Endocrinology



Division Details

Division Data Summary

Research and Training Details

14
1
29
\$1,220,631
\$149,455
29
23

Number of Clinical Staff	50
Number of Clinical Fellows	10
Inpatient Encounters	3,547
Outpatient Encounters	13,419

Division Photo



Row 1: S Rose, A Shah, D Elder Row 2: P Stenger, N Yayah-Jones, B Freedman, N Crimmins, S Lawson, J Katz Row 3: P Backeljauw, D Klein, S Handwerger, L Dolan, M Rutter

Significant Accomplishments

Etiologic Approach to the Classification of Diabetes

In 1997 the American Diabetes Association presented a framework for the classification of the types of diabetes based on etiology. To date, no one has attempted to operationalize these definitions. To achieve this goal, the SEARCH for Diabetes in Youth Study assessed clinical and biochemical data from 2,291 participants attempting to define diabetes type by etiology. Four main categories were established: autoimmune plus insulin sensitive; autoimmune plus insulin resistant; non-autoimmune insulin sensitive; non-autoimmune insulin resistant. This classification offers researchers and clinicians a practical application of the ADA diagnostic criteria and identifies groups of youth in whom further research studies are required to define their type of diabetes.

Racial Differences in Arterial Stiffness among Youth with Diabetes

Adult studies demonstrate African-Americans with type 2 diabetes (T2D) have an increased risk to develop stroke and myocardial infarction compared to Caucasians. Whether similar racial disparities exist in adolescents to suggest African-American youth with T2D are at increased risk to develop early cardiovascular (CV) complications from T2D is not known. To answer this question, a team led by Amy Shah, MD, recruited 215 youth with T2D (55 percent African-American, 65 percent female) in a cross-sectional study and measured arterial stiffness, a known precursor atherosclerosis. They found compared to age and BMI matched Caucasians, African-Americans adolescents with T2D had increased arterial stiffness. Additionally, the investigators demonstrated the CV risk factors that were associated with arterial stiffness differed among the two race groups. In Caucasians, blood pressure appeared to be the largest risk factor contributing to arterial stiffness while in African-Americans age was the largest contributor. Other important risk factors that differed

among groups were lipids and T2D duration. These findings suggest that race-specific risk factor modification approaches should be considered to limit future CV complications associated with T2D.

Regulation of Human Placental Development

Little is known about the transcription factors (TFs) and signaling molecules that are critical for the differentiation of placenta stem cells (cytotrophoblast cells (CTB)) to mature syncytiotrophoblast cells (STB). These cells, which form of the outer layer of placenta villi, are responsible for most functions of the mature placenta, including the synthesis and secretion of hormones and growth factors that modulate fetal growth and development and the transport of nutrients and gases between the maternal and fetal circulations. Recent studies by Stuart Handwerger, MD, and colleagues have demonstrated that the TFs TFAP2A, NR2F2 and FOXF1 are critical for the differentiation of human CTB to a STB phenotype. Binding sites for the TFs were detected on the promoter regions of many genes induced during CTB differentiation; and overexpression of the TFs induced the expression of many of the up-regulated genes. Moreover, silencing of the genes for the three TFs with lentiviruses expressing shRNAs for the factors attenuated CTB differentiation. Immunohistochemical analysis of human placenta sections from normal and pathologic pregnancies have so far demonstrated that AP-2α expression is suppressed in mild preeclampsia (PE), diabetes, hypertension and fetal growth retardation and increased in severe PE. Studies with NR2F2 and FOXF1 are in progress. Taken together, these studies provide important new insights into the pathophysiology of abnormal placenta development.

