Division Introduction

The Division of Pediatric Genetics and Metabolism, under the direction of Ralph DeBerardinis, M.D., Ph.D., is responsible for the evaluation, diagnosis and treatment of children with genetic disorders, including birth defects, malformation syndromes, genetically-defined developmental delays, and inborn errors of metabolism. Approximately one in four admissions to tertiary care pediatric hospitals results from conditions with a genetic basis. Although many genetic conditions are rare, there are hundreds of these diseases and they collectively account for a disproportionate amount of illness and death in children. Furthermore, identifying the genetic basis of rare conditions often leads to specific treatments that dramatically improve the health of the patient.

There are three major components to the Division’s mission: Patient Care, Research, and Education.

Patient Care

With a large and growing team of physicians, genetic counselors, nurse practitioners, dieters, and social workers, we are a major regional resource for children and families with genetic diseases. Our team evaluates more than 250 patients each month with known or suspected genetic diseases. Particular strengths of our clinical program include:

- We have the largest regional practice specializing in the diagnosis and treatment of children with inborn errors of metabolism.
- We have several clinics specializing in malformation syndromes and genetic forms of developmental delay.
- We are experts in the use and interpretation of advanced genetic diagnostics, including tests involving next-generation sequencing.
- We are the only clinic in Dallas that accepts referrals from the Texas Department of Health's newborn screening program for biochemical disorders.
- We have the largest regional multidisciplinary clinic to evaluate and follow children with Down syndrome.
- We provide 24/7 coverage for our patients, with an M.D. Medical Geneticist on call at all times.

Research

Our clinical team is unique in that it is fully synchronized with a state-of-the-art research program in the Children’s Medical Center Research Institute, a joint venture between UT Southwestern and Children’s Health. Our Genetic and Metabolic Disease Program (GMDP) within the CRI is comprised of a team of scientists dedicated to identifying new genetic diseases and developing new ways to treat children with genetic disorders. We use advanced, highly efficient technologies to evaluate each patient’s genetic and metabolic individuality. State-of-the-art laboratory-based approaches in cellular and molecular biology are then used to understand the precise consequences of the DNA mutations identified in our patients. Our research team is funded through federal, state, and private grant support. Specific research goals within the GMDP include efforts to:

- Discover new genetic causes of childhood diseases.
- Understand the genetic basis of metabolic diversity and its relationship to health and disease in children.
- Develop new diagnostic methods to detect genetic diseases in patients.
- Develop imaging techniques to monitor metabolic states non-invasively in patients.
- Establish clinical trials to assess the effect of new treatments.
- Construct new disease models using genetically-modified mice, and use these models to test the effect of experimental therapies.
Education

We are a vital part of UT Southwestern Medical Center’s mission to train medical students, residents, fellows, and allied health professionals in pediatrics, genetics, and metabolism. We teach medical students and pediatric residents throughout their training, manage an accredited residency program to train the next generation of physicians in Medical Genetics, and provide continuing medical education in genetics and metabolism to the Dallas-Fort Worth medical community.

Faculty

The Division has four full-time and one part-time faculty and several residents, all with special interests in the diagnosis and management of a variety of genetic conditions such as inborn errors of metabolism, lysosomal storage disorders, Down syndrome, Marfan syndrome, craniofacial malformation syndromes, incontinentia pigmenti, osteogenesis imperfecta, and other disorders of skeletal development.

Honors / Awards

Ralph DeBerardinis
  - Named a Faculty Scholar by the Howard Hughes Medical Institute
  - Best Pediatric Specialists, D Magazine

Garrett Gotway
  - Best Pediatric Specialists, D Magazine

Angela Scheuerle
  - Best Pediatric Specialists, D Magazine

Luis Umana
  - Texas Rising Stars, Texas Monthly Magazine

Invited Lectures

Luis Umana
  - 1st Course in Neuromuscular Diseases: From Paraclinic to Clinical Practice, Fundacion Santafe de Bogota, Bogota, Colombia November 9 2016
    o Metabolic investigations in neuromuscular disorders
    o Genetic testing in neuromuscular disorders

