Staphylococcus aureus protease drives skin barrier disruption and facilitates allergen-induced inflammation

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Atopic dermatitis (AD) is the most common inflammatory skin disorder characterized by eczematous patches and intense pruritus.

Staphylococcus aureus colonization of AD skin has been shown to correlate with disease severity, potentially leading to the development of allergic conditions in other barrier tissues through a process known as the "allergic march". It is believed that *S. aureus* disrupts the barrier, facilitating penetration of and sensitization to seasonal and environmental allergens, intensifying itch; however, the underlying mechanisms remain unclear.

Our research uncovers that SspA, a serine protease secreted by *S. aureus*, plays a central role in percutaneous sensitization to a panel of clinically relevant allergens in AD: house dust mite, Alternaria alternata, peanut, grass pollen, cat hair, dog epithelia, and white birch pollen. When epicutaneously applied to shaved/depilated mouse skin, SspA destroyed keratinocyte junction proteins and damaged the epidermal permeability barrier, permitting transepidermal allergen penetration and leading to allergen-induced inflammation, allergen-specific immune priming, and itch.

Our results suggest that SspA links *S. aureus* skin colonization to allergen-induced inflammation through its epidermal barrier-directed proteolytic activity.