Hôpital général juif
Jewish General Hospital

Hôpital d'enseignement de l'Université McGill
A McGill University Teaching Hospital

DÉPARTEMENT DE MÉDECINE GÉNÉTIQUE - DEPARTMENT OF MEDICAL GENETICS
3755 Ch. de la Côte-Ste-Catherine, #A-802, Montréal, QC, H3t 1E2 Tél/Tel 514-340-8222 Poste/Local 3965; Fax 514-340-8712

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

PREAMBLE

Medical Genetics has been functioning as a full Department at the Jewish General Hospital in its own right since 2005, while maintaining its status as a Division within the McGill Department of Medicine. This document serves as the annual report for both entities. The academic activities of Dr. David Rosenblatt can be found in the annual report of the Finestone laboratory: www.mcgill.ca/finestone. Information on academic and research activities of all McGill faculty members can also be found in the annual report of the McGill Department of Human Genetics. This report serves as the annual report of both the Department of the Jewish General Hospital and the Division of Medical Genetics in the Department of Medicine.

Clinical Activities

The overall clinical activity is relatively stable since 2013, but there have been some new initiatives. In the hereditary cancer clinic, there were 382 follow-up visits and 523 new visits in 2013. In the Prenatal Diagnosis clinic there were 217 follow-up visits and 316 new visits in 2013. Specialized clinic have been created. In the Urology-Genetics Clinic, which is led by Nassim Taherian, 20 new patients were seen with 19 follow-up visits. In the Hereditary Colorectal Cancer Registry, 6 new patients and 51 follow-up visits or telephone consults have occurred.

The advent of next generation sequencing and the venue of new multiplex genes panel testing, is significantly impacting on current counselling models. The genetic counsellors are currently evaluating new counselling approaches to ensure patients benefit from state of the art genetic services, while ensuring education and patient guided-care. Genetic counsellors share their knowledge with many McGill University students registered in the Genetic Counselling master program, the medical faculty or residents, and fellows from McGill and other universities.

SUMMARY

1. Research and Publications:

The major clinical focus of the department continues to be in the areas of Hereditary Cancer and Prenatal Diagnosis. Prenatal diagnosis activities mainly involve patient care and clinical teaching, whereas Hereditary Cancer has a major research focus at the Jewish

General Hospital and Lady Davis Research Institute. The most exciting work from Dr. Foulkes' group in 2013 continues to be the work on *DICER1* mutations in cancer, but they have also commenced several whole exome sequencing projects that should bear fruit in 2014. The research laboratory of Dr. Rosenblatt is located at the Montreal General Hospital site of the McGill University Health Centre. He has medical responsibility for the prenatal diagnosis program at the Jewish General Hospital.

2. **Teaching and learning (undergraduate and graduate):**
Dr. Foulkes and Dr. Rosenblatt are involved in teaching at all levels-undergraduate, graduate and residency training. The genetic counsellors are actively involved in teaching in the M.Sc. program in Genetic Counselling and with residents in several specialty programs, in particular Medical Genetics and Obstetrics and Gynecology.

McGill Genetic Counselling MSc Program: Role of Genetic Counsellors

Lynn Macrae- on maternity leave in 2013

Carly Pouchet – on Maternity leave in 2013

Prenatal Diagnosis II-HGEN 600-Genetic Counselling
Department: Human Genetics
Format: One group teaching
Role: Facilitator
Title: Maternal Serum Screening
Time: 1.5 hours

Laurence Baret

Unit 8 Small Groups
Department: Human Genetics
Format: Lecture and Small Group Teaching
Role: Facilitator/ Lecturer
Titles: Ethical issues in genetics
Level: Medical Students
Time: 2 hour sessions

Unit 8 Small Groups
Department: Human Genetics
Format: Lecture and Small Group Teaching
Role: Facilitator/ Lecturer
Titles: Cancer Genetics
Level: Medical Students
Time: 2 hour sessions

Genetic counselling Case discussion
Department: Human Genetics
Format: Seminar/ Lecture
Role: Lecturer

Titles: Case discussion and psychosocial issues
Level: Master students
Time: 1.5 hours

Nassim Taherian

Unit 8 Small Groups Department:
Human Genetics
Format: Small Group Teaching
Role: Facilitator
Titles: Genetic Testing in Families and Populations
Level: Medical Students
Time: 2 hour sessions

Unit 8 Small Groups Department:
Human Genetics
Format: Small Group Teaching
Role: Facilitator
Titles: Cancer Genetics
Level: Medical Students
Time: 2 hour sessions

Fundamentals of Medicine and Dentistry
Department: Human Genetics
Format: Small Group Teaching
Role: Facilitator
Titles: Family History Taking and Risk Assessment
Level: Medical Students
Time: 3 hour sessions

