Late-Breaking Abstracts

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Adaptive and Auto-Immunity

LB708

ILC1-like innate lymphocytes in human autoimmunity: Lessons from Alopecia Areata

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Innate lymphoid cells type 1 (ILC1) express NKG2D and produce large amounts of IFN-γ, i.e. two key elements in the pathogenesis of alopecia areata (AA). In this study, we aimed to explore a possible involvement of ILC1-like cells in human AA by using *ex-vivo* and *in-vivo* models for human AA. Triple immunofluorescence staining of AA sections revealed pathological infiltrates of NKG2D+ ILC1-like cells in and around the anagen hair bulb of lesional AA HFs, but also (more discretely) in/around non-lesional AA HFs, together with a dominant infiltrate of CD8+/NKG2D+ cells. Next, autologous circulating human ILC1-like cells were expanded and co-cultured with organ-cultured, stressed human scalp hair follicles (HFs) *ex vivo* or injected into healthy human xenotransplants on SCID mice *in vivo*. Co-culture with ILC1-like cells induced abnormal HLA-DR, HLA-ABC, CD1d and MICA protein expression in the proximal HF epithelium, and down-regulated immunoreactivity for the HF immune privilege (IP) guardians, TGF-β1 and α-MSH, demonstrating the induction HF immune privilege collapse. Adding anti-IFN-γ or anti-NKG2D antibodies or these IP guardians themselves, significantly reduced the AA phenotype induction by ILC1-like cells *ex vivo*. Finally, intradermal injection of autologous, ILC1-like cells into healthy human scalp skin xenotransplants on SCID/beige mice induced classical macroscopic and histological AA lesions *in vivo*, just as seen with CD8+/NKG2D+ T cells. This shows that ILC1-like cells alone suffice to induce autroimmunity in a healthy human (mini-)organ, specifically AA in healthy human HFs, and encourages one to therapeutically target also non-antigen-specific innate lymphocytes in future AA management. Moreover, our findings further support the concept that antigen-specific T cell activities are not absolutely essential for inducing the AA hair loss phenotype.

LB709

Therapeutic Effect of γδTregs cells in Alopecia Areata

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Regulatory γδ T cells (γδTregs) may exert therapeutic effects under some experimental autoimmune disease (AID) conditions. This encouraged us to explore whether this this also applies to alopecia areata (AA), one of the most common human AIDs. Triple immunofluorescence (IF) staining was performed to determine the distribution of γδTregs in human skin presence of γδTregs on skin sections of AA patients. Autologous circulating human γδ Tregs were expanded and either co-cultured with organ-cultured, stressed human scalp hair follicles (HFs) ex vivo or injected into experimentally induced AA lesions on human scalp skin xenotransplants on SCID mice. The IF staining revealed the presence of γδ Tregs around the bulge region of scalp HF and around the hair bulb of lesional and non-lesional scalp skin of AA patients. Next, by using human HFs organ culture, we asked whether γδTregs possess the ability to suppress the premature catagen induction and IP collapse induction by activated CD8+/NKG2D+ T cells. The results demonstrated that γδTregs significantly reduced premature catagen induction as compared to HF co-culture with CD8+/NKG2D+ alone ($p<0.01$). Moreover, γδTregs significantly reduced the staining intensity of HFs immune privilege collapse markers such as HLA-ABC, CD1d, MICA/B and of the AA-associated chemokine, CXCL10. In addition, γδTregs increased the expression of IP guardians, such as TGF-β and α-MSH in the HFs outer root sheath, indicating that γδTregs can restore HF immune privilege. Finally, hair growth with normal histological and IF appearance were observed in the AA induced xenotransplants following transfer of autologous γδTregs . Collectively, this shows that γδTregs play a critical role in suppressing AA and in restoring HF immune privilege and thus deserve targeting in AA management and raises the possibility that expoanded autologous γδTregs may be used directly fas autologous cell-based future AA therapeutics.

LB710

Detection of novel BP180 epitopes in Pemphigoid Gestationis

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Pemphigoid Gestationis (PG) is an autoimmune skin fragility disorder, typically occurring during late pregnancy. Skin blisters and erythematous, itchy plaques are the clinical hallmarks of the disease. Previous studies report that in PG IgG autoantibodies target epidermal collagen XVII/ BP180. Due to the rarity of the disease, the detailed autoantibody profile has not been fully addressed. We retrospectively characterized clinically and serologically 11 PG patients, who were diagnosed and treated in the Skin Fragility Center, Freiburg. The clinical picture was variable with highly pruritic annular papules, urticarial plaques and blisters initially periumbilically. Notably, in three cases blistering started on the extremities. All patients had linear C3c and less obvious IgG, as well as IgG1 and C4d depositions along the basement membrane zone. In half of them anti-full-length BP180 autoantibodies and reactivity against the extracellular non-NC16A domain of BP180 were found. We discovered cases with BP230 antibodies and one patient with antibodies only against the extracellular non-NC16A BP180 domain. The latter had the most severe clinical picture in our cohort. IgE appears not to be relevant for PG pathogenesis. Although this is a limited patient number, our data expand the diagnostic algorithm and clinical characteristics of patients with PG.

LB711

Characterizing Skin Resident Memory T cell formation in Murine Cutaneous Lupus Erythematosus

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Cutaneous Lupus Erythematosus (CLE) is a spectrum of autoimmune connective tissue diseases that are characterized histopathologically by interface dermatitis and lupus band reaction. Current treatment options for CLE are based on SLE treatments and include topical steroids, antimalarials, and other immunosuppressants. Many CLE patients exhibit flares which can be triggered by environmental stimuli such as UV light. Tissue-resident memory T cells (Trm) mediate flares in autoimmune skin disorders, though their specificities, functional molecules, and survival factors in CLE have not yet been described. We used a mouse model of CLE to examine the development of Trm skin lesions. In this model, OVA peptide-activated DO11 CD4+ T cells were injected intravenously into sub-lethally irradiated TLR9KO Ii-TGO mice that express TGO transgene in the MHCII cells after being fed with Dox chow. We also took blister biopsies from CLE patients. Mice in this model developed IgM and IgG1 autoantibodies and exhibited cutaneous T cell accumulation that positively correlated with the severity of skin lesions. We found that approximately 70% of antigen-specific skin T cells in these mice expressed phenotypic markers consistent with Trm, which persisted after antigen withdrawal. Trm cells were enriched in the skin as compared to the draining lymph node and spleen. Disease scores also peaked more rapidly during flare induction than during primary disease, as do ANA titers. Preliminary analysis of human blister biopsies from CLE patients exhibited phenotypic markers of Trm (CD8+CD103+CD69+ T cells) in the skin. Based on our data and previously published studies in other autoimmune skin disorders, we hypothesize that targeting Trm in CLE may be a durable treatment strategy.

LB712

Transcriptomic profiling of Necrobiotic Xanthogranuloma and Necrobiosis Lipoidica provides insight into pathogenic role of T and B cells

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Necrobiotic Xanthogranuloma (NXG) is a chronic cutaneous disorder that results in development of violaceous-yellow papules and nodules that can progress to ulceration. Similarly, Necrobiosis Lipoidica Diabeticorum (NLD) is a chronic skin disease with clinical and histologic features overlapping with NXG. Also, treatment of these two conditions is similar, with anti-TNF agents and other immunomodulators showing promise. Although there is increasing evidence for NXG and NLD being immune-mediated diseases, more precise mechanistic insight is still lacking. To fill this gap, we performed whole-tissue RNA sequencing of healthy control, NXG, and NLD skin. This revealed a broad degree of agreement between the two diseases, including a similar decrease in antimicrobial peptide levels (*DCD*) and upregulation of T and B cell genes activation genes. Genes related to autoinflammation (*SPP1*, *IL1B*, and *IL6*) were also upregulated (FDR < 0.01, FC >5). Biological pathway analysis revealed significant (FDR < 0.01) alterations in B cell receptor signaling, interferon gamma signaling, complement activation, and cell adhesion pathways both in NXG and NLD. Thus, transcriptomic profiling of NXG demonstrates immune alterations paralleling those observed with NLD, and implicate pathologic T and B cell signatures in NXG pathophysiology.

Carcinogenesis and Cancer Genetics

LB713

Proteomic identification of new diagnostic biomarkers of early-stage Cutaneous Mycosis Fungoides

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Primary cutaneous T-cell lymphoma (CTCL) is responsible for two-thirds of cutaneous lymphoma cases. Mycosis fungoides (MF), the most common subtype of CTCL comprises approximately 60% of CTCLs. Due to the similar clinical features of MF and inflammatory diseases such as eczema and psoriasis<!--[endif]---->[2,3], early-stage MF can easily be misdiagnosed as chronic inflammatory dermatoses, posing a diagnostic challenge to the dermatologist. Early-stage MF is characterized by a favorable prognosis with long-term survival similar to or slightly lower than that of age-matched healthy people, with a 5-year survival between 88% and 100%. In contrast, advanced-stage MF shows aggressive progression, and the median survival time of patients with lymph node and visceral involvement is only 13 months. Therefore, it is important to achieve early diagnosis to improve prognosis, yet there are few specific biomarkers for the early diagnosis and prognosis of MF. In this study, we described the pathological features of MF during the early and advanced stages through proteomics technology, providing clues for the pathogenesis of MF as well as biomarkers for malignant tumors in the early stage. More importantly, diagnostic biomarkers of early-stage MF were identified by comparing the proteomic characteristics of early-stage MF and inflammatory diseases, with the goal of preventing delayed therapy due to misdiagnosis.

LB714

Differences in utilization of field therapy of Actinic Keratoses by varying practitioner type

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We aimed to characterize trends in management of field cancerization of actinic keratoses by dermatologists and other clinicians. The 2013-2018 Medicare Public Use File and Physician Compare Tool were analyzed, including 116,441 unique clinicians. Specialties included dermatologists, primary care physicians (PCPs), and advanced practice providers (APPs). Claims of cryosurgery (Healthcare Common Procedure Coding System codes 17000, 17003, and 17004), topical therapies (fluorouracil, imiquimod, or ingenol mebutate), and photodynamic therapy (PDT) were compared. Utilization of each treatment modality was measured as a percentage of all field therapy claims filed. Mean proportions (standard deviation) of individual clinicians were compared. Utilization of each modality was compared versus practitioner type. Longitudinal analyses were performed by calendar year. Statistical significance for all analyses was determined using one-way analysis of variance. PCPs had the greatest mean proportion of cryosurgery (94.9% [21.3%], P<0.0001) vs. dermatologists (93.2% [19.7%]) or APPs (92.2% [22.7%]). APPs most often prescribed topical treatments (7.3%% [22.4%]), while PDT was most utilized by dermatologists (0.6% [3.2%]). Longitudinally, use of cryosurgery decreased from 2013 to 2018 for every specialty (P£0.0005 for all). Use of topicals increased for dermatologists and APPs (P<0.0001 for both) but decreased for PCPs (P=0.0035). PDT use decreased for dermatologists and APPs (P<0.0001 for both) but not PCPs (P=0.95). Our findings demonstrate an important practice gap for non-dermatologists managing field cancerization of actinic keratoses. It may be helpful to educate PCPs on more effective and tolerable therapies than cryosurgery of ill-defined actinic damage. Among dermatologists and APPs, it appears that topical therapies are becoming more prevalent in comparison with cryosurgery or PDT for field cancerization. This may perhaps represent changing reimbursement rates set by Medicare as well as availability of more tolerable topical treatments.

LB715

Epithelioid Hemangioma of the leg: A case report of a rare benign vasoformative lesion

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Background: Epithelioid hemangioma (EH) is a rare, benign vasoformative lesion of unknown etiology that presents clinically as a slowly enlarging smooth-surface nodule. Herein, we report one case of unilateral EH and its clinical presentation. Additionally, we provide a comprehensive review of the literature.
Objective: We aim to illustrate the histopathologic features unique to EH, investigate current theories of pathogenesis, provide differential diagnoses, offer useful diagnostic tools to improve EH detection, and discuss treatment options.
Materials and Methods: A primary literature review was conducted utilizing PubMed/MEDLINE and CINAHL databases with the following search terms: (epithelioid hemangioma OR angiolymphoid hyperplasia with eosinophilia). Exclusion criteria included studies that were written in languages other than English.
Results: Reports of EH with metastatic features, such as multifocality and local aggressiveness, further complicate diagnosis. Ultrasonography (US) paired with color doppler US is the initial imaging modality of choice. EH lesions may be positive for CD34 and factor VIII-related antigen, as well as, show diffuse (>50%) nuclear immunoreactivity for FOSB. With the pathogenesis of EH still in question, cases of EH suggest a reactive pattern may be at play. First-line therapy of EH is said to be surgical excision.
Conclusion: Correct identification and differentiation of EH from similar benign and metastatic pathologies is of fundamental importance due to varying clinical courses, prognoses, and recommended treatments. Better understanding EH's mechanism of action may improve treatment.

LB716

Juxtacrine stimulation of keratinocytes by ultraviolet B (UVB)-exposed melanocytes through the sPmel17-FHL2-TGFb1 axis

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Ultraviolet B (UVB)-based phototherapy has been clinically proven to be effective in inducing vitiligo repigmentation. The repigmentation represents a complicated process in which the depigmentary epidermis is replenished by functional melanocytes (MCs) migrating from undamaged hair follicles or the surrounding skin. We hypothesize that MCs potentially release a secreted form of Pmel17 protein (sPmel17) upon exposure to UVB irradiation, thereby modulating cell-cell adhesions in keratinocytes and allowing melanocytes to go through and enter a vitiliginous region. In this study, we first examined the changes of the sPmel17-FHL2-TGFb1 axis in human keratinocytes (KCs) cocultured with or without human MCs exposed to UVB irradiation. The results demonstrated that the protein and mRNA levels of FHL2 (the four and half LIM domain 2) was significantly increased in the KCs concomitantly with the increase of Pmel17 in the MCs. We also found that there was an intimate interaction between sPmel17 and FHL2 using co-immunoprecipitation assay and double immunofluorescence staining. The conditioned media from UVB-exposed MCs could signal to KCs to perform cytoskeletal remodeling and suppress E-cadherin expression. On the other hand, the conditioned media from Pmel17-silenced and UVB-exposed MCs failed to do this. To further confirm the role of sPmel17-FHL2-TGF b1 axis in vitiligo repigmentation, we examined the expression profiles of FHL2 and Pmel17 in the affected and unaffected skin of vitiligo patients who underwent UVB-based phototherapy using immunohistochemical staining. The data showed that significant downregulations of FHL2 and Pmel17 were seen in the affected skin as compared with those in the unaffected skin, which was reversed in the repigmented skin after UVB phototherapy. In conclusion, the expression of FHL2 in KCs appears to be required by sPmel17 stimulation, the activation of the sPmel17-FHL2-TGFb1 axis offers a potential therapeutic target to hasten vitiligo repigmentation.

LB717

Dipeptide diaminobutyroyl benzylamide diacetate postsynaptically inhibits muscle contraction

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Repetitive facial expressions cause reduction in skin elasticity and, over time, generate noticeable wrinkles. Many procedures that are aimed to reduce expression lines are developed based on the physiochemical and biochemical properties of the synapse between the motor neuron and muscle fiber, known as the neuromuscular junction. Our objective was to assess the inhibitory effects of dipeptide diaminobutyroyl benzylamide diacetate, here after referred to as dipeptide, on myocyte contraction via antagonism of nicotinic acetylcholine receptors (nAChRs). To initially assess the post-synaptic inhibitory properties of dipeptide, fura-2 AM calcium indicator-loaded myocytes were pretreated for 1 h with 2.5 mg/mL, 5 mg/mL, or 10 mg/mL of dipeptide prior to depolarization with 20 μM acetylcholine chloride. Intracellular calcium transients were immediately evaluated fluorometrically as an indirect measure of myocyte excitation-contraction coupling. At all concentrations evaluated, the dipeptide significantly reduced myocyte excitation-contraction coupling almost equivalent to the nAChR competitive antagonist, 5 μM α-bungarotoxin. To corroborate the inhibitory effects of the dipeptide, we evaluated lower concentrations of the dipeptide in a complex skin model system comprised of a coculture of induced human motor neurons and human skeletal myocytes seeded beneath an organotypic epidermis. Muscle contraction frequency was assessed after 2 h and 24 h of topical application (2.5 μL) containing 10 μg/mL or 1 mg/mL of dipeptide. Treatment with 10 μg/mL of dipeptide demonstrated a significant reduction in contraction frequency by 72% after 24 h. A significant decrease in contraction frequency was observe after 2 and 24 h following treatment with 1 mg/mL of dipeptide, with reductions of 54% and 65%, respectively. These data indicate that dipeptide has the potential to significantly reduce post-synaptic signaling associated with muscle contraction.

LB718

Screening method for natural actives in a SIPS fibroblast model

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The interest in understanding the mechanisms of skin aging is growing within the cosmetic scientific field. Aging occurs within skin cells naturally or prematurely when the cells encounter harmful oxidative stresses such as UV light or pollution. Stressors incite a build-up of reactive oxygen species within cells leading to a senesced phenotype. These senesced cells no longer divide, but still maintain a level of cellular respiration, indicating that the cells maintain activity. Senesced cells induce neighboring proliferating cells into a senesced phenotype by secreting cellular signals in a senescence-associated secretory phenotype (SASP), impairing the proliferating cells from dividing. Identifying actives that target senesced cells is important to increase the understanding in the skin aging process. A high throughput stressed induced premature senesced (SIPS) screening model was developed to identify new actives. Using tert-butyl hydroperoxide (t-BHP) SIPS was induced in primary fibroblast. Proliferation, death, and senescence was determined using live cell imaging probes, analyzed via Varioskan Lux plate reader. SASP was determined using reporter assays for IL-6, IL-1-α and TNF-α. Within the SIPS model, t-BHP induced senescence and attenuated proliferation. Furthermore, t-BHP did not induce cell death in the SIPS model. This data supports that t-BHP induced senescence by inhibiting proliferation and not by inducing cell death, creating a senescent model. Additionally, the increase in SASP of the SIPS model at 120hrs further supports the senescence phenotype. Exploiting this high throughput SIPS screening model to identify new actives that target a senesced population will increase our understanding in the skin aging process.

LB719

Cytokine Profiling in Low- and High-Density Small Extracellular Vesicles From Epidermoid Carcinoma Cells

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Exosomes or small extracellular vesicles (sEVs) are membrane-bound, nanoparticles carrying various macromolecules, acting as autocrine and paracrine signaling messengers. Here, sEVs from epidermoid carcinoma cells influenced by membrane presentation of the glycoprotein desmoglein 2 and its palmitoylation state were investigated. sEVs were isolated by sequential ultracentrifugation followed by iodixanol density gradient separation and subjected to multiplex cytokine profiling. Subpopulations of different densities showed active sorting of surface-associated cytokines, chemokines and growth factors. This comprehensive analysis of the cytokine production profile by A431 cell sEVs highlights their contribution to immune evasion, pro-oncogenic and-angiogenic activity and the potential to identify diagnostic disease biomarkers.

LB720

Mechanobiology and periorbital aging: Skin cell response to micromovements and their duration

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Periorbital skin is more vulnerable than the surrounding facial skin since it is much thinner and not have the same appendages as the rest of the face. Another unique characteristic is that it is under constant movement due to daily blinking, and facial expressions including smiling, laughing and crying. As a result, periorbital skin cells are under constant change of mechanical stress with continuous stretching and release. The cells sense the strain (deformation) in the extracellular matrix (ECM) caused by mechanical stresses and, through mechanotransduction, convert this information into very specific cellular responses. Although the molecular signaling and regulatory mechanisms are not fully understood, this constant feedback between external and internal forces have been demonstrated to have a strong impact on cellular behavior. In this study, we mimicked a range of blinking rates through mechanical changes and followed how skin cells from different aged donors respond and adjust to this stress. Using confocal microscopy, we identified changes in skin cell orientation as a function of age and as a function of "blinking times" in terms of ability to adjust. Cell number, inflammation, and collagen levels were also all affected by these micromovements. We have previously demonstrated that these parameters all relate to a specific microRNA, miR-146a; therefore, we also investigated miR-146a level as a function of "blinking times" *in vitro*. For the first time, we show that miR-146a expression level is directly impacted by constant mechanical stress from micromovements. Here, we demonstrate how micromovements and the duration of this mechanical stress directly affect core skin cell activities, creating an accumulation of damage over time. These results provide new insights into why periorbital skin appears to age more rapidly than other areas of facial skin.

LB721

miR-146a, circadian rhythm and impact on collagen

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microRNAs (miRs) are small, non-coding RNAs that function as critical signaling molecules, which can negatively or positively impact cellular health. Even though miRNA biology is a relatively new field of study, hundreds of miRNAs have been identified to date. Expression of these molecules is highly tissue-specific, emphasizing the importance of studying their function within the tissue or cells of interest. In our research on skin cells, we have identified a specific miR involved in skin anti-aging activities: miR-146a. miR-146a was proven not only to help against inflammation but also help to support cell number and production of proteins, such as collagen. miR-146a has also been linked to circadian rhythm and we had shown previously that skin cellular synchronization is essential for skin repair and recovery. Unfortunately, as we age, skin naturally becomes desynchronized from the circadian rhythm and expression of miR-146a decreases in dermal fibroblasts. Here, we show that collagen expression is impacted by a loss of cellular synchronization in relation to circadian rhythm, and that using a combination of actives that promote synchronization and miR-146a levels in skin cells help to increase collagen level in aging skin cells. We believe this is the first demonstration of the critical importance of miR-146a and collagen temporal expression level in skin cells and that technologies addressing both can support natural collagen production and help skin cells resist aging.

LB722

IL-31/IL31RA negatively regulate IL-4 production and cutaneous M2-like macrophage accumulation

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Despite strong clinical associations between "itch cytokine" IL-31 and multiple pruritic inflammatory skin conditions, the impact of IL-31 on cutaneous inflammation remains unclear. In fact, while IL-31 is hypothesized to drive tissue inflammation, and its receptor IL31RA is expressed on multiple myeloid cell populations, cutaneous immune cell-mediated circuits activated by IL-31 have not been characterized. The purpose of this study was to address those unanswered questions by examining the contributions of IL-31 and IL31RA to skin and systemic inflammation in mouse models of dermatitis. To do so, we used existing Il3lra-deficient (IL31RAKO) mice and novel Il31-deficient (IL31KO) mice we developed for this purpose. Analysis techniques included a combination of multi-parameter flow cytometry and scRNA-seq. Unexpectedly, in topical allergen models IL31KO resulted in increased proportions of type 2 cytokine-producing cutaneous T cells. In addition, we observed increased serum IgE, a metric for IL-4-mediated immunoglobulin class-switching. Consistent with this program of increased IL-4 signaling in IL31KO mice, IL-4-responsive M2-like macrophages capable of fueling feedforward pro-inflammatory loops were selectively enriched in IL31RAKO skin. Taken together, these data support a new model wherein IL-31 is not strictly a pro-inflammatory cytokine, but rather an immunoregulatory factor capable of limiting the magnitude of IL-4-mediated allergic skin inflammation. These findings have important implications for allergic skin immunology and for therapeutic targeting of IL31RA in inflammatory skin diseases.

