Epidermal invasion by Malassezia spp. yeasts in 3D-reconstructed tissue

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Being usually harmless commensal components of the skin microbiome, Malassezia spp. sometimes become involved in human disorders like pityriasis versicolor where yeasts proliferate on the skin surface and contribute to skin irritation. Several genome analyses have provided evidence on metabolic functions of the yeast, but these studies have not focused on the 3D architecture of cell layers. We performed genome-wide RNA-seq analyses of 22 human skin fibroblast cell lines (dermal fibroblasts and keratinocytes) and 3D reconstituted human skin models (epidermal and dermal layers). Previous reports on dermal fibroblasts suggest a model for how microorganisms may modulate skin health. To test this, we will use this with ex vivo human skin layers and synthetic skin microbial communities consisting of B12 producers and users to examine the effects on community dynamics when B12 biosynthesis is depleted.

Comprehensive succinylome profiling reveals the pivotal role of lysine succinylation in energy metabolism and quorum sensing of Staphylococcus epidermidis

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Lysine succinylation is a newly identified PTM, which exists widely from prokaryotes to eukaryotes and participates in various cellular processes, especially in the metabolic processes. Staphylococcus epidermidis is a commensal bacterium in the skin, which attracts more attention as a pathogen. However, the significance of lysine succinylation in proteins of S. epidermidis has not been investigated. We performed the first comprehensive succinylome analysis of S. epidermidis (ATCC 12228) using the LC-MS/MS technology and in-depth bioinformatics analysis. A total of 1557 succinylated lysine sites in 649 proteins were identified in S. epidermidis. Gene Ontology, KEGG enrichment, and PPI analysis suggested that lysine succinylation played a pivotal role in energy metabolism, especially the glycolysis/gluconeogenesis process. One succinyltransferase (Skt14A) was identified and further functional analysis showed that Skt14A knockdown significantly impaired growth and biofilm formation. 15 succinyltransferases and 18 desuccinylases were predicted that might be involved in lysine succinylation process. The specific motif KsuD was conserved in model prokaryotes and specific bacterial species. In summary, lysine succinylation plays a pivotal role in energy metabolism, especially the glycolysis/gluconeogenesis pathway, as identified in S. epidermidis. Our findings may provide new insights into the regulation of S. epidermidis and offer potential targets for antibiotic development.

Investigation of vitamin B12 sharing within the skin microbiome

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The skin microbiome has a key role in supporting necessary functions that promote skin health, including protection from pathogens and immunomodulation. One critical element in the skin microbiome is vitamin B12 synthesis. In the legend, we propose a new model for vitamin B12 synthesis in the skin microbiome. Based on this model, we propose a new role for vitamin B12 in the skin microbiome.

Female hormones enhance HIV-1 acquisition in female Langerhans cells, but not in male Langerhans cells

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Hormonal contraceptives, which are composed of progesterone with or without estrogen, are used by women to prevent pregnancy. A recent study reported that the use of combined oral contraceptive pills increased the risk of HIV acquisition about two-fold in women of heterosexual HIV-1-serodiscordant couples. However, the underlying mechanism is not determined. Langerhans cells (LCs) distributed in vaginal epithelium and skin epidermis are the initial cellular target of HIV-1. HIV-1 productively infects LCs through CD4 and CCR5 on LCs, followed by migration of HIV-1-infected LCs to draining lymph nodes. Dendritic cells (DCs) distributed in vaginal lamina propria and skin dermis could be a target of HIV-1 in the female. To determine whether and how vitamin B12 sharing with bacterial or viral pathogens in female and male LCs, we generated monocyte-derived LCs and DCs (mLCs and mDCs, respectively). Pretreatment of female mLCs, but not male mLCs, with 17β-estradiol or progesterone increased HIV-1 infection about two-fold. Pretreatment of female and male mDCs with 17β-estradiol or progesterone did not modulate HIV-1 infection. Both 17β-estradiol and progesterone increased HIV-1 infection in mDCs from both premenopausal and postmenopausal female, suggesting that female hormones enhance the risk of HIV-1 acquisition in female mDCs. Interference of receptors for estrogen and progesterone did not inhibit the increased risk of HIV-1 acquisition by female hormones in female mDCs. Collectively, female hormones enhance risk of HIV-1 acquisition in female LCs thought unknown putative signaling pathway.

Rare presentation of Vesiculobullous Lyme Disease: A case series

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Early Lyme-associated erythema migrans most commonly manifests with a “targetoid” appearance. However, several erythema migrans variants have been reported, which may result in misdiagnosis and delayed diagnosis and treatment. This case series presents a rare variant of bullous erythema migrans. Case 1: A 54-year-old woman presented with a waxy, non-tender, moist, non-widening lesion on her leg. She reported a sudden onset of stinging in the area while walking outdoors. A darkening vesiculobullous rash appeared soon after. A differential of atypical Lyme disease, Sweet’s syndrome, and Herpes Zoster was considered. Her symptoms improved rapidly with empiric doxycycline treatment and serum IgM antibody at three weeks confirmed a Lyme disease diagnosis. Pathology findings showed hyperkeratosis and acanthosis with prominent papillary dermal perivascular lymphocytic infiltrate. Case 2: A 42-year-old female presented four days after the appearance of an enlarging, darkening rash on her leg. The rash developed vesiculobullous changes soon after it appeared. The patient was empirically treated with a 21-day course of doxycycline and rapidly improved. Several weeks later, positive IgM Lyme studies confirmed an atypical Lyme diagnosis. Case 3: A 65-year-old female presented with a three day history of a swollen, painful rash on the left flank. Central dusky papulovesicles developed soon after the appearance of the rash. The patient was empirically treated with a 21-day course of doxycycline and rapidly improved. In summary, our findings highlight the potential for bullous reactions in Lyme disease and the importance of prompt recognition and empirical treatment of atypical presentations. Thus, a low threshold to consider Lyme disease in the differential diagnosis of bullous lesions is warranted in endemic areas.

TNF directs protective neutrophil and IL-17γ T cell responses against Staphylococcus aureus skin infections

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Staphylococcus aureus is the leading cause of skin and soft tissue infections and has become a major health burden due to the emergence of antibiotic-resistant strains. To develop alternative therapies to antibiotics, we sought to understand the protective immune mechanisms against S. aureus skin infections mediated by tumor necrosis factor (TNF). TNF is a pro-inflammatory cytokine that is rapidly induced upon S. aureus exposure and whose inhibition is associated with increased risk of S. aureus infections in humans. However, the contribution of TNF or the cognate receptors, TNFR1 and TNFR2, to host defense against S. aureus skin infection whereby TNF, TNFR1, or TNFR2 deficient mice are protected from S. aureus skin infection. In summary, our findings demonstrated that TNF promotes the previously identified protective neutrophil abscission and IL-17γ T cell responses against S. aureus skin infection. In fact, TNF deficient mice had significantly impaired neutrophil recruitment, abscess formation, and IL-17γ expression and whose inhibition is associated with increased risk of S. aureus skin infection. Together, these findings indicated that differential TNF signaling by TNFR1 and TNFR2 directs protective neutrophil and IL-17γ T cell responses during S. aureus skin infections, which may provide new insights into the development of novel immune-based therapies as alternatives to antibiotic treatment against S. aureus and potentially other bacterial infections.