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MiR-155 modulates morphine-induced immunosuppression by targeting SK3 channel in microglia

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Background: Opioids, especially morphine, have a diversity of effects on immune system. It is well known that morphine has been proved to have immunosuppressive properties both in vivo and in vitro, and is thought to be involved in the increased incidence of infection in heroin addicts. Evidences have shown that microglia, the main active immune defense cell in the central nervous system, plays an essential role in morphine-induced immunosuppression in central nervous system. In addition, recent studies suggest that microRNAs may play a decisive role in the regulation of gene expression during immune responses in microglia. Although numerous studies have shown that multiple factors were involved in morphine-induced immunosuppression, but the precise cellular and molecular mechanisms are still largely unknown.

Objective: This study was to investigate the contribution of a specific microRNA, miR-155, in the modulation of the morphine-induced immunosuppression in microglia.

Methods: We detected morphine-induced immunosuppressive effects in both heroin abused patients and morphine-treated mice primary microglia. MiR-155 expression levels were measured in morphine-treated microglia. In vitro experiments were performed to demonstrate how miR-155 influences the expression of cytokines (TNF- α , IL-6 and IL-10) in morphine-treated microglia at both mRNA and extracellular levels. Moreover, interactions between miR-155 and downstream targets were further evaluated by using western blot and luciferase reporter assay.

Results: Our results showed that morphine could induce immunosuppression by interfering cytokine expression in both heroin abused patients and morphine-treated mice primary microglia cells. Expression of pro-inflammatory cytokines (TNF- α , IL-6) was decreased, while expression of anti-inflammatory cytokine (IL-10) was increased, respectively, compared to control group. We also found that miR-155 was down-regulated in morphine-treated primary microglia. Moreover, up-regulate miR-155 could reverse morphine-induced cytokines expressions by directly targeting SK3 channel in primary microglia.

Conclusions: Our results demonstrated a reversal effect of miR-155 on morphine-induced immunosuppression, and suggested that SK3 channel, the direct target of miR-155, was involved in this process.

Biography

Xiaoni Zhang has completed her MD at Zhongshan School of Medicine, Sun Yat-Sen University, 2012. She is currently a second-year graduate student pursuing a Master's degree within the Department of Neurology, Sun Yat-Sen Memorial Hospital, Sun Yat-Sen University. Her research is focused on the molecular mechanisms of morphine-induced immunosuppressive effects.

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