 years' 5.2 million dollar VECTOR project emphasizing the outstanding quality of anticoagulation/thrombosis research at the JGH. In 2015 the anticoagulation clinic hosted a guest from a foreign university hospital and two staff members of other Québec hospitals in order to broaden their knowledge in the management of clinically demanding anticoagulation problems. Our Anticoagulation Clinic is one of the leading academic Anticoagulation Clinics in Canada, participating in many major peer reviewed Anticoagulation trials in North America. A number of recent peer review publications, in journals such as the New England Journal of Medicine, and the Annals of Internal Medicine, have been produced by this clinic. Early in 2015 the computerization of the clinic has been started and the project successfully advanced. The AC Clinic will be paperless in spring 2016.

Benign Outpatient Clinic

All hematologists and hematology fellows participate in the benign hematology clinic the most involved being still Dr. Arthur Rosenberg in his last year of full clinical activity. Like other clinics the benign outpatient clinic had to redirect many patients with residence outside the 514 area code towards other hematologists. The benign hematology clinic is very interactive with primary care physicians and regularly identifies hereditary red cell disorders related to the multiethnic origin of our patients. Severe iron deficiency anemia and monoclonal gammopathy of unknown significance (MGUS) are frequently diagnosed. Malignant hematologic diseases are picked up at an early stage when patients present with thrombocytosis or or polyglobulia.

Molecular Diagnostics Laboratory

The molecular diagnostics laboratory is located in the 6th floor of the Segal Cancer Center and is run by Yuri Monczak Ph.D. and Tina Haliotis, MD, Ph.D., both associate members of the Division of Hematology. This facility represents a cornerstone for our clinical programs and serves as the referral laboratory for molecular diagnostics for the entire McGill hematology

university network. In 2015 the MYD88 assay (molecular diagnosis of Waldenstroem's macroglobuliemia) and the IS (International Standard) testing for *bcr/abl* qPCR have been introduced and all SOPs (Standard Operating Procedure) for CAP (College of American Pathologists) accreditation have been finalized.

However, a major threat for this top molecular hematology laboratory is the provincial restructuration in the setting of *Optilab*. MPL (trombopoietin receptor) gene mutation analysis was not implemented and transfer of two tests (CALR and NPM1) to another molecular laboratory had led to inacceptably long turnaround times for our Hematology Division. This drawback is now corrected through repatriation. Drs. Monczak and Haliotis had furthermore prepared the bases to implement Next Generation Sequencing (NGN) tremendously needed in a Clinical Research Unit where several phase I trials are open. Unfortunately NGN was put on hold due to financial and personal cuts. Judging this situation dangerous for the future of our Hematology Division, this issue has been recently addressed in common with the director of the Segal Cancer Center, Dr. Gerald Batist, MD, and the director of Pathology, Dr. Alan Spatz, MD, PhD. Both directors agree that NGN for molecular Hematology (IGHV hypermutation analysis for B-CLL and sequencing for B- and T-cell clonality, acute leukemia key gene mutations) has to be performed at the JGH.

2. Research and publications

Dr. Sarit Assouline, director of Clinical Research in Hematology-Oncology and Associate director of the Clinical Research Unit, continues to lead a strong Clinical Research Program in leukemia and lymphoma. It is her first year in the rank of Associate Professor. Her dedication and contribution to research over the past years are also reflected in the attribution of a FRSQ Junior 2 award from July 2015 to July 2018. She also obtained a project grant from the Rossy Cancer Network. Currently she acts as PI in 3 phase I clinical trials and 1 phase 2 trial in acute leukemia as follows: i) ALL - Phase I trial of SYK inhibitor entospletinib in combination with dexamethasone and vincristine in B ALL. ii) AML - Phase I trial of IV MDM2 inhibitor. iii) AML - Phase I trial of oral MDM2 inhibitor with 7+3 for the treatment of newly diagnosed AML. iv) AML - Phase II trial of ribavirin, vismodegib and decitabine for AML M4 and M5. During 2015, Dr. Assouline was involved in 10 peer reviewed published manuscripts, in two as a first, and in one as senior author. In this latter manuscript Dr. Ashley Marton, fellow in hematology, was first author.

