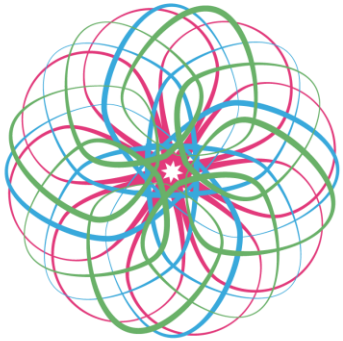


CHDR

Centre for Human Drug Research

Disclosure

- Study co-funded by Cutanea Life Sciences

- No other conflict of interests to declare

Comprehensive, multi-modal characterization of an imiquimod-induced human skin inflammation model

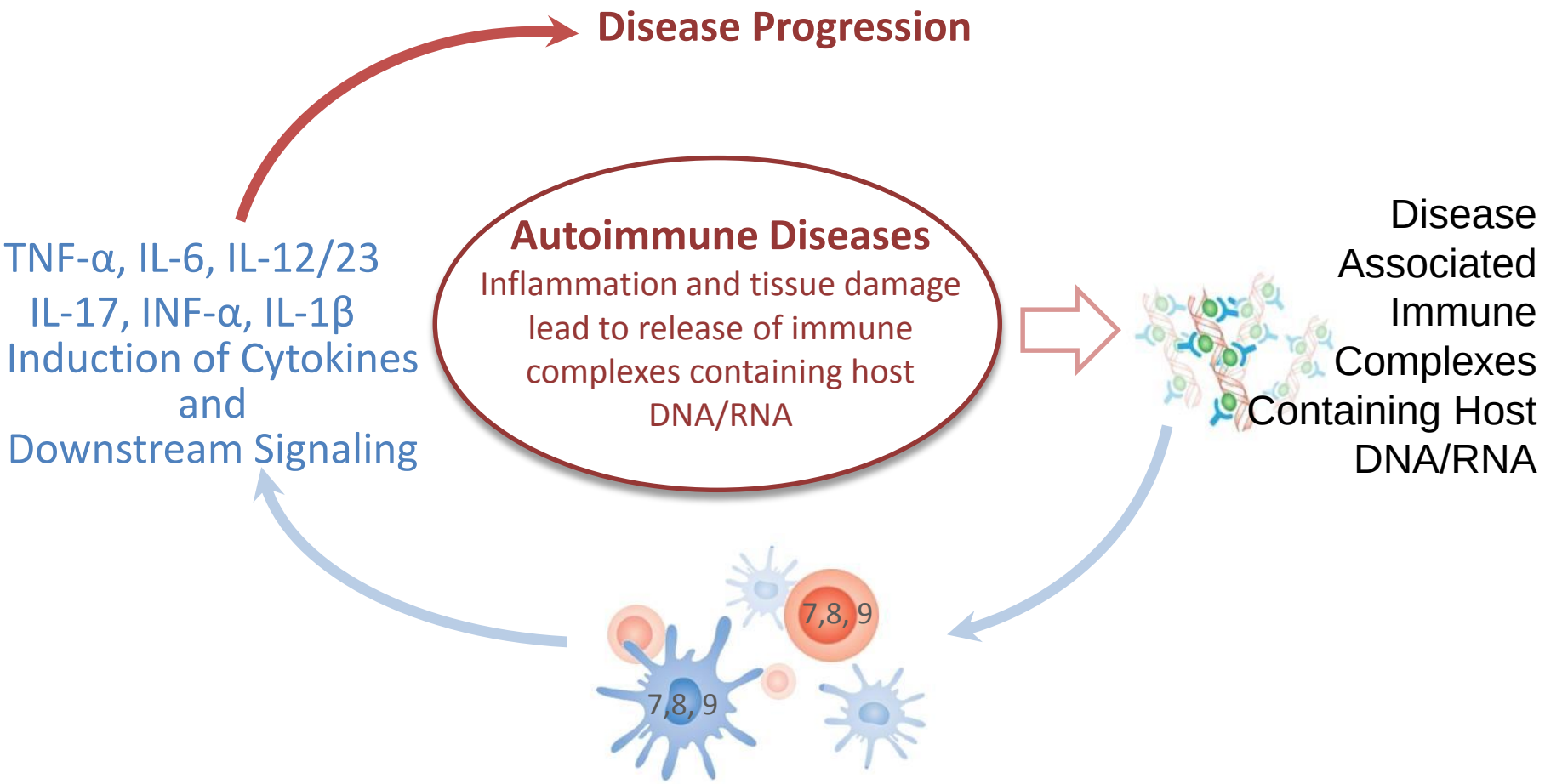
Tessa van der Kolk, MD
Centre for Human Drug Research, Leiden, The Netherlands

Introduction

- Imiquimod; TLR 7/8 agonist
- Local skin inflammation through MyD88 signaling pathway
- Psoriasis exacerbations after treatment
- Development mouse model
- No short human model for drug development

CHDR
Centre for Human Drug Research

Role of TLR 7 in Autoimmune Disease Cycle



Objectives

- To develop an acute skin inflammation challenge model with;

