

## Accepted Manuscript

Title: Kynurenine pathway metabolic balance influences microglia activity: targeting kynurenine monooxygenase to dampen neuroinflammation

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PII: S0306-4530(18)30297-X  
DOI: <https://doi.org/10.1016/j.psyneuen.2018.04.019>  
Reference: PNEC 3906

To appear in:

Received date: 30-3-2018  
Revised date: 12-4-2018  
Accepted date: 20-4-2018

Please cite this article as: Garrison, Allison M., Parrott, Jennifer M., Tuñon, Arnulfo, Delgado, Jennifer, Redus, Laney, O'Connor, Jason C., Kynurenine pathway metabolic balance influences microglia activity: targeting kynurenine monooxygenase to dampen neuroinflammation. *Psychoneuroendocrinology* <https://doi.org/10.1016/j.psyneuen.2018.04.019>

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## **Kynurenine pathway metabolic balance influences microglia activity: targeting kynurenine monooxygenase to dampen neuroinflammation**

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### **Highlights:**

- KMO inhibition attenuates specific elements of microglia activation
- Primary KMO <sup>-/-</sup> microglia recapitulate pharmacologic inhibition of KMO
- Kynurenine negatively modulates microglia responses to LPS
- Exogenous quinolinic acid did not potentiate LPS-induced activity

### **Abstract**

Chronic stress or inflammation increases tryptophan metabolism along the kynurenine pathway (KP), and the generation of neuroactive kynurenine metabolites contributes to subsequent depressive-like behaviors. Microglia regulate KP balance by preferentially producing oxidative metabolites, including quinolinic acid. Research has focused on the interplay between cytokines and HPA axis-derived corticosteroids in regulating microglial activity and effects of KP metabolites directly on neurons; however, the potential role that KP metabolites have directly on

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