

**ANNUAL REPORT  
2018/2019**

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

*Submitted by: Dr. David S. Rosenblatt, Holder, Dodd Q. Chu and Family Chair in Medical Genetics, Professor of Human Genetics, Medicine, Pediatrics and Biology, McGill University*

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## **MEMBERSHIP**

### **PHYSICIANS AND SCIENTISTS**

David S. Rosenblatt

David Watkins

### **CLINICAL SUPPORT STAFF**

Maria Galvez

Leah Ladores

Keo Phommarinh

Jocelyne Tossa

### **RESEARCH SUPPORT STAFF**

#### **GRADUATE STUDENTS**

Lina Sobhy Abdrabo

### **UNDERGRADUATE AND SUMMER STUDENTS**

Camilah Arbabian

Mark Sorin

## ANNUAL REPORT 2018/2019

The Hess B. and Diane Finestone Laboratory in Memory of Jacob and Jenny Finestone was established in 1988. The intent of the donor was to honour the memory of Jacob and Jenny Finestone, and the 80<sup>th</sup> 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.

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### RESEARCH

The Hess B. and Diane Finestone Laboratory in Memory of Jacob and Jenny Finestone is located at the Glen Site of the McGill University Health Centre. Our facility is one of two major international referral laboratories for the diagnosis of patients with inherited disorders of folate and vitamin B<sub>12</sub> 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.

In 2018-2019, longstanding collaborations with Dr. Ruma Banerjee have resulted in two publications. These allowed for the reporting of accumulated data on the levels of cobalamin cofactors in patients with different forms of cobalamin-responsive methylmalonic aciduria. Collaboration with Dr. Chantal Seguin of the Division of Hematology has resulted in a review article on the genetic basis of osteonecrosis of the femoral head.

Ongoing projects in the laboratory include the use of genome and RNA sequencing in patients with undiagnosed methylmalonic aciduria following somatic cell studies, assay of MTHFD1 specific activity in patients with variants in the *MTHFD1* gene, and the hunt for causal mutations in patients with known inborn errors of cobalamin metabolism in whom both causal mutations have not been found. In addition, ongoing collaborations continue with groups at the NIH (Venditti) and at Baylor (Poché) on mouse and zebra fish models of inborn errors of cobalamin metabolism.

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## RESEARCH OPERATING FUNDS

CIHR Operating Grant, PI – 2016-2019. This grant is for the use of next generation sequencing to discover disorders of vitamin B<sub>12</sub> metabolism.

## ORIGINAL PUBLICATIONS

Campanello GC, Ruetz M, Dodge DJ, Gouda H, Gupta A, Twahir UT, Killian MM, Watkins D, Rosenblatt DS, Brunold TC, Warncke K, Smith JL, Banerjee R. Sacrificial cobalt-carbon bond homolysis in coenzyme B<sub>12</sub> as a cofactor conservation strategy. *J Am Chem Soc* 140:13205-13208, 2018

Wang T, Azeddine B, Mah W, Harvey EJ, Rosenblatt D, Séguin C. Osteonecrosis of the femoral head: genetic basis. *International Orthopaedics* 43:519-530

Ruetz M, Campanello GC, McDevitt L, Yokom AL, Watkins D, Rosenblatt DS, Ohi MD, Southworth DR, Banerjee R. Allosteric regulation of oligomerization by a B<sub>12</sub> trafficking G-protein is corrupted in methylmalonic aciduria. *Cell Chem Biol* 26:960-969, 2019

## GRADUATE STUDENTS SUPERVISED

Lina Sobhy Abdrabo

M.Sc.

2016-2019

Title: Next generation sequencing to discover genes underlying methylmalonic aciduria

**FINANCIAL REPORT – 2018/2019**

Starting Balance		<b>\$ 128,907</b>
*Salary Support and Benefits	\$ 89,488	
Conferences, Travel, Special Events	\$ 16,496	
Phones, Pagers, Computer, Printing, Couriers	\$ 451	
Professional Fees	\$ 444	
Total Expenses		<b>\$ 106,878</b>
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**Balance		<b>\$ 22,028</b>

*\*Student: Abdrabo; Research Associate: Watkins*