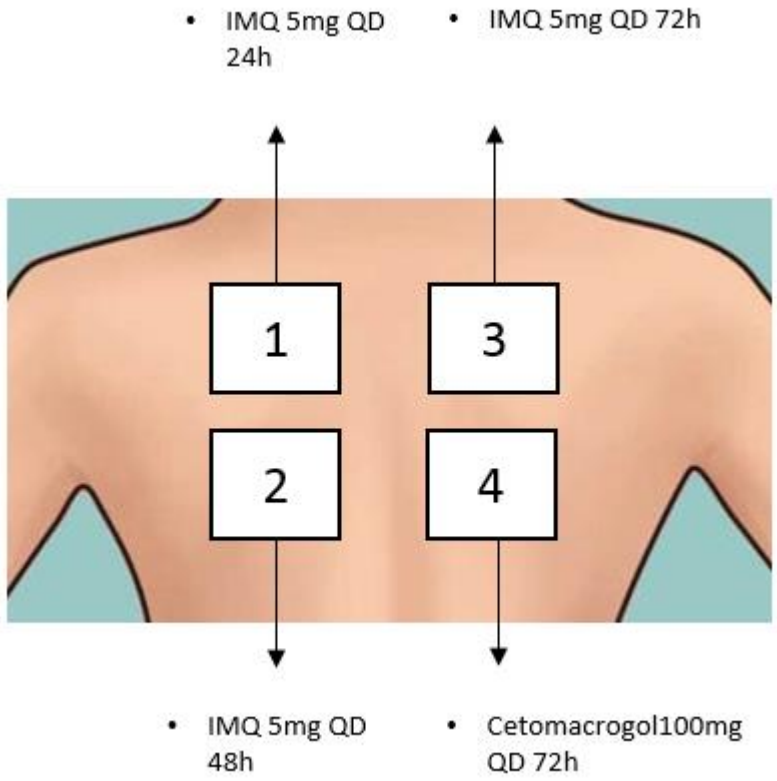
  1) topical IMQ application for 24, 48 and 72 hours on a fully competent skin barrier

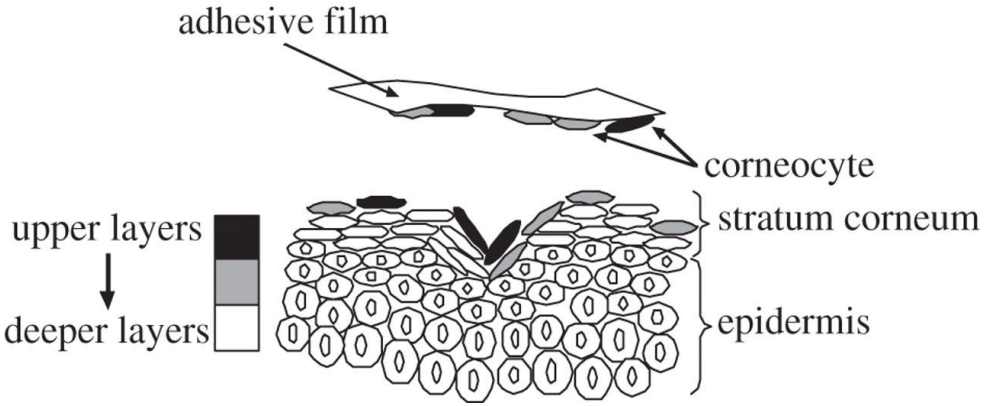
  2) topical IMQ application for 24, 48 and 72 hours on tape stripped skin

CHDR
Centre for Human Drug Research

Study design

- Open label
- Vehicle controlled
- Dose-ranging
- Parallel cohort with tape stripping
- Healthy volunteers (18-45yoa)





