BAYLOR COLLEGE OF MEDICINE

ENDOCRINOLOGY, METABOLISM AND DIABETES FELLOWSHIP PROGRAM

MENTORS' RESEARCH INTERESTS

JANUARY 2012

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Research Interests

- Pathophysiology of type 2 diabetes mellitus: We are examining the metabolic and molecular basis of insulin resistance in T2DM and obesity using insulin clamp studies and muscle biopsies. Vastus Lateralis muscle biopsies from insulin resistant subjects are examined for adiponectin signaling, insulin signaling, inflammation (TLR4, NFkappaB) and mitochondrial gene expression before and after interventions such as weight loss or treatment with PPAR-gamma agonists.
- Imaging studies using MR spectroscopy to measure hepatic, intramyocellular, and myocardial fat and its relationship with insulin resistance and cardiac function in type 2 diabetic patients. The effects of novel type 2 diabetes therapies on fat topography and cardiac function are being studied.
- Vascular Inflammation in type 2 diabetes and obesity using monocyte isolation techniques and measuring TLR pathways and NFkappaB pathways.
- *In vitro* studies examining fat and glucose metabolism in cultured L6 muscle cells.

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Research Interests

Novel syndromes of Ketosis-Prone Diabetes

- Genetic, immunologic and metabolic etiologies of beta cell dysfunction in "atypical" forms of diabetes presenting with diabetic ketoacidosis.

HIV-associated metabolic disease

- Metabolic basis of HIV lipodystrophy syndrome
- Mouse models of HIV lipodystrophy
- Optimal treatment of HIV-associated dyslipidemia and lipodystrophy

Research Projects

Ketosis-Prone Diabetes

- Analysis of natural history and outcomes of different syndromes of KPD
- Stable isotope / mass spectrometry techniques to uncover the metabolic defects in "non-immunologic" forms of KPD
- Genetic and immunologic studies into mechanisms underlying familial and immune-mediated forms of KPD

HIV-associated metabolic disease

- Molecular and cellular studies of the HIV protein Vpr, to investigate its role in HIV associated metabolic disease
- Metabolic studies in a mouse model of HIV lipodystrophy
- Analysis of outcomes in clinical trials for the optimal treatment of HIV-associated metabolic disease.

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Research Interest

- Diabetes management in the cancer patient

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Research Interest

- Targeted treatment of metastatic thyroid cancer. My long-term goal is to design clinical trials targeting known aberrant pathways and/or mutations in patients with metastatic thyroid cancer.

Research projects

- Phase 2 trial of vemurafenib (selective BRAF inhibitor) in patients with BRAF mutated, RAI-refractory papillary thyroid cancer
- Translational clinical trial with vemurafenib, a selective BRAF inhibitor, in the neoadjuvant setting. The primary objective is to correlate clinical response to ERK phosphorylation in the tumor after 2 courses of vemurafenib. I am also exploring mechanisms of resistance to vemurafenib to better understand how to treat these patients. One such mechanism of interest is the role of the immune system in advanced thyroid cancer.
- Second Line Salvage Therapy in Patients with Metastatic Differentiated Thyroid Carcinoma After Sorafenib Failure: Comparison of Efficacy4. Phase 2 trial of XL184 (cabozantinib) in differentiated thyroid cancer
- Retrospective study of efficacy of tyrosine kinase inhibitors therapy in poorly differentiated thyroid cancer
- The efficacy of CASAD in patients with diarrhea related to medullary thyroid cancer: a pilot study
- Tyrosine kinase usage in thyroid cancer database. This is an established database with over 250 patients who have been treated with a TKI (such as sorafenib) for thyroid cancer. Multiple projects can be developed from this database.

Selected publications:

1. Busaidy N, **Cabanillas ME**. Differentiated thyroid cancer: management of patients with radioiodine non-responsive disease. Journal of Thyroid Research 2012, 2/2012.
2. Kim KB, **Cabanillas ME**, Lazar AJ, Williams MD, Sanders DL, Ilagan JL, Nolop K, Lee RJ, Sherman SI. Clinical responses to Vemurafenib in Patients with Metastatic Papillary Thyroid Cancer Harboring V600E BRAF mutation. Thyroid. Accepted for publication
3. Carhill AA, **Cabanillas ME**, Waguespack SG, Jimenez C, Habra MA, Sherman SI, Hu MI, Busaidy NL. The Non-investigational Use of Tyrosine Kinase inhibitors in Thyroid Cancer: Establishing a Standard for Patient Safety and Monitoring. Journal of Clinical Endocrinology & Metabolism. In Press.

4. Ayala-Ramirez M, Chougnet C, Habra MA, Palmer L, Leboulleux S, **Cabanillas ME**, Caramella C, Anderson P, Al Ghuzlan A, Waguespack S, Deandreis D, Baudin E, Jimenez C. Treatment with Sunitinib for Patients with Progressive Metastatic Pheochromocytomas and Sympathetic Paragangliomas. Journal of Clinical Endocrinology & Metabolism. In Press.
5. Choueiri TK, Pal SK, Brose M, McDermott DF, Morrissey S, Miles DR, Holland J, Dutcher JP, Sherman SI, Kaelin WG, **Cabanillas ME**. Activity of Cabozantinib (XL184) in Patients With Renal Cell or Differentiated Thyroid Cancer Evaluated in a Drug–Drug Interaction Study. Clinical Cancer Research. Submitted.
6. Blevins D, Dadu R, Hu M, Baik C, Balachandran D, Ross W, Gunn B, **Cabanillas ME**. Aero-digestive Fistula Formation as a Rare Side Effect of Antiangiogenic Tyrosine Kinase Inhibitor Therapy for Thyroid Cancer. Journal of Clinical Endocrinology and Metabolism. Submitted.
7. **Cabanillas ME**, Varghese JM, Lu C. Role of Cytotoxic Chemotherapy in Advanced Differentiated Thyroid Cancer: a review of the MD Anderson experience. Journal of Clinical Endocrinology and Metabolism. Submitted.
8. **Cabanillas ME**, Hu MI, Durand JB, Busaidy N. Challenges Associated with Tyrosine Kinase Inhibitor Therapy for Metastatic Thyroid Cancer. Special Issue of the Journal Thyroid Research: Thyroid Oncology. e-Pub 10/2011.
9. Dadu R, **Cabanillas ME**. Optimizing therapy for radioactive iodine-refractory differentiated thyroid cancer: Current state of the art and future directions. Minerva Endocrinologica. In Press.

LAWRENCE C.B. CHAN, MD, D.Sc.

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Research Interests

- Gene Therapy for Type 1 Diabetes. We are testing protocols for inducing pancreatic islet formation in the liver and modulating the immune response in NOD mice, a type 1 diabetic mouse model;
- Role of fat cell proteins in glucose and lipid metabolism, obesity and insulin resistance;
- Novel mechanism of diabetic complications.

