

Role of Peptidylarginine Deiminase 2 in a Murine Model of Traumatic Brain Injury

Zaiba Shafik Dawood¹, Marjorie R. Liggett¹, Bowen Wang¹, Kaijie Zhang¹, Guang Jin¹, Wenlu Ouyang², Daniel C. Couchenour¹, Aleezeh Shaikh¹, Kiril Chtraklin¹, Baoling Liu¹, Dinesh Jaishankar¹, Yongqing Li¹, Hasan B. Alam¹.

¹Department of Surgery, Feinberg School of Medicine, Northwestern University, Chicago, IL; ²Department of Surgery, University of Michigan Medical School, Ann Arbor, MI

Introduction

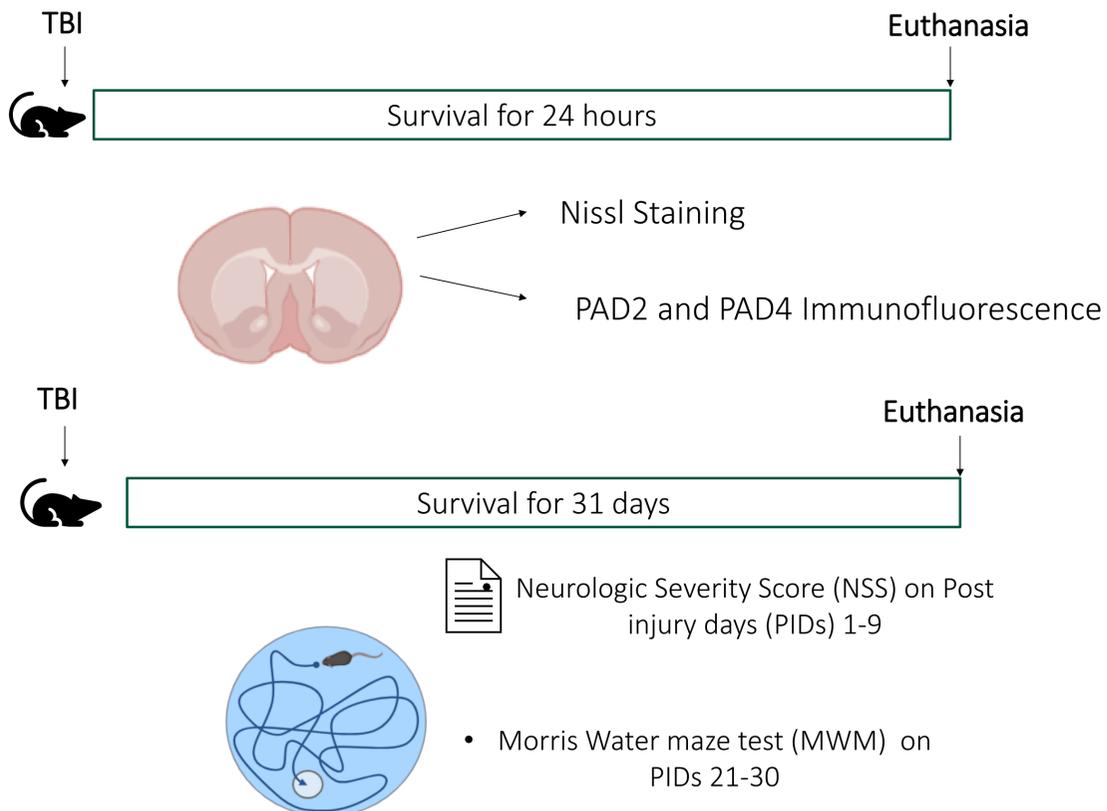
- Traumatic brain injury (TBI) is a leading cause of death and disability worldwide.
- Studies have linked Peptidylarginine deiminases (PADs) with TBI outcomes.
- However, none investigated the exact role of specific PAD enzymes in neurotrauma.
- Since PAD2 and PAD4 have been linked with neurodegeneration, we sought to clearly establish their roles in TBI.

Research Objectives

Aim 1: To investigate the role of PAD2 and PAD4 inhibition on lesion size post TBI

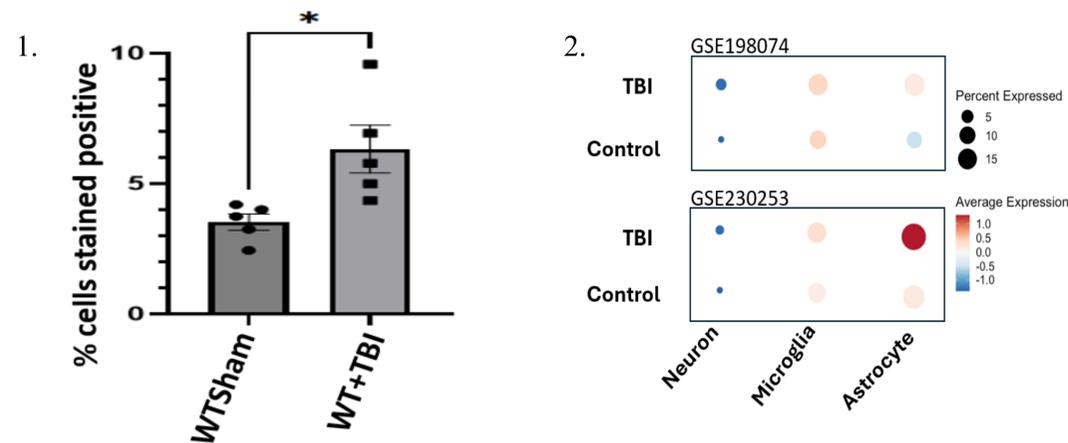
Aim 2: To assess the impact of PAD2 inhibition on motor, sensory and cognitive recovery

