(NCT) numbers identified from internal research administration systems. Business intelligence software (Microsoft PowerBI) was applied to the corresponding dataset to enable end user exploration and analysis of the trials within ClinicalTrials.gov. RESULTS/ANTICIPATED RESULTS: A total of 3,271 studies associated with UM were identified, of which, 3,054 (93.3%) had at least one condition MeSH term linked. A total of 7,711 MeSH terms were associated with the trials overall, representing 1,112 unique MeSH terms; the most common terms were carcinoma (164), lymphoma (155), HIV Infections (139), neoplasms (136), and leukemia (122). Utilizing MeSH hierarchy, trials were characterized were categorized into 36 different trees. The most common top tree nodes were neoplasms (1,181), followed by pathological conditions/signs and symptoms (913), immune system diseases (574), nervous system diseases (513), and digestive system diseases (483). Within trees, a total of 184, 681, and 1057 different MeSH terms were specified at the second, third, and fourth nodes in the hierarchy respectively. DISCUSSION/SIGNIFICANCE: Utilizing existing metadata from trials posted on ClinicalTrials.gov and MeSH tree structures can enable organizations to readily explore the foci of clinical trials research. High rates of MeSH term association to research study conditions are necessary to ensure adequate representation of research foci.

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An umbrella protocol that establishes an enterprise-wide framework for the operation of a Clinical Data Warehouse

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OBJECTIVES/GOALS: To streamline the standards and procedures for operating a research-specific, clinical data warehouse, acheived by defining roles, introducing a common language, and categorizing dataset types to provide transparency regarding data security risks inherent in the use of patient data. METHODS/STUDY POPULATION: We established a Bioethics committee responsible for ensuring clinical data is securely procured, maintained, and extracted in a manner that adheres to all federal, state, and local laws. We created an operational framework in the form of an umbrella IRB protocol and shared it with the bioethics committee for feedback and approval. The protocol was approved first by the bioethics committee and subsequently by the IRB. It was then disseminated across the institution and published online for continuous reference and use by committee members, researchers, and the data warehouse service team. RESULTS/ANTICIPATED RESULTS: The resulting framework defined the roles of researchers, data warehouse service team members, and honest brokers; explains the procedures for accessing and securely delivering data; and lists six categories of datasets according to type and implicit risks: datasets that are preparatory for research/aggregate counts, anonymized datasets, coded datasets, limited datasets, identified datasets for recruitment purposes, and defined identified cohort datasets. The protocol is approved and in use enterprise-wide, has reduced the number of questions from stakeholders, and has given researchers, IRB members, and informatics staff confidence in the use of the clinical research data warehouse. DISCUSSION/SIGNIFICANCE: We offer our framework to CTSAs interested in streamlining their data warehouse operations. We believe the adoption of this framework will establish strong procedures for ensuring compliance with IRB requirements, data privacy, and data security while reducing barriers to clinical research.

Other

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Tyrosine kinase inhibition reduces pathological markers of Alzheimer's Disease*†

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OBJECTIVES/GOALS: Alzheimer's Disease (AD) displays numerous pathological features, including amyloid-beta deposition, extensive neuroinflammation, and vascular fibrosis. However, putative therapeutic options for alleviating these features remain limited, emphasizing the need to develop comprehensive treatments for patients with AD. METHODS/STUDY POPULATION: CSF from human AD patients treated with nilotinib (n=12), a tyrosine kinase inhibitor, or placebo (n=11) was collected and sequenced, and significantly altered miRNAs were identified and analyzed for alterations to disease-associated genes via gene ontology analysis. TgAPP mice were injected intraperitoneally with one of two novel tyrosine kinase inhibitors, BK40143 or BK40197, or DMSO (n=12 per group) daily for six weeks, during which memory deficits between groups were measured, before brains were harvested for analysis of amyloid-beta load via ELISA, microglial activation via Sholl analysis, and vascular collagen levels via immunohistochemistry. RESULTS/ANTICIPATED RESULTS: CSF obtained from AD subjects treated with nilotinib revealed significantly increased ($p<0.05$) levels of miRNAs regulating autophagy, neuroinflammation, and collagen production compared to placebo. These results were validated in vivoin TgAPP mice, who displayed improved recall on the novel object recognition test and Morris water maze following treatment with our drugs, correlating with decreased levels of brain amyloid-beta (30% decrease, $p=0.002$), decreased microglial reactivity and activation (40% decrease, $p=0.01$), and decreased vascular fibrosis (50% decrease, $p=0.005$) along small brain blood vessels compared to controls. DISCUSSION/SIGNIFICANCE: These data identify tyrosine kinase inhibition as a valid therapeutic strategy for alleviating various pathological features associated with AD and warrant further investigation as a treatment option for human patients as a means of slowing cognitive decline.

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Maternal hypertension results in a decreased number of glial cells in offspring during early development

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OBJECTIVES/GOALS: Preeclampsia, a hypertensive disorder in pregnancy, disrupts immune cell profiles at birth in both mice and humans. In mice, it affects offspring's memory and behavior. This study aimed to investigate whether preeclampsia induces lasting immune cell changes after birth and its impact on astrocyte and microglia cell counts in offspring. METHODS/STUDY POPULATION: Preeclampsia was induced in C57BL/6 females by infusion of vasopressin (24 ng/hr) or saline throughout gestation via osmotic minipump. Parturition was allowed to occur naturally. Offspring were euthanized at various timepoints post-delivery for experimental measures. Total urine protein was determined via bicinchoninic acid assay. Single cell suspensions were prepared from thymus spleen, and brain tissue and separated via density gradient.

