Characterization of cell mediated type IV hypersensitivity dermal response in healthy volunteers using Multispectral and Laser Speckle Contrast Imaging

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Introduction

- Challenge models enabling direct pharmacodynamic assessment are necessary for development of immunomodulatory drugs.
- Keyhole limpet hemocyanin (KLH) is commonly used for studying T-cell dependent immune response.

Aim

- To characterize the adaptive immune response after KLH immunization by measuring anti-KLH immunoglobulin (Ig) M and IgG titres
- To assess the skin response after intradermal administered KLH

Methods

- Randomized, double-blind, placebo-controlled study
- 15 male healthy volunteers
- KLH (0.1 mg) or placebo immunization day 0 (4:1 ratio)
- KLH (0.001 mg) intradermal injection day 21 volar left forearm, untreated volar right forearm
- DTH assessment day 21 (pre-dosing) and day 23 (48h post-dosing) including Laser Speckle Contrast Imaging (LSCI), 2D and 3D photography, colorimetry, and visual erythema grading

Results

- Treatments well-tolerated, no significant treatment related AEs
- Anti-KLH IgG and IgM titres significantly increased in KLH compared to placebo ($p<0.0001$ and $p=0.0014$, respectively)
- Average redness values with Antera camera (figure 1) and basal flow with LSCI (figures 2 and 3) after intradermal KLH significantly increased in KLH immunization compared to placebo immunization and untreated right forearm

Conclusions

- KLH administration well-tolerated
- KLH immunization induces quantifiable adaptive immune response
- LSCI and multispectral imaging following DTH assessment after intradermal KLH show potential to serve as novel objective, well-quantifiable assessments to study pharmacodynamic effects of immunomodulators

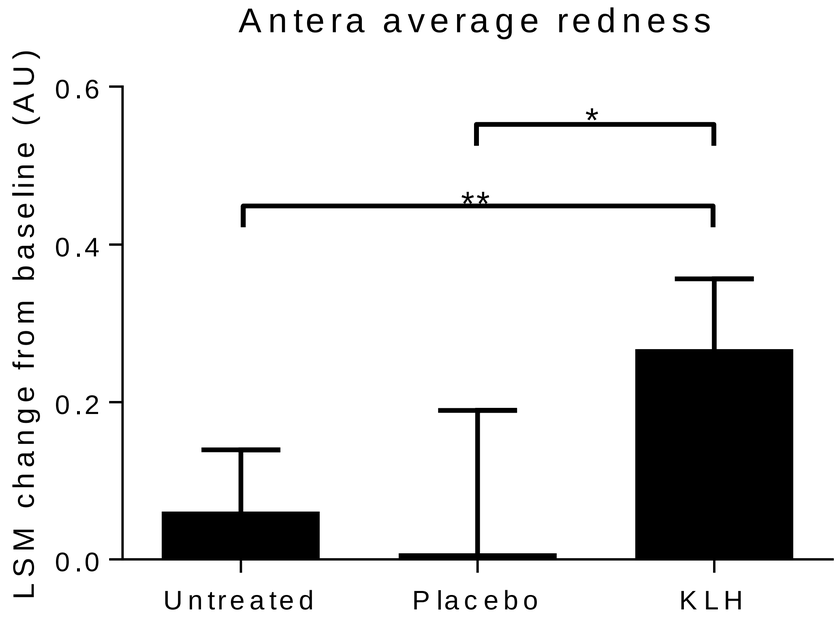

*Figure 1: Least squares means (LSM) change from baseline (95% CI) Antera average redness levels right forearm (untreated) and left forearm (placebo and KLH immunized groups). *p=0.0172; **p=0.0019 (AU, arbitrary unit)*

