Biochemical Genetics

Division of Genetic Medicine, Department of Pediatrics

2017 Newsletter: Seattle Children's Hospital / University of Washington

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OVERVIEW:

The Biochemical Genetics program at Seattle Children's Hospital (SCH) and the University of Washington (UW) provides diagnostic expertise and ongoing follow-up of over 1800 patients with inborn errors of metabolism.

Inborn errors of metabolism are inherited disorders that cause a disruption or abnormality in one of the biochemical pathways involved in the production or breakdown of proteins, fats, or carbohydrates.

Our Biochemical Genetics Program offers immediate resources for intervention by a specialized team of physicians and other specialized health care providers and is supported by a diagnostic laboratory that aids in diagnosis and management of children and adults. Serving the large population of Washington State and neighboring regions, the Biochemical Genetics program provides a comprehensive multidisciplinary evaluation, diagnosis and long-term management program for patients and their families (/http://www.seattlechildrens.org/clinics-programs/biochemical-genetics/.)

Subspecialty clinics include the Cristine M Trahms Program for Phenylketonuria (PKU Clinic-UW), Biochemical/Metabolic Genetics clinics (SCH/UW), Lysosomal Disorders Clinic (UW/SCH), Urea Cycle Disorders Clinic (SCH/UW), Congenital Disorders of Glycosylation Clinic (SCH), and the Wilson Disease Clinic (SCH). Satellite clinics are held two times per year in Spokane.

Biochemical Genetics is actively involved in research studies funded by industry and government. Biochemical Genetics offers clinical trials working to benefit rare metabolic patients. We also provide extensive education for professionals and our patients.

2017 BIOCHEMICAL GENETICS PROGRAM FACULTY AND STAFF

Faculty and Staff changes in 2017:

In 2017 we welcomed **Sirisak Chanprasert**, MD, to the Lysosomal Storage Disorders Program at the University of Washington. He provides clinical services to adult patients with Fabry, Gaucher, Pompe, and the Mucopolysaccharide diseases at the University of Washington Medical Center. Dr. Chanprasert graduated from the Faculty of Medicine, Siriraj Hospital, Mahidol University, Bangkok, Thailand. After completing his internal medicine residency at Bassett Medical Center, Cooperstown, NY, he went on to finish a medical genetics and medical biochemical genetics residency and fellowship at Baylor College of Medicine, Houston, TX. He is one of a few physicians who are board certified in internal medicine, medical genetics, and medical biochemical genetics. In addition, he completed a one-year mitochondrial medicine research fellowship at the Seattle Children's Research Institute in the Center for Developmental Therapeutics. After completing his training, he joined the Division of Medical Genetics, Department of Medicine, University of Washington School of Medicine.

In 2017, we welcomed **Marie Norris**, MS, RDN, CD, CNSC as a new Dietitian to Seattle Children's clinical group. Marie had been with Seattle Children's as a clinical dietitian and moved to our specialty clinic early in 2017. We are so glad she is here. At the same time, we had to say goodbye to Melissa Edwards who moved to another group to better facilitate her career plan. We miss her, but do wish her all the best.

We are also pleased to announce that **Julie Spink**, BSN, RN, CEN has joined Biochemical Genetics as one of our nurses. She is very experienced in pediatrics and emergency room work and is a wonderful addition to our staff. Her presence helps tremendously since Edie Anyieni has shifted to part time due to family needs. Emily Burnham has become the primary Biochemical Genetics RN now.

All the nurses can and do work together and separately as members of the Biochemical Genetics team, handling a multitude of complex communications that often need a lot of choreography, lab testing coordination and paperwork issues as well as the more traditional nursing roles directly connected to clinic.

Another addition to our staff this year is **Jacob Kelliher**, BS, MHA as our Fellowship Coordinator for the new Biochemical Genetics Fellowship Program. Jacob comes to us from Saint Louis University, returning to the area that was once home. In a short time, Jacob has proven to be a very valuable asset to our staff and we look forward to the inaugural year of the fellowship program being well orchestrated.

Another happy note – Jenny Howell, our GC in the group has taken on her husband's name following her wedding and is now Jenny Thies. You can find her under that name now!

Attending Physicians

C. Ronald Scott, MD
Sihoun Hahn, MD, PhD
J. Lawrence Merritt, II, MD
Angela Sun, MD
Christina Lam, MD
Sirisak Chanprasert, MD
Anne Leavitt, MD (PKU Clinic)

Registered Nurses (SCH)

Emily Burnham, RN, BSN, CPN
Julie Spink, BSN, RN, CEN
Siri Sherman-Giere, RN, BSN, CPN
Andrea Hartgraves, RN, BSN, CPN
Edie Anyieni, RNC, BSN

Metabolic Dieticians:

Sarah Sullivan, MS, RDN, CD (SCH)
Marie Norris, MS, RDN, CD, CNSC (SCH)
Kelly McKean, MS, RDN, CSP, CD (SCH)
Beth Ogata, MS, RDN, CD (UW)
Janie Heffernan, MS, RDN, CD (UW)
Mari Mazon, MS, RDN, CD (UW)

Genetic Counselors:

Jenny Thies, MS, LGC (SCH)
Jie Feng, MS, LCGC (UW)

Social Workers

Andrea Barry-Smith, MSW, LICSW, JD (SCH)
Janet Hamovitch, MSW (UW)

Research Associates
Linnea Brody, MPH, CRA

Fellowship Program Coordinator
Jacob Kelliher, BS, MHA

To refer a patient:

- Seattle Children's Hospital: Please visit the website www.seattlechildrens.org and follow instructions for Healthcare Professionals referral process. Alternatively, call 206-987-3012 for additional information.
- University of Washington: 206-598-1800

2017 Clinical Activities:

In 2017, SCH and UW had over 1800 encounters encompassing outpatient visits and inpatient consultations with biochemical genetics. Major disorders seen in our clinic and hospital are summarized in **Table 1**. Some of the subspecialties of our program are highlighted below, but we see and welcome any patient with metabolic disorders or who needs evaluation regarding diagnosis, treatment or ongoing medical care.

Table 1. Major Disorders in 2017 at Seattle Children's & University of Washington Clinics
Lysosomal Storage Disorder
Phenylketonuria
Organic Acid Disorder
Amino Acid Disorder
Urea Cycle Disorder
Peroxisomal Disorder
Fatty Acid Oxidation Disorder
Cobalamin Metabolism Disorder
Mitochondrial Disorder
Congenital Disorders of Glycosylation
Wilson Disease
Developmental Delay
Failure to Thrive
Seizure Disorder
Carbohydrate Metabolism disorders
Biotinidase Deficiency
Biopterin Deficiency
Nephrogenic Diabetes Insipidus

Dietary Management for Inborn Errors of Metabolism at SCH

The Biochemical Genetic Nutrition (BCG) Program at Seattle Children's Hospital provides medical nutrition therapy to a variety of inborn errors of metabolism (IEM). Nutrition therapy for these various IEM disorders is often the cornerstone of the medical treatment, so the dietitians work closely with the BCG physicians to ensure the most appropriate nutrition plan for each patient.

