## Division Data Summary

### Research and Training Details

<table>
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<th>Category</th>
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<tr>
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<td>Direct Annual Industry Support</td>
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<td>Peer Reviewed Publications</td>
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### Clinical Activities and Training

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<td>Outpatient Encounters</td>
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## Division Photo

Row 1: D Elder, N Crimmins
Row 2: N Yayah Jones, I Gutmark-Little, A Sanghavi Shah
Row 3: M Rutter, P Backeljauw, S Lawson
Row 4: D Klein, L Dolan, J Katz

## Significant Publications


This paper provides a detailed description of the type and frequency of cardiovascular anomalies in Turner syndrome that may lead to premature morbidity and mortality.


PTHLP is found in large concentrations in human endometrial Stromal cells during decidualization. The role of PTHLP is not known. This paper demonstrates for the first time that PTHLP represses the induction of human decidualization, stimulates stromal cell apoptosis, and limits the extent of uterine stromal cell differentiation.


In this study Dr. Katz and his research team identified a critical sub-population of dendritic cells responsible for mediating peripheral tolerance to beta cell antigen in vivo.

This paper demonstrates that clustering of risk factors is as reliable but simpler method for assessing cardiovascular risk than the Patholobiological Determinants of Atherosclerosis in Youth score, presently the accepted method of assessing cardiovascular risk.

This manuscript establishes the presence of a progressive increase in vascular stiffness in youth from lean to obese to obese type 2 that cannot be explained by traditional cardiovascular risk factors.

**Division Collaboration**

**Reproductive Sciences** » S.K. Dey, MD; Sanjoy Das, PhD
Research

**Neonatology & Pulmonary Biology** » Cindy Bachurski, PhD; Jeffrey Whitsett, MD
Research

**Biomedical Informatics** » Bruce Aronow, PhD; Anil Jegga, MS, DVM
Research

**Pathology** » Jerzy Stanek, MD, PhD
Research

**Molecular and Developmental Biology** » James Wells, PhD
Research

**Healthworks; Preventive Cardiology; Gastroenterology** » Holly Ippisch, MD; Stavra Xanthakos, MD, MS; Robert Siegel, MD
Center for Better Health and Nutrition clinical collaboration

**Center for Adherance in Psychiatry** » Denny Drotar, PhD; Korey Hood, PhD
Research

**Pulmonary** » Mike Seid, PhD; James Acton, MD; Jamie Wooldridge, MD
Growth hormone therapy in patients with cystic fibrosis; Cystic fibrosis insulin study

**General Pediatrics** » Maria Britto, MD, MPH
Research

**ICU** » Derek Wheeler, MD
Research

**Pharmacy** » Anne Lesko, PharmD; Shannon Saldana, PharmD, MS, BCPP
Research

**Adolescent Gyn; Urology** » Lesley Breech, MD; Curtis Sheldon, MD
Clinical collaboration - Disorders of Sexual Differentiation Clinic

**Gastroenterology** » Lee Denson, MD
Study of the effects of growth hormone on patients with Crohn's disease

**Emergency Medicine** » Mike Gittelman, MD; Wendy Pomerantz, MD
Injury prevention project (RWJ sponsored) in an obesity prevention project in an area experiencing health disparities

**Psychiatry** » Mike Sorter, MD; Mary Matias-Akhtar, MD
Project to see if Metformin given at the initiation of anti-psychotic treatment can prevent weight accretion, which occurs commonly in children on these agents

**Adolescent Medicine** » Heidi Kwalkorf, PhD; Lorah Dorn, RN, PhD
NIH multicenter study of bone mineral in healthy children and adolescents; grant application regarding smoking and pubertal development

**Rheumatology** » Hermine Brunner, MD
NIH funded grant of Triptorelin therapy in lupus patients

**Hematology Oncology; Hematology Oncology** » Franklin Smith, MD; Richard Harris, MD; Stella Davies, MD; Parinda Mehta, MD
Funded study of oxadrolone therapy in children with Fanconi anemia
Research, database, and multicenter care of patients with Fanconi Anemia and other bone marrow failure syndromes

