

Insights into effects of topical application of cis-urocanic acid on the skin microbiome and immune modulation.

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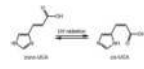
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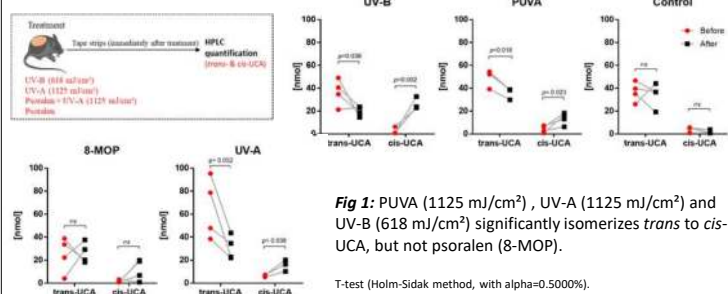
Introduction:

- Urocanic acid (UCA) is present locally in the stratum corneum of the skin in its trans isoform (*trans*-UCA)
- Upon ultraviolet-radiation (UV-R) *trans*-UCA is isomerized to *cis*-UCA.¹
- cis*-UCA is known to induce immune suppression via 5-HT_{2A} receptor, serotonin signaling and various other pathways.²
- Since skin microbiome is established all over the surface of the skin, we investigated the effects of *cis*-UCA on the skin microbiome and antimicrobial peptides (AMPs) expression and further investigated the immune modulation using mouse models.³

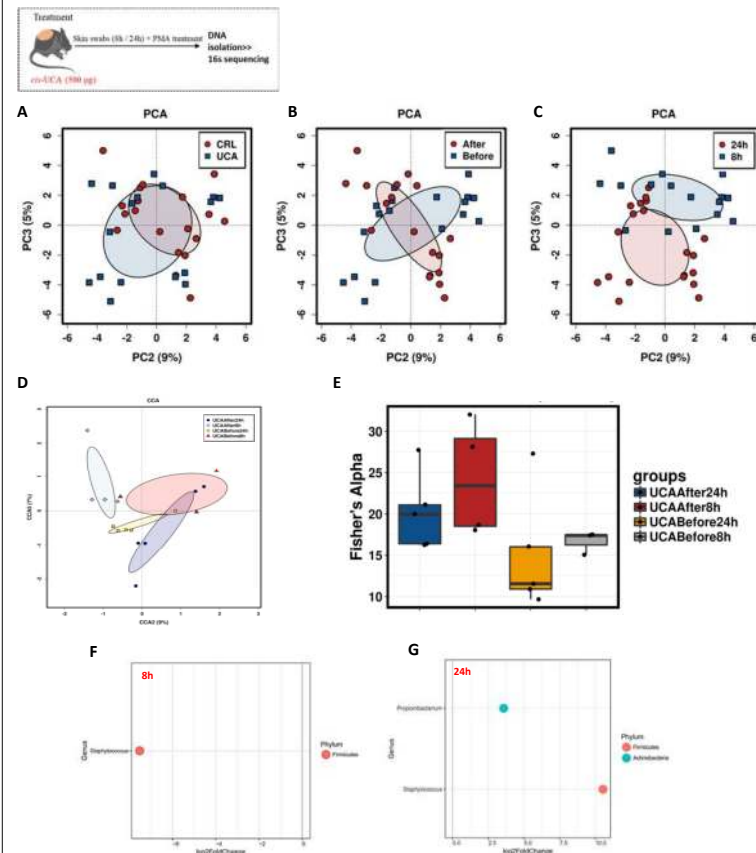


Results:

1. PUVA, UVA and UV-B isomerizes *trans*-UCA to *cis*-UCA.



2. *cis*-UCA modulates microbes on the skin.



Results:

3. *cis*-UCA modulates expression of antimicrobial peptides in the skin.

