The Division of Pediatric Nephrology at UT Southwestern is among the largest pediatric nephrology programs in the United States and is the main provider of clinical services at Children's Medical Center for children with kidney disease, bone disease, and hypertension. The clinical service of the Division consists of the following components: hemodialysis and peritoneal dialysis, kidney transplantation, inpatient services, ambulatory services, and testing services including bone density and GFR measurement. Each of these services is coordinated to provide outstanding state-of-the-art care to children who have kidney disease, bone disease, and/or hypertension.

Concurrently, we are also committed to the training of outstanding physicians and scientists, as well as the discovery of new knowledge that will improve the current standard of care for future patients. Division faculty are devoted to improving the lives of children with renal disease by performing cutting edge research.

Jyothsna Gattineni, M.D.
Associate Professor,
Division Chief

Faculty

There are eleven pediatric nephrologists in the Division, each with a special area of expertise, including renal development, chronic and congenital kidney disease, X-linked hypophosphatemia, bone disease, nephrotic syndrome, hypertension, and renal tubular disorders.

Alexandra Idrovo, M.D.

Assistant Professor

M.D.
Universidad de Guayaquil, Guayas Province, Ecuador, 2010
Postdoctoral Training
Residency, Pediatrics
John H. Stroger Hospital of Cook County, Chicago, IL, 2013-2016
Fellowship, Pediatric Nephrology
Baylor College of Medicine, Houston, TX, 2017-2020
Interests: Dialysis, cardiorenal syndrome, hypertension

Ahmad Mashmoushi, M.D., Ph.D

Clinical Instructor

M.D.
Medical University of South Carolina, Charleston, SC, 2015
Ph.D.
Medical University of South Carolina, Charleston, SC, 2015
Postdoctoral Training
Residency, Pediatrics
UT Southwestern Medical Center, 2015-2018
Fellowship, Pediatric Nephrology
UT Southwestern Medical Center, 2018-2021
Interests: Medical education, CKD, nephrotic syndrome, HUS

Honors/Awards

Best Pediatric Specialists in Dallas, *D Magazine*

- Elizabeth Brown
- Jyothsna Gattineni
- Raymond Quigley
- Mouin Seikaly
- Matthias Wolf

Texas Super Doctors, *Texas Monthly*

- Michel Baum
- Mouin Seikaly

Best Doctors in American

- Michel Baum

DFW Child Mom-Approved Pediatric Specialists – DFW Child Magazine

- Jyothsna Gattineni

Invited Lectures

Jyothsna Gattineni

- World Congress of Nephrology/International Pediatric Nephrology Association, Kuala Lumpur, Malaysia, February 2022
    - *"Hypophosphatemic Rickets"*
- Children's Health Grand Rounds, Children's Health, Dallas, TX, January 2022
    - *"FGF23: A friend, foe or a mere biomarker"*

Matt Wolf

- Drug Development in Nephrology – New Opportunities for our Patients, Nationwide Children's Hospital, Columbus, July, 2022.
- Epithelial Physiology and Cell Biology, Telluride Science Research: Development of a High Throughput Screening (HTS) Assay for ADTKD-, UMOD Center, Telluride, July 2022.
- Uromodulin – from Diagnosis to Physiology and Therapy, C. S. Mott Children's Hospital, University of Michigan Health, Ann Arbor, September 2022
- UMOD, Renal Magnesium Homeostasis, and TRPM6", 3rd Annual ADTKD, International Summit, Boston, USA (virtual), October 2022
- New Therapeutic Opportunities for Autosomal Dominant Tubulo-Interstitial Kidney Disease, University of South Florida Morsani College of Medicine, Department of Pediatrics, Tampa, October 2022

Conference Presentations

Pediatric Academic Society Meeting, Denver CO, April 2022

Gattineni J

Oral Presentation, *"The Kidney and FGF23: Molecular mechanisms and Homeostatic Impact"*

