ANNUAL REPORT
2012/2013

THE HESS B. AND DIANE FINESTONE LABORATORY
IN MEMORY OF
JACOB AND JENNY FINESTONE
http://www.mcgill.ca/finestone

Submitted by: Dr. David S. Rosenblatt

TABLE OF CONTENTS
MEMBERSHIP

PHYSICIANS AND SCIENTISTS
David S. Rosenblatt
David Watkins

ADMINISTRATION
Laura Benner (Maternity Leave)
Ross Mackay
Danielle Veyre

CLINICAL SUPPORT STAFF
Maria Galvez
Leah Ladores

RESEARCH SUPPORT STAFF
Wayne Mah (with James Coulton)
Maira Moreno (with Loydie Jerome Majewski)

GRADUATE STUDENTS
Alison Brebner
Justin Deme (with James Coulton)
Laura Dempsey Nuñez
Peg Illson
Jaeseung Kim
Mihaela Pupavac

UNDERGRADUATE AND SUMMER STUDENTS
Jeehye Jung
Francis Petrella
Kush Prithipaul
Dylan Tanzer
Tracy Wang
ANNUAL REPORT 2012/2013

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. The year 2013 will be the twenty-fifth anniversary of the Finestone 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 is located on Livingston 3 of the Montreal General Hospital Site of the McGill University Health Centre. It 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 Dr. Rosenblatt directs a certified molecular diagnostic laboratory adjacent to the research laboratory, advances in knowledge from research can be immediately translated to clinical diagnostics.

2012-2013 has seen a number of major 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) With colleagues at McGill and in the United States, Switzerland and Germany, we used exome sequencing to discover a novel inborn error of cobalamin metabolism (cblJ), and showed that it is caused by mutations in the ABCD4 gene. These studies showed that at least two different proteins are responsible for the transport of cobalamin across the lysosomonal membrane.

3) Together with James Coulton in the Department of Microbiology and Immunology, we continued studies on the intracellular function of proteins involved in intracellular cobalamin metabolism. We determined the ability of MMACHC and MMADHC to interact, as well as their subcellular locations.
4) With Loydie Jerome-Majewska, we determined the expression of the methylmalonic aciduria related genes, Mmaa, Mmab, and Mut in placental and embryonic tissue during mouse development.

5) With Carl Wittwer of the University of Utah, we have developed the technique of high resolution melting analysis (HRMA) to look for variants in the MMAA and MMAB genes.

---

**RESEARCH OPERATING FUNDS**

CIHR Operating Grant, PI – 2009-2014

---

**INVITED PRESENTATIONS**

July 22-27, 2012
Gordon Research Conference (GRC)
Chemistry and Biology of Tetrapyrroles
Salve Regina University
Newport, Rhode Island

**Title:** Vitamin B$_{12}$ Transport and Metabolism: lessons from Mendelian Disease

September 20-22, 2012
Vitamin B$_{12}$ Symposium
Nancy, France

**Title:** Lessons in Biology from Patients with Inborn Errors of Vitamin B$_{12}$ Metabolism

September 24, 2012
Medical Genetics Seminar
Hôpital Necker
Paris, France

**Title:** Lessons in Biology from Patients with Inborn Errors of Vitamin B$_{12}$ Metabolism

October 24, 2012
The Children’s Hospital of Philadelphia
Grand Rounds-Annual Palmieri Lectureship
Philadelphia, Pennsylvania
Title: Lessons in Biology from Patients with Inborn Errors of Vitamin B₁₂ Metabolism

November 15-16, 2012
Neurometabolic disorders Related to B Vitamins
Orphan Europe Academy
Manchester, UK

Title: Disorders of Cobalamin Transport

February 19-24
Nutrition, Epigenetics and Human Disease
Keystone Symposia on Molecular and Cellular Biology
Santa Fe, New Mexico, USA
Scientific Organizer and Session Chair

Title: Discovering New Genes in the One-Carbon Pathway Using Exome Sequencing-A RaDiCAL Approach

ORIGINAL PUBLICATIONS


Kim JC, Lee NC, Hwu WL, Chien YH, Fahiminiya S, Majewski J, Watkins D, Rosenblatt DS. Late onset symptoms in a patient with the cblJ inborn error of vitamin B₁₂ metabolism:


---

**CHAPTERS**


---

**ABSTRACTS**


TEACHING

David Watkins

Biology 575
Department: Biology/Human Genetics
Format: Lecture
Title: Inborn Errors of Folate and Cobalamin Transport and Metabolism
Role: Lecturer
Level: Undergraduate/Graduate
Time: 3 1.5-hour class lectures

David Rosenblatt

Unit 8
Department: Human Genetics
Format: Lecture and Small Group Teaching
Role: Lecturer-2 sessions
Titles: Introduction to Medical Genetics
Huntington Disease
Level: Medical Students
Time: 2 lectures plus 3 2-hour sessions, 8 hours in total
### FINANCIAL REPORT – 2012/13

<table>
<thead>
<tr>
<th>Description</th>
<th>Amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>Starting Balance</td>
<td>$ 92,310</td>
</tr>
<tr>
<td>Decapitalized</td>
<td>$ 19,651</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>$ 111,961</strong></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Description</th>
<th>Amount</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Salary Support and Benefits</strong></td>
<td>$ 79,831</td>
</tr>
<tr>
<td>Materials and Supplies</td>
<td>$ 3,578</td>
</tr>
<tr>
<td>Conferences, Travel, Special Events</td>
<td>$ 17,942</td>
</tr>
<tr>
<td>Memberships</td>
<td>$ 7,644</td>
</tr>
<tr>
<td>Phones, Pagers, Computer, Printing, Couriers</td>
<td>$ 646</td>
</tr>
<tr>
<td>Miscellaneous</td>
<td>$ 1,637</td>
</tr>
<tr>
<td><strong>Total Expenses</strong></td>
<td><strong>$ 111,278</strong></td>
</tr>
</tbody>
</table>

**Balance**                                        | **$ 683** |

**Notes**

* Rosenblatt, Brebner, Dempsey-Nunez, Illson, Pupavac, Petrella, Prithipaul, Tanzer, Veyre, Wang*