

Endocrinology

Division Details

RESEARCH AND TRAINING DETAILS

| | |
|-------------------------------------|-------------|
| Faculty | 19 |
| Joint Appointment Faculty | 3 |
| Research Fellows and Post Docs | 4 |
| Research Graduate Students | 6 |
| Total Annual Grant Award Dollars | \$1,731,620 |
| Total Annual Industry Award Dollars | \$357,454 |

CLINICAL ACTIVITIES AND TRAINING

| | |
|-----------------------|--------|
| Clinical Fellows | 8 |
| Inpatient Encounters | 4,035 |
| Outpatient Encounters | 15,639 |



Row 1: V Hwa, J Khoury, J Chuang, J Sanchez-Gurmaches, H Wasserman, I Gutmark-Little, N Sheanon, D Elder, A Sanghavi Shah

Row 2: M Rutter, N Crimmins, S Lawson

Row 3: N Yaya Jones, J Wells, T Nakamura, A Dauber, L Dolan, P Backeljauw

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Division Highlights

Amy Sanghavi Shah, MD, MS

Dr. Shah's research continues to study how types of cholesterol (lipids) become dysfunctional as a result of obesity and type 2 diabetes in adolescents. Work in 2016 from the [Shah Laboratory](#), in collaboration with several investigators at Cincinnati Children's and the University of Cincinnati ([Lawrence Dolan, MD](#); Thomas Inge, MD, PhD; and W. Sean Davidson, PhD) has shown that the dysfunctional profile seen in obesity and diabetes is reversible after weight loss surgery. Furthermore, they have shown this reversibility persists for up to eight years post-surgery, despite weight regain and residual obesity. These findings suggest that weight loss surgery influences lipids in a positive way by additional pathways other than weight loss. Future work will focus on determining these pathways.

Deborah Elder, MD

Since April 2014, 19 children and adolescents have undergone total pancreatectomy with islet cell transplantation (TPIAT) for significant, recurrent abdominal pain and impaired quality of life associated with acute or chronic pancreatitis. Dr. Deborah Elder, MD, the endocrine director of the program, in collaboration with other faculty members on the team ([Division of Gastroenterology, Hepatology and Nutrition](#); [Division of Pediatric General and Thoracic Surgery](#); and [Pain Management Service](#)) have used Academic and Research Committee (ARC) funding to establish a database, create several education tools for families (PCC website, educational videos, and patient handbook), and marketing tools to increase referral base. These efforts have resulted in 1-2 TPIAT procedures per month with a vast majority of the individuals coming from outside of Ohio. In March 2017, the team published a manuscript in *Pediatric Transplantation*, "Post-Operative Continuous Glucose Monitoring Following Pancreatectomy with Islet Auto Transplantation". A second manuscript, "Severe Fasting Hypoglycemia in a Child after Total Pancreatectomy with Islet Autotransplantation" is under review at *Pediatric Transplantation*, and submitted abstract, "Thrombocytosis Following Pancreatectomy with Islet Auto Transplantation in Children: Cincinnati Children's Hospital

Experience” sent to the [American Pancreatic Association](#) meeting. In the near future, the team will focus on identifying predictors of glucose intolerance and insulin independence post TPIAT and assessing quality of life after TPIAT.

New International Guidelines for Children and Adults with Turner Syndrome

A published comprehensive, international guideline that incorporates the most up-to-date knowledge on diagnosis, treatment and patient impact of Turner Syndrome (TS), is in the *European Journal of Endocrinology*, with [Dr. Philippe Backeljauw, MD](#), as the senior author. Dr. Backeljauw, and his colleague, Dr. Claus Gravholt, MD, PhD ([Aarhus University](#), Denmark), initiated the guideline project in collaboration with several professional societies, to incorporate the latest evidence-based advice for diagnosis and treatment of girls, and women, with TS throughout the entire lifespan. Drs. Gravholt and Backeljauw, co-chairs of the guideline consensus working group, agree that in particular, “the new cardiovascular-related advice should lead to lower morbidity and mortality, while the recommendations on growth hormone/estrogen replacement therapy and monitoring for co-morbidities, as well as guidance for pregnancy consideration, should lead to improved quality of life for all TS individuals.”

