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**Proceedings Paper:**

Bridgewood, C, Stacey, M [orcid.org/0000-0003-3502-5542](http://orcid.org/0000-0003-3502-5542), Alase, A et al. (3 more authors) (2016) IL-36y stimulation induces proinflammatory effects on human endothelial cells. In: Journal of Investigative Dermatology. European Society for Dermatological Research (ESDR) Annual Meeting, 07-10 Sep 2016, Munich, Germany. Elsevier , S216-S216.

<https://doi.org/10.1016/j.jid.2016.06.343>

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## **IL-36 $\gamma$ stimulation induces proinflammatory effects on human endothelial cells**

C Bridgewood, M Stacey, A Alase, A Graham, D Lagos, M Wittmann

M Wittmann - Leeds Institute of Rheumatic and Musculoskeletal Medicine (LIRMM),  
University of Leeds, Leeds, United Kingdom

M Stacey - School of Molecular and Cellular Biology, Faculty of Biological Sciences,  
University of Leeds, Leeds, United Kingdom,

A Alase - Leeds Institute of Rheumatic and Musculoskeletal Medicine (LIRMM), University of  
Leeds, Leeds, United Kingdom,

D Lagos - Centre for Immunology and Infection, University of York, York, United Kingdom

A Graham - School of Medical Sciences, University of Bradford, Bradford, United Kingdom

C Bridgewood - Centre for Skin Sciences, University of Bradford, Bradford, United Kingdom

Interleukin-36 (IL-36) cytokines are IL-1 family members, predominantly expressed by epithelial cells such as keratinocytes. Significant upregulation of epidermal IL-36 $\gamma$  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-36 $\gamma$  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-36 $\gamma$  stimulation, ECs show increased NF- $\kappa$ B 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-36 $\gamma$  stimulated ECs secrete the proinflammatory chemokines IL-8, CCL2(MCP1) and CCL20. Chemotaxis assays showed increased migration of T cells following IL-36 $\gamma$  stimulation of ECs. These findings add another potential role for IL-36 $\gamma$  in psoriasis immunopathology. Our results suggest IL-36 $\gamma$  has a role in the dermal vascular compartment, and it could potentially enhance inflammation by activating ECs and increasing leukocyte migration to the lesion.