Division Publications

- 1. Backeljauw PF, Chernausek SD. The insulin-like growth factors and growth disorders of childhood. Endocrinol Metab Clin North Am. 2012; 41:265-82.
- 2. Bingham NC, Rose SR, Inge TH. Bariatric surgery in hypothalamic obesity. Front Endocrinol (Lausanne). 2012; 3:23.
- 3. Dabelea D, Pihoker C, Talton JW, D'Agostino RB, Jr., Fujimoto W, Klingensmith GJ, Lawrence JM, Linder B, Marcovina SM, Mayer-Davis EJ, Imperatore G, Dolan LM. **Etiological approach to characterization of diabetes type: the SEARCH for Diabetes in Youth Study**. *Diabetes Care*. 2011; 34:1628-33.
- 4. Edwards NM, Daniels SR, Claytor RP, Khoury PR, Dolan LM, Kimball TR, Urbina EM. Physical activity is independently associated with multiple measures of arterial stiffness in adolescents and young adults. *Metabolism.* 2012; 61:869-72.
- 5. Elder DA, Herbers PM, Weis T, Standiford D, Woo JG, D'Alessio DA. beta-Cell Dysfunction in Adolescents and Adults with Newly Diagnosed Type 2 Diabetes Mellitus. *J Pediatr*. 2012; 160:904-10.
- 6. Elding Larsson H, Vehik K, Bell R, Dabelea D, Dolan L, Pihoker C, Knip M, Veijola R, Lindblad B, Samuelsson U, Holl R, Haller MJ. Reduced prevalence of diabetic ketoacidosis at diagnosis of type 1 diabetes in young children participating in longitudinal follow-up. *Diabetes Care*. 2011; 34:2347-52.
- 7. Guilfoyle SM, Crimmins NA, Hood KK. **Blood glucose monitoring and glycemic control in adolescents** with type 1 diabetes: meter downloads versus self-report. *Pediatr Diabetes*. 2011; 12:560-6.
- 8. Herzer M, Vesco A, Ingerski LM, Dolan LM, Hood KK. Explaining the family conflict-glycemic control link through psychological variables in adolescents with type 1 diabetes. *J Behav Med*. 2011; 34:268-74.
- 9. Hilliard ME, Guilfoyle SM, Dolan LM, Hood KK. Prediction of adolescents' glycemic control 1 year after diabetes-specific family conflict: the mediating role of blood glucose monitoring adherence. *Arch Pediatr Adolesc Med.* 2011; 165:624-9.
- 10. Hilliard ME, Herzer M, Dolan LM, Hood KK. Psychological screening in adolescents with type 1 diabetes predicts outcomes one year later. *Diabetes Res Clin Pract*. 2011; 94:39-44.

- Hood KK, Rausch JR, Dolan LM. Depressive symptoms predict change in glycemic control in adolescents with type 1 diabetes: rates, magnitude, and moderators of change. Pediatr Diabetes. 2011; 12:718-23.
- 12. Katz JD, Janssen EM. Breaking T cell tolerance to beta cell antigens by merocytic dendritic cells. *Cell Mol Life Sci.* 2011; 68:2873-83.
- 13. Khoury JC, Dolan LM, Vandyke R, Rosenn B, Feghali M, Miodovnik M. Fetal development in women with diabetes: imprinting for a life-time?. *J Matern Fetal Neonatal Med*. 2012; 25:11-4.
- 14. Merchant TE, Rose SR, Bosley C, Wu S, Xiong X, Lustig RH. **Growth hormone secretion after conformal radiation therapy in pediatric patients with localized brain tumors**. *J Clin Oncol*. 2011; 29:4776-80.
- 15. Nommsen-Rivers LA, Dolan LM, Huang B. **Timing of stage II lactogenesis is predicted by antenatal metabolic health in a cohort of primiparas**. *Breastfeed Med*. 2012; 7:43-9.
- 16. Patton SR, Dolan LM, Smith LB, Thomas IH, Powers SW. Pediatric parenting stress and its relation to depressive symptoms and fear of hypoglycemia in parents of young children with type 1 diabetes mellitus. *J Clin Psychol Med Settings*. 2011; 18:345-52.
- 17. Patton SR, Midyett LK, Dolan LM, Powers SW. A comparison of average daily risk range scores for young children with type 1 diabetes mellitus using continuous glucose monitoring and self-monitoring data.

 Diabetes Technol Ther. 2012; 14:239-43.
- 18. Rausch JR, Hood KK, Delamater A, Shroff Pendley J, Rohan JM, Reeves G, Dolan L, Drotar D. Changes in treatment adherence and glycemic control during the transition to adolescence in type 1 diabetes.