Sarah D. Corathers, MD

[Dr. Corathers](#)’ research focuses on psychosocial outcomes of adolescents and young adults with diabetes and health system based interventions to improve care. An example of these intersecting interests is the reliable implementation of depression screening of adolescents with diabetes at Cincinnati Children’s Hospital Medical Center, which has resulted in referral and evaluation for treatment needs of approximately 20% of individuals screened who endorse moderate or high symptoms and immediate evaluation for 7% of individuals who endorse suicidal ideation. At a national level, Dr. Corathers is working with colleagues in the Type 1 Diabetes Exchange Learning Network, supported by funding from the [Helmsley Charitable Trust](#), to build a quality improvement community for type 1 diabetes patients, families, clinicians, researchers, and advocates. Currently, as part of her role as faculty leader with the Type 1 Diabetes Exchange, Dr. Corathers is applying the model of integrating patient reported outcomes in clinical diabetes care to spread depression screening to six pilot pediatric and adult diabetes centers across the network.

Andrew Dauber, MD, MMSc

[Dr. Dauber](#)’s research continues to focus on defining the genetic etiologies of severe growth disorders. In a follow up of earlier work, Dr. Dauber published a report in the *Journal of Clinical Endocrinology and Metabolism* describing a large international cohort of patients with mutations in the Aggrecan gene. This cohort included 103 individuals from 20 families spread across seven countries. He found that patients with Aggrecan deficiency have a range of short stature with a median height of -2.8 standard deviations and the majority of children had a significantly advanced bone age at diagnosis. Early onset osteoarthritis was present in 12 of the families. Nineteen individuals had received growth hormone with some evidence of an increased growth velocity in those patients. Dr. Dauber and his colleagues in the [Cincinnati Center for Growth Disorders](#) are now planning on a prospective clinical trial of growth hormone for these patients.

In other work, Dr. Dauber and his collaborators from the [University of Sao Paulo](#) in Brazil, identified a second gene that, when mutated, causes precocious puberty. This gene, DLK1, is an imprinted gene and is only expressed when inherited from the father. This is similar to their prior findings of mutations in the imprinted gene MKRN3 as a major cause of familial precocious puberty. The current study used a combination of genetic techniques including linkage analysis followed by whole genome sequencing to find the mutation in DLK1 in a large Brazilian family.

Vivian Hwa, PhD

[Dr. Hwa](#)’s group continues involvement in a number of projects stemming from genes/variants identified by WES (whole exome sequencing) analysis in patients with monogenic growth disorders. Highlights include: (a) recent functionally proven dominant-negative mutations in the GHR (GH receptor) gene (published in *J. Endocrine Society*) and the STAT5B gene (submitted) expands the spectrum of GHI and IGF-I deficiency, and provided valuable insights into functional properties of the affected proteins; (b) CRISPR/Cas knock-in mouse model of pathological human missense PAPP2 mutation recapitulates patient growth phenotype. Characterization of these mice is on-going; (c) CRISPR/Cas knock-in mouse model of a rare, in-frame, IGF1R homozygous mutation, together with studies involving reconstitution system and primary cells, are currently in progress to understand the mechanism(s) for the microcephalic primordial dwarfism

and insulin resistance phenotype observed in affected children; (d) iPSC lines are being generated from patient cells for future organoid model studies of the human GH-IGF-I axis.

