

Direct and indirect effects of tofacitinib and dupilumab on keratinocytes in skin models of atopic dermatitis

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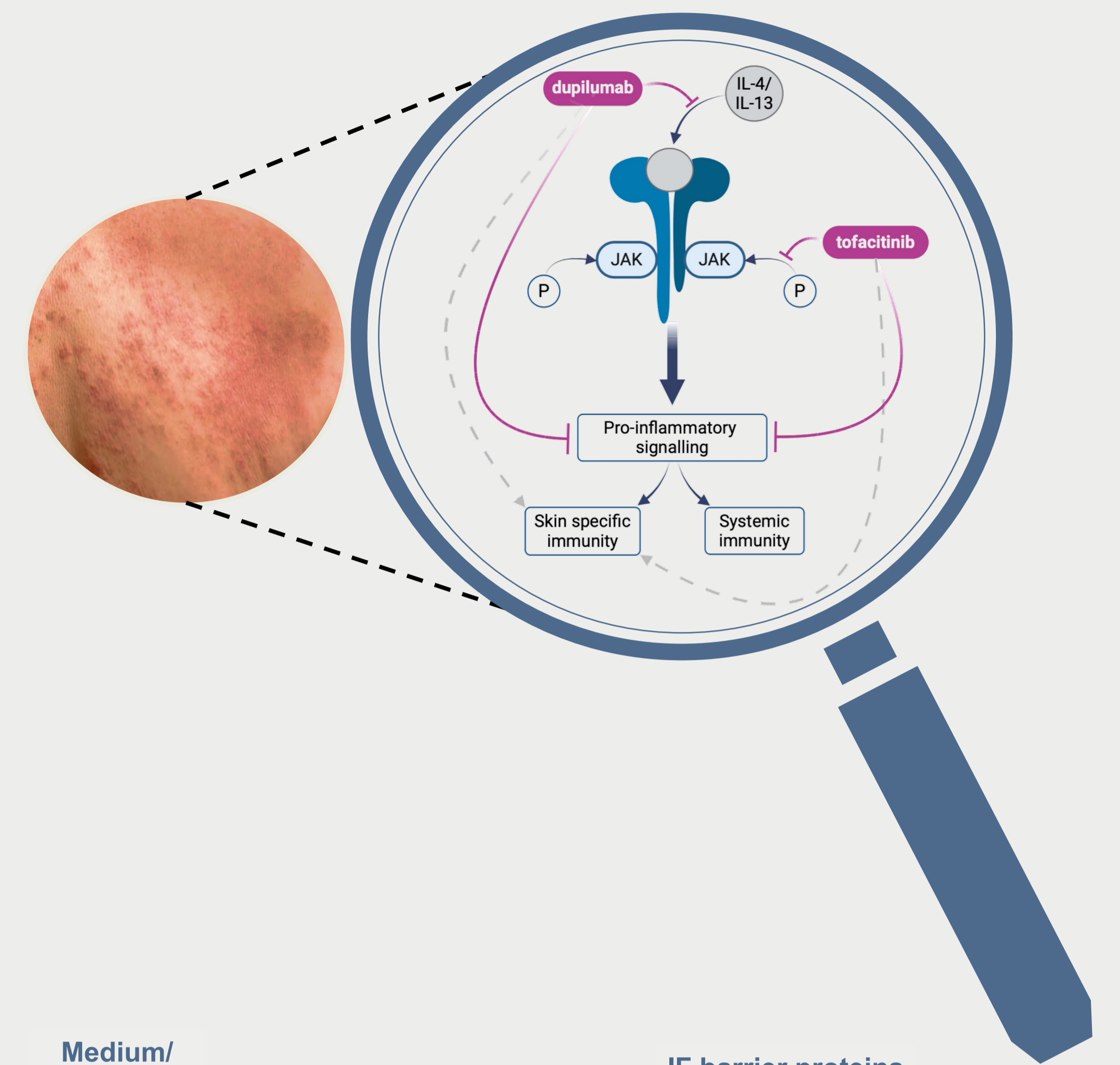
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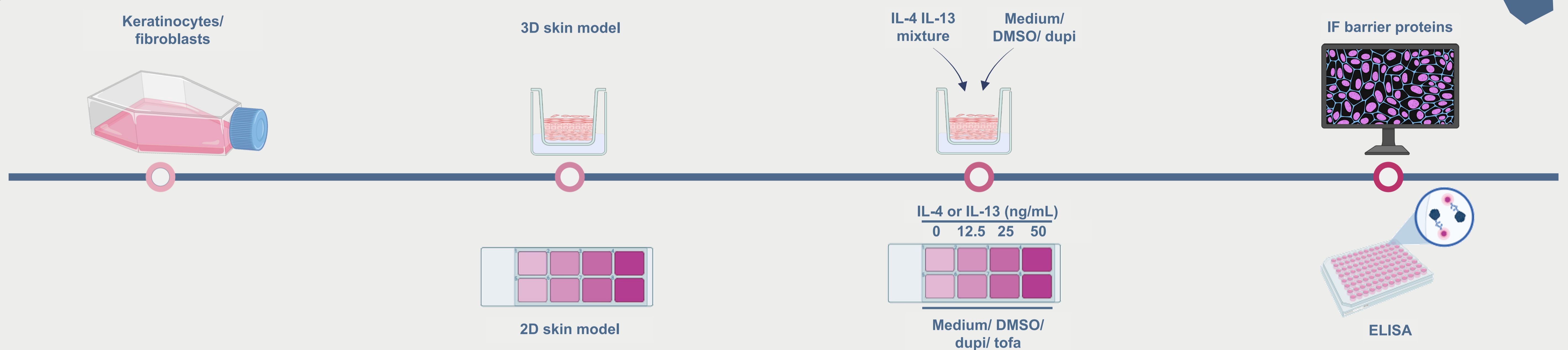
Poster nr:
8