Ralph DeBerardinis
    o “Understanding Metabolic Heterogeneity in Cancer Cells and Tumors
• Foundation IPSEN Conference on Tumor Metabolism, San Pedro De Atacama, Chile, March 2016
  o “Understanding Metabolic Heterogeneity in Cancer Cells and Tumors”
• Company of Biologists Symposium, West Sussex, UK, May 2016
  o “Metabolic Outliers in Human Disease”
• Cancer Biology Training Program, University of Colorado Denver – Anschutz Medial Campus, Aurora, CO, February 2016
  o “Understanding Metabolic Heterogeneity in Cancer Cells and Tumors”
• Cancer Center Seminar Series, Case Western Reserve University, Cleveland, OH, January 2016
  o “Understanding Metabolic Heterogeneity in Cancer Cells and Tumors”
• International VHL Symposium, Boston, MA, April 2016
  o “Cancer Metabolism”
• American Association for Cancer Research Annual Meeting, New Orleans, LA, April 2016
  o “Metabolic Heterogeneity in Cancer Cells and Tumors”
• Department of Biochemistry and Molecular Genetics Seminar Series, University of Illinois, Chicago, May 2016
  o “Metabolic Heterogeneity in Cancer Cells and Tumors”
• American Diabetes Association National Meeting, New Orleans, LA, June 2016
  o “Shared Themes of Metabolic Regulation”
• Department of Biology, Southern Methodist University, Dallas, TX, May 2016
  o “Metabolic Heterogeneity in Cancer Cells and Tumors”
• Department of Experimental Therapeutics, UT MD Anderson Cancer Center, Houston, Texas, October 2016
  o “Understanding Metabolic Heterogeneity in Cancer Cells and Tumors”
• Sanford-Burnham Cancer Metabolism Symposium, La Jolla, CA, June 2016
  o “Understanding Metabolic Heterogeneity in Cancer Cells and Tumors”
• Beatson International Cancer Conference, Glasgow, Scotland, July 2016
  o “Metabolic Heterogeneity in Cancer Cells and Tumors”
• The PI3K-mTOR-PTEN Network in Health and Disease Cold Spring Harbor Symposium, Cold Spring Harbor, NY, August, 2016
  o “Metabolic liabilities in cancer”
• Cold Spring Harbor – Asia Conference on Cancer Metabolism, Suzhou, China, September, 2016
  o “Understanding Metabolic Heterogeneity in Cancer Cells and Tumors”
• Division of Biology and Biological Engineering Seminar Series, California Institute of Technology, Pasadena, CA, November 2016
  o “Establishing Metabolic Phenotypes in Cancer Cells and Tumors”

Angela Scheuerle

• McDermott Center Works-In-Progress Conference, January 2016
  o “Ciliopathies”
• Department of Pediatrics, UT Southwestern Multidisciplinary Conference
  o Co-Moderator: April 26, 2016: Zika Virus
  o Participant: November 8, 2016: Noonan syndrome and Cardiomyopathy
• Texas A&M College of Dentistry, Craniofacial Biology Course (annual). Dallas, Texas September, 2016
  o “Craniofacial Genetic Syndromes”
• Birth Defects Epidemiology and Surveillance Branch, Texas DSHS biannual staff training. November, 2016
  o “Genetic Testing Technology” (90 minutes)
• Pediatric Society of Greater Dallas Quarterly Meeting, Dallas, Texas. November 2016
“Zika Virus”


**Education and Training**

The Division of Pediatric Genetics and Metabolism is committed to providing quality medical education for medical students, residents, and fellows.

**Medical Student Education**

Genetics is an essential component of all facets of medicine, and the Division of Pediatric Genetics and Metabolism is proud to take a major role in the education of medical students and other trainees within the UT Southwestern system.

**First-Year Medical Students**

We are highly involved in the first year medical school curriculum, including:

- Medical Biochemistry Course: protein and amino acid metabolism, hyperammonemia and urea cycle defects, defects in amino acid metabolism (PKU, MSUD, etc.), purine and pyrimidine metabolism, and treatment of inborn errors of metabolism

**Third-Year Medical Students**

Third-year medical students participate in pediatrics rotations involving:

- Case studies in clinical genetics
- Genetics clinic outpatient rotations
- Clinical genetics consultations

**Fourth-Year Medical Students**

We offer an elective in clinical genetics to fourth-year medical students involving outpatient genetics clinics and inpatient genetics consultations.

**Medical Genetics Interest Group**

We provide mentorship to UT Southwestern medical students considering a career in Medical Genetics. This highly successful interest group meets periodically to discuss new developments in clinical and research-based genetics. We seek to provide an environment to educate students about career opportunities in this exciting and rapidly expanding area of pediatrics.