Wolf M

Oral Presentation, *"Autosomal Dominant Tubulointerstitial Kidney Disease"*

Other Conferences

Wolf M

International Pediatric Nephrology Association, Calgary, Canada, September 2022
Oral Presentation, *"Overview of autosomal dominant tubulointerstitial kidney disease (ADTKD) – including Mucin-1"*

American Society of Nephrology, Orlando, Florida, November 2022
Presentation, *"Insulin receptor substrate 4 (IRS4) contributes to hypomagnesemia by mediating the insulin effect on the renal magnesium channel TRPM6."*

Education and Training

The Division of Pediatric Nephrology is one of a hand full of nephrology programs to be funded by an National Institutes of Health (NIH) T32 grant. This grant has funded the training of some of the most successful and productive pediatric nephrologists in the country. Fellows spend a total of 12 months on inpatient clinical service during the three years of training. All fellows spend one day a week seeing outpatients in the nephrology clinic. They also spend time in the metabolic bone clinic at Texas Scottish Rite Hospital for Children. The rest of their training is devoted to clinical or basic research. The trainees may go into one of the Division's basic science laboratories or other laboratories on campus who study renal disease. Some trainees have elected to spend a fourth year of training in renal transplantation.

Research Activities

The Division of Pediatric Nephrology has four basic research laboratories devoted to research into clinically important issues.

Baum Laboratory

The laboratory has published more than 140 research papers and 70 reviews in chapters in areas related to understanding how ions are transported across the renal epithelia in both children and adults. The Baum laboratory has been funded by the NIH for more than 25 years and has investigated the regulation of salt transport by the neonatal and adult kidneys as well as the transporters involved in salt transport. The laboratory has shown that some of the mechanisms involved in both active and passive salt transport are different in neonates than adults. Recently, the laboratory has focused on the mechanism of hypertension with prenatal programming. Small for gestational age infants and very premature infants develop hypertension and chronic kidney disease. The Baum laboratory uses a rat model to explore the pathophysiology of the increase in blood pressure and kidney injury with programming. Most recently, they have made significant discoveries that have shown that hypertension and kidney injury can be prevented by changes in the postnatal environment.

Drake Laboratory

Research in the Drake laboratory uses genetically engineered mouse models to understand how disruptions in normal kidney development lead to Wilms tumor, a rare kidney cancer that primarily affects children in the first years of life. During normal development, nephron progenitor cells are exhausted prior to birth, whereas in Wilms tumor, these specialized cells are abnormally maintained and are thought to drive the development of tumors. Despite this long-recognized link to renal development, the underlying mechanisms of how Wilms tumors originate from renal progenitor cells and can "hijack" developmental programs to result in this rare childhood cancer remain poorly understood, and Dr. Drake's work is aimed at better understanding how fundamental processes in development contribute to the biology of this rare kidney cancer.

Gattineni Laboratory

FGF23 is a phosphaturic hormone that is elevated in many metabolic bone diseases. It is the first hormone to increase in the blood in patients with chronic kidney disease and the levels increase progressively as renal disease worsens. The Gattineni laboratory has characterized the receptors for this hormone and, in so doing, has generated a mouse that has a 25-50-fold increase in FGF23 levels. Dr. Gattineni is using this mouse model to determine if elevated FGF23 contributes to the bone, vascular, and cardiac disease that is seen in patients with chronic kidney disease.

Wolf Laboratory

The Wolf laboratory studies the mechanism and regulation of magnesium and calcium transport. Calcium and magnesium are transported in the distal tubule by channels. His laboratory has made seminal contributions showing how these channels traffic to and stay in the membrane to transport calcium and magnesium. Several diseases, including diabetes, have dysregulated magnesium transport that can make the disease much worse. Dr. Wolf is examining why there is dysregulation of magnesium transport in diabetes and if there are factors that can normalize magnesium transport and improve the outcome of patients with diabetes.