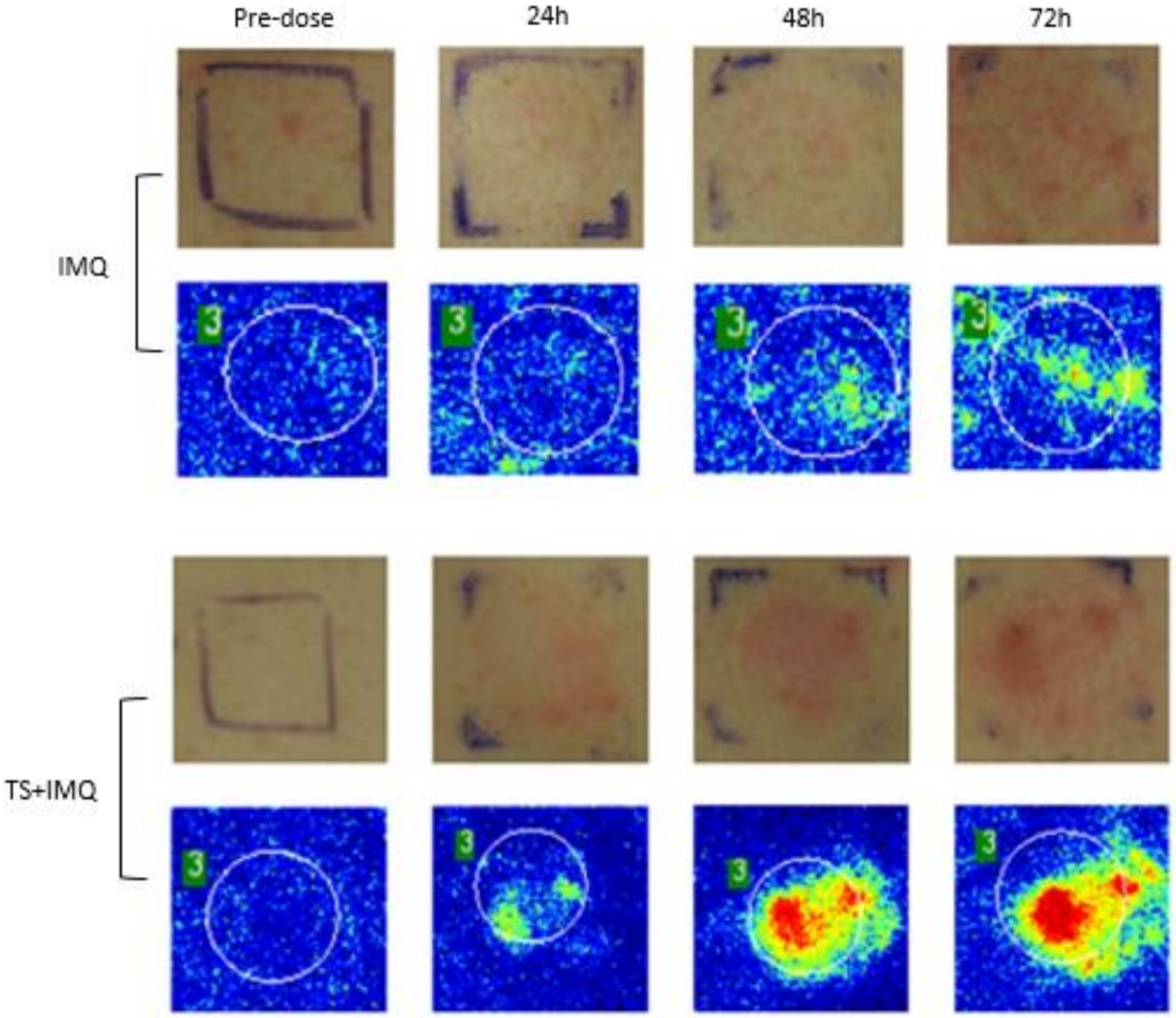
CHDR
Centre for Human Drug Research

Pharmacodynamic endpoints

- Clinical (physician erythema scoring)
- Imaging (colorimetry and erythema index)
- Biophysical (perfusion by Laser Speckle Contrast Imaging)
- Molecular (mRNA expression)
- Cellular (histology and immunohistochemistry)

