Penn Medicine Dermatology

Perelman School of Medicine University of Pennsylvania

SBDRC Scientific Symposium and Trainee Retreat

THURSDAY, MARCH 9, 2023

8:00 - 8:30am — Check-in & Poster Set-up, Breakfast in BRB 0253

8:30 - 8:45am — Welcome & Introduction

George Cotsarelis, MD, Department Chair & Associate Director, Penn SBDRC

Elizabeth Grice, PhD, Director, Penn SBDRC & Vice Chair of Basic Research

8:45 - 9:00am — Highlight on SBDRC Innovations

Donna Brennan-Crispi, PhD, Associate Director of Basic Research

P&F, New Member Highlight, and Trainee Talks

9:00 - 9:15am
- **Wenqin Luo, PhD** (Associate Professor of Neuroscience) SBDRC P&F awardee talk: *"Single-soma deep RNA-seq of human primary somatosensory neurons."*

9:15 - 9:30am
- **Nikhil Jiwrajka, MD** (Rheumatology Research Fellow, Anguera Lab) SBDRC mini-grant talk: *"Elucidating the role of dynamic X-chromosome inactivation maintenance in the pathogenesis of systemic sclerosis"*

9:30 - 9:45am
- **Juan Manuel Inclan Rico, PhD** (Postdoctoral Fellow, Herbert Lab) SBDRC mini-grant talk: *"MrgprA3 neurons selectively control myeloid-derived IL-33 to promote IL-17 dependent cutaneous immunity"*

9:45 - 10:00am
- **DeAnna Diaz** (2022 ECuRE pre-doctoral fellow, Werth Lab): *"Fibroblasts promote increased cannabinoid type 2 receptor expression and inflammatory cytokine production in dermatomyositis"*

10:00 - 10:15am
- **Aakriti Neopaney** (Clinical Research Coordinator, Gelfand Lab): *"Preliminary findings from the prevention of cardiovascular disease and mortality in patients with psoriasis or psoriatic arthritis (CP3) study"*

10:15 - 10:30am
- **Jeromy Gotschall** (4th year medical student & Health Disparities Fellow, Takeshita Lab): *"Minoritized patient race and ethnicity are associated with poorer experiences of access to dermatologic care in the United States"*

10:30 - 11:00am	Break and View Posters, BRB Lobby
11:00am - 12:00pm	Keynote Address **Suephy Chen, MD, MS -** Professor and Chair, Department of Dermatology, Duke University *"Health Services Research in Dermatology""*
12:00 - 12:30pm	Lunch Break, BRB 0253
12:30 - 1:30pm	Poster Session, BRB Lobby
	T32 Trainee Talks
1:40pm - 1:55pm	• **Heather Dingwall, PhD** (T32 Post-Doctoral Fellow, Kamberov Lab) *"A transient dermal niche and dual epidermal programs underlie sweat gland development"*
1:55pm -2:10pm	• **Nina Kuprasertkul** (T32 Pre-Doctoral Fellow, Capell Lab) *"Ferroptosis enhances epidermal cornification through transcriptional and metabolic reprogramming"*
2:10pm - 2:25pm	• **Ariana Majer** (T32 Pre-Doctoral Fellow, Ridky Lab) *"The role of the Y chromosome in melanoma pathobiology and the male sex bias"*
2:30-4:00pm	Trainee Professional Development Workshop BRB Gaulton Auditorium

Location: BRB II/III Gaulton Auditorium and Lobby (421 Curie Boulevard, Philadelphia, PA, 19104)

Please note that there will be a Zoom option for all talk sessions

SBDRC
Penn Skin Biology and Diseases Resource-based Center

Penn Dermatology
T32 Training Programs
Training clinicians and researchers for over 35 years

Penn Medicine
Dermatology

SBDRC Scientific Symposium and Trainee Retreat

Concurrent Sessions

2:30 - 4:00pm

SBDRC
Penn Skin Biology and Diseases Resource-based Center

Advisory Committee Meeting
BRB0253
By Invitation Only

Penn Dermatology
T32 Training Programs
Training clinicians and researchers for over 35 years

Trainee Retreat:
Professional Development Workshop
Gaulton Auditorium
Trainees and Staff only, no faculty
Moderated By Dr. Silvio Manfredo-Vieira

