**205**

Evaluation of SARS-CoV-2 spike protein response on PI3K agonist-mediated IL-8 release

C.E. Borchers, A. Bongers, T. Wright, J.A. Haynes, L. Long, T. McCormick, and R. Sahu

The distinct skin microbiota of congenital ichthyoses

A. Paller, R. Derendorf, R. Wroblewski, J. Seelig, and T. McCormick

**207**

Targeting of HDAC8 and HDAC9 in keratinocytes to enhance skin immune defense


We have recently reported that short-chain fatty acids (SCFA) promote an inflammatory response in keratinocytes by suppression of HDAC8 or HDAC9, specific histone deacetylases whose activity increases tolerance of the skin to inflammatory signals. Upon silencing of HDAC8 or 9 in keratinocytes, subsequent exposure to TRAIL, TNF, or TLR7 ligands augments inflammatory cytokine production in keratinocytes, but this effect does not occur in bone-marrow derived cells, thus demonstrating epidermal specificity of this mechanism. Chip-Seq and signal pathway analysis by RNA-Seq identified MAP2K1 as a key intermediate in this process, with increased acetylation at H3K9 and H3K27 in the MAP2K1 promoter after silencing HDAC8 and HDAC9 or inhibition of HDAC activity by SCFA butyrate. Antibody pull-down analyses showed that HDAC8 and HDAC9 interacted with the FACT complex and promoted FACS on survival of S. aureus. Topical treatment of mice with butyrate upregulated antibacterial peptide production (CAMP and MB4D) and subsequently inhibited S. aureus in mice despite elevated Th2 cytokines generated in an MC903-induced AD model. These observations show a novel approach to enhance host defense against pathogens on skin.

**208**

Sarecycline demonstrates reduced activity against representative fungal and bacterial species commonly found in the human gastrointestinal tract

MA. Channam, L. Long, S. Joussef, T. McCormick and A. Grada

**209**

Epidemial interferon expression is positively regulated by Staphylococcus aureus in SEI and involves the STING pathway

S. Siblosihannana, MK. Sarkar, H. Stickeen, J. Banfield, J. Gudjonsson, and J. M. Kahlenberg

University of Michigan, Ann Arbor, Michigan, United States

Cutaneous infection is exhibited by many systemic lupus erythematosus (SLE) patients. Keratinocytes are an important source of type I interferons (IFNs) which plays crucial roles in surveillance of microbial and environmental stresses as well as in pathobiology of IFN-driven skin diseases. We hypothesized that microbial dysbiosis is an underexplored aspect of cutaneous IFN production. We tested this hypothesis using an unprecedented global pandemic. While the mode of COVID-19 infection, its structural similarity to the SARS coronavirus (SARS-CoV-2), and the cytokine storm associated with it have consequently been the main focus of research, reports have also indicated certain differences in its clinical presentation when compared with SARS-CoV. These differences have been attributed to the adaptation of SARS-CoV-2 to the human host by acquiring glycoprotein genes from the bat SARS-like coronavirus. The recent emergence of SARS-CoV-2 has caused an unprecedented global pandemic. While the mode of COVID-19 infection, its structural configuration, and multiple mechanisms of action including the critical roles of spike proteins have been substantially explored, elucidation of signaling pathways regulating its cellular responses is yet to be fully determined. Among major signaling cascades, phosphoinositide 3-kinases (PI3K) and its downstream pathways have been exploited as the potential therapeutic targets for COVID-19, and its activation induces the release of cytokines such as interleukin-8 (IL-8). Furthermore, HDAC8 and HDAC9 silencing in keratinocytes lead to IFN- 

**210**

Eosinophil-derived IL-17 protects against epicutaneous Staphylococcus aureus infections

NA Orlando, C. Youn, S. Nolan, M. Alphonse, D. Dikeman, Y. Wang, G. Patrick, L. Miller, and N. Anderson

Almirall, Exton, Pennsylvania, United States, 2 Department of Dermatology, Icahn School of Medicine at Mount Sinai, New York, New York, United States

The distinct skin microbiota of congenital ichthyoses

A. Paller, R. Derendorf, R. Wroblewski, J. Seelig, and T. McCormick

The ichthyoses are genetic keratinization disorders with an impaired epidermal barrier and frequent bacterial and fungal infections. Congenital ichthyoses have been recently uncovered as a novel mechanism whereby eosinophil-derived IL-17 protects against S. aureus infections, which has implications in the development of immune-based therapies against S. aureus and potentially other skin infections.