A CTS Team Approach to Investigate Skeletal Muscle Diseases and Countermeasures in a Patient-Derived Bioengineered Muscle Platform

Karly Caples, Zehra Fasih, Elisabeth Barton and Siobhan Malany
University of Florida

OBJECTIVES/GOALS: Our team has developed a high-throughput 3D patient-derived muscle platform to study signaling pathways associated with skeletal muscle disease. This platform will be used to study pathologies of human muscle that arise from genetic mutations and processes of aging along with pharmacologic interventions to improve mass, function, and performance. METHODS/STUDY POPULATION: In the current study, 3D skeletal muscle is formed from young healthy male samples. Samples are treated with urocortin II (UCNII) or vehicle for ten days and evaluated for tissue performance. Functional assessments include real-time contraction magnitudes using digital image correlation (DIC) analysis of video collected during electrical pulse stimulation and end-point measures of initial and repeated tetanic force production. Functional measures provide indices of patient muscle synchronicity, strength, and endurance related to drug efficacy and toxicity which we will correlate to pro-growth protein signaling via Luminex. A subset of these samples will also be analyzed by histology and microscopy to assess muscle fiber density, type, and size, as well as myotube fusion index and sarcomere uniformity. RESULTS/ANTICIPATED RESULTS: We anticipate that healthy muscle treated with UCNII will have increased synchronicity and contraction magnitudes in DIC analysis throughout their seven-day electrical pulse stimulation protocol. We also expect to see sustained contraction magnitudes in DIC analysis at the end of electrical pulse stimulation indicating fatigue resistance in the drug treated group compared to no-drug control. Like our real-time DIC data, we anticipate increases to initial and sustained maximal force production in the drug treated group. We expect that drug treated muscle will present with an increased fiber density, fiber diameter, and fusion index with uniform sarcomeres. Finally, we expect heightened pro-growth signaling pathways in treated vs. controls. DISCUSSION/SIGNIFICANCE: The current study will serve as an initial investigation of the endogenous ligand UCNII for enhancing skeletal muscle mass and performance in human muscle laying the framework for future drug efficacy and toxicity studies. This platform will ultimately enhance the study of muscle diseases and translation of therapeutics to clinical settings.

Improvement of health outcomes and quality of life of Hispanic older adults in Puerto Rico through participation in a Physical Activity (PA) Community-based Program

Felix J. Roman - Hernandez, Maria Danet Lapiz - Bluhm, Abdiel Gomez – Santos and Wilnelys M. Montalvo – Caraballo
University of Puerto Rico Medical Sciences Campus School of Nursing

OBJECTIVES/GOALS: The proposed study aims to improve physical and mental health outcomes among Hispanic older adults who live alone in a low-income San Juan, Puerto Rico community through weekly PA groups. Specific outcomes include measures of loneliness, social isolation, depression, physical mobility, metabolic indicators, and other health indicators. METHODS/STUDY POPULATION: Data will be collected at three time points: Pre (Week 1), Mid (Week 6), and Post (Week 12) intervention. Currently, the community has 50 residents over 65 years old who live under the poverty index and receive multiple social benefits. Various tools will be implemented to measure loneliness (University of California Los Angeles – Loneliness Scale-10 items), social isolation (Lubben Social Network Scale-6 items), depression (Geriatric Depression Scale-10 items), physical mobility (Time Up and Go Test), metabolic health indicators (hemoglobin A1c and glucose) and other health indicators (i.e., blood pressure, cholesterol, as well as body mass index (BMI)). These measurements will determine if participation in PA groups is associated with improvement of the variables measured. RESULTS/ANTICIPATED RESULTS: It is expected that the baseline scores of older Hispanic adults in terms of loneliness, social isolation, depression, physical mobility, metabolic indicators (i.e., cholesterol level and hemoglobin A1c), and other health indicators (blood pressure or BP and BMI) will be lower compared to those after participation in the Physical Activity Program. More frequent participation will be associated with more significant improvement in measured variables. DISCUSSION/SIGNIFICANCE: Results from this study will determine the effectiveness of community-based PA interventions in addressing loneliness, social isolation, depression, physical mobility, and metabolic factors (hemoglobin A1c and glucose) in elderly minority Hispanic populations as a means of improving their health outcomes and quality of life.

Radiographic Changes in the Auditory Pathway to Predict Outcomes of Children with Hearing Loss

Iram Ahmad, Peter Moon, Kristi Ward, Taseer Din, Sara Saki, Alan Cheng and Kristen Yeom
Stanford University

OBJECTIVES/GOALS: Early diagnosis of congenital sensorineural hearing loss (SNHL) is of paramount importance in preventing speech and language impairment.Diffusion tensor imaging (DTI) MRI can identify brain microstructural changes that may potentially contribute towards prognosticating rehabilitation. METHODS/STUDY POPULATION: We retrospectively reviewed pediatric patients with SNHL who obtained DTI MRI between 2011 and 2019, identifying 16 pediatric patients (age <18 years) with at least moderate asymmetric/bilateral SNHL., and gender-matched controlswithout neurological, developmental, or MRI-based brain macrostructural abnormalities. The following brainstem regions and tracts of the auditory pathway were assessed: superior olivary nucleus (SON), inferior colliculus (IC), ipsilateral tracts between the inferior colliculus and superior olivary nucleus (IC-SON). Diffusion values for bilateral regions and tracts were generated, then averaged to calculate a mean value for fractional anisotropy (FA) and mean diffusivity (MD) for each subject. RESULTS/ANTICIPATED RESULTS: Significant differences were identified in FA values of the SON between the SNHL cohort and controls (0.377 ± 0.056 vs 0.422 ± 0.052; p=0.009). No other FA or MD values were significantly different. In children £5 years, MD was significantly decreased in the SNHL cohort compared to controls in the IC (0.918 ± 0.051 vs 1.120 ± 0.142; p<0.001). In children >5 years, there were no significant differences in MD (1.124 ± 0.198 vs 0.997 ± 0.103; p = 0.119). There were no significant differences in MD or FA in the white matter fibers of the IC-SON tract [applewebdata%3A//720AAF0C-C4CF-459C-A42A-6BAA56C4E4CA#_msocom_2]. DISCUSSION/SIGNIFICANCE: This is the first study to assess