**Resident Education**
We play a major role in the education of residents at UT Southwestern. Some of our activities include:

**Medical Genetics Residency Program**

The Department of Pediatrics, through the Division of Pediatric Genetics and Metabolism, is the sponsoring clinical department for our ACGME certified training program in Medical Genetics. Medical Genetics is a specialty of its own, rather than being a subspecialty of Pediatrics, Internal Medicine, or Obstetrics/Gynecology. The training program encompasses many clinical departments at UT Southwestern, including Pediatrics, Internal Medicine, Obstetrics/Gynecology (prenatal diagnosis), Neurology and Pathology (Clinical Molecular Genetics, Cytogenetics, and Biochemical Genetics), among others. The program is directed by Garrett Gotway, M.D., Ph.D., a board certified pediatrician and medical geneticist. Given its interdepartmental nature, the residency is managed through the McDermott Center for Human Growth and Development, the Human Genetics Center of UT Southwestern. Learn more about the Medical Genetics program.

**Pediatrics**

The Division provides didactic teaching for the pediatric residents, including but not limited to:

- Clinical dysmorphology
- Teratology
- Cause and evaluation of birth defects
- Common chromosome anomalies
- Newborn screening
- Acute metabolic disorders
- Genetic storage disorders

We provide direct teaching for the residents in the regular departmental clinical conferences, as well as part of our inpatient consultation service.

Finally, there is a Clinical Genetics elective available for second- and third-year pediatric residents. The residents see outpatients in our clinics and inpatients for consultation services under the supervision of one of the members of the Division faculty. We encourage the residents to participate in clinical research projects if they are interested.

**Other Specialties**

Trainees in other departments also spend time in our clinics. Residents in Neurology, Pathology, and other specialties may receive some of their training through our Division.

**Graduate Student Education**

We teach a variety of courses to students pursuing Ph.D.s and post-doctoral training, including seminars on:

- Human genetics and genomics
- Mendelian genetic diseases
- The use of metabolic tracers and metabolomics in the evaluation of human diseases
- Cancer metabolism
- Regulation of metabolic pathways in health and disease
- Informatic analysis of high-content genomic and metabolomic data sets
Residents

Unlike other subspecialties, training in genetics crosses departmental lines and is considered a residency rather than a fellowship. The Department of Pediatrics is the sponsoring clinical department, and the residency is managed through the McDermott Center for Human Growth and Development, the Genetics Center at UT Southwestern.

Research Activities

The Division has been involved in clinical research projects involving clinical trials of new therapies, as well as multicenter studies in clinical and molecular genetics. We have been involved in translational research, helping to make a bridge between the basic science researchers in molecular genetics and the patients. Our large and varied patient population gives us the ability to conduct clinical studies in several areas.

The laboratory of Dr. DeBerardinis is interested in understanding the metabolic activities that support cell growth and proliferation in normal cells and in cancer. In order to produce daughter cells, which occur with each round of the cell cycle, cells need to double their biomass (proteins, lipids, and nucleic acids). This is a tremendous challenge requiring energy, building blocks, and the coordination of a large number of metabolic pathways.

Dr. DeBerardinis is exploring the idea that these metabolic activities are orchestrated by growth factor-stimulated signal transduction pathways, which direct cells to take up abundant nutrients and allocate them into the proper metabolic pathways. He wants to understand how signal transduction impacts metabolic fluxes during physiologic states of cell proliferation (e.g., embryogenesis, wound healing, activation of the immune system) and during pathological states (e.g., cancer).

To do this, the DeBerardinis Lab uses a combination of techniques in molecular biology, cell biology, and biochemistry, coupled with metabolic flux analysis using mass spectrometry and nuclear magnetic resonance, and animal models of metabolism and cancer. Current projects include developing imaging probes to identify abnormal metabolic activities in tumors and in children with metabolic diseases and using metabolomics and genomics to identify new disease genes.

Dr. Scheuerle’s work with the Texas Department of State Health Services Birth defects Epidemiology and Surveillance Branch (BDES) affords excellent opportunity for both care and research at the public health level. In 2016 this became dramatically important in the state’s preparation for Zika virus. Dr. Scheuerle participated with others in the BDES to define case ascertainment parameters, expand information collected about cases with microcephaly, and provide fast-track surveillance for relevant cases. This work continues as the state establishes a baseline for microcephaly incidence in anticipation of autochthonous Zika transmission.

