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Predicting outcomes of lifestyle and stress reduction interventions for obesity with DNA methylation and psychological measures

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OBJECTIVES/GOALS: Obesity has been classified as a global epidemic and origin of numerous health issues. The central hypothesis of this study is that psychological measures, DNA methylation, and gene transcription will predict obesity-related outcomes after lifestyle interventions, and such interventions may alter DNA methylation profiles. METHODS/STUDY POPULATION: This study consisted of a randomized-controlled trial examining the effects of lifestyle +/- stress reduction interventions in 285 highly stressed parents with obesity, followed for 2 years. Full participants received nutrition and activity counseling, and were randomized to either a stress reduction intervention or a contact control. Those who otherwise qualified for the study but unable to fully participate were included in a no intervention control group. The intervention consisted of 12 weeks of nutrition and activity counseling +/- 2-hour weekly stress reduction interventions using MBSR and CBT-based strategies. DNA methylation was assessed using Illumina EPIC arrays. RESULTS/ANTICIPATED RESULTS: Using linear mixed models (LMMs), this study will first examine the hypothesis that baseline psychological measures and pre-existing methylation sites associated with obesity and glycemic control (e.g., ABCG1, ATP10A, TXNIP, SREBF1, RNF39, and SOCS3) predict changes in BMI, HOMA-IR, and HgbA1C post-intervention and at 1 and 2 year follow-ups. Using sites that demonstrate statistical significance, we will develop a polymethylation risk score predictor of change in BMI. Next, we will examine the hypothesis that interventions which reduce obesity may also lead to improvements in epigenetic aging using LMMs to determine if changes in BMI or HOMA-IR predict changes in epigenetic age acceleration over the course of the study. DISCUSSION/SIGNIFICANCE OF IMPACT: This work examines whether psychological factors and/or epigenetic markers may be used in patient stratification at initiation of treatment, enabling improved treatment selection, fewer years of obesity and decreased risk of comorbidities. This proposal also asks whether lifestyle interventions impact the aging process itself.

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A CTS team approach to investigate skeletal muscle diseases and countermeasures in a donor-derived bioengineered muscle platform*

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OBJECTIVES/GOALS: Our team has developed a 24-well donor-derived skeletal muscle microphysiological system (MPS) to study signaling pathways associated with a variety of muscle diseases. 3D muscle will be utilized to evaluate pharmacologic interventions for these muscle conditions to improve both muscle mass and function. METHODS/STUDY POPULATION: In this study, muscle MPS were formed from healthy young female and male subjects. 3D muscle underwent a 21-day differentiation with an electrical stimulation (e-stim) regimen twice daily beginning on Day 14. Functional assessments in permeabilized fibers of both sexes included isometric and isotonic calcium-induced contractions, allowing for the characterization of force-pCa (-log[Ca2+]), force-velocity and force-power relationships. Samples from Day 17 and Day 21 will be assessed for pro-growth protein signaling via western blotting and a subset of samples will be analyzed by histology and microscopy for fiber type and size. Finally, culture media pre- and post-terminal e-stim on Day 21 will be collected for extracellular vesicle (EV) isolation and EVs will be assessed by standard proteomics analysis. RESULTS/ANTICIPATED RESULTS: Permeabilized fibers from both sexes reproduced the well-established sigmoidal force-pCa and the curvilinear force-velocity and force-power relationships reported in native striated muscle. Maximum specific force and force-pCa relationship were not different between sexes. Isotonic contractile measurements revealed that these male and female fibers also exhibit similar force-velocity and force-power relationships. We anticipate that 3D muscles from day 17 compared to day 21 will exhibit higher levels of pro-growth protein signaling due to e-stim application and no differences in fiber type or size between sexes. Additionally, we expect that EV quantity will depend upon 3D muscle maturity and presence of e-stim. DISCUSSION/SIGNIFICANCE OF IMPACT: This study demonstrates the similarities of functional characteristics and exercise (or e-stim) adaptation between native human skeletal muscle and 3D bioengineered skeletal muscle. Ultimately, this data further validates the muscle MPS system to study muscle diseases and to enhance the translation of therapeutics to clinical settings.

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A systematic review on sleep duration and Alzheimer's disease fluid biomarkers: Preliminary findings

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OBJECTIVES/GOALS: This review examined if sleep duration is associated with established Alzheimer's disease (AD) fluid biomarkers, such as amyloid-β peptides (Aβ40 and Aβ42), total-tau (t-tau), phosphorylated tau (p-tau181 and p-tau217), neurofilament light chain (NfL), and glial fibrillary acidic protein (GFAP).

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