Imiquimod-induced psoriatic inflammation can be attenuated by the application of a Liver X receptor agonist through the production of pro-resolution molecule

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Introduction

- Murine model of psoriasis is achieved by topically applying imiquimod (IMQ).
- Psoriasis is a skin inflammatory disorder known for its hallmark of having abnormal keratinocyte differentiation.
- The expression of LXR and ABCA1 is decreased in keratinocytes in murine model, similar to human.
- LXR plays an essential role in the control of keratinocyte differentiation.

What is Liver X receptor?

Aim

We hypothesized that the topical application of Liver X receptor (LXR) agonist can interfere with the immune cascade that is important for the formation of psoriatic inflammation. We want to investigate the pathway that LXR activation interferes with in psoriatic inflammation. This may provide evidence of a possible target for future treatment for psoriatic inflammation.

Method

Result

FCM

Recruitment of Neutrophils seems to be affected at early phase of inflammation

GW3965 reduced extravascular neutrophil recruitment at Day 3.

Veh + IMQ
GW3965 + IMQ
Blood Vessel (White)
Neutrophils (Red)

Pro-inflammatory lipid mediators are downregulated in GW3965-treated skin.

Conclusion

The topical application of LXR agonist on the mouse ear has shown to be able to attenuate imiquimod induced psoriasis. There is a reduced recruitment of neutrophils into the skin by the down regulation of neutrophil-specific recruitment chemokines, CXCL1 and CCL-20 and lipid mediator, PGD2. LXR agonist has also shown to be able to downregulate key cytokines involve in psoriatic lesion formation such as IL-17 and IL-23. Further studies will be required to determine the inhibitory role of LXR and its mechanism in inflammatory genes.

Sources:

1. Ahmed El Bedewi et al, Int J Pept Res Ther, 2013
2. Gupta et al, Gene and immunity, 2010
3. Yan J Jiang et al, J lipid Res, 2006

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