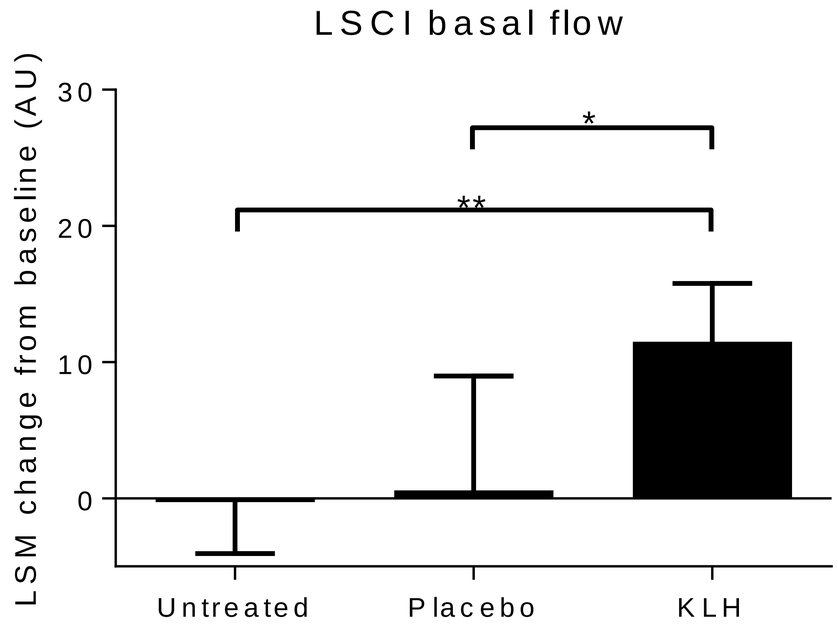

*Figure 2: LSM change from baseline (95% CI) LCSI basal flow right forearm (untreated) and left forearm (placebo and KLH immunized groups). *p=0.0263; **p=0.0002 (AU, arbitrary unit)*

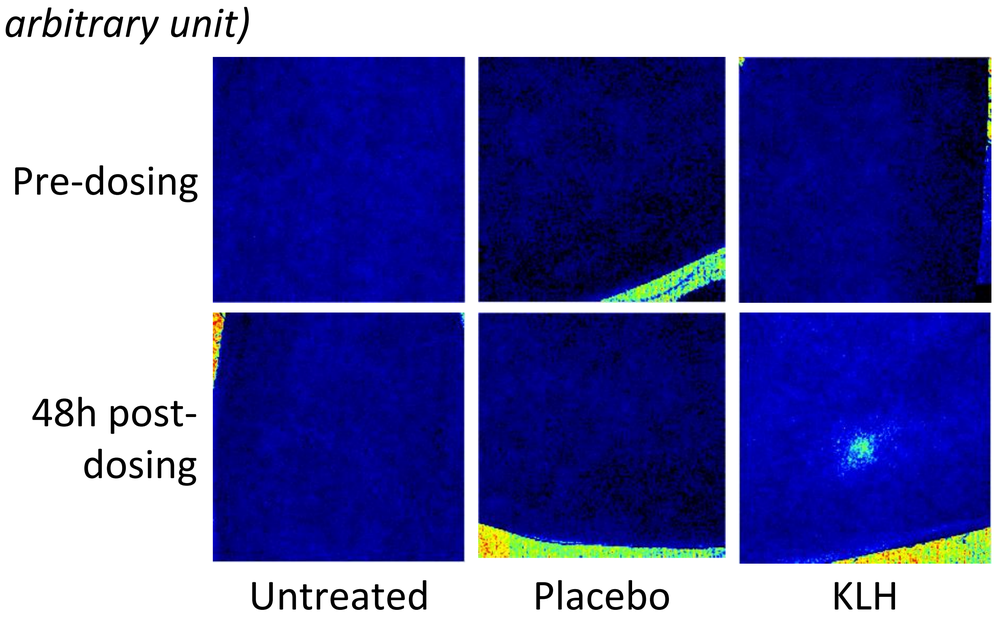

Figure 3: LSCI images right forearm (untreated) and left forearm (placebo and KLH immunized groups) before and after 48h of intradermal KLH administration

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