

Lipopolysaccharide-induced inflammation has no effect on the expression levels of ABC drug transporters in *in vitro* skin models

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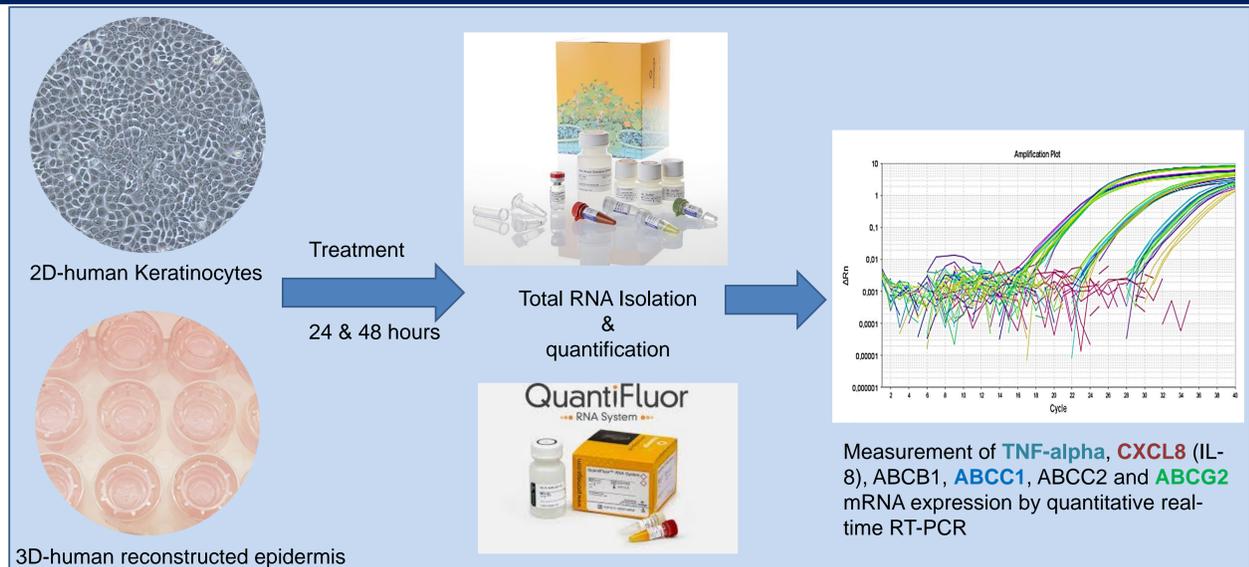
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BACKGROUND

Skin is the largest organ in the human body and is one of the major targets of air pollution. There is increasing evidence indicating that ATP-binding cassette (ABC) family transporters play an important role in the transdermal absorption of their substrates. Atopic dermatitis is a chronic inflammatory disease associated with increasing production of pro-inflammatory cytokines. However, the relationship between skin inflammation and expression of ABC transporters in the skin that might change absorption of anti-inflammatory drugs is not yet known. The aim of this study was to investigate the effect of inflammation on the expression levels of ABC transporters in normal human keratinocytes (NHK) and in 3D-Reconstructed Human Epidermis (RHE).

