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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abnormalities will be exacerbated as the disease state progresses, but at least partially ameliorated with the restoration of dystrophin function. DISCUSSION/SIGNIFICANCE: DMD is a fatal disease with no known cure. Patients develop heart failure in their teens and die in their 20s, so any new insight that may prolong life and improve quality of life for patients is drastically needed. This would be the most accurate preclinical model of DMD cardiomyopathy to date and would investigate yet-untapped aspects of the disease state.

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Analysis of Clinical, Histologic, and Molecular Characteristics of Proliferative Verrucous Leukoplakia

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OBJECTIVES/GOALS: This study aims to develop objectively scored histological characteristics of early oral leukoplakia, which may be correlated with molecular pathways predictive of progression into proliferative verrucous leukoplakia (PVL). The secondary aim is to develop a biomarker profile to be used in diagnosis, staging, and management of PVL. METHODS/STUDY POPULATION: Clinical and pathology records of 120 patients with oral leukoplakia and/or PVL were reviewed. Eight patients were selectedâ€"all had serial biopsies over time leading to PVL suspicion. Specimens were deidentified and subjected to blinded examination by a board certified oral pathologist, then scored relative to the extent of each of the commonly accepted histologic characteristics of PVL: hyperkeratosis, acanthosis, blunt rete ridges, hyperchromatic nuclei, increased nuclear-cytoplasmic ratio, dyskeratosis, and surface corrugation. Given these results, a larger subset of patient samples will be labeled and assayed for expression of epidermal growth factor receptor tyrosine kinases and downstream pro-oncogenic signaling mediators. Expression of these factors will be tested against progression to PVL. RESULTS/ANTICIPATED RESULTS: Histologically, in scoring the specimens from eight subjects, the characteristics of acanthosis, dyskeratosis, and blunted rete ridges had the strongest correlation with eventual progression to PVL. These criteria will therefore be recommended as an objective histopathologic method of identification of patients with high risk of development of PVL, and therefore malignant potential. We expect the results of the biomarker assay to provide a molecular basis for predicting PVL pathogenesis. Particularly, we anticipate pro-oncogenic targets such as EGFR, PI3K, Akt, and mTOR pathways will show increased expression as leukoplakic lesions progress. These results would then provide the basis for testing patient samples for expression of these markers in a longitudinal study of PVL emergence and progression. DISCUSSION/SIGNIFICANCE: The aggressive nature of PVL, with a rate of malignant transformation of 61% and mortality rate of 40%, requires close clinical monitoring in order to improve patient outcomes. Therefore, well defined objective clinical, histologic, and molecular criteria are critical for early detection of sites likely to progress to PVL and subsequent malignancy.

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Assessment of Mental Health Needs of Transgender Adults Seen at a Midwest Transgender Center

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OBJECTIVES/GOALS: Prior studies suggest that transgender individuals are at greater risk of mental health problems. This study aims to determine the mental health care needs of the adult transgender population seen at a tertiary referral hospital in the Midwest region of the United States and assess necessary resources to provide optimal care. METHODS/STUDY POPULATION: This descriptive, retrospective, cross-sectional study included all new transgender patients > 18 years old, seen at the Washington University Transgender Center since December 2019 through May 2022. Electronic medical record data obtained from their initial and subsequent follow-up visits include 1) Demographics: date of birth, age, race, ethnicity, sex assigned at birth, gender identity, zip code of residency 2) Mental health diagnosis: Previous mental health diagnosis, mental health history 3) Mental health care access: mental health providers, mental health treatment, previous mental health admission, resources provided in clinic. RESULTS/ANTICIPATED RESULTS: 487 patient records were reviewed. Median age at initial visit was 24 years (18 - 75 yr), with 46% identify as woman, 37% as man. Predominantly white (84%), 11% were black. 93% had primary health insurance At the first visit, 81% reported having some mental health diagnosis: depression (88%), anxiety (71%), attention deficit disorder (21%). Prior suicide attempt reported on 12% and 5% with self-harm behavior. Only 48% had a therapist and 22% had an established psychiatrist First follow up occurred with a median of 4 months (1-22 months). 4 patients reported new suicide attempt, 3 reported new self-harm behavior. 9 patients required a hospital admission due to a psychiatric condition. 4% reported a new mental health diagnosis (most common: depression and anxiety). No changes noted on access to therapist or psychiatrist DISCUSSION/SIGNIFICANCE: Our study shows that adult transgender individuals have high rates of depression, anxiety, and overall psychological distress which is exacerbated by poor access to mental healthcare. This indicates a critical need to include mental healthcare professionals during the evaluation of adult transgender individuals

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Caspase-1 mediated inflammatory response - a critical player in concussive mild traumatic brain injury (mTBI) associated long term pain

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OBJECTIVES/GOALS: Patients who have experienced conjunctive mild traumatic brain injuries (mTBIs) suffer from a number of comorbidities, including chronic pain. Despite extensive studies investigating the underlying mechanisms of mTBI-associated chronic pain, the role of inflammation after mTBI and its contribution to long-

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