

Division of Endocrinology

DIVISION PROFILE	
Number of Faculty	10
Number of Joint Appointment Faculty	1
Number of Staff Physicians	2
Number of Fellows	
Clinical Fellows	8
Research Fellows	5
Number of Graduate Students	3
Number of Support Personnel	37
Annual Total Grant Support (direct)	\$1,782,154
Annual Total Industry Contracts (direct)	\$253,001
Number of Peer Reviewed Publications	30
Patient Encounters	
Outpatient	8,902
Inpatient	2,024

FACULTY LISTING

Stuart Handwerker, MD, Professor of Pediatrics, Division Director
Philippe Backeljauw, MD, Professor of Pediatrics
Steven Chernausk, MD, Professor of Pediatrics, Associate Director
Lawrence Dolan, MD, Professor of Pediatrics
Deborah Elder, MD, Assistant Professor of Pediatrics
Jonathan Katz, PhD, Associate Professor of Pediatrics, Director, Diabetes Research Center
David Klein, MD, PhD, Associate Professor of Pediatrics
David Repaske, PhD, MD, Associate Professor of Pediatrics, Director, Clinical Diabetes Center
Susan Rose, MD, Professor of Pediatrics
Bo Wang, DVM, PhD, Assistant Professor of Pediatrics

FACULTY JOINT APPOINTMENT LISTING

Jessica Woo, PhD, Assistant Professor, Epidemiology

STAFF PHYSICIAN LISTING

Meilan Rutter, MD, Staff Physician
Peggy Stenger, DO, Staff Physician

OVERVIEW

The major activities in the Division of Endocrinology included patient care, basic and clinical research and the training of physician/scientists, graduate students and postdoctoral fellows for careers in academic medicine. During the past year, approximately 8,900 patient visits were made in the endocrine and diabetic clinics, and inpatient care was provided for approximately 2,000 children. Approximately 256 newly diagnosed patients with diabetes mellitus are admitted yearly. The total number of children followed in the diabetes clinic is about 1,700.

The major basic research projects performed during the past year included investigations of 1) the roles of IGF and IGF-binding proteins in bone development and growth; 2) the regulation of human placental and uterine decidual differentiation; 3) the regulation of human placental lactogen and prolactin gene expression; 4) the development of animal models to study the pathogenesis of type I diabetes mellitus; 5) the role of T-lymphocytes in the pathogenesis of type I diabetes mellitus; and 6) genomic analysis of risk factors in

diabetes mellitus. Clinical research projects included investigations of 1) the use of low dose insulin injections in the prevention of insulin-dependent diabetes in genetically susceptible children; 2) the natural history and etiology of diabetic heart disease and nephropathy; 3) the epidemiology of type II diabetes mellitus in childhood; 4) the roles of growth hormone, IGF and IGF-binding proteins in normal growth and intrauterine growth retardation; and 5) the endocrine consequences of childhood cancer and head trauma.

In addition to participating in the teaching of medical students and house staff, the division was involved in the training of six postdoctoral fellows in pediatric endocrinology, one postdoctoral fellow in Obstetrics/Gynecology, one PhD postdoctoral fellow seeking advanced research training in endocrinology, and four PhD postdoctoral fellows pursuing diabetes research training.



Left to Right: (1st row) S. Chernausek, S. Rose, S. Handwerker, A. Kansra, P. Stenger, A. Dawodu (2nd row) O. Eyal, R. Sherfat (3rd row) M. Rutter, P. Backeljauw, L. Dolan, N. Crimmins, S. Gupta

HIGHLIGHTS

During the past decade, type II diabetes mellitus has increased dramatically in American teenagers, with a prevalence rate now approaching 1:1000. The disease in adolescents affects all ethnic groups and now accounts for about 20% of newly diagnosed diabetes in teenagers. The accelerated prevalence parallels the epidemic of childhood obesity and may be the most significant consequence of increased adiposity in young people. Because type II diabetes mellitus results in striking increases in morbidity and mortality, the recent epidemic of the disease in adolescents constitutes a major public health problem.

