## Division Details

### Division Data Summary

**RESEARCH AND TRAINING DETAILS**

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<td>Direct Annual Industry Support</td>
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**CLINICAL ACTIVITIES AND TRAINING**

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### Significant Accomplishments

**Long-Term (IGF-1) Growth Factor Replacement Therapy is Safe and Effective**

A study led by Philippe Backeljauw, MD, published in July 2013 in *Hormone Research in Paediatrics*, reports that long-term therapy with recombinant human insulin-like growth factor-1 (IGF-1) appears to be effective and safe as a replacement therapy in children with short stature due to severe IGF-1 deficiency (IGFD), a disorder caused by resistance to the effects of growth hormone. Previous reports from this long-term study led to U.S. and European approvals for this treatment. This study reports final height data after tracking participants as they grew to adulthood. For some children with severe short stature, IGF-1 therapy is the only effective option because they are resistant to exogenous growth hormone therapy. Participants who received IGF-1 doses of 120 μg/kg twice daily experienced significant increases in height velocity. Although most did not reach normal heights, many achieved an adult height significantly greater than expected in the absence of therapy. Because the spectrum of growth hormone insensitivity is wider than the patients reported upon in this study, further investigation into the therapeutic applicability of IGF-1 in patients with varying degrees of IGFD is warranted.

**IGF-1 Therapy Improves Height for Boys with Duchenne Muscular Dystrophy**

Backeljauw and Meilan Rutter, MD, FRACP, Endocrinology, also worked with James Collins, MD, PhD, and Brenda Wong, MD, MBBS, Neuromuscular Center, to study recombinant human insulin-like growth factor-1 (IGF-1) as a potential treatment in Duchenne muscular dystrophy (DMD) patients. This progressive, incurable muscle disorder affects one in 3,500 boys. DMD is treated with glucocorticoids (GC), which improve motor
function, but cause significant endocrine adverse effects such as growth failure and insulin resistance. IGF-1 is used to treat children with certain growth disorders. It also has been shown to improve muscle strength and survival in genetically engineered mice with DMD. The investigators hypothesized that IGF-1 therapy would improve statural growth and preserve muscle function in GC-treated DMD boys. They found that six months of a once-daily injection of IGF-1 therapy doubled height velocity and significantly increased height standard deviation scores compared to controls. Markers of insulin resistance also improved. However, there was no difference in motor functional outcomes.

**Functional Hormone Production in Human Intestine Generated from Pluripotent Stem Cells**

Jonathan Howell, MD, PhD, works with James Wells, PhD, to understand the nature of the human intestinal incretin hormones, GIP and GLP-1, which play an important role in regulating glucose homeostasis and are often dysfunctional in diabetes. Wells’ lab has established a method for differentiating human pluripotent stem cells into intestinal organoid tissue, which serves as a novel model for studying intestinal development and function. Howell has shown that the proximal-distal regional identity of intestinal organoids is regulated by bone morphogenetic protein (BMP) signaling, such that BMP inhibition promotes a proximal (small intestinal) fate, whereas activation results in a distal (large intestinal) fate. Importantly, there is segregation of intestinal incretin hormone producing cells within regionalized organoids, which mimics normal human intestine in vivo. These findings have allowed for the study human intestinal incretin pathology in the context of diseases such as diabetes and cystic fibrosis. Howell and colleagues are investigating the dynamics of hormone cell emergence in developing human intestinal tissue, the transcriptional network that controls individual hormone-specific cell fate, and the ability of experimental incretin-secreting drugs to elicit hormone responses. Results of this work will potentially impact new therapeutic regimens for patients with intestinal diseases and disorders of glucose homeostasis.

**Division Publications**


**Faculty, Staff, and Trainees**

**Faculty Members**

**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

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

Bethany Freedman, MD, PhD, Assistant Professor
Research Interests Adrenal disorders, glucocorticoid suppression of the adrenal axis, obesity and quality improvement programs to enhance patient care and clinical efficiency

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

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

Jonathan Howell, MD, PhD, Assistant Professor
Research Interests Using human stem cell derived intestinal tissue to understand human gut hormone development and function in order to facilitate new therapeutic options for diabetes

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

Sarah Lawson, MD, Assistant Professor
Research Interests Turner syndrome; Septo-optic dysplasia; endocrine abnormalities related to oncology and its treatments

Takahisa Nakamura, PhD, Assistant Professor
Research Interests Focus on endogenous dsRNA pathways to address questions concerning why and how inflammatory responses are initiated and thus involved in the pathogenesis of obesity.

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

Amy Shah, MD, Assistant Professor
Research Interests Type 2 diabetes; pre-diabetes; insulin resistance; obesity; lipid disorders

Peggy Stenger, DO, Assistant Professor
Research Interests Disorders of bone and calcium metabolism; 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

Joint Appointment Faculty Members

Jonathan Katz, PhD, Professor (Immunobiology)
Research Interests The immunology of type 1 diabetes mellitus

Jane Khoury, PhD, Associate Professor (Biostatistics & Epidemiology)
Research Interests: Diabetes in pregnancy and effect on offspring; stroke

James Wells, PhD, Professor (Developmental Biology)
Research Interests: Vertebrate gut development, stem cells, mammal