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Cell suspensions were stained with fluorochrome-conjugated monoclonal antibodies for flow cytometry. Statistical significance was determined using a two-tailed Student t test or one way ANOVA multiple comparisons test. The minimal level of confidence deemed statistically significant was $p<0.05$. RESULTS/ANTICIPATED RESULTS: Preeclampsia resulted in lower body and heart masses in offspring. Although T cell populations in the thymus were not altered in preeclampsia offspring, total T cells, Thelper, and cytotoxic T cells were elevated. Total B and isotype-switched B cells were increased in offspring of preeclampsia. Total dendritic cell percentages were not changed in offspring of preeclampsia, however, total anti-inflammatory markers on dendritic cells were reduced. Lastly, offspring of preeclampsia had a reduction in microglia and astrocytes within the brain. DISCUSSION/SIGNIFICANCE: Our study could establish including in utero data in predicting future disease risk, addressing gaps in understanding rising rates of cardiovascular and behavioral diseases. It also uncovers the impact of preeclampsia on early immune programming and reduced glial cell populations, potentially affecting cognitive and behavioral development.

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Validation of a Novel CSF-Based Biomarker of Mitochondrial Function†

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OBJECTIVES/GOALS: Determine the exosome mitochondrial DNA (mtDNA) copy number in cerebrospinal fluid (CSF) as a measure of neuronal mitochondrial integrity in patients with subarachnoid hemorrhage (SAH). Determine the patterns of beta amyloid and tau protein biology in CSF of SAH patients and correlate those measures with the clinical status of the SAH patients. METHODS/STUDY POPULATION: The CSF is collected from SAH patients undergoing ventriculostomy-based continuous CSF drainage. Adults from all ethnicities and sex are included in this study. The exosomes are isolated from CSF samples using a precipitation method and particle count and size are measured using NanoSight. The DNA is extracted using an exosomal DNA isolation kit (XCF kit). The CSF mtDNA copy number is measured using digital drop PCR with mitochondrial DNA primers. The levels of beta-amyloid (a-beta-40 and -42) and tau protein in CSF are measured using a sensitive ELISA-based assay. A quantitative evaluation of mitochondrial DNA copy number, clinical status of the SAH patients and beta amyloid, and tau protein levels will be conducted and reported. RESULTS/ANTICIPATED RESULTS: Preliminary results of four CSF samples showed similar patterns in CSF exosome particle number, particle size and exosomal mtDNA copy number in relation to samples from the admission day. Particle number decreased with time while particle size increased. More patient samples will be analyzed to confirm the patterns. We anticipate that mtDNA copy number will correlate with brain beta-amyloid and tau protein levels. Moreover, we anticipate that the clinical status of the SAH patients will associate with the mtDNA copy number. We specifically predict that higher mtDNA copy number levels will correlate with better clinical outcomes. DISCUSSION/SIGNIFICANCE: Mitochondrial function is critical to brain health, but we lack effective ways to monitor this parameter. Here we focus on a CSF based biomarker, exosome-derived mtDNA, which is intended to reflect the integrity of brain mitochondria. As bioenergetic metabolism influences beta amyloid and tau biology, predicting those levels are important.

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Identification of novel plasma protein biomarkers for diagnosis and prediction of Alzheimer's disease in African Americans*†

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OBJECTIVES/GOALS: To identify novel panel of plasma protein biomarkers to improve prediction and diagnosis of Alzheimer's disease (AD) for African Americans (AA), who are at greater risk of developing AD compared to non-Hispanic White individuals but are underrepresented in AD research. METHODS/STUDY POPULATION: Pre-existing plasma samples from 460 AA individuals with clinical diagnoses of AD, cognitively unimpaired (CU), mild cognitive impairment (MCI), or dementia with Lewy bodies (DLB) will undergo untargeted proteomics using the SomaScan assay, where modified single stranded DNA aptamers bind to protein targets which are quantified by DNA microarray. Protein expression levels will be compared between diagnostic groups to identify differentially expressed proteins. Additional clinical, genetic, and lifestyle factors will be compared with protein expression when available. Proteins of interest, identified by differential protein expression analysis results, will be included in receiver operating characteristic analyses to identify the optimal set of proteins for diagnostic classification. RESULTS/ANTICIPATED RESULTS: A pilot experiment utilizing plasma from 40 individuals identified multiple differentially expressed proteins (DEPs) between AD and non-AD groups. Eight proteins were nominated from the differential protein analysis into a receiver operating characteristic (ROC) analysis based on pvalue and previous implication in AD genome wide association studies. Proteins involved in microglial activation, neuronal adhesion, cell proliferation, and innate immunity were nominated. The ROC model achieved 100% classification accuracy of AD and CU groups using age, sex, and the eight nominated proteins. It is expected that there will be more significant associations when utilizing the full cohort of 460 AA and that DEPs between AD, CU, MCI, and DLB will be identified. DISCUSSION/SIGNIFICANCE: The nomination of a novel panel of plasma biomarkers developed from an AA cohort will directly serve the AA community by improving access to an early and accurate diagnosis of AD. Access to improved prediction and diagnosis will likely improve disease management, thus improving patient outcomes and decreasing burden on families and caregivers.

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Ischemic conditioning improves dynamic balance during treadmill walking in chronic stroke survivors

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OBJECTIVES/GOALS: Evaluate the use of IC to improve stroke survivors' capacity for reactive stepping and adapt their gait cycles in

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