

Annual Report
Division of Endocrinology
Department of Medicine - Jewish General Hospital
April 1, 2010 - March 31, 2011

I HIGHLIGHTS

The Division of Endocrinology and Metabolism has continued its pursuit of excellence in patient care, research and training. The Division has continued to play an active role in joint activities with the other McGill Hospitals counterparts, such as Med-I Endocrine Physiology Course and Calcium Homeostasis, as well as hosting the Lipid-, Thyroid McGill Lectureships, and the newly established McGill/JGH Lecture on Metabolism, supported by a grant from GlaxoSmithKline.

Our members continue to teach in McGill Graduate and Undergraduate courses such as Physiology (Tamilia), Advanced Endocrinology (Tamilia) and Neuroendocrinology (Tamilia). With a grant from GlaxoSmithKline, our Division hosted another McGill Lecture (details under Teaching Activities).

Members of the Division continue to serve in committees of granting agencies, editorial boards and to participate in other high level academic activities at national and international levels. Members have succeeded in the competing renewal of their grants as well as in obtaining additional support from peer-reviewed granting agencies. Dr. Michael Tamilya has continued to receive the recognition of our young colleagues and students as a truly exceptional teacher. Drs. Tina Kader and Morris Schweitzer continue to be remarkable active in CME activities primarily addressed to general practitioners, internists and specialists. Thus, the JGH Endocrine Division has reached a high profile at the university, national and international levels.

In spite of the limited resources and the absence of physical plant, the Metabolic Day Centre under the direction of Dr. Alicia Schiffrin has continued the effort to improve the care of patients with diabetes and bring us to the standards. The Division is grateful to the late Amnon Kahn for having successfully reached donors to support efforts in providing state-of-the art treatment and education of patients with diabetes to palliate the limited resources available for this major current medical problem and for making arrangements with Montreal Children's Hospital to gain access for our patients to insulin pump usage.

Overall, the Division of Endocrinology is one of the most, if not the most, active in contributing its staff to teaching (Professional Skills and Introduction to Internal Medicine and Physiology) and CTU coverage within the Department of Medicine at the Jewish General Hospital.

Our recruits John Brent Richards and Agnieszka Majdan (Aug. 2009) continue to perform as superb academic physicians; Dr. Brent Richards has in short order achieved already much acclaim in his young career.

II EVALUATION OF THE PAST ACADEMIC YEAR

1. Teaching activities

Medical Students

- Metabolic Bone Disease in Unit 5, Med I; preparation of lecture notes, case study, and quiz for students and organizing small group tutors.
- One 1-hour lecture on metabolic bone disorders and two 1.5-hour small group sessions

Residents

- (I) Journal Club
- (ii) Core lectures in Endocrinology
- (iii) Simulated oral examination in Internal Medicine

Postgraduate Students

Advances in Human Genetics: A post graduate course offered by the Department of Human Genetics: Three 1.5-hr lectures on the genetics of metabolic bone diseases.

Endocrine Residents (Fellows) and Medical Residents doing elective rotations participate in all our clinical activities. They are under the direct supervision of the Attending on service. Residents must attend clinics while not busy with the in-patient service. Some clinics are compulsory: Gestational Diabetes, Thyroid, Lipid and Osteoporosis Clinic. Our Division has become very popular for elective rotations among residents and students. All trainees rotating through the Division must attend Endocrine Grand Rounds (every Thursday from 11:30-12:30). This past year we have had an unusually high number of Endocrine Residents, and the same is expected for the next academic year. In addition to McGill Medical Students doing elective rotations, we have received students from UK, Australia, Finland, and Brazil during the last year. Notably, the majority of McGill candidates to McGill Endocrine Residents have come from our Internal Medicine training program over the last several years, a reflection of the positive influence of our staff on the Residents. The McGill Endocrine Teaching Program at large was highly rated by the trainees with our Division receiving the highest ratings in a large number of items, notably conferences, bedside and outpatient teaching, integration with basic sciences. Our weakest mark is on premises and facilities for Endocrine Residents.