PASH
Penn Academy of Skin Heath

PASH Round-Table
10 BRB Conference Room
with current Penn undergrads

Reception

4:30– 6:00pm

14th Floor Lounge

Biomedical Research Building

SBDRC Scientific Symposium & Trainee Retreat

Oral Presentations & Poster Abstracts

March 9, 2023

Oral Presentations

Speaker	Title & Authors
Juan Inclan-Rico	**MRGPRA3 NEURONS SELECTIVELY CONTROL MYELOID-DERIVED IL-33 FOR IL-17 DEPENDENT CUTANEOUS IMMUNITY** Juan M. Inclan-Rico, Camila Napuri, Cailu Lin, Christopher F. Pastore, Li-Yin Hung, Annabel Ferguson, Danielle Reed, and De'Broski R. Herbert
DeAnna Diaz	**FIBROBLASTS PROMOTE INCREASED CANNABINOID TYPE 2 RECEPTOR EXPRESSION AND INFLAMMATORY CYTOKINE PRODUCTION IN DERMATOMYOSITIS** DeAnna Diaz, Muhammad M. Bashir, Rohan Dhiman, Avital Baniel, Julianne Kleitsch, Rachita Pandya, Meena Sharma, Thomas Vazquez, Ming-Lin Liu, Mariko Ogawa-Momohara, Victoria P. Werth
Aakriti Neopaney	**PRELIMINARY FINDINGS FROM THE PREVENTION OF CARDIOVASCULAR DISEASE AND MORTALITY IN PATIENTS WITH PSORIASIS OR PSORIATIC ARTHRITIS (CP3) STUDY** Aakriti Neopaney, Sonia Wang, Daniel Shin, Robert Fitzsimmons, Suzette Baez, April Armstrong, John Barbieri, Rinad Beidas, Michael Garshick, Nehal Mehta, Alexis Ogdie, Joel Gelfand
Jeromy Gotschall	**MINORITIZED PATIENT RACE AND ETHNICITY ARE ASSOCIATED WITH POORER EXPERIENCES OF ACCESS TO DERMATOLOGIC CARE IN THE UNITED STATES** Jeromy W. Gotschall, Robert Fitzsimmons, Daniel B. Shin, Junko Takeshita
Heather Dingwall	**A TRANSIENT DERMAL NICHE AND DUAL EPIDERMAL PROGRAMS UNDERLIE SWEAT GLAND DEVELOPMENT** Heather L. Dingwall, Reiko R. Tomizawa, Adam Aharoni, Peng Hu, Qi Qiu, Blerina Kokalari, Serenity M. Martinez, Daniel Aldea, Meryl Mendoza, Hao Wu, Yana G. Kamberov
Nina Kuprasertkul	**FERROPTOSIS ENHANCES EPIDERMAL CORNIFICATION THROUGH TRANSCRIPTIONAL AND METABOLIC REPROGRAMMING** Nina Kuprasertkul, Claudia Magahis, Shaun Egolf, Cory L. Simpson, Clementina Mesaros, Kathryn E. Wellen, Brian C. Capell
Ariana Majer	**THE ROLE OF THE Y CHROMOSOME IN MELANOMA PATHOBIOLOGY AND THE MALE SEX BIAS** Ariana Majer, Paul Zhang, Todd Ridky

