Annual Report
Division of Endocrinology
April 2005 – March 2006

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. Andrew Karaplis and Mark Trifiro were promoted to Full Professors in the McGill University Faculty of Medicine. 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 again 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 (ICMA, ICMB, Physiology) and CTU coverage within the Department of Medicine at the Jewish General Hospital.

II. Evaluation of Past Academic Year

a. Faculty:

Dr. Stavroula Christopoulos appointment has been approved. She is expected to start in September 2006.

Dr. Brent Richards has also been appointment to our Division and is expected to join us in September 2007.

Dr. J. Enrique Silva, Chief Endocrine Division, left our Hospital in September of 2005 and Dr. Mark A. Trifiro is Acting Chief as of January 2006.

b. 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 focused 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 CLIN ICS

	Monday	Tuesday	Wednesday	Thursday	Friday
AM	-Diab.Clin. (Kader) -Gen.Endo (Schweitzer, Trifiro,Karaplis)	-Thyroid (Tamilia) -Gen. Endo (Trifiro, Assimakopoulos, Schiffrin)	-Gen.Endo -Gestational Diabetes (Kader) - Osteoporosis I (Trifiro)	-non-GFT, Gen. Endo. (Clamen, Kahn) (Rizzo, Komaromi)	-Gen.Endo (Schweitzer) (Trifiro, Tamilia)
PM	-Gen.Endo (Karaplis, Assimakopoulos, Schweitzer)	-Gen.Endo (Assimakopoulos, Schiffrin)	-Gen.Endo (Schiffrin) -Osteoporosis II (Karaplis)	-Lipid Clinic (Schweitzer) -Gen. Endo (Assimakopoulos, Kader)	

c. Honours and Awards (and Promotions) by members, operating grants and salary awards are NOT included- see "g"; for invited lectures, appointments, offices in learned societies, see "e")

Karaplis, Andrew

Invited Oral Presentations

8th International PPP, New Haven, CT, July 2005
Title: The PTHrP signalling in bone
Invited by Dr. J. Wysolmersky, Yale University School of Medicine, New Haven, CT

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

Scholarly Activities

Member of the Health Professionals Awards Committee, CIHR

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.

d. 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 (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, David J. Mangelsdorf, Ph.D., Professor of Pharmacology and Biochemistry, University of Texas Southwestern 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.

Karaplis, Andrew

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.

Beitel, Lenore, K. Ph.D.

- Invited Lecturer: “The Human Androgen Receptor: From Patients to Protein Dynamics”. CHUS, Sherbrooke, QC, June 10, 2005
- Invited Lecturer: “The Human Androgen Receptor: From Genotype-Phenotype Correlations to Molecular Modeling”, MCH Research Institute, Montreal, QC, Nov. 14, 2005”
-Tutor, Endocrine Physiology (Med I)
- Lecturer, Human Biochemical Genetics, McGill University

Tamilia, 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

e. 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
- Tutor Endocrine Physiology (Med I)
- Lecturer, Human Biochemical Genetics, McGill University

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), and Committee Diabetes Prevention Trial-1

Schweitzer, Morris
- Co-Director, Center for Cardiovascular Disease Prevention, JGH
- Director, Lipid Clinic
- Chairman, McGill/Merck-Frosst Lipid Lectureship
- Multiple lectures to medical community on lipid metabolism and its disorders

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

Trifiro, Mark

- Research Director, Department of Medicine
- Ad hoc reviewer, Canadian Institute of Health Research

f. Consulting Activities: None reported

g. Research Activities

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

Grants

Karaplis, Andrew C.

Research Grants

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".

Clinical Grants

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)

2002-2005 CIHR: "A comprehensive assessment of the significance of tissue heterogeneity in the development of androgen independent prostate cancer", operating grant, $79,000/y (co-PI with Dr. Bruce Gottlieb, LDI)

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.

h. Publications

Karaplis, Andrew C.

Refereed papers

--Xue Y, Karaplis AC, Hendy GN, Goltzman D, Miao D. Genetic models show that parathyroid hormone and 1,25-dihydroxyvitamin D3 play distinct and synergistic roles in postnatal mineral ion homeostasis and skeletal development. Hum Mol Genet 2005;14:1515-1528.

--Bedard N, Hingamp P, Pang Z, Karaplis AC, Morales C, Trasler J, Cyr D, Gagnon C, Wing SS. Mice lacking the UBC4-testis gene have a delay in postnatal testis development but normal spermatogenesis and fertility. Mol Cell Biol 2005; 25:6346-6354.

