SIGNIFICANCE: Silicosis is a often fatal disease with no FDA approved therapies. These results suggest that targeted loss of Col1a1+ fibroblasts in Silicosis is sufficient to arrest disease progression. Thus, it is essential to understand how targeted loss of pro-fibrotic fibroblasts can alter disease progression as a tool to develop novel therapeutic strategies.

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Interactions between tumor, age, and chemotherapy in cognitive impairments and neuroinflammation*

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OBJECTIVES/GOALS: We will use a novel syngeneic model of prostate cancer to examine impairments and uncover potential changes in inflammatory signaling in the brains of animals with and without tumors. We will then investigate the interaction between peripheral tumor, age, and chemotherapy on cognitive impairments and any accompanying neuroinflammation METHODS/STUDY POPULATION: Male Copenhagen rats (aged 3 or 10 months) were subjected to tumor fragment implantation (Dunning R2237G cells) or sham surgery. Once tumors were palpable, animals received either docetaxel (4.5mg/kg, intraperitoneal) or it's vehicle once every other day for 5 days (3 injections total) followed by a two-week recovery period. During this time, TNFa and IL-6 was quantified in plasma samples obtained once per week for two weeks. Hippocampal-mediated visuospatial and working memories were assessed using the novel object task and percent alternation in a y-maze, respectively. Afterwards, trunk blood and hippocampal tissue were isolated. TNFa and IL-6 protein was quantified in plasma. Hippocampal tissue was probed for markers of neuroinflammation, including increases in TNFa, IL-6, and reactive microglia RESULTS/ANTICIPATED RESULTS: The presence of a tumor alone produces deficits in hippocampal-mediated visuospatial memory and working memory regardless of treatment and persistent elevations in TNFa and IL-6 in plasma. Docetaxel administration also produces impairments in hippocampal-mediated visuospatial memory, but not in working memory. We anticipate these cognitive impairments will be accompanied by hippocampal neuroinflammation. We expect age and docetaxel chemotherapy to exacerbate working memory deficits and markers in hippocampal neuroinflammation, including increases in TNFa, IL-6 and reactive microglia DISCUSSION/SIGNIFICANCE: This study will provide insight into the interaction between tumor, age, and chemotherapy in impairments in visuospatial memories. This model provides a substrate upon which interventions can be tested to ensure the efficacy of the cancer treatment is maintained when treating these cognitive impairments.

Other

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Rapid SARS-CoV-2 testing with duplexed recombinase polymerase amplification and a bacteriophage internal control

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OBJECTIVES/GOALS: Current COVID-19 rapid molecular tests require cartridge-reader detection, expensive circuitry, and complex microfluidics making the most accurate tests unavailable to the masses. Here we present a rapid molecular diagnostic leveraging isothermal amplification and paper-based microfluidics for a low-cost ultra-sensitive COVID-19 assay. METHODS/STUDY POPULATION: We designed a reverse transcription recombinase polymerase amplification (RT-RPA) assay for the detection of SARS-CoV-2 and bacteriophage MS2 RNA. RT-RPA is a sequence specific, ultrasensitive, rapid isothermal DNA amplification technique that is well suited to home based testing due to its rapid assay time, robustness, ease of use, and readout options. RT-RPA reagents are added to a tube and incubated at 39Â°C in a fluorometer. Realtime fluorometer data gives results in under 15 minutes. This assay also provides visual detection via lateral flow readout with results in 23 minutes. RESULTS/ANTICIPATED RESULTS: We have developed a rapid multiplexed nucleic acid amplification assay with an internal process control for SARS-CoV-2 using single-pot RT-RPA. We screened 21 primer combinations to select primers that demonstrated excellent performance and target specificity against common respiratory viruses. We demonstrate the ability to multiplex SARS-CoV-2 and MS2 detection, utilizing MS2 as an internal process control for lysis, reverse transcription, amplification, and readout. We show duplexed detection using both fluorescence readout and visual readout using lateral flow strips. Duplexed fluorescence detection shows a limit of detection of 25 copies per reaction. Duplexed lateral flow readout shows a limit of detection of 50 copies per reaction DISCUSSION/SIGNIFICANCE: We developed a duplexed RT-RPA assay for SARS-CoV-2 with fluorescence or lateral flow readout. Our assay does not re-quire expensive reader, circuity, or fluid handling. The low material cost, temperature, and robustness make it ideal for a more accurate home-based COVID-19 diagnostic.

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A Human 3D Model of Duchenne Muscular Dystrophy Cardiomyopathy to Investigate Calcium Regulation and Mitochondrial Dysfunction

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OBJECTIVES/GOALS: We will use control- and DMD-engineered heart tissues to better model and investigate DMD cardiomyopathy. We will primarily assess cardiac calcium handling, mitochondrial function, and mitochondrial calcium handling, as calcium regulation and mitochondrial function are known to be affected in DMD. METHODS/STUDY POPULATION: We will use patient-derived stem cells, differentiated into cardiomyocytes in bioprinted 3D heart tissue muscle chambers to better model DMD cardiomyopathy. We will look at calcium handling and general mitochondrial function, as well as mitochondrial calcium handling, using a novel multifunctional genetic probe I previously developed allowing for simultaneous observation of cytosolic and mitochondrial calcium in real time. Optical mapping will also be used for tissue-level analysis. We will establish the functional differences at baseline, and then progress heart failure in the tissues to see how the abnormalities seen in the DMD tissues may get worse. Finally, we will investigate the effects of early restoration of dystrophin function on the effects of DMD cardiomyopathy development. RESULTS/ANTICIPATED RESULTS: We anticipate that DMD tissues will show more irregular/abnormal calcium handling, as seen in 2D hiPSC-CMs, as well as disruptions to mitochondrial function and ultrastructural development, as well as a decreased synchronization between cytosolic and mitochondrial calcium dynamics. We anticipate that these

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