Dr. Mark Blostein is director of the Clinical Investigator Program at McGill University, head of the Anticoagulation Clinic and Associate Chief of the Division of Hematology. Under his guidance the Clinical Investigator Program received accreditation from the Royal College of Physicians of Canada (RCPC) for the first time since 20 years. This accreditation is the result of his longstanding, excellent performance as an academic teacher, researcher and clinician. This year he successfully initiated the transition of the paper chart based AC-Clinic to a paperless clinic. This goal will be completely achieved in spring 2016. Dr. Blostein is a PI in a Heart and Stroke Foundation of Canada grant entitled "*Role of gas6 and inflammation in the pathophysiology of venous thromboembolism*", site-investigator in a prospective cohort study on the safety of interruption of dabigatran therapy for invasive procedures, site-investigator in clinical trials of perioperative management of warfarin, ITP, and three novel anticoagulants (PAUSE). He was involved in 7 peer reviewed published manuscripts, in 3 of them as the senior author. His mice model of cancer-induced venous thrombosis was published in *Blood* and got an Editorial.

Dr. Stephen Caplan, director of the Blood Bank, is a major contributor to the Clinical Research programs and acts as a coordinator and major contributor of the Canadian Paroxysmal Nocturnal Hemoglobinuria (PNH) Network. He was co-author of one peer-reviewed manuscript.

Dr. Martin Gyger, director of the ASCT program and Apheresis Clinic is a major contributor to the Clinical Research programs. He is PI of a novel promising clinical trial for light chain amyloidosis (LA) by NEOD001, a monoclonal antibody that targets specifically circulating and accumulated light chain amyloid. He is also PI of a phase I/II trial of linsitinib (IGF-1 receptor inhibitor) in combination with velcade/dexamethasone for refractory/relapsing MM.

Dr. Nathalie Johnson heads a basic science laboratory with a research program focused on the molecular hematopathology of malignant lymphoma, in particular DLBCL and HL. She is a very active translational researcher and is in charge of the Hematology Flow-Cytometry Laboratory. The new lymphoma and leukemia panels she introduced in 2014 had their successful clinical validation in 2015. These panels are mandatory and have to be run on site since live-saving therapeutic decisions depend on a rapid availability of the results. Out-sorting of the Flow-Cytometry to another hospital in the setting of *Optilab* would be deleterious for our Hematology Division.

In 2015 Dr. Johnson was awarded a 2 years' Canadian Cancer Society Research Institute (CCSRI) grant entitled "*Optimizing Therapy for STAT6-mutated DLBCL*". Another grant where she acts as PI, entitled "*Overcoming therapeutic resistance in lymphoma*", is still running until 2016. She is furthermore co-investigator in three grants dealing with the molecular pathogenesis of lymphoma. Currently she is involved as PI in 5 clinical trials with 3 of them starting recruitment in 2015. Amongst them the study of the PD-1 inhibitor Pembrolizumab in relapsed or refractory HL is of particular importance. This year Dr. Johnson was senior author of a major manuscript dealing with the molecular pathogenesis of relapsing DLBCL published in *Clinical Cancer Research* and co-author of two additional peer-reviewed manuscripts.

Dr. Hans Knecht, in his second year at the JGH, continued his basic and translational research in the molecular pathogenesis of HL. He still works regularly as a visiting scientist in the 3D laboratory of Sabine Mai, PhD, at the Genomic Center for Cancer Research and Detection (GCCRD) at the University of Manitoba. In collaboration with Drs. Johnson and Haliotis he analysed the 3D interaction of telomeres and telomere related factor 2 (TRF2) in primary Hodgkin and Reed-Sternberg cells. These findings were presented in December 2015 at the ASH meeting and confirmed the 3D model for EBV-associated Hodgkin's lymphoma. This model was published with Dr. Knecht as senior author in 2015 in *Blood* and got the journals' cover caption as well as the distinction "*paper of the month*" by the Lady Davis Institute. He is also second author in a further manuscript dealing with Reed-Sternberg cells.

Dr. Yury Monczak was co-author in a *CCR* manuscript and was substantially involved in the composition of the NGN-platform in molecular hematology.

Dr. François Patenaude was second author in a Canadian Urological Association Journal (CUAJ) manuscript dealing with metastatic renal cell carcinoma, accepted in December. He is a leading expert in novel therapeutic approaches for this type of cancer.