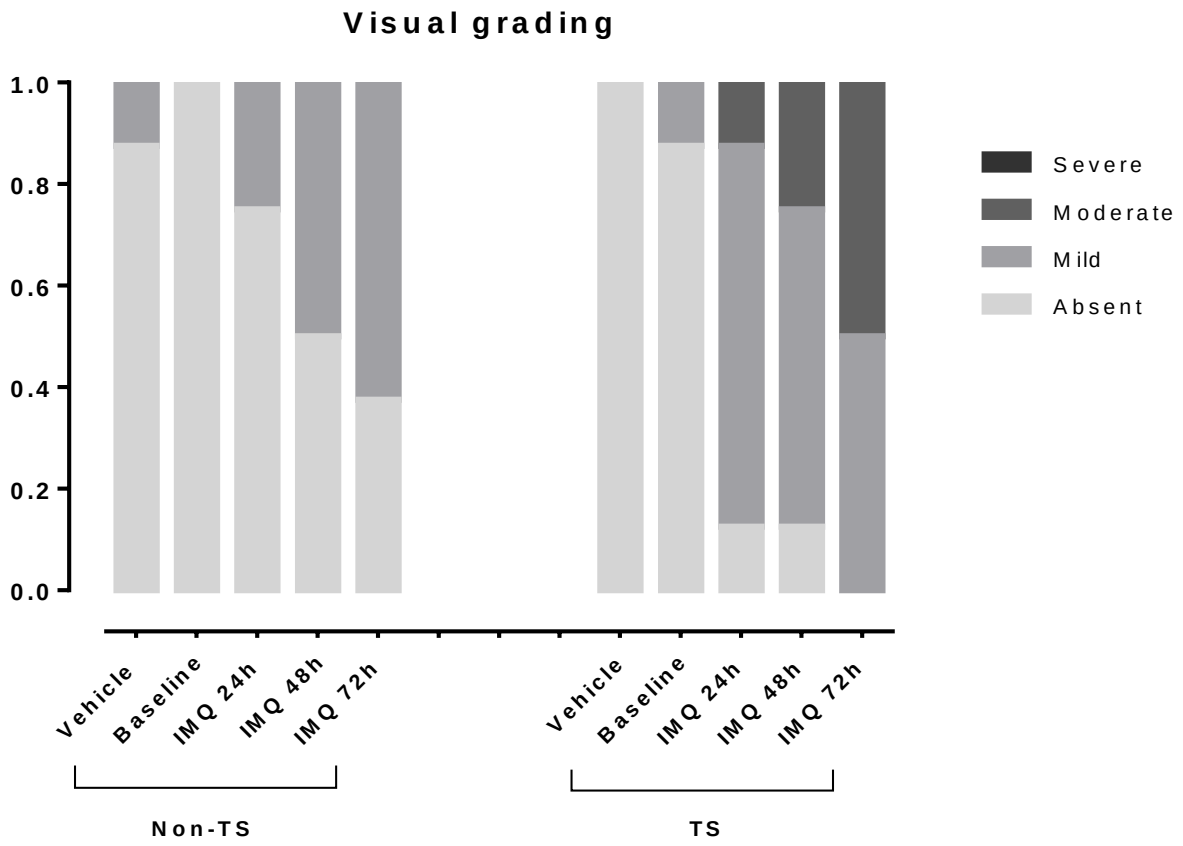
CHDR
Centre for Human Drug Research

Clinical impression



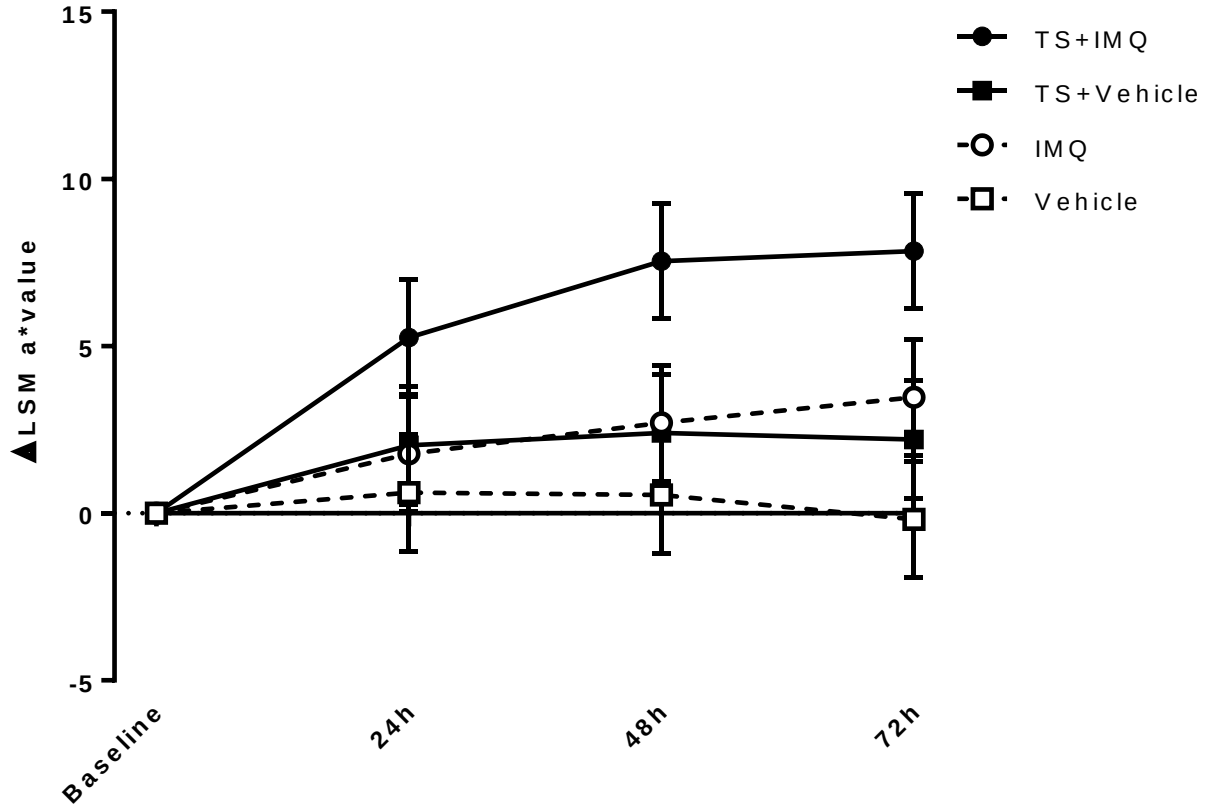
CHDR
Centre for Human Drug Research

CLINICAL



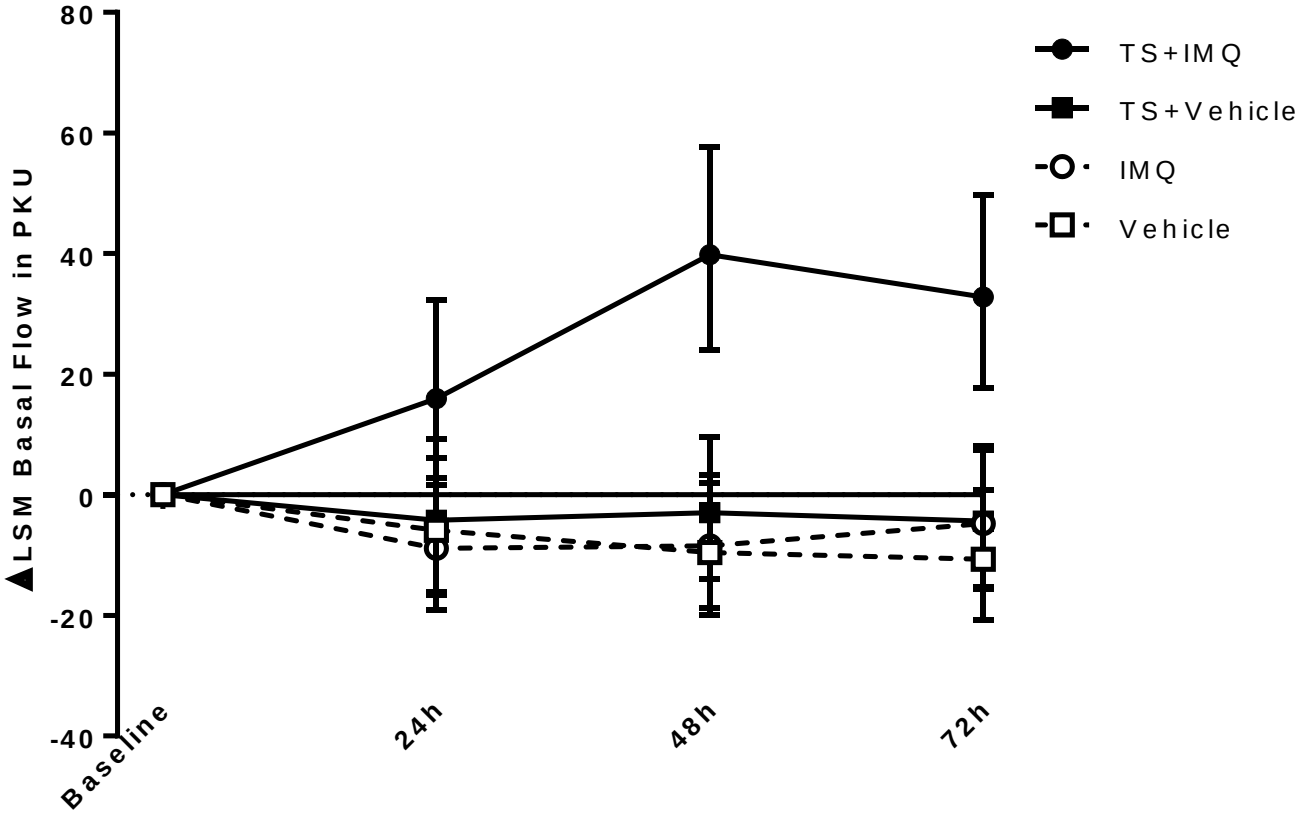
CHDR
Centre for Human Drug Research

IMAGING



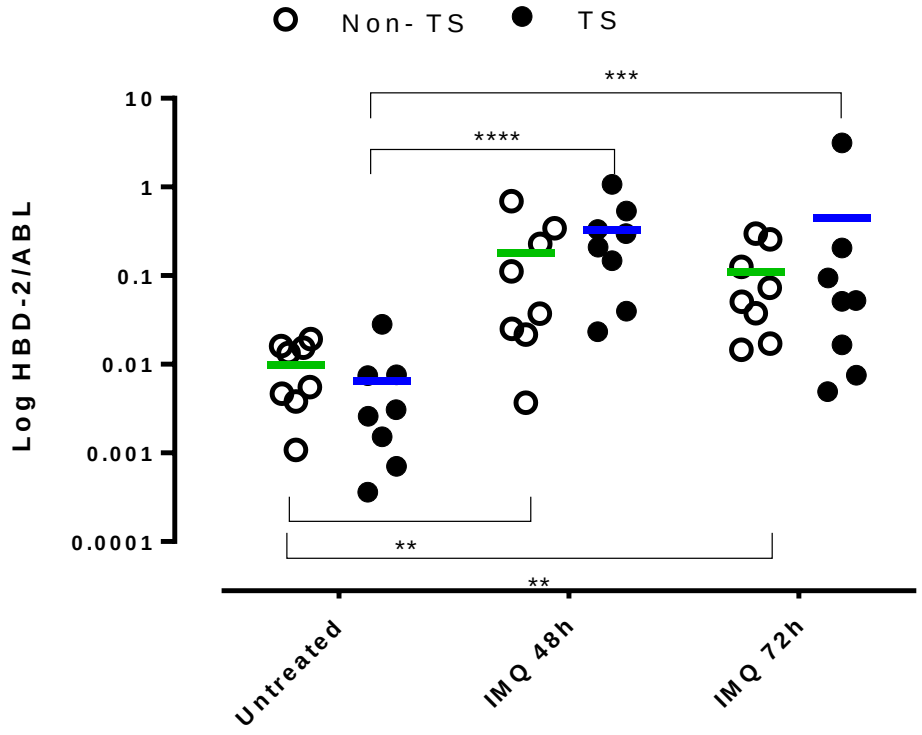
CHDR
Centre for Human Drug Research

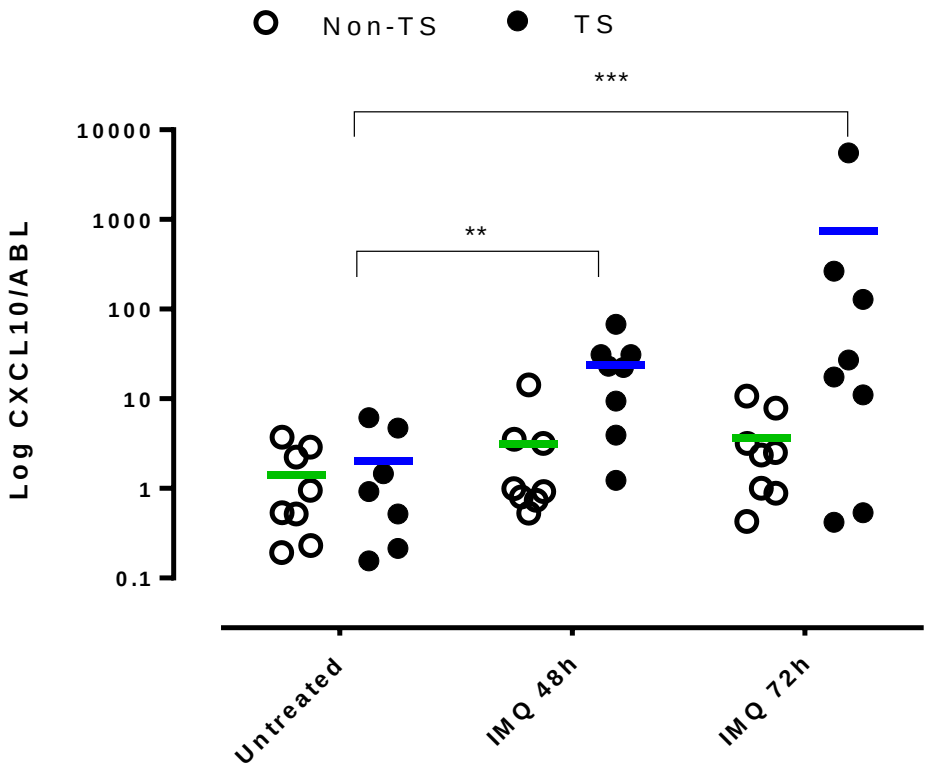