**Mayerson Center** » Kathi Makoroff, MD
Pfizer funded study shaken infants

**Physical Medicine and Rehabilitation** » Linda Michaud, MD
Pfizer funded study of endocrine function after traumatic brain injury

**Neurology** » Brenda Wong, MD
Development of research regarding Duchenne Muscular Dystrophy

**Cardiology** » Elaine Urbina, MD; Thomas Kimball, MD; John Morrison, PhD
Clinical management protocol for cardiac disease in Turner syndrome
The epidemiology of peripheral cardiovascular disease in youth with a specific emphasis on the role of obesity, insulin resistance and diabetes
The epidemiology of central (heart) cardiovascular disease in youth with a specific emphasis on the role of obesity, insulin resistance and diabetes
The ability of pre-teen variables to predict the development of obesity, insulin resistance, diabetes and cardiovascular disease

**Epidemiology and Biostatistics** » Lisa Martin, PhD; Jane Khoury, PhD; Jessica Woo, PhD
Contribution of genetics to obesity in adolescents
The effect of maternal type 1 diabetes on adolescents and young adult offspring with a focus on obesity and carbohydrate metabolism
Creation of clinical database for the Comprehensive Weight Management Center

**Psychology and Behavioral Medicine** » Scott Powers, PhD
Eating behaviors in individuals 16 years of age with type 1 diabetes

**Surgery** » Thomas Inge, MD, PhD
Bariatric surgery in youth: safety, efficacy, and effect on carbohydrate and cardiovascular outcomes
International Hypothalamic Obesity Registry
Faculty Members

Stuart Handwerger, MD, Professor
  *Professor of Cancer and Cell Biology*
  **Research Interests** Growth and thyroid disorders; perinatal endocrinology

Philippe Backeljauw, MD, Professor
  *Director, Cincinnati Turner Syndrome Center*
  **Research Interests** Growth disorders; disorders of bone and calcium metabolism; Turner Syndrome

Nancy Crimmins, MD, Assistant Professor
  **Research Interests** Diabetes; obesity

Lawrence M Dolan, MD, Professor
  *Division Director, Robert and Mary Shoemaker Professor of Pediatrics*
  **Research Interests** Diabetes mellitus; non-insulin dependent diabetes; sexual development disorders; growth disorders; disorders of the thyroid; goiters; hypoglycemia

Deborah Elder, MD, Assistant Professor
  **Research Interests** Diabetes; growth disorders; precocious puberty; calcium disorders

Jonathan Katz, PhD, Associate Professor
  *Director, Diabetes Research Center*
  **Research Interests**

David J Klein, MD, PhD, Associate Professor
  **Research Interests** Diabetes mellitus; intensive diabetes management programs; early detection of renal disease; effects of diabetes mellitus on renal proteoglycan synthesis

Susan Rose, MD, Professor
  **Research Interests** Hypothalamic pituitary function; thyroid disorders; disorders of growth or puberty; endocrine function in cancer survivors; endocrine function after head injury

Meilan Rutter, MD, Assistant Professor
  **Research Interests** Calcium disorders; endocrine function in childhood cancer survivors; endocrine function in muscular dystrophy

Peggy Stenger, DO, Assistant Professor
  **Research Interests** Growth disorders; disorders of sexual development; pubertal disorders; disorders of the thyroid; goiter

Nana-Hawa Yayah Jones, MD, Assistant Professor
  **Research Interests** Adherence/compliance in type 1 diabetes

Iris Gutmark-Little, MD, Assistant Professor
  **Research Interests** Airway and great vessel disorders in Turner syndrome

