TRAINING PROGRAMS IN ENDOCRINOLOGY, DIABETES AND METABOLISM

DEPARTMENT OF MEDICINE
THE UNIVERSITY OF TENNESSEE
HEALTH SCIENCE CENTER
MEMPHIS, TENNESSEE USA 38163

Objectives: The training programs in endocrinology, diabetes and metabolism are designed to develop the skills and attitudes necessary to perform basic and clinical research and to practice clinical endocrinology and diabetes.

Qualifications of Candidates: Applicants for the clinical program who are graduates of United States or Canadian medical schools must have completed at least three years of approved residency training in internal medicine. Foreign medical graduates will not be eligible generally for appointment unless they have completed three years of IM Residency in an approved program in either the United States or Canada. Occasional exceptions may be made in these requirements for outstanding candidates.

Candidates for the NIH-sponsored research programs must have an M.D. or Ph.D., or an equivalent degree, be a U.S. citizen or permanent resident, and be committed to an academic career.

Training Programs Available:
One program is supported by institutional funds. Typically, this program involves two years of predominantly clinical training. Research opportunities, however, will be available during the first year of training and all candidates remaining in the program more than one year will be expected to participate in research. The research activity may be either clinical or basic, or involve a combination of both.

The second program is sponsored by the granting agency and is for the support of individual research training. This is generally a two-year program that is primarily research oriented, although clinically trained individuals will have ample opportunity for maintaining and furthering clinical skills.

Clinical Training: Facilities available for clinical training include Methodist University Hospital (MUH), The Regional Medical Center (MED), the Veterans Administration Medical Center (VAMC), and the outpatient facilities of these institutions. The MED has facilities for both indigent and private patients of the staff of the University of Tennessee. In addition, MUH includes an NIH supported Clinical Research Center which has outpatient and inpatient scatter beds where challenging endocrine issues are studied in depth. This facility, in addition, maintains state-of-the-art equipment for euglycemic clamp and indirect calorimetry equipment.

The clinical trainee will rotate through the VAMC, the MED and MUH. General endocrinology outpatient clinics meet two ½ days per week at VAMC and the MED. In addition, 3-4 private endocrine clinics of the faculty are held at the UT Medical Group offices. Consultation rounds are held twice a week at each institution for the residents and fellows assigned to that institution. At the VAMC a weekly conference is held prior to the outpatient clinic. In addition, a bi-monthly endocrine teaching conference is held for students and general house staff. At UTHSC, an endocrine teaching conference for students, house staff and fellows is held once a week. In addition, tutorial lecture series are held once a week covering a broad range of endocrine topics.

The VAMC serves as a referral center for a five-state area and has an excellent selection of endocrine case material. A consultative service is maintained for complicated diagnostic and therapeutic studies. The VAMC also includes a dedicated RIA endocrine laboratory, a euglycemic clamp facility and research laboratories including facilities for recombinant DNA work.

An active liaison is maintained with the Pediatric Endocrine and Metabolic sections at LeBonheur Children's Medical Center, The West Clinic, and the Section of Reproductive Endocrinology of the Department of Obstetrics and Gynecology at UTHSC. Fellows attend clinics of these services at least three months during their training.

All fellows will be offered courses in ethics and biostatistics at the beginning of their rotation.

An integrated conference, Endocrine Grand Rounds, is held weekly and covers gynecological endocrinology, pediatric endocrinology and neuroendocrinology as well as general endocrine and metabolic topics. A Journal Club covering both basic and clinical journals is also held once a week. A Research Seminar is held once a month.

Research Training: Research experience is an essential component of the training for a qualified endocrinologist. For individuals who plan to become primarily practicing endocrinologists, involvement in research will greatly enhance their clinical abilities. For those individuals who plan to continue a research career, an intensive training in research will provide a solid foundation on which to build.

