IL-17C inhibition reduces skin inflammation in a mouse IL-23-induced psoriasis model

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Introduction
Psoriasis is one of the most common immune-mediated chronic inflammatory skin disorders in adults. The predominant role of cytokines in psoriasis pathogenesis is well established. Among them, IL-17C is the most abundant IL-17 cytokine family member found in human lesional psoriatic skin (Johnson et al, 2013). Moreover, IL-17C-promoted inflammation in a mouse psoriasis model has been demonstrated (Ramirez-Carozzi et al., 2011). These findings suggest IL-17C as a relevant therapeutic target for psoriasis treatment.

Objective
The aim of this study was to evaluate the efficacy of MOR106, a human IgG1 monoclonal antibody that potently and selectively inhibits human and mouse IL-17C, in a mouse IL-23-induced psoriasis model (Rizzo et al., 2011).

Methods
- Human skin samples from 2 healthy and 4 psoriatic donors were immunostained with anti-IL-17C (MOR22420).
- IL-23-induced psoriasis mouse model:
  - Intradermal injection (20μL) of PBS/BSA 1% or rmIL-23 (1μg/ear) in the right ear for 4 days
  - Groups:
    - PBS/BSA 0.1% + isotype Ab (10 mg/kg x2, ip) n=5
    - rmIL-23 + isotype Ab (10 mg/kg x2, ip) n=10
    - rmIL-23 + MOR106 (0.4 mg/kg x2, ip) n=10
    - rmIL-23 + MOR106 (2 mg/kg x2, ip) n=10
    - rmIL-23 + MOR106 (10 mg/kg x2, ip) n=10
  - Daily total ear thickness measurement using caliper
  - Post-sacrifices, the ears were cut in two halves
  - One half ear was fixed in 4% formaldehyde and embedded in paraffin. 4µm thick sections were stained with:
    - Anti-IL-17C (MOR12743) by immunohistochemistry
    - Hematoxylin and eosin solution for Histomorphometry analysis
  - The other half was collected in RNA later for RNA extraction and gene expression was evaluated for relevant cytokines and defenses by qPCR
  - Statistical analysis was performed with one-way analysis of variance (ANOVA) and Dunnett’s post hoc test versus rmIL-23+ isotype Ab control group, *p<0.05; **p<0.01; ***p<0.001

Conclusion
Our data show the protective effect of the anti-IL-17C antibody MOR106 in a mouse model of psoriasis and further support IL-17C inhibition as potential therapeutic approach for treating psoriasis.

IL-17C expression is increased in psoriatic skin

MOR106 prevents skin thickening in an IL-23-induced psoriasis model

Gene expression

References

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