Introduction to Research Ethics-HGEN 600-Genetic Counselling
Department: Human Genetics
Format: One Group Teaching
Role: Lecturer
Titles: Consent Form Design, and the IRB Process
Time: 1.5 hours

Nora Wong

HGEN601
Department: Human Genetics
Format: Lecture
Title: Psychosocial aspects of living with hereditary cancer risk and decision-making under uncertainty
Role: Lecturer
Level: Graduate
Time: 1 X 3 hour session

Unit 8 Small Groups
Department: Human Genetics
Format: Lecture and Small Group Teaching
Role: Lecturer-2 sessions:
Titles: Cancer Genetics
Level: Medical Students
Time: 1 X 2 hour session

Unit 8 Small Groups
Department: Human Genetics
Format: Lecture and Small Group Teaching
Role: Teaching assistant
Titles: Family history taking
Level: Medical Students
Time: 1 X 3 hour session

HGEN 610, HGEN 611
Department: Human Genetics
Format: Independent research project for Laura Dempsey-Nunez
Title: RAD51C/D mutations in women with synchronous cancers of the ovary and endometrium: a hospital cohort
Role: Project advisor
Level: Graduate

Department: Psychiatry
Format: MSc Theses
Title: Psychosocial determinants of decision-making in women newly diagnosed with breast and ovarian cancer
Role: co-supervisor
Level: Graduate

Sonya Zaor

First year Practicum
Department: Human Genetics
Format: Workshop
Title: Psychosocial Issues in Cancer Genetics: a patient testimony
Role: Leader
Level: 1st yr Genetic Counselling student
Time: 2 hours

Summary of McGill Clinical Supervision by Genetic Counsellors

Laurence Baret

Clinical Supervision	Length of Rotation (wks)	Number students	Total time
First Year GC	3	2	6

Visiting fellow	3	1	3
Medical Student	1	2	2
TOTAL		5	11

Maria Lalous

Clinical Supervision	Length of Rotation (wks)	Number students	Total time (wks)
First year GC student	4	2	8
Second Year GC	6	2	12
Medical Student	1	4	4
Medical Residents	2	5	10
MFM fellow	4	1	4
TOTAL		14	38

Heidi Rothenmund

Clinical Supervision	Length of Rotation (wks)	Number students	Total time
Second Year GC	3	2*	6

Co-supervised with Nassim Taherian and Nora Wong
*Please note: one student did not complete her rotation due to medical leave

Nassim Taherian

Clinical Supervision	Length of Rotation (wks)	Number students	Total time
Second Year GC	3	2*	6

Co-supervised with Nora Wong and Heidi Rothenmund
*Please note: one student did not complete her rotation due to medical leave

Nora Wong

Clinical Supervision	Length of Rotation (wks)	Number students	Total time
Second Year GC	3	2*	6

Co-supervised with Nassim Taherian and Heidi Rothenmund
*Please note: one student did not complete her rotation due to medical leave

Sonya Zaor

Clinical Supervision	Length of Rotation (wks)	Number	Total time (wks)
First year GC student	5	1	5
Second Year GC	3	1	3
Visiting fellow	1	1	1
Medical resident	6	2	12
TOTAL		5	21

*3 ad hoc McGill medical students, resident in radiology (CHUM), resident in pathology have not been included

3. Involvement in the community:

Dr. Foulkes has been involved with many activities relating to hereditary cancer. He is often solicited as a resource for the media when expert opinion in this area is required. Nora Wong and Laurence Baret have been involved with many activities relating to hereditary breast and ovarian cancer leading information booth at many events in the community.

4. Partnerships:

The faculty of the JGH Department has close working relationships with the hospital and university Departments of Medicine, Oncology, Pediatrics, and Obstetrics.

5. Milestones:

Dr. Rosenblatt completed twelve years as Chair of the Department of Human Genetics at McGill. Dr. Eric Shoubridge has been appointed as the new Chair.

6. Honours, awards and prizes:

Dr. Rosenblatt is the Chair holder of the Dodd Q. Chu and Family Chair in Medical Genetics at McGill. Dr. Foulkes is a James McGill Professor of Medicine at McGill University. In 2013, Dr. Rosenblatt was named a Champion of Genetics by the Canadian Gene Cure Foundation.

7. Fundraising:

Laura Hayes is supported by funds from the Hereditary Breast and Ovarian Foundation (HBOC).