BIOPHYSICAL



CHDR
Centre for Human Drug Research

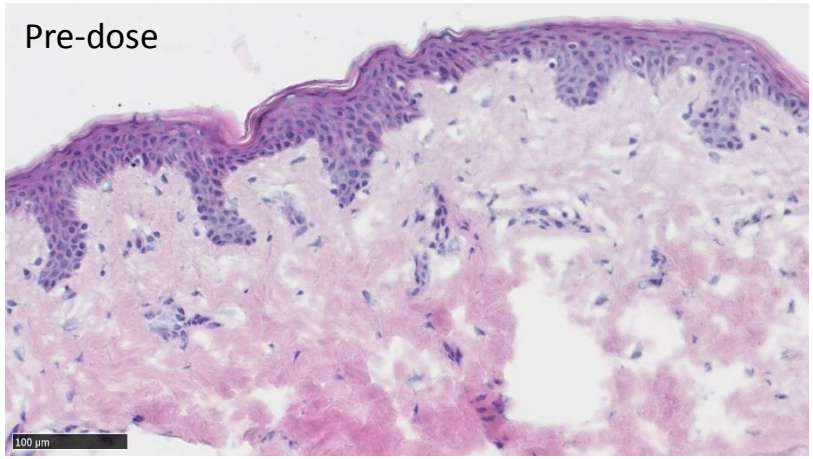
MOLECULAR

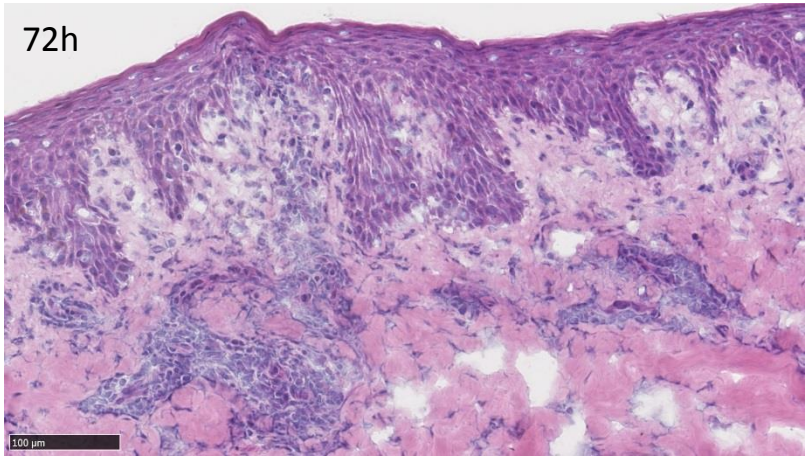


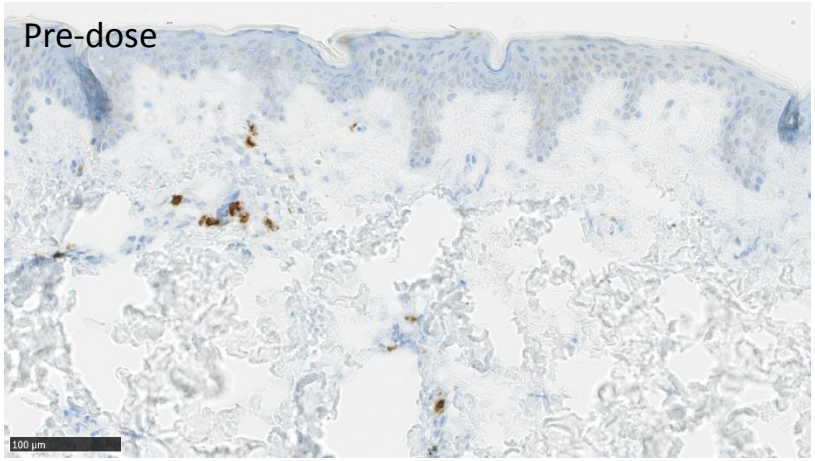


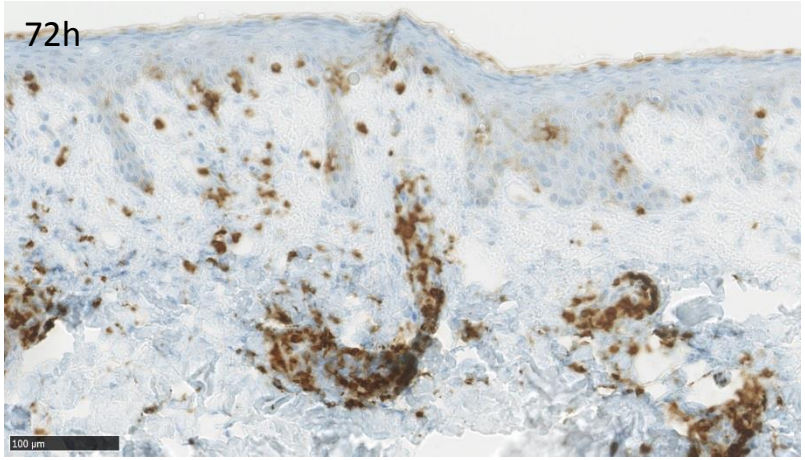
CHDR
Centre for Human Drug Research

Histology impression



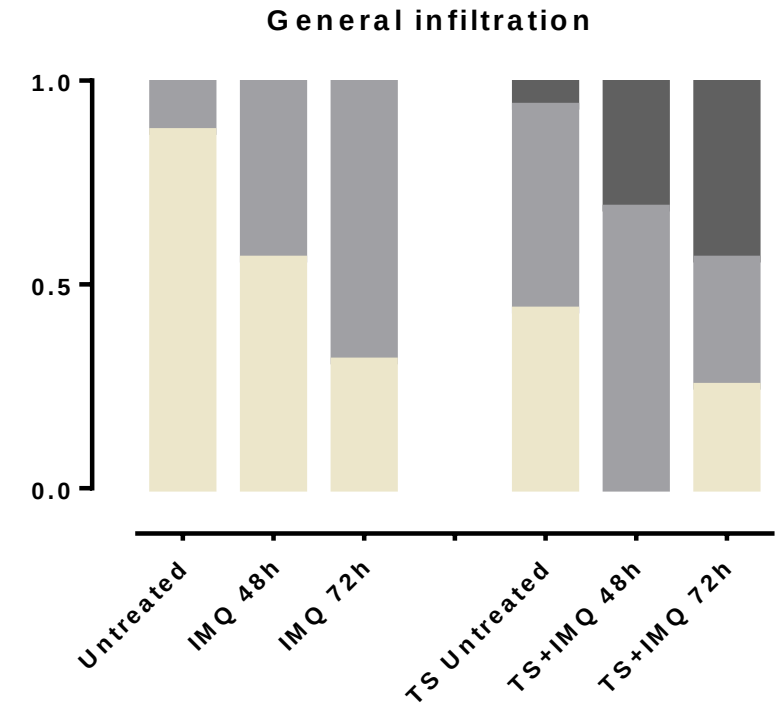


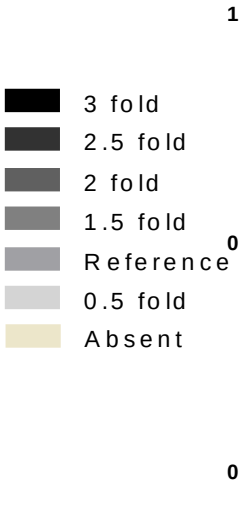


