The Friends of Doernbecher recently awarded five grants, totaling just over $175,000, to support clinical and research projects and programs at OHSU Doernbecher Children’s Hospital. The grant recipients, listed below, were selected from among 45 applicants by a panel of Friends of Doernbecher members.

**Congratulations to the Friends of Doernbecher Grant recipients!**

**Penelope Hogarth, MD**

**Proposal:** Feeding broken brains: nutritional management of an orphan childhood disease

**Award:** $69,189

Pantothenate kinase-associated neurodegeneration (PKAN) is an inborn error of vitamin B5 metabolism that causes severe disability and suffering in children. We have recently shown in a mouse model that we can fix the problem in PKAN by giving a compound that bypasses the enzyme that is broken in PKAN because of a genetic mutation. Our compound can be developed outside of the usual drug pathway, allowing it to move from bench to bedside very quickly and at low cost.

Friends of Doernbecher funding is needed to complete animal dosing and toxicity studies; to refine our existing synthesis method to make larger quantities of the compound; and to develop a formulation for the product in collaboration with Oregon State University. We are already planning a clinical trial of the compound in PKAN, and have just submitted a funding application to the FDA’s Orphan Products Grant Program to support the work going forward. With the OHSU Office of Business Development’s blessing, we are setting up the structure to assure that our product will be financially accessible to every child with PKAN and that any profits from its eventual sale will be used to support further research for PKAN and other disorders.

**Erin Madriago, MD and Lindsay Hamilton-Scott, RDCS**

**Proposal:** Pediatric Echocardiography University at Doernbecher Pilot Project

**Award:** $9,000

Children are born every day throughout Oregon and Washington with congenital heart disease. Depending upon the heart defect, the disease can be life threatening to an adolescent, child or neonate. These children present in dire circumstances to their local hospitals where adult trained sonographers perform ultrasounds on their hearts (echocardiograms) in an effort to identify the problem. Unfortunately, they currently feel poorly trained and equipped to recognize the findings that are specific to children with heart disease. Consequently, there may be delays in initiation of treatment or transfer of care that can lead to significantly worse outcomes for the child including acidosis, shock and even death. As a leader of education, and the premier center for congenital heart care in the region, we receive many of these children. As such, we feel it’s our responsibility to adequately train and equip adult sonographers throughout Oregon and Washington taking care of these children, to quickly recognize life threatening conditions through echocardiography, and directly improve their outcomes.

Pediatric Echo University is a two-day course created by pediatric cardiologists and pediatric sonographers at OHSU Doernbecher Children’s Hospital, designed to help equip adult sonographers already being asked to perform pediatric studies in rural areas, with the tools to perform and recognize certain life threatening conditions in children they may encounter in the field. It will consist of a series of didactic lectures by specially trained pediatric cardiologists and sonographers, engagement in multi-media simulated case studies, and hands-on scanning of volunteer pediatric subjects.

A Friends of Doernbecher Foundation Grant will allow this course to come to fruition, help establish Doernbecher as a premier educator for pediatric echocardiography in Oregon and, most importantly, improve the outcomes of children with heart disease in the Northwest.
Corinne Muirhead, PharmD and Kelvin D. MacDonald, MD
Proposal: Inhaled Glycine as Modifier of Cystic Fibrosis Airway pH and Mucus Viscosity
Award: $26,220

We propose to evaluate in humans with Cystic Fibrosis (CF) a novel inhaled formulation of glycine and evaluate the change in the pH of the exhaled breath condensate (EBC). Glycine is an amino acid that has the properties of both acid and base and is known as a zwitterion. Glycine is currently used in biology labs as a simple buffer. Patients with CF lack the ability to transport bicarbonate (baking soda) ions into the mucus and fluid lining the airways. As a result the airways of CF patients are acidic (low pH) because of a lack of this buffer. This may contribute to the chronic infection of CF lungs. Even subtle changes in pH can have detrimental effects. First, the mucus of the airways increases in thickness (viscosity) with each 0.01 decrease in pH. This has been demonstrated in genetically altered CF pigs. Less viscous mucus is easier to expectorate and this reduces infection risk. Secondly, decreased pH inhibits the growth of antimicrobial substances present in airway fluid from working. In the laboratory, raising the pH of airway fluid dramatically restores the bacterial killing power of these substances.

