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

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Highlights:

- KMO inhibition attenutates specific elements of microglia activation
- Primary KMO -/- 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