3. Teaching and learning:

All doctors in the Division of Hematology participate in teaching activities, whether through the

consultation service (Hematology and Thrombosis), clinics, Introduction to Internal Medicine, Senior Physician Rounds or Clinical Teaching Unit on 7NW, E-7, and Hematology Laboratory. Particularities in teaching are listed as follows:

Dr. Sarit Assouline has been actively involved in the rotation of Hematology Fellows in the Clinical Research Unit. She also gave the 2 lymphoma lectures to Oncology residents and supervised one student in research.

Dr. Mark Blostein taught Approach to Thrombosis and Bleeding throughout the year (4 hours) to undergraduate medical students, 1 hour Bridging Anticoagulation to GIM fellows, Coagulation to Hematology fellows (10 hours a week for 8 weeks, i.e. 80 hours/year), presentation at Thrombosis Rounds 2 hours, and management of Coumadin to residents rotating through the Anticoagulation clinic (4 hours/week). His research trainee supervision included 2 graduate PhD students, 2 post-doctoral fellows, one Internal Medicine resident, and one GIM fellow.

Dr. Stephen Caplan coached a team composed of 2 senior-, 3 junior residents and 2 medical students as a Medicine Ward Attending on 7NW for a 2 weeks' period.

Dr. Chantal Cassis, Program Director of the McGill University Teaching Program prepared in 2014, in collaboration with all McGill Hematologists, an excellent 60 page Residency Training Program for Adult Hematology. The Program was discussed again in detail by all Hematologists in January 2015. Thus, the Division of Hematology, McGill Department of Medicine, was well prepared for the audit of February 4th, 2015 resulting in the accreditation of the Hematology Fellow Program by the RCPC. This success represents a milestone in the history of our Hematology Division. During this first year of the Program Dr. Cassis has already ameliorated some program issues and a proper Residents' room will be ready in 2016. She also participates in the undergraduate lectures (2 hours/year), in the lectures of the academic half-day (3 hours/year) and the EBM curriculum for Hematology residents. Dr. Chantal Cassis has progressed in her Masters' degree in Medical Education, which she plans to finish in 2016.

Dr. Martin Gyger who regularly has several patients hospitalized on 7 NW, discusses these patients every day with the 7NW team. He also spent many hours teaching the residents and Hematology fellows blood and bone marrow morphology and cytology at the microscope.

Dr. Nathalie Johnson has been actively involved in teaching students at the undergraduate, and post-graduate levels at McGill (EXMD 607B, 635, 624, and 516-616A; total of 9.5 hours) as well as in teaching of Hematology fellows (4 hours). In addition to the clinical teaching mentioned above, she supervised in her laboratory a French research trainee who submitted in summer 2015 his Master's degree at the University of Lyon, France. She furthermore supervised 3 PhD candidates in molecular hematology, a medical student, a 3rd year undergraduate in biochemistry and molecular medicine, and two postdoctoral fellows. Jointly with Drs. Patenaude and Knecht she was responsible for teaching Flow Cytometry to the Hematology fellows.

Dr. Hans Knecht was involved in teaching of Hematology/Oncology fellows in classroom (B-cell development and identification/treatment of aggressive B-cell lymphomas, 2x2 hours) and at the microscope (6x1 hour). He also participated in the formation of the Hematology Residents in Flow-Cytometry (2x2 hours). He is still active in the Supervision of two Hematology Residents at Université de Sherbrooke (UdS) for translational research projects. He holds still a minor appointment with the Department of Medicine at the CHUS and is co-supervisor of one MSc

student in Infectiology/Microbiology at UdS.

Dr. Yury Monczak participated with 25 hours in the small group teaching of Hematology and Oncology Residents. He also teaches molecular biology for undergraduates at the Université de Montréal (40 hours) and medical technology at the Dawson College (3h).

Dr. François Patenaude started an 8x1 hours' course entitled "*Introduction to Oncology*" for 3rd year medical students at McGill. This is an excellent initiative and covers the need to address basic oncology already during the formation of future MDs. Ten additional hours of Dr. Patenaude's teaching for Oncology fellows dealt with solid tumors. He also supervised 6 international students during their 1-3 months' elective in Oncology and has twice given a 2 hours seminar on Flow-Cytometry to Hematology-Oncology fellows dealing with basic principles, CD classification, panels of surface markers and their clinical applications.