In addition to these tutorial activities, our Division offers a yearly cycle of lectures on essential endocrinology for residents and non-endocrinologists in general. Our Division also actively participates in the undergraduate teaching of Endocrine Physiology and Calcium Homeostasis (Med-I Physiology) with 6 of our members being small group tutors this year (Assimakopoulos, Beitel, Kader, Karaplis, Schiffrin, and Trifiro). All GFT's have also been very active on CME accredited activities. Dr. Tina Kader has been traditionally active in CME to various groups of physicians, paramedical personnel, as well as in giving talks to the community at large on prevention of obesity and diabetes.

Ms. Joyce Arsenault (Nurse, Certified Diabetes Educator), Ms. Maria Di Narzo (nurse, Certified, Diabetes Educator) and Ms. Sondra Sherman (Dietitian) have worked together with Dr. Tina Kader in this latter endeavour.

The McGill Hospital Endocrine Division hold quarterly combined Endo Rounds, one of which is hosted by our Division. Our Division has for years hosted two major McGill Endocrine lectures, the McGill/Merck Frosst Lipid Lecture and the McGill/Abbott Thyroid Lecture. Invited speakers for the period covered by this report were, respectively, Ronald M. Krauss, MD, University of California, Constantin Polychronakos, MD, from McGill University Health Centre and Jeff Williamson, MD, from Wake Forest University. Nearly 9 years ago, we instituted a third Lectureship, the McGill Lecture on Metabolism, with a restricted grant from GlaxoSmithKline. The Ninth McGill/JGH Lecture on Metabolism was given by Ronald Krauss, MD, from the University of California.

In addition to the teaching activities described under Teaching Activities, above, Endocrine Grand Rounds, under the direction of Dr. Mark Trifiro, have continued to be a great success because of the timeliness of the subjects, the sensible balance of basic and clinical science and the quality of the invited speakers. Endo Grand Rounds are given weekly from September to June.

2. Research Activities

Research activities continue in the rise (see individual reports for details).

Beitel, Lenore

-2009/12-2010/11: Kennedy's Disease Association, \$10,716 total, "Investigating mechanisms contributing to Kennedy's disease: Polyglutamine-expanded androgen receptors and the ubiquitin-proteasome system"

-Opto-impedimetric screening of blood-borne pathogens; **P.I.:** Canadian Institute for Photonic Innovations (CIPI) - Technology Exploitation and Networking Program - Collaboration Grant 12/2010-12/2011; \$30,000 total

Karaplis, Andrew C.

2005-2010: Canadian Institutes of Health Research (Total: \$606,385); "PTHrP and osteoblast biology: Relevance to osteoporosis"

Richards, John Brent

2010: Ministère du développement économique, Innovation et Exportation du Québec. CiPhER: Consortium International pour l'identification des gènes de facture ostéorobotique. Rôle: Principal Investigator. \$491,231 over 3 years.

Trifiro, Mark

2009-2011: Animas Corporation \$50,000/yr Canadian Artificial Pancreas Project

2010-2015: Innovative approaches to functional characterization of the androgen receptor in prostate cancer; **P.I. Mark Trifiro**, Co-Applicants: Miltiadis Paiouras and Edwin Wang; Canadian Institutes of Health Research (CIHR) - Operating Grant: total \$560,279

2009-2012: “Biosenseurs génétiquement modifiés à haute sélectivité et sensibilité” Fonds Québécois de la recherche sur la Nature et les Technologies, Operating \$48,760/yr (Co-Pi)

2009-2012: “Nanoporous silicon catheter device with real-time optical monitoring of bacterial contaminants during hemodialysis”; Canadian Institute for Photonics Innovation (CIPI), \$29,900 total