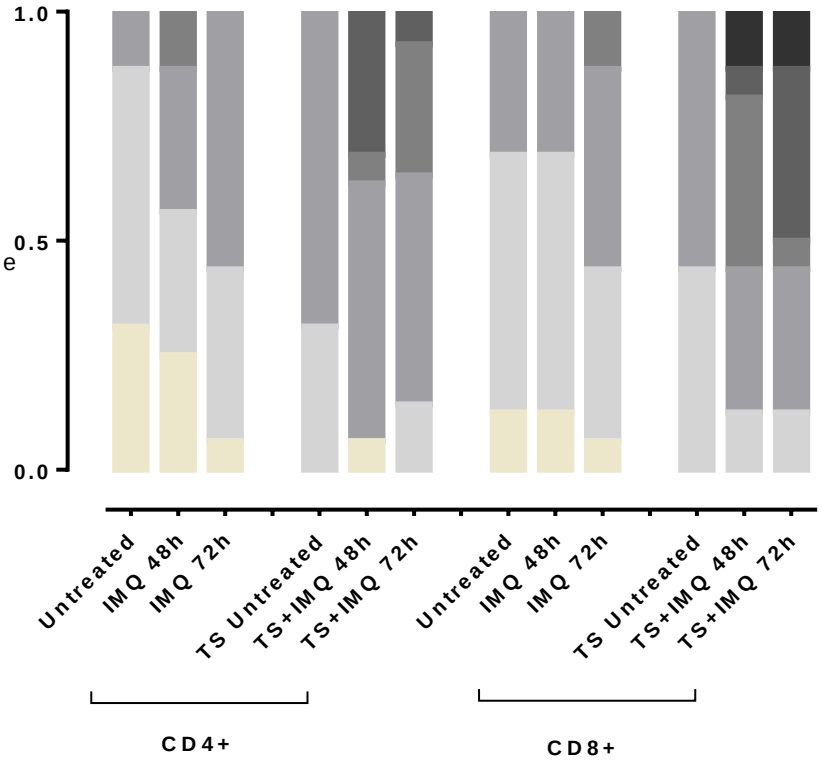


CHDR
Centre for Human Drug Research

CELLULAR

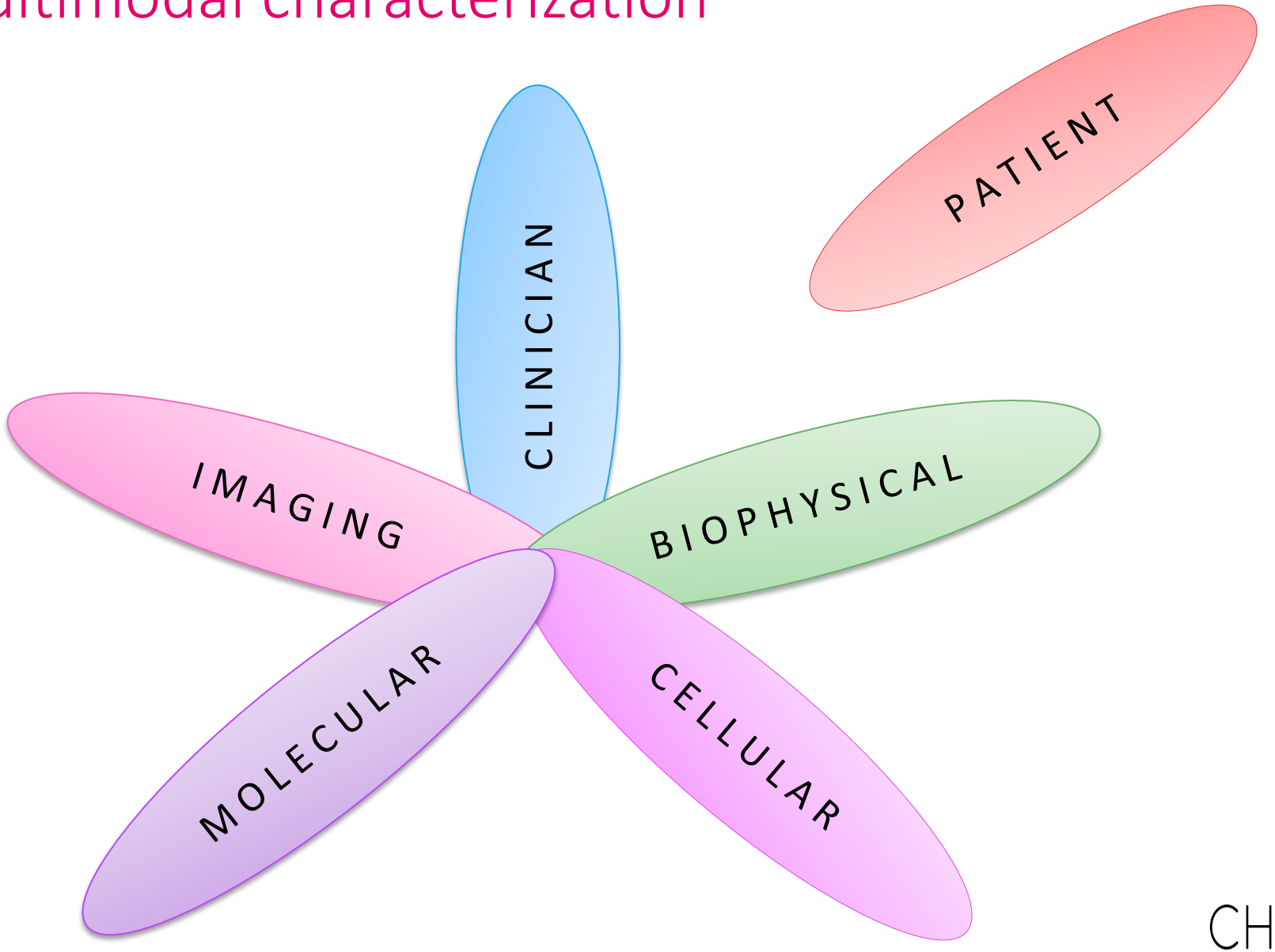






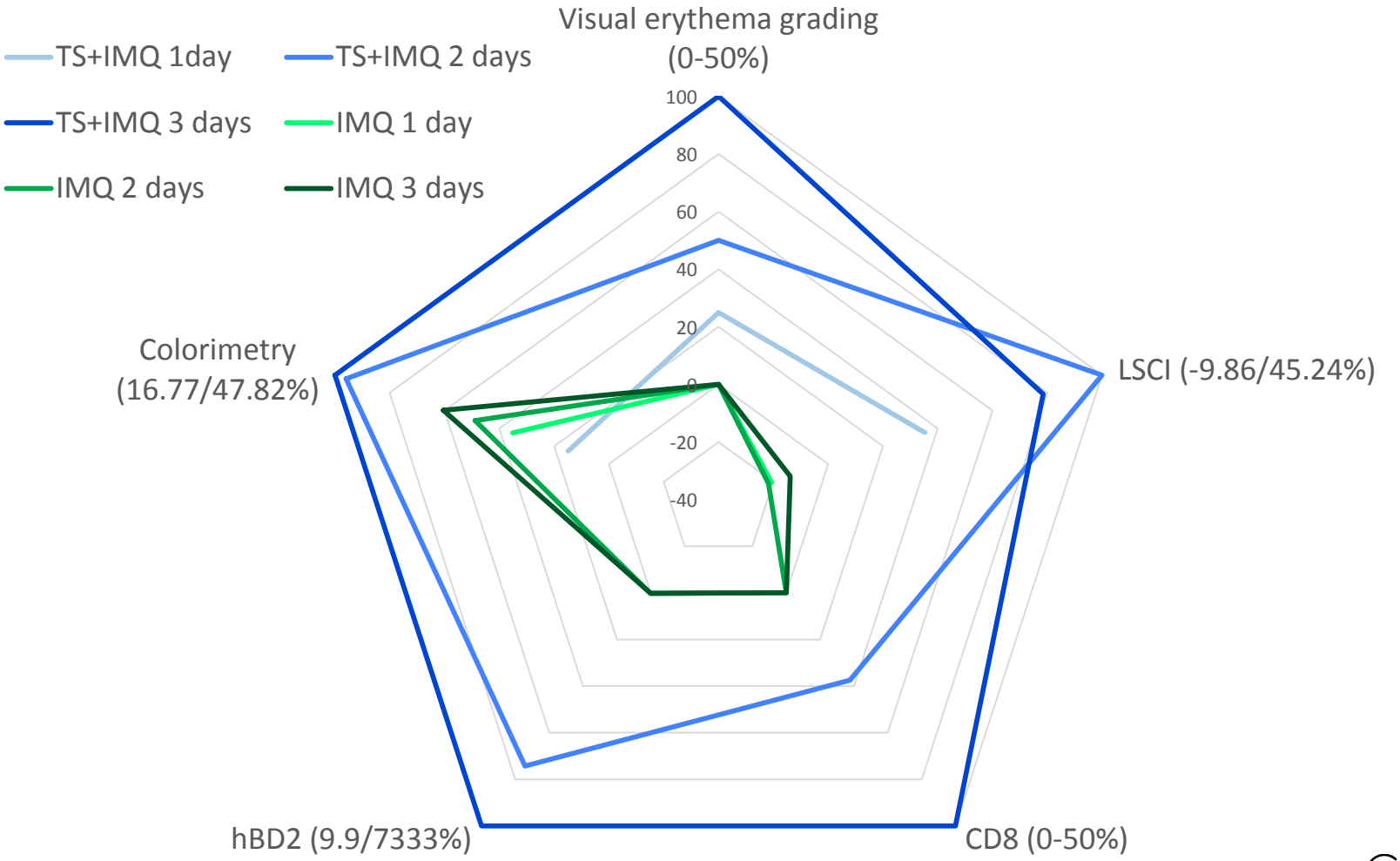
CHDR
Centre for Human Drug Research

Multimodal characterization



CHDR
Centre for Human Drug Research

Multimodal characterization



CHDR
Centre for Human Drug Research

Conclusion

- Successful development of a fully characterized, acute IMQ-induced skin inflammation model
- Well-tolerated (no discontinuations, not shown)

- Clinical and histological phenotype fully concordant in TS+IMQ cohort

- TS of the skin needed for quicker inflammatory response

- 48h application most optimal for the model

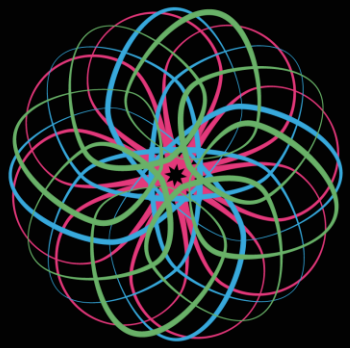
- Future: *proof of pharmacology* and *drug profiling* of novel compounds targeting the innate immune system

CHDR
Centre for Human Drug Research

Acknowledgements

- Salma Assil
- Rianne Rijneveld
- Erica Klaassen
- Gary Feiss
- Eddy Florencia
- Errol Prens
- Martijn van Doorn
- Koos Burggraaf
- Matthijs Moerland
- Robert Rissmann

CHDR
Centre for Human Drug Research



CHDR

Centre for Human Drug Research