Epidermal Structure and Barrier Function

LB723

Face skin changes caused by face mask during the COVID-19 pandemic

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With the prolonged COVID-19 situation, wearing a face mask has become daily routine and we studied facial skin changes caused by wearing a mask for preparing possibilities on changing skin. We analyzed the skin characteristics that changed for about three months from mid-June to mid-September, and compared to skin changes caused by wearing a mask during the day. Measured areas were divided into two groups. Cheeks, perioral area and chin were mask-wearing area and forehead was non-mask-wearing area. Skin temperature, redness, hydration, keratin, elasticity, pore, color and trans-epidermal water loss (TEWL) were measured. Skin changes caused by long-term wearing of mask were shown in TEWL, skin hydration and keratin. Compared to June, TEWL was increased significantly on the cheeks, perioral area and chin. There was significant difference in TEWL increase in the cheeks and perioral area compared to the forehead. Also, skin hydration was significantly decreased on the cheeks. Skin hydration of perioral area was also decrease. There was significant difference in skin hydration decrease in the cheeks compared to the forehead. Compared to June, skin keratin was significantly increased on the cheeks. Skin keratin of perioral area was also increase on the perioral area and chin. There was significant difference in skin keratin increase in the cheeks and chin compared to the forehead. In previous studies, skin characteristics that were quickly affected by wearing a mask were skin temperature and redness. On the other hand, TEWL, skin hydration and keratin were more affected by wearing a mask for a long time so there was difference short-term and long-term effect of mask in changed skin characteristics. In this study, we identified the effect of long-term wearing a mask on the face skin. This result is meaningful in that we studied the effect of wearing a mask in daily life for ordinary people, not those who wear mask in the occupational environment.

LB724

Human epidermal organoids: Establishing a reproducible stratified human epidermal organoid culture system

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Skin is the largest human organ and performs various functions such as protection, temperature regulation, water retention, sensation and immune defense. An organoid is a collection of organ-specific cells that develops from stem cells or organ progenitors and is capable of recapitulating specific functions of the organ. Epidermal organoids are organoids grown from keratinocytes isolated from the epidermis. Here, we describe a well-established and reproducible method for culturing human epidermal organoids (HEOs) in 7 days. We tested different media conditions to develop defined HEO growing and expansion conditions. HEOs were successfully generated from primary keratinocytes isolated from human skin as well as established keratinocyte cell lines (NKc21 and KERTr cells). We characterized these organoids to show that they resemble the human epidermis. We demonstrated that the HEOs express epidermal genes including collagen 17 (col17), keratin 15 (K15), keratin 14 (K14), keratin 5 (K5), keratin 10 (K10), keratin 1 (K1), filaggrin (FLG), transglutaminase 1 (TGM1), and transglutaminase 3 (TGM3). We showed that as the organoids progressed from stem like basal cells to mature organoids. They lost their stemness as indicated by the downregulation of lgr5 and lgr6. They retained their basal layer markers including krt5,14,15 and col17 and the markers for the suprabasal layers, namely tgm1, krt1, krt10, tgm3, and flg were upregulated indicating the differentiation of keratinocytes. This differentiation process is hard to control in regular 2D keratinocyte culture. Overall, our data show that we were able to successfully generate HEOs that recapitulate the complexity and architecture of a human epidermis. HEOs can be derived from patients with different disorders, allowing us to generate *in vitro* models of skin diseases. This makes HEOs an essential tool for physiopathology research, drug development, and personalized medicine of epidermal disorders.

LB725

Skin Barrier Formation by Epigenetic Regulation of EGR3

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Epigenetics is the field of biology that studies the influence of the environment and lifestyle on the expression of genes without changing their DNA sequence, and has recently attracted more and more interest from cosmetic brands. Here, we show that EGR3 plays a critical role on the formation of skin barrier by epigenetic regulation and its application on the cosmetic industry. Skin barrier, the outermost surface of the epidermis, protects our body from external threats of environments. Late epidermal differentiation is a key step of skin barrier formation. We recently found that EGR3 is the transcription factor which is highly expressed in the stratum granulosum by the integrative analysis of various data obtained from open-source database. However, its expression is lost under poorly differentiated conditions, such as parakeratosis-lesional skin. The loss of function study and the analysis of skin tissues data revealed that EGR3 functions as the important regulator of late epidermal differentiation. Further, RNA-seq and ChIP-seq analysis revealed that EGR3 mediated the regulation gene located in the epidermal differentiation complex in which over fifty genes encoding proteins involved in the terminal differentiation and cornification of keratinocytes are located. Interestingly, EGR3 totally regulates the expression of the genes located in epidermal differentiation complex through activation of enhancers and induction of enhancer RNAs, meaning that epigenetic modulation is important for the function of EGR3. Finally, we discovered that Penta-O-galloyl-β-D-glucose from *Paeonia lactiflora Pall.* root extract enhances the expression of skin barrier genes via EGR3 upregulation, and thus it can be a useful cosmetic ingredient to enhance skin barrier function.

LB726

The combination of 0.5% retinol with a naturally derived TRPV 1 antagonist and anti-inflammatory botanical extract helps mitigate retinoid-induced irritation

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The use of topical retinol is recognized as the gold standard for the treatment of photodamaged skin. However, topical application of retinol can potentially cause irritation manifested as burning sensation, erythema, peeling, or dryness. This can contribute to non-compliance or discontinuation of use for many individuals. Studies have shown that adjustments in timing and concentration levels can help mitigate the induced effects of retinol. There is very little understanding of the molecular mechanisms underlying retinoid irritation, however it has been shown that TRVP1 antagonists help mitigate irritation. Here, we designed a cosmetic formulation containing 0.5% retinol and a naturally derived plankton extract shown to antagonize TRPV1, and rosemary extract shown to suppress expression of multiple inflammatory cytokines. In consultation with a dermatologist we designed an 8-week gradual retinization process and using this protocol, subjects who applied the formulation demonstrated high tolerability and reduction in dermatologist-assessed erythema, edema, and dryness. Panelist self-evaluations reported few moderate sensory discomfort scores and reduction in erythema. Separate clinical studies were conducted to evaluate skin pigmentation, global fine lines and wrinkles, skin tone evenness, overall photodamage, and skin texture/smoothness as clinical measurements. The formulation provided statistical improvements in each parameter ($p<0.05$) at both 4 and 8-weeks as expected from a formulation containing retinol. The combination of retinol with naturally-derived anti-inflammatory agents, along with a gradual retinol application is a clinically relevant approach to help mitigate retinoid irritation while improving subject tolerability and compliance over time.

LB727

Using a machine learning approach to identify rare and low-frequency filaggrin variants associated with remission of Atopic Dermatitis

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Rare and low-frequency variants (minor allele frequency (MAF)<5%) within diseased populations are traditionally given less attention than common variants (MAF>5%), primarily because of insufficient statistical power, and because existing methods (burden tests and variant component tests) are primarily useful for examining whether a whole gene, and not particular variants, are implicated in disease. Atopic dermatitis (AD) is a common relapsing inflammatory skin disease, for which common variants, primarily in the skin barrier protein filaggrin (*FLG*), have been associated with disease presence and remission. Loss-of-function (LoF) variants in *FLG* have been consistently associated with AD. However, rare and low-frequency variants (MAF<5%), particularly those that are not LoF, have been given less attention. We developed a machine learning approach, utilizing genetic algorithms, to identify uncommon variants associated with disease. We applied this algorithm to simulated data sets, and demonstrated excellent ability to discriminate associated from unassociated variants (p-values< 0.01 or <0.001 for all groups). We fine-sequenced the *FLG* gene in a longitudinal cohort of individuals with AD, and applied our algorithm to rare and low-frequency variants within *FLG*, searching for associations between groups of these variants and AD remission. We identified a group of 46 rare and low-frequency variants in *FLG* associated with increased AD remission (adjusted p-value=2.76e-11). 16 of our rare and low-frequency *FLG* variants were identified in an independent cohort and associated with decreased incidence of AD (p-value=0.0007). Our study presents a novel application of statistical methods in AD genetics, suggests that rare variants may play a larger role in the pathogenesis of AD than previously appreciated, and uncovers genetic associations which may be valuable for future study of the epidemiology of AD.

LB728

Withdrawn

LB729

A Parthenolide-Depleted Feverfew Extract Reverses Genetic and Epigenetic Changes induced by Particulate Matter Demonstrating Pleiotropic Mechanisms of Action Behind its Anti-Inflammatory Benefits and Protection Against Pollution

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Particulate matter (PM) of pollution causes oxidative stress leading to inflammation and premature skin aging. A parthenolide-depleted (PD) feverfew extract has been shown to reverse these changes induced by PM and provides anti-inflammatory benefits and protection against pollution. However, few studies have examined the genetic and epigenetic mechanisms. The objective of this study was to investigate PD-feverfew's skin protection benefit against PM was also mediated epigenetically. Primary human keratinocytes were treated with PM with or without PD-feverfew extract. Genetic and epigenetic changes were evaluated by transcriptomics RNA-sequencing, microRNA-sequencing and whole-genome bisulfite sequencing. In agreement with previous studies, PM treatment alone significantly induced reactive oxygen species (ROS) generation in a dose-dependent manner, whereas PD-feverfew significantly inhibited PM-induced ROS. Top up-regulated pathways by PM shown by gene ontology analysis were hallmarks of cornification, keratinization and terminal differentiation associated with inflammation. The most down-regulated pathways by PD-feverfew treatment were pro-inflammatory cytokine activity-related signaling pathways. Concomitant with proinflammatory signaling pathways induction, PM also caused epigenetic changes by significantly reducing the expression of multiples miRNAs known to inhibit proinflammatory signaling. Moreover, in agreement with gene expression profiling, PM reduced methylation levels within the differentially methylation promoter regions, which were partially reversed by PD-feverfew treatment. In conclusion, this study revealed that the deleterious pro-inflammatory effects induced by PM are mediated by both genetic and epigenetic changes. PD-feverfew extract treatment reversed these PM-induced genetic and epigenetic changes, uncovering its pleiotropic anti-inflammatory benefits and protection against pollution.

LB730

Quantitative skin-penetration evaluation of active ingredients on *in-vitro* 3D skin model using confocal Raman spectroscopy

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The penetration of active ingredients from topically applied skincare products impacts their efficacy. Many measurement methodologies have been devised to address how fast and how much ingredient molecules penetrate into skin. Here, we established an experimental and analytical method using confocal Raman spectroscopy and demonstrated a quantitative and spatiotemporal penetration profile of active ingredients into skin. We generated standard curves (Raman signal vs. concentration) for certain active ingredients, using agar gel skin phantom. Each active ingredient was solubilized in various vehicles with or without penetration enhancers. 20ul of each solution was topically applied on 3D cell culture model, followed by further incubation for 30min, 1hr, 2hrs, and 3hrs. Raman measurements were performed using a confocal Raman spectroscope and spectra in the fingerprint (400 to 1800 cm-1) region were acquired from top surface to 40um skin depth with an increment of 2um.
The results show that;
1) Raman signal is linearly correlated with active ingredient concentration up to 4mg/ml in agar gel skin phantom.
2) Penetrated active ingredient is highly concentrated in Stratum Corneum (SC) and gradually tapers off along with skin depth.
3) Viscosity of formulation base greatly influences the kinetics of penetration.
We have successfully demonstrated the penetration of certain active ingredients into in vitro 3D skin model using confocal Raman spectroscopy and expect that experimental and analytical method provides valuable information for skincare product development.

LB731

GJA4 somatic mutations drive venous malformation in the skin and liver and reveal a novel pathway for therapeutic intervention

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The term “cavernous hemangioma” has been used to describe vascular anomalies with histology featuring dilated vascular spaces, vessel walls consisting mainly of fibrous stromal bands lined by a layer of flattened endothelial cells, and an irregular outer rim of interrupted smooth muscle cells. Hepatic hemangiomas (HH) and cutaneous venous malformations (cVM) share this histologic pattern, and we examined lesions in both tissues to identify genetic drivers. Paired whole-exome sequencing of lesional tissue and normal liver from HH subjects revealed a recurrent *GJA4* c.121G>T, p.Gly41Cys somatic mutation in 4 of 5 unrelated cases, and targeted sequencing in paired tissue from 9 additional HH subjects identified the same mutation in 8. In cutaneous lesions, paired targeted sequencing in 5 cVMs and normal epidermis, found the same *GJA4* c.121G>T, p.Gly41Cys somatic mutation in 3. *GJA4* encodes gap junction protein alpha 4, also called connexin 37 (Cx37), and the p.Gly41Cys mutation falls within the first transmembrane domain at a residue highly conserved among vertebrates. We investigated the impact of the Cx37 mutant via lentiviral transduction of primary human endothelial cells. We found that the mutant induced changes in cell morphology and led to non-canonical activation of SGK1, a serine/threonine kinase known to regulate cell proliferation and apoptosis. Treatment with spironolactone, an inhibitor of angiogenesis, suppressed SGK1 activation and reversed changes in cell morphology. These findings identify a recurrent somatic *GJA4* c.121G>T mutation as a driver of hepatic and cutaneous venous malformations, revealing a new pathway for vascular anomalies, with spironolactone a potential pathogenesis-based therapy.

LB732

Intravenous gentamicin therapy in adult junctional and recessive dystrophic Epidermolysis Bullosa with nonsense mutations does not result in sustained clinical improvement

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Nonsense mutations lead to premature termination codons and are present in ~15-20% of junctional (JEB) and recessive dystrophic EB (RDEB) patients. Gentamicin allows PTC readthrough to restore protein production and reverses phenotype. While topical gentamicin has shown to be efficacious for EB patients with nonsense mutations, systemic infusion could help the generalized nature of the disease. In this study, two RDEB and one JEB adult patients were given IV gentamicin (7mg/kg/day, once daily) for 2 weeks. EB disease activity and scarring index and wound body surface area were recorded at baseline, the end of therapy, and then one month and three months later. All three patients tolerated the treatment, albeit one RDEB patient developed a urinary tract infection associated with acute kidney injury 9 days after discharge. The three patients had varying responses to gentamicin: one RDEB patient improved, the other RDEB patient deteriorated, and the JEB patient remained stable. None of the patients had restoration of respective proteins (type VII collagen, laminin-332) on immunofluorescence microscopy. Our study indicates that IV gentamicin may not lead to clinicopathologic benefit in all adult EB patients with nonsense mutations at the current maximum recommended dosage. Given the plethora of anecdotal reports and small clinical trial data, it is perhaps time to reach international consensus on recommendations for aminoglycoside therapy in EB, either in further clinical trials or in clinical practice.

LB733

Effect of vitamin C on gene transcription in *ex-vivo* skin model

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Ascorbic acid (Vitamin C) is a potent antioxidant and is also suggested to affect genome activity via modifiable epigenomic processes as an enhancer of demethylases, consequently spatially and temporally altering gene expression. Utilizing ex-vivo skin models and standard RNA sequencing (NOVASEQ™/HISEQ), changes in gene expression within 24 h and 48h posttreatment were observed. Single, topical application of 10% buffered ascorbic acid (AA) altered skin's transcriptional profile at both 24 and 48 hours post-treatment, with a total of 229 and 280 affected gene transcripts, respectively. Analysis of Gene ontology (GO) terms using the Database of essential genes (DEGs) nomenclatures demonstrated that predominantly expression of genes related to cell signaling and differentiation was altered. Notable induction of FOS and FOSB gene transcription suggests that topical application of 10% ascorbic acid is likely activating mitogen-activated protein kinases (MAPK) and consequently causing the induction of number of genes involved in the late stages of cornified envelope formation. Among downregulated transcripts were Insulin Growth Factor (IGF1) and associated regulatory proteins (IGFBPs) that are involved in tissue-specific regulation of cell metabolism. Whether topical application of Vitamin C is modifying the epigenomic dermal processes as previously described in stem cells and cell lines, consequently changing the levels of gene expression, or whether this change in gene transcription is due to a shift in metabolism of the tissue by changes in key glycolytic enzymes and shift to pentose phosphate pathway and NADPH levels, metabolites that are consequently affecting gene transcription, requires further investigation.

LB734

Genome-wide association study of ustekinumab response in Psoriasis

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Ustekinumab is an IL-12/23 inhibitor FDA-approved for the treatment of psoriasis, a chronic immune-mediated skin disease that affects about 2% of the U.S. population. In phase 3 clinical trials of ustekinumab, ~66% of psoriasis patients achieved PASI75 improvement after 12 weeks of treatment. Prior candidate gene studies revealed that individuals with the HLA-C*06:02 allele on chromosome 6 have a more favorable response to ustekinumab. Here, we performed an unbiased genome-wide association study (GWAS) of ustekinumab response at week 12 using data from three placebo-controlled randomized clinical trials (PHOENIX I, PHOENIX II, and ACCEPT). We observed a genome-wide significant signal (p=2E-08) for a single nucleotide polymorphism (SNP) not within the HLA region, and this result was replicated in an independent cohort. Psoriasis patients with at least one copy of the minor allele of this SNP had a PASI75 response rate of 44% after 12 weeks of ustekinumab, while psoriasis patients without the minor allele had a PASI75 response rate of 75% after 12 weeks of ustekinumab. Differences in the response rate of these two groups persisted at weeks 24 and 28. We then evaluated the dual impact of this SNP in conjunction with HLA-C*06:02. Psoriasis patients with the minor allele of the novel SNP and who were HLA-C*06:02 negative had a PASI75 response rate of 35% at week 12, while those without the minor allele and who were HLA-C*06:02 positive had a PASI75 response rate of 82% at week 12. Our findings highlight a novel SNP that is potentially associated with response to ustekinumab in psoriasis. Additional studies are needed to confirm these findings.

LB735

Epidermal growth factor modifies immune gene expression in keratinocytes and Melanoma

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Epidermal growth factor (EGF) ligands play a key role in cellular proliferation and cancer progression via activation of the EGF receptor (EGFR). However, EGFR inhibitors (EGFRIs) frequently induce a rash in patients that is associated with improved cancer survival, suggesting immunomodulatory properties that may be therapeutically beneficial. Human keratinocytes (HaCaT) were treated with IFN-γ (a potent pro-inflammatory cytokine), EGF, both, or neither (control) and differentially expressed genes (DEGs) were analyzed using RNA-seq and gene-set enrichment analyses. The association of top DEGs with tumor-infiltrating lymphocytes (TILs) in primary melanoma and survival of patients registered in the TCGA database (n=414) were estimated using multivariable linear and Cox proportional hazards regression, respectively. Of the 2,792 genes induced by IFN-γ alone in cultured keratinocytes, only 709 (25%) were induced when treated with IFN-γ and EGF. IFN-γ-induced genes modified by EGF were enriched in MHC-class II antigen presentation pathways and cytokine-cytokine receptor interaction, driven by the attenuation of *CXCL10* expression. Consistent with our *in vitro* findings, the association of *IFNG* with *CXCL10* expression in melanoma was weaker in tumors with higher EGF expression. Additionally, among melanoma patients, *CXCL10* expression was associated with increased TILs and better overall survival (upper vs. lowest tertile HR = 0.40, 95% CI: 0.26-0.61, $P = 1.92 \times 10^{-5}$). Our findings suggest that EGF globally attenuates pro-inflammatory gene expression induced by IFN-γ in the skin. The attenuation of *CXCL10*, in particular, may be relevant for melanoma patients given the strong association of *CXCL10* with melanoma TILs and survival. These findings support the hypothesis that the immune effects of EGFR ligands and EGFRIs influence anti-tumor immunity.

Innate Immunity, Microbiology, and Microbiome

LB736

Wearing N95 masks does not disrupt the facial skin microbiome

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The COVID-19 pandemic has elevated concern about mask-related skin problems like so-called 'maskne' which is likely rooted in the skin microbiome. We therefore determined if wearing an N95 mask affects the skin microbiome in a 3-day controlled study. On Day 1, subjects (n=10) followed their normal office routine without a mask. On Days 2 and 3, subjects wore an N95 mask (3M Model 8210) from morning to late afternoon (6 hours). The same mask was used both days. Microbiome diversity and composition (16S rRNA amplicon sequencing, V1-V3), stratum corneum (SC) barrier function (TEWL), SC hydration, skin redness and follicular porphyrins were measured on the cheek (masked site) and forehead (control site) each morning and afternoon. At the end of the study, a sample of each mask was collected for microbiome analysis. Mask wearing showed no significant effect on alpha (Shannon) or beta (Brays-Curtis) microbiome diversity. Mask wearing had no significant effect on *Cutibacterium acnes* relative abundance. Mask wearing corresponded to a small increase in the genus *Staphylococcus* relative abundance on Day 2 ($p=0.03$) but not Day 3. There was no significant effect of mask wearing on SC hydration or follicular porphyrins. TEWL and skin redness were elevated ($p<0.05$) on Day 2 and Day 3 on the masked cheek but not the unmasked forehead; values returned to baseline from Day 2 PM to Day 3 AM. Finally, the mask microbiome reflected that of the subject's skin; the relative abundance of *C. acnes* on the subject's mask correlated with that on the subject's cheek skin ($r^2=0.46$, $p<0.001$). In conclusion, wearing an N95 mask for 6 hours per day on two consecutive days under routine office work conditions did not significantly affect the diversity or composition of the skin microbiome and produced only transient changes in visible skin redness and barrier function. Longer term studies with different types of masks under non-office conditions are needed to further understand the influence of mask wearing on the skin microbiome.

LB737

Lack of stable housing as a risk factor for group A streptococcal skin and soft tissue infection among hospitalized adult patients

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Background: Patients lacking stable housing face significant medical morbidity, including increased rates of skin and soft tissue infections (SSTIs). While outbreaks of invasive group A streptococcal (GAS) disease, such as sepsis and pneumonia, have been reported among persons experiencing homelessness, only a single small study has examined housing status as a risk factor for non-invasive GAS infections, such as SSTIs.
Objective: To determine if housing status is an independent risk factor for GAS SSTIs.
Methods: We performed a retrospective cross-sectional study of hospitalized adult patients receiving dermatology consult services at UCSF Moffitt-Long Hospital or Zuckerberg San Francisco General Hospital between March 2018 and March 2020 who were diagnosed with an SSTI and had skin microbiology data available. We developed logistic regression models to examine whether housing status was independently associated with GAS SSTI in unadjusted analysis and after adjusting for age, gender, alcohol use and injection drug use.
Results: Our analysis captured 209 patients, with 150 having stable housing and 59 lacking stable housing. GAS was cultured from skin in 42% of patients lacking stable housing and 17% of patients with stable housing. In simple logistic regression, patients lacking stable housing had 3.51 times the odds (95% CI 1.80 to 6.84; $p<0.001$) of GAS positivity relative to patients with stable housing. In multiple logistic regression adjusting for potential confounders, patients had 3.95 times the odds (95% CI 1.87 to 8.38; $p<0.001$) of GAS positivity if they lacked stable housing.
Conclusions: Our results suggest that medical providers caring for patients lacking stable housing should have a high index of suspicion for GAS in the setting of SSTIs and consider empiric GAS coverage with a first-line antibiotic.

LB738

Anti-inflammatory activity of traditionally used, bioactive mushrooms in skin

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Mushrooms have long been considered a valuable resource for both nutritional purposes and in traditional medicinal practices. In particular, increasing amounts of research demonstrate that many of the medicinally used mushrooms possess strong anti-inflammatory and immune-modulating properties. In the skin, as elsewhere in the body, inflammation is a natural response to external and internal insults (i.e. physical stimuli, stress, infection, sunlight) and if uncontrolled, can also impact skin cell function, matrix protein degradation, and accelerate skin aging.
In this work, we describe how the inhibition of the recruitment and accumulation of neutrophils to the site of "irritation" (a hallmark of the inflammatory response) can reduce inflammation and help skin cells return to their optimal function. We show the ability of traditionally used, bioactive mushrooms to act on inflammation via this target and suggest a topical application of these mushroom extracts can reduce the visible signs of irritation.

