

**ANNUAL REPORT  
2009/2010**

**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*

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## **MEMBERSHIP**

### **PHYSICIANS AND SCIENTISTS**

David S. Rosenblatt  
David Watkins

### **ADMINISTRATION**

Laura Benner

### **CLINICAL SUPPORT STAFF**

Maria Galvez  
Jocelyne Lavallée

### **RESEARCH SUPPORT STAFF**

Suzanne DufRASne  
Maria Plesa

### **GRADUATE STUDENTS**

Natascia Anastasio  
Junhui Liu  
Isabelle Racine-Miousse  
Mihaela Pupavac

### **SUMMER STUDENTS**

Simon Zhu

### **INDEPENDENT STUDIES STUDENTS**

Lara Reichman  
Laura Nuñez Dempsey

## ANNUAL REPORT 2009/2010

The Hess B. and Diane Finestone Laboratory in Memory of Jacob and Jenny Finestone was established in 1988 to honour the memory of Jacob and Jenny Finestone and the 80<sup>th</sup> birthday of Mr. Hess B. Finestone by providing a permanent endowment 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. This Finestone report will restrict itself to the activities of the Director. Material previously found in this report 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.

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### RESEARCH

The Hess B. and Diane Finestone Laboratory in Memory of Jacob and Jenny Finestone is located at 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 B<sub>12</sub> 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 diagnosis.

2009-2010 has seen a number of scientific accomplishments:

1. With colleagues in California, we have shown that with the advent of expanded newborn screening, there will be unusual clinical presentations of patients. We published, in the *Journal of Pediatrics*, a report of an asymptomatic mother, who was diagnosed as having the *cbIC* inborn error of vitamin B<sub>12</sub> metabolism, based on an abnormal screening result in her baby.
2. With colleagues at the Cleveland Clinic, we showed that the product of the *MMACHC* gene that is responsible for *cbIC* is capable of processing alkylcobalamins. This work was published in *Molecular Genetics and Metabolism*.
3. With Fei Li, a McGill undergraduate student, we published, in *Molecular Genetics and Metabolism*, a systematic review of the role of vitamin B<sub>12</sub> in birth defects.
4. With David Watkins, four chapters relating to folate and vitamin B<sub>12</sub> metabolism were published in major texts.
5. Dr. Rosenblatt presented a plenary session at the International Congress of Inborn Errors of Metabolism (ICIM) in San Diego on the role of homocysteine in heart disease.

## RESEARCH OPERATING FUNDS

CIHR, Operating Grant, PI – 2009-2014  
CIHR, Group Grant, Co-Investigator – 1975-2009

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## MEETINGS AND PRESENTATIONS

August 31, 2009  
International Congress of Inborn Errors of Metabolism (ICIEM)  
Title: *Homocysteine and Coronary Heart Disease*  
San Diego, CA

March 10, 2010  
Medical Grand Rounds  
Title: *Homocysteine and Coronary Heart Disease*  
MUHC – Montreal General Hospital

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## ORIGINAL PUBLICATIONS

Rutsch F, Gailus S, Miousse IR, Suormala T, Sagné, Toliat MR, Nurnberg G, Wittkamp T, Buers I, Shariffi A, Stucki M, Becker C, Baumgartner M, Robenek H, Marquardt T, Hohne W, Gasnier B, Rosenblatt DS, Fowler B, Nurnberg P. Identification of a putative lysosomal cobalamin exporter mutated in the *cbfF* inborn error of vitamin B<sub>12</sub> metabolism. *Nat Genet* 41:234-239, 2009.