While dysfunction of the pancreatic beta cell and insulin resistance are critical factors in the development of type II diabetes in adults, relatively little is known about the pathophysiology of the disease in adolescents and young adults. Consequently, it is unclear whether the disease in adolescents represents a distinct form of diabetes or is simply an early manifestation of the condition seen in adults. Recently, Dr. Deborah Elder, in collaborations with Dr. Larry Dolan and Dr. David D'Allesio (Division of Endocrinology, Department of

Medicine, University of Cincinnati), studied glucose, insulin and glucagons dynamics in a cohort adolescent patients with type II diabetes and non-diabetic lean and obese controls. The major diabetes patients were severely insulin resistant compared to the lean and obese controls and had impaired insulin secretion relative to the degree of insulin resistance. However, in contrast to adult subjects with type II diabetes, the adolescent diabetic subjects had a first phase insulin response to intravenous glucose comparable to lean controls, and did not have hyperproinsulinemia (the precursor form of insulin) or hyperglucagonemia (another measure of beta cell function). This islet phenotype is in marked contrast to the classical findings in adults with T2DM, in whom first phase insulin secretion is very low; the proinsulin/insulin ratio is markedly elevated and glucagon secretion is excessive. These results therefore suggest that the pathophysiology of type II diabetes in youth is different than that in adults. The findings also suggest that the optimal therapy for the disease in adolescent patients may be distinct from that for adult patients.

Drs. You-Hong Cheng and Stuart Handwerger continued their investigations of the regulation of human placental development. They cloned and partially characterized the promoter for a newly-described gene called syncytin that codes for a glycoprotein that is critical early in placental differentiation when mononuclear cytotrophoblast cells fuse to form syncytiotrophoblast cells. In recently completed investigations, they identified a region of the promoter that is essential for placenta-specific expression of the syncytin gene and showed that the activity of the region requires intact binding sites for GATA-2, GATA-3 and Sp1 transcription factors. These studies are of clinical importance since markedly decreased syncytin expression has been observed in placentas from women with pre-eclampsia, a common pathologic condition of pregnancy that is associated with a marked increase in fetal and neonatal morbidity and mortality. An understanding of the regulation of key genes involved in placental development may lead to new therapies for pre-eclampsia and other diseases associated with abnormalities in placental development and function.

TRAINING

Shilpa Gupta, MD	PL-IV	Bronx Lebanon Hospital, New York
Adetokunbo Dawodu, MD	PL-IV	Nassau University Medical Center, East Meadow, NY
Kent Reifschneider, MD	PL-V	Greenville Memorial Hospital
Rosa Sherafat-Kazemzadeh, MD	PL-V	University of Illinois at Chicago
Ori Eyal, MD	PL-VI	Dana Children's Hospital, Tel-Aviv Israel
Nancy Crimmins, MD	PL-VI	Cincinnati Children's Hospital
Alvina Kansra, MD	PL-VII	Hurley Medical Center, MSU
Sumana Sundarajan, MD	PL-VII	New York Medical College and Westchester County Medical Center

GRANTS, CONTRACTS AND INDUSTRY AGREEMENTS

Grant and Contract Awards	Annual Direct/Project Period	Direct
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Cain, J		
Regulatory T Cells in the Control of Type I Diabetes		
National Institutes of Health		
K01 DK 064836	09/30/03 – 06/30/06	\$86,655/\$251,716
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Dolan, L		
SEARCH for Diabetes in Youth 2: Ohio Site		
Centers for Disease Control		
U01 DP 000248	09/30/05 – 9/29/10	\$432,614/\$2,261,046
Understanding Social Status Impact on Adolescent Health		
National Institutes of Health (Brandeis University subcontract)		
R01 HD 041527	07/01/02 – 01/31/07	\$18,422/\$162,644
Type 1 Diabetes Genetics Consortium		
Benaroya Research Institute		
	01/01/04 – 08/31/07	\$20,600/\$82,400