--Miao D, He B, Jiang Y, Kobayashi T, Soroceanu MA, Zhao J, Su H, Tong X, Amizuka N, Gupta A, Genant HK, Kronenberg HM, Goltzman D, Karaplis AC. Osteoblast-derived PTHrP is a potent endogenous bone anabolic agent that modifies the therapeutic efficacy of administered PTH 1-34. J Clin Invest 2005;115:2402-2411.

--Xue Y, Zhang Z, Karaplis AC, Hendy GN, Goltzman D, Miao D. Exogenous PTH-Related Protein and PTH improve mineral and skeletal status in 25-hydroxyvitamin D-1alpha-hydroxylase and PTH double knockout mice. J Bone Miner Res 2005; 20:1766-1777.

--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 .

Hoffer, L. John

--**Hoffer LJ**, Saboohi F, Golden M, Barré PE. Cobalamin dose regimen for maximum homocysteine reduction in end-stage renal disease. *Metabolism* 54:835-40, 2005

--**Hoffer LJ**. Metabolic consequences of starvation. IN: Shils ME, Shike M, Ross AC, Caballero B, Cousins RJ, eds, Modern Nutrition in Health and Disease, 10th Edition. Baltimore, M.D.: Williams & Wilkins, Practice Plan, 730-748, 2005

--**Hoffer LJ**, Hamadeh MJ, Robitaille L, Norwich KH. Human sulfate kinetics. *American Journal of Physiology* 289:R1372-1380, 2005

--**Hoffer LJ**, Djahangirian O, Bourgouin PE, Eid J, Saboohi F. Comparative effects of hydroxocobalamin and cyanocobalamin on plasma homocysteine concentrations in end-stage renal disease. *Metabolism*,54:1362-67, 2005

Trifiro, Mark and Beitel, Lenore K.

--Alvarado C., Beitel L.K., Sircar K., Aprikian A., Gottlieb B., **Trifiro M.** Somatic mosaicism and cancer: A micro-genetic examination into the role of the androgen receptor gene in prostate cancer, Cancer Research 65:8514-8518, 2005

--Beitel L.K., Scanlon T., Gottlieb B., **Trifiro M.** Progress in spinobulbar muscular atrophy research: Insights into neuronal dysfunction caused by the polyglutamine-expanded androgen receptor, Neurotoxicity Research 7:219-230, 2005

--Gottlieb B., Beitel L.K., **Trifiro M.A.** The molecular pathology of the androgen receptor in male infertility. Reproductive BioMedicine Online, 10:42-48, 2005 (www.rbmonline.com)

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 osteoclastic 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 1α-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.

Trifiro, Mark and Beitel, Lenore

Gottlieb B, Lumbroso R, Beitel LK, Trifiro M. Idiopathic male infertility: An investigation into the role of mutations in exon 1 of the androgen receptor gene. Endocrine Society's 87th Annual Meeting, San Diego, CA, June 4-7, 2005. Abst. #P1-279.

Gottlieb B, Alvarado C, Beitel LK, Sircar K, Aprikian A, Trifiro M. A tumor specific examination into the significance of androgen receptor gene alterations with functional consequences in prostate cancer. Endocrine Society's 87th Annual Meeting, San Diego, CA, June 4-7, 2005. Abst. #P2-665.

Gottlieb B, Alvarado C, Beitel LK, Sircar K, Aprikian A, Trifiro M. Single locus gene mutations and prostate cancer. Can mutations in the androgen receptor gene be directly linked to the occurrence of prostate cancer? Oral presentation, Abst. #20. American Society of Human Genetics 53rd Annual Meeting, Salt Lake City, Utah October 25-29, 2005.

Sircar K, Gottlieb B, Aprikian A, Beitel L, Trifiro M, Alvarado C. Genetic heterogeneity of androgen sensitive and androgen independent prostate cancer: An analysis of androgen receptor CAG repeat lengths in germline, somatic and hormone refractory prostate cancer tissues. United States and Canadian Academy of Pathology Meeting, Atlanta, Georgia, February 11-17, 2006 (Poster #84).

Southwell J, Trifiro M. The transactivational effects of androgen receptor CAG repeat lengths in the prostate cancer somatic (T877A) AR mutant. American Society of Clinical Oncology, 2006 Prostate Cancer Symposium, San Francisco, CA, Feb 24-26, 2006.