Sickle cell disease (SCD), the most common genetic blood disease in North America, can be characterized by recurrent episodes of acute severe pain due to blockages of red blood cells. Without pain self-management habits taught at an early age, the pain faced by youth with SCD can impede both everyday activities and their overall health for the long term, trickling into adulthood. By embedding the skills taught in cognitive-behavioral therapy accessibly in web and mobile-based technology, previous research in this interventional medium shows that this format could be beneficial for youth with SCD. Our research, in particular, investigates the effectiveness of iCanCope SCD, a web and mobile-based pain management program with a focus on helping youth build needed skills to handle pain. This study recruited 160 adolescents aged 12-18 with SCD and randomized the participants into an experimental group for the intervention and an attentional-control group. The innovation includes modules teaching coping strategies, symptom and goal-tracking, and peer-based social support, while the attentional-control will contain static education about SCD. The efficacy of the program is determined through self-report scales at pre-treatment, post-treatment (2 months), and follow-up (6-months) periods, targeting the primary outcomes of adaptive coding, pain reduction, and pain-related disability. Secondary outcomes include physical and emotional functioning and disease-specific health-related quality of life. We hypothesize that adolescents in the iCanCope with SCD experimental group will have an increase in adaptive coding and reduced pain and pain-related disability compared to the control condition. Aside from learning how to structure web-based interventions, I have a role in recoding and organizing participant data for this project. The information collected in this study can help to improve web- and mobile-based interventions for not only youth coping with SCD pain but also those with other pain-related conditions, given the flexibility and universality of cognitive-behavioral frameworks.

**Using Metabolomics to Pilot Further Studies in Chronic Pain Management in SMA Patients**

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Spinal muscular atrophy, or SMA, is a term applied to any genetic disorder that affects the spinal motor neuron through gene mutations. Depending on the type of gene mutation, there is an altering of the survival muscular neuron protein (SMN protein) that can affect either the function, quality, or amount of that protein. Due to multiple locations within the genome that produce the SMA protein, different variations of the disease exist and are classified clinically based upon the pattern of nerve loss and the causative gene mutation, with variable onset depending on which gene location has been affected. SMA is unfortunately often fatal in early childhood. Nusinersen is a novel drug treatment that uses an anti-sense oligonucleotide injected directly into the CSF that alters the genome in order to increase the amount of functional SMA protein produced. Pain is unfortunately a common occurrence for those living with SMA, and advancements in treatment and survivability have created a larger patient population and an increased need to address their pain. The scope and experience of pain in the SMA patient can vary widely, manifesting in multiple organ systems simultaneously. Our team proposes utilizing metabolomics to study the cerebrospinal fluid (CSF) of SMA patients currently receiving intrathecal Nusinersen treatment in our clinics. The CSF is already drawn as part of this treatment and is discarded. By utilizing this normally discarded resource, we are provided with a unique opportunity to analyze a human vital fluid without presenting increased harm to the patient. The aim of this proposed study is to ex-
Merkel cell carcinoma (MCC) is an aggressive skin cancer with a high (20%) rate of distant metastases, 80 percent of which occur within 2 years of diagnosis. Metastatic MCC (mMCC) to the heart is rare and presents a management challenge. Our systematic literature review revealed only 11 cardiac mMCC case reports. Most (n=6) patients received chemotherapy which is now known to lack durable response in MCC, and 2 received no treatment due to advanced disease and comorbidities. Hence, to better understand cardiac mMCC we queried an MCC data repository of patients diagnosed between 2011-2021. Progression-free survival (PFS) was measured from date of cardiac mMCC to progression or death. Among 582 MCC patients with distant metastases, 9 developed cardiac mMCC. Median age at initial MCC diagnosis (stage I (1), stage III (6), stage IV (2)) was 69 years. Most (n=8) patients developed mMCC to the right atrium, except for 1 patient (initial stage pIIIA) who had metastasis to the left atrium. Treatment for cardiac mMCC varied: 5 patients received immunotherapy combined with radiotherapy, while the reminder received immunotherapy alone, somatostatin analog, or chemotherapy. Five patients had a complete response in the cardiac lesion after immunotherapy, with or without radiotherapy. Median PFS and overall survival (OS) was 114 and 325 days, respectively. To explore whether presence of cardiac mMCC impacts OS, we matched cardiac mMCC patients to non-cardiac mMCC patients by age, sex, stage, immunosuppression status, and number of prior metastatic episodes. Using Kaplan-Meier statistical analysis, we found no difference in OS for the matched cohort (p=0.96). Taken together, these data indicate the emerging role of immunotherapy and radiotherapy in controlling cardiac mMCC. Furthermore, the location of mMCC to the heart does not appear to confer a worse prognosis compared to non-cardiac sites.