When an individual is diagnosed with an inborn error of metabolism the dietitians work diligently to initiate the most appropriate nutrition plan of care. Significant education and support is provided to the patient and their family to support their success. Each nutrition plan is tailored to each individual in order to support normal growth and development, their specific nutrient requirements and appropriate modifications to macronutrients (such as carbohydrates, proteins or fat). This includes supporting individuals who eat by mouth, as well as those who require feeding tubes to meet their nutrition needs. During acute inpatient admissions sometimes specialized parenteral nutrition solutions are required, which would be managed by the BCG dietitians.

The BCG dietitians have in-depth knowledge of the numerous metabolic formulas available for patients and work with families to find a product that will be best tolerated and meet their needs. This past year they coordinated a cooking class, through support of a formula company, to offer families an opportunity to network and learn new recipes and ideas for home.

All of the biochemical genetic dietitians at Seattle Children's are members of Genetic Metabolic Dietitians International (GMDI), which is an organization that works to provide standards of excellence and leadership in nutrition therapy for genetic metabolic disorders. **Sarah Sullivan** is co-chair of the GMDI technology committee and has worked to support MetabolicPro, an online tool that supports biochemical genetic dietitians with nutrition calculations. **Marie Norris** joined us in March 2017 and is involved in projects to streamline and improve charting. **Kelly McKean,** has been with our team since the start, and now helps cover clinic in Bellevue and is a leader in the nutrition department for patient education.

Table 2. Lysosomal Storage Disorders in 2017
Gaucher Disease
Fabry Disease
Pompe Disease
MPS I (Hurler Syndrome)
MPS II (Hunter Syndrome)
MPS III (Sanfilippo Syndrome)
MPS IV (Morquio Syndrome)
MPS VI (Maroteaux-Lamy Syndrome)
MPS VII (Sly Syndrome)
Mucolipidosis II
GM1 gangliosidosis
Niemann Pick type C
Alpha-mannosidosis
Tay Sachs Disease

At University of Washington, the primary metabolic dietitian is **Beth Ogata**, is also a member of GMDI and a member of the GMDI Technology Committee. She also is in workgroups for Nutrition Management Guidelines for MSUD and Nutrition Management Guidelines for PKU.

The Congenital Disorders of Glycosylation (CDG) Program at SCH

The CDG program at Seattle Children's was established in 2017, with patients scheduled into a quarterly clinic. Dr. Christina Lam is currently the primary physician for these patients and she looks forward also to initiation of a new study for these disorders in 2018. In 2017, there were 2 patients seen here for this relatively new group of diagnoses and interest in the clinic remains high.

The Lysosomal Storage Disease (LSD) Program at UW/SCH

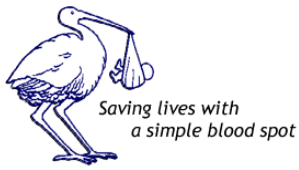
The LSD program provides multidisciplinary care including consultation, examination, testing/ diagnosis, treatment, monitoring, and genetic counseling for patients with lysosomal storage diseases and their families. The patients' medical home is centered with the Biochemical Genetics team. The program is dedicated to the management of these rare diseases and provides care by UWMC and SCH specialists in many areas of medicine including ophthalmology, orthopedics, cardiology, neurology, nephrology, pulmonary, otolaryngology, neurodevelopmental, radiology and anesthesia. Our group also works with local hospitals to facilitate transition of treatment to centers closer to each patient's home or for infusions to be done in the patient's home. Long term follow-up of patients with these rare diseases is essential.

Patient education and support meetings are held periodically, providing patients and their families an opportunity to mingle with other families and hear about recent advances in the field.

There is much ongoing research in the field of lysosomal storage disorders. The UWMC and SCH teams currently have active patient registries for MPS I, MPS II, MPS IV, MPS VI, Pompe disease, Fabry disease, and Gaucher disease. The clinic team follows a large cohort of patients across the spectrum of LSDs as illustrated in **Table 2** and long term follow-up of patients with these rare diseases is essential as is continuing to keep abreast of new developments in therapies and care. A clinical trial for Hunter syndrome is in progress at SCH under IRB approval to evaluate long term safety and clinical outcomes of intrathecal Idursulfase enzyme replacement. Another clinical trial on patients with Pompe disease to evaluate the efficacy and safety of alglucosidase alfa produced at the 4000L scale was successful and the medication was approved by the FDA.

The Newborn Screening Program

Since Washington State's Newborn Screening Program began in 1963 with PKU, the Biochemical Genetics Program has been providing confirmatory diagnostic testing, clinical treatment and care coordination for babies identified with metabolic diseases from infancy to adulthood. The Biochemical and Molecular Genetics Laboratory staff works very hard to prioritize and analyze these samples as quickly as possible. In 2017 Washington State screened for 6 amino acid disorders, 5 fatty acid oxidation disorders, 7 organic acid disorders, and 10 other congenital disorders. Details of each disorder can be found at www.doh.wa.gov/nbs .



We continue to be actively involved with the Western States Regional Genetics Network (http://www.westernstatesgenetics.org/) to study the outcomes of infants with abnormal newborns screens and, in particular, the long-term outcomes of infants identified with Very Long-Chain Acyl-CoA Dehydrogenase (VLCAD) Deficiency.

The Washington State Department of Health (DOH) continues to provide the Newborn Screening confirmation & follow-up program possible with contract funding for the consultative services and

additional testing required to confirm or rule out presumptive diagnoses. This confirmatory diagnosis allows for the earliest possible treatment to begin, giving these children the best quality of life and in some cases a normal or nearly normal lifestyle that would not have been possible without this early care. DOH also continues to provide contract funding for metabolic dietitian services for the Newborn Screening Follow-up Program, as well as for outreach services for semi-annual outreach Biochemical Genetics Clinics in Spokane.

The Newborn Screening Program is partnering with researchers at the University of Washington to refine the lab method for detection of lysosomal storage diseases (LSDs) in infants through newborn screening. The data to date indicates that the prevalence of Fabry, Pompe and Mucopolysaccharidosis Type 1 (MPS-1) is two to four times greater than the prevalence estimates by clinical diagnosis. It is apparent that the tandem mass spectrometry method can be expanded to detect additional LSDs from a single blood spot for which therapy exists or is being developed. Future plans include the addition of at least five more lysosomal storage diseases to the new assay: MPS Type II, MPS Type IV-A, MPS VI, neuronal ceroid lipofuscinosis (NCL-2), and lysosomal acid lipase (LAL) deficiency.