Miousse IR, Watkins D, Lavallée J, Coelho D, Rupar T, Clarke JTR, Crombez EA, Vilain E, Cederbaum S, Bernstein JA, Cowan T, Lee-Messer C, Enns GM, Fowler B, Rosenblatt DS. Clinical and molecular heterogeneity in patients with the *cbfD* inborn error of cobalamin metabolism. *J Pediatr* 154: 551-556, 2009

Loewy AD, Niles KM, Anastasio N, Watkins D, Lavoie J, Lerner-Ellis JP, Pastinen T, Trasler JM, Rosenblatt DS. Epigenetic modification of the gene for the vitamin B<sub>12</sub> chaperone MMACHC can result in increased tumorigenicity and methionine dependence. *Mol Genet Metab* 96: 261-267, 2009

Lerner-Ellis JP, Anastasio N, Liu J, Coelho D, Suormala T, Stucki M, Loewy A, Gurd S, Grundberg E, Morel CF, Watkins D, Baumgartner MR, Pastinen T, Rosenblatt DS, Fowler B. Spectrum of mutations in *MMACHC*, allelic expression and evidence for genotype-phenotype correlations. *Human Mutat* 30:1072-1081, 2009

Li, F, Watkins D, Rosenblatt DS. Vitamin B<sub>12</sub> and birth defects. *Molec Genet Metab* 98:166-172, 2009.

Hannibal L, Kim J, Brasch NE, Wang S, Rosenblatt DS, Banerjee R, Jacobsen DW. Processing of alkylcobalamins in mammalian cells: a role for the *MMACHC (cbfC)* gene product. *Molec Genet Metab* 97:260-2166, 2009.

Lin HJ, Neidich JA, Salazar D, Thomas-Johnson E, Ferreira BF, Kwong AM, Lin AM, Jonas AJ, Levine S, Lorey F, Rosenblatt DS. Asymptomatic maternal combined homocystinuria and methylmalonic aciduria (*cblC*) detected through low carnitine levels on newborn screening. *J Pediatr* 155: 924-927, 2009

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## CHAPTERS

Watkins D, Whitehead VM and Rosenblatt DS. Megaloblastic anemia in Nathan and Oski's *Hematology of Infancy and Childhood* (7<sup>th</sup> ed). Orkin SH, Ginsburg D, Nathan DA, Look AT, Fisher DE (eds). 2009, Chapter 11 pp 467-520

Morel C and Rosenblatt DS. Inborn errors of folate and cobalamin transport and metabolism in *Pediatric Endocrinology and Inborn Errors of Metabolism*. Eds. Sarafoglou K, Hoffman GF and Roth KS. McGraw-Hill Companies. 2009. pp 195-212.

Watkins D and Rosenblatt DS. Vitamin B<sub>12</sub> and folate metabolism. In: *Mechanisms in Hematology*, 4th Edition, Israels LG and Israels, E.D (eds), Core Health Services. 2009, Chapter 11, pp 1-32

Watkins D and Rosenblatt DS. Vitamin B<sub>12</sub>: disorders of absorption and metabolism. In: *Encyclopedia of Life Sciences*, John Wiley and Sons, Chichester. Doi:10.1002/9780470015902.a0002267.pub2, 2010.

Rosenblatt DS, Watkins D. Prenatal diagnosis of miscellaneous biochemical disorders. In: *Genetic Disorders and the Fetus: Diagnosis, Prevention and Treatment*, 6th Edition, A. Milunsky (ed), Wiley-Blackwell, Oxford. 2010, Chapter 19 pp 614-627.

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## TEACHING

### Biology 575

Department: Biology/Human Genetics  
Format: Lecture  
**Title:** *Inborn Errors of Folate and Cobalamin Transport and Metabolism*  
Role: Lecturer and Course Coordinator  
Level: Undergraduate/Graduate  
Time: 6 hours

### Unit 8

Department: Human Genetics  
Format: Lecture and Small Group Teaching  
Role: Lecturer-2 sessions  
**Title:** *Introduction to Medical Genetics  
Huntington Disease*  
Level: Medical Students  
Time: 2 lectures plus 3 2-hour sessions, 8 hours in total

## FINANCIAL REPORT – 2009/2010

Starting Balance **\$105,028**

\*Salary Support and Benefits \$ 58,111

Computer Charges \$ 2,215

Conference, Seminars, & Travel \$ 11,654

Library & Membership \$ 4,443

Materials, Supplies, Phones & Pagers \$ 7,721

Miscellaneous \$ 1,151

Total Expenses **\$ 85,295**

\*\*Balance **\$ 19,733**

### *Notes*

\* *Rosenblatt, Dufrasne, Veyre, Leslie, Benner, Anastasio*

\*\* *Balance was capitalized*