Introduction

- Atopic dermatitis (AD)** is a Th2-driven inflammatory skin disease with a central role for IL-4 and IL-13
- Several **JAK-STAT pathways** are involved in signalling of AD-specific cytokines
- Targeted treatment for AD** are JAK-inhibitors (JAKi) & monoclonal antibodies (mAb)
- What are the **direct modifying effects of JAKi/ mAb** on keratinocytes/ barrier function?

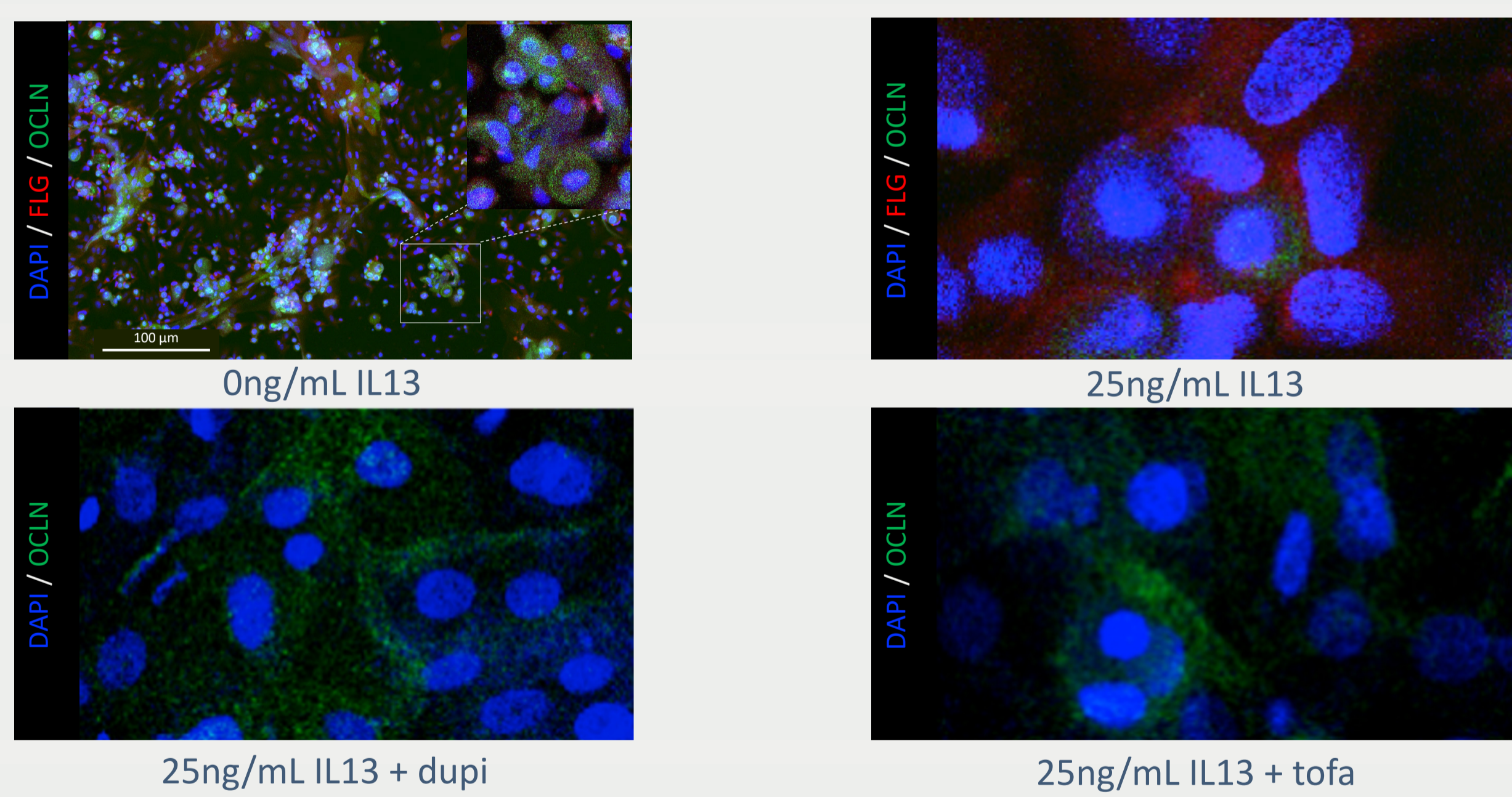


Method



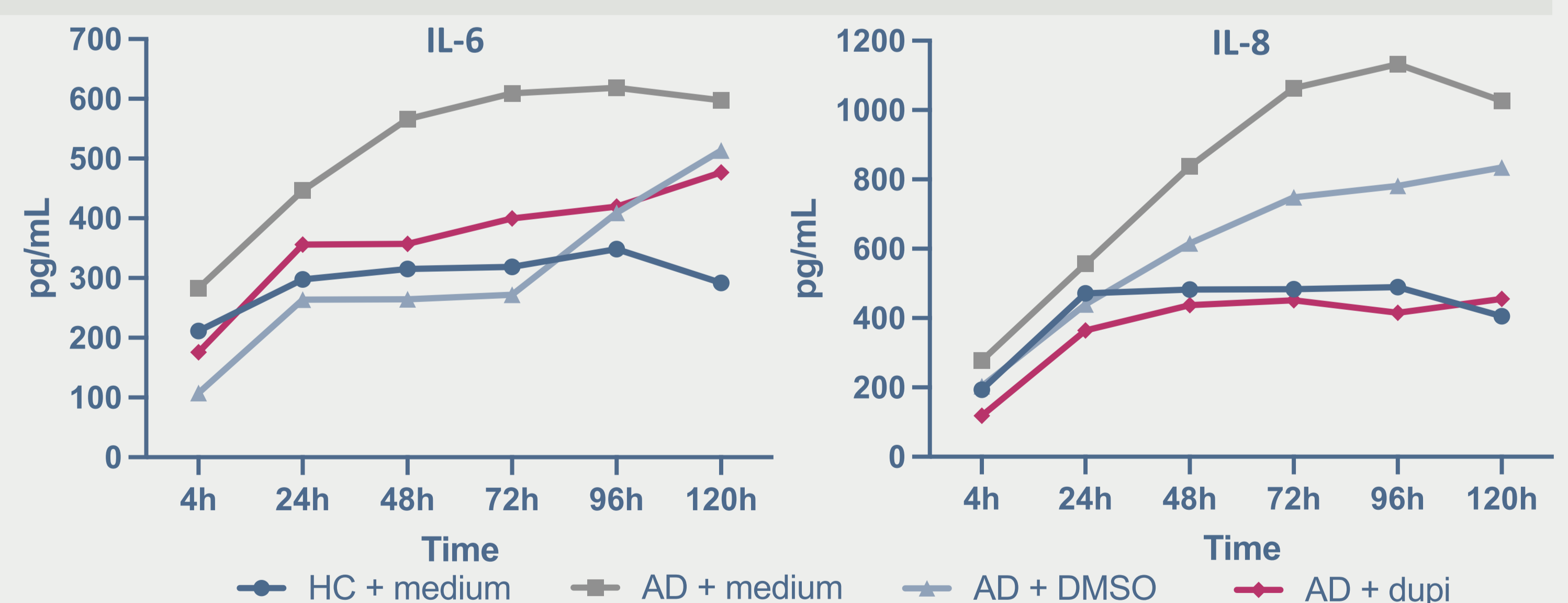
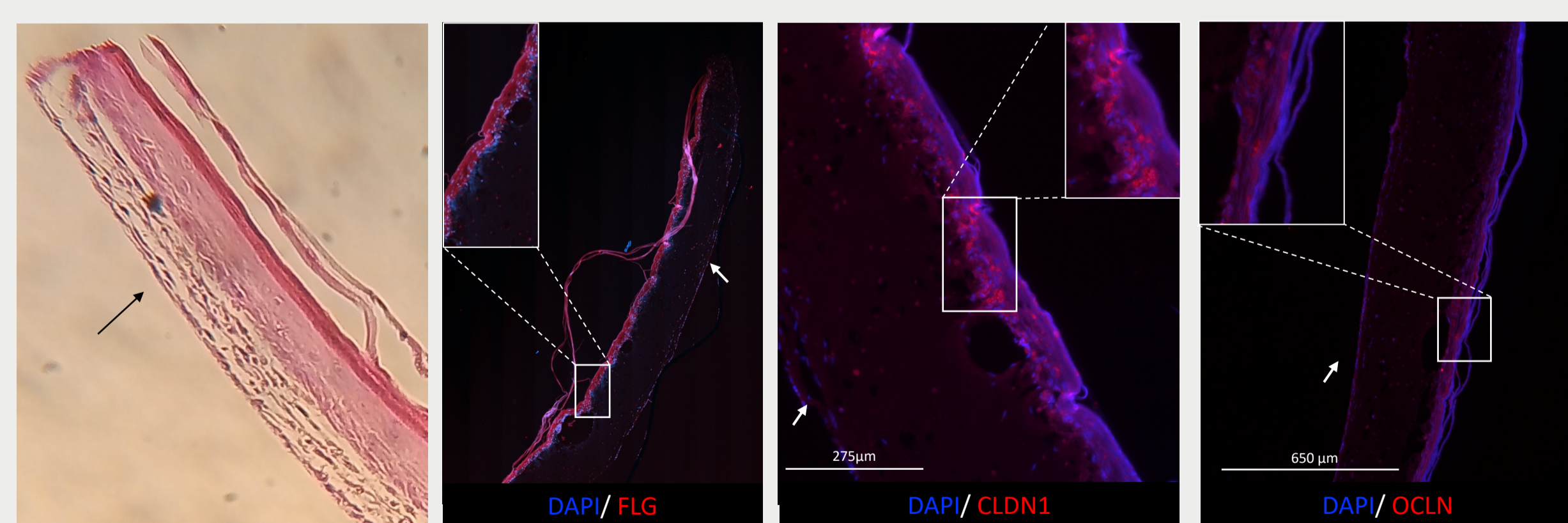
Results

2D skin models



Stimulation	Cytokine secretion					
	IL-4 + medium	IL-4 + dupi	IL-4 + tofa	IL-13 + medium	IL-13 + dupi	IL-13 + tofa
IL-1 α	↑ Dose-dependent	↓↓	↓↓	↑ Dose-dependent	↓↓	↓↓
IL-6	↑ Dose-dependent	↓↓	↓↓	—	↓↓	↓↓
IL-8	—	↓↓	↓↓	—	↓↓	↓↓

3D skin models



Conclusion

- IL-4 and IL-13** exert different distinct effects on keratinocytes, with only IL-13 having the potential to disturb the barrier function
- IL-4 and IL-13** directly affect IL-1 α secretion and Indirectly IL-6 and IL-8 secretion possibly through fibroblasts
- Dupilumab and tofacitinib** have a **direct modifying effect** on the level of **keratinocytes**, even in the absence of immune cells