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LB739

A retrospective analysis of bacterial culture results and disease severity in a cohort of Hidradenitis Suppurativa patients

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The role of bacteria in the initiation and progression of hidradenitis suppurativa (HS) is poorly understood. Likewise, the utility of swab bacterial cultures in guiding antibiotic therapy, a mainstay of treatment, remains controversial. We are seeking to determine if bacterial swabs reveal clinically useful trends in the relationship between bacterial profiles and HS severity. A retrospective chart review of 127 patients seen between March 2019 and November 2020 at the Einstein/Montefiore HS Center was performed. Disease severity was classified according to the HS-Physician Global Assessment (HS-PGA) scale. Chi-square and Fisher's exact tests were computed to analyze the differences in bacterial profile based on disease severity. Those with HS-PGA scores of ≥ 2 and swab bacterial cultures obtained at presentation were included in this study (mean age: 35.8±13.6, female: 70.1%). Participants were grouped by culture results: aerobic, anaerobic, aerobic plus anaerobic, or normal. Patients with aerobic cultures or mixed anaerobic plus aerobic cultures were more likely to have severe disease (HS-PGA 3-5) than mild disease (HS-PGA 2) ($p=0.03$), relative to patients growing anaerobic cultures at first visit. Furthermore, patients with Streptococcal species were more likely to have severe disease than mild disease ($p=0.03$). These findings suggest that superficial microbial cultures in HS may reveal trends in the relationship between bacterial profile and disease severity. Specifically, participants with severe disease were found to have predominantly aerobic or mixed aerobic plus anaerobic flora. Further longitudinal studies are necessary to analyze the shifting relationship between bacterial growth and disease severity in response to treatment.

LB740

SARS-CoV-2-associated 'covid toes:' multiplex immunofluorescent characterization of pathophysiology

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Coincident with the start of the COVID-19 pandemic, dermatologists worldwide have reported an uncharacteristic increase in pernio or chilblains (aka 'COVID toes'). However, the lack of systemic illness, low PCR positivity and lack of consistent seroconversion have led some authors to postulate an epiphenomenon. SARS-CoV-2 spike protein has been identified in a limited number of skin biopsies in few publications, yet there remain conflicting reports regarding other SARS-CoV-2 associated proteins, the presence or absence of viral RNA, and a unifying pathophysiology. In cooperation with the COVID Human Genome Effort, our "COVID toes" biobank was established to identify both the genetic and immunologic basis and provide clinically relevant insights into targeted therapeutics. As of March 2021, we have enrolled 96 patients, creating a prospective biorepository with clinical data, saliva, serial blood collection, and skin biopsies. Here we aim to comprehensively investigate the conflicting findings, detail the inflammatory response, and identify the source of interferon signaling with multiplex immunofluorescence (IFA) and the RNAscope fluorescent assay to detect viral mRNA. Median patient age was 17 (range 2 – 72) and 44/96 (46%) were male. Preliminary IFA results demonstrate detection of SARS-CoV-2 components, robust MxA detection and plasmacytoid dendritic cell (pDC) colocalization, identifying PDCs as the likely primary source of IFN-I production and implicates an excessive localized IFN-I response in affected patients.

LB741

Diet and nutritional behaviors of patients with Psoriasis

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The connection between diet and psoriasis has been of increasing interest to patients and physicians. An IRB approved 30- question survey assessing the popularity of specific diet regimens and nutritional supplements was offered voluntarily to psoriasis patients at the University of Iowa and Saint Louis University Dermatology Clinics. Of the 270 total respondents, 29.5% attempted weight loss as a dietary intervention with 10.8% (slightly more than 1/3 of those attempting weight loss) indicating this helped the severity of their psoriasis. Subjects endorsing dietary experimentation noted psoriasis improvement with ketogenic (50%), Mediterranean (46%), vegetarian (40%), and gluten-free (36%) diets. The most-tried supplement was oral vitamin D (32%), followed by oral fish oil (26%), and probiotics (21%). Of these supplements, probiotic use produced the greatest positive skin response (29%) with vitamin D (27.6%) and fish oil (25.7%) closely following. Out of all participants, 41.85% (113) did not try any of the diets or supplements surveyed while 52.2% (141) attempted between one to four of these interventions and only 5.9% (16) tried five or more of these diets. Wilcoxon tests showed that participants with two or more subtypes of psoriasis (plaque, guttate, flexural, scalp or nail) tried more diets or supplements than those without ($p=0.03$). In addition, participants younger than 55 sought to try more diets or supplements than those who were 55 or older ($p= 0.02$). Chi-squared testing between BMI and severity of psoriasis indicated that participants who were categorized as obese (BMI >30.0), had a higher rate of moderate to severe psoriasis than those who were not obese ($p<0.01$). Probiotics and weight loss are patient endorsed interventions utilized by younger patients in attempt to improve their psoriasis.

LB742

Predictors of post-discharge follow-up attendance among hospitalized dermatology patients

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Background: The transition from the inpatient to outpatient environment is important for patient care. However, this transition has not been studied in the context of hospitalized dermatology patients.
Objective: To determine significant predictors of follow-up attendance among patients seen by the inpatient dermatology teams at Zuckerberg San Francisco General Hospital (ZSFG) or UCSF Medical Center (UCSF) between March 2018 and February 2020 who were recommended for outpatient dermatology follow-up.
Methods: We first performed simple logistic regression to evaluate the association between our outcome variable of post-discharge dermatology visit attendance within 90 days of discharge and each of our 17 predictor variables spanning demographic, psychosocial and clinical categories. Predictor variables significant on simple regression ($P<0.10$) were candidates for the final multiple regression model, which was selected through stepwise backward elimination after false-discovery rate adjustment ($P<0.028$).
Results: Among 435 patients (305 at UCSF and 130 at ZSFG), 69% attended their recommended dermatology visit. Significant positive predictors of follow-up attendance in multiple regression included shorter time from discharge to follow-up ($p<0.001$), prescription of a high-risk discharge medication ($p=0.014$), and Asian race ($p=0.012$), while significant negative predictors included lack of stable housing ($p=0.001$), and active psychiatric disease ($p=0.014$).
Conclusions: Our findings emphasize the importance of systematically collecting information on social determinants of health among hospitalized dermatology patients in order to identify psychosocial risk and connect patients with appropriate resources. These results may also inform patient-centered interventions to improve continuity of care among hospitalized dermatology patients.

LB743

Cutaneous immune-related adverse events are undertreated in advanced cancer patients

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Cutaneous immune-related adverse events (cirAEs) are common complications of immune-checkpoint inhibitors (ICIs). Few cirAE subtypes have established treatment guidelines, which may not be routinely followed. We assessed concordance of delivered care for cirAEs with National Comprehensive Cancer Network (NCCN) recommendations, the standard for treating ICI-associated toxicities. Patients at Massachusetts General Hospital who initiated ICIs between 1/1/16-3/8/19 (N=2,459) were screened for cirAEs using billing data. cirAE status, features, and treatments were further abstracted from the medical record. Undertreatment was defined as failing to provide all NCCN recommended treatments/referrals, based on cirAE subtype/severity. Associations between undertreatment of cirAEs and dermatology consult, severity, and morphology were assessed via logistic regression, adjusting for age, sex, race, cancer/ICI type, and significant covariates (P<0.05). 358 patients developed cirAEs, with 39.9% of diagnoses having established guidelines. Of these 143 patients, 81.1% were undertreated, with a median of 1 treatment met (IQR 0-2) for every 2 recommendations (IQR 2-3). Non-recommended treatments were prescribed in 21.7% of patients. Few patients overall (n=108; 30.2%) were referred to dermatology, including those indicated by NCCN for consultation (n=15, 53.6%). In the multivariable analysis, patients seen by dermatology (aOR: 0.19; 95% CI: 0.06,0.62; P=0.01) and with bullous dermatitis were less likely to be undertreated (aOR: 0.12; 95% CI: 0.02,0.79; P=0.03). Lower cirAE severity was also associated with undertreatment (-0.49 coefficient; 95% CI: -0.80,-0.19; P=0.002). We found that most cirAEs were inadequately managed according to NCCN guidelines, even when controlling for cancer type, cirAE features and ICI regimen. Milder, morphologically ambiguous cirAEs may be less clinically apparent to providers, complicating treatment adherence and decision to consult. Our findings underscore the need for coordinated care with dermatology, and further optimizing cutaneous toxicity management.

LB744

Use of indoor tanning diagnosis codes in claims data

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Efforts to reduce indoor tanning require knowledge on the population at risk. ICD-10 codes (universally implemented in 2015) included indoor tanning codes for the first time. We investigated the patients and settings in which indoor tanning codes are being used, which has not previously been done. We used Truven Health MarketScan data from 2016-2018, including de-identified commercial insurance claims data for approximately 43 million patients. We included encounters with ICD-10 indoor tanning codes and used descriptive statistics to evaluate patient and encounter characteristics. We also normalized to the number of outpatient dermatology encounters. From 2016-2018, a total of 4,550 encounters with indoor tanning codes were recorded. The most common specialty was dermatology (72.3%) and 99.0% of encounters were outpatient. There were 29 encounters with indoor tanning codes per 100,000 dermatology encounters. The majority of patients were female (85.0%). Ages ranged from 7 to 93 with the majority of patients aged 18 to 54, relative to the number of dermatology visits by age group. Encounters with indoor tanning codes were most common in the spring and least common in the fall. The Midwest region had the highest number of indoor tanning encounters per 100,000 dermatology encounters, nearly double that of the next highest region. We also investigated the most frequent CPT codes and found destruction of premalignant lesion was performed in 15.1% and biopsies in 18.4% of encounters, suggesting that many of these encounters may have been for skin cancer surveillance. This study provides insight into encounters with indoor tanning ICD-10 codes, which are relatively uncommon and occur primarily in outpatient dermatology. Increased usage of indoor tanning codes in coming years may strengthen the body of indoor tanning literature. Future research could consider claims data as a tool to better understand patients who have been exposed to indoor tanning and their risk factors, comorbidities, behaviors, and healthcare utilization.

LB745

Population-level study of Hidradenitis Suppurativa (HS) in the United States reveals association with obesity and socioeconomic status

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Hidradenitis suppurativa (HS) is a chronic debilitating skin disease with significant morbidity. Nevertheless, clear epidemiology of HS is incomplete due to challenges in data collection and study designs. With the increasing use of digital approaches to gain health information, digital dermatoepidemiology can help fill the gaps in HS epidemiology. We employed Google Trends data on searches for "hidradenitis suppurativa" between January 1, 2004 and February 1, 2021 as a method to study the geographic variation of HS in the US. With the hypothesis that HS search interest would correlate with lower socioeconomic status (SES) and higher rates of obesity, we examined the association of HS searches with median income and obesity rates based on the US Census Data and Robert Wood Johnson Foundation Obesity Rates & Trend Data, respectively. Our results demonstrate that there are large geographic variations in search interest for HS associated with SES and obesity, where obesity rate is positively correlated (correlation coefficient: 0.70, $p = 2.5 \times 10^{-8}$) and SES is negatively correlated with HS search interest (correlation coefficient: -0.39, $p = 2.1 \times 10^{-6}$). We also identified regions of the country with the highest and the lowest HS search interest and found that the highest HS search interest were in the following regions: Rochester, MN - Mason City, IA - Austin, MN; Shreveport, LA; and Montgomery (Selma), AL whereas the lowest HS search interest were in the following regions: Fresno-Visalia, CA; Monterey-Salinas, CA; and San Francisco-Oakland-San Jose, CA. Our study provides insights into the distribution of HS interest in the US and the potential for precision public health efforts to address areas that may have increased HS burden. Overall, this big data digital dermatoepidemiology approach provides new insights into HS and serves as an important foundation for further public health efforts and epidemiological studies in HS and healthcare disparities.

LB746

Exploring the knowledge, attitude, and practices of chemical shop owners in rural Ghana

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Many rural areas in sub-Saharan Africa face a high prevalence and morbidity of skin disease and are challenged by a lack of accessible dermatologists. In Ghana, community pharmacies, called chemical shops, were established to respond to these inequities. Our study evaluates the dermatologic knowledge, attitudes, and practices (KAP) of Licensed Chemical Sellers (LCS) within several districts of Ghana's Ashanti Region. To assess the dermatologic KAP of LCS, we created a questionnaire and recorded direct interviews over a three-week period with Ghanaian research assistants' help. These were transcribed verbatim and analyzed qualitatively by two US medical students and one board-certified dermatologist, who established common themes based on traditional dermatologic KAP. Over a three-week period, our interviews identified important roles played by LCS within their communities, including dispensing medicines and being the first to assess and treat skin conditions. However, the lack of uniformity in these roles and their training may suggest variation in their knowledge and ability to assess and treat dermatologic conditions properly. And while most mentioned seeing skin disease daily, their clinical thinking and treatment recommendations for all conditions varied. Our interviews also provided insight into the challenges faced by rural LCS, where many commented-on pressures to comply with care-seeking behavior or cultural treatment expectations, including competition faced by therapies offered by traditional healers or street vendors. The KAP of LCS in Ghana's Ashanti Region plays a pivotal role in assessing and treating skin disease, where there is one licensed dermatologist among 11 million people, making it difficult to access dermatologic treatment. Further studies could evaluate the diagnostic and therapeutic accuracy of chemical shop owners and cultural views on dermatology medicines.

LB747

Prevalence of lichen planus across racial/ethnic groups in the *All of Us* research program: a US-based cohort study

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Introduction: Lichen planus (LP) is an inflammatory dermatosis whose epidemiology has not been well described. We sought to describe the prevalence of LP across racial and ethnic groups in the United States-based *All of Us* Research Program.
Methods: We performed a cross-sectional analysis of the *All of Us* Research Program, a US-based cohort study that aims to enroll and share health and genetic data on over 1 million participants with a focus on groups historically underrepresented in biomedical research. We identified LP using participant self-reported survey and electronic health record data. We calculated the prevalence of LP among participants with available data and reported results and demographics across self-identified racial and ethnic groups. We calculated 95% confidence intervals using the Wald method.
Results: Of 203,025 participants with available data, we identified 788 LP cases. The overall prevalence of LP was 0.39% (0.36-0.42) with a 3:1 female predominance (586 females [74.4%]) and an average age of 66 (standard deviation 13). 82% of LP cases were in those age 55 and older, with the highest prevalence seen among the 65-74 year-old group (34% of the LP population). The prevalence of LP varied by racial/ethnic group: prevalence was highest in whites (n=470, 0.45% [0.41-0.49]), followed by Blacks (n= 175, 0.42% [0.36-0.49]), Asians (n=15, 0.26% [0.13-0.42]), and Hispanics (n=93, 0.23%, [0.18-0.28]). The age distribution also varied by race/ethnicity: average age was higher among whites (69 years, SD 11) compared to racial/ethnic minorities (Black, 62 [SD 11]; Asian, 59 [SD 13]; Hispanic, 61 [SD 13]).
Conclusions: In the US-based *All of Us* cohort, the prevalence of LP was 0.36% to 0.42% and varied by racial and ethnic group. These results need validation in other population-based cohorts.

LB748

An epidemiological study on Cutaneous Melanoma, Basal Cell and Epidermoid Carcinomas diagnosed in a sunny city in southeast Brazil in a five-year period

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Skin cancer is increasing worldwide; in tropical places the population is exposed to high levels of solar radiation, raising the risk for developing cutaneous carcinoma. Aimed at encouraging prevention measures and the early diagnosis of these tumors, this study analyzed data on cutaneous melanomas, basal cell and epidermoid carcinomas, using as source the medical records of all patients diagnosed with skin cancer in a pathology service in a Brazilian city from 2015 to 2019. The incidence of skin cancer cases was correlated with the histological type, sex, age, and location. Significant association was observed between age and type of cancer ($p=0.0085$); age and sex ($p=0.0298$); and type of cancer and body region affected ($p<0.01$). Those 161 cases analyzed comprised 93 basal cell, 66 epidermoid carcinomas, and only 2 melanomas. In the group aged 19 to 30 years, the epidermoid form was most prevalent; from 31 to 59 years, the basal cell prevailed; in 60-year-olds or over, both types had higher frequencies. Associating age and sex, in groups aged 19 to 30 women were most affected. There was a gender balance in the age group 60-year-olds or over. As for topography, there was a high prevalence in the head and neck, followed by upper limbs. Relating histological type and topography, there was a prevalence of basal cell carcinomas in head/neck and chest. In upper limbs, the epidermoid form prevailed. About 82% of patients 60-year-olds or over had head and neck skin carcinoma. In conclusion, young people were more affected by the epidermoid form, which manifested itself significantly in the upper limbs, presenting a behavior of this histological type. Patients aged 60 years or older were the most affected; in gender balance, they present intense head and neck involvement, while areas such as chest and lower limbs are little affected, revealing that body areas continuously exposed to solar radiation are more predisposed to the development of skin cancer.

LB749

Association between obesity and sunburn: A cross-sectional analysis in claims data

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A growing body of literature supports a seemingly paradoxical association between obesity and an increased risk for melanoma and a decreased risk for keratinocyte carcinomas (KCs). Investigations using survey data show an association between obesity and sunburn, but this is subject to recall bias. We aimed to assess the association between obesity and sunburn diagnosed in medical encounters. We conducted a cross-sectional study using claims data from the Truven Health MarketScan (2009-2017) and Health Risk Assessment (HRA) Database, which includes commercial insurance claims data and self-reported BMI. Patients ≥18 years old with at least one medical encounter were included. The primary outcome was sunburn diagnosis. We performed multivariate logistic regression, adjusting for age, gender, region, insurance type, and healthcare utilization. Approximately 3.4 million patients met inclusion criteria, with 6,962 having at least one sunburn diagnosis. Multivariate logistic regression showed obesity was statistically significantly associated with sunburn (odds ratio [OR]1.26, 95% confidence interval [CI] 1.20-1.32). Female gender (OR 1.25), younger age (OR 0.98 per 1-year increase in age), and healthcare utilization (OR 1.02 per 1 additional outpatient encounter per year) were also statistically significantly associated with sunburn. Our study shows a positive association between obesity and sunburn diagnosis in a large claims dataset, aligning with self-reported data and supporting the theory that sunburn may partially explain the increased risk for melanoma in patients with obesity. This does not address the lower risk for KCs. Understanding patterns of UV exposure in patients with obesity can inform interventions to minimize melanoma risk.

LB750

Clinical and demographic characteristics of encounters with sunburn in claims data

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Sunburn is a preventable risk factor for skin cancer. Prior investigations of sunburn in healthcare settings have focused on emergency department visits. More epidemiologic information on patients presenting with sunburns is important to inform public health initiatives and further research. Here we characterize the clinical settings and demographic characteristics of patients who receive a sunburn diagnosis. We used Truven MarketScan, a national deidentified commercial insurance database, from 2008-2018. Eligible patients had a sunburn diagnosis code entered (*ICD-9* or *ICD-10*) during an encounter. The primary outcomes were patient demographics, clinical settings, provider specialties, management provided, and geographic location, presented with descriptive statistics. We identified 186,168 patients with 230,987 sunburn encounters. 55.3% were women and 26.9% were <18 years of age. Most of the encounters occurred during summer (57.6%), followed by spring (29.9%). The most common region was the South (38.4%), followed by the Northeast (23.2%). 26.4% of the encounters were in the emergency or urgent care setting, and 73.4% were outpatient. Fewer than 1% of patients were hospitalized. The most common treatments included systemic and topical steroids (7.2% and 5.2%, respectively) and NSAIDs (2.7%). The most common provider specialty was Dermatology (23.5%), followed by Family Medicine (19.9%). This study provides insight into the clinical settings and demographics of patients diagnosed with sunburn across healthcare settings and highlights the importance of sunburn prevention in the pediatric population, which comprised more than a quarter of patients diagnosed with sunburn.

LB751

COVID-19 complications in patients with Hidradenitis Suppurativa: A multicenter study

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Hidradenitis Suppurativa (HS) is a chronic inflammatory skin disorder that causes abscesses in intertriginous areas and is also associated with numerous other conditions. There is limited literature on the outcomes of COVID patients with HS so the goal was to investigate the impact of AD on COVID outcomes. A retrospective cohort study was done using TriNetX, a federated real time database of 63 million records. COVID patient cohorts were identified by validated ICD-10 and serology codes per CDC guidelines from 1/20/2020 to 2/23/2021. A 1:1 matched propensity score analysis was conducted, adjusting for comorbidities and demographics, to calculate adjusted Risk Ratios (aRR) with 95% CI. 30-day COVID complications were examined with severe COVID being defined as a composite of mortality and ventilation. Subgroup analyses were also performed for HS patients on systemic antibiotics. In a matched sample of 2004 patients in each cohort, there was no statistically significant difference between HS-COVID patients and non-HS COVID patients in hospitalization (0.93[0.8-1.1]), acute respiratory distress syndrome (1.31 [0.8-2.2]), mechanical ventilation (1.06 [0.7-1.6]), mortality (1.00 [0.6-1.8]), and severe COVID (1.07 [0.8-1.5]) but there was a difference in sepsis (1.37 [1.0-1.9]). Subgroup analysis revealed that HS-COVID patients with a one-year history of systemic antibiotic use were at a higher risk for hospitalization (1.27 [1.01-1.6]) compared to HS-COVID patients without one-year history of systemic antibiotics wheras all other outcomes assessed had no differences. HS-COVID patients are not at higher risk for more severe COVID outcomes compared to COVID patients without HS. However, HS patients with a history of systemic antibiotics are at a higher risk for hospitalization compared to HS patients without a history of systemic antibiotics. Further studies are warranted to visit the longer-term impacts of COVID on HS patients.

LB752

A cross sectional survey of skin cancer knowledge, attitudes, and sun care practices in an underserved Phoenix population

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The incidence of melanoma and non-melanoma skin cancers is on the rise. The Hispanic population is more likely to be diagnosed with melanoma at an advanced stage and have poorer overall survival. The primary aim of our study was to assess the skin cancer knowledge, attitudes, perceived risk, and sun care practices of an underserved, primarily Hispanic, population in the Phoenix area. A cross sectional survey of 208 patients recruited during a skin cancer screening program was performed. Our population was primarily Hispanic (64.9%), from Mexico (87.9%). The Hispanic population had an average knowledge score of 3.68 for the 6 skin cancer questions asked, the lowest of any group, and significantly lower than the White/Caucasian population ($p<.01$). However, they displayed the highest desire to learn more about skin cancer (64.6%, “strongly agree”). They were the most concerned about developing skin cancer (50.4%, “very concerned”), but had low rates of sun protection usage (45.7% sunscreen, 49.2% protective clothing use). There is a discordance between sun exposure, skin cancer knowledge, and sun care practices in the Phoenix area Hispanic population. This data highlights the opportunity to educate this at-risk population about skin cancer and the importance of sun care practices.

LB753

Erythema nodosum in ulcerative colitis is associated with left-sided colitis and better outcomes: A nationwide inpatient study

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The relationship between erythema nodosum (EN) and ulcerative colitis (UC) prognosis has not been established. Thus, we used the National Inpatient Sample database to evaluate the relationship between EN, anatomical bowel involvement, and inpatient outcomes of UC. Using validated ICD-9 codes, we analyzed adults 2003-2015 with a primary diagnosis of UC with and without EN. Multivariable logistic and linear regression models were used to determine the relationship between EN and UC characteristics after adjusting for patient demographics and hospital characteristics. An estimated 415,247 discharges had a primary diagnosis of UC, of which 778 had a secondary diagnosis of EN. The EN group was less likely to have chronic proctitis (OR=0.30, 95% CI 0.16, 0.58) or universal colitis (OR=0.54, 95% CI 0.42, 0.68), and more likely to have left-sided colitis (OR=1.63, 95% CI 1.23, 2.17). There was no difference in chronic enterocolitis, ileocolitis, proctosigmoiditis, pseudopolyposis, and other or unspecified forms of UC between groups (p-values>0.05). A diagnosis of EN was associated with lower odds of GI hemorrhage (OR=0.74, 95% CI 0.56, 0.98), but higher rates of post-hemorrhagic anemia (OR=1.46, 95% CI 1.17, 1.86) and other anemias or deficiencies (OR=2.22, 95% CI 1.89, 2.60). Healthcare utilization analysis of the EN group revealed a lower rate of colorectal resection (OR=0.36; 95% CI 0.26, 0.49), shorter hospital stay (0.76 days shorter), and lower hospital charges ($671 less) (p-values<0.003). There was no difference in in-hospital mortality between groups (p=0.992). Our study shows that EN as a physical exam finding in patients with UC may be used to identify patients at lower risk of pancolitis, as well as to predict moderate disease severity and better inpatient outcomes.