Recent Publications

1. Samson SL, Gonzalez EV, Yechoor Y, Bajaj M, Oka K, Chan L (2008) Gene therapy for diabetes: Metabolic effects of helper-dependent adenoviral exendin 4 expression in a diet-induced obesity mouse mode. *Molecular Therapy* 16: 1805-1812. PMCID: PMC2582376
2. Yechoor V, Liu V, Espiritu C, Paul A, Oka K, Kojima H, Chan L (2009) Neurogenin3 is sufficient for in vivo transdetermination of hepatic progenitors cells into islet-like structures but not transdifferentiation of hepatocytes. *Developmental Cell* 16: 358-373. PMCID: PMC2676438.
3. Weiqin Chen, Benny Chang, Lan Li and Lawrence Chan (2010) Pnpla3/adiponutrin deficiency in mice is not associated with fatty liver disease. Hepatology 52: 1134-1142.
4. Poungvarin N, Lee JK, Yechoor VJ, Li MV, Assavapokee T, Suksaranjit P, Thepsongwajja JJ, Saha PK, Oka K, Chan L (2012) Carbohydrate response element binding protein (ChREBP) plays a pviotal role in β cell glucotoxicity. *Diabetologia* 55: 1783-1796
5. Yang Y, Chang B H-J, Chan L (2012) Sustained expression of the transcription factor GLIS3 is required for normal beta cell function in adults. *EMBO Mol Med* (in press).

WENHAO CHEN, PhD

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Research Interests

- Define the molecular mechanisms of T-cell tolerance
- Design immune intervention therapies for type 1 diabetes and transplantation
- Develop beta cell replacement therapies for type 1 diabetes

Recent Publications

(1) Xie A, Buras E, Xia J, **Chen W**. (2012) The emerging role of interleukin-21 in transplantation. J Clin Cell Immunol. In press.

(2) Miyahara Y, Khattar M, Schroder P, Mierzejewska B, Deng R, Han R, Hancock WW, **Chen W***,Stepkowski S*. (2012) An anti-TCRβ mAb induces longterm allograft survival as well as prevents and reverses the onset of type-1 diabetes. Am J Transplant. 12:1409. PMID: 22420295. *corresponding authors

(3) Wang G, Khattar M, Guo Z, Miyahara Y, Linkes SP, Sun Z, He X, Stepkowski SM, **Chen W**. (2010) IL-2-deprivation and TGF-beta are two non-redundant suppressor mechanisms of CD4+CD25+ regulatory T cell which jointly restrain CD4+CD25- cell activation. Immunol Lett. 132:61. PMCID: PMC2922908

(4) Wang G, Miyahara Y, Guo Z, Khattar M, Stepkowski S, **Chen W**. (2010) "Default" generation of neonatal regulatory T cells. J Immunol. 185:71. PMID: 20498359

GILBERT COTE, PhD

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Research Interests

- The focus of our laboratory is the study of the genetic mechanisms involved in familial endocrine neoplasias. Specific examples include mutations of the RET proto-oncogene in patients with multiple endocrine neoplasia (type 2) and mutations of the MEN1 gene in patients with multiple endocrine neoplasia (type 1). More recently we have used array-based approaches to study gene copy number and expression. Our experience with genetic analysis of these disorders has allowed a better understanding of disease progression and created the opportunity for the application of genetic diagnosis and treatment. We believe that clarifying the role of genetics in hereditary endocrine neoplasia will lead to a better understanding of sporadic endocrine cancer. Furthermore, these genetic changes have the potential to serve as biomarkers to diagnose and monitor cancer progression. Our recent studies have focused on development of methods to detect circulating tumor cells and cell-free tumor DNA in blood of thyroid cancer patients. These translational studies are performed in close collaboration with faculty within the Endocrine Center.

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Research Interests

- Testosterone replacement therapy in adult hypogonadal males.
- Inpatient glycemia and outcomes.

Clinical research projects

- Inpatient glycemia and various inpatient outcomes (ex: in patients who have undergone CABG or renal transplant).
- Testosterone treatment in men 65 and older.

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Research Interests

- Molecular causation and clinical treatment of medullary thyroid carcinoma (MTC). I have participated in clinical trials of tyrosine kinase inhibitors in the management of MTC. In addition, I have a laboratory program focused on the identification of molecular mechanisms for development and progression of MTC. Recent work has focused on the use of high-density comparative genomic hybridization to identify molecular abnormalities in MTC. These studies have led to the identification of defects of DNA repair, expression of tyrosine kinase receptors, and expression of the transcription factor, ATF4.

- The role of the calcitonin gene in the bone metabolism. We have created a mouse model of calcitonin deficiency. These knock-out mice have a distinctive phenotype characterized by increased bone resorption with thinning of the bone cortex and also an increase of peri-cortical trabecular bone formation. We are currently exploring the mechanism by which this occurs and have discovered a marked increase of expression of sclerostin, an inhibitor of the WNT signaling pathway. These results suggest that calcitonin plays an important role to suppress bone formation. This will be a topic of future interest in the laboratory.

- A third interest is clinical bone biology. The MDACC component of the Bone Disease Program of Texas has a number of clinical studies focused on bone health in patients being treated for cancer and in survivors of cancer.

JOSE GARCIA, MD, PhD

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Research Interests

- My research interests include the role that the novel hormone ghrelin and other anabolic therapies in the setting of cancer-related cachexia and other wasting disorders. I am involved in several clinical trials and in animal studies involving cancer-related cachexia.

Research Projects

- MERIT Review. Department of Veterans Affairs

The role of ghrelin in cancer cachexia.
This project is a randomized controlled trial using a ghrelin mimetic versus placebo in lung cancer subjects.

- MERIT Review. Department of Veterans Affairs

Mechanisms of action of ghrelin in muscle and adipose tissue in cancer-related cachexia.
This project investigates the effects of ghrelin in animal models of cancer cachexia.

- NIH. R03 AG040583

The role of ghrelin and the ghrelin receptor GHSR1a in sarcopenia of aging
The purpose of this grant is to establish the role of ghrelin and the ghrelin receptor GHSR1a in rodent models of sarcopenia of aging.