Clinical Research

Pediatric Nephrology faculty members perform clinical research to study pathogenesis and therapy for children with nephrotic syndrome, chronic kidney disease, end-stage renal disease, hypertension, and transplantation. Dr. Brown is a co-investigator along with one of the adult nephrologists at UT Southwestern on two NIH-funded multicenter observational cohort studies of nephrotic syndrome. She is also a site-principal investigator for the DUPLEX study, a randomized multicenter, double-blind study of Sparsentan in primary focal segmental glomerulosclerosis. Dr. Quigley is a site investigator for an NIH-funded multicenter grant studying the role of ferric citrate as a phosphate binder in children with chronic kidney disease. Patients with end-stage renal disease are at risk for developing metabolic bone disease and secondary hyperparathyroidism. The Division has made significant contributions examining therapy for these complications. Dr. Seikaly cares for many children with metabolic bone disease, and he has made significant strides in improving the care and outcome for patients with X-linked hypophosphatemic rickets.

Clinical Activities

Dialysis

The Division of Pediatric Nephrology cares for 50-60 patients with end-stage renal disease, which places it among the three largest providers of such care for children in the United States. Approximately half of these patients are treated with peritoneal dialysis and the other half with hemodialysis. Under the direction of Dr. Jyothsna Gattineni, the Dialysis Program has met all the federal and state requirements necessary to provide services for the children under its care. The hemodialysis unit provides outpatient dialysis six days a week and two shifts a day. The Division provides 24-hour a day and seven-day a week on-call services for emergency dialysis to support children with acute kidney injuries hospitalized at Children's.

Inpatient Services

The Division provides care to all hospitalized children with all forms of kidney disease at Children's. The average inpatient census is 10-14 patients. The Division also provides inpatient consultation and manages acute dialysis and continuous renal replacement therapy in the intensive care unit.

Two separate inpatient teams (primary nephrology and consult teams) provide care on the Dallas campus. An attending on the primary service staffs a team of two second-year residents, medical students, pharmacists, dietician, social work, and a nurse case manager. The consult team is staffed by an attending who oversees a team of advanced practice providers (APPs) and fellows and provides consultation services on the Dallas campus, Plano campus, Parkland hospital, UT Southwestern hospitals, and telephone consults to pediatricians in town. We currently have three fellows; they rotate between the primary and consult

teams on a pre-determined schedule. There is an Attending Physician on call for consultation 24 hours aday and seven days aweek. All consultations are provided within 24 hours of the time requested.

In addition to providing inpatient services for patients with chronic kidney disease and dialysis requiring hospitalization, the Division also admits and cares for patients who have received renal transplants. This includes patients who have new renal transplants and those who have complications from a transplant such as rejection or opportunistic infection.

Clinic Services

Division faculty provide outpatient treatment for children with kidney disease in Dallas and the surrounding areas. Attending Physicians staff clinics five days a week. The Division also provides outpatient care for those patients who have received renal transplants in the Solid Organ Transplant Program clinic.

24 Hour Ambulatory Blood Pressure Monitoring

The measurement of blood pressure in an outpatient and inpatient setting has been found to be unreliable to assess whether the patient has hypertension. The Division offers 24-hour blood pressure monitoring devices, which are the gold standard for assessment of hypertension.

Testing Services

The Division provides testing services for children with chronic kidney disease and disorders of bone and mineral metabolism. These services are directed by Dr. Mouin Seikaly and include:

- **Bone Mineral Density**
    - The Division oversees a service dedicated to the quantification of bone mineral density. Many patients suffering from endocrine, rheumatologic, orthopedic, and kidney diseases have decreased bone mineral density, which may require therapy to improve bone strength.

- **Renal Function**
    - Renal function has traditionally been assessed using serum creatinine levels. Unfortunately, serum creatinine has been found to be an inaccurate measure of renal function in children. Creatinine levels not only reflect renal function but also muscle mass, which can be quite low in children with chronic disease. To circumvent this limitation, the Division has been providing an accurate measure of renal function using the Glofil technique, which is the gold standard for assessment of glomerular filtration rate in children.

