Imiquimod-induced psoriasis-like dermatitis in rhesus monkey: a novel psoriasis NHP model

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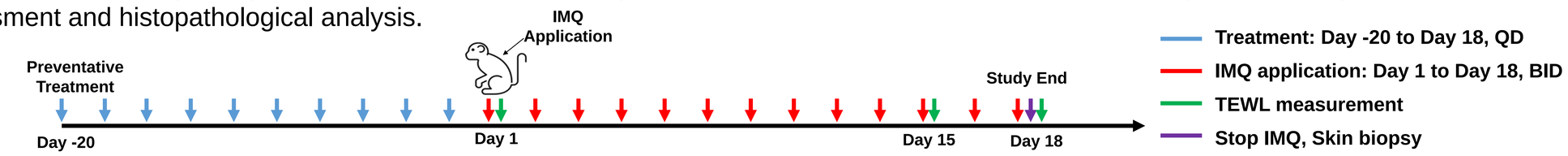
Background

Psoriasis is a chronic autoimmune skin disease characterized by abnormal keratinocyte proliferation and infiltration of inflammatory cells [1, 2]. Nonhuman primates (NHPs) have significantly contributed to preclinical drug evaluation over recent decades due to their high genetic homology with humans [3]. However, the absence of a suitable NHP model that accurately mimics the complex phenotype of psoriasis has hindered the development of promising therapeutics. In this study, we focus on using imiquimod (IMQ) to induce psoriasis-like biological and pathological symptoms in rhesus monkeys, aiming to facilitate the efficacy evaluation of potential psoriasis treatments.

Method

Nine rhesus monkeys were selected and divided into two groups: a model group (n=4) and a treatment group (n=5). The monkeys in the treatment group were pre-treated with oral deucravacitinib once daily, while all monkeys were topically treated with imiquimod on the dorsal back twice daily to induce psoriasis-like symptoms. Throughout the study, general health, trans-epidermal water loss (TEWL), and clinical scores of the imiquimod-treated areas were monitored. Additionally, tissue samples from the treated skin were collected for cytokine assessment and histopathological analysis.



Results

Application of imiquimod in rhesus monkeys resulted in typical psoriasis-like features, including induration, erythema, and crusting, alongside a significant increase in TEWL and clinical scores. Histopathological analysis revealed hyperkeratosis and infiltration of inflammatory cells, along with upregulation of Th1 and Th17 cell-associated signaling pathways and increased mRNA levels of psoriasis-related cytokines. These findings confirm that imiquimod induces psoriasis-like skin inflammation. In contrast, deucravacitinib, an oral tyrosine kinase 2 (TYK2) inhibitor approved for psoriasis treatment, significantly alleviated these symptoms, downregulated related biomarkers, and demonstrated a potent remission effect.

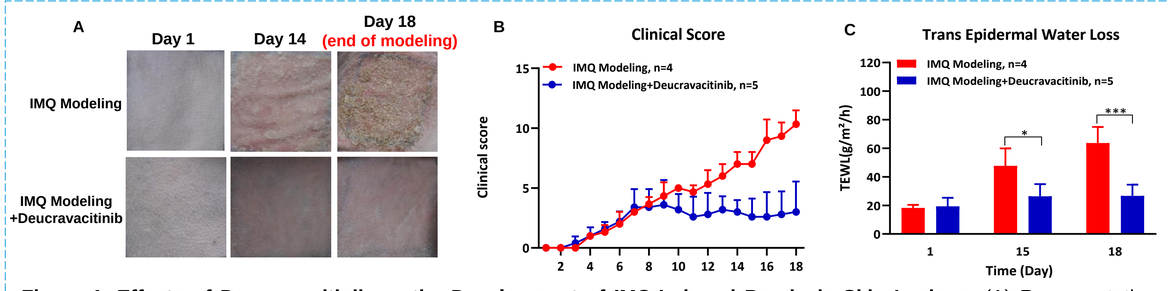


Figure 1. Effects of Deucravacitinib on the Development of IMQ-Induced Psoriasis Skin Lesions. (A) Representative images of the monkey dorsal back skin following IMQ application on different days. (B) Scoring curves for back skin thickness, scaling, and erythema. (C) TEWL data from the IMQ-treated areas.

