Inhibition of GSK-3 by Tideglusib suppresses activated macrophages and inflammatory responses in lipopolysaccharide-stimulated RAW 264.7 cell line

ABSTRACT

Glycogen synthase kinase-3 (GSK-3) is an important immune regulator that controls inflammation via inhibition of its protein kinase activities. Persistent inflammatory responses through the activation of immune cells and excessive production of immune mediators may cause tissue destruction and implicated in the development of chronic inflammatory diseases. The objective of this study was to examine the role of Tideglusib, a GSK-3 inhibitor, in inflammatory responses elicited through macrophage activation by investigating the expression of cell surface biomarkers and inflammatory molecule levels. Method: The effects of GSK-3 inhibition by Tideglusib on the expression of CD11b and CD40 and secretion of pro-inflammatory cytokines in the lipopolysaccharide (LPS)-activated macrophage-derived RAW 264.7 cells were determined by flow cytometry, while the presence of nitric oxide (NO) was determined by Griess assay. Results: Stimulation of RAW 264.7 cells with LPS increased substantial levels of CD11b and CD40 expressions, and secretion of NO, TNF-α, and MCP-1. However, the expression of these molecules was suppressed through inhibition of GSK-3. Conclusion: These findings suggest the significant role of Tideglusib to limit the upregulation of immune responses in activated macrophages, and as a potential anti-inflammatory drug for the intervention and treatment of inflammatory diseases.

Keyword: Glycogen synthase kinase-3 (GSK-3); Tideglusib; CD11b; CD40; Macrophages