 Diabetes Care. 2012; 35:1219-24.
- 19. Rohan JM, Delamater A, Pendley JS, Dolan L, Reeves G, Drotar D. Identification of self-management patterns in pediatric type 1 diabetes using cluster analysis. *Pediatr Diabetes*. 2011; 12:611-8.
- 20. Rose SR, Rutter MM, Mueller R, Harris M, Hamon B, Bulluck AF, Smith FO. **Bone mineral density is normal in children with Fanconi anemia**. *Pediatr Blood Cancer*. 2011; 57:1034-8.
- 21. Schroeder JK, Kessler CA, Handwerger S. Critical role for TWIST1 in the induction of human uterine decidualization. *Endocrinology*. 2011; 152:4368-76.
- 22. Shah AS, Dolan LM, D'Agostino RB, Jr., Standiford D, Davis C, Testaverde L, Pihoker C, Daniels SR, Urbina EM. Comparison of mercury and aneroid blood pressure measurements in youth. *Pediatrics*. 2012; 129:e1205-10.
- 23. Shah AS, Dolan LM, Gao Z, Kimball TR, Urbina EM. Racial differences in arterial stiffness among adolescents and young adults with type 2 diabetes. *Pediatr Diabetes*. 2012; 13:170-5.
- 24. Sontag-Padilla LM, Dorn LD, Tissot A, Susman EJ, Beers SR, Rose SR. Executive functioning, cortisol reactivity, and symptoms of psychopathology in girls with premature adrenarche. *Dev Psychopathol.* 2012; 24:211-23.
- 25. Sung V, Beebe DW, Vandyke R, Fenchel MC, Crimmins NA, Kirk S, Hiscock H, Amin R, Wake M. Does sleep duration predict metabolic risk in obese adolescents attending tertiary services? A cross-sectional study. Sleep. 2011; 34:891-8.
- 26. Tissot A, Dorn LD, Rotenstein D, Rose SR, Sontag-Padilla LM, Jillard CL, Witchel SF, Berga SL, Loucks TL, Beers SR. Neuropsychological functioning in girls with premature adrenarche. *J Int Neuropsychol Soc.* 2012; 18:151-6.
- 27. Tosson H, Rose SR. Absence of mutation in coding regions of CYP2R1 gene in apparent autosomal dominant vitamin D 25-hydroxylase deficiency rickets. *J Clin Endocrinol Metab.* 2012; 97:E796-801.
- 28. Tosson H, Rose SR, Gartner LA. **Description of children with 45,X/46,XY karyotype**. *Eur J Pediatr*. 2012; 171:521-9.
- 29. Urbina EM, Gao Z, Khoury PR, Martin LJ, Dolan LM. Insulin resistance and arterial stiffness in healthy adolescents and young adults. *Diabetologia*. 2012; 55:625-31.

Faculty, Staff, and Trainees

Faculty Members

Stuart Handwerger, MD, Professor

Leadership Professor of Cancer and Cell Biology

Research Interests Growth and thyroid disorders; perinatal endocrinology

Philippe Backeljauw, MD, Professor

Leadership 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

Leadership 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

Leadership Director, Diabetes Research Center

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 proteogycan 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

Sarah Lawson, MD, Assistant Professor

Research Interests Turner syndrome; Septo-optic dysplasia; endocrine abnormalities related to oncology and its treatments

Amy Shah, MD, Assistant Professor

Research Interests Type 2 diabetes; pre-diabetes; insulin resistance; obesity; lipid disorders

Joint Appointment Faculty Members

Jessica Woo, PhD, Assistant Professor (Epidemiology)

Division Collaboration

Reproductive Sciences » S.K. Dey, MD and Sanjoy Das, PhD

Research

Neonatology & Pulmonary Biology » Cindy Bachurski, PhD, Jeffrey Whitsett, MD, and Alexander Lange, PhD

Research

Biomedical Informatics » Bruce Aronow, PhD and Anil Jegga, MS, DVM

Research

Pathology » Jerzy Stanek, MD, PhD and Rachel Sheridan, PhD

Research

Molecular and Developmental Biology » James Wells, PhD

Research

Healthworks; Preventive Cardiology; Gastroenterology » Holly Ippisch, MD, Robert Siegel, MD, and Stavra

Xanthakos, MD, MS

Center for Better Health and Nutrition clinical collaboration

Center for Adherance in Psychiatry » Denny Drotar, PhD and Korey Hood, PhD

Research

Pulmonary » Gary McPhail, MD

Impaired Fasting Glucose and Indeterminant Glucose Tolerance in a Cystic Fibrosis Population (Two and Four Year Clinical Outcomes)

Blood Glucose Monitoring in the hospitalized patient with Cystic Fibrosis - Validation of the expert opinion using Continuous Glucose Monitoring

Solid Organ Transplantation » John Bucuvalas, MD

Screening and Management of Diabetes in youths with solid organ transplantation

Adolescent Medicine » Jennifer Hillman, MD, MS

Diagnosis, screening for comorbidities and management of Polycystic Ovarian Syndrome across three disciplines within an academic hospital

General Pediatrics » Maria Britto, MD, MPH

Research

ICU » Derek Wheeler, MD

Research

Pharmacy » Anne Lesko, PharmD and Shannon Saldana, PharmD, MS, BCPP

Research

Adolescent Gyn, Urology, Genetics » Lesley Breech, MD, Curtis Sheldon, MD, Shumyle Alam, MD, Pramod Reddy, MD, and Howard Saal, MD

