Division of Endocrinology, Diabetes and Metabolism

- **Overview**

The mission of the Endocrinology, Diabetes and Metabolism Division is to provide clinical care, consultation and training, and to perform basic and clinical research in the areas of endocrinology and metabolism.

- **Clinical Activities**

The clinical program is a joint venture with the Joslin Diabetes Center. This collaboration joins the nationally-known BIDMC endocrinology practice with the illustrious and world-renowned diabetes clinical practice at Joslin. The combined program in Endocrinology, Diabetes and Metabolism ranked 12th in the nation in the 2007 US News & World Report of “Best Hospitals” in the US. Dr. James Hennessey is Director of the Clinical Endocrinology Program and Dr. Martin Abrahamson is the Medical Director of the Joslin Diabetes Center.

The greater size and overall strength of the combined clinical program have allowed for growth and development of clinical programs, including initiatives in obesity and nutrition. A full range of outpatient and inpatient endocrine services is available for problems such as diabetes, obesity, thyroid disease, metabolic bone disease (especially osteoporosis), calcium disorders, pituitary disease, adrenal disease, and reproductive and growth disorders. Consultation services are available in the Shapiro Clinical Center. In the last year, the division increased outpatient visits by 25%. The highly successful Thyroid Nodule Clinic offers the coordinated services of radiology, pathology, surgery, and endocrinology. The convenience of the combined services has led to significantly increased patient volume as this program has recently been expanded. The Osteoporosis Prevention and Treatment Center, directed by Dr. Harold Rosen, offers expert consultative services and state-of-the-art dual energy X-ray absorptiometry to diagnose patients with osteopenia and osteoporosis. The Division is also expanding its neuroendocrine-pituitary service in conjunction with neurosurgery, including the recent addition of a multi-disciplinary conference. The conference meets monthly and includes Neurosurgery, Neurology, Endocrinology, Neuroradiology, Neuro-ophthalmology, and Radiation Oncology.

- **Quality Improvement**

Among the Quality Improvement activities of the Division are two programs to monitor the adequacy of thyroid biopsies and to assess renal function in osteoporotic patients. In the thyroid program, the biopsies are measured for accuracy and disposition. Additionally, the Quality Improvement Division has been
tracking the use of Vitamin D and assessing renal function in patients treated within the Division for osteoporosis with drug therapy.

**Educational Programs**

The Division recruits three new subspecialty fellows yearly into a unified fellowship training program with the Joslin Diabetes Center. The director of the Fellowship Program is Evan Rosen, and the site director for the Joslin is Allison Cohen. The BIDMC/Joslin fellowship program was well rated at an ACGME site visit this year and accreditation was renewed for the maximum time of five years. The clinical year is conducted jointly with Brigham and Women’s Hospital, and involves inpatient rotations at BIDMC and Brigham and Women’s Hospital, continuity clinics in endocrinology and diabetes at both BIDMC and Joslin, and sub-specialty clinics in pediatric endocrinology, lipids, reproductive endocrinology, metabolic bone disease, and medical and surgical approaches to obesity. A major aspect of the fellowship training is an in-depth research experience in one of the outstanding laboratories at BIDMC, Joslin or other Boston area research programs. Many graduates remain in academia. The program is supported by two NIH training grants. In addition to nine clinical fellows, there are more than fifty postdoctoral research fellows working within the Endocrine Division research laboratories. Endocrine faculty also participate in the education of our medical students and residents. Recent restructuring of the Endocrine Consult Rotation for residents has resulted in enhanced training in both outpatient and inpatient endocrine and diabetes care. In a recent teaching survey completed by BIDMC Medicine residents, the Endocrine rotation was ranked first or second in all seven categories queried. Endocrine was ranked first in “case specific teaching”, “teaching by attendings”, “teaching by fellows”, and “overall quality of teaching”.

**Research Activities**

The Division has a highly successful, cutting-edge research portfolio which includes research initiatives supported by the National Institutes of Health, private foundations, and the pharmaceutical industry. The key research are clinical trials, in vivo physiology, adipocyte biology, cell signaling, gene transcription, mouse genetics, hormone action and resistance, neuroendocrinology of obesity and glucose homeostasis, insulin secretion, and basic investigations of gene structure and function. The entire research division moved to the new BIDMC Center for Life Science near the Harvard Medical School quadrangle in August, 2008.

