Epidermal barrier maintenance and morphogenesis are molecularly distinct and ceramide synthase 4 (CerS4) is a novel key player in epidermal barrier maintenance

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1. Introduction

The homeostatic maintenance of a functional barrier is crucial for terrestrial life and disturbances in barrier maintenance cause a wide range of common inflammatory diseases.

How these barriers are maintained during homeostatic, adult tissue renewal and whether its malfunction drives barrier diseases are still open questions.

2. CerS4 controls homeostatic barrier maintenance

CerS4 is dispensable for the establishment of a functional epidermal barrier, but is crucial to maintain epidermal barrier homeostasis.

3. Barrier dysfunction precedes acanthosis and hyperkeratosis

Epidermal loss of CerS4 triggers a switch from an initially improved to an impaired barrier function in adult mice, suggesting temporally defined molecular changes in epidermal barrier composition.

4. Altered epidermal lipid barrier homeostasis

The dysbalance in ceramide composition and the excess of cholesterol chronically disturb the proper lipid packing of the lipid matrix, resulting in impaired barrier function.

5. Temporally defined changes in epidermal protein barrier composition

6. Barrier repair response molecularly resembles morphogenetic protein expression signatures

7. Model

Altered epidermal ceramide metabolism resulting from epidermal loss of CerS4, triggers temporally defined changes in skin barrier dysfunction, first disturbing epidermal lipid barrier homeostasis, which leads to an impaired epidermal barrier function, ultimately resulting in chronic skin barrier disease.