

Annual Report
Division of Endocrinology, Department of Medicine
Sir Mortimer B. Davis - Jewish General Hospital
April 1, 2006 - March 31, 2007

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 Glaxo/SmithKline. 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 Glaxo/SmithKline, 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 Tamilia 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. Dr. Amnon Kahn has successfully reached donors to support our effort 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. He has made 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, Physiology) and CTU coverage within the Department of Medicine at the Jewish General Hospital.

II. Evaluation of Past Academic Year

1) Teaching Activities

-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 GFTs 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 (Dietician) 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, David J. Mangelsdorf, Ph.D., Professor of Pharmacology and Biochemistry, University of Texas South-western Medical Center, Rotterdam, The Netherlands. Nearly 5 years ago, we instituted a third Lectureship, the McGill Lecture on Metabolism, with a restricted grant from Glaxo/SmithKline. The Fourth McGill/JGH Lecture on Metabolism was given by Michael W. Schwartz, MD, Professor of Medicine, Division of Metabolism, Endocrinology and Nutrition, University of Washington and Harborview Medical Center, Seattle Washington.

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.

Beitel, Lenore K

-Tutor Endocrine Physiology (Med I)

-Lecturer, Human Biochemical Genetics, McGill University

Karaplis, Andrew

Invited Oral Presentations

-11th and Valedictory Workshop on Cell Biology of Bone and Cartilage in Health and Disease, Davos, Switzerland

March 2006, Title: Mouse genetic evidence for paracrine role of PTHrP in bone, Invited by Dr. H. Fleisch, Switzerland

-Organizer of the McGill Lectures on Metabolic Bone Diseases, a monthly meeting with invited speakers, sponsored by an unrestricted educational grant from The Alliance on Bone Health, Sanofi-Aventis and Procter & Gamble Pharmaceuticals.

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

- Journal Club
- Core lectures in Endocrinology
- 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.
- CME and related: McGill Faculty of Medicine Thursday Evening Lectures, Medical Grand Rounds at RVH and JGH

Schweitzer, Morris

- Multiple lectures to medical community on lipid metabolism and its disorders

Tamalia, Michael

- Medical Update, Thyroid. Family Medicine, McGill University; 2006
- Advanced Endocrinology, Experimental Medicine; Course Directors: Dr. A. Bateman, Dr. HPJ Bennett, Lecturer: since 1997
- Thyroid Physiology, Med-I Students. McGill University; 2006
- Neuroendocrinology, Undergraduate McGill University; 2006
- Endocrinology Core Teaching for Medical Residents; since 1997

2) Research Activities

Research activities continue in the rise. The grants and clinical contracts are listed below:

Karaplis, Andrew C.

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

2005-2008: Canadian Space Agency/ Canadian Institutes of Health Research (Total: \$332,700);, "PTHrP expression and osteoblast apoptosis in microgravity-induced osteoporosis"

2005-2008: Merck-Frosst of Canada, Educational Fund (Total: \$12,000), for Metabolic Bone Disease & Osteoporosis Clinic

Trifiro, Mark

2004-2007: CIHR MOP-69095, "Androgen Receptor: Defining pathological molecular mechanisms in disease states"; operating grant, \$92,960/y (PI; with LK Beitel, co-applicant)

2004-2009: CIHR GR-13297, "CIHR Group in Medical Genetics"; group grant, 19,740/y (Co-applicant)

2004-2006: US Army PC040915, "Development of a transgenic mouse model to investigate the role of the androgen receptor and its CAG repeat in human prostate cancer"; resource development award, \$95,000 total (PI; with LK Beitel, co-applicant)

2006-2009: NCIC, National Cancer Institute of Canada, "Mouse model for prostate cancer", \$140,000/yr

Schweitzer, Morris

2006-2008: Effective statins on Regulation of metalloproteinase gene expression and activity in human abdominal aortic aneurisms. Pfizer, \$220,000 for 2 yrs

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 20,000. Outpatient clinics are run around the week by GFT's. Non-GFT's run a clinic only 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 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 6 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 focussed on a particular condition, as shown in the table below.