Dr. April Shamy is an Osler Fellow in Medicine since 2009. She is the director of the Clinical Teaching Unit (CTU) and acts as a role model for many young Internists in formation. She regularly teaches in the McGill physical exam course (20 hours/year). As an Inpatient Ward Attending on 7NW (twice a 2 weeks' period) Dr. Shamy supervised a team composed of 2 senior and 3 junior residents as well as 2 medical students. During our weekly Friday morning Hematology rounds she is a passionate teacher for house staff and Hematology residents.

4. Involvement in the community:

Dr. Sarit Assouline was an invited speaker at the Mont Gabriel Leukemia/Lymphoma Summit of November 20/21, she has participated in lectures during the Canadian Cancer Research Conference (CCRC) and acted as reviewer for FRSQ Junior 1 grants, *Clinical Cancer Research, and Oncology*.

Dr. Mark Blostein was an invited speaker at the McGill University-Department of Medicine Research Symposium, Montréal, May 13th 2015, as well as at the ISTH 2015 Congress and at 8 occasions within the province of Québec. He was a CIHR reviewer for the Foundation Scheme and reviewed articles for *Blood, Thrombosis & Hemostasis, Journal of Clinical Investigation, and The Journal of Thrombosis and Hemostasis*.

Dr. Chantal Cassis is on the way to assembly quality indicators across the McGill sites for Oncology as a part of the Rossy Cancer Network.

Dr. Martin Gyger was invited to present the opening lecture of the 20th Congress of the AMHOQ April 30, 2015, in Québec City. As a pioneer of bone marrow transplantation in Québec he held a state of the art lecture on bone marrow transplantation from its' beginning to present. He is also the invited speaker for the second *Clinical Arthur Rosenberg Lecture* at the JGH in June 2016.

Dr. Nathalie Johnson was an invited speaker at the Canadian Association of Pathology Annual Meeting where she spoke about the diagnostic workup of double hit lymphomas. She was also an invited speaker at the McGill systems biology training program symposium (Personalized Medicine of Cancer), at the Mont Gabriel Leukemia/Lymphoma Summit of November 20/21, the NCIC annual meeting (predictive biomarkers of response in patients with relapsed or refractory DLBCL), and the CCRC (advances in understanding lymphomas in adolescent/young adults (AYA) patients). Dr. Johnson also acted as a reviewer for *Blood, Leukemia, Oncotarget*,

Leukemia & Lymphoma, and PLOS1.

Dr. Hans Knecht was an invited speaker at the Mont Gabriel Leukemia/Lymphoma Summit of November 20/21, acted as reviewer for an INSERM research project (France), an Elevate Postdoctoral Fellowship Application Mitacs/University of British Columbia, and for *Blood, Leukemia, and British Journal of Haematology*.

Dr. Yury Monczak was an Advisor to the Québec Régie de la Santé, section biologie moléculaire. He also acted as a jury member for the yearly science competition of a private high-school and is a guest lecturer (volunteer activity) in molecular biology at the Catholic University in Lviv, Ukraine (12 hours/year).

Dr. François Patenaude was an invited speaker at 8 occasions in 2015. Amongst the presentations to note this at the 7th Canadian Kidney Cance Conference entitled: “*Immunotherapy for MRCC: The dawn of a new area*“. Apart from his cutting-edge presentations dealing with renal cell carcinoma Dr. Patenaude also addressed in his conferences immuno-therapeutic approaches in breast cancer and melanoma.

Dr. Arthur Rosenberg gave two invited presentations dealing with the basics in Hematology in private institutions in Montreal.

Dr. April Shamy organized this year again a superb Christmas party. This event is essential to our Hematology Division and our daily collaborators. All participants realize how important and precious every person in reality is. It is a great event boosting us with energy for the forthcoming winter.

Apart from that Dr. Shamy as the director of the CTU, -in collaboration with the Head nurse 7NW-, prepared in detail the imminent move to K7 in the new hospital building.

5. Partnerships:

Due to the new CIUSSS organization the Division of Hematology treats now the acute leukemia patients from Rouyn-Noranda and is also in charge of bone marrow reading and flow cytometry from this region.

With Jean Talon, an “Entente de Services en Hématologie” was already signed October 20th 2014 indicating that patients in need of an ultra-specialized treatment will be transferred to the Jewish General Hospital.

Due to budgetary restrictions the division of Hematology is still forced not to accept patients living in the 450 telephone area code unless they insist to be treated at the Jewish General Hospital.