SECTION I – DEPARTMENT/DIVISION STATUS UPDATE

1. Mission and objectives of the Division

Medical Genetics at the JGH is committed to the best possible patient care and teaching in the area of prenatal diagnosis. It is committed to excellence patient care, teaching and research in Hereditary Cancer. In the area of Hereditary Cancer Research, it is committed to being amongst the best centres in the world. The Division strives to provide comprehensive service to our clientele. Its priority is to make it clear that further resources must be made available for prenatal, cancer and other general genetics services at the Jewish General Hospital. The Department of Medical Genetics at the Jewish General Hospital aspires to making the needs of both individuals and families in the area of medical genetics better known to the hospital and the community at large.

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

William Foulkes	Professor
Laurence Baret	Faculty Lecturer
Maria Lalous	Faculty Lecturer
Lynn Macrae	Faculty Lecturer-maternity leave
Carly Pouchet	Faculty Lecturer-maternity leave
David Rosenblatt	Professor
Heidi Rothenmund	Faculty Lecturer
Nassim Taherian	Academic Associate
Nora Wong	Faculty Lecturer
Sonya Zaor	Faculty Lecturer

Laurence Baret, Nora Wong, and Sonya Zaor, are genetic counsellors who are primarily responsible for cancer genetics. Maria Lalous is a full time genetic counsellor in the area of prenatal diagnosis. Heidi Rothenmund and Nassim Taherian are genetic counsellors who are responsible for cancer specialty clinics. Razia Chanda, Martah Urquilla and Samar Edriss provide administrative support for the department. Danielle Veyre has retired from her administrative post in September 2013.

Laurence Baret is a recent graduate from the University of Toronto Genetic Counselling Master Program. She is a full time genetic counsellor in cancer genetics and has been hired for a 1 year maternity leave replacement for Lynn Macrae. With her previous training in Bioethics (M.A. Bioethics), her research interests include the ethical issues in human genetics. Her previous work focused on the communication of genetic research results to research participants, which has been published in the *European Journal of Human Genetics*. Laurence Baret is involved in clinical projects aiming to improve the clinical model of delivering genetic services (*e.g.* developing an alternative model to deliver genetic counselling services for 'low risk' patients, helping to implement referral guidelines for breast and ovarian cancer, helping to implement blood send-outs from a core laboratory and implementing updated genetic testing approaches based on the current literature).

Laura Hayes has the responsibility to help patients who carry mutations in cancer susceptibility genes navigate the medical system and obtain the follow-up care they require. Her work is supported by the Hereditary Breast and Ovarian Cancer (HBOC) Foundation

Heidi Rothenmund is a part-time genetic counsellor who has been working with Dr. Foulkes and Dr. George Chong to develop the Hereditary Colorectal Cancer Registry, which is based in the Cancer Prevention Centre at the Jewish General Hospital. The purpose of the Registry is to follow families affected with hereditary colorectal cancer that have been identified through the Cancer Genetics Clinics in the Department of Medical Genetics as well as other centres throughout the province. The clinical role of the registry is to provide regular contact with these high-risk individuals to update the

family history of cancer, coordinate clinical screening appointments, and to facilitate predictive genetic testing and clinical screening for at-risk relatives, where applicable. Patients and at-risk family members in the Registry may be referred to the GENGI Clinic at the Jewish General Hospital where Heidi and Dr. Polymnia Galiatsatos in the Department of Gastroenterology will follow these high risk patients on an annual basis. For Registry participants who are not able to travel to the Jewish General Hospital, Heidi provides telephone appointments. On a research basis, the Registry recruits high-risk families who are eligible for gene-discovery efforts through the research laboratory of Dr. Foulkes. This involves various local and international collaborations that have been facilitated by both Dr. Foulkes and Dr. Chong. Heidi also works with a part-time research assistant (Angelica Randall) as the study coordinator Canadian Colorectal Cancer Consortium (C4): Clinical and Molecular Screening in Patients with Colorectal Cancer and their Family Members. This is a multi-centre study across Canada that is funded by the Terry Fox Research Institute and for which Dr. Foulkes is the Site Principal Investigator. Eligible patients with newly diagnosed colorectal cancer at the Jewish General Hospital and the Montreal General Hospital will be approached to participate in this study. The main goals of the study are to investigate the frequency of Lynch Syndrome in Canada; to determine the feasibility of implementing routine screening for Lynch Syndrome in newly diagnosed patients; to study quality of life factors for colorectal cancer patients; and to investigate the uptake of colonoscopy screening among at-risk relatives.

Nassim Taherian coordinates a specialty clinic for the evaluation of patients with familial renal cell carcinoma or prostate cancer. She works with the departments of Medical Genetics and Urology. Her clinics are held in the Cancer Prevention Centre with Dr. William Foulkes. She also coordinates various international research studies on prostate cancer genetics and is first author of a paper: Familial prostate cancer: the damage done and lessons learnt. Taherian, N., Hamel, N., Begin, L. R., Bismar, T. A., Goldgar, D. E., Feng, B. J. and Foulkes, W. D. January 2013 Nat. Rev. Urol. 10, 116-122 (2013).

