work includes using VDJ analysis to more closely investigate psoriatic TCR abnormalities and Tregs may amplify several of the pathways behind psoriasis and drive inflammation via IL-32, Cheret1 and R Paus1,2,4 expression analysis was performed between lesional and healthy skin to identify psoriatic psoriasis pathogenesis have not been fully elucidated. This project utilizes single-cell tran-
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Psoriasis is associated with abnormal function of the 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 transcrip-
tomes 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 psoriasis lesional skin were found to be significantly expanded and can be efficaciously targeted using our IL-2 DI pentamer-enabled disables to deliver a recombinant SARS-Cov-2 protein antigen, with or without an innate immune agonist. Immuneization of mice with vaccine-loaded MAPs generates robust antibody and cellular immune responses, and multicomponent (antigen plus adjuvant) MAP vaccination confers robust protection against disease and sSpFc-specific and sSpFc-virus-specific Th1 and IgG2c responses, which are vital for control of SARS-CoV-2 viral infection. Notably, multi-
component MAP vaccination results in increased immune responses compared to immu-
ization 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 freshly-exsanguinated 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 im-
crease the effectiveness of global immunization campaigns against SARS-CoV-2 and other existing or novel pathogens.

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**IL-15** in an unexpected guardian of hair follicle immunity and promotes human hair growth ex vivo

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Successional long-lasting asepsia area (AIA) treatment requires targeting of the key patho-
mechanisms, 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 (HFs).

Specifically, since HF-IP restoration is required for 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 HFs compared to healthy human scalp skin. When organ-cultured, healthy human anagen scalp HFs were treated with recombinant human IL-
15 (rIL-15), angain was significantly prolonged and hair matrix keratinocyte apoptosis inhibited. Moreover, expression of MiCA and MHC class I was reduced while hair bulb expression of the potent IP guardian, a-MSH, was increased by 50 and 100 ng/ml rIL-15 ex vivo. Importantly, if rIL-15 was administered before the HF IP collapse induction by IFNg, the increased expression of the NK2CG-activating "danger" signal, MICA, and MHC class I as well as the decreased expression of a-ASH induced by IFNg were all prevented. Taken together, despite its involvement in autoimmune diseases, IL-15 operates as an IP guardian and hair growth promoter in human HFs, while IL-13RAa signaling is defective in AA.

Therefore, selective stimulation, rather than inhibition, of IL-15RA-mediated signaling is likely to be beneficial in the future management of AA and possibly other inflammatory hair loss disorders.

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**Disregulation 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 MDSCs are increased but functionally impaired in psoriasis (PsO); VISTA knock-out (KO) mice exhibit PsO-like inflammation. VISTA-KO mice exhibit PsO-like inflammation. Whether VISTA signaling is related to PsO MDSC dysregulation is unknown. We analyzed the expression and function of VISTA in PsO and healthy control (HC) monocytes (Mo) using flow cytometry. Mo-MDSC (CD14+HLA-DR+CD16-) were elevated in PsO patients, and, as hypothesized, VISTA surface expression was elevated (1.6±0.9 vs 13±4.0 % of Mo in HC vs PsO, n=3, p<0.01). Intact 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 3 (VSG-3); consistent with a functional role for VISTA in human Mo, we found that VSG-3 stimulation of CD14+ Mo attenuates IL-6 expression. In PsO patients, VSG-3 was less effective in reducing IL-6 in PsO-Mo compared to HC (average IL-6 after VSG-3 relative to LPS alone of 66.±7.1 % in HC versus a minimal effect of IL-6 of 89.±7.0 % in PsO, n=2, p<0.05). In addition, to T cell signals, VISTA expression/signaling is implicated in human Mo activation. PsO dysregulated in PsO. VISTA pathway targeting may represent a novel human imme-

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**Expansion of bacteriophage gp45glycerol reactive CD4+ T cells in atopic dermatitis**

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CD1a, a lipid antigen-presenting molecule structurally related to MHC class I, is constitu-

tively expressed on Langerhans cells in human epidermis. Studies in recent years have sug-
gested a pathogenic role for CD1a in inflammatory and allergic skin disease. We have recently detected a subset of CD1a-restricted CD4+ T cells that specifically responds to bacterial phospatidylglycerol. In particular, lys-phospatidylglycerol (LPG), an amnio-
acylated membrane lipid present in many gram-positive bacteria, including S. aureus, binds to CD1a and is recognized by these T cells. Using CD1a tetramers loaded with LPG, we detected CD1a-LPG staining T cells in the peripheral blood of multiple donors, and were able to isolate and expand these cells in vitro. The majority of tetramer+ T cells were CD4+ CD8- T cells, and responded in a dose-dependent manner to LPG. CD1a-LPG reactive T cell lines showed a predominantly Th2 cytokine profile, with abundant IL-4 and IL-13 release. Beyond the recognition of purified lipid antigen, CD1a-LPG reactive T cells also responded to whole bacteria, as CD1a-expressing dendritic cells pre-incubated with S.aureus induced IL-13 release from the T cell lines. The increased bacterial skin colonization in atopic dermatitis (AD), specifically with S.aureus, prompted us to investigate the presence of CD1a-LPG reactive T cells in AD. A pilot study in atopic dermatitis patients showed a significantly increased frequency of CD4+ CD1a-LPG tetramer+ T cells in the blood of AD patients. Ongoing work aims to understand the contribution of CD1a-LPG reactive T cells to Th2 mediated pathology in AD.

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**IL-23 maintains tissue resident memory Th17 cells in murine and psoriatic skin**

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Tissue resident memory Th17 cells (TmaTh17) are the key cell type driving the chronic skin inflammation of psoriasis. Although IL-23 is strongly associated with autoimmunity and chronic inflammatory disorders including psoriasis, and anti-IL-23 biologic agents have shown efficacy in the treatment of psoriasis, the precise role of IL-23 in supporting IL-17-mediated skin inflammation remains unclear. In mice, we found that circulating memory T cells are dispensable for anamnestic protection from C. albicans skin infection, and TmaTh17 mediated protection from C. albicans reinfection requires IL-23. Administration of anti-IL-23 mAb (AINT17) is devoid of effect in C. albicans-infected mice following resolution of primary C. albicans infection resulted in a selective reduction in the number of CD69+CD101+ TmaTh17 cells in skin compared with isotype controls. TmaTh17 pro-
duction and survival in skin is increased in the absence of IL-23. These results support that IL-23 maintains tissue resident memory Th17 cells in murine and human skin can be efficiently targeted using our 3D printing-enabled dissolving MAPs to deliver a recombinant SARS-CoV-2 protein antigen, with or without an innate immune agonist. Immuneization of mice with vaccine-loaded MAPs generates robust antibody and cellular immune responses, and multicomponent (antigen plus adjuvant) MAP vaccination confers robust protection against disease and sSpFc-specific and sSpFc-virus-specific Th1 and IgG2c responses, which are vital for control of SARS-CoV-2 viral infection. Notably, multi-
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