

## OPEN PEER REVIEW REPORT 1

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**Title:** Dying by fire: noncanonical functions of autophagy proteins in neuroinflammation and neurodegeneration

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### COMMENTS TO AUTHORS

This review is very timely and valuable for the biological scientists in the autophagy field for better understanding of the intricate mechanisms in neuroinflammation and neurodegeneration from an angle of noncanonical functions of autophagy protein. However, I am still interested in some aspects of this paper and hope the authors could discuss more detailed information for dissecting the hot topic.

1. Since the title of this is called noncanonical functions of autophagy proteins, the authors should provide more aspects on noncanonical pathways in neuroinflammation and neurodegeneration, not only from LANDO side but also through LAP, as is largely on researching and little mentioned in pages, or even so forth.
2. Besides the Alzheimer's Disease that is correlated with neuroinflammation and can be promisingly treated through targeting neuroinflammatory cytokines, whether can potential therapeutic methods via non-canonical autophagic induction and neuroinflammatory alleviation utilize in other neurodegenerative diseases, such as Huntington's and Amyotrophic Lateral Sclerosis?
3. It has been reported that some inflammatory diseases in other organs are relevant to noncanonical autophagy deficiency but not canonical autophagy deficiency like lupus-like syndrome in mice. Therefore, in CNS, will the situation be alike? Whether does the noncanonical autophagy like LANDO or LAP independently or primarily influence the progress of neuroinflammation then further to neurodegeneration diseases? If it is, whether can more details be provided such as the basic mechanisms and so on? Or if not, where is the boundary between noncanonical and canonical autophagy and how do they cooperate with each other in the process of neurodegeneration diseases?