In addition to semi-monthly joint lab meetings, the Division has a yearly research retreat at which many of the seventy trainees have an opportunity to present their work.

Division investigators such as Jeff Flier, Barbara Kahn, Brad Lowell, Christian Bjorbaek, Terry Maratos-Flier, Christos Mantzoros and Evan Rosen are well-known for their research in diabetes, obesity, and energy metabolism. A particular strength is investigation of the molecular mechanisms for insulin resistance in diabetes and obesity. Specific studies relate to insulin signaling including the role of protein tyrosine phosphatases and suppressors of cytokine signaling, regulation of glucose transport in insulin resistance and the role of novel adipocyte-secreted molecules in insulin resistance. Studies of insulin secretion focus on the role of uncoupling proteins. These investigators also have strong programs investigating the pathogenesis of obesity, including leptin biology and signaling, hypothalamic peptides and appetite regulation, neuronal circuitry and regulation of adipogenesis. Techniques include sophisticated mouse genetics, viral vectors, state-of-the-art in vivo metabolic assessment of rodent models of obesity, electrophysiology, as well as patient-based studies.

### Research Funding - AY’07

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The Division has a large NIH-funded Program Project in Obesity Pathophysiology with a primary focus on the biology of the fat-derived hormone leptin, including the physiologic role of this hormone in the integration of energy balance, signaling pathways mediating the biological effects of leptin, leptin receptor biology, and mechanisms of leptin resistance. Other work using mouse genetics and gene targeting technologies investigates the basic mechanisms regulating energy expenditure and thermogenesis, including the biology of brown adipose tissue, novel uncoupling proteins and beta adrenergic receptors. Studies using neuron-specific knockout and knockin approaches are defining the functional neurocircuitry of body weight control. The Division has a second Program Project Grant from the American Diabetes Association which supports studies of the neuroendocrine regulation of hypothalamic function, including reproduction, growth, and the thyroid and stress axes. Three members of the Division were awarded funding from the Picower Foundation as part of a new Picower Diabetes Program grant involving four institutions.

Tony Hollenberg is a leader in the area of thyroid hormone action and nuclear receptor function. His group also studies the role of nuclear co-activator and co-repressor proteins and their involvement in cell signaling. Anny Usheva is exploring basic mechanisms of gene regulation at the transcription level. A specific interest is the effect of nutrition on transcription, and computational analyses are carried out in collaboration with the Theoretical Physics Division at the National Laboratory in Los Alamos.

Clinical and translational research activities of Christos Mantzoros’ group, are focused on leptin physiology, the etiology and treatment of the HIV-associated metabolic syndrome, and the role of IGF-1 in the pathogenesis of malignancy.

**Selected Publications**


**Awards and Honors**

Dr. Tim Graham was awarded the Smith Family Medical Foundation New Investigator Award, the Doris Duke Charitable Foundation Clinical Scientist Development Award, the Howard Hughes Medical Institute’s Physician Scientist Early Career Award, and the Klarman Award for Junior faculty from BIDMC. Dr. Anthony Hollenberg received an Honorary Phi Beta Kappa from Harvard University. Harvard Medical School awarded Drs. Mark Herman and Naaznin Lokhandwala Excellence in Tutoring awards. HMS also awarded Dr. Effie Tzameli a Scholars in Medicine Fellowship. Dr. Barbara Kahn received a Pfizer Visiting Professorship from the Mayo Clinic. Dr. Brad Lowell received a National Institutes of Health Merit Award. The American Federation of Medical Research awarded Dr. Christos Mantzoros the outstanding investigator award for 2008. Dr. Evan Rosen received an American Diabetes Association Career Development Award as well as a Richard and Susan Smith Family Foundation Pinnacle Program Project.


Zabolotny JM, Kim YB, Welsh LA, Kershaw EE, Neel BG, Kahn BB. Protein tyrosine phosphatase 1B (PTP1B) expression is induced by inflammation in vivo. J Biol Chem 2008; 283:14230-14241.