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, dieticians, 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 perform initial evaluations in children with Down syndrome.
- We participate in multidisciplinary clinics specializing in relatively common disorders such as 22q11.2 deletion syndrome.
- We provide 24/7 coverage for our patients, with a 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 Research Institute (CRI), a joint venture between UT Southwestern and Children’s Health. The 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 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.
• Use multidisciplinary approaches (chart review, public health databases, 2- and 3-dimensional image analyses, etc.) to identify and characterize novel malformation syndromes.

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, co-direct a fellowship program in Laboratory Genetics and Genomics, and provide continuing medical education in genetics and metabolism to the Dallas-Fort Worth medical community.

Faculty

The Division has four full-time faculty members, all with special interests in the diagnosis and management of a variety of genetic conditions such as inborn errors of metabolism, newborn screening, lysosomal storage disorders, Down syndrome, craniofacial malformation syndromes, and incontinentia pigmenti.

Honors / Awards

Best Pediatric Specialists, D Magazine

• Ralph DeBerardinis
• Garrett Gotway
• Angela Scheuerle
• Luis Umaña

Texas Super Doctor, Texas Monthly

• Angela Scheuerle

Ralph DeBerardinis

• Elected to the Association of American Physicians
• Elected to the National Academy of Medicine

Garrett Gotway

• Promoted to Associate Professor

Angela Scheuerle

• Elected to Alpha Omega Alpha, Alumni Section by the Univ of South Florida Morsani College of Medicine
Invited Lectures

Ralph DeBerardinis (selected from over 20 extramural lectures)

- UCSF Symposium on Quantitative Biology, February, 2020
  - “Metabolic phenotypes and liabilities in human cancer.”
- Cancer Institute of New Jersey, June, 2020
  - “Metabolic phenotypes and liabilities in human cancer.”
- St. Jude Cancer Biology Program, August, 2020
  - “Metabolic phenotypes and cancer progression in humans”
- Mechanisms & Models of Cancer Cold Spring Harbor Meeting, August, 2020
  - “Metabolic phenotypes and cancer progression in humans.”
- American Association for Cancer Research Conference on Epigenetics and Metabolism, September, 2020
  - “Metabolic phenotypes and liabilities in human cancer.”
- European Association for Cancer Research, Virtual Conference on Cancer Metabolism, September, 2020
  - “Human tumor metabolism in vivo.”
- University of Illinois – Chicago Costa Symposium, October, 2020
  - “Metabolic phenotypes and cancer progression in humans.”
- EMBO Virtual Symposium, November, 2020
  - “Inter-Organ Communication in Physiology and Disease”
- American Association for Clinical Chemistry, Plenary Lecture, December 2020
  - “Metabolic Reprogramming in Human Cancer.”

Angela Scheuerle

- UTSW Pediatric Hematology/Oncology Grand Rounds, February 2020
  - “Genetic Testing in Childhood Cancer and Informed Consent”

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:

- Tissues 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.

Summer Genetics Fellowship

Starting summer 2020 we offer two rising second year medical students the opportunity for a clinical experience in Genetics and Metabolism. This is a paid fellowship covering two months. It includes clinical observation, experience in the clinical laboratories, and a series of lectures. The 2020 curriculum was impacted by Covid-19 but was still well received by the students - one of whom now says she wants to pursue Genetics as a career. Calls for applications for the 2021 summer have gone out.

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 and other specialties may receive some of their training through our Division. This includes the Laboratory Genetics and Genomics Fellow in the Department of Pathology, who has dedicated clinical rotations in both Metabolic Genetics and General Genetics.

Graduate Student Education

We teach a variety of courses to students pursuing Ph.Ds. 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

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

Our faculty are involved in clinical, translational, and basic research projects. Our over-arching goal is to better understand the genetic basis of human disease, and to advance new knowledge into new approaches to diagnose and treat our patients. Our large and varied patient population inspires research in numerous 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. Gotway is participating in a new endeavor at the McDermott Center for Human Growth and Development to enhance the discovery of new gene – disease associations in patients with novel clinical presentations. The Human Gene Discovery Laboratory will analyze whole exome and genome data from patients with unknown clinical syndromes to identify variants in novel genes that will expand our knowledge and understanding of human genetics.

Dr. Scheuerle is a co-investigator on Dr. A.J. Agopian’s study out of the University of Texas School of Public Health entitled A Multidisciplinary Approach for Identifying and Characterizing Novel Congenital Malformation Syndromes (NIH 1R01HD093660-01A1). This study uses a combination of Texas Department of State Health Services Birth Defects Registry data and chart review with the goal of identifying previously unrecognized malformation associations. Additionally, this study links birth defects with other health databases, such as cancer, to evaluate potential associations.

Dr. Scheuerle additionally has ongoing research in the natural history of Incontinentia Pigmenti. This is a survey generating study that has the current goal of elucidating the adult phenotype.
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 Clinics

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. Efforts in newborn screening are led by Dr. Luis Umaña.