Metabolic Bone Disease

Dr. Mouin Seikaly runs the Metabolic Bone Disease clinic at Texas Scottish Rite Hospital for Children and consults for disorders of metabolic bone disease at Children's Medical Center. Metabolic bone disease comprises several inherited disorders that can often be treated. Dr. Seikaly is a world's expert on the diagnosis and treatment of metabolic bone disease and has made research discoveries that have translated to improved patient care.

Patient Statistics

Nephrology Patient Stats by Type of Visit by Location By Year; Along With Patient Treated By Type.

	2016	2017	2018	2019	2020	2021	2022
Total number of admissions to C5	354	391	473	388	283	316	285
New Nephrology Clinic outpatient visits	1,014 Dallas: 883 Plano: 131	1,106 Dallas: 993 Plano: 113	1,058 Dallas: 880 Plano: 178	886 Dallas: 744 Plano: 142	915 Dallas: 791 Plano: 124	955 Dallas: 955 Plano: 0	 Dallas: 506 Plano:
Follow up Nephrology Clinic outpatient visits	3,591 Dallas: 3,118 Plano: 473	3,378 Dallas: 2,970 Plano: 408	3,447 Dallas: 3,045 Plano: 402	3,064 Dallas: 2,619 Plano: 445	2,792 Dallas: 2,387 Plano: 404	3,043 Dallas: 3,043 Plano: 0	 Dallas: 1,943 Plano:
Patients seen at Legacy	641 New Pt: 131 Follow Up: 473 Nurse Visit: 37	568 New Pt: 113 Follow Up: 408 Nurse Visit: 47	602 New Pt: 178 Follow Up: 402 Nurse Visit: 22	612 New Pt: 142 Follow Up: 445 Nurse Visit: 25	567 New Pt: 124 Follow up: 404 Nurse Visit: 20 TeleMed Audio: 19		 New Pt: 192 Follow up: 250 Nurse Visit:
Patients seen at UT Plano						295 New Pt: 145 Follow Up: 150	791 New Pt: 241 Follow Up: 550
Acute hemodialysis procedures: Inpatient hemodialysis	429	697	729	735	372	413	
Patients treated with CVVH	76	84	110	52	52	42	
Renal transplants: Living and Deceased	14	11	22	33	5	19	
Average number of hemodialysis patients	30	33	35	31	21	20	
Average number of peritoneal dialysis patients	36	38	29.5	28	31	36	

Current Grant Support

Michel Baum

Grantor: NIH-National Institute of DDK Diseases
Title of Project: George M. O'Brien Kidney Research Core Center
Role: Co-Principal Investigator
Dates: 09/2017 – 06/2023

Elizabeth Brown

Grantor: National Institutes of Diabetes and Digestive and Kidney Disease (NIDDK), and the Office for Rare Diseases Research (ORDR) at the National Institutes of Health (NIH), and The NephCure and Halpin Foundations
Title of Project: Nephrotic Syndrome Study Network ("NEPTUNE")
Role: Co-Investigator
Dates: 2013 – Present

Grantor: National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) at the National Institutes for Health (NIH).
Title of Project: Cure Glomerulonephropathy (CureGN)
Role: Co-Investigator
Dates: 2013 – Present

Sponsor: Retrophin, Inc
Title of Project: A Randomized, Multicenter, Double-Blind, Parallel, Active Control Study of the Effects of Sparsentan, A Dual Endothelinreceptor and Angiotensin Receptor Blocker, on Renal Outcomesin Patients With Primary Focal Segmental Glomerulosclerosis(FSGS)
Role: Principal Investigator
Date: 2019 – Present

Keri Drake

Grantor: NIH-National Institute of DDK Diseases
Title of Project: Wilms tumor 1 (Wt1) mutation reveals mechanisms of cell lineage crosstalk in the developing kidney
Role: Principal Investigator
Dates: 08/2022 – 05/2025

Jyothsna Gattineni

Grantor: NIH-National Institute of DDK Diseases
Title of Project: Consequences of Elevated Fibroblast Growth 23 in the Presence and Absence of Kidney Disease
Role: Principal Investigator
Dates: 07/2018 – 06/2023