Division Publications

1. Mayer-Davis EJ; Lawrence JM; Dabelea D; Divers J; Isom S; Dolan L; Imperatore G; Linder B; Marcovina S; Pettitt DJ. **Incidence Trends of Type 1 and Type 2 Diabetes among Youths, 2002-2012.** *The New England journal of medicine.* 2017; 376:1419-1429.
2. Dabelea D; Stafford JM; Mayer-Davis EJ; D'Agostino R; Dolan L; Imperatore G; Linder B; Lawrence JM; Marcovina SM; Mottl AK. **Association of Type 1 Diabetes vs Type 2 Diabetes Diagnosed During Childhood and Adolescence With Complications During Teenage Years and Young Adulthood.** *Journal of the American Medical Association.* 2017; 317:825-835.
3. Guo MH; Dauber A; Lippincott MF; Chan YM; Salem RM; Hirschhorn JN. **Determinants of Power in Gene-Based Burden Testing for Monogenic Disorders.** *The American Journal of Human Genetics.* 2016; 99:527-539.
4. Sheanon N; Simpson B; Shaughnessy E. **Teenager With Hip Pain and Limp.** *JAMA Pediatrics.* 2017; 171:297-298.
5. Newton KP; Hou J; Crimmins NA; Lavine JE; Barlow SE; Xanthakos SA; Africa J; Behling C; Donithan M; Clark JM. **Prevalence of Prediabetes and Type 2 Diabetes in Children With Nonalcoholic Fatty Liver Disease.** *JAMA Pediatrics.* 2016; 170:e161971.
6. Shah AS; Maahs DM; Stafford JM; Dolan LM; Lang W; Imperatore G; Bell RA; Liese AD; Reynolds K; Pihoker C. **Predictors of Dyslipidemia Over Time in Youth With Type 1 Diabetes: For the SEARCH for Diabetes in Youth Study.** *Diabetes Care.* 2017; 40:607-613.
7. Garvey KC; Foster NC; Agarwal S; DiMeglio LA; Anderson BJ; Corathers SD; Desimone ME; Libman IM; Lyons SK; Peters AL. **Health Care Transition Preparation and Experiences in a US National Sample of Young Adults With Type 1 Diabetes.** *Diabetes Care.* 2017; 40:317-324.
8. Swertfeger DK; Li H; Rebholz S; Zhu X; Shah AS; Davidson WS; Lu LJ. **Mapping Atheroprotective Functions and Related Proteins/Lipoproteins in Size Fractionated Human Plasma.** *Molecular and Cellular Proteomics.* 2017; 16:680-693.
9. Subramaniam DR; Stoddard WA; Mortensen KH; Ringgaard S; Trolle C; Gravholt CH; Gutmark EJ; Mylavarapu G; Backeljauw PF; Gutmark-Little I. **Continuous measurement of aortic dimensions in Turner syndrome: a cardiovascular magnetic resonance study.** *Journal of Cardiovascular Magnetic Resonance.* 2017; 19:20.
10. Dauber A; Cunha-Silva M; Macedo DB; Brito VN; Abreu AP; Roberts SA; Montenegro LR; Andrew M; Kirby A; Weirauch MT. **Paternally Inherited DLK1 Deletion Associated With Familial Central Precocious Puberty.** *Journal of Clinical Endocrinology and Metabolism.* 2017; 102:1557-1567.
11. Gkourogianni A; Andrew M; Tyzinski L; Crocker M; Douglas J; Dunbar N; Fairchild J; Funari MFA; Heath KE; Jorge AAL. **Clinical Characterization of Patients With Autosomal Dominant Short Stature due to Aggrecan Mutations.** *Journal of Clinical Endocrinology and Metabolism.* 2017; 102:2016-3313.
12. Muñoz-Calvo MT; Barrios V; Pozo J; Chowen JA; Martos-Moreno GÁ; Hawkins F; Dauber A; Domené HM; Yakar S; Rosenfeld RG. **Treatment With Recombinant Human Insulin-Like Growth Factor-1 Improves Growth in Patients With PAPP-A2 Deficiency.** *Journal of Clinical Endocrinology and Metabolism.* 2016; 101:3879-3883.
13. Davidson WS; Inge TH; Sexmith H; Heink A; Elder D; Hui DY; Melchior JT; Kelesidis T; Shah AS. **Weight loss surgery in adolescents corrects high-density lipoprotein subspecies and their function.** *International Journal of Obesity.* 2017; 41:83-89.