Nora Wong continues her clinical focus on increasing the accessibility of genetic testing for cancer susceptibility and looking into alternative models for service delivery. Her two papers have been accepted for publication (see below). She also continues to devote time in various research projects, advisory boards and community programs. Experience of BRCA1/2 mutation-negative young women from families with hereditary breast and ovarian cancer: a qualitative study. Macrae L, de Souza AN, Loiselle CG, Wong N. Cultural aspects of healthy BRCA carriers from two ethnocultural groups in qualitative health research. Hered Cancer Clin Prac. October 2013. 16;11(1):14.

Sonya Zaor devotes her efforts in delivering and improving cancer genetic counselling services. The increase in referrals and recent implementation of new genetic testing technologies in the clinical setting, have synergistically impacted the current practice of genetic counseling. Sonya was instrumental in implementing referral criteria to increase accessibility to genetic testing for a greater number of families who are at high risk. Sonya is interested in other projects such as addressing the utility and acceptance of gene panels in the clinical setting for providers and their patients. Her efforts are also focused on addressing the needs for patients at lower genetic risk. She is looking at alternative models to delivery information for these individuals by developing alternative clinics as

well as improving access to information for patients and physicians using various media sources (McGill Website, educative pamphlet).

Dr. William Foulkes also continues to play a major role in clinical and research aspects of hereditary cancer predisposition at the JGH. In his role as Director of the Program in Cancer Genetics, housed in the Departments of Human Genetics and Oncology at McGill, he has played a major role in bringing expertise together from these two different but crucially important disciplines.

On the eighth floor of the A Pavilion, the department has administrative space and a dedicated counselling room, primarily used for prenatal diagnosis. Much of the clinical work in cancer genetics takes place in the Cancer Prevention Centre in the Segal Cancer Centre and provides state of the art facilities for managing individuals and families with a hereditary predisposition to cancer.

Dr. David Rosenblatt continues to be Director of the University Division of Medical Genetics in the McGill Department of Medicine; this enhances integrated service delivery and allows the Department to share in the larger talent pool of the Department of Medicine. He completed his term as Chair of the McGill Department of Human Genetics and his term at the end of June 2013. The report of the academic activities of Dr. Rosenblatt for the past year can be obtained at www.mcgill.ca/finestone/. Dr. Rosenblatt has assured the full involvement of the JGH Department in all aspect of the McGill RUIS.

Dr. William Foulkes continues to run the cancer genetics service, dividing his time between the MUHC and the JGH. There are close links to the Departments of Oncology and Pathology, and to a number of surgical divisions, reflecting the multidisciplinary nature of the clinical service.

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

1. Grants and awards received

William Foulkes

CURRENT COMPETITIVE GRANTS

As Principal Investigator

- CCSRI: DICER1 and pituitary blastoma: Keys to understanding pituitary development and tumorigenesis

- Alex’s Lemonade Stand Foundation: DICER1, microRNAs and pediatric cancer: an emerging story

- Ride to Conquer Cancer: Establishing a Quebec Hereditary Colorectal Cancer Registry,

- Prostate Cancer Canada: Funding for the Canadian BRCA1/2 Prostate Cancer Network, Susan G Komen for the Cure Komen Scholar: Hereditary breast cancer: cause and effect

- Cancer Research Society: Assessing the contribution of spindle assembly checkpoint genes to colorectal carcinoma

- Comité mixte Québec-Catalogne, du Ministère des Relations internationals: Identification de nouveaux gènes de susceptibilité à la néoplasie colorectale.

Co-investigator -

- Dorval, M

Co-applicants: Foulkes WD et al.
CRS/QBCF: Cancer screening practices of non-carriers from BRCA1/2 mutation-positive families: Extent, determinants and psychosocial impact of over-screening

- Mes-Masson, A

Co-applicants: Foulkes WD et al.
FRQS: Budget alloué dans le cadre du projet FRQS-Réseau de recherche sur le cancer (Axe banque de tissus et de données)

- Tischkowitz, M

Co-applicants: Foulkes WD et al.
Cancer Research Society: A multimodal genomic analysis strategy to identify novel breast cancer genes

David Rosenblatt
-CIHR, Operating Grant, PI – 2009-2014
Inborn Errors of Folate and Cobalamin Metabolism

3. **Scholarly works published in the 2013 calendar year**:

William Foulkes:

1. Xu J, Lange EM, Lu L, Zheng SL, Wang Z, Thibodeau SN, Cannon-Albright LA, Teerlink CC, Camp NJ, Johnson AM, Zuhlke KA, Stanford JL, Ostrander EA, Wiley KE, Isaacs SD, Walsh PC, Maier C, Luedeke M, Vogel W, Schleutker J, Wahlfors T, Tammela T, Schaid D, McDonnell SK, Derycke MS, Cancel-Tassin G, Cussenot O, Wiklund F, Grönberg H, Eeles R, Easton D, Kote-Jarai Z, Whittemore AS, Hsieh CL, Giles GG, Hopper JL, Severi G, Catalona WJ, Mandal D, Ledet E, Foulkes WD, Hamel N, Mahle L, Moller P, Powell I, Bailey-Wilson JE, Carpten JD, Seminara D, Cooney KA, Isaacs WB; International Consortium for Prostate Cancer Genetics. HOXB13 is a susceptibility gene for prostate cancer: results from the International Consortium for Prostate Cancer Genetics (ICPCG). Hum Genet. 2013 Jan;132(1):5-14.

2. Tischkowitz M, Sabbaghian N, Hamel N, Pouchet C, Foulkes WD, Mes-Masson AM, Provencher DM, Tonin PN. Contribution of the PALB2 c.2323C>T [p.Q775X] Founder mutation in well-defined breast and/or ovarian cancer families and unselected ovarian cancer cases of French Canadian descent. BMC Med Genet. 2013 Jan 9;14:5.

3. Narod SA, Metcalfe K, Lynch HT, Ghadirian P, Robidoux A, Tung N, Gaughan E, Kim-Sing C, Olopade OI, Foulkes WD, Robson M, Offit K, Jakubowska A, Byrski T, Huzarski T, Sun P, Lubinski J. Should all BRCA1 mutation carriers with stage I breast cancer receive chemotherapy? Breast Cancer Res Treat. 2013 Feb;138(1):273-9.

4. Zhang J, Shi Y, Lalonde E, Li L, Cavallone L, Ferenczy A, Gotlieb WH, Foulkes WD, Majewski J. Exome profiling of primary, metastatic and recurrent ovarian carcinomas in a BRCA1-positive patient. BMC Cancer. 2013 Mar 22;13:146.

5. Sabbaghian N, Bahubeshi A, Shuen AY, Kanetsky PA, Tischkowitz MD, Nathanson KL, Foulkes WD.Germ-line DICER1 mutations do not make a major contribution to the etiology of familial testicular germ cell tumours. BMC Res Notes. 2013 Apr 1;6:127.

6. Domchek SM, Tang JB, Stopfer J, Lilli DR, Hamel N, Tischkowitz M, Monteiro AN, Messick TE, Powers J, Yonker A, Couch FJ, Goldgar DE, Davidson HR, Nathanson KL, Foulkes W, Greenberg RA. Biallelic Deleterious BRCA1 Mutations in a Woman with Early-Onset Ovarian Cancer. Cancer Discov. 2013 Apr;3(4):399-405.

7. Foulkes WD, Real FX. Many mosaic mutations. Curr Oncol. 2013 Apr;20(2):85-7.

8. Wark L, Novak D, Sabbaghian N, Amrein L, Jangamreddy JR, Cheang M, Pouchet C, Aloyz R, Foulkes WD, Mai S, Tischkowitz M. Heterozygous mutations in the PALB2 hereditary breast cancer predisposition gene impact on the three-dimensional nuclear organization of patient-derived cell lines. Genes Chromosomes Cancer. 2013 May;52(5):480-94.

9. Finch A, Valentini A, Greenblatt E, Lynch HT, Ghadirian P, Armel S, Neuhausen SL, Kim-Sing C, Tung N, Karlan B, Foulkes WD, Sun P, Narod S; Hereditary Breast Cancer Study Group. Frequency of premature menopause in women who carry a BRCA1 or BRCA2 mutation. Fertil Steril. 2013 May 99(6):1724-8.

10. Wu M, Sabbaghian N, Xu B, Addidou-Kalucki S, Bernard C, Zou D, Reeve A, Eccles M, Cole C, Choong C, Charles A, Tan T, Iglesias D, Goodyer P, Foulkes W. Biallelic DICER1 mutations occur in Wilms tumours. J Pathol. 2013 Jun;230(2):154-64.

11. Chen Z, Greenwood C, Isaacs WB, Foulkes WD, Sun J, Zheng SL, Condreay LD, Xu J. The G84E mutation of HOXB13 is associated with increased risk for prostate cancer: results from the REDUCE trial. Carcinogenesis. 2013 Jun;34(6):1260-4.

12. Foulkes WD. Preventing ovarian cancer by salpingectomy. Curr Oncol. 2013 Jun;20(3):139-42

13. Segev Y, Iqbal J, Lubinski J, Gronwald J, Lynch HT, Moller P, Ghadirian P, Rosen B, Tung N, Kim-Sing C, Foulkes WD, Neuhausen SL, Senter L, Singer CF, Karlan B, Ping S, Narod SA; Hereditary Breast Cancer Study Group. The incidence of endometrial cancer in women with BRCA1 and BRCA2 mutations: An international prospective cohort study. Gynecol Oncol. 2013 Jul;130(1):127-31.