6. Milestones: new hires, highlights, promotions, and retirements:

Accreditation of the Hematology Fellow Program by the Royal College of Physicians of Canada under the lead of Dr. Chantal Cassis, Program Director.

Accreditation of the Clinical Investigator Program at McGill University by the Royal College of Physicians of Canada under the lead of Dr. Mark Blostein, Program Director.

Dr.Sarit Assouline, Director CRU, successfully accomplished her first year in the rank of Associate professor.

This year our Hematology Division has a strong publication record. For two *Blood* manuscripts and one *CCR* manuscript staff physicians sign as senior authors. The first *Blood* paper got the journal's front cover, the second an Editorial. All 3 senior authors were or are invited speakers at the McGill University-Department of Medicine Symposium (2014, 2015, 2016).

6. Honours, awards, and prizes: None reported

SECTION I - DIVISION STATUS UPDATE

1. Mission and objectives of the Division:

The principle goals for the next years will be (unchanged):
to offer cutting-edge treatment to the very sick hematology patients,
to increase patient recruitment for phase I and II trials,
to progress in our Hematology Fellowship program,
to strengthen and expand laboratory hematology,
to increase the collaboration with the other Hematology McGill sites,
to increase top-level research production in basic, translational and clinical research,
to solidify the administrative (secretarial) domain of the Division,
and to improve our Clinical Programs despite forthcoming financial restrictions and reorganization of the current healthcare system.

Concerning the recruitment of new young staff Hematologists the vision remains exactly the same as that formulated by Dr. Stephen Caplan in the 2013 Annual Report, as follows (verbatim):
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	Associate 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. Hans Knecht	Full Professor	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

2015-2018	Fonds de Recherche en Santé du Québec, chercheur clinicien boursier Junior 2
2013-2017	Co-applicant with Dr. Wilson Miller on CIHR grant; \$150,000 for 4 years
2014-2017	Co-applicant with Dr. Nathalie Johnson for “Optimizing therapy for STAT6-mutant DLBCL”, CCSRI, \$ 199,600 for three years.
2014-2016	Co-investigator with Katherine Borden on a grant from The Leukemia & Lymphoma Society of Canada.
2015-2016	Rosy Cancer Network Grant (project to be determined)

Dr. Mark Blostein

2014-2016	Principal Investigator: Operating Grant of the Heart and Stroke Foundation of Canada (HSFC). \$440,00 for 3 years
2014-2015	Site Investigator: Clinical trial for perioperative management of Dabigatran. HSFC funded. \$ 10,000/year
2014-2015	Site Investigator: Clinical trial for perioperative management of warfarin. NIH funded. \$ 34,000
2014-2015	Site Investigator: Clinical trial for perioperative management of ITP. Funded by Glaxo.
2014-2015	Site Investigator for PAUSE, a CIHR funded clinical trial that uses a standardized protocol for peri-operative management for all three novel anticoagulants
2014-2015	Funding from Bayer for the development of an INR measurement for rivaroxaban based on patient samples

Dr. Nathalie Johnson

2011-2015	Fonds de Recherche en Santé du Québec (FRSQ), chercheur clinicien boursier Junior 1
2013-2016	CIHR; Principal Investigator. Overcoming therapeutic resistance in lymphoma. \$449,166.00

- 2013-2018 CIHR; co-PI; (PI Dr. Ryan Morin); \$612,720 total but \$22,500 for her work Investigating the mutations driving non Hodgkin lymphomas and developing plasma-based assays for tumour detection and monitoring
- 2014-2016 Co-PI. (PI Dr Koren Mann) RASGRP4 mutations in R-CHOP resistant DLBCL. The Leukemia & Lymphoma Society of Canada. \$ 120,000
- 2014-2016 Merck, Sharp & Dohme Corp./McGill Faculty of Medicine Grant. (PI Dr. Jerry Pelletier). Conditional Genome Engineering in Mice. Dr. Johnsons' part is sequencing of human Burkitt lymphoma exomes (4,000/year)
- 2015-2017 CCSRI Innovation Grant; Principal Investigator. "Optimizing therapy for STAT6-mutant DLBCL", CCSRI, \$ 199,600 for three years.