14. Wasserman H; Ikomi C; Hafberg ET; Miethke AG; Bove KE; Backeljauw PF. **Two Case Reports of FGF23-Induced Hypophosphatemia in Childhood Biliary Atresia.** *Pediatrics.* 2016; 138:e20154453.
15. Wallace G; Jodele S; Myers KC; Dandoy CE; El-Bietar J; Nelson A; Taggart CB; Daniels P; Lane A; Howell J. **Vitamin D Deficiency in Pediatric Hematopoietic Stem Cell Transplantation Patients Despite Both Standard and Aggressive Supplementation.** *Biology of Blood and Marrow Transplantation.* 2016; 22:1271-1274.
16. Smego A; Woo JG; Klein J; Suh C; Bansal D; Bliss S; Daniels SR; Bolling C; Crimmins NA. **High Body Mass Index in Infancy May Predict Severe Obesity in Early Childhood.** *The Journal of Pediatrics.* 2017; 183:87- 93.e1.
17. Wong BL; Rybalsky I; Shellenbarger KC; Tian C; McMahon MA; Rutter MM; Sawnani H; Jefferies JL. **Long-Term Outcome of Interdisciplinary Management of Patients with Duchenne Muscular Dystrophy Receiving Daily Glucocorticoid Treatment.** *The Journal of Pediatrics.* 2017; 182:296-303.e1.
18. Gordon SM; Li H; Zhu X; Tso P; Reardon CA; Shah AS; Lu LJ; Davidson WS. **Impact of genetic deletion of platform apolipoproteins on the size distribution of the murine lipoproteome.** *Journal of Proteomics.* 2016; 146:184-194.
19. Gonzalez Ballesteros LF; Ma NS; Gordon RJ; Ward L; Backeljauw P; Wasserman H; Weber DR; DiMeglio LA; Gagne J; Stein R. **Unexpected widespread hypophosphatemia and bone disease associated with elemental formula use in infants and children.** *Bone.* 2017; 97:287-292.
20. Shah AS; Urbina EM. **Vascular and Endothelial Function in Youth with Type 2 Diabetes Mellitus.** *Current Diabetes Reports.* 2017; 17:36.
21. Myers KC; Howell JC; Wallace G; Dandoy C; El-Bietar J; Lane A; Davies SM; Jodele S; Rose SR. **Poor growth, thyroid dysfunction and vitamin D deficiency remain prevalent despite reduced intensity chemotherapy for hematopoietic stem cell transplantation in children and young adults.** *Bone Marrow Transplantation.* 2016; 51:980-984.
22. Corathers SD; Kichler JC; Fino NF; Lang W; Lawrence JM; Raymond JK; Yi-Frazier JP; Dabelea D; Liese AD; Saydah SH. **High Health Satisfaction Among Emerging Adults With Diabetes: Factors Predicting Resilience.** *Health Psychology.* 2017; 36:206-214.
23. Golekoh MC; Cole CR; Jones NHY. **Severe Hypothyroidism From Iodine Deficiency Associated With Parenteral Nutrition.** *Journal of Parenteral and Enteral Nutrition.* 2016; 40:1191-1193.
24. Brady CC; Vannest JJ; Dolan LM; Kadis DS; Lee GR; Holland SK; Khoury JC; Shah AS. **Obese adolescents with type 2 diabetes perform worse than controls on cognitive and behavioral assessments.** *Pediatric Diabetes.* 2017; 18:297-303.
25. Wasserman H; Hufnagel RB; Utz VM; Zhang K; Valencia CA; Leslie ND; Crimmins NA. **Bilateral cataracts in a 6-yr-old with new onset diabetes: a novel presentation of a known INS gene mutation.** *Pediatric Diabetes.* 2016; 17:535-539.