Table 3. 2017 Newborn Screening Totals of Confirmed Conditions

Condition	Severe	Mild
ASA/CIT	1	
BIO	1	
CUD		
GAI	1	
GALT	4	
HCY		
HMG/MCD		
IVA	2	
LCHAD	1	
MCAD	7	1
MMA	3	
MSUD		
PKU	3	
VLCAD		
Total	**23**	**1**

Does not include 9 other non-panel conditions identified: one Citrin deficiency, six 3-MCC cases, one 2-MBDH deficiency case, and one GA-2 case.

Current Newborn Screening Staff:

Office Director: John D.Thompson, PhD, MPA, MPH
Laboratory Supervisor: Fonda Olsen, MS
Laboratory Quality Assurance Coordinator: Santosh Shaunak, BS
Follow-up Supervisor: Lani Culley, MPH
Health Services Consultants: Carol Nucup-Villaruz, MD, Megan McCrillis, MPH, Christine Nguyen, BS
Quality Assurance Supervisor: Ashleigh Ragsdale, MPH
Quality Assurance: Gauri Gupta, MScPH; Heidi Lovejoy
Laboratory Leadworkers: Tim Davis, Bill Hoffman, Greg Olin, Aihong Thai, Arun Singh
Laboratory Chemists & Microbiologists: Brenda Angulo, Aaron Boyce, Sarah Hasselbalch, Luis Loyola, Joshua Oakes, Benjamin Peprah, Aranjeet Singh, Abbey Werede, Gretchen Zych
Support Staff: Relasha Sampson, Elizabeth Rankin

The Urea Cycle Disorders (UCD) Program at SCH provides multidisciplinary care including consultation, examination, testing, diagnosis, treatment, and genetic counseling for patients with urea cycle disorders and their families. Our goal is to provide patients and families with a comprehensive medical home that is centered on the patient and family. Our mission is to provide each patient with the knowledge, ability, and proper tools to allow them to manage their disorder. The biochemical genetics team is the core within a larger program dedicated to the management of these diseases and providing care by UWMC and SCH specialists in many areas of medicine including psychology, neurodevelopment, neurology, gastroenterology, and organ transplant. The clinic team follows a large group of children and adult patients across the spectrum of UCDs. Our group also works with local hospitals to coordinate the treatment of care during acute emergencies and in routine follow-up closer to each patient's home.

We are active members of the Urea Cycle Disorders Consortium Longitudinal study, sponsored by the Rare Disease Clinical Research Network at the National Institute of Health (http://rarediseasesnetwork.epi.usf.edu/ucdc/) along with the National Urea Cycle Disorders Foundation (www.nucdf.org) in order further improve treatment, quality of life, and our understanding of UCDs and to implement newborn screening for all UCDs – including ornithine transcarbamylase deficiency. We are also actively involved in multiple collaborations with urea cycle disorder support groups and with clinical research trials developing novel treatments of UCDs.

2017 LABORATORY UPDATE:

Biochemical Genetics Laboratory (SCH)

Molecular Genetics Laboratory (SCH) (http://www.seattlechildrens.org/geneticslab)

The Biochemical Genetics Laboratories (SCH) are led by Dr. Sihoun Hahn and Dr. Rhona Jack. In 2017, they were joined by Dr. Anna Scott. Test volumes in the labs are summarized in **Table 5**. The Biochemical and Molecular Genetics

Laboratories serve as a key component of the Biochemical Genetics Program. The laboratories provide rapid, comprehensive diagnostic and monitoring results along with guidance for follow-up.

Our laboratory is committed to high quality results. To ensure accuracy, the laboratory is participating in a variety of external proficiency testing programs offered by various national and international agencies (ERNDIM; European network, CAP; College of American Pathologists, CDC; Center for Disease Control).

The Molecular Development Laboratory (UW)
(http://depts.washington.edu/moleclab)

The molecular development lab is directed by Dr. C. Ronald Scott, a pioneer in the area of research and development for diagnosis and treatment of metabolic disorders. Additional scientist Jie-Yu Huang, PhD, has 25 years research experience in molecular biology. The laboratory is in its tenth year and is a CLIA-certified clinical lab that offers DNA analysis for Gaucher, Congenital Sucrase-Isomaltase Deficiency (CSID), and Tyrosinemia.

Research and Development (R&D) Laboratory
http://www.seattlechildrens.org/research/integrative-brain-research/our-labs/hahn-lab/

The Biochemical Genetics program's CLIA-certified R&D Laboratory is located at the Seattle Children's Research Institute (SCRI): Center for Integrative Brain Research (Center Director. Dr. Jan-Marino Ramirez). The facility is fully equipped with a LC-MS/MS and an Illumina Genome Analyzer IIx. Since 2007, the R&D team has continuously focused their efforts on refining current methodologies and developing new tests, with a fundamental goal to improve clinical practice through the implementation and integration of routine laboratory testing. In particular, the lab aims to develop and validate clinical tests to diagnose various metabolic and genetic disorders by utilizing tandem mass spectrometry.

Table 5. High Volume Tests in 2017

Test	Analytic Method	# Analyses
Fragile X	Fragment Analysis, Southern Blot	254
Prader Willi /Angelman Syndrome	Methylation PCR	33
Gaucher Disease	Sequencing	1
MCAD	Sequencing	29
Muscular Dystrophy	MLPA	6
Pyridoxine-Dependent Seizure	Sequencing ALDH7A1 gene	0
POLG 1	Sequencing	14
Spinal Muscular Atrophy	PCR	14
Spinal Muscular Atrophy Carrier Testing	MLPA	23
VLCAD	Sequencing	4
Wilson Disease	Sequencing	12
GCK	Sequencing	5
KCNJ11	Sequencing	2
HNF1A	Sequencing	11
HNF4A	Sequencing	11
ABCC8	Sequencing	0
INS	Sequencing	0
MODY Panel	Sequencing	35
CHI panel	Sequencing	2
Neonatal Diabetes panel	Sequencing	1
Connexin	Sequencing	17
Amino Acid Analysis	HPLC	1807
Phenylalanine / Tyrosine	HPLC	690
Organic Acid Analysis	GC/MS	1192
Acylcarnitine profile	MS/MS	993
Carnitine profile	MS/MS	581
Alpha aminoadipic semialdehyde	LC/MS/MS	245
Pipecolic acid	LC/MS/MS	39
Oligosaccharide	TLC	107
Very long chain fatty acids (peroxisomal)	GC/MS	119
MPS	Dye Binding	137
Succinylacetone QNT	GC-MS	21
MMA, plasma	LC-MS/MS	228
Enzyme Testing	Fluorometric	
Lysosomal Acid Lipase		4162
Alpha-galactosidase		20
Alpha-glucosidase		86
Beta-galactosidase		1
Hexosaminidase		5
TPP Tripeptidyl peptidase (NCL2)		70
PPT Protein palmitoyl transferase (NCL1)		68
Arylsulfatase A		10
Beta-glucosidase		13
Biotinidase		12
Galactose 1 Phosphate		39
Galactose-1-PUT		12
Miscellaneous enzymes		18
Total number as noted		11149

