

عنوان مقاله:

Effect of A-۷۶۹۶۶۲, a direct AMPK activator, on Tlr-۴ expression and activity in mice heart tissue

محل انتشار:

مجله علوم پایه پزشکی ایران, دوره 19, شماره 12 (سال: 1395)

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خلاصه مقاله:

Objective(s): TLR-۴ activates a number of inflammatory signaling pathways. Also, AMPK could be involved in anti-inflammatory signaling. The aim of this study was to identify whether stimulation of AMPK could inhibit LPS-induced Tlr-۴ gene expression in mice hearts. Materials and methods: Heart AMPK activity and/or Tlr-۴ expression was stimulated in different mice groups, using respectively IP injection of A-۷۶۹۶۶۲ (1۰ mg/kg) and LPS (۲ mg/kg) or a combination of both agents. Moreover, compound-C (۲۰ mg/kg), as an AMPK antagonist, was intraperitoneally co-administrated with both A-۷۶۹۶۶۲ and LPS in another group to investigate the role of AMPK activity on Tlr-۴ regulation. After ۸ hr, in addition to peripheral neutrophil cell count, myocardial p-AMPK, p-ACC as well as MyD۸۸ protein contents and Tlr-۴ expression was assessed by Western blotting and real-time qRT-PCR, respectively. TNF- α and IL-۶ expression levels were also determined by ELISA. Results: LPS induced heart Tlr-۴ expression ($P<۰.۰۰۱$) associating with an increase in the myocardial MyD۸۸ protein content ($P<۰.۰۰۱$), elevation of heart TNF- α ($P<۰.۰۱$) and IL-۶ ($P<۰.۰۵$) concentrations, and rise in the peripheral neutrophil cell count ($P<۰.۰۰۱$). Administration of A-۷۶۹۶۶۲ decreased LPS-induced Tlr-۴ expression ($P<۰.۰۱$) and alleviated peripheral neutrophil cell count ($P<۰.۰۱$). The inhibitory effect of A-۷۶۹۶۶۲ on LPS-induced Tlr-۴ expression was reversed by antagonizing AMPK with compound-C ($P<۰.۰۰۱$) which reduced p-AMPK ($P<۰.۰۵$) and p-ACC ($P<۰.۰۱$) myocardial protein contents in the LPS+A-۷۶۹۶۶۲ group. Conclusion: This study demonstrated that activation of AMPK, by A-۷۶۹۶۶۲ agent, could inhibit Tlr-۴ expression and activity, suggesting a link between AMPK and Tlr-۴ in heart tissue.

کلمات کلیدی:

ACC, A-۷۶۹۶۶۲, AMPK, Compound-C Lipopolysaccharide, TLR-۴

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