This is a repository copy of *IL-36y stimulation induces proinflammatory effects on human endothelial cells*.

White Rose Research Online URL for this paper:
http://eprints.whiterose.ac.uk/110850/

Version: Accepted Version

**Proceedings Paper:**

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

© 2016 Published by Elsevier Inc. Licensed under the Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International
http://creativecommons.org/licenses/by-nc-nd/4.0/

**Reuse**
Unless indicated otherwise, fulltext items are protected by copyright with all rights reserved. The copyright exception in section 29 of the Copyright, Designs and Patents Act 1988 allows the making of a single copy solely for the purpose of non-commercial research or private study within the limits of fair dealing. The publisher or other rights-holder may allow further reproduction and re-use of this version - refer to the White Rose Research Online record for this item. Where records identify the publisher as the copyright holder, users can verify any specific terms of use on the publisher's website.

**Takedown**
If you consider content in White Rose Research Online to be in breach of UK law, please notify us by emailing eprints@whiterose.ac.uk including the URL of the record and the reason for the withdrawal request.

https://eprints.whiterose.ac.uk/eprints@whiterose.ac.uk
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.