Sponsor: Mark and Marcia King Foundation
Title of Project: FGF23: Friend, Foe or Innocent Bystander
Role: Principal Investigator
Date: 08/2013 – 07/2024

Raymond Quigley

Grantor: University of California, Los Angeles/ NIH-National Institute of DDK Diseases
Title of Project: Ferric Citrate and Chronic Kidney Disease in Children (FIT4KiD)
Role: CO-Principal Investigator
Dates: 06/2020 – 04/2025

Grantor: ABBVIE INC
Title of Project: A Phase 3, Prospective, Open-Label, Multicenter Study to Evaluate the Safety, Efficacy and Pharmacokinetics of Paricalcitol Oral Solution for the Treatment of Secondary Hyperparathyroidism in Pediatric Subjects Ages 0 to 9 Years with Stage 5 Chronic Kid
Role: Principal Investigator
Dates: 08/2021 – Present

Mouin Seikaly

Sponsor: RELYPSA INC
Title of Project: A Phase 2, Open-Label, A Phase 2, Open-Labe, Multiple dose Study to Evaluate the Pharmacodynamic Effects, safety, and tolerability of Patiromer for Oral Suspension in Children and Adolescents 2 to < 18 Years of Age with Chronic Kidney Disease and Hyperkalemia (EMERALD)
Role: Principal Investigator
Date: 09/2017 – Ongoing

Matthias Wolf

Grantor: NIH R01DK119631
Title of Project: Assay Development and Optimization for a High Throughput Screen to Detect Compounds Increasing Secretion of C150S Mutant Uromodulin
Role: Principal Investigator
Dates: 03/2020 – 12/2024

Grantor: NIH R01HL151632 (PI Mizuno)
Title of Project: Targeting insulin resistance to improve abnormal cardiovascular control in diabetes
Role: Co-Investigator
Dates: 06/2020 – 05/2024

Grantor: NIH P30 DK079328-11 (PI Moe)
Title of Project: George M. O'Brien Kidney Research Core Center
Role: Co-Investigator
Dates: 09/2017 – 06/2023

Grantor: Department of Defense W81XWH1910205
Title of Project: Urinary magnesium regulation by Mucin-1 and Uromodulin – an unexpected role in the development of type 2 diabetes mellitus
Role: Principal Investigator
Dates: 09/2019 – 08/2022

Grantor: CTSA Pilot Program 5UL1TR003163-02 NIH/UT Southwestern Medical Center, Pilot and Feasibility grant
Title of Project: Development of New Therapies Against Renal Fibrosis
Role: Principal Investigator
Dates: 2022 – 2023

Peer-Reviewed Publications

1. Bleyer AJ, **Wolf MT**, Kidd KO, Zivna M, Kmoch S. Autosomal dominant tubulointerstitial kidney disease: more than just HNF1β. *Pediatr Nephrol.* 2022 May;37(5):933-946. PMID:34021396

2. Chaney CP, **Drake KA**, Carroll TJ. Integration of Multiple, Diverse Methods to Identify Biologically Significant Marker Genes. *J Mol Biol.* 2022 Oct 15;434(19):167754. PMID:35868363

3. **Drake K**. Updates in the Management of Antenatal Hydronephrosis–from Current Practices to On-going Challenges. *Current Treatment Options in Pediatrics*. 2022 Mar;8(1). https://doi.org/10.1007/s40746-021-00233-8

4. **Drake KA**, Chaney C, Patel M, Das A, Bittencourt J, Cohn M, Carroll TJ. Transcription Factors YAP/TAZ and SRF Cooperate To Specify Renal Myofibroblasts in the Developing Mouse Kidney. *J Am Soc Nephrol.* 2022 Sep;33(9):1694-1707. PMID:35918150