Elder, D		
Beta Cell Function in Adolescents with Type II Diabetes National Institutes of Health K23 DK 070775	09/01/05 – 08/31/10	\$116,500/\$582,500
Handwerker, S		
Decidual Prolactin in Normal and Pathological Pregnancies National Institutes of Health R01 HD 015201	04/01/03 – 03/31/08	\$219,713/\$1,125,000
Training in Developmental and Perinatal Endocrinology National Institutes of Health T32 HD 007436	05/01/06– 04/30/11	\$181,170/\$905,850
Microarray Analysis of HCMV-Placental Trophoblast Interaction March of Dimes – National (University of Minnesota subcontract)	06/01/05 – 05/31/07	\$54,294
The Physiology of Placental Lactogen National Institutes of Health R01 HD 007447	04/01/02 – 03/31/07	\$219,713/\$1,125,000
Katz, J		
Using Genomics to Understand Autoimmune Diabetes National Institutes of Health R01 DK 062274	06/01/02 – 04/30/07	\$179,127/\$950,002
Klein, D		
A School-Based Diabetes Awareness & Prevention Program American Diabetes Association	07/01/04 – 06/30/06	\$87,360/\$173,910
Rose, S		
Thyroid Hormone in Children with Fanconi Anemia Fanconi Anemia Research Fund	04/01/05 – 03/31/08	\$15,986/\$47,687
Wang, B		
Spatiotemporal Control of Insulinitis in NOD Mice American Diabetes Association	01/01/04 – 12/31/08	\$150,000/\$758,500
Current Year Direct		\$1,782,154
Industry Contracts		
Backeljauw, P		
AstraZeneca		\$1,779
Tercica		\$5,716
Pharmacia		\$2,310
Eli Lilly & Co		\$2,194
Chernausek, S		
Tercica Inc		\$73,345
Eli Lilly & Co		\$1,051
Growth Research Fund		\$2,019

Klein, D	
American Diabetes Association	\$61,600
Eli Lilly & Co	\$65,299
Repaske, D	
Aventis	\$8,493
Rose, S	
Eli Lilly & Co	\$16,470
Unimed	\$12,725
Current Year Direct Receipts	
	\$253,001
TOTAL	
	\$2,035,155

PUBLICATIONS

1. Backeljauw PF, Chernausek SD. Treatment of insulin-like growth factor deficiency with IGF-I: studies in humans. *Horm Res* 2006;65 Suppl 1:21-7.
2. Kilbane BJ, Mehta S, Backeljauw PF, Shanley TP, Crimmins NA. Approach to management of malignant hyperthermia-like syndrome in pediatric diabetes mellitus. *Pediatr Crit Care Med* 2006;7(2):169-73.
3. Lomenick JP, Backeljauw PF, Lucky AW. Growth, bone mineral accretion, and adrenal function in glucocorticoid-treated infants with hemangiomas-- a retrospective study. *Pediatr Dermatol* 2006;23(2):169-74.
4. Chernausek SD. Treatment of short children born small for gestational age: US perspective, 2005. *Horm Res* 2005;64 Suppl 2:63-6.
5. Chernausek SD. Mendelian genetic causes of the short child born small for gestational age. *J Endocrinol Invest* 2006;29(1 Suppl):16-20.
6. Chernausek SD, Abuzzahab MJ, Kiess W, Osgood D, Schneider A, Smith RJ. IGF resistance: the role of the type 1 IGF receptor. In: Carel J-C, Kelly PA, Christen Y, editors. *Deciphering growth*. Berlin ; New York: Springer; 2005. p. 121-130.
7. Pinhas-Hamiel O, Chernausek SD, Zeitler P. Acute necrotizing pancreatitis in an adolescent with type 2 diabetes. *Curr Opin Pediatr* 2006;18(2):206-8.
8. Dabelea D, D'Agostino RB, Jr., Mayer-Davis EJ, Pettitt DJ, Imperatore G, Dolan LM, Pihoker C, Hillier TA, Marcovina SM, Linder B, Ruggiero AM, Hamman RF. Testing the accelerator hypothesis: body size, beta-cell function, and age at onset of type 1 (autoimmune) diabetes. *Diabetes Care* 2006;29(2):290-4.
9. Goodman E, McEwen BS, Dolan LM, Schafer-Kalkhoff T, Adler NE. Social disadvantage and adolescent stress. *J Adolesc Health* 2005;37(6):484-92.
10. Martin LJ, Woo JG, Daniels SR, Goodman E, Dolan LM. The relationships of adiponectin with insulin and lipids are strengthened with increasing adiposity. *J Clin Endocrinol Metab* 2005;90(7):4255-9.
11. Martin LJ, Woo JG, Geraghty SR, Altaye M, Davidson BS, Banach W, Dolan LM, Ruiz-Palacios GM, Morrow AL. Adiponectin is present in human milk and is associated with maternal factors. *Am J Clin Nutr* 2006;83(5):1106-11.
12. Patton SR, Dolan LM, Powers SW. Parent report of mealtime behaviors in young children with type 1 diabetes mellitus: implications for better assessment of dietary adherence problems in the clinic. *J Dev Behav Pediatr* 2006;27(3):202-8.
13. Patton SR, Dolan LM, Powers SW. Mealtime interactions relate to dietary adherence and glycemic control in young children with type 1 diabetes. *Diabetes Care* 2006;29(5):1002-6.
14. Woo JG, Dolan LM, Daniels SR, Goodman E, Martin LJ. Adolescent sex differences in adiponectin are conditional on pubertal development and adiposity. *Obes Res* 2005;13(12):2095-101.