Grants, Contracts, and Industry Agreements

Annual Grant Award Dollars

| Investigator | Title | Sponsor | ID | Dates | Amount |
|----------------------------|--|---|----------------------|-------------------------|-----------|
| Amy Sanghavi Shah, MD | Understanding the Role of HDL Subspecies in Adolescents with Type 2 Diabetes | National Institutes of Health | K23 HL118132 | 04/15/2014 - 03/31/2019 | \$190,391 |
| Nancy Abigail Crimmins, MD | Long Term Investigative Follow-up in Trial Net (LIFT) | National Institutes of Health (University of South Florida) | USF - Crimmins,Nancy | 03/10/2014 - 06/30/2017 | \$1,750 |

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|----------------------------|---|--|----------------------|------------|------------|
| Vivian Hwa, PhD | Roles of STAT5b in IGF-1 Production and Human Growth | National Institutes of Health | R01 HD078592 | 09/01/2014 | \$353,270 |
| | | | | - | 06/30/2019 |
| Lawrence M Dolan, MD | Limited Competition for the Continuation of the SEARCH for Diabetes in Youth Cohort Study (UC4) - SEARCH for Diabetes in Youth Cohort Study | National Institutes of Health (Wake Forest University Health Sciences) | UC4 DK108175 | 09/25/2015 | \$359,372 |
| | | | | - | 09/24/2020 |
| Nancy Abigail Crimmins, MD | Anti-CD3 MAB (Teplizumab) for Prevention of Diabetes in Relatives At-Risk for Type-1 Diabetes Mellitus | National Institutes of Health (University of South Florida) | USF - Crimmins,Nancy | 02/27/2015 | \$10,530 |
| | | | | - | 06/30/2017 |
| Lawrence M Dolan, MD | SEARCH for Diabetes in Youth Registry Study, Phase 4: Ohio Center | Ctr for Disease Control and Prevention | U18 DP006134 | 09/30/2015 | \$358,934 |
| | | | | - | 09/29/2020 |
| Takahisa Nakamura | Role of Hepatic RNA Silencing in Insulin Resistance and Obesity | National Institutes of Health | R01 DK107530 | 09/01/2016 | \$351,000 |
| | | | | - | 07/31/2021 |
| Nancy Abigail Crimmins, MD | CTLA-A Ig (Abatacept) for Prevention of Abnormal Glucose Tolerance and Diabetes in Relatives At-Risk for Type-1 Diabetes Mellitus | National Institutes of Health (University of South Florida) | TN18 | 04/01/2016 | \$5,590 |
| | | | | - | 06/30/2017 |
| Jacob M Redel, MD | Molecular Epidemiology in Children's Environmental Health Training Program | University of Cincinnati | T32 ES010957 | 07/18/2016 | \$50,945 |
| | | | | - | 06/30/2017 |
| Vincent E Horne, MD | Molecular Epidemiology in Children's Environmental Health Training Program | National Institutes of Health (University of Cincinnati) | T32 ES010957 | 07/26/2016 | \$49,838 |
| | | | | - | 06/30/2017 |

Total Annual Grant Award Dollars

\$1,731,620

Annual Industry Award Dollars

| Investigator | Industry Sponsor | Amount |
|--|-------------------------------|------------------|
| Amy Sanghavi Shah, MD | Sanofi Synthelabo | \$72,212 |
| Andrew Dauber, MD | Alexion Pharmaceuticals, Inc. | \$100,000 |
| Andrew Dauber, MD | IPSEN, US | \$11,610 |
| Andrew Dauber, MD | OPKO Biologics | \$66,360 |
| Philippe Ferdinand Backeljauw, MD | Versartis, Inc. | \$107,272 |
| Total Annual Industry Award Dollars | | \$357,454 |