Dr. Hans Knecht

- 2015-2016 Principal Investigator : Nouvelles cibles thérapeutiques dans le lymphome de Hodgkin réfractaire. Pilot project \$ 15,000. CRC Étienne-Le Bel, CHUS.
- 2016-2017 Prolongation of the above grant in the setting of a MSc thesis \$ 10'000.- CRC Étienne-Le Bel, CHUS.

2. Scholarly works published in the 2015 calendar year (*in press not included*):

Sarit Assouline

Morin RD, **Assouline SE**, Alcaide M, Mohajeri A, Johnston RL, Chong L, Grewal J, Yu S, Fornika D, Bushell K, Holm Nielsen T, **Petrogiannis-Halotis T**, Crump M, Tosikyan A, Grande BM, Macdonald D, Rousseau C, Bayat M, Sesques P, Froment R, Albuquerque M, **Monczak Y**, Klein-Oros K, Greenwood C, Riazalhosseini Y, Arseneault M, Camlioglu E, Constantin AM, Pan-Hammarström Q, Peng RJ, Mann KK, **Johnson NA**. Genetic landscapes of relapsed and refractory diffuse large B cell lymphomas. Clin Cancer Res. 2015 Dec 8. [Epub ahead of print]

Andreeff M, Kelly KR, Yee K, **Assouline S**, Strair R, Popplewell L, Bowen D, Martinelli G, Drummond MW, Vyas P, Kirschbaum M, Iyer SP, Ruvolo V, González GM, Huang X, Chen G, Graves B, Blotner S, Bridge P, Jukofsky L, Middleton S, Reckner M, Rueger R, Zhi J, Nichols G, Kojima K. Results of the Phase I Trial of RG7112, a Small-Molecule MDM2 Antagonist in Leukemia. Clin Cancer Res. 2015 Oct 12. [Epub ahead of print]

Owen C, **Assouline S**, Kuruvilla J, Uchida C, Bellingham C, Sehn L. Novel Therapies for Chronic Lymphocytic Leukemia: A Canadian Perspective. Clin Lymphoma Myeloma Leuk. 2015 Nov;15(11):627-634.

Mori S, Vagge E, le Coutre P, Abruzzese E, Martino B, Pungolino E, Elena C, Pierri I, **Assouline S**, D'Emilio A, Gozzini A, Giraldo P, Stagno F, Iurlo A, Luciani M, De Riso G, Redaelli S, Kim DW, Pirola A, Mezzatesta C, Petroccione A, Lodolo D'Oria A, Crivori P, Piazza R, Gambacorti-Passerini C. Age and dPCR can predict relapse in CML patients who discontinued imatinib: the ISAV study. Am J Hematol. 2015 Oct;90(10):910-4.

Palanca-Wessels MC, Czuczman M, Salles G, **Assouline S**, Sehn LH, Flinn I, Patel MR, Sangha R, Hagenbeek A, Advani R, Tilly H, Casasnovas O, Press OW, Yalamanchili S, Kahn R, Dere RC, Lu D, Jones S, Jones C, Chu YW, Morschhauser F. Safety and activity of the anti-CD79B antibody-drug conjugate polatuzumab vedotin in relapsed or refractory B-cell non-Hodgkin

lymphoma and chronic lymphocytic leukaemia: a phase 1 study. *Lancet Oncol*. 2015 Jun;16(6):704-15.

Assouline S, Bucchieri V, Delmer A, Gaidano G, McIntyre C, Brewster M, Catalani O, Hourcade-Potelleret F, Sayyed P, Badoux X. Pharmacokinetics and safety of subcutaneous rituximab plus fludarabine and cyclophosphamide for patients with chronic lymphocytic leukaemia. *Br J Clin Pharmacol*. 2015 Nov;80(5):1001-9.

Mistry PK, Lukina E, Ben Turkia H, Amato D, Baris H, Dasouki M, Ghosn M, Mehta A, Packman S, Pastores G, Petakov M, **Assouline S**, Balwani M, Danda S, Hadjiev E, Ortega A, Shankar S, Solano MH, Ross L, Angell J, Peterschmitt MJ. Effect of oral eliglustat on splenomegaly in patients with Gaucher disease type 1: the ENGAGE randomized clinical trial. *JAMA*. 2015 Feb 17;313(7):695-706.

Marton A, Kezouh A, Petrogiannis-Halioitis T, **Assouline S**. Barriers to enrollment of patients with recurrent diffuse large B-cell lymphoma onto clinical trials. *Leuk Lymphoma*. 2015 Sep;56(9):2747-9.

