STATE OF THE SCIENCE MITOCHONDRIA SPECEFIC-TARGETS, THERAPEUTICS AND BIOMARKER INVESTIGATIONS FOLLOWING TRAUMATIC BRAIN INJURY IN THE US MILITARY

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Introduction: In a preclinical model of penetrating traumatic brain injury (PTBI), our post-injury time-course of mitochondrial function observed a biphasic response of bioenergetic failure, together with calcium and redox homeostasis dysregulation between 30 minutes to 7 days post-injury period (1-3). Our results imply that targeted therapy directed at mitochondrial functions could be an effective neuroprotection approach following PTBI. Additionally, the presence of such mitochondria-specific markers in biofluids may offer new theragnostic and prognostic values to alleviate TBI pathology. The invited talk will present mitochondria-centric state of the science updates on preclinical military medicine approaches undertaken to mitigate TBI pathology.

Material & Methods: We used both Sprague-Dawley rats and Yorkshire swine to evaluate post-injury pathophysiological responses after TBI. Assessments conducted in isolated mitochondria from injury core, CSF, and biofluids following TBI. Mitochondrial functions such as bioenergetics, calcium, redox, and cell death analysis were performed during acute post-injury period. Statistical comparisons were analyzed using either unpaired t-test or ANOVA (N=6-8, *$p < 0.05$).

Results: Our results indicated that mitochondria-targeted neuroprotection therapeutics have potential to mitigate secondary injury responses after TBI. Additionally, mitochondrial markers are detectable in biofluids.

Conclusion: Mitochondria-centric mechanisms may serve as novel therapeutic targets for TBI, which further contribute to the assessment of neuroprotection therapies for TBI.

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References:

1. Pandya JD, et.al., Comprehensive evaluation of mitochondrial redox profile, calcium dynamics, membrane integrity and apoptosis markers in a preclinical model of severe penetrating traumatic brain injury. Free Radic Biol Med. 2023 Mar;198:44-58. Pandya JD, Leung LY, Hwang HM, Yang X, Deng-Bryant Y, Shear DA.
2. Pandya JD, et.al.,Time-Course Evaluation of Brain Regional Mitochondrial Bioenergetics in a Pre-Clinical Model of Severe Penetrating Traumatic Brain Injury. J Neurotrauma. 2021 Aug 15;38(16):2323-2334. PMID: 33544034.
3. Pandya JD, et.al., Intranasal delivery of mitochondria targeted neuroprotective compounds for traumatic brain injury: screening based on pharmacological and physiological properties. J Transl Med. 2024 Feb 16;22(1):167. PMID: 38365798.