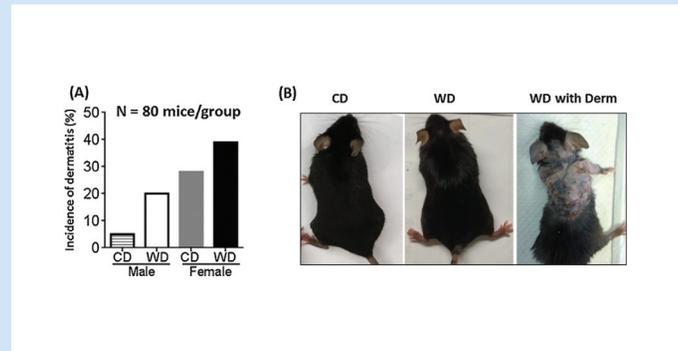


## Long-term Western diet intake leads to dysregulated bile acid signaling and dermatitis with Th2 and Th17 pathway features in mice

Dietary interventions are implicated in the development of atopic dermatitis, psoriasis, and acne. Jena PK et al investigate the effect of diet and the bile acid (BA) receptors, such as TGR5 and S1PR2 in the development of dermatitis. WD intake substantially increased the incidence of dermatitis. Cutaneous antimicrobial peptide genes were reduced in WD-fed mice, but increased when mice developed skin lesions. *Trpa1* and *Trpv1*, which mediate itch, were also increased in dermatitic lesions. The expression of *S1pr2* and genes encoding sphingosine kinases, S1P phosphatases, binding protein, and transporter were all reduced by WD intake but elevated in dermatitic lesions. Dermatitis development increased total cutaneous BA with an altered profile, which may change TGR5 and S1PR2 activity. In summary, activation of TGR5 and S1PR2 keratinocyte proliferation, metabolism, and inflammation, may contribute to WD-exacerbated dermatitis with Th2 and Th17 features. In addition, elevated total BA play a significant role in inducing dermatitis and cutaneous inflammation.



**Fig. 1.** The incidence of dermatitis lesions in CD- and WD-fed male and female mice,  $n = 80$  mice per group (A). The morphology (B), histopathology

## A proinflammatory role of KLK6 protease in Netherton syndrome

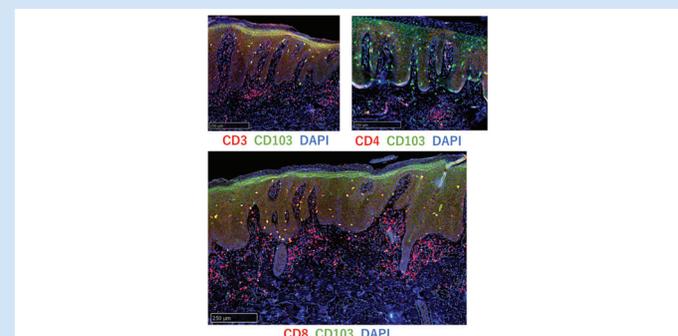
Netherton syndrome (NS) is a rare but severe type of ichthyosis characterized by atopy, allergies, and potentially lethal skin overdesquamation associated with highly elevated proteolytic activities in LEKTI-deficient epidermis. NS symptoms are recapitulated in *Spink5*<sup>-/-</sup> mouse where the gene encoding *Lekti* has been invalidated. The KLK6 protease is expressed by epidermal keratinocytes and shown in vitro to cleave desmosomal components. Zingkou E et al investigated whether KLK6 is implicated in epidermal overdesquamation and inflammation associated with NS. Elimination of Klk6 in *Spink5*<sup>-/-</sup> remarkably suppresses the expression of *Tslp*. *Spink5*<sup>-/-</sup>*Klk6*<sup>-/-</sup> mice display normalized keratinocyte differentiation, nevertheless, epidermal proteolytic activities and the associated overdesquamation were not ameliorated. Ablation of *Klk6* largely suppresses epidermal inflammation but cannot rescue over-desquamation leading to the lethal NS phenotype. Nonetheless, these findings demonstrate that KLK6 is implicated in skin inflammation and may represent a novel druggable target for NS and other inflammatory conditions e.g. atopic dermatitis.



**Fig. 1.** Deletion of Klk6 in Lektin-deficient epidermis does not rescue the lethal NS phenotype. (A) Macroscopic appearance of newborn wt, *Klk6*<sup>-/-</sup>, *Spink5*<sup>-/-</sup>, and *Spink5*<sup>-/-</sup>*Klk6*<sup>-/-</sup> mice. *Spink5*<sup>-/-</sup>*Klk6*<sup>-/-</sup> appear macroscopically indistinguishable from the *Spink5*<sup>-/-</sup> displaying, detachment of the stratum corneum from the stratum granulosum and extensive desquamation.

## Significance of IL-17A-producing CD8+CD103+ skin resident memory T cells in psoriasis lesion and their possible relationship to clinical course

A number of studies have shown the relationship between the pathogenesis of psoriasis and skin resident memory T ( $T_{RM}$ ) cells. Kurihara K et al investigated the cytokine profile of TRM cells from skin lesions of psoriasis and the relationship of skin  $T_{RM}$  cells to the future clinical course of psoriasis. The biopsied skin revealed CD8+CD103+  $T_{RM}$  cells were present in the epidermis of psoriasis and associated with acanthosis. Sorted CD103+ T cells were mostly CD8+ memory T cells expressing CD69 with a skin-homing potential. A part of CD8+CD103+ T cells produced interferon- $\gamma$ , IL-17A or IL-22. Notably, CD8+CD103+  $T_{RM}$  cells more frequently produced IL-17A than did CD8+CD103- T cells. The frequency of CD8+CD103+IL-17A+  $T_{RM}$  cells tended to be higher in the advanced therapy group. These results suggest that IL-17A-producing CD8+CD103+  $T_{RM}$  cells are associated with a progressive clinical course of psoriasis.



**Fig. 1.** Fluorescence immunostaining of  $T_{RM}$  cells in psoriasis lesions. (a) Double immunofluorescent staining for CD3, CD4 or CD8 (red), and CD103 (green). The merged cells exhibit yellow.