Nielsen TH, Diaz Z, Christodoulopoulos R, Charbonneau F, Qureshi S, Rousseau C, Benlimame N, Camlioglu E, Constantin AM, Oros KK, Krumsiek J, Crump M, Morin RD, Cerchietti L, **Johnson NA**, Petrogiannis-Halioitis T, Miller WH Jr, **Assouline SE**, Mann KK. Methods for sample acquisition and processing of serial blood and tumor biopsies for multicenter diffuse large B-cell lymphoma clinical trials. *Cancer Epidemiol Biomarkers Prev*. 2014 Dec;23(12):2688-93.

Assouline S, Culjkovic-Kraljacic B, Bergeron J, **Caplan S**, Cocolakis E, Lambert C, Lau CJ, Zahreddine HA, Miller WH Jr, Borden KL. A phase I trial of ribavirin and low-dose cytarabine for the treatment of relapsed and refractory acute myeloid leukemia with elevated eIF4E. *Haematologica*. 2015 Jan;100(1):e7-9.

Mark Blostein

Aghourian MN, Lemarié CA, Bertin FR, **Blostein MD**. Prostaglandin E synthase is upregulated by Gas6 during cancer-induced venous thrombosis. *Blood*. Epub 2015 Nov 19

Bertin FR, Lemarié CA, Robins RS, **Blostein MD**. Gas6 regulates thrombin-induced expression of VCAM-1 through FoxO-1 in endothelial cells. *J Thromb Haemost*. 2015 Sep 28. [Epub ahead of print]

Ibrahim, R., B. Kucukyazici, V. Verter, M. Gendreau, **M. Blostein**, "Designing Personalized Treatment: An Application to Anticoagulation Therapy", forthcoming in *Production and Operations Management*, (accepted September 2015)

Marc Carrier, M.D., Alejandro Lazo-Langner, M.D., Sudeep Shivakumar, M.D., Vicky Tagalakakis, M.D., Ryan Zarychanski, M.D., Susan Solymoss, M.D., Nathalie Routhier, M.D., James Douketis, M.D., Kim Danovitch, C.C.R.P., Agnes Y. Lee, M.D., Gregoire Le Gal, M.D., Philip S. Wells, M.D., Daniel J. Corsi, Ph.D., Timothy Ramsay, Ph.D., Doug Coyle, Ph.D., Isabelle Chagnon, M.D., Zahra Kassam, M.D., Hardy Tao, M.D., and Marc A. Rodger, M.D., for the SOME Investigators*. Screening for Occult Cancer in Unprovoked Venous

Thromboembolism. N Engl J Med. 2015 Aug 20;373(8):697-704.

* **M Blostein** Local site investigator

Charles V. Pollack, Jr., M.D., Paul A. Reilly, Ph.D., John Eikelboom, M.B., B.S., Stephan Glund, Ph.D., Peter Verhamme, M.D., Richard A. Bernstein, M.D., Ph.D., Robert Dubiel, Pharm.D., Menno V. Huisman, M.D., Ph.D., Elaine M. Hylek, M.D., Pieter W. Kamphuisen, M.D., Ph.D., Jörg Kreuzer, M.D., Jerrold H. Levy, M.D., Frank W. Sellke, M.D., Joachim Stangier, Ph.D., Thorsten Steiner, M.D., M.M.E., Bushi Wang, Ph.D., Chak-Wah Kam, M.D., and Jeffrey I. Weitz, M.D.* Idarucizumab for Dabigatran Reversal.

N Engl J Med. 2015 Aug 6; 373:511-520.

* **M Blostein** Local site investigator

Schulman S, Carrier M, Lee AY, Shivakumar S, **Blostein MD**, Spencer FA, Solymoss S, Barty R, Wang G, Heddle N, Douketis JD. Perioperative Management of Dabigatran: A Prospective Cohort Study. Circulation. 2015 Jul 21;132(3):167-73.

James D. Douketis, M.D., Alex C. Spyropoulos, M.D., Scott Kaatz, D.O., Richard C. Becker, M.D., Joseph A. Caprini, M.D., Andrew S. Dunn, M.D., David A. Garcia, M.D., Alan Jacobson, M.D., Amir K. Jaffer, M.D., M.B.A., David F. Kong, M.D., Sam Schulman, M.D., Ph.D., Alexander G.G. Turpie, M.B., Vic Hasselblad, Ph.D., and Thomas L. Ortel, M.D., Ph.D. for the BRIDGE Investigators.* Perioperative Bridging Anticoagulation in Patients with Atrial Fibrillation. N Engl J Med, 2015; 373:823-833.

