The extracellular serine protease from Staphylococcus epidermidis elicits a type 2 immune response in atopic dermatitis patients

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Abstract

Background: Atopic dermatitis (AD) is a chronic inflammatory skin disease caused by skin barrier defects and a misdirected type 2 immune response against antigens. The skin microbiome in AD is characterised by a reduction in microbial diversity with a dominance of staphylococci, including Staphylococcus epidermidis (S. epidermidis). To assess whether S. epidermidis antigens play a role in AD, we studied the immune response against the extracellular serine protease (Esp). Methods: We analyzed the binding of human IgG4 to S. epidermidis extracellular proteins using immunoblotting and mass spectrometry. We then measured serum antibodies specific for recombinant Esp by ELISA in healthy and AD individuals. We also stimulated T cells from AD patients and control subjects with Esp and measured the secreted cytokines. Finally, we analyzed the proteolytic activity of Esp against IL-33 and determined the cleavage sites by mass spectrometry. Results: We identified Esp as the dominant IgG4-binding antigen of S. epidermidis. Esp-specific IgE was present in human serum; AD patients had higher concentrations than controls. The T cell response to Esp in healthy adults was characterized by IL-17, IL-22, IFN-γ, and IL-10, whereas the AD patients' T cells lacked IL-17 production and released only low amounts of IL-22, IFN-γ, and IL-10. In contrast, Th2 cytokine release was higher in T cells from AD patients than from healthy controls. Mature Esp cleaved and activated the alarmin IL-33. Conclusions: Esp elicits type 2-biased response in AD patients. This suggests that S. epidermidis can aggravate AD through the allergenic properties of Esp.

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