15. Woo JG, Dolan LM, Deka R, Kaushal RD, Shen Y, Pal P, Daniels SR, Martin LJ. Interactions between noncontiguous haplotypes in the adiponectin gene ACDC are associated with plasma adiponectin. *Diabetes* 2006;55(2):523-9.
16. Elder DA, Prigeon RL, Wadwa RP, Dolan LM, D'Alessio DA. Beta-cell function, insulin sensitivity, and glucose tolerance in obese diabetic and nondiabetic adolescents and young adults. *J Clin Endocrinol Metab* 2006;91(1):185-91.
17. Cheng YH, Handwerger S. A placenta-specific enhancer of the human syncytin gene. *Biol Reprod* 2005;73(3):500-9.
18. Cheng YH, Handwerger S. Mitogen-activated protein kinase activation induces corticotrophin-releasing hormone gene expression in human placenta. *Life Sci* 2005;77(11):1263-72.
19. Grinius L, Kessler C, Schroeder J, Handwerger S. Forkhead transcription factor FOXO1A is critical for induction of human decidualization. *J Endocrinol* 2006;189(1):179-87.
20. Kessler CA, Schroeder JK, Brar AK, Handwerger S. Transcription factor ETS1 is critical for human uterine decidualization. *Mol Hum Reprod* 2006;12(2):71-6.
21. Kong S, Aronow BJ, Handwerger S. Gene expression microarray data analysis of decidual and placental cell differentiation. In: Soares MJ, Hunt JS, editors. *Placenta and trophoblast : methods and protocols (Methods in molecular medicine; v.121-122)*. Totowa, N.J.: Humana Press; 2006. p. 425-438.
22. Allen D, Rose SR, Reiter E. Normal growth and growth disorders. In: Kappy MS, Allen DB, Geffner ME, editors. *Principles and practice of pediatric endocrinology*. Springfield, Ill.: Charles C. Thomas; 2005. p. 77-216.
23. Kaste SC, Rai SN, Fleming K, McCammon EA, Tylavsky FA, Danish RK, Rose SR, Sitter CD, Pui CH, Hudson MM. Changes in bone mineral density in survivors of childhood acute lymphoblastic leukemia. *Pediatr Blood Cancer* 2006;46(1):77-87.
24. Leung W, Rose SR, Merchant TE. Neuroendocrine complications of cancer therapy. In: Schwartz CL, editor. *Survivors of childhood and adolescent cancer : a multidisciplinary approach (Pediatric oncology); . 2nd ed*. Berlin: Springer; 2005. p. 51-80.
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28. Rose SR, Brown RS, Foley T, Kaplowitz PB, Kaye CI, Sundararajan S, Varma SK. Update of newborn screening and therapy for congenital hypothyroidism. *Pediatrics* 2006;117(6):2290-303.
29. Rose SR, Shulman DI, Larsson P, Wakley LR, Wills S, Bakker B. Gender does not influence prepubertal growth velocity during standard growth hormone therapy--analysis of United States KIGS data. *J Pediatr Endocrinol Metab* 2005;18(11):1045-51.
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