LB754

Demographics and features of hospital admissions for Hermansky-Pudlak Syndrome: A national inpatient sample analysis

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We conducted the first ever nationwide analysis of Hermansky-Pudlak Syndrome (HPS) in the United States (US) using the National Inpatient Sample database. Discharges with a primary or secondary diagnosis of HPS during 2015-2018 were selected using ICD-10 codes. Demographics, reasons for admission, and outcomes were analyzed using multivariable logistic and linear regression models. An estimated 510 inpatient discharges had a diagnosis of HPS, a nationwide prevalence of 4.4 per million discharges. Compared to the standard inpatient population, HPS was more common in the 18-44 years age group (OR=1.79, 95% CI 1.18, 2.73), and more common in Hispanic patients (53.9%) than white (34.3%) or other races or ethnicities (9.8%) (OR=7.24, 95% CI 5.11, 10.27). HPS was also more common in large, urban teaching hospitals in the Northeastern US (OR=1.60, 95% CI 1.00, 2.54). The most frequent reasons for admission were gastrointestinal (GI) disease (often misdiagnosed as Crohn's disease) (18.6%), pulmonary disease including pulmonary fibrosis and pneumonia (16.7%), infections (most often sepsis) (8.8%), and renal failure or electrolyte derangement (7.2%). Bleeding was a less frequent reason for admission (3.9%). The mean length of stay was 10.3 days with a total hospital charge of $174,673. In-hospital mortality was 4.9%, with all deaths occurring with pulmonary disease. We discovered that the Hispanic population constitutes the majority of HPS admissions in the US, likely due to HPS Type 1 (pulmonary fibrosis, granulomatous colitis, and mortality from pulmonary disease). We also found that HPS is most common in the Northeastern US, which is also where the Puerto Rican population is most concentrated. Finally we found that electrolyte derangements and renal injury occur more than previously recognized, while non-GI hemorrhage was less common than expected.

LB755

Patient-reported outcomes with sarecycline treatment for Acne Vulgaris: Pooled analysis of phase 3 clinical studies

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Introduction: Acne vulgaris is associated with anxiety, depression, and suicidal ideation. Sarecycline is a narrow-spectrum antibiotic approved by the FDA for treatment of moderate-to-severe acne. This post hoc analysis evaluated health-related quality of life (HRQOL) outcomes using pooled data from 2 multicenter, randomized, double-blind, placebo-controlled, Phase 3 studies of sarecycline in moderate-to-severe acne (ClinicalTrials.gov IDs NCT02320149 and NCT02322866).
Methods: Patients with acne vulgaris (age, 9-45 years) were randomized to receive sarecycline 1.5 mg/kg/d or placebo for 12 weeks. Patient-related HRQOL was assessed at baseline and week 12 using the Skindex-16 questionnaire, which evaluates the effects of skin disease on HRQOL across domains of symptoms, emotion, and functioning. The total score averages the 3 domain scores, normalized to a scale of 0 (no effect) to 100 (maximum effect). Change from baseline and least squares means (LSM) difference (sarecycline vs placebo) were assessed in the overall population and stratified by age (<18 and ≥18 years).
Results: Improvement in HRQOL was significantly greater in the sarecycline group (n=1002) vs placebo (n=1000; change from baseline in total score, -16.8 vs -12.0). Sarecycline demonstrated improved HRQOL vs placebo for total score (LSM difference sarecycline vs placebo, -4.8 [95% CI, -6.4 to -3.1]) and each domain: symptoms (-4.9 [-6.5 to -3.3]), emotion (-6.4 [-8.8 to -4.1]), and functioning (-3.2 [-5.1 to -1.3]). The LSM difference for each score in both age groups significantly favored sarecycline over placebo (total score, P<0.001), though reduction from baseline in total score was numerically greater in patients aged ≥18 years vs <18 years (-21.6 vs -11.6).
Conclusion: Sarecycline demonstrated significant improvements in HRQOL across each age group.

LB756

Patient-reported outcomes for sarecycline effectiveness in Acne Vulgaris in real-world settings: PROSES study protocol

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Introduction: The detrimental psychosocial impact of acne vulgaris is well established. Patient-reported outcomes are needed to fully understand the psychosocial benefits of acne treatment. Sarecycline, a novel narrow-spectrum antibiotic, demonstrated efficacy, safety, and improvement in health-related quality of life (HRQOL) in clinical trials and is approved for treatment of moderate-to-severe acne. In 2020, a consensus panel generated a 10-question expert panel questionnaire (EPQ), which, along with the validated acne symptom and impact scale (ASIS), was considered a high-quality tool for real-world assessment of patient-reported HRQOL. The HRQOL benefits of sarecycline will be assessed using these instruments.
Methods: This single-group, prospective, 12-week cohort study is expected to enroll 300 patients (age, ≥9 years) with moderate-to-severe acne treated with sarecycline as part of routine care in up to 50 US community practices. The primary endpoint is patient-reported outcomes at week 12. At the baseline and week-12 visits, patients and caregivers of pediatric patients will complete the EPQ and ASIS. Additional endpoints include sarecycline

effectiveness (success on investigator global assessment), satisfaction, safety, and tolerability.
Conclusions: This real-world study of sarecycline will be the first to use the most recent expert panel recommendations to evaluate HRQOL for patients with acne.

LB757

Hospitalization for Chediak-Higashi Syndrome: A national inpatient sample analysis

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Chediak Higashi syndrome (CHS) is a rare autosomal recessive disease that presents as oculocutaneous albinism and immunodeficiency. We performed the first ever national inpatient analysis of CHS in the United States. Patients with a primary or secondary diagnosis of CHS during 2015-2018 were selected using ICD-10 codes to determine the most common reasons for hospitalization, demographic features, and inpatient burden and outcomes. An estimated 155 discharges had a primary or secondary diagnosis of CHS nationwide, representing an inpatient prevalence of 1.3 per million discharges. Approximately 58.1% were male and 42.9% were female, and the mean age of hospitalization was 18 years. The predominant race was white (41.9%), followed by black (38.7%), other (16.1%), and Asian/Pacific Islander (3.2%). No patients were Hispanic or Native American. The most common reasons for admission were hematological or coagulation dysfunction (36.7%), infection (16.7%), and major organ dysfunction or endocrine disease (13.3%). Hemolytic anemia was the most frequent principal diagnosis (10%), followed by hemophagocytic lymphohistiocytosis (HLH), complications of bone marrow transplant, cellulitis of the lower extremity, and acute renal failure (each 6.7%). The mean length of stay was 9.9 days, mean hospital charge of $89,893, and mean inpatient mortality of 3.3%. Although infection remains a hallmark of CHS, our study showed that other common reasons for inpatient care in CHS were anemia, hematologic malignancies, and bone marrow transplant or complications. Notably, we found an absence of the disease in the Hispanic population, as well as renal morbidity in some patients. These demographic results, along with the frequent presentation of hemolytic anemia, are useful characteristics to aid in diagnosing this rare disease in the clinical setting.

LB758

Erythema nodosum in Crohn's Disease is associated with lower risk of enteritis and surgery: A nationwide inpatient study

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Erythema nodosum (EN) indicates a better prognosis in sarcoidosis and coccidiomycosis, but its predictiveness of outcomes in Crohn's disease (CD) is not well-established. Therefore, we used the National Inpatient Sample database to evaluate the relationship between EN, anatomical bowel involvement, and outcomes in patients with CD. Using validated ICD-9 codes, we analyzed adults 2003-2015 with a primary diagnosis of CD with and without EN. Multivariable logistic and linear regression models were used to determine the relationship between EN and CD characteristics after adjusting for patient and hospital characteristics. Patients with CD and EN had a higher odds of isolated colon involvement (OR=2.03, 95% CI 1.77, 2.33,) and combined colitis-enteritis (OR=1.38, 95% CI 1.17, 1.63) compared to those without EN. The EN group also had significantly lower rates of isolated enteritis (OR=0.45, 95% CI 0.37, 0.55). The EN group had lower rates of intestinal obstruction (OR=0.32, 95% CI 0.26, 0.39) and non-anorectal intestinal fistulas (OR=0.39, 95% CI 0.27, 0.58), but higher rates of anal fistulas (OR=3.87, 95% CI 3.15, 4.76). There was no difference in gastroduodenal fistulas (p=0.99). Healthcare utilization analysis revealed lower rates of small bowel resection (OR=0.10, 95% CI 0.04, 0.24) and colorectal resection (OR=0.44, 95% CI 0.35, 0.55) in the EN group. No difference was seen in cost, length of stay, or inpatient mortality (p-values>0.05). Our study

shows that EN indicates a specific disease state in CD that involves higher rates of colonic involvement and lower rates of enteritis. Thus, the dermatologic finding of EN may be useful for predicting odds of bowel involvement and disease stage in CD.

LB759

Post-operative radiation therapy to prevent local recurrence of low-risk Merkel cell carcinomas of the head and neck versus other sites

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Merkel cell carcinoma (MCC) is a rare, aggressive skin cancer with a recurrence risk of ~40%; however, prognosis for low-risk, stage I disease is excellent with primary surgical management and wide local excision. The role of post-operative radiation therapy (PORT) is controversial. Here, we assess the efficacy of PORT on local recurrence (LR) rates in a cohort of patients with low-risk, pathological stage I MCC with primary tumors on the head/neck (HN) vs. non-head and neck (Non-HN) sites. One hundred forty-seven MCC patients treated from 2006-2020 were identified from an IRB-approved prospective registry who had 'low risk' disease: pathological T1 primary tumor resected with negative microscopic margins, negative pathologic node status, and no immunosuppression or prior systemic therapy. LR was defined as tumor recurrence within 2 cm of the primary surgical bed and its frequency was estimated with the cumulative incidence method. Seventy-nine patients received PORT (30 HN, 49 Non-HN) with a median dosage of 50 Gy (range: 5-64 Gy) while 68 patients were treated with surgery alone (30 HN, 38 Non-HN). Median follow-up time was 5.1 years (range: 7 days to 16 years). Addition of PORT was associated with a decreased risk of LR across the entire cohort (5-year rate: 9.5% vs. 0%, p=0.004), with 6 LRs in the surgery alone group. Importantly, the addition of PORT significantly reduced LR rates among HN patients (21% vs. 0%, p=0.034). Conversely, no LRs were observed in Non-HN patients. There was no significant difference in MCC-specific survival. For low-risk, pathological stage I MCC of the extremities and trunk, excellent outcomes were achieved with surgery alone. However, HN MCC was a risk factor for LR that was significantly reduced with PORT. Therefore, MCC of the head and neck should be considered an independent indication for PORT.

LB760

Statin use in patients with pre-existing inflammatory myopathies

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Systemic autoimmune myopathies (SAM) are a group of rare rheumatic diseases associated with high morbidity and disability. Recent studies have shown a high prevalence of hyperlipidemia in patients with SAM. While statins are commonly used lipid-lowering medications, the safety of statin use in patients with SAM is still unclear. The objective of this study was to evaluate the safety of statin use in patients with pre-existing SAM. We performed a single-center retrospective cohort study of adult patients with clinically diagnosed SAM between 2008-2018. Data on type of myopathy, statin use, patient demographic, and clinical information were collected from electronic medical records. The primary outcome of interest was the incidence of new myalgia or myopathy, as determined by a physician. Patients taking statins prior to SAM diagnosis were excluded. 151 patients met inclusion criteria. 104 (69.3%) patients had dermatomyositis, 45 (30%) had polymyositis, and 2 (0.7%) had another SAM. Patients prescribed statins were significantly older at the time of SAM diagnosis compared to those who were not prescribed statins (58.2 vs 46.6 years, p<0.001). Incidence of a new myopathy did not differ significantly between patients prescribed statins versus those not prescribed statins (6.25% vs 4.24%, p=0.632); this difference remained insignificant when adjusted for age (p=0.313). No differences were observed in the incidence of adverse cardiovascular or cerebrovascular events. Of the two patients on statins who developed a new myopathy, one discontinued their statin medication.

Overall, patients with SAM prescribed statins do not appear to have a significantly higher incidence of new myopathies compared to those not prescribed statins. Given their widespread use and well-studied benefits for cardiovascular health, physicians caring for patients with inflammatory myopathies can counsel them accordingly regarding the safety of statin use.

LB761

Clinical outcomes in Pemphigoid and Pemphigus patients with COVID-19

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Pemphigoid and Pemphigus are both blistering autoimmune skin diseases that can have systemic manifestations. Little information exists on the outcomes of COVID patients with these blistering diseases, so the goal was to investigate the impact of both on COVID outcomes. A retrospective cohort study was done using TriNetX, a federated real time database of 63 million records. COVID patient cohorts were identified by validated ICD-10 and serology codes per CDC guidelines from 1/20/2020 to 2/5/2021. A 1:1 matched propensity score analysis was conducted, adjusting for comorbidities and demographics, to calculate adjusted Risk Ratios (aRR) with 95% CI. 30-day COVID outcomes were examined with severe COVID being defined as a composite of mortality and ventilation. Subgroup analyses were also performed for pemphigoid and pemphigus patients on systemic immunosuppressants. In a matched sample of 260 patients in each cohort, there was no significant difference between pemphigus/pemphigoid-COVID patients and non-pemphigus/pemphigoid COVID patients in hospitalization (1.1[0.85-1.43]), acute respiratory distress syndrome (1.1[0.47-2.5]), mechanical ventilation (1.64[0.8-3.4]), mortality (1.75[0.9-3.5]), and severe COVID (1.53[0.9-2.7]) but pemphigus/pemphigoid patients were at a higher risk for sepsis (1.87[1.1-3.4]) . Subgroup analysis revealed that pemphigus/pemphigoid-COVID patients with a one-year history of immunosuppressants had no difference in complication risk compared to pemphigus/pemphigoid-COVID patients without one year history of immunosuppressants. Overall pemphigus/pemphigoid-COVID patients are not at higher risks for severe COVID complications compared to COVID patients without pemphigus/pemphigoid. History of systemic Immunosuppressants also do not increase complication risk in pemphigus/pemphigoid patients. Additional research is needed to examine the long term impacts.

LB762

Initiation patterns among novel systemic agents for U.S. adults with Psoriasis and Psoriatic Arthritis

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Background: Biologic agents and PDE-4 inhibitors are a growing, but high cost drug class for severe psoriasis patients, especially those refractory to conventional therapies. Factors that drive treatment selection are unknown.
Type of Study: Retrospective cohort study
Methods: Commercial and Medicare Advantage adult enrollees with a pharmacy claim for a TNF-a, IL-12/23, IL-17, or PDE-4 between 2015 and 2018 were grouped into psoriasis only (1-Ps, n=8013) or those with psoriasis plus psoriatic arthritis (2-Ps+PsA, n=5233). Multinomial logistic regression was used to generate odds ratios and 95% confidence intervals for receiving IL-12/23, IL-17, or PDE-4 compared with TNF-a and adjusted for demographics, prescriber specialty, insurance, and Charlson Comorbidity Index.
Results: TNF-a (referent) was the most common biologic for both groups (1-Ps 36%, 2-Ps+PsA 55%), followed by PDE-4 (1-Ps: 38%, 2-Ps+PsA: 27%), IL-12/23 (1-Ps: 21%, 2-Ps+PsA: 12%) and IL-17 (1-Ps: 5%, 2-Ps+PsA: 6%). Only 1.1% of 1-Ps patients were prescribed by a rheumatologist and 43% of 2-Ps+PsA. From 2015 to 2018, the proportion of IL-17 and PDE-4 increased, but TNF-a remained the most common. Prescribing of IL-12/23 is also increasing over time driven by the newer IL-23 medications. For 2-Ps+PsA patients, patients seen by

rheumatologists were less likely to have a claim for non-TNF-a treatment i.e. IL-12/23 (OR=0.22[0.18-0.27)], IL-17 (0.36[0.28-0.46]) and PDE-4 (0.53[0.27-0.46]) versus those seen by dermatology. For 1-Ps, fills for IL-12/23 and PDE-4 (0.45[0.33-0.61], 0.48[0.38-0.60]) were less likely to be observed in Medicare compared to commercial.
Conclusion: IL-17 and PDE-4 inhibitors have been increasingly utilized compared to older biologics , however TNF-a remained the most commonly used. IL-23s should be monitored as their prescribing increases. Psoriasis type, insurance, and provider specialty were associated with selection of these agents.

LB763

Characteristics and outcomes of dermatologic patient assistance programs

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Several biologics and small molecule inhibitors are approved for psoriasis and atopic dermatitis; however, high costs limit accessibility for patients with inadequate insurance. Patient Assistance Programs (PAPs) are designed to provide free or discounted medications. This study characterizes PAPs for patient-administered biologics and small molecule inhibitors with FDA-approval for psoriasis and atopic dermatitis. Online PAP application forms for 13 medications were reviewed for application characteristics, patient eligibility, and outcomes. Application readability was determined using the Flesch-Kincaid grade level. All PAPs accepted uninsured and insured patients with no or limited drug coverage. 92% disclosed that they accepted Medicare Part D patients. The median maximum eligible annual income per one-person household was $57,420. 69% required financial documentation. 92% noted that coverage could be obtained for up to one year. Only one PAP specified the number of patients directly assisted in the past year. 69% of applications had a reading level of college or above. 38% were offered in Spanish. 31% did not require applicants to be legal US residents. PAPs were transparent regarding eligibility criteria and coverage duration. All PAPs accepted patients without insurance or with zero or limited drug coverage, and all but one disclosed that they accept Medicare Part D patients. The 4 PAPs that did not require legal US residency represent coverage opportunity for undocumented patients. While PAPs can provide a safety net for patients who cannot afford medications, most applications were unavailable in non-English languages and required at least a college reading level, representing a significant health literacy discrepancy. Furthermore, most PAPs were not transparent about percent of patients obtaining coverage. Greater transparency, language availability and readability may better inform patients of viable options to treat their disease.

LB764

Factors associated with Dermatoporosis

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Objective: To determine factors associated with this diagnosis in >60 years old patients of the outpatient clinic in the Hospital Central “Dr. Ignacio Morones Prieto ” San Luis Potosí, México.
Materials and methods: An observational, cross-sectional, descriptive, and analytical study was performed. Patients >60 years old were selected. A clinical history, clinical examination, and application of a validated diagnostic self-questionnaire were performed.[2]
Results: 315 subjects were evaluated, the prevalence was 29% (n = 91), 70% women (n = 64), and 30% men (n = 27). The risk factors were age> 75 years (61% vs 27%; p = 0.001); prolonged sun exposure (77% vs 58%; p = 0.002); intake of anticoagulants / antiplatelets (40% vs. 23%; p = 0.004), intake of oral steroids (13% vs. 6%; p = 0.03); and kidney disease (12% vs 6%; p = 0.03). Maternal age> 40 years in their last child (p = 0.02), lactation> 7 months per pregnancy and cumulative> 18 months (p = 0.01). On the contrary, age <20 years in their first pregnancy, and menopause> 45 years were associated with their absence. The correlation between self-assessment and clinical diagnosis was significant (95% CI 4-12.2%; p <0.001).
Conclusions: Dermatoporosis in Mexico was less prevalent compared to Caucasian population. As in other studies, it was more common in women. Associated factors were age> 75 years, significant sun exposure, chronic anticoagulant / antiplatelet intake, oral steroids, and kidney disease. Late pregnancy and prolonged lactation

predispose; premature pregnancy and late menopause seem to prevent it. The self-diagnostic questionnaire correlates with the clinical diagnosis.

LB765

Pseudofolliculitis barbae in the barbershop: A survey of barbers and patients identifying needs and possible solutions

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Pseudofolliculitis barbae (PFB) is an inflammatory condition with an incidence of up to 83% in Black men. Prior studies called for partnerships between dermatology and barbers. We aimed to understand population needs and identify opportunities for improving access. We recruited barbers and individuals affected by razor bumps and ingrown hairs (representing PFB) via social media to complete a survey. 1063 participants responded (77% male and 24% Black). 41% (n=389) experienced PFB in the past two years, of which PFB "sometimes" or "always" impacted their quality of life with symptoms related to physical (48%) emotional (40%) or function (43%). 68% of individuals reported seeking advice from doctors and 78% from barbers on how to treat PFB. Over 20% did not know dermatologists treat PFB. Of individuals treated by dermatologists, 92% were satisfied with care provided compared to 83% from primary care doctors and 46% from barbers. Barriers to seeking dermatology were: lack of knowledge of where to find a dermatologist (25%) and not having time to schedule (27%). Overall, 36% said they would interact with dermatologists on telehealth platforms, 30% would like a directory of local providers, and 23% would like PFB treatment recommendations. Barbers comprised 41% (n=421) of our study population. 17% did not know clients could see a dermatologist but 95% would refer clients to dermatology. Barbers prefer a personal connection with a dermatologist (48%), access to a directory (37%) or in-shop services or seminars (14%). Our findings demonstrate both needs and receptiveness to increased access to dermatologic care in the population with high incidence of PFB. Our results may prompt further exploration of potential means to bridge identified access barriers: namely, programming development based on barbers and individual needs, possible applications offering product recommendations, building connections to local dermatologists, and facilitated appointment scheduling.

LB766

Prevalence and adverse events of special interest among COVID19-vaccinated patients with chronic inflammatory skin diseases: An early look

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Despite increasing rates of COVID-19 vaccination among those living in the United States, there is little known about the prevalence of vaccination among patients with chronic inflammatory skin diseases and if any significant adverse reactions have occurred within these specific groups. The goal of this study was to further analyze these trends. A retrospective analysis was conducted from December 2020 to March 2021 using TriNetX, a national federated, real time database of 69 million records. The prevalence of COVID-19 vaccination among patients with inflammatory skin diseases including psoriasis (Pso), atopic dermatitis (AD), and hidradenitis suppurativa (HS) was calculated. A 1:1 matched propensity score analysis was then conducted, adjusting for comorbidities and demographics, to generate adjusted risk ratios (aRR) with 95% CI. The outcome was any adverse event of special interest (AESI), as defined by the CDC and FDA, that occurred at any point after vaccination. In a sample of 301,878 patients who were vaccinated,1.5% had Pso, 1.4% had AD, and 0.3% had HS. After matching, cases had no significant differences compared to controls for any AESIs after either the first dose (Pso: 1.1[0.5-2.3], AD: 1.4[0.7-2.8], HS:1.0[0.4-2.4]) or second dose of vaccine (Pso: 1.4[0.7-2.7], AD: 1.0[0.6-1.7], HS: 1.0[0.4-2.4]). Matched subgroup analysis among the two major COVID-19 vaccine brands also revealed no differences in AESIs among Pso, AD, and HS patients. While preliminary, the current data reveals that patients with chronic inflammatory skin

diseases are not at higher risk of any AESIs after receiving the COVID-19 vaccine. Further studies are warranted to continuously evaluate the trends in side effect profiles of these vaccines.