Trainees

Bethany Auble, MD, PL-6, University of Rochester
Nathan Bingham, MD, PhD, PL-6, Cincinnati Children's Hospital Medical Center
Cassandra Brady, MD, PL-4, Vanderbilt University
Janet Chuang, MD, PL-6, Rainbow Babies Children's Hospital
Sarah Corathers, MD, PL-6, University of Cincinnati
Marjorie Golekoh, MD, PL-4, Cincinnati Children's Hospital Medical Center
Pranati Jha, MBBS, PL-5, Albany Medical Center
Christel Keefe, MD, PL-4, Cincinnati Children's Hospital Medical Center
Arti Shah, MBBS, PL-5, University at Buffalo Program
Nicole Sheanon, MD, PL-6, University of Massachusetts
Stephanie Sisley, MD, PL-8, Indiana University
Halley Wasserman, MD, PL-4, Cincinnati Children's Hospital Medical Center

Division Collaboration

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)

Adolescent Medicine » Jennifer Hillman, MD, MS
Diagnosis, screening for comorbidities and management of Polycystic Ovarian Syndrome across three disciplines within an academic hospital

Behavioral Medicine and Psychology » Jessica Kichler, PhD
Depression Screening in Type 1 Diabetes clinical care and research projects

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

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
HDL Subspecies and Vascular Function

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

Epidemiology and Biostatistics » Lisa Martin, PhD, Jane Khoury, PhD, Jessica Woo, PhD, Heidi Sucharew, PhD, and Lindsey Hornung
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
Study of Clinical Efficacy of Three Month Depot GnRH Agonist in Suppression of Central Puberty
Study of birth length, growth patterns and GH therapy in patients with Diamond Blackfan anemia
Study on Endocrine phenotype of children with Shwachman-Diamond syndrome
Analysis of Prospective Annual Adrenocorticotropin (ACTH) Stimulation Testing among Survivors of Intracranial Tumor, a retrospective study

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

General Pediatrics » Maria Britto, MD, MPH
Research

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

Hematology Oncology » Richard Harris, MD, Stella Davies, MD, Parinda Mehta, MD, Karen Burns, MD, Kasiani Myers, MD, and Maryam Fouladi, 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
Study of endocrine phenotype of children with Shwachman-Diamond syndrome
Analysis of Prospective Annual Adrenocorticotropin (ACTH) Stimulation Testing among Survivors of Intracranial Tumor, a retrospective study
Study of endocrine effects after reduced intensity BMT
Study of endocrine effects after new treatment modality for high risk medulloblastoma

ICU » Derek Wheeler, MD
Research

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

Molecular and Developmental Biology » James Wells, PhD
Research

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

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

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

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

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

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

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

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

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

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

Solid Organ Transplantation » John Bucuvalas, MD
  Screening and Management of Diabetes in youths with solid organ transplantation

Sports Medicine » Gregory Myer, PhD
  Research

Surgery » Thomas Inge, MD, PhD
  Bariatric surgery in youth: safety, efficacy, and effect on carbohydrate and cardiovascular outcomes
  International Hypothalamic Obesity Registry
  HDL Subspecies and their changes post bariatric surgery

Grants, Contracts, and Industry Agreements

Grant and Contract Awards

CRIMMINS, N

  Type I Diabetes TrialNet
  National Institutes of Health(George Washington University)
DOLAN, L

Air Pollution, Subclinical CVD and Inflammatory Markers in the SEARCH Cohort
National Institutes of Health (University of Maryland)
R01 ES 019168 09/27/11-06/30/15 $16,299

SEARCH for Diabetes in Youth, Phase 3: Registry Study
Center for Disease Control and Prevention
U18 DP 002709 09/30/10-09/29/15 $427,358

Vitamin D and Arterial Stiffness in Youth
University of Cincinnati
11/01/12-06/14/13 $44,363

HANDWERGER, S

Transcriptional Control of Human Placental Differentiation
National Institutes of Health
R01 HD 065339 02/01/11-01/31/16 $192,924

KATZ, J

Control of Diabetes by Manipulation of Bc12 Family Members
National Institutes of Health
R01 DK 081175 07/01/11-06/30/15 $217,500

Dendritic Cells in the Breaking of Peripheral Tolerance in Type 1 Diabetes
National Institutes of Health
R01 DK 090978 09/20/10-08/31/13 $183,150

Dissecting Dendritic Cell Function in Autoimmune Diabetes
National Institutes of Health
R01 DK 078179 08/01/09-07/31/14 $213,173

NAKAMURA, T

Analysis of Pathogenic Double-Stranded RNA in Chronic Inflammatory Disease
Japan Science and Technology Corporation
02/11/13-03/31/16 $59,900

Functional Analysis of PKR, JNK, and RISC in Metabolic Inflammation and Homeostasis
American Heart Association
11SDG5270010 01/01/13-12/31/14 $70,000

RUTTER, M

DMD Insulin Growth Factor - 1
Charley's Fund
11/1/10-10/31/13 $200,000
### CNS NFκB Regulation of Glucose Homeostasis

**National Institutes of Health**

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**Current Year Direct**

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**Industry Contracts**

**BACKELJAUW, P**

- Eli Lilly and Company: $3,503
- Tercica, Inc: $8,952
- Versartis, Inc: $7,469
- Novo Nordisk Pharmaceuticals: $20,400

**DOLAN, L**

- Jaeb Center: $9,447

**KLEIN, D**

- Novo Nordisk Pharmaceuticals: $24,533

**ROSE, S**

- Debiopharm SA: $10,295

**Current Year Direct Receipts**

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**Total**

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