- VA Seed Fund Grant

A Pilot Study on the Mechanisms of Action and Effects of Ghrelin Mimetics in Patients with Cancer Anorexia - Cachexia Syndrome.
This proposal is design to study the role of the ghrelin mimetic macimorelin on the central mechanisms regulating appetite in the setting of cancer cachexia

Publications

1. Garcia JM, Garcia-Touza M, Hijazi RA, Taffet G, Epner D, Mann D, Smith RG, Cunningham GR, Marcelli M 2005 Active ghrelin levels and active to total ghrelin ratio in cancer-induced cachexia. J Clin Endocrinol Metab 90:2920-2926
2. Garcia JM, Iyer D, Poston WS, Marcelli M, Reeves R, Foreyt J, Balasubramanyam A 2006 Rise of plasma ghrelin with weight loss is not sustained during weight maintenance. Obesity (Silver Spring) 14:1716-1723
3. Garcia JM, Li H, Mann D, Epner D, Hayes TG, Marcelli M, Cunningham GR 2006 Hypogonadism in male patients with cancer. Cancer 106:2583-2591
4. Garcia JM, Polvino WJ 2007 Effect on body weight and safety of RC-1291, a novel, orally available ghrelin mimetic and growth hormone secretagogue: results of a phase I, randomized, placebo-controlled, multiple-dose study in healthy volunteers. Oncologist 12:594-600

5. Sun Y, Garcia JM, Smith RG 2007 Ghrelin and growth hormone secretagogue receptor expression in mice during aging. Endocrinology 148:1323-1329
6. Garcia JM, Cata JP, Dougherty PM, Smith RG 2008 Ghrelin prevents cisplatin-induced mechanical hyperalgesia and cachexia. Endocrinology 149:455-460
7. Sun Y, Butte NF, Garcia JM, Smith RG 2008 Characterization of adult ghrelin and ghrelin receptor knockout mice under positive and negative energy balance. Endocrinology 149:843-850
8. Garcia JM, Polvino WJ 2009 Pharmacodynamic hormonal effects, a novel oral ghrelin mimetic and growth hormone secretagogue in healthy volunteers. Growth Horm IGF Res. 2009 Jun;19(3):267-73. PMID: 19196529
9. Tan HY, Garcia JM 2010 Association between Insulinoma and Adrenal Insufficiency: A Case Report and Review of the Literature. Pancreas. May;39(4):544-6. PMID: 20418760
10. Smiechowska J, Utech AE, Taffet G, Hayes T, Marcelli M, Garcia JM. 2010 The role of adipokines in patients with cancer anorexia and cachexia. J Investig Med. Mar;58(3):554-9. PMID: 20215915.
11. Garcia, J.M., Sharafkhaneh, H., Hirshkowitz, M., Elkhatib, R., and Sharafkhaneh, A. 2011 Weight and metabolic effects of cpap in obstructive sleep apnea patients with obesity. *Respir Res* 12:80. PMID:
21676224
12. Engineer DR, Garcia JM. 2012 Leptin in anorexia and cachexia syndrome. Int J Pept. 2012;2012:287457.
13. Burney BO, Hayes TG, Smiechowska J, Cardwell G, Papusha G, Bhargava P, Konda B, Auchus R, Garcia JM. 2012 Low testosterone levels and increased inflammatory markers in patients with cancer and relationship with cachexia. J Clin Endocrinol Metab. 2012 May;97(5):E700-9
14. Burney BO, Garcia JM. 2012 Hypogonadism in male cancer patients. J Cachexia Sarcopenia Muscle. Apr 20. [Epub ahead of print]
15. Utech AE, Tadros EM, Hayes TG, Garcia JM. 2012 Predicting survival in cancer patients: the role of cachexia and hormonal, nutritional and inflammatory markers J Cachexia Sarcopenia Muscle. May 31. [Epub ahead of print]
16. Garcia JM, Friend S, Allen S. 2012 Therapeutic potential of anamorelin, a novel, oral ghrelin mimetic, in patients with cancer-related cachexia: a multicenter, randomized, double-blind, crossover, pilot study. Support Care Cancer. Jun 16. [Epub ahead of print]
17. Guillory B, Splenser AE, Garcia JM. 2012 The role of ghrelin in anorexia-cachexia syndromes. Vitam Horm. 92, In press.

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Research Projects

- PI, Molecular Profiling of Adrenocortical Tumors, 2009−present
- Beverlin Fund and Institutional Start up research Fund
- PI, Phase 3 clinical trial of E7080 vs. placebo in radioiodine resistant differentiated thyroid carcinoma.
- Retrospective reviews of Adrenal neoplasms

Publications

1. **Habra MA**, Hijazi R, Verstovsek G, Marcelli M. Medullary thyroid carcinoma associated with hyperthyroidism: a case report and review of the literature. Thyroid 14(5):391-6, 5/2004.
2. Busaidy NL, Jimenez C, **Habra MA**, Schultz PN, El-Naggar AK, Clayman GL, Asper JA, Diaz EM, Evans DB, Gagel RF, Garden A, Hoff AO, Lee JE, Morrison WH, Rosenthal DI, Sherman SI, Sturgis EM, Waguespack SG, Weber RS, Wirfel K, Vassilopoulou-Sellin R. Parathyroid carcinoma: a 22-year experience. Head Neck 26(8):716-26, 8/2004.
3. Jimenez C, **Habra MA**, Huang SC, El-Naggar A, Shapiro SE, Evans DB, Cote G, Gagel RF. Pheochromocytoma and Medullary Thyroid Carcinoma: A New Genotype-Phenotype Correlation of the RET Protooncogene 891 Germline Mutation. J Clin Endocrinol Metab 89(8):4142-5, 8/2004.
4. **Habra MA**, Vassilopoulou-Sellin R. Cervical spine metastasis mimicking thyroid bed uptake in follicular thyroid carcinoma. Thyroid 15(3):298-9, 3/2005.
5. **Habra MA**, Feig BW, Waguespack SG. Image in endocrinology: adrenal pseudocyst. J Clin Endocrinol Metab 90(5):3067-8, 5/2005.

6. **Habra M**, Sarlis NJ. Thyroid and aging. Rev Endocr Metba 6(2):145-54, 6/2005.
7. Picolos MK, **Habra M**, Safdar A, Sarlis NJ. Inactive pulmonary tuberculosis mimicking metastasis from papillary thyroid carcinoma in diagnostic radioiodine whole-body scintigraphy. Images in Thyroidology. Thyroid 15(9):1105-6, 9/2005.
8. **Habra MA**, Jimenez C, Wallace M, Evans, DB, Vassilopoulou-Sellin R. Insulinoma in a Marathon Runner Illustrating the Effects of Exercise on Insulin Sensitivity and Glucose Homeostasis. The Endocrinologist 16(1):20-24, 1/2006.
9. **Habra MA**, Vassilopoulou-Sellin R. Contribution of routine chest x-ray in the long-term follow-up of patients with differentiated thyroid carcinoma. Thyroid 16(3):303-6, 3/2006.
10. **Thompson MA, Habra MA,** Routbort MJ, Holsinger FC, Perrier ND, Waguespack SG, Rodriguez MA. Primary adrenal natural killer/T-cell nasal type lymphoma: first case report in adults. Am J Hematol 82(4):299-303, 4/2007.
11. **Habra MA,** Weaver EJ, Prewitt PV. Primary cutaneous large B-cell lymphoma of the leg and acute hypercalcemia. J Clin Oncol 25(36):5825-6, 12/2007.
12. **Habra MA,** Jimenez C, Huang SC, Cote GJ, Murphy WA, Gagel RF, Hoff AO. Expression analysis of fibroblast growth factor-23, matrix extracellular phosphoglycoprotein, secreted frizzled-related protein-4, and fibroblast growth factor-7: identification of fibroblast growth factor-23 and matrix extracellular phosphoglycoprotein as major factors involved in tumor-induced osteomalacia. Endocr Pract 14(9):1108-14, 12/2008.
13. **Habra MA,** Nunez R, Chuang H, Ayala-Ramirez M, Rich T, Kyle K, Jimenez C. Fatal hypoglycemia in malignant pheochromocytoma: direct glucose consumption as suggested by 18F-2-fluoro-2-deoxy-D-glucose positron emission tomography/computed tomography imaging. Endocrine 37:209-212, 1/2010.
14. Santarpia L, **Habra MA,** Jiménez C. Malignant Pheochromocytomas and Paragangliomas: Molecular Signaling Pathways and Emerging Therapies. Horm Metab Res 41(9):680-6, 9/2009. e-Pub 4/2009**.**