LB767

A multicenter analysis of patients using telemedicine for dermatological conditions during the COVID-19 pandemic

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The COVID-19 pandemic caused medical facilities to modify healthcare delivery and incorporate more telemedicine to reduce the spread of COVID-19. Multicenter studies assessing the impact of telemedicine in dermatology remains sparse. The aim of this study was to quantify the national impact of the pandemic on telemedicine utilization for common dermatologic conditions. A descriptive study was done using TriNetX, a national federated real time database of 69 million records. ICD-10 codes of the most common dermatologic diagnoses were determined *a priori*. The prevalence of common dermatologic conditions diagnosed via telemedicine encounters (TME) was assessed from 3/20/2020 to 3/19/2021 and compared to the preceding year. The number of TME across all dermatological conditions (ICD10:L00-L99) increased 805% from 150 to 1,358 per 100,000 of all healthcare encounters (HCE). Every dermatological disease assessed had a significant increase in TME when compared to the prior year. This increase was most significant for acne vulgaris (808%), psoriasis (792%), malignant skin neoplasms (716%), atopic dermatitis (609%), rosacea (566%) and contact dermatitis (529%). Others with increased TME include viral warts (497%), follicular cysts (415%), seborrheic keratosis (365%), actinic keratosis (351%), and benign skin neoplasms (275%). The most common dermatologic conditions seen via TME were seborrheic keratosis (146/100,000 HCE), actinic keratosis (106), malignant skin neoplasms (103), contact dermatitis (82), psoriasis (75), acne vulgaris (57), follicular cysts (48), benign skin neoplasms (42), atopic dermatitis (39), rosacea (39), and viral warts (31). Common dermatological diagnoses saw a drastic increase in telemedicine utilization from 2020 to 2021 compared to the prior year. Further research is warranted to determine whether these trends persist.

LB768

Adult and pediatric emergency department visits for dermatological conditions during the COVID-19 pandemic: A multicenter analysis

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During the early phases of the COVID-19 pandemic, many emergency departments (EDs) across the United States experienced significant declines in patient volumes. The aim of this study was to quantify the degree to which COVID-19 impacted ED visits for adult and pediatric dermatologic conditions. A descriptive study was performed using TriNetX, a national federated real time database of 69 million records. Common dermatologic conditions were identified *a priori* via ICD-10 codes. The prevalence of adult and pediatric ED encounters (EDE) with each skin condition was assessed from 3/20/2020 to 3/19/2021 and compared to the preceding year. The number of EDE for any dermatological condition (ICD10: L00-L99) decreased 23% overall from 19,705 to 15,218 per 100,000 of all healthcare encounters (HCE). All dermatological disease categories assessed in both adult and pediatric patients showed a significant decrease in total EDE compared to the prior year. Diagnoses assessed included cellulitis (-38% and -53% for adult and pediatrics, respectively), other skin infections (-38%, -56%), bullous skin disorders (-46%, -53%), dermatitis/eczema (-40%, -61%), papulosquamous disorders (-35%, -64%), urticaria/erythema (-46%, -64%), radiation-related skin disorders (-44%, -38%), skin appendages disorders (-43%, -54%), and other skin disorders (-39%, -53%). Adult and pediatric ED visits for dermatological conditions significantly decreased during the pandemic compared to the prior year with decreases in pediatric ED visits being more notable. Further studies are

necessary to determine if these patients received care in other settings (i.e. outpatient offices, telehealth), and associated outcomes. Future studies are also needed to examine the degree to which ED visits for dermatologic conditions resume and if COVID-19 has lasting impacts on the setting in which skin care is sought.

LB769

A report of Basal Cell Carcinoma hospitalizations: An analysis from the national inpatient sample database

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There is a scarcity of national population studies on hospitalizations of Basal cell carcinoma (BCC) patients in the United States (U.S). This study aims to compare comorbidities of BCC to non-BCC hospitalizations and determine the most common reasons for BCC hospitalizations resulting in inpatient mortality. Data were obtained from the National Inpatient Sample (NIS) 2016-2018 databases, which contained about 105 million hospitalizations. The NIS is the largest inpatient database in the U.S. We abstracted data for adult hospitalizations, with any diagnosis of BCC, using ICD-10 codes. Analyses were performed using STATA,16. By using a "rank" command in STATA, diagnoses were placed in descending order of frequency. We compared comorbidities using chi-square test between BCC and non-BCC hospitalizations. A total of 30,345 hospitalizations had a diagnosis of BCC, of these 850 resulted in inpatient mortality. BCC patients had more comorbidities such as prior myocardial infarction (7.2% vs 5.5%), prior stroke (8.3% vs 6.5%), hypertension (40.7% vs 34.4%), congestive heart failure (19.6% vs 15.4%), peripheral vascular disease (4.4% vs 2.9%), smoking (41% vs 35.9%), coronary artery disease (23.1% vs 16.9%), vascular dementia (0.9% vs 0.5%), and Alzheimer's dementia (2.1% vs 1.3%) compared to non-BCC patients ($p<0.0001$).The most common principal diagnosis categories for BCC hospitalizations resulting in inpatient mortality were infections (27.1%), cardiovascular CV (17.1%), respiratory (15.3%), and hemato-oncologic (14.1%). Sepsis (20%), acute kidney injury (2.9%) and inhalational pneumonitis (2.4%) were the most common specific diagnosis. The most common reasons for BCC hospitalizations resulting in inpatient death were infections, cardiovascular and respiratory diseases. CV risk factors, smoking, and dementia are more common in BCC hospitalized patients than non-BCC patients. Management of co-morbidities is important in reducing inpatient mortality.

LB770

Analysis of pediatric Hidradenitis Suppurativa hospitalizations: A national population-based study

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There is a scarcity of large national population-based studies on hospitalized pediatric hidradenitis suppurativa (HS) patients in the United States (U.S). This study aims to determine the most common reasons for hospitalizations of pediatric HS patients and compared baseline characteristics of HS and non-HS pediatric hospitalizations. We searched the 2016 Kids' Inpatient Database (KID), which contains about 7 million weighted discharges. The KID is the largest inpatient pediatric database in the U.S. We abstracted data for pediatric patients aged <21 years, with a principal or secondary diagnosis of HS, using the ICD-10 code "L732". Analyses were performed using STATA, version 16. By using a "rank" command in STATA, diagnoses were placed in descending order of frequency. The most common principal discharge diagnoses were divided into categories based on organ system, and the most common specific principal discharge diagnosis was recorded. We compared baseline socio-demographic characteristics and comorbidities between HS and non-HS hospitalizations using chi-square test. A total of 1,290 hospitalizations had a diagnosis of HS, of these 356 had a principal diagnosis of HS. HS patients were older (16.9 vs 4 years), had more females (72.6% vs 51.5%), African Americans (45.4% vs 14.7%), dyslipidemia (3.2% vs 0.2%), hypertension (8.7% vs 0.8%), hypothyroidism (3.5% vs 0.5%), Diabetes Mellitus type 2 (6.9% vs 0.2%), obesity (32.5% vs 1.4%), liver disease (1.9% vs 0.4%), smoking (7.9% vs 2.1%), and anemia (20.2% vs 3.9%) compared to non-HS patients ($p<0.0001$). The most common principal diagnosis categories of HS hospitalizations were "diseases of the skin and subcutaneous tissue" (50.7%), digestive (6%), mental and behavioral (5.2%), and endocrine (5.1%).

HS (27.6%) was the most common specific principal diagnosis. Establishing multidisciplinary clinics with dermatologists and psychologists, screening for endocrine, metabolic, and other associated comorbidities may reduce unnecessary hospitalizations of pediatric HS patients.

LB771

Racial and Ethnic Disparities in COVID-19-Related Infection in Patients with Psoriasis: A Cross-Sectional Study

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Psoriasis severity may vary due to demographics and geography, yet data on the risk, racial disparities, and outcomes for COVID-19 in patients with psoriasis is limited. We evaluated rates of COVID-19 infection, hospitalization, and mortality among psoriasis patients in a California-based population through a cross-sectional study utilizing the University of California COVID Research Data Set (UC CORDS). Psoriasis diagnosis, COVID-19 testing, demographics, hospitalizations, and mortality were collected. Specific biologic (adalimumab, ustekinumab, secukinumab, guselkumab, and etanercept) and systemic (cyclosporine and methotrexate) treatment for at least 30 days prior to COVID-19 testing were identified. Data from 290,838 patients is included in UC CORDS with a 3.59% positive COVID-19 test rate. Of these, 3,566 patients had a diagnosis of psoriasis, with a 2.44% positive infection rate; lower than the 3.56% infection rate for those without psoriasis ($p=0.00021$). There were no significant differences in hospitalization or mortality rate for COVID-19-positive psoriasis patients compared to those without psoriasis ($p=0.5523$, $p=0.1152$, respectively). Lastly, no significant difference in infection rate for psoriasis patients on systemic (2.92%, $p=0.579$) or biologic agents (2.46%, $p=0.986$) in comparison to psoriasis patients not on these treatments. UC CORDS data showed higher COVID-19 infection rates in non-white (3.05%) and Hispanic (8.35%) patients compared to non-Hispanic Caucasians (1.95%, $p<0.00001$). No significant differences were seen in infection, hospitalization, or mortality rates between non-Hispanic races (Caucasian, African American, and Asian). Overall, psoriasis patients did not have increased risk for COVID-19 infection, hospitalization, or mortality, regardless of treatment modality.

Patient-Targeted Research

LB772

Prognostic role of beta-blockers for Melanoma: A systematic review and meta-analysis

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Beta-blockers (BB) are widely used antihypertensive agents shown to have anti-tumorigenesis properties in cutaneous metastatic melanoma (CMM) but results of current observational and experimental studies have been inconsistent. Given these controversies and absence of randomized controlled trials (RCTs), we performed a systematic review and meta-analysis to evaluate the association between BB use and survival outcomes in CMM. A comprehensive search of PubMed, Embase and Scopus was performed to identify all studies published before February 2, 2021 investigating the association between survival outcomes and BB use in patients with CMM. Pooled hazard ratios (HR) and 95% confidence intervals (CI) were calculated using a random-effects model. Subgroup analyses examined receptor selectivity, timing of initiation and use in concert with immune checkpoint inhibitors (ICIs). Ten of 589 studies (18,919 patients) met criteria for inclusion. Use of BB was significantly associated with improved overall survival (OS) (HR= 0.80, 95% CI: 0.65-0.98), melanoma-specific survival (MSS) (HR= 0.72, 95% CI: 0.54-0.96), progression-free survival (HR= 0.53, 95% CI: 0.29-0.95) and disease-free survival (HR= 0.23, 95% CI: 0.06-0.82). Receptor selectivity was heterogenous, with most studies including mixed cardioselective and non-selective agents. Initiation of BB prior to diagnosis was associated with prolonged OS (HR=

0.81, 95% CI: 0.70-0.93) but not MSS (HR= 0.50, 95% CI: 0.23-1.09) and there was no evidence to suggest BB use in concert with ICIs improved OS (HR= 0.54, 95% CI: 0.17-1.71). Few studies assessed specific agents or stratified findings by receptor selectivity, and there was considerable heterogeneity between studies. Overall, BB use correlated with improved prognosis and repurposing of these agents in treatment of CMM appear promising, but additional RCTs are needed.

LB773

Treating pemphigus vulgaris (PV) and foliaceus (PF) by inhibiting the neonatal Fc receptor: Phase 2 multicentre open-label trial with efgartigimod

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Efgartigimod, an engineered Fc fragment that inhibits the activity of the neonatal Fc receptor (FcRn), was evaluated in an open-label phase 2 adaptive trial (NCT03334058). Thirty-four mild to moderate PV or PF patients were enrolled to evaluate the safety, pharmacodynamics, pharmacokinetics, and efficacy of efgartigimod. In four sequential cohorts, efgartigimod was dosed at 10 or 25 mg/kg intravenously with various dosing frequencies, as monotherapy or add-on therapy to low-dose oral prednisone. Efgartigimod demonstrated a favorable safety and tolerability profile, consistent with previous studies of this FcRn inhibitor. We observed a strong association between serum IgG level reduction, autoantibody level reduction and improvement of pemphigus disease area index (PDAI) scores and clinical outcomes. 90% (28/31) of patients achieved disease control with a median time of 16 days. Fourteen of 22 (64%) patients on efgartigimod treatment with prednisone 0.1-0.5 mg/kg/d achieved complete remission (10 mg/kg: median 35 days, range 13-93; 25 mg/kg: 43 days, range 41-287). These results add to the interim analysis previously presented and support the further evaluation of efgartigimod as a therapy for pemphigus.

LB774

Comparison of clinical and pathologic assessment of lesions in Mycosis Fungoides

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Evaluate concordance between clinical and pathologic classification of lesions as it relates to mycosis fungoides staging. Sequential patients with a clinical diagnosis of non-erythrodermic mycosis fungoides in a tertiary care referral center from 2015 to present date and who had undergone biopsy with histologic lesion staging were included in this retrospective study, and changes in TNMB stage with follow-up assessed. Pathologic and clinical diagnosis agreed in 72% of cases (weighted kappa statistic=0.82). Clinical patches with more advanced pathologic stage at initial diagnosis were more likely to progress compared to pathologic patches (12.5 v 10.3%); clinical plaques with lower pathologic stage were less likely to progress than pathologic plaques (14.3 v 21.4%) and more likely to regress (42.9% v 14.3%) with a median follow-up of 189 days (range 0-1426); statistical significance was not achieved.

LB775

Characterization of sensitive scalp in Korean females

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Sensitive scalp is a common phenomenon in a general population according to studies conducted worldwide. Previous studies have reported that 35-56% of population claim to have sensitive scalp condition. Despite high prevalence of the condition, there is no standard predictive method to diagnose sensitive scalp. In this study, survey and biophysical measurements were conducted to assess sensitive scalp in Korean females and identify parameters associated with sensitive scalp. A total of 760 women aged 20-50 years participated in the questionnaire concerning self-perception of scalp sensitivity, lifestyle, environmental factors, hair products utilization pattern, and health status. Among the participants who answered the survey, twenty subjects with non-sensitive scalp and twenty four self-declared sensitive scalp subjects were examined by instrumental measurements including transepidermal water loss (TEWL), skin hydration, pH, and sebum content. In addition, desquamation and erythema were graded on a 4-point ordinal scale (grades 0-3). According to the self-assessment, three percent of the subjects perceived themselves to have very sensitive scalp, 10.5% had sensitive scalp, and 61.5% had slightly sensitive scalp. Scalp itching, heat sensation and redness were main symptoms of sensitive scalp. Sensitive scalp group was more likely to experience hair cosmetics related adverse reactions and more reactive to environmental factors, hormonal changes, and stress. The mean TEWL of the occipital and temporal scalp of the subjects with sensitive scalp were significantly higher compared to that of non-sensitive scalp subjects ($p<0.01$). Sensitive scalp group also had significantly higher sebum level at temporal area ($p<0.05$). The results indicate that questionnaire and biophysical measurements of sebum content and TEWL can be used to diagnose sensitive scalp and contribute to a better understanding of the sensitive scalp.

LB776

Dermatologists Are More Likely Than Oncologists to Prescribe Skin Directed Therapies for Early Stage Cutaneous T-Cell Lymphoma, A Retrospective Review.

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Purpose:
Based on the guidelines of stage-based treatment set by the national comprehensive cancer network (NCCN), we retrospectively analyzed the differences in treatment regimen preferences between the two specialties at our tertiary care university hospital. Our goal was to determine whether oncologists were as likely as dermatologists to start skin directed therapies for early stage disease.

Methods:
Skin directed therapy was defined using the NCCN guidelines, and included local radiation, phototherapy, and the following topical medications: corticosteroids, imiquimod, mechlorethethamine, retinoids and carmustine. Patients included in our investigation were those that met the criteria of either stage IA-IB or IIA disease based on NCCN guidelines and who also had a pathologic diagnosis rendered by a dermatopathologist. Cases were excluded if there was insufficient data to calculate the stage or if the medical records were not available. Our review identified 72 patients diagnosed between 2009 and 2019 with stage IA-IB or IIA primary cutaneous T-cell lymphoma. Of this population, 31 (43%) patients were diagnosed with stage IA disease, 39 (54%) patients were diagnosed with stage IB disease, and 2 (3%) patients were diagnosed with stage IIA disease.

Results:
Of these patients, 51 were managed solely by dermatologists, 9 were managed solely by oncologists and 12 were co-managed by both specialties. Our data showed that there was a statistically detectable relationship between the presence or absence of oncologist involvement and whether a patient would be prescribed skin directed therapy ($p = 0.0003$; Fisher's Exact Test). Limitations identified in our study included the retrospective design, small sample size, and being a single academic center. Our findings suggest that early stage CTCL patients may benefit from having a dermatologist involved in their care.

LB777

Atypical presentation of Bullous Pemphigoid unmasked by radiation therapy

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This is a rare case of a 73-year-old female who developed generalized classic bullous pemphigoid (BP), likely from smoldering pre-bullous or eczematous BP, during radiation therapy (RT) for breast cancer. Prior to RT for invasive ductal carcinoma of the right breast, the patient was referred to dermatology for a chronic pruritic rash. Given the pruritic erythematous papules with overlying erosions, excoriations, and white atrophic scars on her chest, back, arms and legs that had been present for several years without specific triggers, she was diagnosed with prurigo simplex with non-specific eczematous dermatitis and prescribed 0.1% triamcinolone cream BID. After 11 fractions of RT, the patient developed new pruritic bullae and vesicles on the right breast, arms and legs. She continued to acquire worsening dermatitis with moist desquamation of the right breast (grade 4), and numerous urticarial plaques, tense vesicles and bullae scattered on the torso, arms and legs. After 13 fractions (3471 cGy), RT was discontinued. Biopsy of a bulla showed superficial perivascular and interstitial mixed cell infiltrate with many eosinophils under a subepidermal blister. DIF staining showed IgG and C3 staining in a linear pattern at the dermal-epidermal junction, confirming BP. Serum BP180 and BP 230 IgG were both positive at 180U/mL and 10U/mL respectively. The patient was treated with prednisone taper (starting at 1mg/kg) and mycophenolate mofetil (titrated to 2000mg), and had complete response after 6 months. While localized BP that occurs months after completion of RT is somewhat common, the timing and generalized nature of our patient's BP is unusual. We conclude that this is a rare case of generalized BP triggered by RT in a patient who likely had smoldering pre-bullous BP. Atypical variants of BP that test positive for basement membrane autoantibodies are well-documented, and we suggest that physicians managing patients with non-specific eczematous eruptions should consider evaluating for BP prior to commencing RT.

LB778

A quantitative scoring system for cutaneous immune-related adverse events

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Immune checkpoint inhibitor (CPI) therapy has revolutionized the treatment of many types of malignancy. Unfortunately, patients treated with these medications frequently develop immune-related complications of therapy, immune-related adverse events (irAE), which occur most commonly in the skin. These cutaneous irAE cause significant morbidity and may lead to interruption or discontinuation of cancer therapy. Current scoring and therapeutic guidelines for cutaneous irAE are relatively nonspecific, and comparative studies of therapies for these reactions have not yet been published. As treatment of these eruptions with systemic immunosuppression may impact antitumor efficacy, there is a need to compare responses to interventions in a quantitative way. Current staging systems rely on broad ranges of body surface area involvement and lack the granularity necessary for meaningful comparison. Building on prior systems developed for research use in psoriasis, atopic dermatitis, and lichen planus, we have developed a scoring system for this purpose. While designed for our murine model of cutaneous irAE, it is easily extrapolated for use in patients, and produces results that correlate well with qualitative clinical evaluations. This system provides a needed objective tool for the comparative study of cutaneous irAE and their treatment.

LB779

Comparison of outcomes for intravenous and intralesional administration of sodium thiosulfate for treatment of Calciphylaxis

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Calciphylaxis is a vasculopathy characterized by calcium deposition in cutaneous vessels resulting in skin ulceration. Sodium thiosulfate (STS) has been used to treat calciphyaxis and can be administered via intravenous (IV) or intralesional (IL) injection. Retrospective chart review of patients treated for calciphylaxis at a tertiary hospital was conducted. Skin lesions were followed for at least two years following STS treatment initiation for three outcomes: 1) clinical improvement defined by reduction in lesion size or halted progression of purpura; 2) resolution of disease activity characterized by resolution of purpura; and 3) healing of ulcers. Hazard ratios for each treatment modality were calculated by a shared frailty model with random effects per patient and adjustment for confounders. 32 patients were treated with ILSTS and 47 patients treated with IVSTS alone. Each treatment outcome was achieved at a higher frequency and within a shorter timeframe for patients receiving ILSTS. ILSTS had a higher hazard ratio for lesion improvement and resolution of disease activity in both the unadjusted (HR: 16.3; 95% CI: 6.4- 41.1 and HR: 5.3; 95% CI: 2.3-12.4) and adjusted (HR: 10.4; 95% CI: 3.5-30.4 and HR: 3.8; 95% CI: 1.3-11.2) shared frailty model. ILSTS and IVSTS had comparable hazard ratios for lesion healing. ILSTS alone or in combination significantly hastened lesion improvement and resolution of disease activity compared to IVSTS even upon adjustment for possible confounders. This benefit may be due to targeted delivery of STS to active areas of disease by IL injection. ILSTS may play a therapeutic role for patients who cannot tolerate the systemic side-effects of IVSTS treatment.

LB780

Risk factors predicting Cellulitis diagnosis in a prospective cohort undergoing dermatology consultation in the Emergency Department

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Cellulitis is a skin and skin-associated structure infection with many clinical mimickers called pseudocellulitis. Dermatology consultation is considered the gold standard for diagnosis. A prospective cohort of adult patients presenting to the emergency department with concern for lower extremity cellulitis received dermatology consultation with conferral of a final diagnosis. Patients with signs of complicated cellulitis, such as abnormal vital signs, or infection overlying hardware, animal bites, or sites of recent surgery were excluded. Possible risk factors independently associated with cellulitis diagnosis ($p<0.1$) were used in a logistic regression model. Factors significantly predicting cellulitis diagnosis ($p<0.05$) were used to create a simplified integer scoring system. Of 104 patients meeting inclusion criteria evaluated by dermatology consultation for presumed lower extremity cellulitis, 63 patients (60.7%) received a final diagnosis of cellulitis. Factors significantly predicting cellulitis diagnosis via multivariate logistic regression were past history of cellulitis (OR 2.6; 95% CI 1.2, 5.8), unilateral presentation (OR 5.8; 95% CI 2.1, 16.1), and white blood cell count greater than 10 thousand/mL^3 (OR 9.6; 95% CI 3.5, 26.4). When assigned score values of 1, 2, and 2 points, respectively, a cutoff score of 3 points had a 80% sensitivity and 68% specificity for predicting cellulitis diagnosis. Prior cellulitis, unilateral presentation, and leukocytosis independently predict lower extremity cellulitis. This simplified scoring system retains predictive performance and can distinguish from clinical mimickers.

