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2020 Friends of Doernbecher Grant Recipients

Ramon F Barajas Jr MD, Dexing Zeng PhD
Project Title: Improved Detection and Therapy of Pediatric Medulloblastoma Brain Tumors with Sequential-Multi-Agents Receptor-Targeting (SMART) Imaging
Award: $69,501
Primary brain tumors are the most common pediatric solid tumor and leading cause of childhood cancer-related deaths. Through the recent advances in surgical resection and chemoradiotherapy, the five-year survival rates have improved to ~70%. Unfortunately, the tradeoff of improving survival is the morbidity of treatment. This is particularly true for children whose tumor arises within eloquent brain. Therapeutic irradiation has significant and long-lasting side effects upon the developing central nervous system (CNS); irreversible neurologic and intellectual damage is very common. Herein, we hypothesize that normal pediatric brain can be spared from high dose radiotherapy toxicity by combining Sequential-Multi-Agents Receptor-Targeting (SMART) with blood brain barrier (BBB) opening.

Kelvin D. MacDonald, M.D; Anindit Mukherjee Ph.D.
Project Title: Primary Human Nasal Epithelial Cell Repository for Nanoparticle Development in Cystic Fibrosis
Award: $30,742
Cystic fibrosis (CF) is an inherited disorder with more than 1500 known gene mutations in the cystic fibrosis transmembrane receptor gene (CFTR). The result is defective CFTR protein production leading to crippling pulmonary disease and shortened life expectancy. Gene mutation specific CFTR protein rescue drug therapy has proven beneficial and effective. However, this therapy has variable efficacy with some patients having no clinical response. Moreover at least 10% of CF patients are not eligible for the treatment as they lack the specific mutation, thereby demonstrating the need for ongoing therapeutics development. Recently a collaboration between OSU and OHSU (Sahay and MacDonald) demonstrated for the first time that nanoparticle encapsulated mRNA encoding for normal CFTR protein can restore native CFTR function in CF cells and in animal models. This approach promises to be effective for all CF patients, not just for the ones carrying a specific CFTR mutation.

Erin Madriago, MD
Project Title: Fetal Cardiac Imaging Symposium at Doernbecher
Award: $7,700
Every year in the United States approximately 40,000 babies are born with congenital heart disease (CHD). As prenatal detection and imaging technology have improved over the last several decades, still less than 35 percent of CHD cases in the United States are diagnosed in utero. As a result, these vulnerable infants are born under suboptimal conditions in local hospitals that do not have the expertise to care for an infant with a serious heart condition. With the success of our previous Doernbecher Foundation grant supported “Sonographer University”,

we have improved the ability of local hospitals to identify defects after birth. However, we still need to push the diagnostic accuracy earlier. Doernbecher has become a regional center of excellence for multidisciplinary fetal diagnosis and therapy. In this effort, it is crucial that medical professionals (sonographers, radiologists, obstetricians, maternal fetal medicine specialists, midwives and family practitioners) who care for pregnant women and perform prenatal heart screenings have learning opportunities to improve their ability to recognize heart defects in babies during routine prenatal screening. Enabling our local providers to recognize that something is wrong in utero allows families to access our multidisciplinary team early in pregnancy and ensure the safest delivery possible.

This inaugural one-day event will be held at Doernbecher and will provide an instructive and interactive program aimed at increasing prenatal detection rates. Program highlights will include didactic lectures, interactive case studies with audience feedback, evaluation of pathological specimens, live-scanning fetal echocardiography and a parent experience presentation.

Ashok Muralidaran, MD
Project Title: Designing and implanting a better heart valve, using 3D-printing technology to create personalized aortic valves for children
Award: $49,248
An infant or small child who is born with a severely diseased aortic valve has no good treatment options. The aortic valve is the most important valve in the heart because it guards the blood going out to the body. Companies do not make replacement aortic valves for the very young as they do for older children and adults because the valve cannot grow with a rapidly growing child. In addition, manufactured valves are not durable and have associated risks like infection and clotting. Using resources from the Doernbecher 3D-printing laboratory, we propose to create a new kind of aortic valve made from a child's own tissue called pericardium, the sack that surrounds the heart.

The aorta will be imaged using MRI and then valve templates will be created with 3D printing tools utilizing these images of the child's aortic root. The aortic root is the expanded base of the aorta that houses the aortic valve. The pericardial tissue is cut by the surgeon to conform to the 3D-printed template. Such a personalized valve, we hypothesize, will function as well as a normal aortic valve, avoiding the ill effects of the currently available artificial valves. As a first step to creating this innovative type of valve we propose to study valve function in a porcine model. We will profile the blood flowing through the animal's natural aortic valve using a new imaging technique called 4D-flow MRI. The blood flow profile before and after implantation of the personalized valve will be compared. This study blends the skills and knowledge of OHSU experts from pediatric cardiology, pediatric heart surgery and advanced cardiac imaging research. Infants and children who face having their hearts permanently damaged because of the lack of a suitable valve replacement option will be the principal beneficiaries of this project. In addition, cardiologists and radiologists will benefit by gaining significant experience in the application of new blood flow imaging techniques like 4D-flow MRI. Basic biology researchers will benefit.