progression, showing remarkable early biomarker potential. These findings lay the groundwork for early detection and innovative therapies to halt DKD and improve patient outcomes.

38

Biomarkers and neurocognitive impairment in traumatic brain injury patients

Manuel Mas[1], Valerie Wojna[1], Bexaida Díaz, Pérez[2], Tanlix Bartolomei-Traviza, Rosario-Rodriguez Lester[2] and Yisel M. Cantres-Rosario[2]
[1]University of Puerto Rico, Medical Sciences Campus and [2]School of Medicine (Postdoctoral Researcher)

OBJECTIVES/GOALS: This study aims to explore the relationship between plasma biomarkers (GFAP, NF-L, and IL-1β) and cognitive impairment in moderate to severe TBI patients. We will assess biomarker levels and their link to neurocognitive outcomes at acute and chronic stages of injury. METHODS/STUDY POPULATION: We will recruit 100 patients aged 21 years and older with moderate to severe TBI (Glasgow Coma Score 3–12) from a trauma hospital. Blood samples will be collected at 24–72 hours post-injury and again at 3 and 6 months. Plasma levels of GFAP, NF-L, and IL-1β will be measured using multiplex ELISA. Neurocognitive tests will be administered at 3 and 6 months to assess cognitive function. Correlations will be made between biomarker levels, neurocognitive performance, and disability scores (Disability Rating Scale and Glasgow Outcome Scale). Exosome isolation from plasma will allow for detailed analysis of astrocyte-derived biomarkers and their association with long-term cognitive impairment and recovery. RESULTS/ANTICIPATED RESULTS: We anticipate that plasma levels of GFAP, NF-L, and IL-1β will be elevated in the acute phase of moderate to severe TBI and will correlate with injury severity. At 3 and 6 months, higher levels of IL-1β, in particular, are expected to be strongly associated with cognitive deficits. We also anticipate that biomarkers in astrocyte-derived exosomes will provide more specific insights into long-term neuroinflammation and its impact on cognitive function. These findings could pave the way for targeted, personalized interventions to improve recovery in TBI patients. DISCUSSION/SIGNIFICANCE OF IMPACT: This research focuses on inflammation's role in cognitive impairment and disability in TBI patients. We propose using multiple biomarkers – GFAP, IL-1β, NF-L – paired with advanced techniques like exosomes and multiplex analyses to identify novel therapeutic targets, aiming for personalized treatment strategies, as well as prognosis.

39

Nanoscale imaging of pT217-tau in aged rhesus macaque entorhinal and dorsolateral prefrontal cortex: Evidence of interneuronal trafficking and early-stage† neurodegeneration

Dibyadeep Datta, Isabella Perone, Denethi Wijegunawardana, Feng Liang, Yury M. Morozov, Jon Arellano, Alvaro Duque, Zhongcong Xie, Christopher H. van Dyck, Mary Kate P. Joyce and Amy F. T. Arnsten
Yale School of Medicine

OBJECTIVES/GOALS: pT217-tau is a novel fluid biomarker that predicts onset of Alzheimer's disease (AD) symptoms, but little is known about how pT217-tau arises in brain, as soluble pT217-tau is dephosphorylated postmortem in the humans. Aging macaques naturally develop tau pathology with the same qualitative pattern and sequence as humans, including cortical pathology. METHODS/STUDY POPULATION: The etiology of pT217-tau in aging brains can be probed in rhesus macaques, where perfusion fixation allows capture of phosphorylated proteins in their native state. We utilized multi-label immunofluorescence and immunoperoxidase and immunogold immunoelectron microscopy to examine the subcellular localization of early-stage pT217-tau in entorhinal cortex (ERC) and dorsolateral prefrontal cortex (dlPFC) of aged rhesus macaques with naturally occurring tau pathology and assayed pT217-tau levels in blood plasma using an ultrasensitive nanoneedle approach. RESULTS/ANTICIPATED RESULTS: pT217-tau labeling is primarily observed in postsynaptic compartments, accumulating in: 1) dendritic spines on the calcium-storing smooth endoplasmic reticulum spine apparatus near asymmetric glutamatergic-like synapses and 2) in dendritic shafts, where it aggregated on microtubules, often "trapping" endosomes associated with Aβ42. The dendrites expressing pT217-tau were associated with autophagic vacuoles and dysmorphic mitochondria, indicative of early neurite degeneration. We observed trans-synaptic pT217-tau trafficking between neurons within omega-shaped bodies and endosomes, specifically near excitatory, but not inhibitory synapses. We also examined pT217-tau in blood plasma in macaques across age-span and observed a statistically significant age-related increase in pT217-tau. DISCUSSION/SIGNIFICANCE OF IMPACT: We provide direct evidence of pT217-tau trafficking between neurons near synapses to "seed" tau pathology in higher brain circuits, interfacing with the extracellular space to become accessible to CSF and blood. The expression of pT217-tau in dendrites with early signs of degeneration may help to explain why this tau species can herald future diseases.

40

Impact of feminizing hormone therapy on rectal mucosal HIV target cells in Thai TGWSM†

Jadah Keith, Colleen Kelley and Stacey Smith
Emory University

OBJECTIVES/GOALS: Transgender women who have sex with men (TGWSM) have higher HIV risk. The rectal mucosal (RM) immune environment of TGWSM who choose feminizing hormone therapy (FHT) has been shown to be distinct from the RM of cisgender men who have sex with men (MSM). We studied the impact of FHT on the adaptive immune cellular composition of the RM. METHODS/STUDY POPULATION: We sampled cross-sectional and longitudinal cohorts of TGWSM and cisgender MSM from The Silom Clinic in Bangkok, Thailand from December 2020 to December 2023. We included participants aged >18 years, all cisgender MSM and TGWSM with FHT levels in the therapeutic range for cisgender women. We performed RM biopsies and analyzed the adaptive immune cell characteristics via flow cytometry. We will perform binary linear regression to assess the association between systemic FHT levels and the percentage of CD4+ T cells expressing key biomarkers. Primary outcomes include the percentage of CD4+ T cells that express CCR5, with a secondary outcome of the percentage of CD4+ T cells that express Ki67. RESULTS/ANTICIPATED RESULTS: The cross-sectional cohort included 100 TGWSM on FHT and 50 cisgender MSM. The longitudinal cohort included 25

https://doi.org/10.1017/cts.2024.725 Published online by Cambridge University Press