A dedicated clinic is also provided for teenagers with IEMs transitioning into adult medicine. This clinic at Children’s is staffed by Dr. Markey McNutt, who is board certified in both Medical Genetics and Internal Medicine, and follows these patients after age 18 at a clinic in the Aston Center.

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 has been available at the Children’s Specialty Center at THR Presbyterian in addition to the Children’s Health Dallas campus, though it is on hold right now due to Covid restrictions and space limitations at that site.

Down Syndrome Clinic

Faculty and staff with the Down Syndrome Clinic have decades 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 sees adult patients as referred from both UTSW and community obstetricians and maternal fetal medicine specialists. These are coordinated through the Children’s FETAL program. She continues on the Parkland Hospital Stillbirth Committee, an organ of the Obstetrics & Gynecology department that reviews all the Parkland Hospital stillbirths. In early December, a small group consisting of Dr. Scheuerle, and Pathology, Obstetric, and Neonatology providers at Clements University Hospital met to work through best practices for managing stillbirths and early neonatal deaths. The goal is to provide optimum evaluation and testing of those fetuses/babies.

Beginning in summer 2019, under the direction of Dr. James Seaward in Plastic Surgery, a multidisciplinary group was formed for care and management of patients with 22q11.2 deletion syndrome. This has evolved quickly into a formal multidisciplinary clinic - the first one at Children’s Dallas and the first dedicated 22q11.2 deletion syndrome clinic in Texas. As of January 8, 2020, this became an in-person clinic held in the Plastic Surgery space on the 6th floor of the Ambulatory Services Center. Because Genetics evaluations and counseling are time intensive, all patients are being seen separately in the Genetics clinic once, then will be followed in the 22q11.2 deletion clinic. This clinic was on hiatus starting in March, then restarted with Genetics and Endocrinology continuing virtual visits while all other specialties see the patients in person.

**Current Grant Support**

**Ralph DeBerardinis**

- **Grantor:** National Institutes of Health/National Cancer Institute – R35  
  **Title of Project:** Metabolic Regulators of Tumor Cell Growth and Progression  
  **Role:** Principal Investigator  
  **Dates:** 09/2017 – 08/2024

- **Grantor:** Howard Hughes Medical Institute  
  **Title of Project:** HHMI Investigator Program  
  **Role:** Principal Investigator  
  **Dates:** 09/2018 – 08/2025

- **Grantor:** NIH – Project 3 (1 P50 CA196516-01A1)  
  **Title of Project:** UTSW SPORE in Kidney Cancer  
  **Role:** Principal Investigator of Metabolomics Project (Overall PI: James Brugarolas)  
  **Dates:** 08/2016 – 07/2021

- **Grantor:** Cancer Prevention and Research Institute of Texas – MIRA  
  **Title of Project:** Mechanisms of Melanoma Metastasis  
  **Role:** Co-investigator (Overall PI: Sean Morrison)  
  **Dates:** 12/2016 – 11/2022

- **Grantor:** CPRIT RP180778  
  **Title of Project:** Metabolic Enablers of Melanoma Progression  
  **Role:** PI of Project 3 and Metabolism Core (Overall PI: Sean Morrison)  
  **Dates:** 08/2018 – 08/2022
Grantor: 2P50CA070907-21A1  
**Title of Project:** The University of Texas SPORE (Special Program of Research Excellence) in Lung Cancer  
**Role:** PI of Project 1 (Overall PIs: John Minna and Jack Roth)  
**Dates:** 09/01/20-08/31/25

Grantor: Lawrence Steinberg Endowment  
**Title of Project:** Joel B. Steinberg, M.D. Chair in Pediatrics  
**Role:** Principal Investigator  
**Dates:** 12/2018 – Ongoing

Grantor: Robert L. Moody, Sr. Faculty Scholar Endowment  
**Title of Project:** Moody Faculty Scholar  
**Role:** Principal Investigator  
**Dates:** 10/2018 – Ongoing

Grantor: Once Upon a Time Foundation  
**Title of Project:** Discovering and Treating Genetic Metabolic Diseases in Children  
**Role:** Principal Investigator  
**Dates:** 03/2016 – 02/2020

**Angela Scheuerle**  
Grantor: National Institutes of Health/National Institute of Child Health and Human Development (R01)  
**Title of Project:** A Multidisciplinary approach for identifying and characterizing novel congenital malformation syndromes  
**Role:** Co-Investigator  
**Dates:** 9/2018 – 9/2023

**Peer-Reviewed Publications**


4. DeBerardinis RJ, Chandel NS. *We need to talk about the Warburg effect.* Nat Metab. 2020 Feb;2(2):127-129. PMID:32694689


7. Faubert B, Solmonson A, DeBerardinis RJ. *Metabolic reprogramming and cancer progression.* Science. 2020 Apr 10;368(6487):. PMID:32273439


16. Lesner NP, Gokhale AS, Kota K, DeBerardinis RJ, Mishra P. α-ketobutyrate links alterations in cystine metabolism to glucose oxidation in mtDNA mutant cells. *Metab Eng.* 2020 Jul;60():157-167. PMID:32330654


**Book Chapters**