031 Single cell transcriptomic analysis of cutaneous T cells in psoriasis

S Aher1, J Liu2, D Bhatt1, M Pauli1, M Rosenblum1, P Nanzanilo1 and W Liao1
1 University of California San Francisco, San Francisco, California, United States and 2 Immunology and Oncology, Argen Research, South San Francisco, California, United States

Psoriasis is a chronic immune-mediated disease 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 transcriptomics of T cells from healthy and psoriatic skin 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 express a predominantly Th2 cytokine profile, with abundant IL-4 and IL-13 release. Beyond Th2 cytokines, regulatory CD4+ T cells were found to express a Th17-like cytokine profile, with increased IL-17A and IL-22 production. This study demonstrates the complexity of the immune response in psoriasis and highlights the potential for targeted therapies to modulate specific T cell subtypes.

032 A multicomponent skin-targeted COVID-19 vaccine elicits robust humoral and cellular immune responses

K Abu-Salah1, J Liu2, D Bhatt1, M Pauli1, M Rosenblum1, P Nanzanilo1 and W Liao1
1 University of California San Francisco, San Francisco, California, United States and 2 Immunology and Oncology, Argen Research, South San Francisco, California, United States

Considerable progress has been made toward development of COVID-19 vaccines in the past year. However, there is still a need for vaccines that are effective against new and existing SARS-CoV-2 variants. In this study, we developed a multicomponent skin-targeted vaccine using 3D printing technology. This vaccine was shown to be highly immunogenic and effective against a range of SARS-CoV-2 variants. The vaccine was tested in a murine model and was shown to elicit robust humoral and cellular immune responses, including high levels of neutralizing antibodies and CD8+ T cells specific to the SARS-CoV-2 spike protein. This study demonstrates the potential of multicomponent skin-targeted vaccines for the treatment of COVID-19 and other infectious diseases.

033 IL-15 is an unexpected guardian of hair follicle immune privilege and promotes human hair growth ex vivo

T Suzuki1, T Scala1, G Ehrhardt2, C Nicu3, J Sullivan4, G Epstein-Kuka5, T Purba6, J Chen7, R Rausch1, T. Naksoud1, J. Gaffli1, A. Holmfeldt1, K. Oberschall2, T. Norman3, T. Hlaing4, G. Sillers4, A. Jiao4, J. Segal5, Y. Qian5, S. Ng6, L. Bao6, Z. Wang6, W. Bao6, J. Shanks6, R. Van Der Meulen7, M. P. Van Den Berghe8, M. Ghishan9 and K. J. Coyle1
1 Department of Dermatology, University of California, San Francisco, California, United States, 2 Department of Immunology, Hair Research Institute, Los Angeles, California, United States, 3 Department of Dermatology, United Medical Hospital, Sapporo, Japan, 4 Department of Immunology, Showa University, Koshigaya, Saitama, Japan, 5 Department of Medicine, University of California San Francisco, California, United States, 6 Department of Medicine, University of California San Francisco, California, United States, 7 Department of Dermatology, Stanford University, Stanford, California, United States, 8 Department of Dermatology, University of Oxford, Oxford, United Kingdom, 9 Department of Dermatology, University of California Berkeley, Berkeley, California, United States

Psoriasis is an immune-mediated 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 express a predominantly Th2 cytokine profile, with abundant IL-4 and IL-13 release. Beyond Th2 cytokines, regulatory CD4+ T cells were found to express a Th17-like cytokine profile, with increased IL-17A and IL-22 production. This study demonstrates the complexity of the immune response in psoriasis and highlights the potential for targeted therapies to modulate specific T cell subtypes.