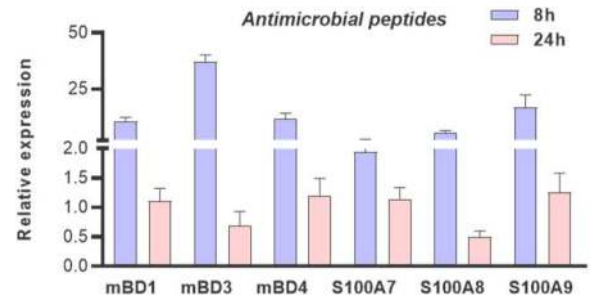


Fig 3: AMPs gene signature significantly differs at 8h and 24h. Expression of AMPs is reduced at 24h after *cis*-UCA (500 µg), compared to 8h.

4. Disinfecting the skin results in reduced isomerization of *trans*- to *cis*-UCA.

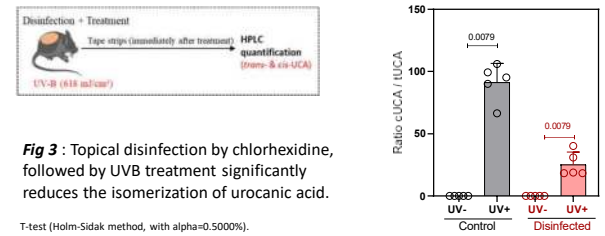


Fig 3: Topical disinfection by chlorhexidine, followed by UVB treatment significantly reduces the isomerization of urocanic acid.

5. *cis*-UCA, PUVA and UV-B suppress immune reaction to contact allergen DNFB.

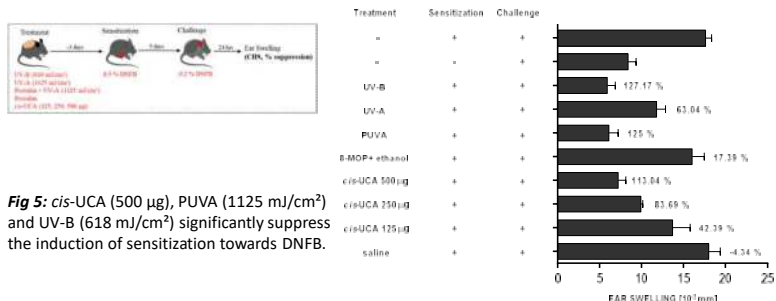
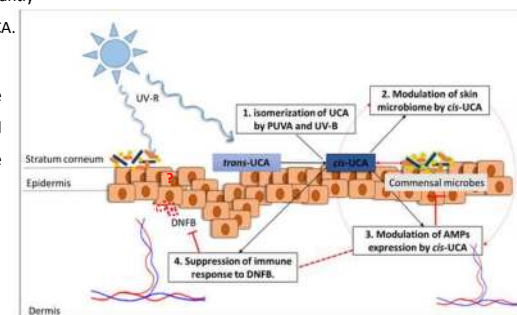


Fig 5: *cis*-UCA (500 µg), PUVA (1125 mJ/cm²) and UV-B (618 mJ/cm²) significantly suppress the induction of sensitization towards DNFB.

Summary and Conclusion:

- ✓ PUVA, UV-A and UV-B significantly increase the formation of *cis*-UCA.
- ✓ Application of *cis*-UCA on the skin alters the microbial landscape and AMP gene expression of the skin.
- ✓ Disinfecting the skin reduces the isomerization of urocanic acid.
- ✓ There is dose-dependent increase in immune suppression against the contact allergen DNFB, when the mice are pre-treated with *cis*-UCA.
- ✓ *cis*-UCA may have a role in immune suppression through affecting skin microbiome and AMPs expression.



References:

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- Jeffrey P. Walterscheid, Dat X. Nghiem, Nasser Kazimi, Leta K. Nutt, David J. McConkey, Mary Norval, and Stephen E. Ullrich: *cis*-urocanic acid, a sunlight-induced immunosuppressive factor, activates immune suppression via the 5-HT_{2A} receptor *PNAS* 2006; 103 (16): 17420-17425
- Patra, V; Wagner, K; Arulampalam, V; Wolf, P. Skin Microbiome Modulates the Effect of Ultraviolet Radiation on Cellular Response and Immune Function. *Science*. 2019; 15: 211-222.

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