The R&D team has a long-standing interest in developing a mass spectrometry based assay for

diseases characterized by the absence and/or reduction of protein markers. We use a highly sensitive and targeted analytical technology, selected reaction monitoring mass spectrometry (SRM-MS), to measure peptides of our interest, which enables more efficient translation of protein markers into clinical use as screening and diagnostic tests. As proof-of-concept, we previously demonstrated that SRM-MS analysis of signature peptides can correctly identify patients lacking specific protein markers of three life-threatening Primary Immunodeficiency Disorders (Proteomics Clin Appl, 2012, R21AI85488). Our efforts (R56AI106784, R21HD069890, and CRFS-2015-004) to improve the sensitivity of our assay by combining SRM-MS with antibody-based enrichment of target peptides (immuno-SRM) showed that the method can detect extremely low abundance marker proteins of congenital disorders such asCD3e (for SCID), BTK (for XLA), WASP (for WAS), CTNS (for Cystinosis), and ATP7B (for Wilson disease) in dried blood spots. In 2016, we published the proof-of-concept study demonstrating that the immuno-SRM assay readily distinguishes affected cases of Wilson disease from normal controls (p<0.0001) (Journal of proteome research, 2016). We also received a NIH grant (R01AI123135) to further study and develop a multiplexed immuno-SRM assay for screening11 different primary immunodeficiency disorders. We believe that our proteomics based approach will provide an efficient and inexpensive screening for a broad range of genetic disorders.

At the heart of translational research, the R&D Laboratory's goal is to bridge basic research and the clinical applications of novel tests developed for effective patient diagnosis and treatment. Current staffs of the R&D team include Christopher Collins, PhD and Remwilyn Dayuha, BS which is led by Dr. Sihoun Hahn.

Dr. Irene Chang has been working in Dr. Hahn's laboratory in 2017 to develop a novel and innovative assay for Pompe disease using tandem mass spectrometry. Her work titled as "Immunogenicity screening and predicting need for immunomodulation by quantification of proteolytic peptide biomarkers in dried blood spots of patients with Pompe Disease and Mucopolysaccharidosis Type I" has been recently granted as ACMGG fellowship award.

Pompe disease (PD) and MPS I are recessive diseases characterized by decreased or absent acid α-glucosidase (GAA) and alpha-L-iduronidase (IDUA) enzymes, respectively. Enzyme replacement therapy (ERT) is effective at prolonging survival and protecting cognitive development in patients with infantile PD and improve pulmonary functioning, stabilize disease progression, and reduce biochemical parameters in patients with MPS I. However, a universal efficacy is limited as some patient populations will develop immune-mediated inhibitory reactions (neutralizing antibodies) to the exogenously supplied therapeutic enzymes. Patients with PD who develop sustained high titers of neutralizing antibodies to ERT that render the treatment ineffective usually also have poor clinical outcomes. Immunomodulation for these groups of patients, ideally before ERT begins, would improve treatment efficiency. Rapid detection of immunogenic potential would allow for pre-emptive patient immunomodulation and increased therapeutic efficacy. Her work aims to harness this technology in the quantification of peptides of target proteins associated with immunogenicity to ERT in patients with PD and MPS I. By developing a rapid and accurate assay for detecting specific biomarkers, she hopes to reduce immunogenic reactions to ERT and improve the clinical outcomes of patients with these treatable metabolic disorders.

EDUCATION / TRAINING IN CLINICAL BIOCHEMICAL GENETICS

Fellowship in Medical Biochemical Genetics:

The University Of Washington School Of Medicine's, Medical Biochemical Genetics Fellowship is based at Seattle Children's Hospital and provides care to children and adults at Seattle Children's Hospital and the University of Washington. Our program covers a diverse population from a large region covering five states in the Pacific Northwest. Fellows will have an opportunity to participate in clinical care and learn from patients from all areas of inborn errors of metabolism in clinic, will act as a member of the primary admitting in-patient service and hospital consultation service. Fellows will also have opportunities to participate in the vast clinical and basic science research programs at both

institutions and in the clinical biochemical genetics laboratory to learn the complex interpretation of biochemical genetic testing.

During the year, fellows have an intensive exposure to inpatient and outpatient biochemical genetics and nutrition. Fellows are exposed to a wide variety of acute and chronic inborn errors of metabolism with exposure to treatment through nutritional manipulation, medications, enzyme replacement therapy, and solid organ or bone marrow transplantation. Through the year, fellows will have the opportunity to rotate in the Biochemical Genetics Laboratory. Fellows are encouraged and supported in presenting their research at national and international meetings. This training focuses on providing fellows the skills necessary to become independent academic medical biochemical geneticists.

http://www.washington.edu/medicine/pediatrics/fellowships/overview/medical-genetics

We are excited to announce our first Medical Biochemical Genetics Fellow will be Irene Chang, MD, starting in July, 2018.

In addition to the formal fellowship program, the Biochemical Genetics training program at UW is accredited by the American Board of Medical Genetics and leads to eligibility to sit for the Clinical Biochemical Genetics examination. The goal of the program is to provide medical genetics residents with a sound academic, clinical, and laboratory understanding of the diagnosis, treatment and management of patients with inborn errors of metabolism. These residents are also exposed to and review the complexities and processes of the Newborn Screening program, a crucial tool in detecting these disorders as early as possible.

In 2017, **Dr. Ken Ndugga-Kabuye** had a three month rotation in clinical biochemical genetics from January through March at Seattle. **Dr. Jennifer Dines** was with us for a similar rotation from April through June 2017. Biochemical Genetics also provides rotations for residents of other specialties to provide a greater knowledge of the complexities and range of many of the conditions and disorders referred here. There is emphasis on the need to maintain a coordinated collegial approach in the diagnosis and care of these patients, whose conditions cross the boundaries of many specialties.

In 2017, **Jeongho Lee**, MD, PhD took on a year-long program with Dr. Hahn. Dr. Lee came to us from Korea as a neurologist with special interest in clinical biochemical genetics. He worked with Dr. Hahn in his research lab and was also at the hospital campus regularly. He has returned to Korea to the directorship of his own clinical group.

The PKU and Biochemical Genetics Programs also provide ongoing training to residents, medical students, nutritionists, social workers, and others through didactic instruction and clinical experiences.