Clinical Activities

We accept referrals from all pediatricians and children's hospitals in the Dallas/Fort Worth metroplex, as well as from more distant areas within and beyond Texas. The Division’s clinical activities at Children’s Medical Center are focused in the following areas:

Metabolic Disease Clinic

The Metabolic Diseases Clinic provides evaluation and testing for children with known or suspected inborn errors of metabolism (IEMs). IEMs are a family of hundreds of rare diseases caused by mutations in the genes that allow the body to produce energy and grow. We are a regional center of excellence in these diseases, establishing the diagnosis in affected children, counseling and educating their families about these conditions, and optimizing therapy tailored to the needs of each child. Blood, urine, enzyme, and DNA analyses are performed for diagnosis. Patients with a confirmed diagnosis are
then provided with nutritional evaluation, genetic counseling and psychosocial assessment as well as long-term care.

The Metabolic Disease Clinic is closely associated with the Newborn Screening Clinic. We are a major referral center for the Texas Newborn Screening Program. This statewide program seeks to identify newborn babies with any of 30 different treatable diseases, many of which are genetic/metabolic in nature. A large fraction of the approximately 400,000 babies born in Texas each year are evaluated through our Division. When a baby in North Texas is found to have a metabolic abnormality on the newborn screen, the family is referred to our team for definitive diagnosis, treatment, and long-term care if necessary. Through the Texas Newborn Screening Program, more than 75 children with genetic metabolic diseases are identified each year, and the coordinated care of these children by the Metabolic Disease Clinic at Children’s significantly improves their development and survival.

**Genetics/Dysmorphology Clinic**

Children with conditions involving birth defects, developmental delay or mental retardation, or other known or suspected genetic disorders receive evaluation and testing in the Genetics/Dysmorphology Clinic. Chromosomal and DNA analysis for diagnosis of genetic disease is provided, as well as psychosocial assessment, counseling, and comprehensive case management with referral to medical specialists, community resources, and support groups. Family history analysis and risk counseling to discuss reproductive options also are available through a team of board-certified genetic counselors. As of August, 2016, this clinic is now available at the Children’s Specialty Center at THR Presbyterian in addition to the Children’s Health Dallas campus.

**Down Syndrome Clinic**

Faculty and staff with the Down Syndrome Clinic have more than 50 collective years of experience in caring for children with Down Syndrome and provide comprehensive treatment for children and their families, including medical management, genetic counseling, physical, speech and motor development evaluation and recommendations, psychosocial support, screening and referral for behavioral and psychiatric problems, and referral to community agencies for educational intervention or therapies. New patients are seen at the Children’s Health Dallas campus with follow up available both there and at the Legacy campus.

**Interdivisional and Interdepartmental Collaborations**

The genetic basis of many human diseases, and the broad utility of genetic testing across numerous subspecialties of Pediatrics and Internal Medicine, make the consultative services of our physicians essential to the clinical and academic missions of UT Southwestern.

Dr. Scheuerle is a key contributor to the Children’s Craniofacial program, participating in weekly care conferences involving Plastic Surgery, Dentistry, Otolaryngology, Medical Genetics, Psychology, and various ancillary services such as speech therapy and social work. She also attends the monthly FETAL conferences, a patient report and management planning meeting run by the department of Obstetrics & Gynecology and including Neonatology, Pediatric Surgery, Diagnostic Imaging, and Medical Genetics. Dr. Scheuerle sees adult patients as needed in the FETAL center. She also has joined the Stillbirth Committee, an organ of the Obstetrics & Gynecology department that reviews all the Parkland Hospital stillbirths.

Dr. Gotway provides Medical Genetics service in an outpatient clinic in the Aston Center, performing diagnostic evaluations and ongoing management of adult patients with Mendelian genetic disorders. This clinic is administered by the department of Internal Medicine and the Eugene McDermott Center for Human Growth and Development.
Current Grant Support

Ralph DeBerardinis

Grantor: NIH 2R01 CA157996 06
Title of Project: Metabolic regulators of tumor cell growth
Role: Principal Investigator
Dates: 5/2016 – 4/2021

Grantor: Howard Hughes Medical Institute
Title of Project: HHMI Faculty Scholar
Role: Principal Investigator
Dates: 11/2016 – 10/2021

Grantor: V Foundation Translational Research Award
Title of Project: Translational studies in lung cancer metabolism: creating new paradigms in diagnosis and therapy
Role: Principal Investigator

Grantor: CPRIT RP130272
Title of Project: The metabolic phenome of human lung cancer
Role: Principal Investigator

Grantor: CPRIT RP160089
Title of Project: CPS1: A new metabolic liability in non-small cell lung cancers
Role: Principal Investigator
Dates: 03/01/16 – 02/28/19