However, raising the pH of the airway is not so simple. Bicarbonate is highly irritating to inhale and is quickly neutralized and absorbed by the lung. Other biological buffers might be toxic when inhaled chronically and have not been studied in people. Fortunately, alkalinized glycine has been studied as an inhalant in humans. In those studies, investigators were hoping changing the airway pH to improve the uptake of asthma medication. They showed that they could increase the airway pH 0.23 units. Moreover, there were no side effects or change in breathing tests. However, neither persons with CF nor the effects on mucus viscosity were studied. This research potentially benefits all CF children. Friends of Doernbecher support will allow us to collect initial data that will be critical for a government or CF Foundation funding application. An invention statement for inhaled glycine as modifier of CF airway mucus viscosity has been filed with the OHSU Tech Transfer office.

Louise Elaine Vaz, MD MPH and Michael A. Harris, PhD
Proposal: The Most Vulnerable Project (MVP): Improving the health of our socially fragile children
Award: $20,334

Children sick enough to be admitted to the hospital, who also live in challenging home situations, are at high risk for poor health outcomes. These outcomes include deterioration in their health after hospitalization, frequent emergency department visits, missed school days, and lower quality of life. Socially fragile children experience challenges in the home such as poverty and emotional stress. Studies now demonstrate that screening for social vulnerabilities can significantly improve health outcomes. Currently, at Doernbecher Children’s Hospital (DCH), we do not identify social vulnerabilities for inpatients. While social work consultations are delegated to the most complicated cases, it is not feasible, or even necessary, to have a social worker see every patient. But, not having a systematic approach to identify a child’s home life greatly limits our ability to provide the highest level of care to vulnerable children. This is especially true during the critical transition from hospital to home, called the discharge period. If our doctors and nurses were to have this information, then care could be crafted to meet the demands of a child's particular living situation. With this grant, we aim to characterize and evaluate the social complexity of children hospitalized at DCH. We hypothesize that identifying social vulnerabilities will prevent a deterioration in health after discharge, fewer missed school days, fewer avoidable emergency department visits, and an increase in quality of life. In addition, these data will later be used to customize health care such that it is cost effective and high impact by including the lived experience of children and their families in the care plan.
GRANT RECIPIENTS (CONTINUED)

David C. Sheridan, MD
Proposal: QuickBrain MRI for Pediatric Head Trauma: A Pilot Study
Award: $51,188

Head CT is the recommended first-line imaging study for evaluation of children with head trauma. CT is an effective test in the setting of trauma, allowing for rapid and accurate diagnosis of intracranial hemorrhage and other potential neurosurgical emergencies. Unfortunately, the ionizing radiation associated with CT exposes children's developing brains to radiation and increases risk of future malignancy. Previous studies have shown that approximately 1 in 1000 head CTs in children will result in a future brain tumor or leukemia.

Considering head trauma is one of the most common traumatic injuries and a leading cause of morbidity/mortality in children, a large number of pediatric head CTs are performed annually in the US. Previous research studies have aimed to identify low risk groups, but a large number of children and adolescents continue to undergo neuroimaging yearly for this indication. A recent nationally representative study showed that approximately 600,000 CTs were ordered in the US in children less than 15 years of age with over 90% of those being of the head. These previous studies showed that only 2.5% of the head CTs were positive for an acute intracranial injury suggesting that we are exposing many children to pediatric trauma patients are being exposed to an unnecessary amount of ionizing radiation.

Magnetic resonance imaging (MRI) is an alternative form of cross-sectional diagnostic imaging of the head that does not use ionizing radiation. Routine brain MRI is not used for trauma work-up due to the longer time required for scanning as compared to head CT (up to an hour compared to minutes, respectively) and uncertainty of the diagnostic accuracy of MRI for assessment of trauma-related pathology. Some hospitals are using abbreviated MRI protocols (Quick brain MRI (QbMRI)) for various indications that obtain images in minutes. Our center was one of the first to study its use for ventriculoperitoneal shunt evaluation in the emergency department and we now use this modality as the standard in our assessment of patients with ventricular shunts.

The use of MRI in the emergency department is becoming more common with these established indications, but has not been prospectively studied for acute head trauma. A recent retrospective study we performed showed a good ability of QbMRI to detect acute pediatric traumatic brain injuries with a sensitivity of 100% (95% CI: 89,100) using head CT as a reference standard. However, that study had limitations including an average 24 hour gap between acquisition of the CT and QbMRI and in its retrospective nature. A prospective pilot study with a much shorter time between CT and QbMRI acquisition, more generalized ED population and prospective data collection is needed to better assess the diagnostic accuracy and potential utility of QbMRI in the setting of pediatric head trauma. This data will then direct a future, multicenter study that could change the standard of care for imaging work-up of pediatric head trauma in the U.S. with a dramatic reduction in the exposure of children to ionizing radiation.