

educational preparation, hands-on observation of value of ACP in surgical patients and influences from attending and residents. **DISCUSSION/SIGNIFICANCE:** While current ACP research in surgery focuses on physician-led patient engagement in ACP discussions, there is a paucity of research focusing on how to develop a team-based approach to ACP discussions in surgery. This study will provide information necessary for the development of interventions that increase team-based ACP for surgical patients.

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### Potential Drug Therapy for Fragile X Tremor/Ataxia Syndrome<sup>\*,†</sup>

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**OBJECTIVES/GOALS:** Fragile X-associated tremor/ataxia syndrome (FXTAS) is a devastating rare neurological disorder that negatively impacts movement and cognition. To date, there are no effective pharmacological treatments for FXTAS. Our goal was to develop a cell culture model of FXTAS to investigate promising therapeutics. **METHODS/STUDY POPULATION:** To establish mitochondrial dysfunction, normal human cell lines and human-induced pluripotent cells were treated with multiple concentrations of glucose/ glucose oxidase (GluOx) at 2, 12, and 24 hour time points to induce varying intensities of oxidative stress. The degrees of oxidative stress were measured by apoptosis and mitochondrial reactive oxygen species (ROS) production. Curcumin and MSKE compounds effective against oxidative damage in mitochondria were used to rescue glucose oxidase-induced oxidative damage in both cell lines. To test the ability of these drugs to restore mitochondrial health, cell viability and cellular superoxide production were assessed by propidium iodide and the MitoSox fluorescence assay, respectively. **RESULTS/ANTICIPATED RESULTS:** We anticipated that GluOx at varying concentrations and time points would proportionally increase levels of apoptosis and mitochondrial ROS, reflective of mitochondrial damage, with the most severe dysfunction occurring at a dose of 25 nM and the longest duration of 24-hr exposure. Administration of MSKE in concentrations ranging from 10<sup>-8</sup> to 10<sup>-5</sup> M in half log increments, did not reverse the oxidative defects induced in the cell lines. However, curcumin concentrations increased cell viability at the 2, 12, and 24 hour time period. Results indicate that the research design should be modified by increasing the concentration of both glucose and MSKE to provide a reliable test of the hypothesis. **DISCUSSION/SIGNIFICANCE:** These studies illustrate the usefulness of this in vitro model to test novel therapeutics in neuronal FXTAS models and expand the discovery of mitochondrial markers for the syndrome.

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### Eliminating System xc- Signaling Between Astrocytes and Neurons Selectively Impairs Complex Cognition

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**OBJECTIVES/GOALS:** We aim to determine whether non-neuronal, non-synaptic glutamate signaling mechanisms can be targeted

to produce highly specific, narrow changes in brain function that would benefit CNS disorders. To do this, we investigated cognitive changes produced through manipulating the activity of the astrocytic glutamate release mechanism system xc-. **METHODS/STUDY POPULATION:** System xc- (Sxc) activity was eliminated by mutating the gene *Slc7a11* through pronuclear injection of zinc-finger nucleases into Sprague Dawley rat embryos to create a line of rats lacking Sxc (MSxc rats). To confirm a lack of Sxc activity, we verified that tissue from MSxc rats had a complete lack of xCT, which is the regulatory subunit of Sxc that is encoded by *Slc7a11*. We also verified that astrocyte cultures generated from MSxc tissue lacked cystine-evoked glutamate release. Next, we measured development (body weight), CNS regulation of metabolism, and other indicators of generalized, non-specific brain function as well as behaviors that are reliant on executive function, such as cognitive flexibility, impulse control, decision-making, and response inhibition. **RESULTS/ANTICIPATED RESULTS:** Eliminating Sxc was not lethal and did not impair development or produce widespread changes in brain function as is commonly observed when deleting other glutamate mechanisms. MSxc rats did not differ from wildtype in growth rate, central regulation of metabolism as reflected by absolute or diurnal changes in core body temperature, locomotor activity in a familiar or novel environment, or simple forms of cognition such as novel object recognition, or operant responding (food and cocaine-reinforced). In contrast, behaviors that rely on executive function were impaired. MSxc rats displayed deficits in cocaine reinstatement and attentional set-shifting. We anticipate MSxc rats to also show impairments in decision-making in the rat gambling task and response inhibition in the stop-signal reaction time task. **DISCUSSION/SIGNIFICANCE:** Eliminating Sxc activity in rats produced deficits in behaviors reliant on executive function without impacting development or simple brain function. These results highlight the potential of targeting Sxc to enhance cognition without generating therapeutically limiting adverse effects resulting from non-specific changes in brain function.

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### Quantifying Heavy Metals in Interstitial Fluid for Remote Monitoring of Chronic Exposures

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**OBJECTIVES/GOALS:** Our hypothesis is that microneedle array (MA) extraction of interstitial fluid (ISF) will enable minimally invasive quantitation of heavy metal (HM) exposure. We aim to establish analytical parameters for ICP-MS analysis of HMs, quantify baseline HM content in ISF vs other fluids, and characterize a mixed HM exposure model. **METHODS/STUDY POPULATION:** Ten healthy human volunteers were recruited into the study, approved by the UNM Human Research and Resource Committee. Each subject had blood and urine collected. ISF was also collected using 3D-printed MAs inserted into the forearm. Additionally, twelve Sprague Dawley rats were unexposed (n=6) or exposed (n=6) to ad libitum water containing a mixture of uranium (U), cadmium (Cd), vanadium (V), and arsenic (As), each at 5X the maximum contaminant level (MCL) for drinking water under a protocol approved by the UNM animal care and use program. Human and animal fluids were analyzed, using ICP-MS, to quantify the levels of U, Cd, V, and As. **RESULTS/ANTICIPATED RESULTS:** Recent advances in ISF extraction and analysis suggest a minimally invasive method that can be adapted to monitor HM exposure and biological loads