3. Clinical Activities:

Endocrinology is largely an outpatient specialty. Including the Gestational Diabetes Clinic and Bone and Osteoporosis Clinics that do not function in our premises, the number of visits per year exceeded the 25,000. Outpatient clinics are run around the week by GFT's. Non-GFT's run clinics on Monday and Thursday mornings. The increase in the number of patients is still too long. It has been due to space and support personnel constraints that we have not been able to recruit more new members. Constraints also result from the RAMQ that is trying to restrict the number of endocrinologists. This problem has been solved at the expense of physician scientists increasing their clinical hours, reducing their research time. We also have established a triage system to see first those patients in most urgent need (e.g. decompensated diabetics, thyrotoxic patients). To enhance the use of the space, examining space has been arranged in three of the largest physician offices. We have stretched to the limits the secretarial time available, which has not increased in over 7 years in spite the doubling of the numbers of patient visits. Although all staff physicians see patients spanning the whole spectrum of endocrine and metabolic diseases, some clinics are focused on a particular condition, as shown in the table below.

In-patient activities are centered on the Endocrine Consulting Service, attended by our staff physicians in a 2-week rotating schedule through the year. The endocrine service is largely covered by 7 of the 8 GFT's, which burden's them – including the physician scientists- with a minimum of 6 weeks per year. Volume of consults is approximately 1200/year. In addition, our staff is actively involved in CTU rotations. The Division does not have assigned beds and endocrine patients are admitted to general wards.

The Survival Skills Program of self-management education for patients with diabetes has continued to function regularly with private donations. No additional resources have been provided this year for the essential program.

Outpatient Clinics:

Monday AM

Diabetic Clinic (Kader)

General Endocrinology (Schweitzer, Karaplis, Trifiro, Kahn)

Monday PM

General Endocrinology (Karaplis, Assimakopoulos, Schweitzer)

Tuesday AM

Thyroid (Tamilia)

General Endocrinology (Trifiro, Assimakopoulos, Schiffrin)

Tuesday PM

General Endocrinology (Assimakopoulos, Schiffrin, Christopoulos, Richards)

Wednesday AM

General Endocrinology (Kader, Trifiro, Majdan)

Gestational Diabetes (Kader)

Osteoporosis I (Trifiro)

Wednesday PM

General Endocrinology (Christopoulos, Richards, Majdan)

Osteoporosis II (Karaplis)

Lipid Clinic (Schweitzer)

Thursday AM

General Endocrinology (Schiffrin, Tamilia, Clamen, Kahn, Rizzo, Jukier)

Thursday PM

General Endocrinology (Assimakopoulos, Kader)

Friday AM

General Endocrinology (Schiffrin, Schweitzer, Trifiro, Christopoulos, Majdan)

4. Academic Staff

- Dr. Lillian Jukier now participates only in the tumor clinic.

- Dr. Amnon Kahn passed away in November 2010.

5. Consulting Activities:

None reported

6. Honours, Awards, Prizes:

None reported

7. Other

Publications

Beitel, Lenore

--Gottlieb B, Beitel LK, Alvarado C, **Trifiro M**: Selection and mutation in the "new" genetics: an emerging hypothesis. *Human Genetics* 127:491-501, 2010

Karaplis, Andrew

--Zhang HW, Ding J, Jin JL, Guo J, Liu JN, **Karaplis A**, Goltzman D, Miao D: Defects in mesenchymal stem cell self-renewal and cell fate determination lead to an osteopenic phenotype in Bmi-1 null mice. *Journal of Bone and Mineral Research*, 25:640-652, 2010

--Simmonds CS, Karsenty G, **Karaplis AC**, Kovacs CS: Parathyroid hormone regulates fetal-placental mineral homeostasis. *Journal of Bone and Mineral Research*, 25:594-605, 2010 PMID:19968565

--Sun W, Sun W, Liu J, Zhou X, Xiao Y, Karaplis A, *Pollak MR, Brown E, Goltzman D, Miao D: Alterations in phosphorus, calcium and PTHRP contribute to defects in dental and dental alveolar bone formation in calcium-sensing receptor-deficient mice. *Development*,137:985-992, 2010 Epub. PMID: 20150282

