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IL-36γ stimulation induces proinflammatory effects on human endothelial cells

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Interleukin-36 (IL-36) cytokines are IL-1 family members, predominantly expressed by epithelial cells such as keratinocytes. Significant upregulation of epidermal IL-36γ is now a recognised characteristic of psoriatic skin inflammation. IL-36 is known to induce inflammatory responses in dendritic cells, fibroblasts and epithelial cells. Whilst vascular alterations are a hallmark of psoriatic lesions and dermal endothelial cells are known to play a critical role in skin inflammation, the effects of IL-36γ on endothelial cells have not been documented. We report that endothelial cells (EC), including dermal microvascular cells, express a functionally active IL-36 receptor. Following IL-36γ stimulation, ECs show increased NF-κB and AP-1 activation and adhesion molecules ICAM-1 and VCAM-1 are both upregulated and this is reversed by the presence of the endogenous IL-36 receptor antagonist (IL-36RA). Furthermore, IL-36γ stimulated ECs secrete the proinflammatory chemokines IL-8, CCL2(MCP1) and CCL20. Chemotaxis assays showed increased migration of T cells following IL-36γ stimulation of ECs. These findings add another potential role for IL-36γ in psoriasis immunopathology. Our results suggest IL-36γ has a role in the dermal vascular compartment, and it could potentially enhance inflammation by activating ECs and increasing leukocyte migration to the lesion.