NLRP3 is involved in the development of morphine analgesic tolerance

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Abstract

Objective: Microglia-mediated inflammation plays an important role in morphine tolerance. However, the underlying mechanism remains largely unknown. Nucleotide-binding domain-like protein 3 (NLRP3) is an important member of nucleotide-binding oligomerization domain-like receptor family, which could recognize a variety of pathogen- and host-derived "danger" signals. NLPR3 can form inflammasome with adaptor protein ASC and pro-caspase-1, which is a multiprotein complex that can activate caspase-1 and ultimately lead to the processing and secretion of interleukin (IL)-1β and IL-18. The present study is to explore the role of NLRP3 in morphine tolerance in vivo and in vitro. Methods: The antinociceptive responses were determined by mechanical (Von Frey filaments) and thermal (tail-flick) test paradigms. The levels of protein and mRNA are examined by Western Blot and RT-PCR methods. Results: (1) Morphine induced the activation of NLRP3 inflammasome. (2) The inhibition of NLRP3
inflammasome suppresses the development of morphine analgesic tolerance. (3) Morphine activates NLRP3 inflammasome by activating the P2X7 receptor signaling pathway, thereby promoting the maturation and release of IL-1β and IL-18. **Conclusion:** These results confirm that NLRP3 inflammasome is involved in the development of morphine analgesic tolerance and elucidates the signaling pathway of morphine-activated NLRP3 inflammasome. This study provides a new target for the effective prevention and treatment of morphine analgesic tolerance.

**Keywords:** morphine tolerance, NLRP3 inflammasome, inflammation

**Acknowledgements**

This study was supported by the National Natural Science Foundation of China (No.31360246, and No.81300973), the Fund of the Applied Basic Research Programs of Yunnan Province in China (No.2013FB100), and the Special Fund of the Applied Basic Research Programs of Yunnan Province associated with Kunming Medical University in China (No.2014FB100).