ABSTRACTS | Adaptive and Auto-Immunity

031 Single cell transcriptomic analysis of cutaneous T cells in psoriasis
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Psoriasis is a chronic skin condition characterized by skin inflammation that affects 125 million people worldwide. However, the underlying pathways contributing to psoriasis pathogenesis have not been fully elucidated. This project utilizes single-cell transcriptomes of T cells from healthy and psoriatic skin to aid in identifying key biomarkers and pathways of psoriasis. T cells were clustered into subtypes and differential gene expression analysis performed was between lesional and healthy skin to help identify psoriatic marker genes in each T cell subtype. Regulatory CD4+ T cells in psoriatic lesional skin were found to have less IL-17, but more TNF, IL-6, IFN-g production compared to CD4+ T cells from healthy skin. This suggests the presence of a unique regulatory T cell subset in psoriasis.

032 A multiplex skin-targeted COVID-19 vaccine elicits robust humoral and cellular immune responses
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Considerable progress has been made toward development of COVID-19 vaccines in the past year. However, there is still a need for effective, safe, self-administered vaccines. We are developing an alphanumeric COVID-19 SARS-CoV-2 vaccines to enable sustainable immunization programs against COVID-19. To address this need, we hypothesized that harnessing the immune-responsive cutaneous microenvironment using microray patches (MAPs) to deliver integrated SARS-CoV-2 vaccine components would bring together biologic advantages of targeted vaccine delivery and induce skin-specific immune responses.

For this study, we injected C57BL/6 mice with 1 µg of MAPs in a 5 µl volume via traditional intramuscular injection, and MAP immunization obviates adverse effects of intramuscular delivery of adjuvants, suggesting improved safety and efficacy compared to conventional vaccination routes. These results are supported by our translational studies utilizing ex vivo human skin. The MAP vaccines are under development for human clinical trials.

033 IL-15 is an unexpected guardian of hair follicle immune privilege and promotes human hair growth ex vivo
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Contrary to its pro-inﬂammatory role in chronic inﬂammatory disorders including psoriasis, IL-15 enhances HA growth in human epithelia. Studies in recent years have suggested a pathogenic role for IL-15 in human epidermis. Studies in recent years have suggested a pathogenic role for IL-15 in human psoriasis. In this study, we have investigated the role of IL-15 in human HA growth. Using organ-cultured HA, we found that IL-15 increases HA growth. IL-15 signaling is mediated by the IL-15 receptor, which is expressed on keratinocytes. These findings suggest that IL-15 plays a role in human HA growth.

034 Dysregulation of VISTA expression and functionality in psoriatic monocytes and Mo-MDSCs
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V-domain Immunoglobulin Suppressor of T cell activation (VISTA) is an inhibitory B7 family member that is involved in immune modulation in tumors. We are currently investigating whether VISTA is involved in immune modulation in psoriasis.

Recent research has suggested that VISTA is upregulated in psoriasis. We have found that VISTA expression is increased in psoriatic monocytes and Mo-MDSCs. These findings suggest that VISTA may have a role in immune modulation in psoriasis.

035 Expansion of bacterial phosphatidyglycerol reactive CD4+ T cells in atopic dermatitis
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CD1a, a lipid antigen-presenting molecule structurally related to MHC class I, is constitutively expressed on Langerhans cells in human epidermis. Studies in recent years have suggested that the expression of CD1a is regulated by the immune system. In this study, we have investigated the role of CD1a in human epidermis. Using organ-cultured HA, we found that the expression of CD1a is increased in human epidermis. These findings suggest that CD1a plays a role in human epidermis.

036 IL-23 maintains tissue resident memory TH17 cells in murine and psoriatic skin
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Tissue resident memory TH17 cells (Tρ17) are the key cell type driving the chronic skin inflammation of psoriasis. Although IL-23 is strongly associated with autoimmune and chronic inflammatory disorders including psoriasis, anti-IL-23 biologic agents have variable efficacy in the treatment of psoriasis, the precise role of IL-23 in supporting Tρ17-mediated skin inflammation remains unclear. In mice, we found that circulating memory Tρ17 cells are dispensable for anamnestic protection from C. albicans skin infection, and Tρ17-mediated protection from C. albicans re-infection requires IL-23. Administration of anti-IL-23 zolotumab to adult mice following resolution of primary C. albicans infection resulted in a selective reduction in the number of CD69+CD103+ Tρ17 in skin in comparison with isotype controls. Tρ17 pro-inflammatory cytokine production was increased in skin following their rechallenge in skin. In human skin, anti-IL-23 therapy increased the expression of cDC2 as the principal source of IL-23, but increased keratinocytes and cDC4 T cells were additional sources of IL-23 in psoriatic skin. Analysis of human psoriatic skin before and after clinical anti-IL-23 therapy revealed reduced retention of Tρ17 in association with reduced IL-23 expression. These findings suggest that IL-23 is an important enhancer of the major mechanism by which anti-IL-23 therapy induces uniquely durable disease-free intervals in psoriasis patients.