LB781

Comparison of surgical incision healing using cold plasma scalpel versus standard steel blade

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Infection of surgical sites by skin dwelling bacteria, such as *C. acnes* and others can have devastating effects. Cold plasma generates an antimicrobial mixture of reactive oxygen and nitrogen species (ROS/RNS) through ionization of atmospheric gases. We investigated whether a cold plasma scalpel device (J-Plasma, Apyx Medical Inc.) could be a viable tool for creating surgical incisions. J-plasma scalpel incisions were compared to incision by 11-blade steel scalpel. To determine the least damaging settings with optimal ROS/RNS generation, variable power and gas flows used to generate plasma were tested in an *ex vivo* rat model and analyzed using trichrome and H&E stains. The J-Plasma device was used at a gas flow of 3L/min at 40% power to create a 2 cm long incision along the rat dorsum in the *in vivo* study, a matching incision was created using the 11 blade scalpel. Wound healing appearance was assessed daily by photographing the external wound and graded blindly using Southampton wound scoring system. Histology was performed at 3, 8 or 20 days after surgery using H&E and Masson's trichrome from 3 sections, acquired at different levels within the incision, and evaluated using the Stoney Brook scar scale. The blinded assessments were made by at least 4 surgical associates. Results showed wounds were visually undiscernible from each other at days 8 and 20. At Day 3, a slightly higher but non-significant score was calculated. Histological parameters revealed day 8 showed a slight delay in granulation tissue resolution in the plasma incision, but this was variable and similar observances of this occurred in some 11 blade scalpel wounds. All incisions were equally resolved by day 20. This study demonstrates the efficacy of J-Plasma scalpel used in a surgical setting, which may prove invaluable in cases of high potential contamination of the surgical site. Further studies will explore incisions through acne lesions to determine level of mitigation.

LB782

A retrospective case series of Ustekinumab therapy in patients with severe and recalcitrant Hidradenitis Suppurativa

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Hidradenitis suppurativa (HS) is a chronic inflammatory skin disease characterized by painful nodules and sinus tracts in areas of high sweat gland and hair follicle density, such as the axilla and groin. These debilitating features may impair quality of life and cause significant psychosocial burden. Though the pathophysiology of HS is complex and incompletely understood, various cytokines are under investigation as targets for biologic therapy. Adalimumab, a monoclonal antibody that targets tumor necrosis factor-a (TNF-a), is currently the only FDA-approved antibody therapy for HS. Despite its efficacy, as demonstrated by the phase III trials (PIONEER I and II), we have observed that a subset of HS patients failed to respond to adalimumab. This case series aims to characterize clinical response in 6 patients with HS refractory to anti-TNF-α therapy who underwent treatment with ustekinumab in our clinic between 2017 – 2021. Ustekinumab has demonstrated success in patients with severe and recalcitrant HS in several case series and one open phase II trial. We found that 50% of patients achieved Hidradenitis Suppurativa Clinical Response at 11 – 43 weeks of ustekinumab therapy. Additionally, 67% of patients experienced over 50% reduction in the International Hidradenitis Suppurativa Score at 2 – 27 weeks of therapy. We demonstrate that ustekinumab may be a promising therapy for HS refractory to anti-TNF-α treatment and hope that our study can support its investigation in randomized-controlled trials.

LB783

Skin-tethered bifunctional antibodies for treatment of autoimmune and inflammatory skin diseases

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Current treatment approaches for autoimmune conditions comprise primarily of systemic immunosuppressants or cytokine blockade. Concentration of therapeutic molecules to the tissues that are the sites of autoimmune and inflammatory diseases is a promising approach with the potential to induce therapeutic benefit and avert risks associated with systemic immunotherapies. Pandion Therapeutics is developing a bifunctional antibody platform that can drive localized immune modulation. The platform combines a "tether antibody" that targets a tissue of choice and "an effector end" that activates specific regulatory immune pathways to restore immune-homeostasis. Here we report the engineering of a skin-tethered PD-1 agonist and a skin-tethered CD39 that inhibit T cell activation and function and deplete local ATP, respectively, modulating different arms of the immune system in a tissue specific manner. These skin-tethered immune effectors were assessed for drug-like properties in biophysical assays and *in vitro* and *in vivo* assays for target binding, cellular activity and tissue specific-localization. Moreover, these bifunctionals were tested in pathway-relevant preclinical models such as vitiligo and contact Hypersensitivity. Strikingly, a selective accumulation of the tethered bifunctionals to the skin was observed and correlated with a tether-dependent efficacy compared to a non-tether control. We believe that this localized therapeutic approach has the potential to drive the resolution of cutaneous inflammation, providing an opportunity for developing new targeted therapies for autoimmune and inflammatory skin diseases.

LB784

Anticancer activity of Ramalin isolated from *ramalina terebrata* on human Squamous Cell Carcinoma *in vitro* and *in vivo*.

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Squamous cell carcinoma (SCC) is the second most common skin cancer, after basal cell carcinoma. Locally advanced or metastatic SCC requires multi-modality therapy with radiation and systemic treatment. However, management of these lesions are a therapeutic challenge because of the scarce amount of available prospective data. Recent studies have revealed that constituents of lichen extracts exhibit potent pharmaceutical activities, including anticancer activity, making them promising candidates for new anticancer therapeutic drugs. Ramalin is a chemical compound derived from the Antarctic lichen Ramalina terebrata and its effect on human breast cancer and colorectal cancer was already known in vivo. We examined the ability of ramalin in normal human epidermal keratinocytes (NHEK), HSC-1 and A431 (human squamous cell carcinoma) cells *in vitro* and *in vivo*. Ramalin reduced viability and ability of migration and induced caspase-independent apoptosis in A431 cells. It also affects the MAPK and NFkB signaling pathway in A431 and HSC-1 cells *in vitro*. Based on these results, we evaluated the effect of ramalin on human squamous cell carcinoma by xenograft tumor mice. Ramalin was administered intralesionally and the mice were divided into 3 groups: I (control group), II(10mg/kg), and III (20mg/kg). Hematoxylin and eosin stained sections of tumor and other organs were investigated. Relative tumor volumes were decreased 51% and 29% in group II and III respectively compared with control group at the end of the observation periods. Tumor inhibition rate were 57.0% and 71.7% in group II and III respectively. Histopathological study revealed that mice in group II and III showed decreased tumor cells than those in group I. There were no abnormal histological findings upon normal organs. Therefore, ramalin induces apoptosis and it results tumor volume decrease in squamous cell carcinoma. These findings suggest that ramalin is a potential anticancer agent for the treatment of patients with squamous cell carcinoma.

LB785

Efficacy and safety of baricitinib in adults with Alopecia Areata: Phase 3 results from a randomized controlled trial (BRAVE-AA1)

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The efficacy and safety of baricitinib, an oral, selective Janus kinase (JAK)1/JAK2 inhibitor, were assessed in a double-blind, placebo-controlled Phase 3 trial of adults with alopecia areata (AA). Patients (n=654) were randomized 3:2:2 to once-daily baricitinib 4 mg or 2 mg or placebo. Outcomes were analyzed using logistic regression with non-responder imputation. At Week 36, greater proportions of patients achieved the primary endpoint, Severity of Alopecia Tool (SALT) score ≤20, with baricitinib 4 mg (35.2%, p≤0.001) and 2 mg (21.7%, p≤0.001) versus placebo (5.3%); statistical significance over placebo was observed by Week 8 with 4 mg and Week 24 with 2 mg. With baricitinib 4 mg, 2 mg, and placebo, respectively, 26.0% (p≤0.001), 12.5% (p≤0.01), and 3.7% had SALT score ≤10 at Week 36; among those with baseline Clinician-Reported Outcome Measures for Eyebrow Hair Loss™/Eyelash Hair Loss™ scores ≥2 (significant gaps to no notable hair), 31.4%/33.5% (both p≤0.001), 19.1%/13.5% (p≤0.001/p≤0.05), and 3.2%/3.1% scored 0 or 1 (full coverage or minimal gaps) with ≥2-point improvement from baseline at Week 36. For baricitinib 4 mg, 2 mg, and placebo, respectively, 59.6%, 50.8%, and 51.3% had any treatment-emergent adverse event (AE); 2.1%, 2.2%, and 1.6% had serious AEs. There were no deaths, opportunistic infections, thromboembolic events, or malignancies. One major adverse cardiovascular event occurred in a patient with multiple risk factors; details are not reported to maintain ongoing study blinding. In this first Phase 3 trial of baricitinib for AA, baricitinib 4 mg and 2 mg were superior to placebo in achieving hair regrowth after 36 weeks; findings were consistent with the established safety profile.

LB786

Associations between cutaneous and non-cutaneous adverse effects in patients with Melanoma receiving immunotherapy: A retrospective chart review

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Understanding the relationship between cutaneous adverse effects (CAE) and non-cutaneous adverse effects (NCAE) associated with immunotherapy used to treat melanoma may promote early identification, treatment, or prevention of severe NCAE. We aimed to examine associations between CAE and NCAE among a cohort of patients with grade III or IV melanoma receiving immunotherapy. Participants were identified from a prospective cohort study conducted at Emory University from October 2018 to June 2020. Electronic medical record data on immunotherapy and adverse effects were extracted retrospectively starting from first immunotherapy infusion up until one year later. CAE were defined as rash or symptoms of itch. NCAE for each organ system were defined as symptoms and or laboratory abnormalities documented by the clinical provider as being related to immunotherapy. Participants were grouped as developed CAE versus did not develop CAE. NCAE incidence and time to NCAE onset between groups were compared using odds ratios and t-tests, respectively. 35 participants were included: 11 (31.4%) developed no adverse effects, 8 (22.9%) developed only CAE, 3 (8.6%) developed only NCAE, and 13 (37.1%) developed both CAE and NCAE. Gastrointestinal (n=7, 20.0%) and endocrine (n=9, 25.7%) adverse effects were most common. Those who developed CAE were significantly more likely (OR=5.96; 95% CI, 1.26-28.1) to develop NCAE. Mean time to NCAE onset was shorter in those that developed CAE (mean, standard deviation; 85.3 days, 62.8) than those that did not develop CAE (148 days, 115.3) but differences were not statistically significant (p=0.44). Study limitations were small sample size and limited ability to examine specific NCAE separately. CAE were significantly associated with development of NCAE. Patients receiving immunotherapy should be monitored for CAE during routine clinical follow up as that may aid in identifying NCAEs before symptoms become severe.

LB787
CLE-400: A potent alpha-2 adrenergic receptor agonist for the treatment of chronic itch
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Pruritus (itch) is a major symptom of several dermatological diseases but has limited therapeutic options available. Itch stimuli are transmitted via primary sensory neurons in the skin by activating pruriceptors/nociceptors on small unmyelinated C-fibers, through the spinal cord for final processing in the brain. CLE-400 is an aqueous gel of detomidine that is being developed for the topical treatment of itch. Detomidine is a potent α2-adrenergic receptor (α2-AR) agonist. α2-AR have been shown to be expressed on skin nociceptors and their activation by topical administration of detomidine could lead to inhibition of itch neural signalling. To assess this hypothesis, the ability of topical administration of CLE-400 to suppress itch was evaluated in the well-established chloroquine-induced pruritus mice model. Chloroquine, an antimalarial drug, induces itching in humans and mice by activating Mrgpr receptors in peripheral primary sensory neurons, suggesting a histamine independent mechanism of itch. CLE-400 was applied to CD-1 mice once daily (QD) for five consecutive days prior to chloroquine challenge. A single subcutaneous injection of chloroquine in vehicle-treated animals produced significant scratching behaviors lasting over 30 min after administration. Topical application of CLE-400 (0.1, 0.33 and 1%) at a dose volume of 75 μL/cm^2 QD for 5 days, with the last dose applied 30 min prior to chloroquine injection, significantly reduced and almost completely blocked chloroquine-induced scratching behaviors at all dose levels tested ($p < 0.0001$ compared to control), suggesting that topical detomidine could be an effective peripherally acting antipruritic agent. The positive control, U-50,488, a kappa-opioid receptor agonist, administered intraperitoneally 30 min prior to chloroquine, significantly attenuated scratching, confirming the validity of the model. CLE-400 was generally well tolerated locally and systemically when administered topically QD for 5 days up to 1% at 75 μL /cm^2, and did not produce any significant side effects as observed by CNS Irwin test battery and dermal clinical score

LB788
Withdrawn

LB789
Novel IFNγ aptamer TAGX-0003 protected hair follicles from immune privilege collapse and reversed Alopecia Areata like phenotype in humanized mouse model.
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Alopecia areata (AA) is an autoimmune disease of the hair follicle (HF). Central to the disease is IFNγ which accumulates in HFs leading to a Th1 autoimmune response, failure of the hair bulb immune privilege (IP), premature catagen induction followed by HF dystrophy. Currently, combination of steroid and minoxidil is considered to be the first line of treatment, providing protection through the suppression of inflammation. Some JAK inhibitors are under clinical trials for AA and demonstrate fairly good efficacy. However, systemic administration of JAK inhibitors has potential side-effects due to its broad immunosuppressive activities. Therefore, the selective inhibition of IFNγ could provide a more effective treatment of AA with fewer side-effects. Here, we investigated whether TAGCyx's proprietary ssDNA aptamer TAGX-0003, characterized by high affinity against IFNγ (Kd=33pM), protects HFs from experimentally induced IP collapse and rescues HFs from AA-like phenotype in the humanized mouse model for AA. Systemic administration of 0.3 or 3nM TAGX-0003 significantly inhibited 100IU/ml IFNγ-induced STAT1 phosphorylation in human HF organ culture. In the humanized mouse model of AA, intradermal injection of TAGX-0003 drastically reduced MHC class I and II expression in and around hair bulbs, rescued HFs from IP collapse and significantly promoted hair regrowth during the dose escalating period (12-300nM). Moreover, TAGX-0003 significantly reduced peri- and intra-follicular CD8 positive T cells around the bulb. Further, melanogenesis was clearly observed by TAGX-0003 treatment. In conclusion, TAGX-0003 prominently protected HFs from IP collapse, potentially preventing disease relapse, and it could be developed as a potent medicine for treatment of AA.

LB790

Toward new depigmenting agents through drug repurposing: Melanogenesis inhibition by para-aminophenols

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Inhibitors of the enzyme tyrosinase have found clinical utility as agents to treat disorderrs of hyperpigmentation. Potential toxicity and carcinogenicity of currently approved depigmenting agents motivates the discovery of safer and more effective alternatives. We report the identification and characterization of tyrosinase inhibitors that are "repurposed" exisiting drugs. Acetmaniophen, a para-aminophenol analgesic, displayed inhibitory activity against mushroom tyrosinase with a Ki of approximately 400 microM. Detailed analysis of enzyme kinetics showed acetaminophen acts as a non-competitive inhibitor. Further, spectrophotometric analysis revealed acetaminophen is converted in the presence of tyrosinase to an oxidation product, hydroxy-para-benzoquinone. Select substituted analogs of acetaminophen were also found to block tyrosinase activity; in contrast to the parent molecule, the susbstituted analogs behaved as competitive inhibitors. Both acetaminophen and its chloro-substituted derivative inhibited melanin production in human MNT-1 melanoma cells. The differing kinetic behavior of acetaminophen and its substituted analogs reflects differing interactions of the inhibitors with the active site of the enzyme.

LB791

Avacopan, a highly selective small molecule inhibitor of c5a receptor, in patients with Hidradenitis Suppurativa: Initial results from a randomized, double-blind, placebo-controlled, phase 2 study (aurora)

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Hidradenitis suppurativa (HS) is a chronic, debilitating, inflammatory skin disorder. Neutrophils are prominent in nodules, abscesses, and tunnels. Complement C5a is a key source of inflammation promoting neutrophil recruitment, activation and localized inflammation in HS via the C5a receptor (C5aR). Current HS therapy with antibiotics, corticosteroids or TNF-α inhibitors is insufficient. Avacopan (CCX168) is an orally-administered inhibitor of C5aR (which leaves the beneficial actions of a second C5a pathway via CC5L2 intact) which was tested as a novel therapeutic approach in HS. A Phase II clinical study (NCT03852472) evaluated avacopan in moderate-to-severe HS, (Hurley Stage II/III) ≥6 months, with HS lesions in ≥2 distinct anatomic areas, and inadequate response to antibiotics. Patients were treated with avacopan 10 or 30 mg BID, or placebo BID in a 1:1:1 ratio for 12 weeks (wks), followed by avacopan 10 or 30 mg BID (blinded) in all patients from Wk 12-36. The primary efficacy endpoint was the proportion of patients (398 enrolled in the intend-to-treat, ITT, population) achieving HiSCR (Hidradenitis Suppurativa Clinical Response) at week 12. While the proportion of patients achieving HiSCR in the overall ITT population did not statistically separate at Wk 12, there was a significantly greater HiSCR response in the Hurley Stage III patients with avacopan 30 mg BID vs. placebo (42.6% vs. 22.2% P=0.0349). Avacopan also demonstrated a favorable safety profile in HS, with a lower incidence of treatment emergent adverse events (48.5% in avacopan groups vs. 55% with placebo), and serious adverse events (1.5% in the avacopan groups vs 2.3% in placebo). Avacopan's use in a Hurley Stage III HS population warrants further investigation.

LB792

Minoxidil and dutasteride drug tattooing for male Androgenetic Alopecia

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Men are frequently affected by androgenetic alopecia. A variety of drug therapies, including, but not limited to, topical or oral minoxidil, oral 5-alpha-reductase inhibitors (finasteride, dutasteride), and new therapies such as platelet-rich plasma injections have been adopted by dermatologists in the management of androgenic alopecia. The drug tattooing technique is a drug delivery technique that utilizes tattoo machine and disposable microneedles cartridges to deliver drug formulations to the superficial dermis and has been employed for the treatment of scars and idiopathic guttate hypomelanosis. The aim of this study is to understand the effectiveness of dermal delivery of minoxidil and dutasteride through the tattooing technique in the treatment of androgenic alopecia among men. Ten men treated with at least 3 monthly sessions were evaluated by standardized overhead photography. Drug tattooing technique consisted of monthly sessions with endpoint of pinpoint bleeding, using a 27-Magnum Soft-Edges needle cartridge, using a rotatory tattoo machine under sterile conditions. The sterile drugs (1mL of minoxidil sulfate 0.5% and 1mL of dutasteride 0.1%) were placed in a sterile ink cup, and needles were kept moist by dipping the needle cartridge in the ink cup throughout the procedure. Changes in the Severe Alopecia Tool (SALT) scores were calculated for each patient before and after treatment as a means to monitor response to treatment. The combination of minoxidil and dutasteride delivered to the superficial dermis resulted in significant hair growth in the majority of patients as measured by the regrowth % based on the SALT score. Some patients that did not respond to 3 sessions were identified as having longer course of androgenetic alopecia (over 40 years of disease), and had associated features of scalp photoaging from chronic sun exposure. Delivery of minoxidil and dutasteride via the drug tattooing technique could be considered as an effective technique to promote hair follicle stimulation and hair growth in young male patients with androgenic alopecia.

LB793

A phase 1, open-Label, single ascending dose study in healthy subjects of the safety, tolerability and pharmacokinetics of ASLAN004, a novel IgG anti-IL-13 receptor alpha 1 Inhibitor

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ASLAN0004 is a novel fully human IgG4 anti-IL-13 receptor alpha 1 (IL-13Rα1) monoclonal antibody, that blocks the signaling of IL-4 and IL-13 through the Type II receptor, hence is a potential therapy for atopic dermatitis, asthma and diseases of related etiology. The study aim was to evaluate the safety, tolerability and pharmacokinetics of single ascending doses of ASLAN0004 in healthy male subjects. The study had 2 parts: in the first, 5 sequential ascending dose cohorts (0.1 to 10 mg/kg) were administered ASLAN0004 intravenously as a single dose. In the second, 4 cohorts (75 to 150 mg) were administered ASLAN0004 subcutaneously, as a single dose. The primary outcome measure was safety and tolerability; secondary outcomes comprised of pharmacokinetic parameters. Pharmacodynamic outcomes were assessed as exploratory endpoints and included IL-13Rα1 receptor occupancy and the inhibition of STAT6 phosphorylation. Peak ASLAN004 serum concentration was 2–4 hours post intravenous administration and approximately 4 days post subcutaneous administration. Duration of pharmacodynamic effect was shown to increase with increasing ASLAN004 intravenous and subcutaneous dose. In all cases, subcutaneous administration showed a higher degree of subject variation for both pharmacokinetic and pharmacodynamic effect when compared with intravenous administration. As a single dose, ASLAN004 was well tolerated with no adverse events that led to study discontinuation and no serious adverse events were reported. Mild itch at the injection site was reported in one individual, resolving within 24 hours. There were no adverse events of special interest associated with ASLAN004. Data from this study support and encourage further development of ASLAN0004. Clinical trials registration: NCT03721263.

LB794

Synthesis and biological evaluation of a small molecule library identifies novel anti-skin cancer agents

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Treatment of melanoma (MSC) and non-melanoma skin cancers (NMSCs, basal cell carcinoma (BCC), and squamous cell carcinoma (SCC)), affecting one-fifth of the US population, is hampered by drug resistance, side effects, and low bioavailability. Owing to low molecular weight and the ability to enter cells, small molecules are gaining ground towards enhancing bioavailability and minimizing some of the side effects associated with classical cancer drugs. Herein, we synthesized a mini-library of 86 compounds via C-N/C-C coupling, direct substitution on the aromatic ring, or a modified Skraup–Doebner–von Miller approach, and their solubility and biological properties were characterized. These agents were tested for *in-vitro* anticancer activity against human NMSC (SCC-12 and A431) and MSC (SKMel-28 and A375) cell lines compared with nontumorigenic HaCaT keratinocyte cell line as control. Potent hits with low-micromolar anticancer activities displayed IC_{50} values of 3.1±0.68, 5.0 ±0.80, 5.3±0.88, and 6.2±1.05 μM for SCC-12, A431, SkMel-28, and A375, respectively, versus minimal effects on HaCaT. Cisplatin, used as positive control drug had a lesser cytotoxic effect in cancer cells and more toxicity in normal cells, compared to some of the identified agents. Using SwissTargetPrediction web-based tool, the potent hits identified CDK8, CLK4, nuclear receptor ROR, tyrosine protein-kinase Fyn/LCK, ROCK, and PARP that are dysregulated in skin cancers as targets. Using SwissADME web-tool, the potent compounds were identified with high GIT absorption, skin permeation (log KP), Log Po/w (below 5), compliance to Lipinski rule, and high biodegradable profile characteristics. In summary, the results highlight the promising anti-skin cancer characteristics of these low molecular weight compounds.

LB795

Topical Product Development: Role of Barrier Function, *In-vitro* Skin Irritation & Permeation Testing for a model drug.

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The Purpose of the study was to evaluate a model drug for topical application using various invitro screening models; skin barrier, *invitro* skin irritation and *invitro* skin permeation testing. The skin barrier function assessment was performed by Trans Epithelial Water Loss (TEWL) measurements. The skin irritation potential was assessed using the EpiDerm® in vitro model in which tissue viability was determined using the MTT conversion assay. The IVPT study was performed across dermatomed human fresh frozen skin using Franz type diffusion cells and drug content was analyzed using LCMS/MS.

Results: 4 prototypes of TER 001 were formulated and screened.The skin barrier function results showed that TER001 in 2 silicone-based prototypes showed occlusion effect for T24h, comparable to positive control over stripped skin. The other 2 spray type prototypes showed less than T6h. The relative tissue viability with secreted levels of the proinflammatory mediator IL-1a indicated optimum dose . A dose-dependent upregulation of IL-1a secretion was noted at 2% w/w, TER001. *Invitro* permeation testing of the applied dose presented tissue retention in the epidermal and dermal layers of the tissue. 1.0±1.0 and 0.5± 0.2% applied dose was found in the epidermal and dermal layers respectively and higher epidermal retention.

Conclusions: Topical and Dermatological product development aims at safe drug limits, active availability and biological activity intended at the site. This can be evaluated using *invitro* tools. The model drug evaluated here presented better emollient properties, was classified as non-irritant at intended dose and IVPT results supported the selection of the prototype for CMC consideration and non-clinical tox studies.