Laboratory Facilities for basic and clinical investigation at the University of Tennessee Health Science Center consist of a well-equipped four-room laboratory located in the Coleman Building on the UT Health Science Center (UTHSC) campus in Memphis with all of the necessary equipment to carry out molecular biological, biochemical, and immunologic assays. There is a well-established storage system to preserve clinical samples (plasma, RNA, DNA). The UT Molecular Resource Center is located in the adjacent area to the principal investigator's laboratories and provides easy access to flow cytometers, ABI 7900 for quantitative PCR, DNA sequencing and mutation detection equipment. Some of the equipment in the

investigator's lab includes: microplate reader for ELISA, cell probe labeling, etc., assays with O. D., fluorescent and glow chemiluminescence capabilities; thermal cyclers for PCR & RT-PCR; gel (agarose and polyacrylamide) 1 and 2-D electrophoreses and blotting equipment; gel scanner-viewer; -80°C & -20°C freezers and refrigerators; DPC Immulite Analyzer; incubators; Olympus CK-2 microscope and inverted microscope; a PE HPLC with gradient pump system, diode array detector and data analysis software; refrigerated and laboratory centrifuges, Savant Speedfuge, Eppendorf microcentrifuge, and Beckman refrigerated high speed centrifuge; Bio Rad Fluor-S Imager; 2 Nuaire CO_2 incubators; Milli Q Water System; Coulter AcT diff cell counter; and biological safety hoods.

Evaluation: At the beginning of training, each fellow will be asked to take the Pathophysiology examination in order to assess the basic knowledge in endocrinology and metabolism and to provide a guideline as to the area in which additional basic knowledge needs to be enhanced. Each fellow will be evaluated for his/her performance and clinical knowledge at the end of each rotation (two or three months) by the attending staff. These evaluations will be reviewed by the Executive Committee with each fellow biannually. In addition, each year a formal examination, both oral in the form of a seminar, and written, is administered to the fellows. The results of these evaluations and examinations are used to apprise the fellows of their eligibility for the Endocrinology Board examination.

Appointments: Appointments are made for one year and may be renewed for up to two additional years. Stipends are commensurate with training and experience and conform to the University of Tennessee's guidelines.

The University of Tennessee is an equal opportunity employer.

Following is the list of selected faculty members who have active research programs:

ONGOING RESEARCH PROGRAMS

Abbas E. Kitabchi, Ph.D., M.D., Division Director

1. *Diabetes Prevention Program (DPP):* A multi-center NIH Sponsored (10 year) trial to investigate effects of 3 arm interventions (placebo, metformin or intense lifestyle [ILS]) on conversion of patients with impaired glucose tolerance (IGT) and high risk to diabetes and its long term follow-up studies (DPPOS) on cardiovascular events by the use of the 3 arm interventions *(Diabetes 54:2404-2414; Diabetes Care 29:1997-2002, 2006).*

2. *Mechanisms of Action of Treatment in DPP: An NIH supported program* (RO1 DK53061) multicenter grant inquiring into the role of ethnicity and gonadal (testosterone and androstenedione) versus adrenal (DHEA, DHEAS) androgens in regard to premenopausal IGT patients' response to three arm interventions of the DPP. *(Diabetes Care 22:1524-1529, 1999)*

3. *Action for Health in Diabetes (Look AHEAD):* A 11.5 year multi-center NIDDK funded grant to study various interventions for weight reduction in type 2 DM and effects of these on cardiovascular events as compared to a control group without such interventions. (U01DKES57078) *(Diabetes Care 30: 1374-83, 2007)*

4. *Mechanisms of Action of Insulin in Insulin Resistant State:* Using human isolated T-lymphocytes (T-cells) before and after activation by PHA we have demonstrated that activated cells metabolize insulin similar to human fibroblasts to smaller A and B chain peptides (J Biol Chem 1989; 264:20275-20282). Some of these intermediates have been synthesized and have been injected into the cells by electroporation to study their effects on insulin action. These intermediates are shown to stimulate DNA synthesis, protein synthesis and cytokine production (Current Drug Targets 4:493-503, 2003). The proposed studies will inquire into the role of these intermediates in PHA-activated T-lymphocytes from various insulin resistant states individuals such as obesity and PCOS. This is done in collaboration with Dr. Frankie Stentz.