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Research Interests

- Thyroid cancer – medullary thyroid carcinoma and novel therapeutics
  Multiple endocrine neoplasia, Types 1 and 2 – surveillance and management
  Bone and mineral metabolism disorders, including osteoporosis and calcium disorders
  Parathyroid disorders
  Pituitary tumors – management and surveillance
  Endocrine sequelae of cancer and its therapies

Ongoing Clinical Research Protocols (serving as PI)

- Principal Investigator, A Single-arm, Multicenter, Proof-of-Concept Study of Denosumab in the Treatment of Hypercalcemia of Malignancy in Subjects with Elevated Serum Calcium Despite Recent Treatment with IV Bisphosphonates, 2009-0595, 2009−present, Sponsor

- Principal Investigator, An International, Randomised, Double-Blind, Two-Arm Study to Evaluate the Safety and Efficacy of Vandetanib 150 and 300 mg/day in Patients with Unresectable Locally Advanced or Metastatic Medullary Thyroid Carcinoma with Progressive or Symptomatic Disease, 2011-1097, 2011−present, $440,752, Sponsor

- Principal Investigator, Genetic risk of Osteonecrosis of the Jaw (ONJ) in Patients with Metastatic Cancer: Case Control Study, PA11-0573, 2011−present, $20,010, NIH

- Co-Principal Investigator, Efficacy of CASAD for Patients with Diarrhea in Medullary Thyroid Cancer, 2012-0584, PI - Maria Cabanillas, 2012−present, Sponsor

- Co-Principal Investigator, An Open-Label, Expanded Access Study of Cabozantinib (XL184) in Subjects with Unresectable, Locally Advanced, or Metastatic Medullary Thyroid Cancer, 2012-0446, PI - Camilo Jimenez, 2012, Sponsor

- Principal Investigator, A Retrospective Chart Review of Patients with Non-Islet Cell Tumor Hypoglycemia Due to Excessive IGF2 Production, RCR06-1066, 2006−present

Publications

1. Carhill AA, Cabanillas ME, Jimenez C, Waguespack SG, Habra MA, **Hu M**, Ying A, Sellin RV, Gagel RF, Sherman SI, Busaidy NL. The non-investigational use of tyrosine kinase inhibitors in thyroid cancer: establishing a standard for patient safety and monitoring. The Journal of Clinical Endocrinology & Metabolism. In Press.
2. Cabanillas ME, **Hu MI**. A randomized, double blinded study of risedronate versus placebo for the prevention of bone loss in adult patients receiving high dose corticosteroids for the treatment of acute lymphocytic leukemia and lymphoblastic lymphoma. Cancer. Submitted.
3. Blevins D, **Hu MI**, Waguespack SG, Balachandran D, Dadu R, Cabanillas M. Aero-digestive fistula formation as a rare side effect of antiangiogenic tyrosine kinase inhibitor therapy for thyroid cancer. J Clin Endo Metab. Submitted.
4. **Hu MI**, Glezerman I, Gucalp R, Insogna K, Leboulleux S, Misiorowski W, Yu B, Ying W, Jain R. Denosumab for hypercalcemia of malignancy in patients refractory to IV bisphosphonates. JNCI. Submitted.
5. Chae YK, **Hu MI**, Katz RL, Chavez-MacGregor M, Haluska P, Meric-Bernstam F, Gonzalez-Angulo AM, Melhem-Bertrandt A. Two birds with one stone: octreotide treatment for acromegaly and breast cancer. J Clin Oncol. Submitted.

Invited Articles

1. **Hu MI**, Gagel RF, Jimenez C. Bone loss in patients with breast or prostate cancer. Curr Osteoporos Rep 5(4):170-8, 2007.
2. Jiménez C, **Hu MI**, Gagel RF. Management of medullary thyroid carcinoma. Endocrinol Metab Clin North Am 37(2):481-96, 2008.
3. **Hu MI**, Cote G, Gagel RF. RET gene: a therapeutic target in medullary thyroid carcinoma (within issue on "Recent advances in thyroid cancer"). Current Problems in Surgery 45(3):202-212, 2008.
4. Stava CJ, Jimenez C, **Hu MI**, Vassilopoulou-Sellin R. Skeletal sequelae of cancer and cancer treatment. J Cancer Surviv 3(2):75-88, 6/2009. e-Pub 5/2009.
5. **Hu MI**, Lu H, Gagel RF. Cancer Therapies and Bone Health. Curr Rheumatol Rep 12(3):177-85, 6/2010.
6. Hoff AO, Toth B, **Hu M**, Hortobagyi GN, Gagel RF. Epidemiology and risk factors for osteonecrosis of the jaw in cancer patients. Ann N Y Acad Sci 1218(1):47-54, 2/2011. e-Pub 9/2010.
7. Khan MI, Waguespack SG, **Hu MI**. Medical management of postsurgical hypoparathyroidism. Endocr Pract 17 Suppl 1:1-19, Mar-Apr, 3/2011. e-Pub 12/2010.
8. **Hu MI**. Updates in the management of medullary thyroid cancer. Clin Adv Hematol Oncol 9(5):1-3, 5/2011.
9. **Hu MI**, Gagel RF. Multiple endocrine neoplasia type 2. Translational Endocrinology & Metabolism 2(4):45-76, 12/2011.
10. Cabanillas ME, **Hu MI**, Durand JB, Busaidy NL. Challenges associated with tyrosine kinase inhibitor therapy for metastatic thyroid cancer. J Thyroid Res 2011:985780, 2011. e-Pub 10/2011. PMCID: PMC3189619.
11. Rich TA, **Hu MI**, Martin JW, Perrier ND, Waguespack SG. CDC73-related disorders. GeneReviews at GeneTests, www.genetests.org, 5/2012.

Editorials

1. **Hu MI**, Cote GJ. Medullary thyroid carcinoma: who's on first? Thyroid 22(5):451-3, 5/2012.