LB796

Protective Effect of the Aqueous Extract of *Polypodium leucotomos* (Fernblock®) on Skin Cells against Blue Light Emitted from Digital Devices

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Introduction. The effects of sun exposure on the skin and specifically those related to pigmentation disorders are well known. It has recently been shown that blue light leads to the activation of metalloproteinases, the induction of oxidative stress, and long-lasting pigmentation. The protective effect of the aqueous extract of *Polypodium leucotomos* (Fernblock®) is known.
Objective. To investigate the action mechanism of Fernblock® against pigmentation induced by blue light from digital devices.
M&M. Human fibroblasts (HDF) and murine melanocytes (B16-F10) were exposed to artificial blue light (a 400-500 nm LED lamp). Fernblock® was used as photoprotector. Cell viability, mitochondrial morphology and the expression of the mitogen-activated protein kinase (MAPK) p38 as markers involved in the melanogenesis pathway, were evaluated. The activation of Opsin-3, a membrane protein sensitive to blue light that triggers the activation of the enzyme tyrosinase responsible for melanogenesis in melanocytes, was also analyzed.
Results. The pretreatment with Fernblock® prevents cell death, alteration of mitochondrial morphology and phosphorylation of p38 in HDF. In addition, Fernblock® significantly reduces the activation of opsin 3 in melanocytes and the photo-oxidation of melanin, preventing its photodegradation.
Conclusions. The photoprotective role of Fernblock® could be due to a reduction of the activation of opsin 3 and the formation of the oxidized form of melanin, preventing hyperpigmentation and exerting beneficial effects against the detrimental impact of blue light from digital devices and preventing early photoaging.

LB797

Immune nano-scintillator mediated novel triad photodynamic therapy reversing the tumor immunosuppressive microenvironment against invasive skin Squamous Cell Carcinoma

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Therapy of cutaneous squamous cell carcinoma (cSCC) is a big challenge when it progresses into invasive cSCC which involves a deep range with a high degree of malignancy. Photodynamic therapy is a promising method utilized in tumor therapy while its applications are limited due to the low penetration depth of light in tissues and weak efficacy of each single treatment. Herein, a novel nanoplatform of X ray responsive, photosensitizer and immunologic adjuvant imiquimod loaded nano-scintillator (ScMMI) mediated triad photodynamic therapy (X-IPDT) was constructed to accomplish the inhibition of cSCC growth, benefiting from the deep penetration ability of X ray and simultaneous enhanced immunological effect. Results indicated that the photosensitizer loaded nano-scintillator (ScMM) mediated X-PDT could suppress tumor growth and integrating of imiquimod into the nanocomposite could enhance the anti-tumor immunity and eradicate the tumor. ScMMI mediate X-IPDT induced mutation of DCs, secretion of INFα, IL-4, IL-12A, and IL-10, reduced proliferation and activation of M2-type macrophages, recruited $CD4^+$ and $CD8^+$ T cells, released the immunosuppress of microenvironment in invasive cSCC bearing mice, increased mobilizing and activating of B cells, thus up-regulating the anti-tumor efficiency. The integrated therapy model of X-ray excitation, photodynamic therapy and immunologic adjuvant mediated X-IPDT could overcome the shortcomings of traditional treatment and implement synergistically anti-cSCC effect.

LB798

Particulate matter-induced atmospheric skin aging is aggravated by UVA and inhibited by a topical *L*-ascorbic acid compound

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Ambient particulate matter (PM) is a major contributor to environmental air pollution-associated skin damage. However, most published studies are observational or epidemiologic and have not mechanistically investigated the combined effects of air pollutants on cellular senescence and aging, particularly in combination with Ultraviolet (UV) radiation. Herein, we analyzed whether UVA aggravated PM induced inflammatory cascade, which contributes to aging of skin-derived cells. We hypothesized that the cell senescence is involved PM&UVA-induced aging and tested whether an *L*-ascorbic acid compound, containing vitamin E and ferulic acid, can inhibit PM&UVA-induced aging. In the results, PM&UVA exposed HDFs showed further increased in ROS levels detected by flow cytometry. We then demonstrate that PM induces MAPK signaling activation and the expression of AhR and NF-κB – responses that are exacerbated by UVA. The levels of inflammatory cytokines, IL-1β and IL-6 were significantly higher in PM&UVA exposed group which, induced increase transcription of MMPs, causing down regulation of type I collagen. Meanwhile, treatment with *L*-ascorbic acid compound mixture, reduced increased levels of ROS and inflammatory cytokines. Additionally, PM&UVA induced increase in SA-β-gal staining assay was reduced by the *L*-ascorbic acid compound (LAC). These findings demonstrate the relationship between atmospheric pollution and markers of inflammation and cellular aging. AhR inhibition by topical antioxidants represent prospective strategies for preventing atmospheric pollution-induced skin aging.

LB799

Role of mitochondria in keratinocyte responses to acute UVB irradiation.

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Solar ultraviolet B (UVB) radiation is the major environmental risk factor for skin cancers. In order to develop new strategies to prevent and treat those malignant tumors, a better understanding of the different pathways involved in the cellular responses to UVB radiation is needed. The study of the energy metabolism is essential by its central function in many cellular processes like cell cycle, autophagy, senescence and apoptosis. In this study, we examined the contribution of the mitochondrial metabolism in the keratinocyte responses to acute UVB radiation. To this end, we first evaluated the modifications in the metabolic pathways involved in energy metabolism at different time points after UVB irradiation using a global quantitative proteomic approach. Results showed that UVB irradiation induces a biphasic modification in the expression of proteins implicated in oxidative phosphorylation, TCA cycle and glycolysis. Biochemical functional analysis showed that an increase in the oxygen consumption rate (OCR) occurs in concomitant with the accelerated phase of DNA damage removal. Interestingly, the immediate removal of UVB-induced damage through expression of photolyase abrogates the observed upregulation in the OCR. Our results further revealed a particular modification in the mitochondrial network morphology. However, the number of mitochondria did not significantly affected by UVB irradiation. Altogether, our data suggest a tight interrelationship between UVB-induced DNA damage, DNA repair system and energy metabolism, which finally governs cell-fate decision between survival, differentiation, and death.

LB800

Blue Light Phototherapy as a Treatment of Transient Acantholytic Dermatosis

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Transient acantholytic dermatosis (Grover disease) is a recurring cutaneous papulovesicular skin disorder classically occurring on the chest in middle aged Caucasian males. The disease is often recalcitrant and difficult to induce complete remission in a subset of patients with current standard therapies. Currently, there is a need for more therapeutic options for these patients. In prior studies, non-ionizing blue light exposure has been shown to be efficacious in the treatment of a wide range of skin conditions from acne to rosacea, and psoriasis. Its efficacy in these skin pathologies is thought to be mediated by its ability to alter keratinocyte proliferation, generate reactive oxygen species, and increase T-cell mobility. Our purpose was to elucidate the possible clinical utility of blue light phototherapy in treating transient acantholytic dermatosis (TAD). Seven patients with biopsy proven TAD, after a 2 week washout of therapies they were using for their disease, underwent blue light phototherapy treatment for 15 sequential treatments over five weeks for 16 minutes using the DUSA BLU-U device. Cumulative dosage of light given was 160 J/cm^2 directed at the torso. Clinical status was assessed by visual inspection and photography before, during (midpoint), and at treatment conclusion along with administration of the DLQI (0-30 points) and 12-item pruritis severity score (0-22 points). We found that blue light phototherapy reduced the number of lesions (-70±27%, P <0.001, 95% CI, .438 .98), improved the severity of itching as shown by a reduction in the 12-item pruritis severity survey (-6±5.5 points, P .04261, 95% CI, 0.283, 12.1) and improved the quality of life of Grover's patients (mean DLQI -Δ 3±2.8 points) as when compared to baseline. Patients with intractable TAD may benefit from blue light therapy in addition to current standard therapies with regards to lesion reduction and itch severity.

LB801

High-Energy Visible (HEV) Light: Blue Light Poses Potential Harmful Effects on Human Skin Cells.

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Skin is being increasingly exposed to artificial blue light due to the extensive use of electronic devices. Studies have suggested that blue light, also known as high-energy visible (HEV) light can produce cytotoxic effects associated with oxidative stress, and damage to mitochondrial and DNA repair systems. The work described in this presentation was carried out in order to better understand the deleterious effects of HEV light on the skin. Studies were conducted using primary human keratinocyte and melanocyte cells in 2D culture. The impact of artificial blue light on cell viability, oxidative stress, DNA repair pathways, and mitochondrial function were assessed using gene and protein expression methods. Our results showed that cells exposed to 60 minutes and 120 minutes of blue light each day for 4 consecutive days (total intensity of 3.8 and 7.6 J/cm^2 respectively) produced a significant decrease in cell viability. In addition, gene expression data showed an increase in the expression of genes that regulate inflammation (IL1A, CSF2) and a decrease in the expression of genes that regulate mitochondrial function and DNA repair (PARP1, EGR1 and FOXO1). HEV light also decreased the expression of TP73, which plays an integral role in regulating keratinocyte proliferation, suggesting disruption to skin repair mechanisms. Changes in specific proteins were confirmed using ELISAs and plate-based enzyme assays. Our results showed blue light caused alterations to mitochondrial and DNA repair pathways, demonstrating a significant decrease in mitochondrial biogenesis and an increase in DNA damage. Our findings suggest that artificial blue light poses significant damage to skin cells.

LB802

Strengthening nuclear envelope attenuates NETosis and ameliorates UVB-triggered skin inflammation and kidney damage in lupus mice

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Background: Ultraviolet B (UVB) triggers lupus flare by worsening skin lesions and systemic symptoms, i.e., lupus nephritis. The effects of UVB-induced skin inflammation on kidney damage are not well understood. NETosis has been implicated in lupus. Our mechanistic study revealed that nuclear envelope rupture and NET formation is driven by PKCα-mediated lamin B disassembly. Strengthening nuclear envelope by lamin B overexpression decreases NETosis and NET-associated cytokine exhibition in skin of UVB-irradiated lmnb1$^{Tg/+}$ mice. Other studies report that UVB can trigger an IFNα signature both in skin and kidneys, and neutrophils in the inflamed skin can migrate back to the circulation and are recruited by kidneys, resulting in transient proteinuria in WT mice. However, the involvement of NETosis in UVB-mediated lupus flare in skin and kidneys has not been studied.
Method: We generated lupus-like mice with lamin B overexpression by backcrossing lmnb1$^{Tg/+}$ mice with MRL/lpr (lpr) mice for 10 generations. Female lpr-lmnb1$^{Tg/+}$ mice and their lpr littermates (8-week-old) were exposed to UVB at 150 mJ/cm^2 for 5 consecutive days. We examined skin lesion, proteinuria, and NET formation in skin and kidney in these mice. *Aggregate lesion severity (ALS) score was evaluated based on skin thickness and infiltrates of the H&E staining of skin sections.*
Results: UVB exposure induced NET formation and inflammatory responses in skin, as well as proteinuria and NETotic neutrophils in kidneys of lpr mice. Strengthening nuclear envelope by lamin B overexpression decreased NET formation both in skin and kidneys compared to controls ($p<0.05$), and ameliorated skin inflammation with attenuated skin thickness, ALS score*, and reduced* proteinuria in lpr-lmnb1$^{Tg/+}$ mice as compared to those in lpr mice with UVB exposure. Skin ALS score or NETs ($r=0.6$, $p<0.05$) are positively correlated with proteinuria.
Conclusion: Inhibition of NETosis by strengthening nuclear envelope integrity can ameliorate UVB-triggered skin inflammation and proteinuria in young lupus-like mice.

Pigmentation & Melanoma

LB803

Resveratrol's effect on the androgen receptor pathway as a target for decreasing growth and invasion of Melanoma and methods of application

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Although melanoma affects both sexes, current literature shows it is more prevalent and more deadly in men. Several potential reasons for this difference have been proposed. That said, the androgen receptor has been proven to play a role in melanoma growth and metastasis, and may play a part in the difference in incidence and mortality rates between sexes. Resveratrol, a naturally occurring compound with poor bioavailability, has been shown to decrease melanoma cell growth in both *in vitro* and *in vivo* studies. Its effects on the expression of several genes involved in the androgen receptor pathway in non-melanoma cancer are well documented. Although several mechanisms have been proposed in which resveratrol affects melanoma cell growth, we suspect the androgen receptor pathway may be another target that warrants further investigation. Our objective is to reiterate the potential for resveratrol as a treatment in melanoma and to propose that it changes melanoma behavior at least partially through its interaction in the androgen receptor pathway. We also will discuss pros and cons of the various ways resveratrol may be delivered as a treatment for melanoma. To support our hypothesis we reviewed current literature and performed scratch wound assay, qPCR, and Western Blotting. Melanoma cells treated with resveratrol showed a decrease in the distance traveled during scratch wound assay. Additionally, androgen receptor pathway gene expression and protein level was altered in cells treated with resveratrol. The androgen receptor pathway plays a role in melanoma cell growth and metastasis. Resveratrol is a potential therapeutic that decreases melanoma growth at least partially through its effects on this pathway. Further melanoma *in vivo* studies that explore the various methods of treatment with resveratrol are needed to help the transition from bench to bedside.

LB804

Study of the expression of cellular senescence markers in Melasma

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The aim of this study was to evaluate the presence of cellular senescence markers in the skin of patients with melasma. The study included female patients with melasma who attended the outpatient consultation, aged between 30 and 35 years. Biopsies of skin with melasma and non-photoexposed healthy skin were taken, in which the expression of the cellular senescence markers p16, p53, IGF1, TGFβ, BCL2, mTOR and SIRT1 was measured at the RNA level by means of RT-PCR. Twelve patients were included, with a mean age of 32.8 years and an average mMASI of 11.5. It was found that p16 had a 1.3-fold (p=0.04) and p53 a 3-fold (p=0.006) higher expression in skin with melasma compared to healthy skin. In contrast, SIRT1 had a 7-fold (p=0.02) and BCL2 an 8-fold (p=0.049) lower expression in skin with melasma compared to healthy skin. The levels of TGFβ and IGF1 were similar in both groups and no measurable expression of mTOR was found. By multivariate analysis, p53 and p16 were related with statistical significance to the mMASI values (p=0.0001 in both cases). In agreement with previous studies, an increase in p53 and p16 levels was found; this finding had not been previously reported in young patients with melasma. This is the first time that a decrease in SIRT1, as well as BCL2, has been described in lesional skin with melasma, and it is also the first time that the mMASI has been associated with markers of cellular senescence. These findings support the theory of cellular senescence in the pathophysiology of melasma and could have implications for prevention, treatment, and future research.

Skin of Color

LB805

A Study of the Human Skin Changes According to UV Shock.

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Introduction: Ultraviolet (UV) is one of the important environmental factor affecting skin aging. Therefore, there are many people who are reluctant to expose themselves to ultraviolet rays. On weekdays, workers are exposed to UV rays for less than an hour, but on weekends, they are exposed to UV rays for more than two hours due to outdoor activities, according to a survey. Therefore, the purpose of this study is to study skin changes when skin without UV exposure followed to strong UV light and skin with suberythemal doses of UV followed to strong UV light.
Method: Ten women between the ages of 20 and 39 have been recruited in the study. The test area was untanned middle or lower part of back skin. The test sites were two. (Test group : 0 minimal erythema dose (MED) + 2 MED, **Control group :** 0.5 MED + 2 MED) Ultraviolet radiation of 0 MED or 0.5 MED was investigated for five days and 2 MED was investigated in both areas on Day 6. The measurement points were baseline, five days after 0.5 MED, immediately after 2 MED and follow up three days after 2 MED. The skin color, melanin, erythema, hydration and elasticity were measured
Result: The melanin level was increased that received 0.5 MED for five days. And immediately after receiving 2 MED, the area that examined 0.5 MED immediately showed a stronger immediate pigment darkening reaction than those that 0 MED area. Skin erythema was stronger those with 2 MED after receiving 0 MED than those with 2 MED after receiving 0.5 MED and it was lasted for 3 days. Skin elasticity was lower that of 2 MED after 0 MED than that of 2 MED after 0.5 MED.
Discussion: Skin that did not receive UV radiation showed weak immediate pigment darkening reaction and significant damage from strong UV because it took time for melanin to reach the surface of the skin to protect the skin. Therefore, the erythema lasted for a long time and elasticity decreased. Therefore, back skin and inner skin of the thighs, such as those with little UV exposure, need to be applied with high UV protection index product before receiving strong UV rays.

LB806

YouTube as a source of information on treatment of hyperpigmentation in skin of color

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YouTube has become an important resource for patients who are looking to find more information about how to treat conditions in skin of color. One of the most common concerns in patients with skin of color is hyperpigmentation. The objective of this study was to assess the usefulness of information on treatment of hyperpigmentation presented on YouTube in order to assess areas of potential areas of patient outreach and education for practicing Dermatologists who are interested in Skin of Color. The YouTube site was searched systematically using the following keywords: “hyperpigmentation”, “hyperpigmentation treatment for black skin”, “hyperpigmentation treatment”, and “hyperpigmentation home remedies”. Eight hundred and forty-five videos met the inclusion criteria. Videos were assessed based on views, duration, days since upload, number of likes and number of dislikes. A usefulness score was given to each video according to the following score: “slightly informative”, “informative”, and “very informative” based on the quality of information provided in the video. Eight hundred and forty-five videos (233 for the ‘hyperpigmentation’ search term, 294 for the ‘hyperpigmentation treatment for black skin’ search term, and 280 for the ‘hyperpigmentation treatment’ search term), were included in the analysis. Treatment of hyperpigmentation in Black skin yielded 34.7% of the results. 33.9% of the videos were categorized as very informative, 41.6% were categorized as ‘informative’ and 24.5% were categorized as slightly informative. Measure of usefulness did not correlate with the number of views. Video length did not correlate with usefulness score. YouTube search and video production trends point to an marked interest in the treatment of hyperpigmentation in skin of color. Physicians interested in treating skin of color can use the queries seen on YouTube to inform patient education and outreach parameters for their patient populations.

Skin, Appendages, and Stem Cell Biology

LB807

Evidence for epithelial cells in human and murine blood and bone marrow

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Cytokeratin positive cells are frequently found in the blood (BL) and bone marrow (BM) of patients with epithelial cancers and attributed to metastasis. We document here epithelial cells in normal BL and BM (Lonza) using four different methods: immunofluorescence microscopy (IF), Krt1-14CreERT;mTmG transgenic mice, NanoString Gene Expression Assays, and flow cytometry. We have made several novel findings. First, we observed rare but reproducible pan-cytokeratin immunoreactive cells (Dako) in untreated human and murine BL and BM. We found that Epithelial Cell Adhesion Molecule+ (EpCAM; 9C4 Biolegend) cells in human BL and BM constituted 1,719/10^6 viable cells (0.17% n=4 biological replicates), and 25,697/10^6 viable cells (2.57%; n=3 biological replicates) of mononuclear cells, respectively, regardless of the number of cells counted (4 experimental replicates). Virtually 100% of the EpCAM+ cells were immunoreactive to pan-cytokeratin as determined by IF microscopy. Second, using Krt1-14CreErt;mTmG transgenic mice, we found low (8.6 native GFP+ cells per 10^6 cells analyzed), but significant numbers ($p<0.0005$) of GFP+ cells in normal murine BM that were not the result of randomness when compared with multiple negative controls. Third, NanoString Gene Expression Assays detected cytokeratins 17 and 18, and traces of cytokeratin 5 in human BL and BM. Moreover, flow cytometric analyses disclosed heterogeneity among the EpCAM+ cells when compared with CD34 (19% of EpCAM+ cells) CD45 (0.58% of EpCAM+ cells in BM and 0.13% in BL; HG12, BD Pharmingen) and CD44 (0.13% of Epcam+ cells from BL; IM7, Biolegend) lineage markers. We conclude from these observations that cells expressing cytokeratin proteins, and mRNA as well as EpCAM are reproducibly detectable among mononuclear cells from human and murine BL and BM. These observations set the stage for determining the functions of these most curious and interesting epithelial cells.

LB808

A humanized mouse model of androgenetic alopecia (AGA) shows that platelet-rich plasma (PRP) stimulates hair regrowth

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Xenografts of human AGA scalp skin on SCID mice provide the only model system for interrogating human AGA preclinically *in-vivo*, yet are rarely used. This experimental design was to investigate the effect of PRP on hair growth in the AGA mice. We obtained intermediate balding scalp skin areas from 7 male AGA patients . On day 30 following transplantation, the mice were divided into two groups that received once monthly intradermal PRP (standard protocol) injections for 4 months: (i) eight control mice received non-activated PRP (ii) eight were injected with activated PRP. 120 days after the first PRP injection, xenografts were processed for quantitative hair cycle histomorphometry and immunohistomorphometry to measure proliferation/apoptosis of hair matrix keratinocytes *in situ*. This showed that the mean number of macroscopically visible, photodocumented hair shafts was significantly higher in the xenografts treated with activated PRP compared to the non-activated PRP controls. Xenografts of 5/7 patients showed impressive hair regrowth ,while the xenografts of two patients were unresponsive to autologous PRP treatment – roughly corresponding to the % of AGA patients that reportedly do not respond to PRP injection. Quantitative hair cycle histomorphometry revealed a significantly increased anagen:telogen and vellus to terminal HFs ratio in responder mice treated with activated PRP-treated versus those treated with non-activated PRP ($p<0.001$, $p<0.001$). This corresponded to significantly increased proliferation and decreased apoptosis of hair matrix keratinocytes in responders HFs (Ki-67/TUNEL). Thus, our study presents the first preclinical evidence that PRP stimulates hair regrowth in male pattern AGA scalp *in vivo*. Additionally, the humanized AGA mice should be optimally suited to screen candidate AGA therapeutics in a highly relevant preclinical model.

LB809

IL-33 contributes to skin ulcer formation in ischemia-reperfusion-induced decubitus mouse model.

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Decubitus ulcers are injuries to skin and underlying tissue resulting from prolonged pressure on the skin, which become serious problems in aging long-term bedridden patients. Currently, there is no effective treatment or efficient prevention method in early phase of decubitus. Ischemia-reperfusion (I/R) injury is associated with vascular infarction or vasospasm in various organs and decubitus ulcers are considered as cutaneous I/R injury. Interleukin-33 (IL-33) is a member of IL-1 cytokine family that enhance Th2 immune reaction. IL-33 is one of danger signals, and we speculated that copious amount of IL-33 would be released in the formation of decubitus ulcers. In this study, we aimed to determine if IL-33 acted an important role in the decubitus ulcer formation following I/R and investigate the mechanism. Dorsal skin of IL-33KO and wild type (WT) mice was trapped with two magnetic force to make I/R injury model. Ulcers were formed time-dependently in WT and KO mice, but the ulcer area was significantly reduced in IL-33KO mouse compared to WT mice. The number of mast cells and neutrophils was increased in WT mice compared to that in IL-33KO mice by I/R, but the number of infiltrating macrophage was higher in IL-33KO mice at the stage of I/R ulceration and the major increasing macrophage was M2 macrophage in IL-33KO mice. Flow cytometric analysis showed that M2-like macrophages were increased by I/R injury in IL-33KO mice. Microarray analysis also indicated that there were more M2-associated genes in IL-33KO mice at I/R day 2. We checked expression of inflammasome-related molecules, revealing IL-1 beta was decreased in IL-33KO mice and the expression of CCL17, related to M2 macrophage differentiation, was increased in IL-33KO mice compared to WT mice. We conclude that IL-33 was released by I/R injury in the skin, contributed to M1/M2 macrophage increase through CCL17 suppression, and that IL-33 induced inflammasome-related molecules, such as

IL-1 beta, causing ulcer formation probably through increasing M1/M2 ratio and mast cell and neutrophil infiltration.

