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Differential Regulation of Toll-Like Receptor and CD14 Pathways by Retinoids and Corticosteroids in Human Sebocytes

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The combination of *13-cis*-retinoic acid (RA) and corticosteroids has been shown to be markedly effective in severe inflammatory acne, such as acne fulminans. We have currently shown human epithelial cells to induce and modulate inflammatory signals by Toll-like receptors (TLRs) and CD14 in acne. By this pathway the innate immunity is able to recognize microbial components and to induce cytokine/chemokine synthesis. We examined the effects of retinoids, hydrocortisone and the microbial components lipopolysaccharide and lipoteichonic acid on TLR2, TLR4 and CD14 expression as well as on cytokine/chemokine expression in human SZ95 sebocytes. Human SZ95 sebocytes were found to constitutively express TLR2, TLR4, CD14, interleukin (IL)-1α, IL-1β, IL-6 and IL-8 that was augmented by exposure to components of Gram-negative (lipopolysaccharide) and Gram-positive (lipoteichonic acid) bacteria. Retinol was the most active retinoid by slightly upregulating mRNA levels of TLR2, TLR4 and CD14, while 13-*cis*-RA and all-*trans*-RA were practically inactive. Retinoids did not affect mRNA levels of IL-1α, IL-1β and IL-8 mRNA and their release. However, IL-6 mRNA levels and release were significantly reduced under treatment with 13-*cis*-RA and all-*trans*-RA being more potent than retinol, indicating a selective, TLR-independent, anti-inflammatory effect of retinoids on SZ95 sebocytes. Hydrocortisone slightly upregulated TLR2 mRNA levels but markedly reduced TLR4 and CD14 mRNA levels. Furthermore, hydrocortisol induced an overall reduction of cytokine/chemokine expression, a finding that undersigns its global anti-inflammatory activity. We provide evidence that the pharmacological regulation of TLR and CD14 expression may provide a novel mechanism in the treatment of inflammatory acne lesions.

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