In-patient activities are centred 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 Programme 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

-Diabetes Clinic: (Kader)

-General Endocrinology: (Schweitzer, Trifiro, Karaplis)
Monday PM
-General Endocrinology: (Karaplis, Assimakopoulos, Schweitzer)

Tuesday AM
-Thyroid: (Tamilia)
-General Endocrinology: (Trifiro, Assimakopoulos, A. Schiffrin)
Tuesday PM
-General Endocrinology: (Assimakopoulos, A. Schiffrin)

Wednesday AM
-General Endocrinology
-Gestational Diabetes: (Kader)
- Osteoporosis I: (Trifiro)
Wednesday PM
-General Endocrinology: (A. Schiffrin)
-Osteoporosis II: (Karaplis)

Thursday AM
General Endocrinology: (PT Clamen, Kahn, Rizzo, Komaromi)
Thursday PM
-Lipid Clinic: (Schweitzer)
-General Endocrinology: (Assimakopoulos, Kader)

Friday AM
-General Endocrinology: (Schweitzer, Trifiro, Tamilia)

4) Academic Staff

Dr. Stavroula Christopoulos' appointment has been approved. She started in September 2006.
Dr. Brent Richards has also been appointment to our Division and is expected to join us in July 2008.

5) Consulting Activities

None reported

6) Honours, Awards and Prizes

7) Service to Academic Community and other contributions

Assimakopoulos, Peter
-In charge of dynamic function testing for Endocrinology by Day Hospital

Beitel, Lenore K
-Program Committee of Canadian Society of Endocrinology and Metabolism

Hoffer, L. John

-Metabolism and Nutrition Committee of the Canadian Institutes of Health Research (CIHR)

Kader, Tina

-Director, Gestational Diabetes Clinic

Karaplis, Andrew C.

-Member JGH Department of Medicine Management Committee

-Ad hoc reviewer, Canadian Institutes of Health Research

-CME and related: McGill Faculty of Medicine Thursday Evening Lectures, Medical Grand Rounds at RVH and JGH

Schiffrin, Alicia

-Director, Metabolic Day Center, JGH

-Past President, Canadian Diabetes Association National Research Council

-Consultant National Institutes of Health (USA); Ethics Committee for Prevention Trials. Study Section Diabetes Prevention Trials (TrialNET 2001) & Committee Diabetes Prevention Trial-1

Schweitzer, Morris

-Co-Director, Center for Cardiovascular Disease Prevention, JGH

-Director, Lipid Clinic

-Chairman, McGill/Merck-Frosst Lipid Lectureship

Tamalia, Michael

-Founding Member, Director, Thyroid Tumor Study Group, JGH

Trifiro, Mark

-Research Director, Department of Medicine

-Ad hoc reviewer, Canadian Institute of Health Research

8) Publications

Refereed papers:

Karaplis, Andrew C.

--Gao J, Tiwari-Pandey R, Samadfam R, Yang Y, Miao D, Karaplis AC, Sairam MR, Goltzman D. Altered ovarian function affects skeletal homeostasis independent of the action of follicle-stimulating hormone. *Endocrinology* 2007, Jun; 148 (6) 2613-21

--Hendy GN, Li T, Girard M, Feldstein RC, Mulay S, Desjardins R, Day R, Karaplis AC, Tremblay ML, Canaff L. Targeted ablation of the chromogranin A (Chga) gene: normal neuroendocrine dense core secretory granules and increased expression of other granins. *Mol Endocrinol* 2006

--Xue Y, Karaplis AC, Hendy GN, Goltzman D, Miao D. Exogenous 1,25-dihydroxyvitamin D3 exerts a skeletal anabolic effect and improves mineral ion homeostasis in mice that are homozygous for both the 1alpha-hydroxylase and parathyroid hormone null alleles. *Endocrinology* 2006, Oct; 147 (10)

Hoffer, L. John

--Hoffer LJ. Tube feeding in advanced dementia: the metabolic perspective. *BMJ*. 2006 Dec 9;333(7580):1214-5

--Hoffer LJ. Testing the homocysteine hypothesis in end-stage renal disease: Problems and a possible solution. *Kidney Int*. 2006 May; 69(9):1507-10

--Padayatty SJ, Riordan HD, Hewitt SM, Katz A, Hoffer LJ, Levine M. Intravenously administered vitamin C as cancer therapy: three cases. *CMAJ*. 2006 Mar 28; 174(7):937-42

Trifiro, Mark and Beitel, Lenore K.

