Effects of Kaponane Diterpenoids Compound PV006 on M1 Polarization of THP1 derived Macrophages

Xinyu Li, Jiafen Zhang, Shasha Song, Yongfang Wang

Department of Skin Pharmacology, Institute of Dermatology, Chinese Academy of Medical Sciences, China

Background: Macrophages involved in the pathogenesis of chronic inflammatory diseases. M1 type macrophages may constitute the basis of chronic inflammatory disease. The differentiation of macrophages can be induced and regulated by various signals in microenvironment. Intracellular signal transduction and transcription activator (STAT1) and nuclear transcription factor B (NFκB) are the key factors to promote M1 polarization of the macrophage. It is important to regulate the differentiation of M1 subtype macrophages for therapeutic interventions of inflammatory processes. Kaurane Diterpenoids have been found to have anti-tumor and anti-inflammatory effects. In this study, human monocyte cell line THP1 cells were induced to M1 type differentiation in vitro. The effect of Kauri Diterpenoids PV006 on regulation of M1 type polarization of macrophages were studied.

Methods: The human monocyte cell line THP1 cells were stimulated to differentiate into M1 type macrophages by phorbol 12 myristate 13 acetate (PMA) combined with lipopolysaccharide (LPS) and recombinant human interferon r (rhIFNr). M1 type polarization of THP1 derived macrophages was confirmed by observing morphological changes of cells with microscope, detecting the mRNA expression of IL1β, TNFa, IL6 and IL8 by real time fluorescence-based quantitative PCR, as well as analyzing expressions of NFκB phospho p65 and phospho STAT1 by western blotting. After synchronously treatment with PV006, above parameters of stimulated cells were detected.

Results: After THP1 cells were induced in vitro, the shape of cells changed from round to characteristic long fusiform or spindle shape, the expression of IL1β, TNFa, IL6, IL8 mRNA increased, the expression of NFκB phospho p65 and phospho STAT1 proteins enhanced. After treatment with different concentrations of PV006, long fusiform or spindle shape cells did not be observed and most cells remains round in M1 polarization stimulated THP1 cells. PV006 down regulated the expression of IL1β, TNFa, IL6, IL8 mRNA(P<0.05), and attenuated the expression of NF-kB phospho p65, phospho STAT1 proteins.

Conclusions: M1 type polarization of macrophages derived from THP1 cells can be induced by stimulation of PMA combined with LPS and rhIFNr. PV006 compound could inhibit the differentiation of macrophages into M1 subtype.