5. *Effect of hyperglycemia and hyperlipidemia on denovo emergence of growth factor receptors (insulin, IGF, and IL2) in human T-lymphocyte (T-cells) and endothelial cells (E-cells).* We have demonstrated that in vivo condition characterized by hyperglycemia or hyperlipidemia such as DKA is associated with activation of T-cells in vivo *(Biochem Biophys Res Commun 315:404-7, 2004 & Diabetes 53:2079-2086, 2004).* To further investigate mechanism of this phenomenon we studied effect of high glucose on T-cells (Biochem Biophys Res Commun 335:491-495, 2005) and endothelial cells *(Am J Physiol Endocrinol Metab 290:E516-E522, 2006)* as well as effect of palmitate and unsaturated fatty acids on both T-cells and endothelial cells (Biochem Biophys Res Commun 346:721-726, 2006). This study clearly demonstrated that both high glucose and high palmitate (but not unsaturated fatty acids) activate T and E-cells by generation of reactive oxygen species (ROS) lipid peroxidation and conversion of these non-insulin responsive cells to insulin responsive cells.

6. *Use of Bicarbonate in the Treatment of Severe DKA: A Prospective Randomized Trial.* Effectiveness of NaHCO3 is being studied in severe diabetic ketoacidosis (DKA). These patients (with pH < 7.0) will be admitted to ICU and randomized to receive IV bicarbonate or saline control. Their cardiac states will be monitored by the use of portable echocardiogram and compared in the two groups. In addition, the efficacy of bicarbonate in recovery and outcome of DKA by measuring various clinical and biochemical parameters during treatment of these patients will be assessed.

7. *Factors Affecting Ketogenesis in Diabetic Ketoacidosis (DKA) and Hyperglycemic Hyperosmolar State (HHS).* One major unresolved problem in pathogenesis of DKA vs HHS regardless of low levels of serum insulin and high levels of counter-regulatory hormones in both, is that HHS is characterized by low levels or absence of ketoacidosis *(Diabetes Care 24:131-154, 2001).* We propose to measure biochemical parameters in patients with DKA and HHS at baseline, including C-peptide, free insulin, counter-regulatory hormones, ketone bodies, leptin, FFA and lipid panel, pyruvate and lactate, as well as C- peptide in response to IV glucagon after recovery from DKA and HHS. These studies for the first time will provide us with available information on important components responsible for ketogenesis or lack of it in these two conditions. *(J. Clin. Metabol., In Press 2008)*

8. *ACTOS NOW for Prevention of Diabetes ("ACT NOW"):* This is a multi-center prospective double blind randomized protocol to study efficiency of Actos in prevention of diabetes in subjects with impaired glucose tolerance.

9. *Glucommander Study: Comparative Trial Between Computer-Guided Intravenous Infusion Protocol (Glucommander) Versus a Standard Insulin Infusion Algorithm in the ICU*. This protocol is used in any patients with admitting blood glucose of >140 mg/dl excluding those on insulin therapy, in DKA or hyperosmolar state. *(Metabolism 57: 116-120, 2008)*

10. *Effect of diet composition on weight change and metabolic parameters in premenopausal obese women without prediabetes or diabetes.* The aims of this project are to 1) Compare the effects of high protein (HP) vs. high carbohydrate (HC) diet during energy restriction on weight loss and body composition (lean and fat body mass) and bone mineral density in a free living outpatient setting and 2) to assess the effect of HP vs. HC on metabolic parameters including insulin sensitivity, protein and lean muscle metabolism, lipoprotein metabolism and degree of oxidative stress and activation of T-lymphocytes during oral glucose tolerance and the two meal tolerance tests.

11. *Risk of New Onset Diabetes in Men Undergoing Androgen Deprivation Therapy (ADT)* for prostate cancer and protective effect of Vitamin D on risk of developing new diabetes (British Journal of Urology Int. 100: 1060-1065, 2007)

Solomon S. Solomon, M.D., Section Chief, VAMC

1. *Pathogenesis of Diabetes Mellitus: Studies of Insulin Action and Calmodulin:* This is a VA Merit Review Grant in which pathogenesis of DKA is studied and involves the mechanism by which insulin stimulates Calmodulin, an activator of PDE. These effects are transcriptional and involve the transcription factor Sp1. (J. Biol. Chem. 281 (16): 3642, 2006)

2. *Tumor Necrosis Factor-alpha (TNF-α) in Insulin Resistance of Obesity and NIDDM:* Role for biguanides and thiozolidinediones. TNF-α, a cytokine induces insulin resistance in animals and is implicated in insulin resistance in NIDDM. We have been able to induce insulin resistance in tissue culture of rat liver cells, using TNF-α. (J Lab Clin Med 130:139-146, 1997, also editorial). Using metformin or pioglitazone in the presence of insulin, we have reduced the insulin resistance by 50-100%. Current experiments involve both troglitazone and roseglitazone.