034 Dysregulation of VISTA expression and functionality in psoriatic monocytes and Mo-MDSCs

K Ohno1, S McCormick2, G Hill3, J Wang4 and KD Cooper1
1 Dept. Dermatology, University of California San Francisco, San Francisco, California, United States and 2 Dermatology, University of Oxford, Oxford, United Kingdom

VISTA (V-domain Immunoglobulin Domain Containing A Member 1) is an immune-checkpoint molecule. VISTA is highly expressed on myeloid, hematopoietic and cancer cells and participates in T cell-mediated autoimmunity and antitumor 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. VISTA knockout (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 ex vivo human monocytes and Mo-MDSCs and healthy control (HC) monocytes (Mo) using flow cytometry. Mo-MDSCs CD14+HLA-DR+CD11c+ were elevated in PsO patients, and, as hypothesized, VISTA surface expression was elevated (CD84:0.9; CD85:1.2, n=4, p<0.01). Immune 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 (VSIG-1); consistent with a functional role for VISTA in human Mo, we found that VSIG-1 stimulation of CD14+ Mo attenuates IL-6 expression. In PsO patients, VSIG-1 was less effective in reducing IL-6 in PsO-Mo compared to HC (average IL-6 after vs 1/3 relative to LPS alone of 66.7±1.7% in HC versus a minimal effect on IL-6 of 89±7.0% in Pso, n=3, p>0.05). This, in addition to T cell signals, VISTA expression/signaling is implicated in human Mo activation and is regulated 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 VSIG-1 inhibition of anti-CD3-induced IL-17 secretion in PBMCs.

035 Expansion of bacterial phosphatidylglycerol reactive CD4+ T cells in atopic dermatitis

GC Monod1, M Wegerki2, BN Sailer3, L Bavonde4, CH Rohde5, J Rossohn5 and A de Jong6
1 Dermatology, Columbia University Irving Medical Center, New York, New York, United States, 2 Monash University, Clayton, Victoria, Australia, 3 Cardiff University Cardiff Institute of Infection and Immunology, Cardiff, United Kingdom, 4 Columbia University Irving Medical Center, New York, New York, United States

Psoriasis is a chronic immune-mediated disease 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 transcriptomics of T cells from healthy and psoriatic skin 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 express a predominantly Th2 cytokine profile, with abundant IL-4 and IL-13 release. Beyond Th2 cytokines, regulatory CD4+ T cells were found to express a Th17-like cytokine profile, with increased IL-17A and IL-22 production. This study demonstrates the complexity of the immune response in psoriasis and highlights the potential for targeted therapies to modulate specific T cell subtypes.

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

Sk Whitley1, M Li2, T Hirai3, H O, R Lalayas4, N McGreathy4 and DH Kaplan1
1 Dermatology, University of Pittsburgh, Pittsburgh, Pennsylvania, United States, 2 Immunology, University of Pittsburgh, Pittsburgh, Pennsylvania, United States, 3 Medicine, University of Pittsburgh, Pittsburgh, Pennsylvania, United States

IL-23 is a pro-inflammatory cytokine that plays a critical role in the pathogenesis of psoriasis. However, the mechanisms by which IL-23 maintains tissue resident memory Th17 cells in murine and psoriatic skin are not fully understood. In this study, we used a murine model of psoriasis to investigate the role of IL-23 in the maintenance of tissue resident memory Th17 cells. We found that IL-23 is required for the maintenance of tissue resident memory Th17 cells in murine and psoriatic skin. These findings suggest that IL-23 may be a potential therapeutic target for the treatment of psoriasis.

037 A multicomponent skin-targeted COVID-19 vaccine elicits robust humoral and cellular immune responses

1 Depts. Dermatology, University of Pittsburgh, Pittsburgh, Pennsylvania, United States

Considerable progress has been made toward development of COVID-19 vaccines in the past year. However, there is still a need for vaccines that are effective against new and existing SARS-CoV-2 variants. In this study, we developed a multicomponent skin-targeted vaccine using 3D printing technology. This vaccine was shown to be highly immunogenic and effective against a range of SARS-CoV-2 variants. The vaccine was tested in a murine model and was shown to elicit robust humoral and cellular immune responses, including high levels of neutralizing antibodies and CD8+ T cells specific to the SARS-CoV-2 spike protein. This study demonstrates the potential of multicomponent skin-targeted vaccines for the treatment of COVID-19 and other infectious diseases.