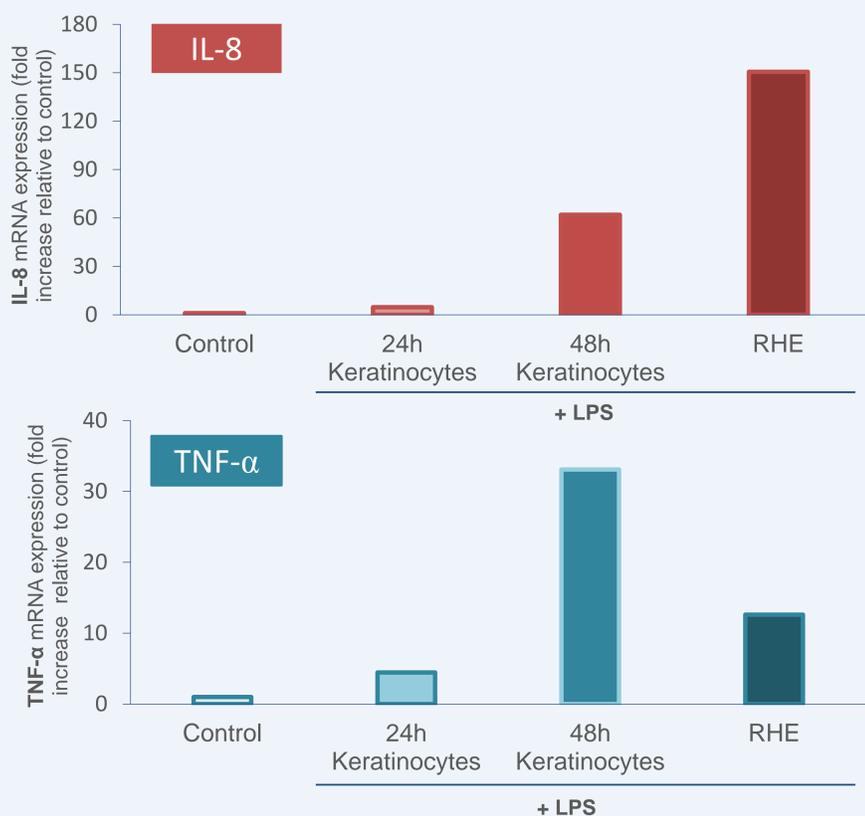
METHODS

Normal human epidermal keratinocytes, (Sterlab France), were treated for 24 and 48 hours with the well-known inflammation inducer lipopolysaccharide (LPS, 100 µg/mL in culture medium). Untreated NHEK were used as control. On the other hand, 3D-reconstructed human epidermis, (Sterlab France), was treated for 24 hours with LPS. Incubation was done in cell incubator set at 37°C, 5% CO₂ and saturated humidity. mRNA expression of inflammation markers (TNF- α , CXCL8 (IL-8)), and ABC drug transporters (ABCB1, ABCC1, ABCC2 and ABCG2) was measured by quantitative real time RT-PCR, using TaqMan® technologies.

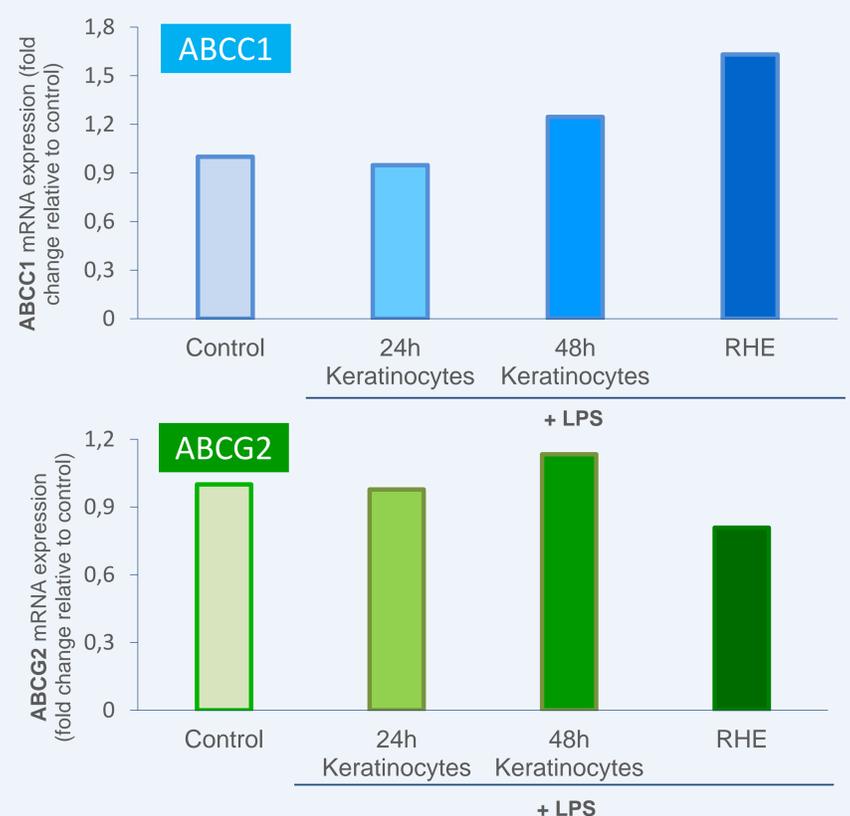


RESULTS

mRNA expression of TNF- α and IL-8 in 2D-Human Keratinocytes and 3D-Reconstructed Human Epidermis



mRNA expression of ABCC1 and ABCG2 in 2D-Human Keratinocytes and 3D-Reconstructed Human Epidermis



• Inflammatory markers :

- LPS increases mRNA expression of both inflammatory markers (IL-8 and TNF- α) in both Keratinocytes and in 3D-Reconstructed human epidermis models
- LPS-increased expression of inflammatory markers in keratinocytes is higher after 48-hour treatment period than after 24-hour treatment period

• ABC transporters:

- Treatment with LPS does not induce any significant increase or decrease of ABCC1 and ABCG2 mRNA expression in human epidermal keratinocytes and in 3D-Reconstructed human epidermis

CONCLUSION

This study clearly shows there is **no** relationship between inflammation induced by LPS and the expression of ABC transporters in the two *in vitro* skin models, 2D-Human Epidermal Keratinocytes and 3D-Reconstructed Human Epidermis