3. *Mechanisms of Tumor Necrosis Factor-alpha (TNF-α) Induction Insulin Resistance (IR):* Using the discovery science approach (proteomics), work from our laboratories has identified 13 unique proteins involved in IR in the TNF-α model. (J. Lab. Clin. Med 145:275, 2005). We have recently extended this approach to the use of genomics, or gene chips, and have identified 108 unique genes in 7 different networks (J. Invest. Med. 55(1): S297, 2007 abstract). We hope to continue this work reversing the IR with thalazolidindiones and metformin, as we have already shown (Horm. Met. Res. 29(8): 379, 1997) and analyzing both proteome/genome before and after treatment.

4. *BARI-2D.* Dr. Solomon is the Diabetes PI on the local site for BARI (Bypass Angioplasty Revascularization Investigation in DM2).Similarly, Dr .Dale Childress is the co-PI on the ACCORD(Action to Control Cardiovascular Risk in Diabetes) study. These clinical trials are both active at VA Memphis.

5. *NIH (NIDDK) Short Term Medical Students Research Training grant.* This grant is in its 27th year of operation under Dr. Solomon's direction and offers research opportunities to UT medical students.

Samuel Dagogo-Jack, M.D., FRCP

1. *Pathobiology of Prediabetes in A Biracial Cohort (POP-ABC):* This is a 5-yr NIH-funded study initiated in 2006. The overall objective of POP-ABC is to understand the predictors of progression from normoglycemia to prediabetes in African-Americans and Caucasians at high risk for development of type 2 diabetes. We wish to test the hypothesis that ethnic disparities manifesting during the earliest stages in the pathogenesis of type 2 diabetes result in a higher rate of progression from normal glucose tolerance (NGT) to prediabetes in African-Americans than Caucasians. The project is organized under 4 specific aims: 1) To compare the rate of progression from normal glucose tolerance to prediabetes (IFG or IGT) between African-American and Caucasian offspring of type 2 diabetes parents during a 5-year follow-up period; 2) To determine whether progression from normal glucose tolerance to prediabetes is influenced by a) accumulation of body fat; b) impairment in insulin action; c) beta cell dysfunction, and d) socioeconomic status. 3) To determine whether progression from normal glucose tolerance to prediabetes is associated with a) alterations in energy expenditure; b) expression of proinflammatory markers; and c) dysregulation of leptin and other adipocytokines. and 4) To determine whether progression to impaired fasting glucose is associated with a) accumulation of components of the metabolic syndrome; b) impairment in insulin action; and c) beta cell dysfunction.

Our ultimate goal is to understand the natural history and determinants of ethnic disparity during transition from NGT to prediabetes. By studying African-American and Caucasian offspring of parents with type 2 diabetes, we hope first to establish whether ethnic disparities exist at the earliest stages of glucose impairment, and then dissect the pathophysiologic mechanisms that drive the progression from NGT to prediabetes. Of equal importance is understanding the protective mechanisms that predict long-term maintenance of normoglycemia in high risk subjects. Because an interplay of protective genetic and environmental factors may be involved, we plan to collect specimens for future genomic and proteomic analyses. Thus, our proposed studies will add fundamentally to current understanding of the pathobiology and natural history of the earliest stages of dysglycemia, while simultaneously assessing the role of ethnic disparities.

2. *Metabolic Significance and Regulation of Leptin in Humans:* Our overall objective is to understand the hormonal and metabolic regulation of leptin in humans and the pathophysiologic significance of aberrant regulation, especially with regard to obesity and the related disorders of insulin resistance, impaired glucose tolerance (IGT), and diabetes. Another is to expand knowledge of hormonal interaction in the context of adaptations to intermediary metabolism and bioenergetics in directions relevant to human disease. Studies from Dr. Dagogo-Jack's lab have shown I) that glucocorticoid regulation of human leptin is expressed rapidly, dose-dependently, and in proportion to intrinsic glucocorticoid potencies, and ii) that regulation of leptin by glucocorticoids is defective in diabetes. Current studies focus on exploring the mechanism, physiological significance and reversibility of the impaired leptin secretion in

diabetes. (Supported by American Diabetes Association clinical research award.)