LB810

A stabilized retinol and myrtle complex with enhanced antiaging efficacy induces beneficial transcriptomic and epigenetic skin changes, leading to a clinical visible reduction in the skin's signs of aging

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Retinol is a gold-standard treatment for anti-aging. Previously it was shown that a stabilized retinol and myrtle complex delivered enhanced antiaging benefits. The addition of myrtle complex increased the biological activity of retinol and enhanced its clinical antiwrinkle efficacy, as well as its tolerability, resulting in a 1-week fast acting claim. Here, using non-invasive ultrasound imaging, we show visual evidence of its dermal-matrix building effect. Furthermore, we aimed to discover if the benefits of this complex could be associated with transcriptomic and epigenetic changes in human skin. mRNA, miRNA and protein expressions were evaluated. Differentially expressed genes (DEG) were identified and analyzed using Gene Ontology (GO) to examine enriched biological processes that were modulated by the retinol complex. The retinol complex modulated 961 genes. GO analysis revealed several antiaging biological pathways were enriched, including epithelial cell migration, epidermis development, epithelial cell proliferation, glycosaminoglycan metabolism and positive regulation of the extracellular-matrix. Concomitant with induction of multiple biological antiaging pathways, the retinol complex caused epigenetic changes by significantly reducing the expression of multiples miRNAs known to inhibit anti-aging genes. Overall, this study demonstrated that the retinol complex provides its antiaging benefit through pleiotropic mechanisms of action including beneficial epigenetic and transcriptomic skin changes working together, leading to the clinically visible reduction in the skin's signs of aging.

LB811

Exosomes from human neonatal fibroblasts conditioned media play an important role in skin rejuvenation

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Extracellular vesicles (EVs), including exosomes, are lipid bilayer delimited particles that are naturally released from a cell and play a major role in the communication of various cells by serving as vehicles to transfer cytosolic proteins, lipids, and RNAs between cells. Cell culture conditioned media (CCM) from human neonatal fibroblasts cultured under hypoxic conditions have demonstrated potential to stimulate wound healing and skin regeneration. EVs are known to secrete into medium from cultured cells; therefore we characterized the content of exosomes from CCM to investigate its potential role in skin.
Method: Exosomes isolated from CCM were characterized by western blotting, qNano nanoparticle analyzer and transmission electron microscopy. Total proteins were extracted from the isolated exosomes and then proteomic analysis was performed. Furthermore, identified proteins were performed through bioinformatic analysis, such as gene ontology (GO) and KEGG pathway. We also performed efficacy testing of isolated exosomes by applying on fibroblasts and keratinocytes in a monolayer and 3D skin cell culture model followed by performing gene expression analysis.
Result: 1635 proteins were identified from proteomic analysis. GO biological process (GOBP) and KEGG pathway analysis results indicated isolated exosomes have strong involvements in cell adhesion, extracellular matrix organization, and cell signaling pathways related to cell differentiation and proliferation. Gene expression analysis from *in vitro* monolayer study showed upregulation of longevity associated gene FOXO3 and with 3D cell culture study showed strong upregulation of extracellular matrix genes which primarily participate in skin regeneration.
Conclusion: The results indicate that exosomes from human neonatal fibroblasts conditioned media may be an important component that contribute to skin regeneration.

LB812

Natural history of recessive dystrophic Epidermolysis Bullosa wounds using a home photography app

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Recessive dystrophic epidermolysis bullosa (RDEB) is a devastating, genetic blistering condition caused by the absence of type VII collagen (C7), affecting the mucosa and skin. Patients often have recurrent and chronic open wounds, but one of the major barriers to the development of clinical trials is the lack of understanding of the natural history of RDEB wounds, as the measurement of target wound change has not been studied prospectively or validated. We conducted a longitudinal, clinical observational study of 10 patients with RDEB who used a mobile phone photography application, with built-in machine learning, to outline and track RDEB wounds autonomously. Patients used this mobile application to capture photographs weekly, alongside reporting associated pain and itch. 507 photos of 10 participants with RDEB were collected: 202 of chronic open wounds (unhealed >12 weeks) and 290 of recurrent wounds (heal but re-open), with an average of 44.7 wound photos per participant. The top three locations recorded were hips or legs (n=241), feet (n=115) and upper extremity (n=82). For chronic open wounds, there was a statistically significant positive correlation for both wound size and pain (0.76, $p<0.001$), and wound size and itch (0.74, $p<0.001$). Recurrent wounds also had a significant association between wound size and pain and itch, but the strength of the correlation was weaker; pain (0.37, $p<0.0009$), itch (0.32, $p<0.005$). Neither wound types significantly healed over an average follow up time of 95.5 days. This validated previously known information about the nature of RDEB wounds, and we found that use of a mobile application can be a valuable method to track the natural history. The covid-19 travel restrictions have shown the value of being able to obtain weekly wound images whilst participants are at home. The challenges we faced included encouraging regular submission of wound photographs, loss-to-follow up due to enrollment in other clinical trials, and technical difficulties associated with using the application.

LB813

Intelligent acid responsive nanocomposite mediated sonodynamic-immunotherapy for Cutaneous Squamous Cell Carcinoma

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The aberrant tumor microenvironment (TME) featured with hypoxia, acidosis and vascular anomaly are reported to be related with the therapeutic resistance in cancer. SDT has received increasing attention for cancer therapy, because of its unique features, including minimal invasiveness, deep tissue penetration, low systemic toxicity and high controllability. Herein, an acid-degradable metal-organic framework nanocomposite (ZIF-8) which encapsulated ALA, hemoglobin and imiquimod (AIHZNPs) was design and synthesized for sonodynamic-immunotherapy of cutaneous squamous cell carcinoma (cSCC). The AIHZNPs is composed of ALA as the sonosensitizer, which could be activated with ultrasound to perform anti-tumor effect. Hemoglobin was used as an oxygen molecules co-carrier to relieve intra-tumoral hypoxia and increase the production of reactive oxygen species during treatment for curative effect improvement. The co-loaded imiquimod could upregulate anti-tumor immune response during therapy. The organic framework ZIF-8 can be degraded under acidic condition to increase the drug release of the nanoparticles in the tumor tissue. The results show that the as prepared AIHZNPs exhibited good stability, acid degradation ability, ultrasound responsiveness and biosafety. Under ultrasound stimulation, AIHZNPs could damage cSCC cells, activate anti-tumor immunity *in vivo*, effectively eliminate skin squamous cell in cSCC bearing mice and prolong their survival time. This study presented a tumor responsive nanocomposite mediated sonodynamic-immunotherapy for cSCC *in vitro* and *in vivo*, highlighted its great potential for clinically translatable cSCC therapy.

LB814

Therapeutic drug monitoring: The way towards individualized Secukinumab dosing in Psoriasis

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With the introduction of new biologics for psoriasis, achieving optimal response is a realistic goal. However, real life data reveal that response varies from optimal to non-response and loss of response urging physicians to explore off-label intensification. Therapeutic drug monitoring (TDM) could prevent these 'blind' modifications by guiding physicians in their clinical decision-making. In order to perform TDM, two fundamental requirements are 1) assay accessibility and 2) knowledge about an optimal therapeutic window. Therefore, we developed an secukinumab immunoassay and determined the optimal therapeutic window. Sera from 77 psoriasis patients treated with secukinumab were collected at least once at trough (maintenance). Secukinumab trough levels (C_{trough}) were determined using an in-house developed ELISA and disease severity was assessed through the PASI. Using mixed effect model analysis, the effect of several variables on PASI or C_{trough} were studied. During maintenance, the mean C_{trough} were lower in moderate compared to good responders (PASI $\leq$ 2 or ΔPASI $\geq$ 90), respectively 32.9 µg/ml and 45.7 µg/ml. In addition, absolute PASI increased (p=0.015), while C_{trough} (p=0.002) decreased with incremental treatment duration. Furthermore, the absolute PASI decreased significantly with -0.055 (95% CI [-0.086;-0.023]) with increasing C_{trough}(p=0.001). By targeting an PASI of 2, a minimal effective C_{trough} of 37.3 µg/ml was determined. Based on a concentration-effect curve, a maximal beneficial C_{trough} of 52.3 µg/ml could be deduced. In this study, we used an in-house developed secukinumab ELISA and determined the optimal therapeutic window, being 37.3 - 52.3 µg/ml, in psoriasis patients, thereby achieving two essential requirements for TDM implementation in the clinic.

LB815

Differences in characteristics between sensitive and non-sensitive lips applying lip products

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Compared to other skin, the tissue of lip has no sebum and sweat glands, and the stratum corneum is thinner. Because of these properties of the lips, people with sensitive lips may frequently experience the dryness, tingling, itching, allergic skin reactions, etc. In this study, we statistically evaluated the lifestyle and lip sensitivity questionnaires of about 300 people in order to select sensitive lips. The sensitive lip group selected through the questionnaire has a high level of experience with problems after the use of lip products, and lip skin troubles such as the lip dryness, cracking and other symptoms due to changes environment and body condition. In addition, sensitive lip groups tend to have sensitive skin and have a habit of licking lips or using lip balms. We also found out the characteristic differences between sensitive and non-sensitive lips in the application of lip products. Sensitive lip group showed higher TEWL values than non-sensitive lip group. (P <0.001) Although not statistically significant, water content and pH were also lower in the sensitive lip group. When using the lip tint product, the TEWL was significantly decreased between D7 and D14 in the sensitive lip group. In the non-sensitive group, there were no statistically relevant changes or tendencies before and after using the lip tint. Based on the results of these studies, it was confirmed that people with sensitive lips may experience many side effects from the use of lip products. We also confirmed that the selection criteria developed in this study is suitable to select subject with sensitive lips using a questionnaire.

LB816

Wavelet-based image enhancement of confocal data

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Wavelet-based signal processing provides a powerful mechanism for image enhancement, while avoiding noise amplification. Fractional wavelet algorithms function as a family of filters that can be used for an array of image processing applications. Our objective was to employ fractional wavelet transforms (FRWT) for improving image quality and visibility of structures seen in confocal images of human skin. Images were acquired from deep dermal levels using reflectance confocal microscopy (RCM). The original images are very dark and have a low signal due to decreased reflectance of near infrared light in deeper levels. Initially, simple histogram based approaches in the spatial domain were performed, including histogram equalization and normalization. These methods redistribute intensities; contrast is altered indiscriminately and images incur data loss and noise artifact is amplified. This led us to combine FRWT with contrast limited adaptive histogram equalization (CLAHE) to improve image quality. We compared the different approaches for image enhancement by asking 3 expert observers to rank resulting image sets, which were then used to generate aggregate mean opinion scores (MOS). Statistically significant differences in image quality were observed among image sets ($p<0.05$). Specifically, the FRWT+CLAHE transformation was consistently rated with the highest quality among enhancement strategies in all image sets. The FRWT+CLAHE transformation displayed 3.0 MOS points higher than the original dermal level RCM in all RCM image sets ($p<0.05$). Image MOS rating demonstrated substantial agreement between raters ($\kappa=0.704$, 95% CI 0.699-0.708, $p<0.001$). We anticipate a wavelet-based combined algorithm could be developed specifically for data contained in deep dermal level RCM images, leveraged for AI applications for improving image quality, and ultimately improve the diagnostic capacity of RCM.

LB817

Transcriptomic characterization of Prurigo Nodularis and the therapeutic response to Nemolizumab.

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Prurigo Nodularis (PN) is a debilitating, difficult to treat, intensely pruritic, chronic inflammatory skin disease characterized by hyperkeratotic skin nodules. The pathogenesis of PN is not well understood but is believed to involve cross talk between itch-related neuronal cells, immune cells, and the epidermis, and centered around the pro-inflammatory cytokine IL-31, driving an intractable itch-scratch cycle. Here we provide a comprehensive view of the transcriptomic changes in PN skin and characterize the mechanism of action of the anti-IL-31 receptor inhibitor nemolizumab. Our results demonstrate that nemolizumab effectively decreases IL-31 responses in PN skin leading to collapse of downstream inflammatory responses including Th2/IL-13 responses. This is accompanied by decreased keratinocyte proliferation and normalization of epidermal differentiation and function. Furthermore, our results demonstrate how transcriptomic changes associated with nemolizumab treatment correlate with improvement in lesions, pruritus, stabilization of extracellular matrix remodeling, and processes associated with cutaneous nerve function. In summary, these data demonstrate a broad response to IL-31 receptor inhibition with nemolizumab and confirm the critical upstream role of IL-31 in PN pathogenesis.

LB818

Diverse immune response changes during different adjuvant treatments in Epidermal Necrolysis patients

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Stevens-Johnson Syndrome (SJS) and toxic epidermal necrolysis (TEN) are life-threatening cutaneous adverse reactions. There is no consensus on the use of adjuvant treatments in SJS/TEN. This is the first study to explore the effects of intravenous immunoglobulins (IVIG), cyclosporine A (CSA) and best supportive care (BSC) on the systemic immune response. 16 patients with SJS/TEN received IVIG (n=8), CSA (n=4) or BSC only (n=4). Serum samples were obtained prior-, 5-7 days and 21 days after treatment. High-throughput proteomics (OLINK) and ELISA were performed to measure inflammation-associated proteins. Nanostring was performed on RNA extracted from skin biopsies collected prior treatment. SJS/TEN patients showed increased levels of Th1-associated chemokines and regulatory proteins. Few proteins were expressed differently between SJS/TEN severity grades (CD8, TGFb, IL-33, CX3CL1, CCL11, IL-17A, GDNF, ITM2A and IRAK1). Serum overexpression of Th1-associated chemokines correlated with their upregulation in mRNA of lesional skin. Serial measurements showed diverse dynamics between the 3 treatment groups, without any difference in clinical outcome. Both IVIG- and CSA-treated patients showed a decrease in Th1-associated proteins at day 5-7, while BSC patients showed an increase of regulatory and TNF-associated proteins. In all 3 groups, Th1-associated proteins were decreased at day 21.
BSC only, CSA and IVIG have diverse effects on the systemic inflammatory response in SJS/TEN.

LB819

Multiple mediators of inflammation correlate with IRAK4 expression in the skin of Hidradenitis Suppurativa patients and are blocked by the IRAK4 protein degrader KT-474 in TLR-activated monocytes

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IRAK4 is involved in immune activation by interleukin-1 (IL-1) family cytokines and toll-like receptor (TLR) ligands. Kymera is developing the IRAK4 protein degrader KT-474 for the treatment of TLR/IL-1 receptor (IL-1R)-driven inflammatory diseases, including hidradenitis suppurativa (HS) and atopic dermatitis (AD). To understand the role of IRAK4 in HS and AD, we undertook a non-interventional study to evaluate IRAK4 levels in the blood and skin and its relationship to inflammatory biomarkers and disease stage. The study is designed to enroll up to 30 HS patients and 10 AD patients at a single center (York Dermatology Clinic and Research Center). Patient participation consists of a single visit for evaluation of disease status, skin biopsies and blood draws. Levels of IRAK4 and inflammatory biomarkers are measured in skin and blood. Enrollment of HS patients is complete (n=30), and skin biopsies analyzed for IRAK4 by mass spectrometry (MS) and immunofluorescence (IF). IRAK4 expression was highest in HS lesions and lowest in non-lesional skin (MS: $p<0.0001$; IF: $p<0.001$). The expression of gene transcripts involved in TLR-myddosome signaling, inflammasome activity, prostaglandin generation, Th1 and Th17 inflammation, and monocyte/neutrophil migration and activation was significantly upregulated in HS lesions and correlated with IRAK4 protein levels measured by MS or IF, but not with IRAK4 mRNA expression. The upregulation of many of these same genes in human monocytes stimulated *ex vivo* with the TLR7/8 agonist R848 was blocked by KT-474, including IL-1β, TNF-α, IL-6, IL-8, NLRP3, PTGS2, CXCL2/3, IRF7, IFN-γ, IL-2RA, granzyme B and perforin. These findings suggest a central role for IRAK4 in the pleiotropic inflammation in HS, and support the development of KT-474, currently in Phase 1 testing in healthy volunteers and patients with HS or AD.

LB820

ATR inhibition for potentiation of immunogenicity and cell death in Merkel Cell Carcinoma refractory to PD-1 pathway blockade

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ATR (Ataxia telangiectasia and Rad3-related kinase) ensures completion of DNA replication prior to mitosis and its inhibition is known to sensitize cancer cells to DNA damage. Excitingly, with the recent availability of potent, selective ATR inhibitors (ATRi), multiple studies indicate that ATR inhibition can potentiate anti-tumor immunity, largely through unknown mechanisms that may induce cGAS/STING/interferon. Here we explore if ATR inhibition could target Merkel cell carcinoma (MCC) which is immunogenic but often becomes refractory to PD-1 pathway blockade. We treated three MCC cell lines (two virus-positive, one virus-negative) with an ATRi, ceralasertib, on a continuous or intermittent dosing schedule (~4 days on/off) while being serially passaged. Cells were assessed for viability and expression of PD-L1 and class I MHC, both of which are closely linked to immune recognition of cancer cells. Compared to intermittent dosing, continuous ATR inhibition more potently limited the proliferative capacity of all cell lines, suggesting that a continuous dosing schedule may be preferred in a clinical trial without a DNA damaging agent. Although the extent of the effect was variable between cell lines and dependent on dose/schedule, both PD-L1 and class I MHC were frequently induced by ATRi in the absence of DNA damage. Given its inherent immunogenicity, cell-cycle checkpoint deficiencies (p53 and Rb inactivation and upregulation of Myc proteins), and high replication stress, MCC is an ideal tumor to explore the potential of ATR inhibition to overcome resistance to PD-1 pathway blockade. Based on these concepts and data, a clinical trial is currently being developed to help the >50% of patients whose advanced MCC tumors do not persistently respond to PD-1 blockade.

LB821

Human hair follicle dermal papilla as an *in vitro* model to study stress-induced hair growth arrest

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Stress induced hair loss, such as Telogen Effluvium, has been growing in recent years, due to an increased environmental and psychological pressure. Stress is responsible for activating the HPA axis within the human hair follicle. Studies have shown that isolated human hair follicles secrete substantial levels of cortisol when activated by corticotropin releasing hormone (CRH). This activity is linked to hair growth arrest and a shift from anagen to catagen. However, the extreme variability of isolated hair follicles in response to either CRH or cortisol limits the investigation of possible therapeutics. We have observed this variability between donors and between hair follicles (data not shown). With the goal to investigate potential therapeutics to address stress induced hair loss, we have tested human hair follicle dermal papilla cells (HFDPC), but differently than previous investigators, we used cortisol (hydrocortisone) as the stressor, and we fully characterized cell's genetic response. Cortisol (300 nM) induced a statistically significant, non-cytotoxic, proliferation arrest (HFDPC seeded in 96 well plates, cortisol added for 72 hours, then BrDU for 24 hours, -63% $p<0.01$ vs untreated control). The effect was reproducible in multiple experiments. CRH used as a control at different concentrations did not show any effect on HFDPC proliferation (data not shown). To further investigate the molecular mechanism associated with cortisol induced cell arrest, we ran a gene panel (qRT-PCR). After 24 h incubation with Cortisol (300 nM), we observed a strong upregulation of DKK1 (+598%) and PAI-1 (+218%) while inhibition of WNT10A (-60%), VEGFa (-54%), POMC (-61%) and SFRP5 (-62%). At 72 hours, DKK1 was still upregulated (+599%) and VEGFa still inhibited (-74%), but WNT10A (+104%) and POMC (+147%) expression level increased, while SFRP5 returned to baseline. Overall, the data correlated well with HFDPC proliferation arrest. In conclusion, we believe that cortisol as an inducer is a good choice for stress induced growth arrest models *in vitro*. Ingredients will be further tested to modulate this mechanism.

LB822

Nutraceuticals known to promote hair growth do not interfere with the inhibitory action of tamoxifen in breast cancer cells

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A common side effect of tamoxifen therapy in estrogen receptor (ER) positive breast cancer is hair loss/thinning. Some nutraceutical ingredients known to promote hair growth are avoided during breast cancer therapy for fear of phytoestrogenic activity. However, not all botanical ingredients have similarities to estrogens or they don't necessary activate proliferation inducer ERα, and in fact, no information exists as to the true interaction of these ingredients with tamoxifen. Kelp, Astaxanthin, Saw Palmetto, Tocotrienols, Maca, Horsetail, Resveratrol, Curcumin and Ashwagandha were assessed, alone or in combination, for MCF7, T47D and BT483 breast cancer cell line proliferation (Alamar Blue and BrdU, +/- 17β-estradiol 10nM, and/or tamoxifen 2-5μM) and for ERα/β expression (qRT-PCR, western blot and immunocytochemistry). 17β-estradiol significantly stimulated DNA synthesis in MCF-7 (17%, $p<0.0001$); TD47 (34%, $p<0.0001$); BT483 (101%, $p<0.0001$), which was inhibited by tamoxifen ($p<0.0001$). None of the nutraceuticals stimulated cell proliferation at low concentrations. Furthermore, either alone or in combination, none interfered with the tamoxifen inhibition of estrogen, some even induced further inhibition when combined with tamoxifen. Although ratios varied, ERα was more strongly expressed than ERβ in all cell lines at the mRNA, 39:1 (MCF7), 50:1 (T47D), 15:1 (BT483), and protein, 7:1 (MCF7), 5:1 (T47D), 11:1 (BT483) level. Incubation with combined nutraceuticals induced a shift in the ratio of ERα:ERβ, with increased ERβ and ERs localization at the nuclear periphery. Since ERβ triggers proliferation inhibition and antagonizes ERα in reproductive tissues, the finding can explain the synergy with tamoxifen. Overall, our in vitro data in three different breast cancer cell lines, demonstrate the ingredients safety on not interfering with tamoxifen anti-proliferative action. Further clinical studies are needed to fully demonstrate their safety during cancer therapy when used to limit hair loss/thinning.

LB823

Investigating the role of skin resident memory T-cells in a mouse model of DRESS

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Drug Rash Eosinophilia and Systemic Symptoms (DRESS) is a severe cutaneous adverse reaction with high morbidity and mortality. The pathogenesis of the disease is poorly understood, and research has been hampered by the lack of an available animal model. A recently developed mouse model of DRESS employed C57BL/6 mice transgenically expressing human HLA-B*57:01 and treated with abacavir intraperitoneally (i.p.) and topically to induce ear dermatitis at the site of topical treatment. We have modified this model to investigate T cell activation, migration and function in disease pathogenesis. Clinically we observed dermatitis and increased ear thickness in 100% of treated and contralateral untreated ears of HLA-B*57:01 mice administered abacavir i.p. and topically. Disease correlated with activation of $CD3^+CD8^+$ T cells in cervical lymph nodes and migration through blood with accumulation in both treated and untreated ears. Skin-infiltrating $CD8^+$ T cells expressed the skin homing molecule CLA as well as the activation phenotype CD44hi $CD62L^{lo}$ $CD69^+$ and produced the proinflammatory cytokines IFNg and TNFa and the cytotoxic molecule Granzyme B ex vivo. Disease resolved slowly in mice in parallel to human disease. Despite complete clinical and histologic resolution, a population of $CD8^+CD44^{hi}CD62L^{lo}CD69^+CLA^+$ T cells remained both in treated and untreated ears 90+ days later consistent with skin resident memory T cells. HLA-B*57:01 negative mice treated with abacavir and HLA-B*57:01 positive mice treated with vehicle served as controls and failed to develop inflammation indicating T cell responses were drug and HLA-B*57:01 specific. Taken together these data indicate that skin resident memory T cells develop as a result of drug/HLA specific DRESS-like dermatitis. We are currently testing whether these skin-resident memory T cells can mediate repeated episodes of DRESS-like dermatitis in response to drug, consistent with true drug allergy.

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