Book Chapters

1. **Hu MI**, Gagel RF. Calcitonin gene family of peptides. In: Principles of Bone Biology, 3rd edition. Ed(s) Bilezikian J, Raisz L, Rodan G, 2008.
2. **Hu MI**, Sherman SI. Endocrine complications of head and neck surgery. In: Complications in Head and Neck Surgery, 2nd edition. Ed(s) Eisele, DW, 2009.
3. **Hu MI**, Yeung SJ, Gagel RF. Endocrine paraneoplastic syndromes. In: Internal Medicine Care of Cancer Patients. Ed(s) Escalante C, Yeung J, Gagel RF. BC Decker Inc; the Holland-Frei Series: Ontario, 2009.
4. **Hu MI**, Vassilopoulou-Sellin R, Lustig R, Lamont J. Thyroid and parathyroid cancers. In: Cancer Management: A Multidisciplinary Approach, 11th Edition. CMPMedica, 2009.
5. **Hu M**, Gagel RF. Multiple endocrine neoplasia type 2. In: Endocrinology, 6th edition. Ed(s) JL Jameson, LJ DeGroot. Saunders, 2010.
6. **Hu MI**, Ahn P, Lamont JP. Thyroid and parathyroid cancers. In: Cancer Management: A Multidisciplinary Approach, 12th Edition. CMPMedica, 51-70, 2010.
7. Alford E, **Hu MI**, Ahn P, Lamont JP. Thyroid and parathyroid cancers. In: Cancer Management: A Multidisciplinary Approach, 13th Edition. CMPMedica, 2011.
8. **Hu MI**, Jimenez C, Cote GJ, Gagel RF. Medullary thyroid carcinoma. In: The Thyroid, 10th. Ed(s) Braverman L, Cooper D. Lippincott Williams & Wilkins: Philadephia, PA, 744-65, 2012.
9. Thosani S, Ahn P, **Hu MI**. Thyroid and parathyroid cancers. In: Cancer Management: A Multidisciplinary Approach, 14th. CMP Medica, http://www.cancernetwork.com/cancer-management-app via http://itunes.apple.com, e-Book 2012.
10. **Hu MI**, Jimenez C, Busaidy NL, Habra M. Long-term and late endocrine effects of cancer survivorship. In: Cancer Survivorship, 1st. In Press.
11. Waguespack SG, Grubbs EG, **Hu MI**. Multiple endocrine neoplasia type 2. In: Clinical Genomics: Practical Applications in Adult Patient Care. McGraw Hill. In Press.

CAMILO JIMENEZ, MD

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Research Interests

- Novel Therapeutics for Malignant Pheochromocoytomas and Sympathetic Paragangliomas: Recent advances in understanding the role of mutations of succinate dehydrogenase and hypoxia, signaling kinases in oncogenesis and tumor progression of malignant pheochromocytomas has led to identification of attractive targets for therapy. We have demonstrated the utility of multi-targeted kinase inhibitors to lead to durable tumor control in patients with malignant pheochromocytoma. Future efforts will continue to target angiogenesis through inhibition of VEGF receptors, but additional kinases that will be targeted in clinical trials include oncogenic fibroblast growth factor receptor mutants and the mTor pathway.
- Circulating Tumor Cells (CTCs) in malignant pheochromocytomas and sympathetic paragangliomas: The presence of CTCs is associated with a poor prognosis in breast, prostate and colon cancer, because they are believed to be the primary mediator for development of hematogenous metastases. We have developed a project with the goal to identify CTCs using immunomagnetic separation systems in the blood of patients with malignant pheochromocytoma and sympathetic paraganglioma. Further studies will focus on identifying the prognostic value of these findings in both newly diagnosed patients as well as those entering clinical trials for advanced disease. A secondary goal is to identify methods to extract CTCs from blood that permit additional analysis of gene expression and mutations as biomarkers to disease biology as well as response to treatment.
- The MDACC malignant pheochromocytoma and sympathetic paragangliomas database: We have created the biggest single institution database on pheochromocytomas and paragangliomas with >500 patients. We study the outcomes of patients with this tumor to delineate their follow-up and treatment and to understand the roles of primary interventions of surgery, MIBG, azedra, and chemotherapy. Further analyses to be undertaken will focus on the predictive value of diagnostic testing modalities during the first few years of patient follow-up, as well as the identification of clinical predictors for metastases, prognostic factors,

the best surgical approaches, etc. We will also identify families at risk, we will offer screening for affected individuals and early prevention of complications.

VICTOR LAVIS, MD

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Research Interest

- Hyperglycemia at M.D. Anderson Cancer Center:

At M.D. Anderson, patients with severe hyperglycemia are more likely to develop infection or renal insufficiency, stay longer in the hospital, and experience higher mortality in the hospital and over the 6 months after discharge than non-hyperglycemic patients. These relationships persist after adjustment for age, gender, hospital service, type and stage of cancer.

As has been reported for other institutions, the associations of hyperglycemia with adverse outcomes are more pronounced in patients with "new" hyperglycemia (no prior diagnosis of diabetes) than in those with known diabetes mellitus. In comparison with known diabetics, patients with "new" hyperglycemia at M.D. Anderson are more likely to be treated with high-dose glucocorticoids, and less likely to be treated with scheduled insulin. At M.D. Anderson, "new" hyperglycemia is associated with excess inpatient and post-discharge mortality only among those patients who are treated with high-dose glucocorticoids.

Research Projects

We have several projects focused on understanding and treating hyperglycemia related to treatment with glucocorticoids:

- Case-control study of patients on high-dose steroids, attempting to identify clinical characteristics that correlate with increased risk of hyperglycemia;
- Development and testing of algorithms for treatment of steroid-induced hyperglycemia with multiple-dose insulin in the hospital;
- Proposed clinical trial of treatment of steroid-induced hyperglycemia with GLP-1 agonists in patients with acute lymphoid leukemia.

Additionally, there are opportunities to design studies of optimal treatment of hyperglycemia related to treatment of cancer with experimental drugs that block steps in the insulin and IGF-1 signaling pathways.

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Research Interests

- Mechanisms associated with transition of prostate cancer to the castration resistant phenotype

- Role of the androgen receptor isoform AR3 in castration resistant prostate cancer

- Drug discovery program for novel compounds blocking the androgen receptor isoform AR3

- Development of new diagnostic tools for the management of androgen insensitivity syndromes.

Basic research:

- Identify molecular mechanisms associated with the activation of the outlaw form of the androgen receptor variant AR-V7. AR-V7 selection in tissue of patients with prostate cancer is thought to be a major cause of treatment resistance in patients with castration resistant prostate cancer. The work implies screening libraries of drugs to identify molecules inhibiting the activation of AR-V7 using established in vitro protocol. Candidate drug are then tested for their ability to inhibit this AR variant, and various experimental approach (in vitro and in vivo) are used to identify the mechanism involved.

Translational Research:

- Identify the genetic signature(s) of bone marrow obtained from patients with prostate cancer metastatic to the bone marrow who have failed Abiraterone. Bone marrow biopsies form these patients and from healthy control will be analyzed with various molecular approaches to understand the genetic abnormalities causing prostate cancer to develop resistance to Abiraterone.