3. *The Epidemiology of Diabetes Interventions and Complications (DCCT-EDIC):* This 10-year study is an ancillary study to the landmark Diabetes Control and Complications Trial (DCCT) in which tight control of diabetes mellitus was shown to prevent or retard the development of microvascular complications. DCCT participants are being followed for additional evaluation of pertinent metabolic, systemic and molecular genetic endpoints relevant to diabetes complications.

4. *A multinational, randomized, double blind, placebo-controlled, forced-titration, 2x2 factorial design study of long term administration of nateglinide and valsartan in the prevention of diabetes and cardiovascular outcomes in subjects with impaired glucose tolerance (IGT*). This study, which will run from September 2001 through September 2009, is supported by a grant from Novartis Pharmaceuticals Corporation.

Ivan C. Gerling, Ph.D.

1. *Experimental studies on function of human islets in a physiological environment:* Human islets are isolated from cadaveric donors and placed under the renal capsule of immunodeficient NOD-scid mice. The mice provide a relatively normal physiological environment for the human tissue. The final goal of this project is to develop new procedures and treatments, of patients or islets, that can improve the engraftment and function of human islets transplanted into diabetic patients. (Supported by a 4-year ADA grant.)

2. *Comprehensive molecular characterization of tissue in disease and health.* This project attempts to use the latest modern technologies, "expression arrays" (gene chips) and "proteomics", to compare the complete molecular structure of health and diseased tissues. This comparison is conducted both at the gene expression (mRNA) level and at the protein level. A comprehensive knowledge of molecular differences between the state of health and the state of disease will help both in understanding the processes leading to disease and in finding new therapeutic targets. (Supported by NIH RR15373)

Recent Publications:

Wu J, Lenchik N, Pabst MJ, Solomon SS, Shull J, Gerling IC. Functional characterization of two-dimensional gel-separated proteins using sequential staining. Electrophoresis 2005; 26: 225-37.

Gerling IC, Singh S, Lenchik NI, Marshall DR, Wu J. New data-analysis and mining approaches identify unique proteome and transcriptome markers of susceptibility to autoimmune diabetes. Mol Cell Proteomics 2006; 5:293-305.

Cesar Magsino, Jr., MD

Research Interests:
Neuroendocrinology
Methods of Evaluating Pituitary Functions in Hormonally Challenged Patients

Ebenezer A. Nyenwe, MD

1. *Glucommander Study: Comparative Trial Between Computer-Guided Intravenous Infusion Protocol (Glucommander) Versus a Standard Insulin Infusion Algorithm in the ICU*. This protocol is used in any patients with admitting blood glucose of >140 mg/dl excluding those on insulin therapy, in DKA or hyperosmolar state. *(Metabolism 57: 116-120, 2008)*

Harold Sacks, M.D.

Human Epicardial Adipose Tissue: A Review.

We discuss the anatomy, physiology, and pathophysiology of epicardial adipose tissue and its relationship to coronary atherosclerosis. Epicardial fat stores triglyceride to supply free fatty acids for myocardial energy production and produces adipokines. It shares a common embryological origin with mesenteric and omental fat. Like visceral abdominal fat, epicardial fat thickness, measured by echocardiography, is increased in obesity. Epicardial fat could influence coronary atherogenesis and myocardial function because there is no fibrous fascial layer to impede diffusion of free fatty acids and adipokines between it and the underlying vessel wall as well as the myocardium. Segments of coronary arteries lacking epicardial fat or separated from it by a bridge of myocardial tissue are protected against the development of atherosclerosis in those segments. However, when epicardial fat is totally absent in congenital generalized lipodystrophy, coronary atherosclerosis can still occur. Macrophages are more numerous and densely packed in the periadventitial fat of human atherosclerotic coronary arteries with lipid cores than in that of fibrocalcific or nonatherosclerotic coronary arteries. In obese patients with multiple cardiovascular risk factors, epicardial fat around atheromatous coronaries secretes several proinflammatory cytokines and is infiltrated by macrophages, lymphocytes, and basophils. Epicardial adipokine expression in obesity without coronary atherosclerosis has not been determined. In nonobese patients, epicardial fat around atheromatous coronary arteries expresses proinflammatory cytokines but produces either less adiponectin, a vasoprotective adipokine, than fat around nonatheromatous coronaries or a similar amount compared with thoracic subcutaneous fat. Further studies should be done to test the hypothesis that adipokines produced by and released from human epicardial adipose tissue might contribute locally to the pathogenesis of coronary atherosclerosis. *Am Heart J. 2007 Jun;153(6):907-17*

Burt M. Sharp, M.D.

