

**ANNUAL REPORT
2015/2016**

THE HESS B. AND DIANE FINESTONE LABORATORY
IN MEMORY OF
JACOB AND JENNY FINESTONE

Submitted by: Dr. David S. Rosenblatt

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MEMBERSHIP

PHYSICIANS AND SCIENTISTS

David S. Rosenblatt

David Watkins

ADMINISTRATIVE SUPPORT STAFF

Danielle Piazzoli (Veyre)

CLINICAL SUPPORT STAFF

Maria Galvez

Leah Ladores

RESEARCH SUPPORT STAFF

GRADUATE STUDENTS

Jordan Chu

Mihaela Pupavac

ANNUAL REPORT 2015/2016

The Hess B. and Diane Finestone Laboratory in Memory of Jacob and Jenny Finestone, was first established in 1988. The intent of the donor was to honour the memory of Jacob and Jenny Finestone, and the 80th birthday of Mr. Hess B. Finestone. A permanent endowment was created at McGill University devoted to the advancement of medical genetics. The specific objectives of the endowment are to a) fund research projects related to the field of medical genetics; b) fund trainees in the field of medical genetics; and c) publicize the field of medical genetics through the support of special lectures, visiting professorships and other appropriate means. Dr. David S. Rosenblatt has been Director of the laboratory since its inception, and this annual report describes the activity of his laboratory. Material relating to members of the Department of Human Genetics at McGill and the Departments of Medical Genetics at the McGill University Health Centre and the Jewish General Hospital should be sought in the respective university or hospital annual reports.

RESEARCH

The Hess B. and Diane Finestone Laboratory in Memory of Jacob and Jenny Finestone, had been located on Livingston 3 of the Montreal General Hospital Site of the McGill University Health Centre. This is the first year that it has been located at the new Glen Site. The new site has the advantage of grouping many leading scientists from the hospital communities on one site. Our facility is one of two major international referral laboratories for the diagnosis of patients with inherited disorders of folate and vitamin B₁₂ transport and metabolism. It is involved in studying the biochemical and molecular bases of these diseases. Since the MUHC has a CLIA certified cellular and molecular diagnostic laboratory, advances in knowledge from research can be immediately translated to clinical diagnostics.

2015-2016 has seen a number of scientific highlights:

- 1) Dr. Rosenblatt has continued to champion the concept of **RaDiCAL** (Rare Disease Collaboration for Autosomal Loci). He has proposed the use of single patients with Mendelian disorders to discover new genes. With colleagues at McGill he has continued to use exome sequencing for new gene discovery.
 - 2) The group has compared the results that have been obtained over decades using a somatic cell genetic approach, with those that can now be obtained using next generation sequencing panels. This has confirmed the utility of both techniques.
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RESEARCH OPERATING FUNDS

CIHR Operating Grant, PI – 2009-2014. A one year no cost extension was granted until October 2015. Much of the current year was structured in anticipation of being successful in the Project Grants competition in 2016.

ORIGINAL PUBLICATIONS

Wong D, Tortorelli S, Bishop L, Sellars DA, Schimmenti L, Gallant M, Prada CE, Hopkin RJ, Leslie ND, Berry SA, Rosenblatt DS, Fair AL, Matern D, Raymond K, Oglesbee D, Rinaldo P, Gavrilov D. Outcomes of four patients with homocysteine remethylation disorders detected by newborn screening. *Genet Med* 18:162-167, 2016.

Gupta S, Fahiminiya S, Wang T, Dempsey Nunez L, Rosenblatt DS, Gibson WT, Gilfix BM, Bergeron JJM, Jerome-Majewska LA. Somatic overgrowth associated with homozygous mutations in both *MAN1B1* and *SEC23*. *Cold Spring Harb Mol Case Stud* 2:a000737 2016.

Pupavac M, Tian X, Chu J, Wang G, Feng Y, Chan S, Fenter R, Zhang VW, Wang J, Watkins D, Wong LJ, Rosenblatt DS. Added value of next generation gene panel analysis for patients with elevated methylmalonic acid and no clinical diagnosis following functional studies of vitamin B₁₂ metabolism. *Mol Genet Metab* 117:363-368, 2016.

Chu J, Pupavac M, Watkins D, Tian X, Feng Y, Chen S, Fenter R, Zhang VW, Wang J, Wong LJ, Rosenblatt DS. Next generation sequencing of patients with *mut* methylmalonic aciduria: validation of somatic cell studies and identification of 16 novel mutations. *Mol Genet Metab* 118:264-271, 2016.

Watkins D, Rosenblatt DS. Lessons in biology from patients with inherited disorders of vitamin B₁₂ and folate metabolism. *Biochimie* 126:3-5, 2016.

Mah W, Sonkusare SK, Wang T, Azeddine B, Pupavac M, Carrot-Zhang J, Majewski J, Harvey EJ, Russell L, Chalk C, Rosenblatt DS, Nelson MT, Séguin C. Gain-of-function mutation in TRPV4 identified in patients with osteonecrosis of the femoral head. *J Med Genet* doi:10.1136/jmedgenet-2016-103829, 2016.

ABSTRACTS

Chu J, Pupavac M, Watkins D, Tian X, Feng Y, Chen S, Fenter R, Zhang VW, Wang J, Wong LJ, Rosenblatt DS. Next-generation sequencing analysis of 53 patients diagnosed with *mut* methylmalonic aciduria. Genomics of Rare Disease: Beyond the Exome, Cambridge UK, April 2016

Chu J, Pupavac M, Watkins D, Tian X, Feng Y, Chen S, Fenter R, Zhang VW, Wang J, Wong LJ, Rosenblatt DS. Next-generation sequencing analysis of 53 patients diagnosed with *mut* methylmalonic aciduria. Annual Meeting-Association des Médecins Généticiens du Québec, Montreal, May 2016

TEACHING

David Watkins

Biology 575

Department: Biology/Human Genetics
Format: Lecture
Title: *Inborn Errors of Cobalamin Transport and Metabolism*
Role: Lecturer
Level: Undergraduate/Graduate
Time: 2 1.5-hour class lectures

David Rosenblatt

Unit 8

Department: Human Genetics
Format: Lectures
Role: Lecturer-2 sessions
Titles: *Introduction to Medical Genetics*
Huntington Disease
Level: Medical Students
Time: 2 lectures -1 hour each

FINANCIAL REPORT – 2015/2016

Starting Balance		\$ 112, 042
*Salary Support and Benefits	\$ 70, 522	
Materials and Supplies	\$ 9, 441	
Conferences, Travel, Special Events	\$ 6, 447	
Phones, Pagers, Computer, Printing, Couriers	\$ 1, 118	
Miscellaneous	\$ 602	
Total Expenses		\$ 88, 130
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**Balance		\$ 23, 912

* *Chu, Pupavac, Rosenblatt, Veyre, Watkins*