Clinical Research:

- Diabetes Mellitus E-Consultation Service (DMECS) is a new form of telehealth being pioneered by the VHA. It is unknown whether DMECS is an effective approach, since no outcome studies have been performed. We have established one of the first DMECS services of the country at the Houston VA. We have a number of retrospective and prospective studies organized to understand whether this new way of delivering DM care is effective, what are the mechanisms of success or of failure, and the impact on end points such as prevention of days of inpatient care, clinic visits, ER visits, and medication use.

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Research Interests

- Innovative Approaches to Diabetes Management: Diabetes mellitus is a multisystem disease of immense clinical impact and growing prevalence among veteran patients. The Veterans Health Administration (VHA) has been a pioneer in telehealth services to manage chronic diseases. I am currently investigating the role of teleconsultation in the management of diabetic veterans.

- Truncated Androgen Receptors in Prostate Cancer: The androgen receptor is involved in prostate cancer growth, and androgen-ablation therapy is the primary therapy if surgical therapy fails or is not an option. Androgen ablation therapy, however, invariably fails, and once PC has transitioned in to castrate resistance it may progress to a fatal outcome. The precise mechanism of castrate resistance remains controversial, but constitutively active truncated androgen receptor isoforms may play a role. I work in the Marcelli lab to investigate the role of truncated AR isoforms in castrate resistant prostate cancer.

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Research Interests

- Ketosis prone diabetes: We are investigating the etiology and pathogenesis of ketosis prone diabetes. We have categorized patients presenting with diabetic ketoacidosis based on the presence or absence of autoantibodies and beta cell function and have characterized and studied them longitudinally.
- Metabolic syndrome and heart failure: In collaboration with a cardiologist with heart failure expertise, we have investigated the benefits of collaborative care with focus on health education in patients with metabolic syndrome and heart failure.
- Bone and mineral metabolism disorders
- Endocrine complications in pregnancy

Publications

(1) Hampe C, **Nalini R**, Maldonado M, Garza G, Hall T, Balasubramanyam A. Association of Amino-terminal-Specific Antiglutamate Decarboxylase (GAD65) Autoantibodies with {beta}-Cell Functional Reserve and a Milder Clinical Phenotype in Patients with GAD65 Antibodies and Ketosis-Prone Diabetes Mellitus. J Clin Endocrinol Metab. 2007 Feb; 92(2):462-7.

(2) **Nalini R**, Maldonado M, Balasubramanyam A. A comparison of classification schemes for ketosis- prone diabetes. Nat Clin Pract Endocrinol Metab 2007 Dec; 3(12):E1.

(3) **Nalini R**, Gaur LK, Maldonado M, Hampe CS, Rodriguez L, Garza G, Lernmark A, Balasubramanyam A: HLA Class II Alleles Specify Phenotypes of Ketosis Prone Diabetes (KPD) Diabetes Care 2008 Jun;31(6):1195-200.

(4) Balasubramanyam A, **Nalini R**, Hampe CS, Maldonado M. Syndromes of ketosis prone diabetes. Endocrine Reviews 2008 May; 29(3):292-302.

(5) Haaland WC, Maldonado MR, Mansouri DL, **Nalini R**, Iyer D, Hampe CS, Balasubramanyam A, Metzker ML . The "A-β-" subtype of Ketosis-Prone Diabetes is not predominantly a monogenic diabetic syndrome. Diabetes Care. 2009 May; 32(5):873-7

(6) Shaw S, **Nalini R**: Celiac disease and Metabolic Bone Disease: Case Study. Endocrine News. July 2007

(7) **Nalini R**, Ozer K, Maldonado MR, Patel SG, Villanueva J, Rodriguez L, Hampe CS, Gaur LK, Balasubramanyam A. Presence or absence of a known DKA precipitant defines distinct syndromes of "A-β+" Ketosis-Prone Diabetes (KPD) based on long-term beta cell function, HLA class II alleles, and gender predilection. Metabolism, , 2010 Oct;59(10):1448-55

(8) Shahani S, Nudelman RJ, **Nalini R**, Kim HS, Samson SL. Ectopic corticotropin-releasing hormone (CRH) syndrome from metastatic small cell carcinoma: a case report and review of the literature**.** Diagn Pathol. 2010 Aug 31;5:56

(9) Balasubramanyam A, **Nalini R.** "Syndromes of Ketosis Prone Diabetes" in UpToDate: Updated May 2012.

(10) Carhill A, Gutierrez A, Lakhia R and **Nalini R.** Surviving the storm**:** two cases of thyroid storm successfully treated with plasmapheresis. BMJ Case Rep. 2012 Oct 19;2012

(11) Fernandez R, Misra R, Hampe C, **Nalini R**, Ozer K, Balasubramanyam A. Characteristics of Patients with Ketosis-Prone Diabetes (KPD) Presenting with Acute Pancreatitis: Implications for the Natural History and Etiology of a KPD Subgroup In press, Endocrine Practice 2012.

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Positions:
• Assistant Professor
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Clinical Research Interests

- Use of biomarkers and imaging in risk prediction and management of patients at risk for CVD
- Peripheral and multi-bed atherosclerotic disease.
- Diabetes and vascular disease: assessment of vascular function

Selected Publications (from 78):

1. Hyperglycemia and arterial stiffness: The Atherosclerosis Risk in the Communities study. Rubin J, Nambi V, Chambless LE, Steffes MW, Juraschek SP, Coresh J, Sharrett AR, Selvin E. Atherosclerosis. 2012 Sep 13. pii: S0021-9150(12)00616-8.

2. Nambi V, Boerwinkle E, Lawson K, Brautbar A, Chambless L, Franeschini N, North KE, Virani SS, Folsom AR, Ballantyne CM. The 9p21 genetic variant is additive to carotid intima media thickness and plaque in improving coronary heart disease risk prediction in white participants of the Atherosclerosis Risk in Communities (ARIC) Study. Atherosclerosis. 2012 May;222(1):135-7. Epub 2012 Feb

3.PMID:22349088 3. Yang EY, Chambless L, Sharrett AR, Virani SS, Liu X, Tang Z, Boerwinkle E, Ballantyne CM, Nambi V. Carotid Arterial Wall Characteristics Are Associated With Incident Ischemic Stroke But Not Coronary Heart Disease in the Atherosclerosis Risk in Communities (ARIC) Study. Stroke. 2011 Oct 27. [Epub ahead of print]

4. Saunders J*, Nambi V*,de Lemos J, Chambless L, Virani S, Boerwinkle E, Hoogeveen RC, Liu X, Astor B, Mosley T, Folsom AR, Heiss G, Coresh J, Ballantyne, CM Cardiac Troponin T Measured by a Highly Sensitive Assay Predicts Coronary Heart Disease, Heart Failure, and Mortality in the ARIC Study: Circulation. 2011 Apr 5;123(13):1367-76. Epub 2011 Mar 21 (* co-primary authors)