14. Foulkes WD, Shuen AY. In Brief: BRCA1 and BRCA2. J Pathol. 2013 Aug;230(4):347-9.

15. Tessier Cloutier B, Clarke AE, Ramsey-Goldman R, Wang Y, Foulkes W, Gordon C, Hansen JE, Yelin E, Urowitz MB, Gladman D, Fortin PR, Wallace DJ, Petri M, Manzi S, Ginzler EM, Labrecque J, Edworthy S, Dooley MA, Senécal JL, Peschken CA, Bae SC, Isenberg D, Rahman A, Ruiz-Irastorza G, Hanly JG, Jacobsen S, Nived O, Witte T, Criswell LA, Barr SG, Dreyer L, Sturfelt G, Bernatsky S. Breast cancer in systemic lupus erythematosus. Oncology. 2013;85(2):117-21.

16. Yu OH, Foulkes WD, Dastani Z, Martin RM, Eeles R, Richards JB. An assessment of the shared allelic architecture between type 2 diabetes and prostate cancer. Cancer Epidemiol Biomarkers Prev. 2013 May 23. [Epub ahead of print]

17. Witkowski L, Lalonde E, Zhang J, Albrecht S, Hamel N, Cavallone L, May ST, Nicholson JC, Coleman N, Murray MJ, Tauber PF, Huntsman DG, Schönberger S, Yandell D, Hasselblatt M, Tischkowitz MD, Majewski J, Foulkes WD. Familial Rhabdoid Tumour "Avant la Lettre" - from pathology review to exome sequencing and back again. J Pathol. 2013;231(1):35-43.

18. de Kock L, Plourde F, Carter MT, Hamel N, Srivastava A, Meyn MS, Arseneau J, Soglio DB, Foulkes WD. Germ-line and somatic DICER1 mutations in a pleuropulmonary blastoma. Pediatr Blood Cancer.2013 Jul 19. [Epub ahead of print]

19. Sabbaghian N, Srivastava A, Hamel N, Plourde F, Gajtko-Metera M, Niedziela M, Foulkes WD. Germ-line deletion in DICER1 revealed by a novel MLPA assay using synthetic oligonucleotides. Eur J Hum Genet. 2013 Sep 25. [Epub ahead of print]

20. Foulkes WD. BRCA1 and BRCA2 - Update and Implications on the Genetics of Breast Cancer: A Clinical Perspective. Clin Genet. 2013 Oct 1. [Epub ahead of print]

21. Joly Y, Burton H, Knoppers BM, Feze IN, Dent T, Pashayan N, Chowdhury S, Foulkes W, Hall A, Hamet P, Kirwan N, Macdonald A, Simard J, Van Hoyweghen I. Life insurance: genomic stratification and risk classification. Eur J Hum Genet. 2013 Oct 16. [Epub ahead of print]

22. Witkowski L, Mattina J, Schönberger S, Murray MJ, Huntsman DG, Reis-Filho JS, McCluggage WG, Nicholson JC, Coleman N, Calaminus G, Schneider DT, Arseneau J, Stewart CJ, Foulkes WD. DICER1 hotspot mutations in non-epithelial gonadal tumours. Br J Cancer. 2013 Oct 17. [Epub ahead of print]

23. Valentini A, Lubinski J, Byrski T, Ghadirian P, Moller P, Lynch HT, Ainsworth P, Neuhausen SL, Weitzel J, Singer CF, Olopade OI, Saal H, Lyonnet DS, Foulkes WD, Kim-Sing C, Manoukian S, Zakalik D, Armel S, Senter L, Eng C, Grunfeld E, Chiarelli AM, Poll A, Sun P, Narod SA; The Hereditary Breast Cancer Clinical Study Group. The impact of pregnancy on breast cancer survival in women who carry a BRCA1 or BRCA2 mutation. Breast Cancer Res Treat. 2013 Oct 18. [Epub ahead of print]

24. Tomiak E, de Kock L, Grynspan D, Ramphal R, Foulkes WD. DICER1 mutations in an adolescent with cervical embryonal rhabdomyosarcoma (cERMS). Pediatr Blood Cancer. 2013 Oct 22. [Epub ahead of print] No abstract available.

25. Rothenmund H, Singh H, Candas B, Chodirker BN, Serfas K, Aronson M, Holter S, Volenik A, Green J, Dicks E, Woods MO, Gilchrist D, Gryfe R, Cohen Z, Foulkes WD. Hereditary colorectal cancer registries in Canada: report from the Colorectal Cancer Association of Canada consensus meeting; Montreal, Quebec; October 28, 2011. Curr Oncol. 2013 Oct;20(5):273-8. Doi.

