Peroxisome Proliferator-Activated Receptor Activators Target Human Endothelial Cells to Inhibit Leukocyte-Endothelial Cell Interaction

Division of Cardiology, UCLA School of Medicine, 47-123 CHS, Box 951679, Los Angeles, CA, USA

An early event in acute and chronic inflammation and associated diseases such as atherosclerosis and rheumatoid arthritis is the induced expression of specific adhesion molecules on the surface of endothelial cells (ECs), which subsequently bind leukocytes. Peroxisome proliferator-activated receptors (PPARs), members of the nuclear receptor superfamily of transcription factors, are activated by fatty acid metabolites, peroxisome proliferators, and thiazolidinediones and are now recognized as important mediators in the inflammatory response. Whether PPAR activators influence the inflammatory responses of ECs is unknown. We show that the PPAR activators 15-deoxy-Δ12,14-prostaglandin J2 (15d-PGJ2), Wyeth 14643, ciglitazone, and troglitazone, but not BRL 49653, partially inhibit the induced expression of vascular cell adhesion molecule-1 (VCAM-1), as measured by ELISA, and monocyte binding to human aortic endothelial cells (HAECs) activated by phorbol 12-myristate 13-acetate (PMA) or lipopolysaccharide. The “natural” PPAR activator 15d-PGJ2 had the greatest potency and was the only tested molecule " protection assay; however, we results suggest that certain PPAR activators may help limit chronic inflammation mediated by VCAM-1 and monocytes without affecting acute inflammation mediated by E-selectin and neutrophil binding.

Simon Jackson, Division of Cardiology, UCLA School of Medicine, 47-123 CHS, Box 951679, Los Angeles, CA, USA, E-mail: smjak@ucla.edu

02-S ضر : 18

mediators-neutrophil binding and E-selectin expression. ese results suggest that PPAR activators may be bene cial in ameliorating chronic in ammatory disease such as atherosclerosis by reducing extravasation of monocytes to the involved tissue without limiting the response to acute infection [9].

Overview

ese results indicate that some synthetic PPAR activators, such as a peroxisome proliferator and certain thiazolidinediones, inhibit monocyte binding by activated HAECs and their expression of

Jackson S, Parhami F, Xi XP, Berliner J, Hsueh W (2022) Peroxisome Proliferator-Activated Receptor Activators Target Human Endothelial Cells to Inhibit Leukocyte-Endothelial Cell Interaction. Atheroscler Open Access 7: 184.