Grantor: Welch Foundation Grant I-1733
Title of Project: Compartmentation of a redox-balancing metabolic activity in the cancer cell peroxisome
Role: Principal Investigator
Grantor: NIH/NCI 1 R01 CA154843-01A1
Title of Project: Defining the metabolic phenotype of low grade gliomas in vivo
Role: Co-Investigator (PI-Maher)
Dates: 4/2012 – 3/2017

Grantor: DOD W81XWH-12-1-0464
Title of Project: Oxygen-Regulated Metabolic Homeostasis: Therapeutic Implications of Paradigm Shift
Role: Principal Investigator of Metabolomics sub-contract (PI-Semenza)
Dates: 9/2012 – 9/2017

Grantor: NCI R01 CA168815 03
Title of Project: Metabolic Adaptive Responses in Cancer
Role: Principal Investigator of Metabolomics sub-contract (PI-Plas)
Dates: 4/2013 – 3/2018

Grantor: UL1TR001105 03
Title of Project: UT Southwestern Center for Translational Medicine
Role: Co-Director of Core 1 (PI-Toto)
Dates: 7/2013 – 6/2018

Grantor: NIH 5 R01 CA174786 02
Title of Project: Signaling and Targeting of 6-Phosphogluconate Dehydrogenase in Human Cancers
Role: Principal Investigator of Metabolomics sub-contract (PI-Chen)

Grantor: NIH 1 P50 CA196516-01A1
Title of Project: UTSW SPORE in Kidney Cancer
Role: Principal Investigator of Metabolomics project (Overall PI: James Brugarolas)
Dates: 8/2016 – 7/2021

Jonathan Rios

Grantor: Texas Scottish Rite Hospital for Children
Title of Project: Genomic Characterization of Hereditary Spastic Paraplegia
Role: Principal Investigator

Grantor: Children’s Clinical Research Advisory Council (CCRAC)
Title of Project: Genetics of IMAGe Syndrome
Role: Principal Investigator

Grantor: Pediatric Orthopaedic Society of North America
Title of Project: Uncoupling Cell Signaling and Mineralization Defects in Neurofibromin Deficient Tibial Psuedoarthrosis
Role: Principal Investigator
Dates: 5/2015 – 4/2017

Grantor: NIH
Title of Project: Genetic and Metabolic Basis of Familial Lipodystrophies
Role: Co-Investigator
Dates: 9/2012 – 8/2017
Grantor: NIH  
**Title of Project:** UT Southwestern Center for Translational Medicine  
**Role:** Key Personnel  
**Dates:** 9/2013 – 4/2018

Grantor: Texas Scottish Rite Hospital for Children  
**Title of Project:** Solving the Genetics of Pediatric Musculoskeletal Disorders  
**Role:** Co-Investigator  
**Dates:** 6/2012 – 5/2016

Grantor: Texas Scottish Rite Hospital for Children  
**Title of Project:** Genetic Studies of Idiopathic Clubfoot  
**Role:** Principal Investigator  
**Dates:** 11/2014 – 10/2019

Grantor: Texas Scottish Rite Hospital for Children  
**Title of Project:** MAPK Signaling in Stem Cell Function and Bone Development  
**Role:** Principal Investigator  
**Dates:** 5/2015 – 4/2020

Grantor: NIH  
**Title of Project:** Target Pyrophosphate Excess to Prevent, Predict and Treat NF1 Pseudoarthrosis  
**Role:** Co-Investigator  
**Dates:** 12/2015 – 11/2020

Grantor: NIH  
**Title of Project:** The G.O.O.D. for Kids Program  
**Role:** Principal Investigator  
**Dates:** 9/2015 – 8/2016

Grantor: Pediatric Orthopaedic Society of North America  
**Title of Project:** Genome-wide Approach to Genetic Causes of Congenital Pseudoarthrosis of the Tibia (CPT)  
**Role:** Principal Investigator  
**Dates:** 5/2013 – 4/2015

Grantor: Texas Scottish Rite Hospital for Children  
**Title of Project:** Program for Medical Genetics  
**Role:** Co-Investigator  
**Dates:** Annual institutional support

Grantor: Texas Scottish Rite Hospital for Children  
**Title of Project:** Identification of *de novo* mutations causing Spina Bifida in discordant twins  
**Role:** Principal Investigator  
**Dates:** 2/2013 – 2/2016

---

**Peer-Reviewed Publications**