5. Gipson DS, Troost JP, Spino C, Attalla S, Tarnoff J, Massengill S, Lafayette R, Vega-Warner V, Adler S, Gipson P, Elliott M, Kaskel F, Fermin D, Moxey-Mims M, Fine RN, **Brown EJ**, Reidy K, Tuttle K, Gibson K, Lemley KV, Greenbaum LA, Atkinson MA, Hingorani S, Srivastava T, Sethna CB, Meyers K, Tran C, Dell KM, Wang CS, Yee JL, Sampson MG, Gbadegesin R, Lin JJ, Brady T, Rheault M, Trachtman H. Comparing Kidney Health Outcomes in Children, Adolescents,

and Adults With Focal Segmental Glomerulosclerosis. *JAMA Netw Open.* 2022 Aug 1;5(8):e2228701. PMID:36006643

6. Hanudel MR, Laster ML, Portale AA, Dokras A, **Quigley RP**, Guzman GAL, Zaritsky JJ, Hayde NA, Kaskel FJ, Mitsnefes MM, Ramirez JA, Imani PD, Srivaths PR, Kogon AJ, Denburg MR, Blydt-Hansen TD, Reyes LZ, Greenbaum LA, Weidemann DK, Warady BA, Elashoff DA, Mendley SR, Isakova T, Salusky IB. A review of ferric citrate clinical studies, and the rationale and design of the Ferric Citrate and Chronic Kidney Disease in Children (FIT4KiD) trial. *Pediatr Nephrol.* 2022 Nov;37(11):2547-2557. PMID:35237863

7. Khin EE, Elmaghrabi AY, Alvarado LA, Modem V, **Quigley R**. Fluid balance assessment in pediatric hemodialysis patients by using whole-body bioimpedance spectroscopy (WB-BIS). *Pediatr Nephrol.* 2022 Oct;37(10):2449-2456. PMID:35166921

8. **Mashmoushi A**, **Wolf MTF**. A narrative review of Hyporeninemic hypertension-an indicator for monogenic forms of hypertension. *Pediatr Med.* 2022 May;5():. PMID:36325202

9. Sambharia M, **Gattineni J**, Noureddine L, Mansilla MA, Thomas CP. Familial hyperkalemic hypertension: hyperkalemia not hypertension defines dominant KLHL3 disease and may permit earlier recognition and tailored therapy. *J Nephrol.* 2022 Jul;35(6):1737-1742. PMID:35000137

10. van Megen WH, Beggs MR, An SW, Ferreira PG, Lee JJ, **Wolf MT**, Alexander RT, Dimke H. Gentamicin Inhibits Ca(2+) Channel TRPV5 and Induces Calciuresis Independent of the Calcium-Sensing Receptor-Claudin-14 Pathway. *J Am Soc Nephrol.* 2022 Mar;33(3):547-564. PMID:35022312

11. Wood WD, Elmaghrabi A, Gotway G, **Wolf MTF**. The roles of homocysteinemia and methylmalonic acidemia in kidney injury in atypical hemolytic uremic syndrome caused by cobalamin C deficiency. *Pediatr Nephrol.* 2022 Jun;37(6):1415-1418. PMID:34854955

12. Yang K, Han J, Gill JG, Park JY, Sathe MN, **Gattineni J**, Wright T, Wysocki C, de la Morena MT, Yan N. The mammalian SKIV2L RNA exosome is essential for early B cell development. *Sci Immunol.* 2022 Jun 3;7(72):eabn2888. PMID:35658009

13. Yang K, Han J, Asada M, Gill JG, Park JY, Sathe MN, **Gattineni J,** Wright T, Wysocki CA, de la Morena MT, Garza LA, Yan N. Cytoplasmic RNA quality control failure engages mTORC1-mediated autoinflammatory disease. *J Clin Invest.* 2022 Jan 18;132(2):. PMID:35040435

Book Chapters

1. **Wolf MTF**, Besse W, Bleyer AJ, Dahl NK (2022) Genetic Diseases Associated with Tubulointerstitial Nephritis. In: Atta MG, Perazella MA (Eds), *Tubulointerstitial Nephritis* (1st ed. Pp 139-160) Cham, Switzerland: Springer Nature