INBORN ERRORS OF METABOLISM CONFERENCE, HOSTED MONTHLY BY BIOCHEMICAL GENETICS AT SEATTLE CHILDREN'S HOSPITAL (CME Level II attached)

IEM Conference is held every first Wednesday of the month, with the exception of the August hiatus. This Conference is open to any interested members of all specialties and provides a chance to hear and present new interesting cases and diagnostic puzzles, as well as laboratory tests and process updates. Presentations are made by a variety of providers, fellows, visiting experts from many specialties and topics can vary widely. This conference provides an interesting and open venue for the presentation of varied types of cases and histories.

This conference functions as a teaching event for fellows, residents, students and it also provides ongoing educational credit at CME Leve II category.

2017 Schedule of IEM Conference presentations:

Topic	Presenter
January Hiatus – schedules in conflict	
"Role of liver transplantation for glycogen storage disease type 4." "Of transport and Golgi organization 2..."	Niviann Blondet, MD Ken Ndugga-Kabuye, MD
"Hyperkalemic Periodic Paralysis." "Sly Syndrome."	Sarah Bauer Huang, MD Ken Ndugga-Kabuye, MD
"Metabolic Liver Disease in Children: Who Can Benefit from Liver Transplantation?" "Inborn errors of ketogenesis and ketone body utilization."	Simon Horslen, MB, ChB Ken Ndugga-Kabuye, MD
"Epilepsy in Inborn Errors of Metabolism" "Novel Therapies in Inborn Errors of Metabolism."	Jenn Dines, MD Angela Sun, MD

"The many faces of POLG1 - mitochondrial DNA depletion syndromes." "Proteolytic Quantification of GAA in Dried Blood Spots by Peptide Immuno-SRM: Potential Screening for Immunogenicity in Pompe Disease."	Juliane Gust, MD Irene Chang, MD
"Newborn Screening and Post-Screening Biochemical Analysis of Lysosomal Storage Diseases and a Few Others." "The Heart of it: Cardiomyopathy and IEM."	Michael Gelb, PhD Jenn Dines, MD
Hiatus – August (8/2/17)	
"Update on treatments in Duchenne Muscular Dystrophy and Spinal Muscular Atrophy."	Susan Apkon, MD
"Niemann-Pick Disease Type C: A review and an update. If they can't look up, you need to look it up." "PIGA Deficiency: Not Just Paroxysmal Nocturnal Hemoglobinuria"	Michael Raff, MD Irene Chang, MD
"Atypical PKU - BH4 deficiency."	Jeongho Lee, MD, PhD
"HSD10 Mitochondrial disease." "Creatine Deficiency Syndromes."	Ken Ndugga-Kabuye, MD Angela Sun, MD

FUNDED CLINICAL TRIALS AND RESEARCH PROJECTS AT SEATTLE CHILDREN'S AND THE UNIVERSITY OF WASHINGTON

CLINICAL TRIALS:

Longitudinal Study of Urea Cycle Disorders, O'Malley Family Foundation. Children's Research Institute (Batshaw) (10/1/11 – 7/31/18) Site PI: J Lawrence Merritt, II

A Phase 1/2 Open-Label Study In Patients with Arginase I Deficiency to Investigate the Safety, Pharmacokinetics, and Pharmacodynamics of Intravenous AEB1102 (Protocol# CAEB1102-101A) Aeglea Biotherapeutics, Inc. (12/22/17 – present) Site PI: J Lawrence Merritt, II; Co-investigator: Angela Sun

An Open Label Study of the Safety, Efficacy and Pharmacokinetics of Glycerol Phenylbutyrate (GPB; RAVICTI®) in Pediatric Subjects under Two Years of Age with Urea Cycle Disorders (UCDs) (HPN-100-009) Horizon Therapeutics, Inc. (4/22/2015-1/27/2017) Site PI: J. Lawrence Merritt, II

Development of a Long-term Outcome Study of Newborn Screening for Urea Cycle Disorders (NBS+UCD) Horizon Therapeutics, Inc. Investigator Initiated Study 2/5/2015-2/4/2017 (2014-2017) PI: J Lawrence Merritt, II

HGT-HIT-046 An Open-Label Extension Study of HGT-HIT-045 Evaluating Long-Term Safety and Clinical Outcomes of intrathecal idursulfase -IT Administered in Conjunction with Intravenous Elaprase® in Pediatric Patients with Hunter Syndrome and Cognitive Impairment; P.I.: Angela Sun; Co PI: Sihoun Hahn. Funding: Shire

A Four-Part, Phase 3, Randomized, Double-Blind, Placebo-Controlled, Four-Arm, Discontinuation Study to Evaluate the Efficacy and Safety of Subcutaneous Injections of BMN 165 Self Administered by Adults with Phenylketonuria. 7/1/2015 – 12/31/2018, 165-302, BioMarin. Scott, C. Ronald (PI), Leavitt, Anne M. (Co-PI), Jie Feng (Coordinator)

Individual Patient, Emergency IND (FDA IND # 123292 July 2014 to present) **Emergency Use of Triheptanoin (UX007) in Neonatal-Onset Very Long-Chain Acyl-CoA Dehydrogenase Deficiency.** PI: Lawrence Merritt, II

Individual Patient, Non-Emergency FDA IND # 129399 Individual Patient, IND. Non-Emergency Single Patient Expanded Access Treatment of an individual patient with carnitine-acylcarnitine translocase (CACT) deficiency with UX007 (triheptanoin). PI: J. Lawrence Merritt, II

Wilson Therapeutics 101-201. A multi-center study for the assessment of copper parameters in Wilson Disease subjects on standard of care treatment. P.I.:Sihoun Hahn, MD, PhD Period:2016-present. Funding: Wilson Therapeutics Inc.

Wilson Therapeutics 101-301. A Phase 3, Randomised, Rater-Blinded, Multi-Centre Study to Evaluate the Efficacy and Safety of WTX101 Administered for 48 Weeks versus Standard of Care in Wilson Disease Subjects Aged 18 and Older with an Extension Phase of up to 60 Months. PI: Sihoun Hahn. Funding: Wilson Therapeutics Inc.

DISEASE REGISTRIES:

The LSD Registry Program. Principal Investigators: Site PI, J Lawrence Merritt, II, MD; Co-PI, Angela Sun, MD. Funding: Genzyme Corporation. Four long-term natural history studies of treated and untreated patients with Gaucher, Fabry, MPS I and Pompe diseases. These four registries are also at UW with Principal Investigators C. Ronald Scott, and Jie Feng, MS, LCGC

Morquio A Registry Study (MARS), Angela Sun, PI. 2014 – present.

A Global Multi-Center, Long-Term, Observational Survey of Patients with Hunter Syndrome (Mucopolysaccharidosis II). A long-term natural history disease registry of treated and untreated patients with MPS II. Funding: Shire Human Genetic Therapeutics. Angela Sun,: PI; Sihoun Hahn, Christina Lam, Lawrence Merritt: Co-investigators

The MPS VI Clinical Surveillance Program. A long-term natural history disease registry of treated and untreated patients with MPS VI. Funding: BioMarin Pharmaceuticals. Angela Sun,: PI.