-- **Karaplis AC**, Chouha F, Djandji M, Sampalis JS, Hanley DA. Vitamin D status and response to daily 400 IU vitamin D3 and weekly alendronate 70 mg in men and women with osteoporosis. *Ann Pharmacother*. 2011 May; 45(5):561-8. Epub. PMID: 21521859

--Shu L, Ji J, Zhu Q, Cao G, **Karaplis A**, Pollak MR, Brown E, Goltzman D, Miao D. The calcium sensing receptor mediates bone turnover induced by dietary calcium and parathyroid hormone in neonates. *J Bone Miner Res*. 2010 Nov 23. [Epub ahead of print]PMID: 21105080

Richards, J. Brent

--LS Greene-Finestone, C Berger, M de Groh, DA Hanley, N Hidioglou, K Sarafin, S Poliquin, J Krieger, JB Richards, D Goltzman; CaMos Research Group. 25-Hydroxyvitamin D in Canadian adults: biological, environmental, and behavioral correlates. *Osteoporosis International*, DOI: 10.1007/s00198-010-1362-7, Epub Aug 21, 2010

--Ladouceur M, Leslie WD, Dastani Z, Goltzman D, **Richards JB**. An Efficient Paradigm for Genetic Epidemiology Cohort Creation. *PLoS One*, 5:e14045, 2010

--Panicker V, SG Wilson, JP Walsh, **JB Richards**, SJ Brown, JP Beilby, AP Bremner, GL Surdulescu, E Qweitin, I Gillham-Naseny, N Soranzo, EM Lim, SJ Fletcher, TD Spector. A locus on chromosome 1p36 is associated with thyrotropin and thyroid

function as identified by genome-wide association study. *American Journal of Human Genetics*, 87:430-5, 2010

--Wang TJ, Zhang F, Richards JB, Kestenbaum B, van Meurs JB, Berry D, Kiel DP, Streeten EA, Ohlsson C, Koller DL, Peltonen L, Cooper JD, O'Reilly PF, Houston DK, Glazer NL, Vandenput L, Peacock M, Shi J, Rivadeneira F, McCarthy MI, Anneli P, de Boer IH, Mangino M, Kato B, Smyth DJ, Booth SL, Jacques PF, Burke GL, Goodarzi M, Cheung CL, Wolf M, Rice K, Goltzman D, Hidiroglou N, Ladouceur M, Wareham NJ, Hocking LJ, Hart D, Arden NK, Cooper C, Malik S, Fraser WD, Hartikainen AL, Zhai G, Macdonald HM, Frouhi NG, Loos RJ, Reid DM, Hakim A, Dennison E, Liu Y, Power C, Stevens HE, Jaana L, Vasani RS, Soranzo N, Bojunga J, Psaty BM, Lorentzon M, Forouzi T, Harris TB, Hofman A, Jansson JO, Cauley JA, Uitterlinden AG, Gibson Q, Jarvelin MR, Karasik D, Siscovick DS, Econs MJ, Kritchevsky SB, Florez JC, Todd JA, Dupuis J, Hyppönen E, Spector TD: Common genetic determinants of vitamin D insufficiency: a genome-wide association study. *Lancet*, 376:180-188, 2010

--Heid IM, Henneman P, Hicks A, Coassin S, Winkler T, Aulchenko YS, Fuchsberger C, Song K, Hivert MF, Waterworth DM, Timpson NJ, **Richards JB**, Perry JR, Tanaka T, Amin N, Kollerits B, Pichler I, Oostra BA, Thorand B, Frants RR, Illig T, Dupuis J, Glaser B, Spector T, Guralnik J, Egan JM, Florez JC, Evans DM, Soranzo N, Bandinelli S, Carlson OD, Frayling TM, Burling K, Smith GD, Mooser V, Ferrucci , Meigs JB, Vollenweider P, Dijk KW, Pramstaller P, Kronenberg F, van Duijn CM: Clear detection of ADIPOQ locus as the major gene for plasma adiponectin: results of genome-wide association analyses including 4659 European individuals. *Atherosclerosis*, 208:412-420, 2010

