ABSTRACTS | Adaptive and Auto-Immunity

031 Single cell transcriptomic analysis of cutaneous T cells in psoriasis
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Psoriasis is a chronic inflammatory disease characterized by skin and systemic 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 transcriptomics of T cells from healthy and psoriatic skin in an effort to identify key biomarkers and pathways of psoriasis. T cells were clustered into subtypes and differential gene expression analysis was performed between lesional and healthy skin to identify psoriatic marker genes in each T cell subtype. Regulatory CD4+ T cells in psoriatic lesional skin were found to be increased, which can be efficaciously targeted by our CD1a-LPG tetramer-induced signaling, NF-kB signaling, and cutaneous pathological pathways. As a result, psoriatic Tregs may suppress several of the pathways behind psoriasis and drive inflammation via IL-33, which has been previously found to be significantly upregulated in plaque psoriasis. Future work includes using VDJ analysis to more closely investigate psoriatic TCR abnormalities and to incorporate more patient data.

032 A multicomponent skin-targeted COVID-19 vaccine elicits robust humoral and cellular immune responses
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To address this need, we hypothesized that harnessing the immune-responsive cutaneous microenvironment using microarray patches (MAPs) to deliver integrated SARS-CoV-2 vaccine can provide a unique solution. Here, we present our 3D printing-enabled dissolving MAPs to deliver a recombinant SARS-CoV-2 protein antigen, with or without an innate immune agonist. Immune microarrays of vaccine-loaded MAPs generate robust antibody and cellular immune responses, and multicomponent (antigen plus adjuvant) MAP vaccination ameliorates 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 freshly-excised human skin, suggesting that multicomponent MAPs induce greater expression of co-stimulatory molecules by human skin-migratory DCs, which may contribute to enhanced immune responses. Ultimately, the simplicity, thermostability, immunogenicity, and versatility of MAPs may enable novel vaccination strategies and improve the effectiveness of global immunization campaigns against SARS-CoV-2 and other existing or novel pathogens.

033 IL-15 is an unexpected guardian of hair follicle immune privilege and promotes human hair growth ex vivo
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Success of long-lasting aleukemia eradication (AA) treatment requires targeting of the key pathomechanisms, i.e., collapse of hair follicle (HF) immune privilege (IP) and premature catagen induction. Recent research has suggested that the pleiotropic cytokine, interleukin-15 (IL-15), is involved in AA pathobiology and that inhibiting IL-15-induced signaling may be beneficial in AA therapy. Yet, this concept has not yet been assessed in human scalp hair follicles (HHFs). Specifically, since HHF-IP is restored following re-initiating hair growth and for preventing relapse of AA, it is crucial to clarify the impact of IL-15 on human HF-IP and HF cycling. Here we show that IL-15+ cell number is increased while IL-15 receptor alpha protein expression is decreased in AA-affected human scalp HHFs compared to healthy human scalp skin. Organ-cultured, healthy human anagen scalp HHFs were treated with recombinant human IL-15 (rhIL-15), while IL-15 receptor expression was restored in AA-affected human scalp HHFs when treated with IL-15. rhIL-15 was significantly prolonged and hair matrix keratinocyte apoptosis inhibited. Moreover, expression of MICA and MHC class I was restored while hair bulb transformation was decreased. Differences in these target genes between AA and healthy scalp HHFs indicate that IL-15 is responsible for AA. Overall, our results suggest a novel role for IL-15 in human scalp HHFs in facilitating HF cycling, and re-initiating hair growth and preventing AA relapse.

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 immune-checkpoint molecule. VISTA is highly expressed on myeloid, hematopoietic and cancer cells and participates in T cell-mediated autoimmunity and antimicrobial immunity, playing a broad role in regulation of myeloid- and T cell-mediated immunity. VISTA is upregulated on myeloid-derived suppressor cells (MDSCs) from AML patients. We previously reported MICA and MHC class I were less effective in reducing IL-6 in Pso-Mo compared to HC (average IL-6 after VSIG-3 relative expression is 4.0% of Mo in HC vs Pso, n=4, p<0.01). Intracellular signaling for human Mo activation via LPS attenuated VISTA gene expression in HC and Pso patients, suggesting VISTA expression is sensitive to inflammatory status. A novel VISTA ligand in V-Set and Immunoglobulin domain containing 1 (VSG-15); consistent with a functional role for VISTA in human Mo, we found that VSG-1 stimulation of CD14+ Mo attenuates IL-6 expression. In Pso patients, VSG-1 was less effective in reducing IL-6 in Pso-Mo compared to HC average IL-6 after VSG-1 stimulation was lower than VSG-1 stimulation in HC (average IL-6 after VSG-1 stimulation was 66% ± 7.1% in HC versus a minimal effect on IL-6 of 69% ± 7.0% in Pso, n=2, p<0.05). Thus, in addition to T cell signals, VISTA expression/signaling is implicated in human Mo activation/dysregulation in Pso. VISTA pathway targeting may represent a novel immune rebalancing approach in Pso and related inflammatory diseases whose engagement inhibits T cell proliferation as well as cytokine and chemokine production, demonstrated previously by VSG-1 inhibition of anti-CD3-induced IL-17 secretion in PBMCs.

035 Expansion of bacterial phosphatidylglycerol reactive CD4+ T cells in atopic dermatitis
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Bacterial phosphatidylglycerol (PG) is a major component in lipid A from Gram-negative bacteria. PG elicits T cell immune responses in atopic dermatitis (AD) patients. A Pilot study in atopic dermatitis (AD) patients with self-reported disease characteristics that affect 125 million people worldwide. However, the underlying pathways contributing to psoriasis pathogenesis have not been fully elucidated. This project utilizes single-cell transcriptomics of T cells from healthy and psoriatic skin in an effort to identify key biomarkers and pathways of psoriasis. T cells were clustered into subtypes and differential gene expression analysis was performed between lesional and healthy skin to identify psoriatic marker genes in each T cell subtype. Regulatory CD4+ T cells in psoriatic lesional skin were found to be increased, which can be efficaciously targeted by our CD1a-LPG tetramer-induced signaling, NF-kB signaling, and cutaneous pathological pathways. As a result, psoriatic Tregs may suppress several of the pathways behind psoriasis and drive inflammation via IL-33, which has been previously found to be significantly upregulated in plaque psoriasis. Future work includes using VDJ analysis to more closely investigate psoriatic TCR abnormalities and to incorporate more patient data.