RESEARCH PROJECTS:

Assay validation for MPS II, IIIA, and IIIB in a real-time newborn screening lab. MPS II/III Pilot Study, Shire Genetic Therapies. 5/8/2014 – 6/30/2019. C. Ronald Scott (PI); Michael H. Gelb (Co-PI); Jie Feng (Coordinator)

Clinical and Basic Investigations into Known and Suspected Congenital Disorders of Glycosylation NHGRI Intramural Protocol – 14-HG-0071 Christina Lam,Co-Investigator. (NCT02089789) (2014-2016 – PI)

Assay validation for MPS II, IIIA, and IIIB in a real-time newborn screening lab. MPS II/III Pilot Study, Shire Genetic Therapies 5/8/2014 - 5/7/2018. Scott, C. Ronald (PI); Gelb, Michael (Co-PI); Feng, Jie (Coordinator)

Multiplex Analysis of Inborn Errors of Metabolism to develop sensitive, reproducible assays for the measurement of lysosomal enzymes for the detection of lysosomal storage diseases in dried blood spots. R01 DK DK67859, NIDDK 4/1/2014 – 3/31/2018. Gelb, Michael H. (PI) Scott, Turecek, Frantisek (Co-PI) C. Ronald (Co-PI), Jie Feng (Coordinator)

MLD Studies. To field-test a novel assay in a working newborn screening lab to determine its effectiveness in identifying newborns with metachromatic leukodystrophy. 2/26/2016-2/25/2019. Michael H Gelb (PI), C. Ronald Scott (Co-PI), Jie Feng, MS, LCGC (Coordinator).

Assay validation for MPS-VII in a real-time newborn screening lab. Ultragenyx 2-18-2016 - 12 - 30-2019. Scott, C. Ronald, PI

Multiplexed immune-SRM screening for primary immunodeficiencies; Funding: NIH/National Institute of Allergy and Infectious Diseases. (2016-2020). PI: Sihoun Hahn.

Newborn screening for Cystinosis. Cystinosis Research Foundation. 2017-2019. Sihoun Hahn (PI)

2017 AWARDS, GRANTS, HONORS

Dr. C. Ronald Scott co-chaired the Clinical and Laboratory Standards Institute's (CLSI's) Committee on Pompe and Other Lysosomal Storage Disorders, whose purpose was to develop and publish national guidelines for screening newborn blood spots for Pompe disease (CLSI Report NBS07).

Dr. C. Ronald Scott serves on the national North American Tyrosinemia Guidelines committee, hosted by Emory University, to develop national recommendations for the treatment of tyrosinemia.

Sihoun Hahn, MD, PhD: Chair, Department of Genome Medicine and Science, Gachon University School of Medicine, Incheon, Korea (2015 – present)

Sihoun Hahn, MD, PhD: Director, Gachon Institute of Genome Medicine and Science, Gachon University School of Medicine, Incheon, Korea (2015 – present)

Beth Ogata, MS, RD, CSP received the Excellence in Practice – Clinical Practice Award from the Academy of Nutrition and Dietetics (October 2017, Chicago, IL)

2017 EXTRAMURAL PRESENTATIONS

Invited Presentations

Sihoun Hahn: Newborn Screening for Rare Disorders. Korean Society of Newborn Screening, April 6, 2017, Seoul, Korea

Sihoun Hahn: Improving Clinical Practice through Integrated Translational Research: Transforming the Lives of Future Patients with Rare Disorders. Ilchun Memorial Lecture, The Korean Society for Molecular and Cellular Biology. September 14, 2017, Seoul, Korea

B Ogata: Networking with Quality. Co-present with Barbara Grant. Academy of Nutrition and Dietetics Food & Nutrition Conference & Exhibition. October 24, 2017, Chicago, IL.

B Ogata: Diet and Nutrition. Connecting Families, UCD Foundation Podcast. Published August 2017. http://www.ucdfamily.org/ucdtalk/

B Ogata: Connecting Families UCD Foundation. Co-present with CR Scott and Jie Feng. Urea Cycle Foundation Parent Meeting. May 6, 2017, Seattle, WA.

Poster/Oral Presentations

Sunhee Jung, Jeffrey R. Whiteaker, Lei Zhao, Troy Torgerson, Amanda G. Paulovich, and **Si Houn Hahn.** Dried Blood Spot Screening for Primary Immunodeficiencies using Immuno-SRM. MSACL annual meeting, Palm Springs, CA, Jan 22-26, 2017

S. Hahn, S. Jung, Remwilyn Dayuha, J.Whiteaker, L. Zhao, W. Gahl, A. Paulovich. Proteomic Peptide Screening of Dried Blood Spots for Cystinosis. Pediatric Academic Society, San Francisco, CA, May 6-9, 2017

S. Hahn, S. Jung, R. Daiyuha, J. Whiteaker, L. Zhao, T. Torgerson, W. A. Gahl, A. Paulovich; Proteomic Peptide Screening of Dried Blood Spots: A Potential Clinical Application, European Society of Human Genetics, Copenhagen, Denmark, May 27-31, 2017

Dines J, LaCroix A, Golden-Grant K, McWalter K, **Sun A**, Mefford H. Exome Sequencing Reveals Family Affected with Biallelic *TANGO2* Variants. American College of Medical Genetics Meeting, Phoenix, 2017. Poster. Presenting author: Dines.

Zarate YA, Gambello M, Pandya Arti, Saenz M, Siu V, Ray J, Sellars E, **Sun A**, Smith W, Robin N, Picker J, Kirby A, Slavotinek A, Bebin M, Calhoun A, Smith-Hicks C, Balasubramanian M. Phenotype and Natural history in 49 individuals with *SATB2*-associated syndrome. David W. Smith Workshop on Malformations and Morphogenesis, Stowe, 2017. Platform. Presenting author: Zarate.

Chang IJ*, Starr MC*, Finn L, **Sun A**, **Howell J**, Hingorani SR, **Lam C**. Novel Variants in COQ2 in Primary Coenzyme Q10 Deficiency and Steroid-Resistant Nephrotic Syndrome. ACMG Annual Clinical Genetics Meeting. Phoenix, Arizona; poster, presenting author Howell J; (2017).

Lam C, Hall PL, Alexander JJ, Asif G, Berry GT, Ferreira C, Freeze HH, Gahl WA, Nickander KK, Sharer JD, Watson CM, Wolfe L, Raymond KM. Urine Oligosaccharide Screening by MALDI-TOF for the Identification of NGLY1-CDDG. Third World Conference on CDG. Leuvan, Belgium; poster, presenting author Lam C; (2017).