--Hsu YH, Zillikens MC, Wilson SG, Farber CR, Demissie S, Soranzo N, Bianchi EN, Grundberg E, Liang L, **Richards JB**, Estrada K, Zhou Y, van Nas A, Moffatt MF, Zhai G, Hofman A, van Meurs JB, Pols HA, Price RI, Nilsson O, Pastinen T, Cupples LA, Lusi AJ, Schadt EE, Ferrari S, Uitterlinden AG, Rivadeneira F, Spector TD, Karasik D, Kiel DP: An integration of genome-wide association study and gene expression profiling to prioritize the discovery of novel susceptibility Loci for osteoporosis-related traits. *PLoS Genetics* 6, e1000977, 2010

--Kung AW, Xiao SM, Cherny S, Li GH, Gao Y, Tso G, Lau KS, Luk KD, Liu JM, Cui B, Zhang MJ, Zhang ZL, He JW, Yue H, Xia WB, Luo LM, He SL, Kiel DP, Karasik D, Hsu YH, Cupples LA, Demissie S, Styrkarsdottir U, Halldorsson BV, Sigurdsson G, Thorsteinsdottir U, Stefansson K, **Richards JB**, Zhai G, Soranzo N, Valdes A, Spector TD, Sham PC: Association of JAG1 with bone mineral density and osteoporotic fractures: a genome-wide association study and follow-up replication studies. *American Journal of Human Genetics*, 86:229-239, 2010

--EL Duncan, P Danoy, JP Kemp, P Leo, E McCloskey, GC Nicholson, R Eastell, RL Prince, JA Eisman, G Jones, PN Sambrook, IR Reid, EM Dennison, J Wark, **JB Richards**, AG Uitterlinden, TD Spector, C Esapa, RD Cox, SDM Brown, RV Thakker, KA Addison, LA Bradbury, JR Center, C Cooper, C Cremin, K Estrada, D Felsenberg,

CC Glueer, J Hadler, MJ Henry, A Hofman, MA Kotowicz, J Makovey, SC Nguyen, TV Nguyen, JA Pasco, K Pryce, DM Reid, F Rivadeneira, C Roux, K Stefansson, U Stykarsdottir, G Thorleifsson, R Tichawangana, DM Evans, MA Brown. Genome-wide association study using extreme truncate selection identifies novel genes affecting bone mineral density and fracture risk. **PLoS Genetics**. 2011 Apr; 7(4):e1001372. Epub 2011 Apr 21.

Schweitzer, Morris

--**Schweitzer M**, Mitmaker B, Obrand D, Sheiner N, Abraham C, Dostanic S, Meilleur M, Sugahara T, Chalifour LE: Atorvastatin modulates matrix metalloproteinase expression, activity, and signaling in abdominal aortic aneurysms. *Vascular and Endovascular Surgery*, 44:116-122, 2010

Trifiro, Mark

--Ghafar-Zadeh E, Chowdhury SF, Aliakbar A, Lumbroso R, Chodavarapu V, **Beitel LK**, Sawan M, **Trifiro M**. Handheld impedance biosensor system using engineered proteinaceous receptors. *Biomedical Microdevices* 12: 967-975, 2010.

III OBJECTIVES AND PRIORITIES

The Division of Endocrinology moved to its renovated space which has been helpful in providing excellent care as the division continues to place a high priority on patient care and in doing so seeks new clinical recruits either as full-time or as part time members. Efforts are being made to add another diabetic nurse to help with the ever-increasing referral of diabetic patients. Other priorities include the expansion of both clinical research and basic research personnel that will start in the next few years. This will be a very arduous task given the many roadblocks at the university, government and hospital level; however the Division remains confident that when the right recruits come along, it will find the mechanisms to have them join its staff.

Respectfully submitted,

Marc Trifiro, MD
Chief, Division of Endocrinology