Methods

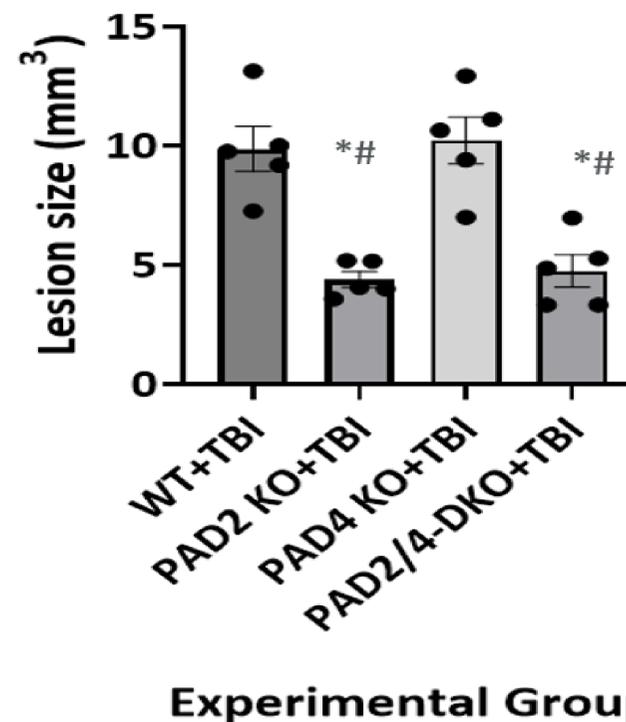


Results

PAD2 levels increased significantly post TBI as shown by (1) immunofluorescence and (2) single-cell RNA sequencing of previous databases (2) while PAD4 levels remained unchanged

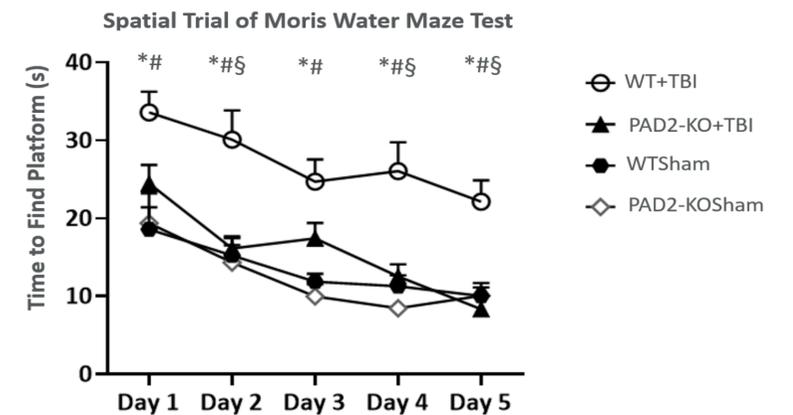
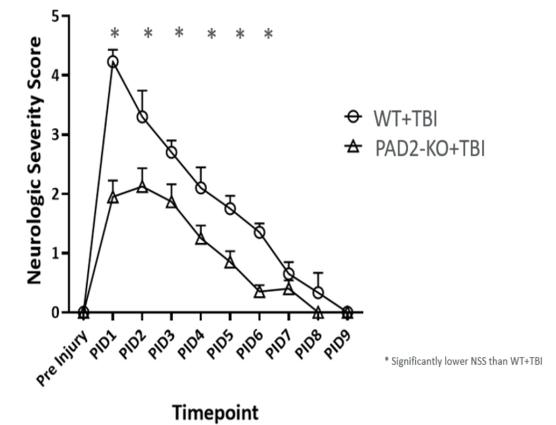


PAD2 knockout (PAD2-KO+TBI) and PAD2/4 double knockout (PAD2/4-DKO+TBI) mice had a significantly smaller lesion size than wildtype (WT+TBI) and PAD4 knockout (PAD4-KO+TBI) mice



*Significantly smaller lesion size compared with Wild Type TBI Mice
Significantly smaller lesion size compared with PAD4-KO TBI Mice

PAD2-KO+TBI mice had significantly improved motor and sensory recovery (as shown by NSS) and cognition (as shown by MWM) compared with WT+TBI



Conclusions/Future Directions

- Our results suggest that PAD2, but not PAD4, as a potential therapeutic target for TBI management.
- **Future Directions:** To elucidate downstream mechanisms of PAD2 in the central nervous system.

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References

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2. Mi L, Min X, Shi M, et al. Neutrophil extracellular traps aggravate neuronal endoplasmic reticulum stress and apoptosis via TLR9 after traumatic brain injury. *Cell Death Dis*. 2023;14(6):374..