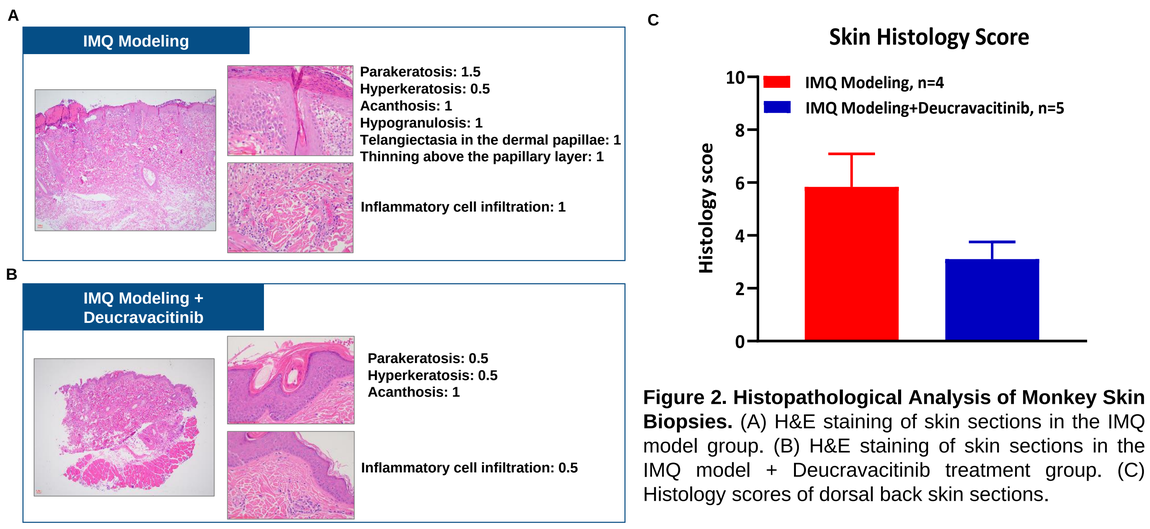


Figure 2. Histopathological Analysis of Monkey Skin Biopsies. (A) H&E staining of skin sections in the IMQ model group. (B) H&E staining of skin sections in the IMQ model + Deucravacitinib treatment group. (C) Histology scores of dorsal back skin sections.

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TLR Signaling	JAK-STAT Signaling	Th17 Lymphocyte	Th1 Lymphocyte	Th2 Lymphocyte
IRAK4, IRAK1, NFKB1, IRAK2, MAPKAPK2, TRAF6, CHUK, IRF3, IRF7, TLR7, MYD88, TLR8	TYK2, JAK1, STAT6, JAK2, STAT3, STAT4, STAT1, STAT2	IL1B, IL23A, IL6, TGFB1, SMAD2, STAT3, IL23R, IL17F, IL17A, IL22, IL12RB1, IL21, STAT4	IFNG, IL12RB1, STAT1, NFKB1, IL12RB2, STAT5A, STAT5B, IL18, IL2, IL12A, IL12B	GATA3, NFATC1, IFNG, IL10, IL4, IL13, IL5, MAF, STAT6

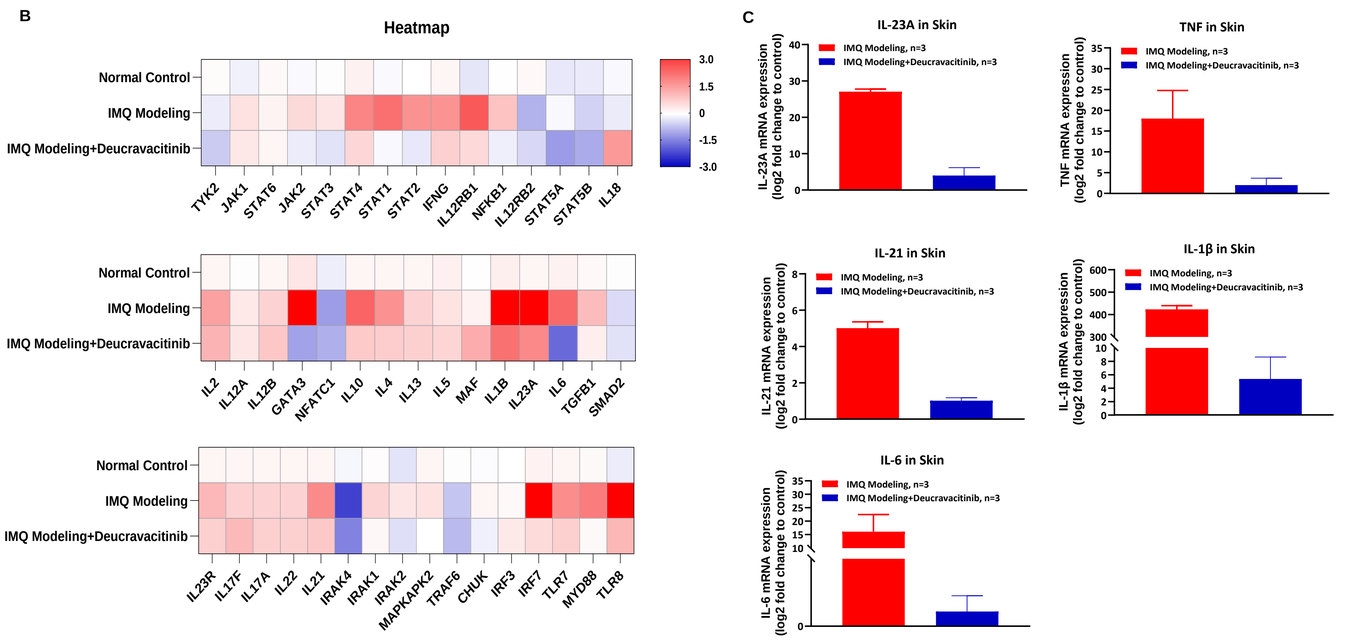

Figure 3. Gene Expression Characterization in the IMQ-Induced Psoriasis Model Using NanoString Analysis. (A) Signaling pathways associated with psoriasis. (B) Heatmap of differentially expressed genes in IMQ-induced psoriasis model animals with and without Deucravacitinib. (C) Cytokines showing significant differences between IMQ-induced psoriasis model animals with and without Deucravacitinib.

Conclusion

This study successfully established a psoriasis NHP model by applying imiquimod topically to the dorsal skin of rhesus monkeys, which replicated key pathological features of human psoriasis, including clinical appearance, histological changes, and inflammatory cytokine profiles. Our results suggest that this model could serve as a valuable tool for preclinical pharmacokinetic/pharmacodynamic (PK/PD) studies and the screening of anti-psoriasis therapeutics.

Reference

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3. Harding, John D. “Nonhuman Primates and Translational Research: Progress, Opportunities, and Challenges.” *ILAR journal* vol. 58, 2 (2017): 141-150.