Clowes Candadai SV, Sikes MC, **Howell JM**, Dines J, Ndugga-Kabuye MK, Byers H, Conta JH, Hendricks E, Stasi SM, Sternen DL, Bennett JT. Rapid inpatient genomic testing: doing it the RIGhT Way. Poster presented at: NSGC 36th Annual Conference; September, 2017; Columbus, OH

Küry S, van Woerden GM, Besnard MT, Cho MT, Sanders S, Sellars EA, Berg J, Waugh JL, Kobak L, Bernstein JA, Deardorff M, Hoganson GE, Johnson DS, Dabir T, Sarkar A, Terhal PA, Prescott TE, Grange DK, Haeringen A, **Lam C**, Mirzaa G, Helbig KL, Rosenfeld JA, Agrawal PB, Odent S, Mercier S, Elgersma Y, Bezieau S. De novo mutations in protein kinase genes CAMK2A and CAMK2B cause intellectual disability. 67th Annual Meeting of the American Society of Human Genetics. Orlando, Florida; platform, presenting author Küry S; (2017).

2017 INTRAMURAL PRESENTATIONS

C. Lam, Invited Speaker; Glycosylation: A Sweet Branch of Neuro-Metabolics. Oral presentation at Seattle Children's Hospital Neurology Friday Morning Conference, Seattle, WA

C. Lam, Invited Speaker: Congenital Disorders of Glycosylation, a Sweet Branch of Biochemical Genetics at Seattle Children's Hospital Pediatrics Grand Rounds, Seattle, WA

A Sun, Novel Therapies in Inborne Errors of Metabolism, IEM Conference, Seattle Children's Hospital 5/3/17

A Sun, Creatine Deficiecy Syndromes, IEM Conference, Seattle Childrens, 12/6/17

B Ogata, Guest lecturer: Treatment of Metabolic Disorders. NUTR 520 (Protein and Carbohydrate Metabolism), University of Washington Nutritional Sciences Program. November 2017.

B Ogata: Instructor: NUTR 526 (Maternal, Infant, and Pediatric Nutrition), University of Washington Nutritional Sciences Program. Fall 2017

2017 PUBLICATIONS

[Chapters & Educational Publications]

Chang IJ, **Hahn SH** (2017). The genetics of Wilson disease. In Anna Czlonkowska, Michael L. Schilsky eds. Wilson Disease, Handbook of Child Neurology, Volume 142, Pages 2-248.

Merritt, II, JL and Vockley J. UpToDate. Overview of fatty acid oxidation disorders. Updated December 6, 2017. https://www.uptodate.com/

Thomas JA, **Lam C**, Berry GT. Lysosomal Storage, Peroxisomal, and Glycosylation Disorders and Smith Lemli Opitz Syndrome in the Neonate. In Avery's Diseases of the Newborn 10th edition (CA Gleason, SU Devaskar, eds) Philadelphia, PA: Elsevier/Sauders (accepted 2016 pending 2017).

CLSI. *Newborn blood spot screening for Pompe disease by lysosomal acid alpha-glucosidase activity assays*, 1st ed. CLSI report NBS07. Wayne, PA: Clinical and Laboratory Standards Insittute; 2017. Joseph Orsini and **C. Ronald Scott**, editors.

Sniderman King L, Trahms C, **Scott CR.** Tyrosinemia Type I. In: Adam MP, Ardinger HH, Pagon RA, Wallace SE, Bean LJH, Stephens K, Amemiya A, eds. *GeneReviews*® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2018. [updated 2017 May 25]. Available from: https://www.ncbi.nlm.nih.gov/books/NBK1515/ PM ID: 20301688

[Peer-Reviewed Journals]

Jung S, Whiteaker JR, Zhao L, Yoo HW, Paulovich AG, **Hahn SH**. Quantification of ATP7B Protein in Dried Blood Spots by Peptide Immuno-SRM as a Potential Screen for Wilson's Disease. *J Proteome Res*. 2017 Feb 3;16(2):862-871

Gericke B, Amiri M, **Scott CR**, Naim HY. Molecular pathogenicity of novel sucrase-isomaltase mutations found in congenital sucrase-isomaltase deficiency patients. *Biochim Biophys Acta* 1863(3):817-826. 2017. PMID: 28062276

Liu Y, Yi F, Kumar AB, Kumar Chennamaneni N, Hong X, **Scott CR**, Gelb MH, Turecek F. Multiplex Tandem Mass Spectrometry Enzymatic Activity Assay for Newborn Screening of the Mucopolysaccharidoses and Type 2 Neuronal Ceroid Lipofuscinosis. *Clin Chem*, Jun;63(6):1118-1126, 2017. PMID: 28428354

Liao HC, Spacil Z, Ghomashchi F, Escolar ML, Kurtzberg J, Orsini JJ, Turecek F, **Scott CR**, Gelb MH. Lymphocyte Galactocerebrosidase Activity by LC-MS/MS for Post-Newborn Screening Evaluation of Krabbe Disease. *Clin Chem*., Aug;63(8):1363-1369, 2017. PMID: 28592445, PMCID: PMC5533636

Bodamer OA, **Scott CR**, Giugliani R, on behalf of the Pompe Disease Newborn Screening Working Group. Newborn Screening for Pompe Disease. *Pediatrics* 140(S1):S4-S13, July, 2017.

Mistry PK, Batista JL, Andersson HC, Balwani M, Burrow TA, Charrow J, Kaplan P, Khan A, Kishnani PS, Kolodny EH, Rosenbloom B, **Scott CR**, Weinreb N. Transformation in pretreatment manifestations of Gaucher disease type 1 during two decades of alglucerase/imiglucerase enzyme replacement therapy in the International Collaborative Gaucher Group (ICGG) Gaucher Registry. *Am J Hematol*, 92: 929-939, 2017. PMID: 28569047

Chinsky JM, Singh R, Ficicoglu C, van Karenbeek CDM, Grompe M, Mitchell G, Waisbren CDE, Gucsavas-Calikoglu M, Wasserstein MP, Coakley K, **Scott CR**. Diagnosis and treatment of tyrosinemia type I: a US and Canadian consensus group review and recommendations. *Genet Med*, Vol 19, 2017.

Buroker NE, Ning X-H, Zhou Z-N, Cen W-J, Wu, X-F, Zhu W-Z, **Scott CR**, Chen S-H. SNPs, linkage disequilibrium, and chronic mountain sickness in Tibetan Chinese. *Hypoxia* 5:67-74, 2017. PMID 28770234

Phowthongkum P, **Sun A**. Novel truncating variant in *DNA2*-related congenital onset myopathy and ptosis suggests genotype-phenotype correlation. Neuromuscul Disord. 2017 Jul;27(7):616-618. PMID 28554558.