Joint Appointment Faculty Members

Jessica Woo, PhD, Assistant Professor
  Epidemiology

Significant Accomplishments

  *Turner Syndrome Research*
The Turner Syndrome Center has investigated cardiovascular anomalies in Turner syndrome (TS) patients by cardiac MRI, including aortic abnormalities and partial anomalous pulmonary venous return (PAPVR). The prevalence of PAPVR was found to be 18 percent. Six of the newly diagnosed patients had not been diagnosed by echocardiogram. Another study found the prevalence of hypertension in TS girls to be under-recognized. More attention should be given to careful determination, interpretation and follow-up of blood pressure monitoring in TS girls, including a recommendation to manually perform all blood pressure measurements in TS girls. A prospective study comparing the prevalence of vasculopathy in TS patients showed evidence of increased arterial stiffness. This puts TS girls at greater risk for cardiovascular disease later in life. As a next step, measurements of TS-specific comorbidities will be evaluated in an attempt to determine the specific at-risk TS population. These studies underscore the importance of a multidisciplinary approach to TS care, together with the development of a large patient database. New studies being developed will focus on further evaluation of large vessel disease, assessment of airway dysfunction and studies looking at abnormalities of glucose metabolism.

Placental Development in Normal and Pathologic Pregnancies

Many pathologic conditions of pregnancy that result in infant morbidity and mortality, such as preeclampsia and intrauterine growth retardation (IUGR), are characterized by abnormal placental development. Research by Stuart Handwerger, MD, and his colleagues examines the roles for protein hormones, transcription factors and other signaling molecules in the development of normal and pathologic placentas. They postulate that a better understanding of the factors that regulate placental growth and development may lead to the discovery of therapeutic modalities that prevent or correct abnormal placental development and that improve fetal outcome. Their recent investigations have shown that placental development is critically dependent upon the transcription factors TFAP2A and NR2F2, both of which modulate cell structure, cell growth and hormone expression. The mRNA and protein levels of both transcription factors were shown to increase markedly during placental development; silencing the expression of either transcription factor was observed to markedly inhibit development. NR2F2 and TFAP2A were shown to form a positive feedback loop in which NR2F2 induces TFAP2A expression and TFAP2A in turn induces NR2F2. NR2F2 also potentiated the effect of retinoic acid on TFAP2A. Having demonstrated that TFAP2A and NR2F2 are critical for normal placental development, Handwerger, in collaboration with Jerzy Stanek, MD, PhD, and Rachel Sheridan, MD, of the Division of Pathology, recently observed by immunohistochemical analyses that TFAP2A protein levels in preeclampsia and IUGR placentas are markedly decreased compared to levels in gestational age-matched control placentas. Similar NR2F2 studies have not as yet been completed. Since these studies suggest that the abnormal placental development and function in preeclampsia and IUGR may be due, at least in part, to abnormalities in TFAP2A (and possibly NR2F2) expression, subsequent studies will examine whether correcting TFAP2A (and possibly NR2F2) expression in cultures of pathologic placentas will result in normal development.

Causes and Control of Type 1 Diabetes

Our research focuses on type 1 diabetes (T1D) by using a non-obese diabetic (NOD) mouse model. During the past year, our NIH-funded work has focused mainly on three areas: the role plasmacytoid dendritic cells and natural killer T cells play in establishing an immunoregulatory environment in mice that are protected from disease; the role mercury dendritic cells play in breaking peripheral T cell tolerance to islet cell antigen (in collaboration with Edith Janssen, PhD, in the Division of Molecular Immunology); and the potential use of small molecule inhibitors of Bcl-2 family members in targeting diabetogenic CD4+ and CD8+ T cells for specific destruction to enhance long-term tolerance and to facilitate a novel therapeutic strategy to
re-establish tolerance in T1D patients (in collaboration with David Hildeman, PhD, in the Division of Immunobiology). Together these studies are designed to understand what normally controls T1D development, what underlies the basic response to beta cell antigens and, finally, what can be done to facilitate the restoration of normal beta cell function and glucose regulation in T1D patients.

**Division Publications**


## Grants, Contracts, and Industry Agreements

### Grant and Contract Awards

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<td>National Institutes of Health (University of Colorado)</td>
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<td><strong>SEARCH for Diabetes in Youth, Phase 3: Registry Study</strong></td>
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<td>SHAH, A</td>
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<td>SISLEY, S</td>
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| **Current Year Direct** | **$1,656,184** |

### Industry Contracts

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**Current Year Direct Receipts**

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