Clinical collaboration - Disorders of Sexual Development Clinic

(Cincinnati Disorders of Sex Development Center)

Gastroenterology » Lee Denson, MD

Study of the effects of growth hormone on patients with Crohn's disease

Emergency Medicine » Mike Gittelman, MD and Wendy Pomerantz, MD

Injury prevention project (RWJ sponsored) in an obesity prevention project in an area experiencing health disparities

Psychiatry » Michael Sorter, MD and 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

Rheumatology » Hermine Brunner, MD

NIH funded grant of Triptorelin therapy in lupus patients

Hematology Oncology » Richard Harris, MD, Stella Davies, MD, Parinda Mehta, MD, and Karen Burns, 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 and James Collins, MD

IGF-I therapy and muscle function in Duchenne Muscular Dystrophy research study

Research, database and interdisciplinary team care of patients with Duchenne Muscular Dystrophy

Cardiology » Elaine Urbina, MD, Thomas Kimball, MD, and 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, and Heidi Sucharew, 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

Contribution to collaborative research in Duchenne Muscular Dystrophy

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

Grants, Contracts, and Industry Agreements

Grant and Contract Awards		Annual Direct
BINGHAM, N		
Effect of High Fat Diet on Hypothala	mic Microglia	
Endocrine Fellows Foundation		
	05/01/12-04/30/13	\$12,500
CRIMMINS, N		
Type 1 Diabetes TrialNet		
National Institutes of Health (Univ. of S	outh Florida	
National institutes of Health (Only, of S	06/16/11-06/30/13	\$32,348
DOLAN, L		
·	flammatory Markers in the SEARCH Cohort	
National Institutes of Health(University	-	
R01 ES 019168	09/27/11-06/30/15	\$16,137
SEARCH for Diabetes in Youth, Phas		\$10,137
Ctr for Disease Control and Prevention		
U18 DP 002709	09/30/10-09/29/15	\$409,298
T1D Exchange Registry	09/30/10-09/29/13	\$409,290
Jaeb Center for Health Research Foun	dation Inc	
Jaeb Center for Fleath Nesearch Foun	12/01/10-02/28/13	\$14,079
HANDWERGER, S		
·	acental Differentiation	
Transcriptional Control of Human PI National Institutes of Health	acental Differentiation	
R01 HD 065339	02/01/11-01/31/16	\$216,358
1011ID 003339	02/01/11-01/31/10	φ210,330
HOWELL, J		
Incretin Expression and Regional Pa	ttering in Human Pluripotent Stem Cell Derived	Intestine
Endocine reliows roundation	07/01/11-06/30/12	\$15,000
	07/01/11 00/00/12	ψ10,000
KATZ, J		
Dissecting Dendritic Cell Function in	Autoimmune Diabetes	
National Institutes of Health	00/04/00 07/04/44	0040.470
R01 DK 078179	08/01/09-07/31/14	\$213,172

KATZ, J / HILDEMAN, D

	Total	\$1,370,086
	Current Year Direct Receipts	\$149,455
Pfizer Inc.		\$28,721
ROSE		Ţ.0,300
LAWSON, S Pfizer, Inc		\$13,860
Novo Nordisk Pharmaceuticals		\$42,478
KLEIN, D		
Tercica, Inc.		\$48,833
Eli Lilly and Company Novo Nordisk Pharmaceuticals		\$3,138 \$12,425
BACKELJAUW, P		¢2 120
Industry Contracts		
	Current Year Direct	
National Institutes of Health F32 DK 091077	07/01/11-06/30/13	\$59,582
CNS NFkappaB Regulation of Glucose Ho		ψ1,000
Center for Environmental Genetics New Ir National Institutes of Health(University of Cin P30 ES 006096		\$4,500
SISLEY, S		
Tercica, inc.	11/01/10-12/31/11	\$2,657
IGF Drug Only Tercica, Inc.		
DMD Insulin Growth Factor-1 Charley's Fund	11/01/10-10/31/12	\$100,000
RUTTER, M		
National Institutes of Health R01 CA 138617	09/10/10-08/31/13	\$\$115,121
KATZ, J / JANSSEN, E Dendritic Cells in the Breaking of Periphe	ral Tolerance in Type 1 Diabetes	
R01 DK 081175	07/01/11-06/30/15	\$125,000
D04 D1/ 004475	07/04/44 00/00/45	¢405.000