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, 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 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 five 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 Down syndrome, Marfan syndrome, osteogenesis imperfecta, and other disorders of skeletal development.

Honors / Awards

Ralph DeBerardinis

- Named organizer of 2015 Keystone Symposium on “Integrating Metabolism and Tumor Biology”
- Named Chair of Metabolism and Cancer Section for American Association for Cancer Research

Mary Carlin

- Texas Super Doctors, Texas Monthly Magazine

Garrett Gotway and Angela Scheuerle

- Best Pediatric Specialists, D Magazine

Invited Lectures

Ralph DeBerardinis (from over 20 regional, local and international invited lectures in 2015)

  - Conventional and Unconventional Roles of Mitochondrial Enzymes in Tumor Cell Metabolism
- AACR, Society for Nuclear Medicine and Molecular Imaging, National Meeting, San Diego, CA, January 2015
  - Understanding Metabolic Heterogeneity in Cancer Cells and Tumors
- American Association for Cancer Research, Annual Meeting, Philadelphia, PA, April 2015
  - Understanding Metabolic Heterogeneity in Cancer Cells and Tumors
- AACR Special Conference on Cancer Metabolism, Bellevue, WA, June 2015
  - Metabolic Heterogeneity in Cancer Cells and Tumors
  - Metabolomics and Metabolic Flux Analysis
  - Metabolic Heterogeneity in Cancer Cells and Tumors
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
- Medical Genetics Course: population genetics, inborn errors of metabolism, assessing genetic risk/pedigree analysis, genetic screening, genetic counseling, and ethical issues in genetics

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
- 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.
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 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.

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.

**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.

Altogether, the Division staffed over 2,600 outpatient encounters in these clinics in 2015. This volume more than doubles the volume from two years ago.

**Current Grant Support**

**Ralph DeBerardinis**

- **Grantor:** NIH 1R01 CA157996 05  
  **Title of Project:** Metabolic regulators of tumor cell growth  
  **Role:** Principal Investigator  
  **Dates:** 7/2011 – 8/2016

- **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  
  **Dates:** 11/2013 – 10/2016

- **Grantor:** CPRIT RP130272  
  **Title of Project:** The metabolic phenome of human lung cancer  
  **Role:** Principal Investigator  
  **Dates:** 6/2013 – 5/2016
Grantor: Welch Foundation Grant I-1733  
**Title of Project:** Glutamine-Dependent Reductive Carboxylation (GDRC): A Metabolic Achilles' Heel in Cancer  
**Role:** Principal Investigator  
**Dates:** 7/2013 – 6/2016

Grantor: CPRIT RP101243  
**Title of Project:** Metabolic Imaging of Hyperpolarized $^{13}$C Substrates in Animal Models of Cancer  
**Role:** Co-Principal Investigator of sub-project (PI-Sherry)  
**Dates:** 9/2010 – 8/2015

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 – 3/2018

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)  
**Dates:** 4/2014 – 2/2019

**Jonathan Rios**

Grantor: Texas Scottish Rite Hospital for Children  
**Title of Project:** Genomic Characterization of Hereditary Spastic Paraplegia  
**Role:** Principal Investigator  
**Dates:** 4/2012 – 4/2016

Grantor: Children's Clinical Research Advisory Council (CCRAC)  
**Title of Project:** Genetics of IMAGe Syndrome  
**Role:** Principal Investigator  
**Dates:** 2/2013 – 1/2016

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  

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  

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  

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  
Peer-Reviewed Publications