Lam C, Ferreira C, Krasnewich D, Toro C, Latham L, Wadih ZM, Lehky T, Brewer C, Baker EH, Thurm A, Farmer CA, Rosenzweig SD, Lyons JJ, Schreiber JM, Gropman A, Lingala S, Ghany MG, Solomon B, Macnamara E, Davids M, Stratakis CA, Kimonis V, Gahl WA, Wolfe L. "Prospective Phenotyping of NGLY1-CDDG, the First Congenital Disorder of Deglycosylation." Genet Med. 19(2):160-168, 2017.

Carlson RJ, Bond MR, Hutchins S, Brown Y, Wolfe LA, **Lam C**, Nelson C, DiMaggio D, Jones N, Rosenzweig SD, Stone KD, Freeman AF, Holland SM, Hanover JA, Milner JD, Lyons JJ. "Detection of phosphoglucomutase-3 (PGM3) deficiency by lectin-based flow cytometry." J Allergy Clin Immunol. 140(1): 291-294, 2017. PMCID none. PMID 28063873.

Küry S*, van Woerden GM*, Besnard T*, Onori MP, Latypova X, Towne MC, Cho MT, Prescott TE, Ploeg MA, Sanders S, Stessman HAF, Pujol A, Distel B, Robak LA, Bernstein JA, Denommé-Pichon AS, Lesca G, Sellars EA, Berg J, Carré W, Busk ØL, van Bon BWM, Waugh JL, Deardorff M, Hoganson GE, Bosanko KB, Johnson DS, Dabir T, Holla ØL, Sarkar A, Tveten K, de Bellescize J, Braathen GJ, Terhal PA, Grange DK, van Haeringen A, **Lam C**, Mirzaa G, Burton J, Bhoj EJ,, Douglas J, Santani AB, Nesbitt AI, Helbig KL, Andrews MV, Begtrup A, Tang S, van Gassen KLL, Juusola J, Foss K, Enns GM, Moog U, Hinderhofer K, Paramasivam N, Lincoln S, Kusako BH, Lindenbaum P, Charpentier E, Nowak CB, Cherot E, Simonet T, Ruivenkamp CAL, **Hahn S**, Brownstein CA, Xia F, Schmitt S, Deb W, Bonneau D, Nizon M, Quinquis D, Chelly J, Rudolf G, Sanlaville D, Parent P, Gilbert-Dussardier B, Toutain A, Sutton VR, **Thies J**, Peart-Vissers LELM, Boisseau P, Vincent M, Grabrucker AM, Dubourg C, Undiagnosed Diseases Network, Tan W, Verbeek NE, Granzow M, Santen G, Shendure J, Isidor B, Pasquier L, Redon R, Yang Y, State MW , Kleefstra T, Cogné B, GEM HUGO, Deciphering Developmental Disorders study, Petrovski S, Retterer K, Eichler EE, Rosenfeld JA, Agrawal PB, Bézieau S*, Odent S*, Elgersma Y*, Mercier S*. "De novo mutations in protein kinase genes CAMK2A and CAMK2B cause intellectual disability." Am J Hum Genet. 101(5): 768-788, 2017. PMID 29100089

Hall PL, **Lam C**, Alexander JJ, Asif G, Berry GT, Ferreira C, Freeze HH, Gahl WA, Nickander KK, Sharer JD, Watson CM, Wolfe L, Raymond KM. "Urine Oligosaccharide Screening by MALDI-TOF for the Identification of NGLY1 Deficiency." J Inherit Metab Dis. (accepted 2017).

Starr MC*, **Chang IJ***, Finn L, Sun A, **Thies J**, Hingorani SR, **Lam C**. "COQ2 Nephropathy – A Treatable Cause of Nephrotic Syndrome."Pediatr Nephrol. (accepted 2017).

Other Activities:

Sihoun Hahn, MD, PhD

- is on the Medical Advisory Committee, Wilson Disease Association International
- is a Genetics Section Editor for UpToDate, since 2011
- is on the Advisory Committee for WA State Newborn Screening
- is a Member of the IRB Committee, Seattle Children's Hospital

J. Lawrence Merritt, II, MD,

- is on the American Academy of Pediatrics, Subcommittee on Apparent Life Threatening Events (ALTE). August 2013 to 2017. (Goal: to create an evidence-based guideline on the Management of Apparent Life Threatening Events)
- is a Western States Regional Genetics Collaborative Representative for National Newborn Screening Translational Research Network
- is a Peer Reviewer for UpToDate, Inborn Errors of Metabolism topics

Angela Sun, MD,

- is a member of the Seattle Children's Hospital Clinical Exome Sequencing Committee
- is a Peer Reviewer for UpToDate, Inborn Errors of Metabolism topics
- is a member of the Washington State Newborn Screening Technical Advisory Committee
- serves as the rotation coordinator for students, residents and fellows who rotate through Biochemical Genetics
- serves as Preceptor, American College of Medical Genetics and Genomics Summer Scholars Program

Christina Lam, MD

- is on the Program Evaluation Committee for Medical Biochemical Genetics Fellowship at Seattle Children's Hospital, Chair
- is an Interviewer for Pediatric Residency Candidates
- is on the Rapid Exome Committee for Seattle Children's Hospital.
- is on the Medical Advisory Board Member for CDG Care (CDG Family Support Group), since 2015.
- is a Medical Advisory Board Member for NGLY1.org (NGLY1-CDDG)
- is Guest Researcher, NHGRI, NIH, Bethesda, MD.

Kelly McKean, MS, RD, CSP, CD is a member of the Genetic Metabolic Dietitians International (GMDI) organization.

Sarah Sullivan, MS, RDN, CD is a member of the Genetic Metabolic Dietitians International (GMDI) organization.

Marie Norris MS, RDN, CD, CNSC

- is a member of the Genetic Metabolic Dietitians International (GMDI) Organization
- is a member of American Society for Parenteral and Enteral Nutrition (ASPEN)
- is a member of the NASPGHAN Council for Pediatric Nutrition Professionals (CPNP)

Beth Ogata, MS, RD, CD

- is a Working Group Member of the NIH Phenylketonuria Review Conference (Diet Control & Management)
- is a member of the Western Regional Genetics Collaborative
- is a Grant Reviewer for the Galactosemia Foundation.
- is a member of the Genetic Metabolic Dietitians International (GMDI) Technology Committee and a member of the GMDI Nutrition Guidelines Work Groups for MSUD and PKU
- Co-Chair Scope and Standards Work Group, Academy of Nutrition and Dietetics

Mari Mazon, MS, RD is Co-chair of the GMDI Technology Committee

Jenny Thies, MS, LGC, is a member of the National Society of Genetic Counselors and the Metabolic/Lysosomal Storage Disease SIG.

- Involved in the Rapid Inpatient Genomic Testing (RIGhT) study at Seattle Children's Hospital

Jie Feng, MS, LCGC is a member of the National Society of Genetic Counselors and the Metabolic/Lysosomal Storage Disease SIG.