5. Carotid intima-media thickness and presence or absence of plaque improves prediction of coronary heart disease risk: the ARIC (Atherosclerosis Risk In Communities) study. Nambi V, Chambless L, Folsom AR, He M, Hu Y, Mosley T, Volcik K, Boerwinkle E, Ballantyne CM J Am Coll Cardiol. 2010 Apr 13;55(15):1600-7

6. Clinical implications of JUPITER (Justification for the Use of statins in Prevention: an Intervention Trial Evaluating Rosuvastatin) in a U.S. population insights from the ARIC (Atherosclerosis Risk in Communities) study. Yang EY, Nambi V, Tang Z, Virani SS, Boerwinkle E, Hoogeveen RC, Astor BC, Mosley TH, Coresh J, Chambless L, Ballantyne CM.J Am Coll Cardiol. 2009 Dec 15;54(25):2388-95

7. Obesity: an independent predictor of in-hospital postoperative renal insufficiency among patients undergoing cardiac surgery? Virani SS, Nambi V, Lee VV, Elayda MA, Pan W, Petersen LA, Wilson JM, Willerson JT, Ballantyne CM.Tex Heart Inst J. 2009;36(6):540-5.

8. Impact of adding a single allele in the 9p21 locus to traditional risk factors on reclassification of coronary heart disease risk and implications for lipid-modifying therapy in the Atherosclerosis Risk in Communities study. Brautbar A, Ballantyne CM, Lawson K, Nambi V, Chambless L, Folsom AR, Willerson JT, Boerwinkle E. Circ Cardiovasc Genet. 2009 Jun;2(3):279-85. Epub 2009 Apr 21.

9. Differences in responses of platelets to fluid shear stress in patients with peripheral artery disease (PAD) and coronary artery disease (CAD). Nambi V, Kimball KT, Bray PF, Bergeron AL, Johnson SL, Morrisett JD, Chen C, Lin PH, Lumsden AB, Ballantyne CM, Dong JF. Platelets. 2009 May;20(3):199-205

10. Lipoprotein-associated phospholipase A2 and high-sensitivity C-reactive protein improve the stratification of ischemic stroke risk in the Atherosclerosis Risk in Communities (ARIC) study. Nambi V,Hoogeveen RC, Chambless L, Hu Y, Bang H, Coresh J, Ni H, Boerwinkle E, Mosley T, Sharrett R, Folsom AR, Ballantyne CM. Stroke. 2009 Feb;40(2):376-81. Epub 2008 Dec 18.

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Research Interests

Behavioral and social science approaches to diabetes care in co-morbid patients

- Qualitative and survey research on diabetes self-management
- Testing of coach-led interventions for personalized self-management plans
- Rapid induction clinics for hypertension control in diabetes

Current Research Projects

VA Mental Health Funded Pilot Intervention

- Development and testing of a coach-led telephone intervention to improve diabetes and depression outcomes in rural-living comorbid veterans.

DDCF funded pilot intervention in Breast Cancer Survivors with Diabetes

- Development and testing of a coach-led telephone intervention to improve retention in care (cancer survivorship and diabetes) and diabetes outcomes in co-morbid breast cancer survivors.

Validation of a novel measure of goal-setting behaviors in chronically ill patients

- Analysis of data from a pilot RCT to validate a novel tool for measuring the quality of goal-setting in diabetes self-management.

Post-Doctoral Research Fellowships in Health Services Research

- Director of the fellowships and education program in HSR at the VA. Open to MDs/PhDs who have completed all their clinical training, are US citizens, and eligible to sit for any US board (for physicians).

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Research Interests

Role of Wnt signaling for beta cell development and function

- We currently have two mouse conditional knockouts – beta-catenin and transcription factor 7-like 2 (TCF7L2). Beta-catenin is an important co-factor of Wnt signaling and the transcription regulation of developmental and cell proliferation genes. TCF7L2 encodes a Wnt responsive transcription factor which recently has been found to be an important gene conferring risk for diabetes in humans. We are using beta-cell specific knockouts of these genes to understand their role in the islet responses to 1) insulin resistance and obesity, and 2) agents which induce beta cell proliferation. Through these studies, we hope to understand the cell signaling that fails when humans develop type 2 diabetes and how we may be able to harness these signals to increase beta-cell regeneration.

Glucagon-like peptide 1 receptor agonists in type 1 and type 2 diabetes models

- GLP-1 receptor agonists improve beta cell function in humans. In mouse models, they also increase beta cell proliferation, leading to improved glucose control in diabetic or obese mouse models. In addition, we have found that another important action is to decrease liver production of glucose and decrease hepatic steatosis. Our studies are designed to understand how GLP-1 analogues cause signaling in the liver to allow improvements in glucose both in mice and in cultured cells.

Research Projects Appropriate for Clinical Fellows and Residents:

- The conditional knockouts (TCF7L2 and beta-catenin) are being used in specialized diet studies which have a definite timeline and could be started and completed with physiologic studies in vivo and analysis of tissues and blood samples within a 1-2 year period, including writing and publishing the data.

Select Publications

1. Samson SL*, Sathyanarayana P*, Jogi M, Gonzalez EV, Absalon Gutierrez, Ramkumar Krishnamurthy, Raja Muthupillai, Chan L, Bajaj M. Exenatide decreases hepatic fibroblast growth factor 21 resistance in NAFLD. 2011. *Diabetologia* 54:3093-100. PMID: 21956711 (*co-first authors).
2. Sathyanarayana P, Jogi M, Muthupillai R, Samson S, Bajaj M. 2011. Effects of combined Exenatide and Pioglitazone therapy on hepatic fat content in Type 2 diabetes. *Obesity* 19: 2310-2015. PMID: 21660077
3. Samson SL. 2011. Incretin therapies for type 2 diabetes: the liver takes a bow. *Treatment Strategies: Diabetes.* 3: 93-97.