--Gottlieb B, Beitel LK, Trifiro M. Will knowledge of human genome variation result in changing cancer paradigms? *Bioessays*. 2007 Jul; 29(7):678-85

--Sircar K, Gottlieb B, Alvarado C, Aprikian A, Beitel LK, Alam-Fahmy M, Begin L, Trifiro M. Androgen receptor CAG repeat length contraction in diseased and non-diseased prostatic tissues. *Prostate Cancer Prostatic Dis*. 2007 Apr 17

--Elhaji YA, Stoica I, Dennis S, Purisima EO, Trifiro MA. Impaired helix 12 dynamics due to proline 892 substitutions in the androgen receptor are associated with complete androgen insensitivity. *Hum Mol Genet*. 2006 Mar 15; 15(6):921-31

Abstracts:

Karaplis, Andrew C.

--Panda D, Juppner H, Goltzman D, Karaplis AC. TIP39/Parathyroid hormone receptor 2 signaling inhibits chondrocyte proliferation and differentiation by negatively regulating Sox9 gene expression. *ASBMR 27th Annual Meeting, Nashville, Tennessee*. Presentation Number: SA490

--Shimomura J, Amizuka N, Kojima T, Maeda T, Goltzman D, Karaplis AC, Shimooka S. Intracellular localization of mutant PTH/PTHrP receptors in cultured osteoblasts. *ASBMR 27th Annual Meeting, Nashville, Tennessee*. Presentation Number: SA488

--Fu H, Bai X, Miao D, Gao J, Goltzman D, Karaplis AC. Reduced 25-hydroxyvitamin D3-1alpha-hydroxylase activity impacts negatively on the secondary hyperparathyroidism arising from FGF23 overexpression. *ASBMR 27th Annual Meeting, Nashville, Tennessee*. Presentation Number: SA453

--Miao D, Su H, He B, Gao J, Xia Q, Goltzman D, Karaplis AC. Deletion of the mid- and carboxyl regions of PTHrP produces growth retardation and early senescence in mice. *ASBMR 27th Annual Meeting, Nashville, Tennessee*. Presentation Number: 1050

--Gao J, Yang Y, Miao D, Sairam MR, Karaplis AC, Goltzman D. Follicle-stimulating hormone

receptor deficiency in female mice results in an osteoporotic phenotype characterized by impairment of osteoblastic bone formation and stimulation of osteoblastic bone resorption. ASBMR 27th Annual Meeting, Nashville, Tennessee. Presentation Number: SA516

--Xue Y, Karaplis AC, Hendy GN, Goltzman D, Miao D. PTH and 1,25-dihydroxyvitamin D3 each independently exert skeletal anabolic effects and improve mineral ion homeostasis in mice which are homozygous for both the 1 α -hydroxylase and PTH null alleles. ASBMR 27th Annual Meeting, Nashville, Tennessee. Presentation Number: 1203

--Christopoulos S, Djiana R, Lipman ML, Sampalis JS, Thibeault D, MacNamara E, Karaplis AC. Influence of serum phosphorus levels on circulating intact FGF23 in hemodialysis patients. The Endocrine Society 87th Annual Meeting, San Diego, California. Presentation Number: OR30-6

--Gupta A, Välimäki V-V, Välimäki MJ, Löyttyniemi E, Richardson M, Goltzman D4, Karaplis AC. Variable number of tandem repeats (VNTR) polymorphism in the PTHRP gene as diagnostic predictor of peak bone mass in Young Finnish males. International Osteoporosis Foundation World Congress on Osteoporosis, Toronto, Ontario. Presentation Number: P754SA.

III. Objectives and Priorities

The objective of the division is to develop its academic and research profile. This is a distinct possibility given the fact that the division is endeavouring to recruit more junior members with the primary aim to bolster its academic profile. The immediate and major priority is to expand the physical space as it is woefully inadequate for the present needs of patients and staff. The expected newly appointed chief of division will no doubt have space as a major issue for the Endocrinology Division.

Respectfully submitted,

Mark Trifiro, MD, FRCPC
Acting Chief, Division of Endocrinology