**ABSTRACTS**

**LB789**

Novel IFNγ-antagonist TAGX-0003 protected hair follicles from immune privilege collapse and reversed Alopecia Areata like phenotype in immunized mouse models. K Harada1, M Fehrholz2, A Piccini1, G Hilgers2, S Prasad1, T Schall1, P Staehr1 and J Fotie3. 1) monoclonal TACGx Biotechnologies Inc, Tokyo, Japan and 2) Monasterium Laboratory, Munster, Germany. Alopecia areata is a chronic, idiopathic inflammatory skin disorder of unknown etiology. Skin inflammation of the hair follicle (HF), central to the disease is IFNγ which accumulates in HF's leading to a Th1 autoimmune response, failure of the hair bulb immune privilege (IP), premature catagen induction followed by HF dystrophy. Currently, combination of sensual 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, a selective inhibition of IFNγ could provide a novel therapeutic approach with fewer side-effects. Here, we investigated whether TACGx's proprietary sIgA antagonist TAGX-0003, characterized by high affinity against IFNγ (Kd=1.3pM), protects HFs from experimentally induced IP collapse and rescues HFs from AA-like phenotype in the humanized mouse model for AA. Systemically administered (5mg/kg, SC) or IV (10mg/kg) significantly inhibited 100U/mI IFNγ-induced SATL phosphorylation in human HF organ culture. In the humanized mouse model of AA, intradermal injection of TAGX-0003 drastically reduced MCH 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 (12-300mM). Moreover, TAGX-0003 significantly reduced peri- and intra-folicular CD8 positive T cells around the bulbs. Further, melanogenesis was clearly observed by TAGX-0003 treatment. In all cases, subcutaneous administration on the aromatic ring, or a modified Skraup reaction, could be considered as an effective therapeutic approach to promote hair follicle stimulation and hair growth in young male patients with androgenic alopecia.

**LB790**

Toward new depigmenting agents through drug repurposing: Melanogenesis inhibition by para-aminophenols. F. Kalaparala1, KP Kim1 and T Germanas1. 1) Maryland Dermatology Associates, Annapolis, Maryland, United States, 2) Dermatology, University of Maryland School of Medicine, Baltimore, Maryland, United States, 3) Biochemistry and Molecular Biology, University of Maryland, Baltimore, United States. Melanogenesis is a complex process that is regulated by a large number of genes. However, the exact mechanisms that lead to the development of hyperpigmentation are still not fully understood. Therefore, the selective inhibition of IFNγ could provide a novel therapeutic approach with fewer side-effects. Here, we investigated whether TACGx's proprietary sIgA antagonist TAGX-0003, characterized by high affinity against IFNγ (Kd=1.3pM), protects HFs from experimentally induced IP collapse and rescues HFs from AA-like phenotype in the humanized mouse model for AA. Systemically administered (5mg/kg, SC) or IV (10mg/kg) significantly inhibited 100U/mI IFNγ-induced SATL phosphorylation in human HF organ culture. In the humanized mouse model of AA, intradermal injection of TAGX-0003 drastically reduced MCH 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 (12-300mM). Moreover, TAGX-0003 significantly reduced peri- and intra-folicular CD8 positive T cells around the bulbs. Further, melanogenesis was clearly observed by TAGX-0003 treatment. In all cases, subcutaneous administration on the aromatic ring, or a modified Skraup reaction, could be considered as an effective therapeutic approach to promote hair follicle stimulation and hair growth in young male patients with androgenic alopecia.

**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) J Scaccia1,2, C Jenne3, B Maling3, S Prasad1, T Schall1, P Staehr1 and I investigators1. 1) ChemoCentric, San Carlos, California, United States, 2) ChemoCentric, San Carlos, California, United States, 3) 3 Zeeland Univ. Hospital, Sore, Denmark, 4) Penn State Health, Hershey, Pennsylvania, United States and 5) Erasmus Med Center, Rotterdam, Netherlands. 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 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 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. S Ghajan1 and C Wamberi Department of Dermatology, Brown University Warren Alpert Medical School, Providence, Rhode Island, United States. 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 androgenetic alopecia. The drug tattooing technique is a novel 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 alopecia. Minoxidil and dutasteride delivery through the tattooing technique in the treatment of androgenetic alopecia among men. Ten men treated with at least 3 monthly sessions were evaluated by standardized overhead photography. Drug tattooing technology can be considered as an effective technique to promote hair follicle stimulation and hair growth in young male patients with androgenetic 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-1 receptor alpha 1 Inhibitor. L Lee1, JH Hajireen1, A Ward1 and C Firth1. 1) Asian Pharmaceuticals, Singapore, Singapore. ASLAN004 is a novel fully human IgG anti-IL-1 receptor alpha 1 (1L-1Ralpha1) monoclonal antibody, that blocks the signaling of IL-1α and IL-1β through the Type II receptor, hence is a potential target for treatment of dermatoses, asthma and diseases of related etiology. The study aim was to evaluate the safety, tolerability and pharmacokinetics of single ascending doses of ASLAN004 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 ASLAN004 intravenously as a single dose. In the second, 4 cohorts (75 to 150 mg/kg) were administered ASLAN004 subcutaneously, as a single dose. The primary outcome measure was safety and tolerability; secondary outcomes comprised of pharmacokinetic parameters. Pharmacodynamic outcomes were evaluated by dermatologist endpoint of HF occupency 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. The most common adverse events that led to study discontinuation and 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 ASLAN004. Clinical trials registration: NCT03127263.

**LB794**

Synthesis and biological evaluation of a small molecule library identifies novel anti-skin cancer agents. ST Boating1, T Roy1, RN Chanchev1, S Banang-Mbeum1, AL WALKER1, A KISS1, E TIMOVA1, J FOTIE2 and J Chanchev1. 1) College of Pharmacy, University of Louisville at Monroe, Monroe, Louisiana, United States, 2) Department of Dermatology/Cell Biology, The George Washington University, Washington, United States. Melanoma (MCA), squamous cell carcinoma (SCC), and 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 MCA (SCC-12 and A431) and MCA and SCC (SKMel-28 and A175) cell lines compared with nonmalignant HaCaT keratinocyte cell line as control. Potent hits with low-micromolar anticancer activities displayed IC50 values of 3.1±0.68, 5.0±0.80, S.±0.88, and 6.2±1.05 µg for SCC-12, A431, SKMel-28, and A175, respectively, versus minimal effects on HaCaT. Ciplatin, 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 were screened for their ability to bind to Lipinski and high biodegradable profile characteristics. In summary, the results highlight the promising anti-skin cancer characteristics of these low molecular weight compounds.