Dear Editor

Journal of Neuroinflammation

We are herewith submitting our manuscript entitled " RasV12 expression in microglia promotes retinal inflammatory circuits and impairment of photoreceptor ".

Microglial activation is commonly observed in neurodegenerative diseases, and recent evidence suggests involvement of microglia in the pathogenesis of diseases associated with neuronal degeneration including retinal neurons. However, its role in the complex inflammatory network remains unclear. In this study, we generated a microglial activation mouse model by inducing the expression of a constitutively active form of Ras in microglia. RasV12 expression in retinal microglial cells promoted its activation accompanied with activation of Müller glia in the retina in few days after expression of RasV12. Interestingly, we observed loss of the photoreceptors in the ONL in close proximity to microglial cells, suggesting that activation of microglia could lead acute photoreceptor degeneration. However, neurodegeneration was observed in the INL or GCL was not observed although RasV12-microglia migrated to these regions. Consistent with specific degeneration in ONL, we found that RasV12-expressing microglia in the ONL were smaller in size and engulfed photoreceptors; in contrast, the morphology of RasV12-expressing microglia in the GCL and INL resembled resting microglia. In conclusion, RasV12-induced microglial activation impaired rod photoreceptor survival in the ONL, but not in other regions of the retina. Therefore, we hypothesized that microenvironment cues may modulate the microglial phenotypic features and effects of microglial activation.

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Thank you for your consideration.

Sincerely yours,

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