26. Teerlink CC, Thibodeau SN, McDonnell SK, Schaid DJ, Rinckleb A, Maier C, Vogel W, Cancel-Tassin G, Egrot C, Cussenot O, Foulkes WD, Giles GG, Hopper JL, Severi G, Eeles R, Easton D, Kote-Jarai Z, Guy M, Cooney KA, Ray AM, Zuhlke KA, Lange EM, Fitzgerald LM, Stanford JL, Ostrander EA, Wiley KE, Isaacs SD, Walsh PC, Isaacs WB, Wahlfors T, Tammela T, Schleutker J, Wiklund F, Grönberg H, Emanuelsson M, Carpten J, Bailey-Wilson J, Whittemore AS, Oakley-Girvan I, Hsieh CL, Catalona WJ, Zheng SL, Jin G, Lu L, Xu J; International Consortium for Prostate Cancer Genetics, Camp NJ, Cannon-Albright LA. Association analysis of 9,560 prostate cancer cases from the International Consortium of Prostate Cancer Genetics confirms the role of reported prostate cancer associated SNPs for familial disease. Hum Genet. 2013 Oct 26. [Epub ahead of print]

27. Nguyen-Dumont T, Teo ZL, Pope BJ, Hammet F, Mahmoodi M, Tsimiklis H,Sabbaghian N, Tischkowitz M, Foulkes WD, Giles GG, Hopper JL, Southey MC, ParkDJ. Hi-Plex for high-throughput mutation screening: application to the breast cancer susceptibility gene PALB2. BMC Med Genomics. 2013 Nov 8;6(1):48. [Epub ahead of print]

28. Phelan CM, Iqbal J, Lynch HT, Lubinski J, Gronwald J, Moller P, Ghadirian P, Foulkes WD, Armel S, Eisen A, Neuhausen SL, Senter L, Singer CF, Ainsworth P, Kim-Sing C, Tung N, Llacuachaqui M, Chornokur G, Ping S, Narod SA; the Hereditary Breast Cancer Study Group. Incidence of colorectal cancer in BRCA1 and BRCA2 mutation carriers: results from a follow-up study. Br J Cancer. 2013 Nov 28. doi:10.1038/bjc.2013.741.

David Rosenblatt

1. Mah W, Deme JC, Watkins D, Fung S, Janer A, Rosenblatt DS, Shoubridge EA, and Coulton JW. Subcellular location of MMACHC and MMADHC, two human proteins central to intracellular vitamin B_{12} metabolism. *Mol. Genet. Metab.* 108:112-118, 2013.

2. Watkins D, Rosenblatt DS. Lessons in biology from patients with inborn errors of vitamin B_{12} metabolism. *Biochimie* 95:1019-1022, 2013.

3. Keller MD, Ganesh J, Heltzer M, Paessler M, Bergqvist AGC, Baluarte JJ, Watkins D, Rosenblatt DS, Orange JS. Severe combined immunodeficiency resulting from mutations in *MTHFD1*. *Pediatrics* 131:e629-e634, 2013.

4. Rosenblatt DS. Who's on first in exome and whole genome sequencing? Is it the patient or the incidental findings? *Mol Genet Metab* 110:1-2, 2013.

5. Illson ML, Dempsey-Nunez L, Kent J, Huang Q, Brebner A, Raff M, Watkins D, Gilfix BM, Wittwer CT, and Rosenblatt DS. High resolution melting analysis of the MMAB gene in cblB patients and in those with undiagnosed methylmalonic aciduria. *Mol. Genet. Metab.* 110:86-89, 2013.

6. Yu HC, Sloan JL, Scharer G, Brebner A, Quintana A, Achilly NP, Manoli I, Coughlin CR, Geiger EA, Schneck U, Watkins D, Van Hove JLK, Fowler B, Baumgartner MR, Rosenblatt DS, Venditti CP and Shaikh TH. An X-linked cobalamin disorder caused by mutations in the transcription coregulator *HCFC1*. *Am J Hum Genet* 93:506-514, 2013.

7. Moreno-Garcia MA, Rosenblatt DS, Jerome-Majewska LA. Vitamin B_{12} metabolism in man and in embryonic mouse models. *Nutrients* 5:3531-3550, 2013.

8. Prasad C, Melançon SB, Rupar CA, Prasad AN, Dempsey-Nunez L, Rosenblatt DS and Majewski J. Exome sequencing reveals a homozygous mutation in *TWINKLE* as the cause of multisystemic failure in three siblings. *Mol. Genet. Metab.* 108:190-194, 2013.