* **M Blostein** Local site investigator

Steven Caplan

Assouline S, Culjkovic-Kraljacic B, Bergeron J, **Caplan S**, Cocolakis E, Lambert C, Lau CJ, Zahreddine HA, Miller WH Jr, Borden KL. A phase I trial of ribavirin and low-dose cytarabine for the treatment of relapsed and refractory acute myeloid leukemia with elevated eIF4E. Haematologica. 2015 Jan;100(1):e7-9.

Nathalie Johnson

Morin RD, **Assouline SE**, Alcaide M, Mohajeri A, Johnston RL, Chong L, Grewal J, Yu S, Fornika D, Bushell K, Holm Nielsen T, **Petrogiannis-Halioitis T**, Crump M, Tosikyan A, Grande BM, Macdonald D, Rousseau C, Bayat M, Sesques P, Froment R, Albuquerque M, **Monczak Y**, Klein-Oros K, Greenwood C, Riazalhosseini Y, Arseneault M, Camlioglu E, Constantin AM, Pan-Hammarström Q, Peng RJ, Mann KK, **Johnson NA**. Genetic landscapes of relapsed and refractory diffuse large B cell lymphomas. Clin Cancer Res. 2015 Dec 8. [Epub ahead of print]

Lim EL, Trinh DL, Scott DW, Chu A, Krzywinski M, Zhao Y, Robertson AG, Mungall AJ, Schein J, Boyle M, Mottok A, Ennishi D, **Johnson NA**, Steidl C, Connors JM, Morin RD, Gascoyne RD, Marra MA. Comprehensive miRNA sequence analysis reveals survival differences in diffuse large B-cell lymphoma patients. Genome Biol. 2015 Jan 29;16:18.

Chan FC, Telenius A, Healy S, Ben-Neriah S, Mottok A, Lim R, Drake M, Hu S, Ding J, Ha G, Scott DW, Kridel R, Bashashati A, Rogic S, **Johnson N**, Morin RD, Rimsza LM, Sehn L, Connors JM, Marra MA, Gascoyne RD, Shah SP, Steidl C. An RCOR1 loss-associated gene

expression signature identifies a prognostically significant DLBCL subgroup. Blood. 2015 Feb 5;125(6):959-66.

Hans Knecht

Righolt CH, **Knecht H**, Mai S. DNA Superresolution Structure of Reed-Sternberg Cells Differs Between Long Lasting Remission Versus Relapsing Hodgkin's Lymphoma Patients. J Cell Biochem. 2015 Dec 7. doi: 10.1002/jcb.25456. [Epub ahead of print]

Lajoie V, Lemieux B, Sawan B, Lichtensztein D, Lichtensztein Z, Wellinger R, Mai S, **Knecht H**. LMP1 mediates multinuclearity through downregulation of shelterin proteins and formation of telomeric aggregates. Blood. 2015 Mar 26;125(13):2101-10. This manuscript got the Cover Caption of the journal and was chosen as paper of the month at the LDI.

Yury Monczak

Morin RD, **Assouline SE**, Alcaide M, Mohajeri A, Johnston RL, Chong L, Grewal J, Yu S, Fornika D, Bushell K, Holm Nielsen T, **Petrogiannis-Haliotis T**, Crump M, Tosikyan A, Grande BM, Macdonald D, Rousseau C, Bayat M, Sesques P, Froment R, Albuquerque M, **Monczak Y**, Klein-Oros K, Greenwood C, Riazalhosseini Y, Arseneault M, Camlioglu E, Constantin AM, Pan-Hammarström Q, Peng RJ, Mann KK, **Johnson NA**. Genetic landscapes of relapsed and refractory diffuse large B cell lymphomas. Clin Cancer Res. 2015 Dec 8. [Epub ahead of print]

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

This issue has already been dealt with under: 4. Involvement in the Community.

SECTION III - CONFIDENTIAL INFORMATION

1. Consulting activities:

Three staff physicians reported Consulting activities in the private sector ranging from 3 – 7 days over the year.

Respectfully submitted,



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