Two major areas of interest 1) the basic neuro-chemistry and molecular neurobiology of nicotine and (2) cellular and biochemical approaches to understand the action of opioid peptides on the immune system.

The nicotine research uses in vivo microdialysis coupled with measurements of biogenic amines and excitatory amino acids to understand both the neurochemical basis for addiction to nicotine and the beneficial therapeutic effects of nicotinic agonists on hypothalamic and hippocampal function. In many of these studies, nicotine is delivered acutely through intra-jugular catheters and cannulae that are chronically implanted in specific CNS sites. Animals also learn to self-administer nicotine through operant conditioning that mimics human smoking. In vivo microdialysis in these self-administering animals permits analysis of changes in brain neurochemistry and direct correlation of these with drug-dependent behavior. Using RT-PCR, analyses are made of specific gene expression in micropunched areas of brain. Similarly, in situ hybridization analyses are used to characterize the effects of nicotine self-administration on short and longterm changes in CNS gene expression. NIH support - USPHFGRDA 04196-13.

Dr. Sharp's research on opioid immunobiology seeks to understand the cellular and molecular basis for the modulatory effects of opiates and opioid peptides on lymphocytes, specifically T-cells. Using fluorescence flow cytometry and RT-PCR, his lab is characterizing the expression of delta opioid receptors on specific subsets of T lymphocytes. Biochemical and immunological approaches (e.g.,

immunoprecipitation, Western immunoblotting, receptor binding, etc.) are used to elucidate the signal transduction pathways that mediate the anti-proliferative actions of delta opioid receptors on T-cells. Their current focus is on the role of mitogen-activated protein kinases (MAPKs) in opioid signaling, as this pertains to the effects of opioids on MAPK-dependent interleukin-2 production. . NIH Support - USPHFGRDA 03977-16.

Frankie Stentz, Ph.D

1. *Genomic and Proteomic Studies in Activated T-Lymphocytes and Muscle Tissue in Human Subjects with and without Type 2 Diabetes* (GCRC 741) :
The major goal of this study is to determine the genes activated, transcribed and translated during T-lymphocyte activation and the differences in this activation between normal and type 2 diabetic subjects and compare this to muscle tissue in these subjects.

2. *Mechanisms of Action of Insulin in Insulin Resistant State:* Using human isolated T-lymphocytes (T-cells) before and after activation by PHA we have demonstrated that activated cells metabolize insulin similar to human fibroblasts to smaller A and B chain peptides (J Biol Chem 1989; 264:20275-20282). Some of these intermediates have been synthesized and have been injected into the cells by electroporation to study their effects on insulin action. These intermediates are shown to stimulate DNA synthesis, protein synthesis and cytokine production (Current Drug Targets 4:493-503, 2003). The proposed studies will inquire into the role of these intermediates in PHA-activated T-lymphocytes from various insulin resistant states individuals such as obesity and PCOS. This is done in collaboration with Dr. Abbas Kitabchi.

3. *Effect of hyperglycemia and hyperlipidemia on denovo emergence of growth factor receptors (insulin, IGF, and IL2) in human T-lymphocyte (T-cells) and endothelial cells (E-cells).* We have demonstrated that in vivo condition characterized by hyperglycemia or hyperlipidemia such as DKA is associated with activation of T-cells in vivo *(Biochem Biophys Res Commun 315:404-7, 2004 & Diabetes 53:2079-2086, 2004).* To further investigate mechanism of this phenomenon we studied effect of high glucose on T-cells (Biochem Biophys Res Commun 335:491-495, 2005) and endothelial cells *(Am J Physiol Endocrinol Metab 290:E516-E522, 2006)* as well as effect of palmitate and unsaturated fatty acids on both T-cells and endothelial cells (Biochem Biophys Res Commun 346:721-726, 2006). This study clearly demonstrated that both high glucose and high palmitate (but not unsaturated fatty acids) activate T and E-cells by generation of reactive oxygen species (ROS) lipid peroxidation and conversion of these non-insulin responsive cells to insulin responsive cells.

