Longitudinal changes in skin microbial populations as a function of atopic dermatitis severity
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Atopic dermatitis (AD) is an inflammatory skin disease associated with increased Staphylococcus aureus (SA) colonization. We and others have found an inverse relationship between levels of SA and a common skin commensal, Catheterium acnes (CA). As a intra-individual changes in the quantity of CA and SA from the skin of human subjects have not been well studied, we initiated a single-center, pragmatic, longitudinal study to address this, the design of which we present here. We hypothesize that CA, which produces antimicrobial peptides including cutumycin, limits SA growth in nonatopic (NA) and psoriasis (PS) subjects with low SA levels. The corollary is that AD subjects have higher SA levels due to lower levels of CA and/or CA strains producing lower levels of antimicrobial peptides. We are enrolling subjects (13-65 years) with moderate to severe AD (n = 30) receiving standard care, as well as age- and gender-matched subjects with moderate to severe PS (n = 30) and NA (n = 30) and following them for 1 year. At each visit, we assess disease severity, collect lesional and non-lesional skin swabs and serum, and measure skin barrier (transepidermal water loss). Our primary endpoint is relative abundance of SA, other Staphylococcus species from swabs are cultured on CHROMagar Staphylococcus. CA is confirmed with mannitol salt agar and PCR of Protein A (spa). CA is cultured anaerobically on tryptic soy agar with 0.5% Tween80 and confirmed by PCR of CA recombinase A (recA). Our primary endpoint is relative abundance of SA, other Staphylococcus species, and CA, as measured by CFUs. Our secondary endpoint will be to determine if conditioned media from CA clinical samples inhibits SA growth. We will also identify if CA samples contain genes necessary for the synthesis of antimicrobial peptides (cutumycin or lantibiotics) by PCR. Finally, we will evaluate this data across disease states (AD, PS, NA), disease severity, and treatments. The intra-individual changes observed in CA and SA over time and as a function of disease will provide valuable insights into host-microbe relationships in inflammatory diseases.

Tacrolimus induced pseudo-allergic reaction via Mas-related G protein coupled receptor-X2
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Tacrolimus is widely used in atopic dermatitis (AD), but the side effects of topical application effect the patient’s compliance with medication, such as itching and burning, of which the mechanism is not clear. Recent studies have revealed that Mas-related G protein-coupled receptor X2 (MRGRX2), a receptor on mast cells, mediating pseudo-allergic reaction in many contact dermatitis caused by topical drugs, which is similar to the side effects of tacrolimus. In this study, the mechanism in pseudo-allergic reaction caused by tacrolimus was investigated. Wild-type (WT) and Mrgr2β/-/- mice were used to observe local inflammation by Haematoxylin & Eosin and immunofluorescence staining. Release of tryptase, histamine and MCP-1 were measured in D2 cells with special hindered targeting MRGRX2 siRNA. We found WT mice exhibited inflammatory reaction in dorsal skin and footpad induced by tacrolimus, while Mrgr2β/-/- mice showed slighter reaction. The level of tryptase, histamine and other inflammatory cytokines were lower in mutated mice. Downregulation of Mrgr2β expression by siRNA. We found WT mice exhibited inflammatory reaction in dorsal skin and footpad following them for 3 years. At each visit, we assess disease severity, collect lesional and non-lesional skin swabs and serum, and measure skin barrier (transepidermal water loss). Our primary endpoint is relative abundance of SA, other Staphylococcus species from swabs are cultured on CHROMagar Staphylococcus. CA is confirmed with mannitol salt agar and PCR of Protein A (spa). CA is cultured anaerobically on tryptic soy agar with 0.5% Tween80 and confirmed by PCR of CA recombinase A (recA). Our primary endpoint is relative abundance of SA, other Staphylococcus species, and CA, as measured by CFUs. Our secondary endpoint will be to determine if conditioned media from CA clinical samples inhibits SA growth. We will also identify if CA samples contain genes necessary for the synthesis of antimicrobial peptides (cutumycin or lantibiotics) by PCR. Finally, we will evaluate this data across disease states (AD, PS, NA), disease severity, and treatments. The intra-individual changes observed in CA and SA over time and as a function of disease will provide valuable insights into host-microbe relationships in inflammatory diseases.

A case of phaeohyphomycosis caused by Corynespora cassicola, a plant pathogen
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Corynespora cassicola is a common plant pathogen. Humans infected by C. cassicola are extremely rare. We report a case of subcutaneous and pulmonary phaeohyphomycosis caused by C. cassicola in a 68-year-old male Chinese. The clinical manifestations were ulcers on the upper arm skin with erosions, scabs, and infiltrative plaques. The pulmonary manifestations presented with cough, chest tightness, and fever. The organism was identified as C. cassicola based on the morphology and the sequence of the internal transcribed spacer region of the ribosomal RNA gene. CARD9 deficiency has been reported to underlie several fungal infections. By employing whole-exome capture, compound heterozygous sequence variants were found in the CARD9 gene, c.106C>T (p.Gln36*) and c.1118G>C (p.Arg373-Pro). The patient was cured by the antifungal drug voriconazole, based on repeated fungal microscopy and culture which were negative. The skin lesion gradually healed, leaving scar and erosive surface. There are less than 10 reports on subcutaneous infection by C. cassicola, and this case is unique with concomitant subcutaneous and pulmonary phaeohyphomycosis highlighting the role of CARD9 in the human immune response in controlling fungal infections. In summary, this case emphasizes the importance of genes susceptibility to certain microbial infections.

S. aureus superantigens enhance viral pathogenesis of the skin epithelium
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Staphylococcus aureus (SA) is a frequent skin pathogen that can cause infection by a number of different virulence factors (SAgs) including superantigens (SAgs). Previously we had observed that eczema herpeticum, another AD viral infection, is enhanced by SA superantigens. To test this we decided to create a primary human keratinocyte model to observe the effect of superantigens on primary human keratinocytes (PHFK) cultured with purified SE Q, as a virulence factor of interest. Treatment of PHFK with purified SE Q, namely SE Q, enhanced epithelial cell death and beta III tubulin expression in PHFK. To test the effect of SA superantigens on keratinocytes we incubated USA300 supernatant with USA300 supernatant with purified SE Q, as a virulence factor of interest. Treatment of PHFK with purified SE Q, namely SE Q, enhanced epithelial cell death and beta III tubulin expression in PHFK. To test the effect of SA superantigens on keratinocytes we incubated USA300 supernatant with purified SE Q, as a virulence factor of interest.