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

TABLE OF CONTENTS

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

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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 80th 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.

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_{12} 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 immediate 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 diagnosis as having the *cblC* inborn error of vitamin B_{12} 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 *cblC* 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_{12} in birth defects.

4. With David Watkins, four chapters relating to folate and vitamin B_{12} metabolism were published in major texts.

5. Dr. Rosenblatt presented a plenary session at the International Congress of Inborn Errors of Metabolism (ICIEM) 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

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

ORIGINAL PUBLICATIONS

Rutsch F, Gailus S, Miousse IR, Suormala T, Sagné, Toliat MR, Nurnberg G, Wittkampf 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 *cblF* inborn error of vitamin B_{12} 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 *cblD* inborn error or 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_{12} 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_{12} 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 (cblC)* 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

CHAPTERS

Watkins D, Whitehead VM and Rosenblatt D**S**. Megaloblastic anemia in Nathan and Oski's *Hematology of Infancy and Childhood* (7th 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_{12} 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_{12}: 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.

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*