Lester VanMiddlesworth, Ph.D., M.D.

1. *Natural Radioactive Isotopes in Human Thyroid Glands.*

2. *Thyroid Function During Pregnancy.*

Supported by grants from:

1. National Cancer Institute.
2. UT Medical Group.

Beverly J. Williams-Cleaves, M.D.

1. *UTHSC VITAMIN D DEFICIENCY(VitDD) PROJECT:* VitDD appears to be present in nearly epidemic proportions in some populations. Obviously, further studies are necessary to document the true prevalence of this finding. In our preliminary studies looking at the sickle cell (SCD) population and a general endocrine population (GEP) here at UTHSC, the percentages of deficiency were 98.6 and 100, respectively. However, if the prevalence is only half of what it proved to be in the preliminary UTHSC Project, there are potentially broad implications for the many at risk and for the entire US population. Vit D, especially in the Vit D(1,25) form is being associated with metabolic and immunologic effects that expand its already important benefits known in calcium, bone and connective tissue metabolism. Therefore, at UTHSC, we are proposing a campus-wide prevalence survey, as we begin to try to define mechanisms in the SCD population, so severely affected and look at the broader possible needs for public health intervention.

2. *"Enhance the Metabolic Profile of Women With Insulin Resistance (EMPOWIR)"*: This study is designed to evaluate the efficacy of three treatment protocols in improving insulin sensitivity, preventing weight gain, and reducing visceral adiposity in African American, Hispanic, South Asian and other high-risk populations. The study will compare the effect of a carbohydrate modified diet alone and in combination with metformin (MF) and Avandamet (metformin plus rosiglitazone (RSG) on insulin parameters in a wide range of ethnically and economically diverse non-diabetic women (aged 35-55) who meet study selection criteria, seen at three academic medical centers: The Hispanic Center of Excellence and The Menopause Research and Treatment Center at Albert Einstein College/Montefiore Hospital Diabetes Center; The Diabetes Center of Excellence at the MedPlex, Ground Floor, a part of the Regional Medical Center, affiliated with the University of Tennessee Health Science Center and the Center for Diabetes and Endocrine Care at New York Medical College/Westchester Medical Center and other affiliated practices. All women will receive the calorie-reduced, carbohydrate modified (sugar restricted, low glycemic index) diet, based on large servings of vegetables, fruits, low fat proteins and dairy products and limited refined carbohydrates and treats.

3. *Hypopituitary Complications and Control Trial (HypoCCS):* This is a 5-7 year drug treatment assessment of Growth hormone in growth hormone-deficient adults.

4. *Regional Variance in the Prevalence of Non-Classical Congenital Adrenal Hyperplasia 21-OH'ase Deficiency vs. 3 B' Hydroxysteroid Dehydrogenase Deficiency.*

For further information regarding our fellowship program, address inquiries to:
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Samuel Dagogo-Jack, M.D., F.R.C.P. Professor of Medicine; Fellowship Training Director; and Associate Director, GCRC

Solomon S. Solomon, M.D., Professor of Medicine and Pharmacology & Section Chief, VAMC

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Cesar Magsino, Jr., M.D., Asst. Professor of Medicine, Section Chief, Methodist University Hospital

Ivan C. Gerling, Ph.D., Professor of Medicine

Burt M. Sharp, M.D., Professor of Medicine and Chair, Department of Pharmacology

Thomas A. Hughes, M.D., Professor of Medicine

Ebenezer Nyenwe, M.D., Assistant Professor of Medicine

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John W. Runyan, Jr., M.D. MACP, Professor Emeritus of Medicine

Lester VanMiddlesworth, Ph.D., M.D., Distinguished University Professor, Medicine & Physiology

Dale Childress, M.D., Clinical Assistant Professor/VAMC

Hooman Oktaei, M.D., Clinical Assistant Professor of Medicine

Volunteer Faculty

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Harold Sacks, M.D., Clinical Professor of Medicine

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