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View Abstract

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AUTHORS

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Commercial Relationships Disclosure: Kayla Bernstein: Commercial Relationship: Code N (No Commercial Relationship) | Tyler Heisler-Taylor: Commercial Relationship: Code N (No Commercial Relationship) | Sumaya Hamadmad: Commercial Relationship: Code N (No Commercial Relationship) | Abhay Satoskar: Commercial Relationship: Code N (No Commercial Relationship) | Colleen Cebulla: Commercial Relationship: Code N (No Commercial Relationship)

Study Group: (none)

ABSTRACT

TITLE: MIF Genetic Depletion Prevents Retinal Cell Death in Murine Excitotoxic Retinal Damage

ABSTRACT BODY:

Purpose: Our preliminary data show that the pro-inflammatory cytokine macrophage migration inhibitory factor (MIF) is upregulated in a murine N-methyl-D-aspartate (NMDA) excitotoxic model. We evaluated the effect of MIF genetic depletion on retinal ganglion cell (RGC) death and retinal thickness in a murine NMDA model, which simulates glutamate excitotoxicity involved in retinal ischemic disease.

Methods: Under an IACUC approved protocol, MIF-knockout (MIFKO) mice and C57BL/6 wild type background controls (WT) were treated with intravitreal injection of NMDA (0.1M/2ul) in the left eye and vehicle in the right eye. Eyes were enucleated and fixed 24 hrs after treatment (n=6 WT, 11 MIFKO) for analysis of dying cells or 9 days for retinal thickness measurement (n=7 WT, 6 MIFKO). Dying cells in the ganglion cell layer (GCL) were evaluated by TUNEL assay. GCL thickness measurements were performed using fluorescent microscopy of DAPI stained sections. Analysis was done via NIS Elements software using the MCT threshold method for cell death and cell density calculation for retinal thickness. Statistics were performed in JMP with a Wilcoxon Signed Rank and two-sample Wilcoxon Rank Sum test.

Results: Within each WT and MIFKO group at 24h post damage, the proportion of dying cells in the GCL was significantly higher in the NMDA treatment eye compared to vehicle eye (0.35 ± 0.05 vs 0.01 ± 0.01, p=0.0313; 0.15 ± 0.03 vs 0.001 ± 0.001, p=0.0010 respectively). Moreover, the proportion of dying cells in the GCL was significantly reduced by 58.6% in the MIFKO mice compared to WT group (0.15 ± 0.03 vs 0.35 ± 0.05, p=0.0077). At day 9 post damage (D9), the MIFKO eyes did not lose RGC density (1138.01 ± 235.69 vs 1102.74 ± 126.10, p=1.00) while the WT mice had significantly lower RGC density after NMDA treatment (737.62 ± 120.72 vs 1253.56 ± 143.98, p=0.0313). The RGC density at D9 was preserved relative to fellow control eye in the MIFKO mice compared to WT group (1.13 ± 0.27 vs 0.60 ± 0.13, p=0.05). There was no difference in TUNEL and GCL thickness between vehicle-treated MIFKO and WT groups.

Conclusions: Our results indicate that MIF has a significant impact on cell survival in excitotoxic damage as genetic depletion reduced cell death and preserved the retinal layer thickness. Future studies should further evaluate MIF inhibition as a potential therapeutic for excitotoxic retinal damage and preservation of retinal neurons.

(No Image Selected)

Layman Abstract (optional): Provide a 50-200 word description of your work that non-scientists can understand. Describe the big picture and the implications of your findings, not the study itself and the associated details.: Inhibition of MIF with a genetic model reduced ganglion cell death and preserved ganglion cell layer thickness after excitotoxic damage in the retina.

DETAILS

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TRAVEL GRANTS and AWARDS APPLICATIONS

AWARDS: ARVO Members-in-Training Outstanding Poster Award|ARVO and ARVO Foundation Travel Grants