9. Gupta IR, Baldwin C, Auguste D, Ha KC, Andalousi EI, Fahiminiya S, Bitzan M, Bernard C, Akbari MR, Narod SA, Rosenblatt DS, Majewski J, Takano T. ARHGDIA: a novel gene implicated in nephritic syndrome. *J Med Genet* 50:330-338, 2013.

10. Rosenblatt DS. Book Review: Victor McKusick and the History of Medical Genetics. *J Med Genet* 50:640, 2013.

11. Paul E, Guttenberg M, Kaplan P, Watkins D, Rosenblatt DS, Kaplan BS. Atypical glomerulopathy associated with the cblE inborn error of vitamin B12 metabolism. *Pediatr. Nephrol.* 28:1135-1139, 2013.

12. Watkins D, Rosenblatt DS. Cerebral folate deficiency. *MedLink Neurology* http://www.medlink.com/MedLinkContent.asp, 2013.

13. Watkins D, Rosenblatt DS. Folic acid deficiency. *MedLink Neurology* http://www.medlink.com/MedLinkContent.asp, 2013.

14. Armour C, Brebner A, Watkins D, Geraghty MT, Chan A, Rosenblatt DS. A patient with an inborn error of vitamin B_{12} metabolism (*cblF*) detected by newborn screening. *Pediatrics* 132:e257-e261, 2013.

15. Fofou-Caillierez MB, Mrabet N, Chéry C, Dreumont N, Flayac J, Pupavac M, Paoli J, Alberto JM, Coelho D, Camadro JM, Feillet F, Watkins D, Fowler B, Rosenblatt DS, Guéant JL. Interaction between methionine synthase isoforms and MMACHC: characterization of cblG-variant, cblG and cblC inherited causes of megaloblastic anemia. *Hum Mol Genet* 22:4591-4601, 2013.

16. Zawati MH, Parry D, Thorogood A, Nguyen MT, Boycott,KM, Rosenblatt D, Knoppers BM. Reporting results from whole-genome and exome sequencing in clinical practice: a proposal for Canada? *J Med Genetics* 51:68-70, 2014, 2013.

17. Trakadis YJ, Alfares A, Bodamer O, Boyukavci M, Christodoulou J, Connor P, Glamuzina E, Gonzalez-Fernandez F, Haim B, Echenne B, Manoli I, Mitchell J, Nordvall M, Prasad C, Scaglio F, Schiff M, Schrewe B, Touati G, Tchan MC, Varet B, Venditti C, Zafeiriou D, Rupar T, Rosenblatt DS, Watkins D, Braverman N. Update on transcobalamin deficiency: clinical presentation, treatment and outcome. *J Inher Metab Dis* doi:10.1007/s10545-013-9664-5, 2013

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

William Foulkes

February 5 2013
Title: Triple negative breast cancer: germ-line mutations, classification and emerging targets
Sírio Libanês Hospital
São Paulo, Brazil

March 13 2013
Title: Triple Negative Disease: Molecular heterogeneity and emerging targets
13th International St-Gallen Breast Cancer Conference
St-Gallen, Switzerland

April 6th 2013
Title: Deconstructing the complexity of Triple Negative Breast Cancer
2013 AACR Meeting
Walter E. Washington Convention Center
Waashington, DC

October 4th 2013
Title: Clinical aspect of digestive diseases
10th International Symposium on the Physiology and Diseases of the Digestive Tract
Estrimont Suites and Spa Orford
Orford, Qc

David Rosenblatt

February 19, 2013
Title: Discovering New Genes in the One-carbon Pathway Using Exome Sequencing-A RaDiCAL Approach
Keystone Symposia on Molecular and Celular Biology
Santa Fe, New Mexico

September 11, 2013
Title: Discovering new genes in the one-carbon pathway using exome sequencing: a RaDiCAL approach
9th International Conference on Homocysteine and One
Carbon Metabolism
Dublin, Ireland

November 5, 2013
Title: Using next generation sequencing to discover novel steps in one-carbon Metabolism
Genomics in Metabolism
Copenhagen, Denmark

December 13, 2013
Title: Les maladies héreditaires du metabolisme de la vitamine B_{12}: contribution à la connaissance du metabolism cellulaire
Journées francophones de nutrition
Bordeaux, France

SECTION III - CONFIDENTIAL INFORMATION

1. Consulting activities:

Both Dr. Foulkes and Dr. Rosenblatt are involved in editorial reviews of manuscripts, and on various committees at the local, provincial and national levels.

Respectfully submitted,

David S. Rosenblatt, MD
Chief, Department of Medical Genetics, Jewish General Hospital
Head, Division of Medical Genetics, Department of Medicine, Jewish General Hospital and McGill University

January 26, 2014