2022 Friends of Doernbecher Grant Recipients

Luiz E. Bertassoni, DDS, PhD, Ramesh Subbiah, PhD, Rahul Madathiparambil Visalakshan, PhD
Project Title: Development of an osteosarcoma-on-a-chip model for personalized screening and evaluation of anticancer drugs
Award: $43,700

Osteosarcoma (OS) is the most common primary tumor of bone and predominately affects the pediatric and young adult population. Osteosarcoma treatments still have low efficacy which mostly arise from the limited ability to predict the patient tumor responses to therapeutic agents, resistance to anti-cancer drugs and tumor heterogeneity among patients. The major reason that current therapeutics often cannot translate into a successful clinical outcome is because cancer biology investigation and therapeutic testing rely heavily on monolayer, monoculture methods developed over half a century ago. However, these methods often lack essential hallmarks of the cancer microenvironment that contribute to tumor pathogenesis. Therefore, the successful engineering of a personalized three-dimensional (3D) tumor ecosystem that can recapitulate the tumor microenvironment and heterogeneity *in vitro* is strongly desired to accurately predict patients' responses to anti-cancer drugs and thus further improve patient outcomes. Here we propose to develop a first of its kind personalized 3D osteosarcoma-on-a-chip platform using our recently developed biomineralization engineering strategy and patient-derived tumor cells. Our system will offer an ideal platform to understand cancer progression and to evaluate the patient specific (precision medicine) anticancer potential of existing chemotherapeutics and newly developed drugs with high accuracy.

Trang Huynh, MD, Garth Meckler, MD, MSHS, Matthew Hansen, MD, MCR, Jeanne-Marie Guise, MD, MPH
Project Title: Emergency Medical Services (EMS) Neonatal Resuscitation Curriculum to Improve Out-of-Hospital Newborn Resuscitation
Award: $17,241

Out-of-hospital births have a higher risk of poor outcomes, including death. Oregon's out-of-hospital birth rate is double the national average. Emergency Medical Services (EMS) personnel may be the primary and most experienced medical providers at these deliveries when people seek help through the 9-1-1 emergency services system. Most newborns transition successfully after birth, however, up to 10% require some assistance to breathe effectively when they are born. For those requiring help, actions taken within the first seconds to minutes can make the difference between life, death, or lifelong disability. EMS personnel are poorly-equipped to manage out-of-hospital birth emergencies due to limited exposure and proficiency in newborn resuscitation. Our prior research testing emergency medical providers' response to out-of-

hospital newborn resuscitation shows deficiencies in critical steps of warming and drying, and initiating bag mask ventilation (BMV) for a baby in crisis. Failure to perform these basic first steps can lead to death, which we unfortunately see as neonatologists when babies arrive to the emergency room by ambulance. Currently there is no standardized curriculum for neonatal resuscitation for medical providers who do not work in the delivery-room/hospital environment. Neonatal Resuscitation Program (NRP) guidelines, based on recommendations by the American Academy of Pediatrics (AAP) and American Heart Association (AHA), provide evidence-based practice guidelines that are the standard of care for infants born in the United States (US) and are hospital-based. Based on our simulation study results, we developed an EMS-tailored, NRP-based educational curriculum that we propose to disseminate to EMS providers in Oregon. Our curriculum is accessible and we hypothesize that it will better prepare Oregon EMS teams to take the evidence-based care available in hospitals to babies born in the out-of-hospital setting.

Henry Milczuk, MD
Project Title: Speech and Language Outcomes in Cleft Palate
Award: $24,675

Cleft palate (with or without cleft lip) is one of the most common congenital differences in children, affecting approximately 1 in 500 births. These children and families face a number of challenges including recurrent ear disease, speech development, and speech understandability. For more than 20 years, clinical data for most patients who have attended the Craniofacial Disorders Clinic (CFD) at Doernbecher Children's Hospital (DCH) have been collected. These data have focused on outcomes during and after surgical and medical treatments. For example, which patients born with a cleft palate are more likely to need additional surgery to correct speech understandability, and how might that be influenced by speech therapy versus surgery. We currently have data for 2,000 patients and more than 31,000 encounters, which allows for the statistical power often lacking in other studies in this field. Preliminary work by our team of investigators indicate that clinically important questions regarding treatment outcomes for cleft palate, and the frequently associated problem of temporary hearing loss, will be answered by further analysis of this large and rich data set. We believe that the results of these studies will lead to increased understanding of which patients with cleft palate are at a greater risk for speech problems, and that we may be able to recommend treatment strategies for school and community speech therapists, as well as the medical community that cares for children born with cleft palate, that may lead to improved outcomes and resource utilization.

Rita Somogyi, BA, Matthew Halsey, MD
Project Title: SRS-22 Outcomes in Adolescents with Scoliosis Possessing Borderline Surgical Indications 12 Months Following Surgical Intervention Versus Conservative Management
Award: $8500

Idiopathic adolescent scoliosis is a lateral curvature of the spine that often presents in late childhood or early teens, frequently during times of rapid growth. While many kids have a mild curvature that does not affect their daily functioning, severe curvatures can occur and causing pain, impaired movement, self-consciousness related to body-image, or even difficulty breathing due to restricted lung movement. A curvature of over 40 is considered severe with surgical correction considered for curves greater than 50; alternative options such as bracing, physical therapy, and simple observation are considered because surgery carries its own set of risks. Spinal fusion, the most common surgical intervention, necessarily restricts movement, which can

ultimately limit patients' future job prospects, recreational activities, and even contribute to worsening pain.

The goal of this study is to assess healthcare-related quality of life outcomes, namely pain, function, self-image, and mental health, using a well-established Scoliosis Research Society questionnaire, the SRS-22, already applied in clinical practice. For patients that choose to undergo surgery, their scores just prior to surgery and then at their 12-month follow-up will be compared. For those not undergoing surgery, scores obtained at the time they were found to have severe curvatures and then scores at a 12-month follow-up will be compared. The difference in scores for each group will be analyzed to assess whether surgery actually improves quality of life for these young patients in order to help guide future decision-making.

Elizabeth Super, MD, Jillian Sanford, MD
Project Title: Wake Up! Using Evidence-based Actigraphy to Accurately Diagnose and Treat Pediatric Sleep
Award: $8,899

As pediatric sleep medicine physicians, some of the most challenging patients are children with disrupted circadian sleep-wake cycles, complex insomnia, and those who are too sleepy (hypersomnia). These sleep disorders wreak havoc by impacting school attendance, mood, and all aspects of family functioning and are especially difficult in patients with comorbid complex medical conditions and neurodevelopmental disabilities. The International Classification of Sleep Disorders, Third Edition, 2014, published by the American Academy of Sleep Medicine (AASM), recommends actigraphy monitoring for circadian disorders and disorders of hypersomnia. Actigraphy is a validated method of objectively measuring sleep parameters over a period of days to weeks using a small device that is worn like a wristwatch. Despite the AASM recommendation to use actigraphy and the relative ease of obtaining actigraph data, the Doernbecher Pediatric Sleep Medicine Program does not have reliable access to actigraphy monitoring.

Lack of actigraphy monitoring leaves providers and parents with incomplete diagnostic and treatment information. Imagine treating diabetes without monitoring sugars, or blood pressure without a blood pressure cuff. We are truly in the dark! Please support the children of Oregon with sleep disorders and the Doernbecher Pediatric Sleep Medicine Program faculty with a grant of $8,899 to purchase eight actigraphy units. You will sleep better at night knowing children are getting the right medical care at the best hospital in Oregon.