4. Yang Y, Chang BH, Samson SL, Li MV, Chan L. 2009.The Krüppel-like zinc finger protein Glis3 directly and indirectly activates insulin gene transcription. *Nucleic Acids Res*. 37:2529-38. PMID: 19264802.
5. Samson SL, Kohjima M, Chan L. 2009. News and commentary: A fine balance - an autoregulatory gene therapy approach to treat obesity and achieve energy homeostasis. *Gene Therapy: 16: 1175-1177.* PMID: 19626055.
6. Yechoor V, Liu V, Paul A, Burras EB, Ozer K, Samson SL, and Chan L. 2009. Hepatic gene therapy with Neurogenin3 and betacellulin reverses all the major metabolic derangements in insulin-deficient diabetic mice. *Endocrinology.*105: 4863-73. PMID:19819964.
7. Samson SL, Gonzalez EV, Yechoor V, Oka K, Bajaj M, Chan L. 2008. Gene therapy for diabetes: Metabolic effects of helper-dependent adenoviral expression in a diet induced obesity model. *Mol Ther*.18:1605-1612 PMID: 18781141.
8. Samson SL, Chan L. 2006. Gene therapy for diabetes: Re-inventing the islet. *Trends Endo Met*. 17: 92-100. PMID: 16504534

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Research Interests

- I am interested in understanding how abnormalities in fuel and energy metabolism lead to insulin resistance, obesity and dyslipidemia in diabetes, HIV and aging. Out approach is to 'think outside the box' to test ideas, and our research approach typically begins at the bedside in humans, and is complemented by animal models in the lab, where we identify mechanisms and test interventions, before applying these to human studies in a 'translational' approach. Our focus is in the following areas:
- **Role of glutathione on impaired mitochondrial fuel oxidation:** we have found that glutathione, a vital endogenous antioxidant, is critically important for mitochondrial health. Glutathione deficiency results in mitochondrial dysfunction and predisposes to obesity and insulin resistance, and correction of glutathione deficiency reverses these defects. We are currently conducting a human study to investigate the role of glutathione on correcting these defects in elderly humans.
- **Diabetic microvascular complications:** if hyperglycemia is the only cause for diabetic complications, why was the reduction in the risk of developing microvascular complications not higher than 60% (DCCT) or 35% (UKPDS)? We are investigating innovative strategies independent of glycemic controls in preventing diabetic micovascular complications.
- **Metabolic complications of HIV:** Why do patients with HIV develop obesity and lose muscle stength? We are investigating novel defects in fat, glucose and protein metabolism which can provide a unifying solution to the multiple metabolic defects afflicting HIV infected patients.

Why should you consider joining our lab?

Research training at your level is very important, especially if you want an academic career. In these two years you need to build a solid foundation on which to base your research career. In my lab you will be in charge of your own project from beginning to completion. This will permit you to not only acquire valuable experience in how to conduct research, but also the joy of beginning independent thinking and development of your own ideas in a friendly, productive and cooperative environment. If metabolism and translational research focused on finding solutions to human health and disease is something that interests you, then we are a lab you should consider.

RENA SELLIN, MD

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Research Interests

- Thyroid and adrenal neoplasms

Research Projects

- I am currently a part-time faculty member, and do not have active individual projects. However, I continue to collaborate with other faculty in clinical projects related to thyroid and adrenal neoplasms. I would not be a primary mentor to a fellow or resident at this point, but I am available to participate in projects with other faculty and provide joint mentorship.

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Research interests:

- Opportunities to write reviews on:
    1. Management of thyroid nodules
    2. Diagnosis and treatment of pituitary tumors and hypopituitarism

STEVEN I. SHERMAN, MD

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Research Interests

- Novel Therapeutics for Advanced Thyroid Cancers: Recent advances in understanding the role of signaling kinases in oncogenesis and tumor progression of thyroid carcinomas has led to identification of attractive targets for therapy. We have demonstrated the utility of multi-targeted kinase inhibitors to lead to durable tumor control in patients with both metastatic differentiated thyroid carcinoma and medullary carcinoma. Future efforts will continue to target angiogenesis through inhibition of VEGF receptors, but additional kinases that will be targeted in clinical trials include oncogenic BRAF mutants.
- Circulating Tumor Cells (CTCs) in Thyroid Cancers: The presence of CTCs is associated with a poor prognosis in breast, prostate and colon cancer, because they are believed to be the primary mediator for development of hematogenous metastases. We have recently demonstrated the feasibility to detect CTCs using immunomagnetic separation systems in the blood of patients with medullary thyroid carcinoma. Further studies will focus on identifying the prognostic value of these findings in both newly diagnosed patients as well as those entering clinical trials for advanced disease. A secondary goal is to identify methods to extract CTCs from blood that permit additional analysis of gene expression and mutations as biomarkers to disease biology as well as response to treatment.
- National Thyroid Cancer Treatment Cooperative Study: Through creating a large, multicenter registry of >5000 patients with thyroid cancer, we study the outcomes of patients with both low risk and high risk presentations of thyroid cancer to understand the roles of primary interventions of surgery, radioiodine, and thyroid hormone. Further analyses to be undertaken will focus on the predictive value of diagnostic testing modalities during the first few years of patient follow-up, as well as the long-term need for continued TSH-suppressive therapy for patients with differentiated thyroid carcinoma.

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Research Interests

- Diabetes management in the cancer patient
- General endocrinology

Current Projects

- Quality improvement projects for inpatient diabetes service

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Research Interests

- Pediatric Thyroid Cancer
- Multiple Endocrine Neoplasia Syndromes

Research Projects

- I am developing a multicenter database for the study of pediatric thyroid tumors. I aim to study the clinical, pathological, etiological, and treatment differences between children and adults with thyroid cancer. As part of a collaborative effort, I also hope to study the clinical presentations and treatment of the multiple endocrine neoplasia syndromes, in order to better clarify optimal screening strategies in MEN1 and timing of prophylactic thyroidectomy in MEN2.

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Research Interests

- Cell and Gene therapy of diabetes mellitus: We have demonstrated that it is possible to cure insulin deficient diabetes in diabetic mouse models by inducing the formation of new insulin secreting islets in the liver with gene therapy using islet developmental genes. However, this therapy does not work in the autoimmune setting as the newly generated islets are also destroyed. We are now working on ways to circumvent this by engineering islets with gene therapy that can resist the autoimmune attack. We are also working on identifying the mechanisms that are involved which result in adult stem cells differentiating into islet beta cells and apply it towards potential cell therapy for diabetes.

- Islet function and dysfunction in diabetes: We are investigating the mechanisms that underlie an inability of the islets to compensate for increasing peripheral insulin resistance resulting in type 2 diabetes.

- Circadian control of islet function: The circadian clock regulates many metabolic processes including islet function and a disruption of this leads to diabetes and metabolic syndrome. Using gene knockout mouse models we are investigating the mechanisms that underlie this regulatory control.

ANITA K. YING, MD

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Clinical interests

- MEN syndromes, thyroid cancer in adults and children, endocrine sequelae of childhood cancers.

Research interests

- Clinical effectiveness, quality and process improvement

Research projects

- "Post op calcium algorithm, applying LEAN principles to clinic and new patient scheduling processes"

OTHER MENTORS (Molecular Endocrinology Training Grant)

Trainees in the Division of Diabetes, Endocrinology and Metabolism also have access to mentors, resources and projects under the umbrella of a long-standing NIH T32 Training Grant, the "Molecular Endocrinology Training Grant". This program is for endocrine residents and fellows who desire intensive training (usually at least 2 years in duration) in various aspects of molecular endocrinology. Several of the faculty listed above are also participants in this program. In addition, the following mentors / labs listed below are available to residents and fellows interested in intensive training in molecular endocrine-related research. Please visit their websites for more information regarding their research.

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