Adolescent Perceptions of Prescription Pain Medicines
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The opioid epidemic is a growing challenge facing the US, and adolescents are an under-researched population susceptible to opioid addiction and overdose. After surgery, many adolescents are prescribed pain medicines such as opioids to treat severe pain they may experience, but this exposes teens to opioids which have strong addictive properties. The aim of this study is to 1) understand teens’ perceptions and attitudes about prescription pain medicines that influence opioid use decisions and behaviors, and 2) develop a measure assessing perceptions and beliefs as risk factors for adolescent opioid misuse and abuse. We performed a literature review identifying existing measures that ask children, adolescents, and young adults about their perceptions of prescription pain medicines. Next we conducted semi-structured brief phone interviews about opioid decision making with adolescents aged 12-18 years, who either had recent surgery/ICU admission or were healthy, from 3 existing studies at Seattle Children’s Research Institute. After consent, interviews were audio recorded, transcribed, and coded to identify themes across the interviews. We conducted 15 interviews. Emerging nodes are “It’s important that I understand risks of opioids so I can balance this with helping my pain,” and “Having a support system, including family support, helps me use my opioids safely”. An example quote of the family support theme is “I just think it’s a lot easier to be able to monitor [my meds] when I had a strong support system” (15 year old participant). Once coding is complete, findings will be combined with expert input to develop a measure which will undergo pilot testing with adolescents. Understanding perceptions about prescription pain medicines will allow researchers to measure factors which place youth at higher risk for opioid addiction and to develop interventions for youth requiring opioid treatment, for example in the context of surgery.

The Rate of Skin Biopsy Closure Correlates with Resilience to Aging in Mice
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Mentor: Katie Nickel
Mentor: Zhou Jiang
Mentor: Warren Ladiges, Comparative Medicine

The ability to respond to and recover from a physically stressful event is defined as physical resilience. Because of the inherent individual variation in response to a specific stressor with increasing age, the ability to document resilience at a younger age would likely predict that an individual would be more resilient at an older age. In a preliminary experiment, this concept was tested in a mouse model of wound healing consisting of a through and through 2 mm biopsy within the central area of each ear. A cohort of 20 female and 20 male C57BL/6 mice (an inbred mouse strain used extensively in aging research), 18 months of age, were biopsied and the area of closure measured after two weeks using a digital imaging procedure. The area of closure showed that the biopsy
opening healed at variable rates depending on each individual mouse independent of sex, but clustering resulted in two main groups of approximately equal numbers, a fast-healing group and a slow-healing group. The data were analyzed by me (student first author), and I was able to assess the correlation of the two groups six months later with data on aging parameters for learning, strength, and agility when mice were 24 months of age. I found that mice with faster ear biopsy closures were better learners, and showed increased strength compared to mice with slower ear biopsy closures. I will be doing a special stain for collagen on formalin fixed ear wound areas to confirm the healing process and see if digital imaging staining intensity correlates with healing rate and aging parameters. These preliminary observations suggest that a simple skin biopsy procedure can be used to predict levels of resilience to aging phenotypes and identify mice at increased risk for age-related frailty conditions.

**Identifying Neural Biomarkers of Pain**

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*Mentor: Rajesh Rao, Computer Science & Engineering*

*Mentor: Samantha Sun, Bioengineering*

Chronic pain is characterized by persistent pain following the healing process or even in the absence of injury. The neural basis of chronic pain has been linked to several structures and pathways in the brain. However, the underlying neural electrophysiology behind chronic pain is not yet well understood. Here, we present a novel pain intensity decoder that inputs segments of neural electrophysiology and outputs predicted pain intensity values. We work with epilepsy patients who have week-long electrode implants for clinical monitoring. Using historical patient-reported pain intensities, scaled from 0 to 10, we identified segments of neural electrophysiology time-synched to when patients reported their pain levels. From these time segments, we extracted neural features, such as power-in-band values from the delta (1-4Hz), theta (4-8Hz), alpha (8-12Hz), beta (13-30Hz), gamma (30-55Hz), and high gamma (65-115Hz) frequency bands. We then used these neural features as inputs to train supervised machine learning models to predict pain intensity. We expect that prediction accuracy will depend on electrode location, where increased accuracy would occur in pain-related regions such as the anterior cingulate and insular cortex. Our classification model demonstrates that pain can be successfully decoded from neural electrophysiology and indicates potential for informing pain interventions and treatment methods for chronic pain.