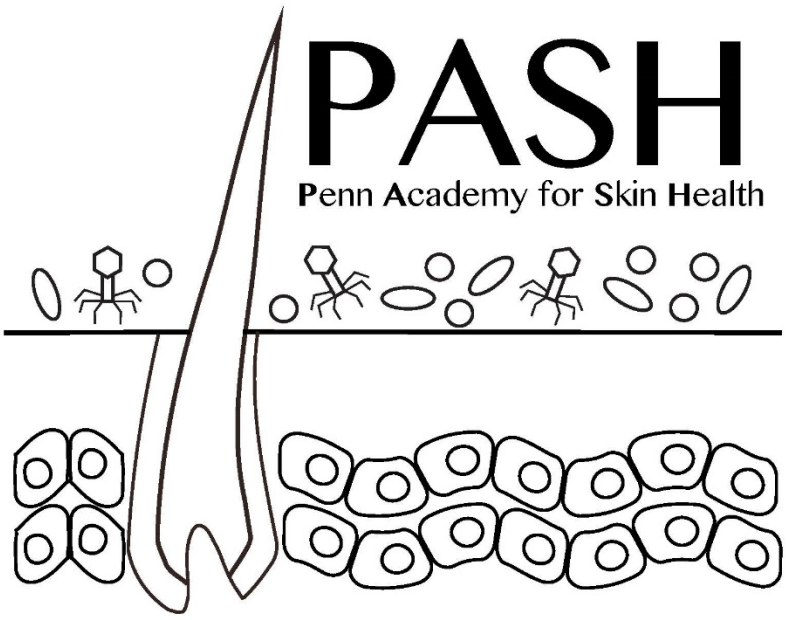
Poster Presentations

Poster Number	Title & Authors
1	**ECTODYSPLASIN SIGNALING VIA XEDAR IS REQUIRED FOR MAMMARY GLAND MORPHOGENESIS** Abigail R. Wark, Daniel Aldea, Reiko R. Tomizawa, Blerina Kokalari, Bailey Warder, Yana G. Kamberov
2	**PROTEIN CARGO OF PLASMA-DERIVED EXTRACELLULAR VESICLES DRIVES INNATE MEDIATED INFLAMMATION IN DERMATOMYOSITIS** Avital Baniel, Mariko Momohara-Ogawa, Rachita Pandya, Julianne Kleitsch, Felix Chin, Ming-Lin Liu, Victoria P. Werth
3	**A CROSS-SECTIONAL GOOGLE TRENDS ANALYSIS OF ONLINE SEARCHES AMONG US SPANISH SPEAKERS WITH DERMATOLOGIC CONCERNS** Tatiana M. Barrera, BA, Stephanie Marín, BS, Omar Venegas, BS, Hollie St. Claire, BS, David Lee, BS, David J. Margolis, MD, PhD, Susan Taylor, MD
4	**ASSOCIATION OF CHRONIC GRAFT-VERSUS-HOST DISEASE CLINICAL SUBTYPE WITH HEALTH-RELATED QUALITY OF LIFE AND SYMPTOM BURDEN: A COHORT STUDY** Emily Baumrin MD, Stephanie J Lee MD, MPH, Nandita Mitra PhD, Alison W Loren MD, MSCE, Joel M Gelfand MD, MSCE
5	**FITZPATRICK SKIN TYPE GROUP 1/2 BASELINE CHARACTERISTICS FOR THE LITE STUDY** Brooke E. Bishop, Suzette Baez, Daniel B. Shin, Robert Fitzpatrick, Joel M. Gelfand
6	**MERGED AND HARMONIZED IMAGING MASS CYTOMETRY DATASETS REVEAL NEW FINDINGS FROM LENABASUM-TREATED DERMATOMYOSITIS SKIN FROM PHASE 3 DETERMINE TRIAL** Chin F, Vazquez T, Chou R, Werth VP

7	**AGE-DEPENDENT UPREGULATION OF CHEMOKINE CCL11 IN SKIN FIBROBLASTS IS ESSENTIAL FOR HOMEOSTATIC SUBCUTANEOUS ADIPOGENESIS** Rahul Debnath, Zhaoxu Chen, Kang I Ko
8	**LENABASUM AND ITS INTERACTION WITH DERMATOMYOSITIS LEUKOCYTE SIGNALING PATHWAYS** Rohan Dhiman, Nilesh Kodali, DeAnna Diaz, Julianne Klietsch, Rachita Pandaya, Ming-Lin Liu, Meena Sharma, Muhammad Bashir, Avital Baniel, Victoria Werth
9	**HUMANS ARE A DOG'S BEST FRIEND: ENHANCING CANINE CART WITH HUMAN CAR DOMAINS** Emma Goodman, Roderick S. O'Connor, Nicola J. Mason, Aimee S. Payne
10	**MICROBIAL AND IMMUNE ENVIRONMENTAL STATES ARE TRANSMITTED VIA TRANSGENERATIONAL EPIGENETIC INHERITANCE** Jordan Harris, Natalie Trigg, Bruktawit Goshu, Colin Conine, Elizabeth Grice, Taku Kambayashi
11	**TUMOR AND TME COMPARTMENT-SPECIFIC SPATIAL TRANSCRIPTOMICS IN SCCIS** Matthew Hedberg, Stephen Prouty, Wan-Jung Chang, Joseph Fraietta and John Seykora
12	**MRGPRA3 NEURONS SELECTIVELY CONTROL MYELOID-DERIVED IL-33 FOR IL-17 DEPENDENT CUTANEOUS IMMUNITY** Juan M. Inclan-Rico, Camila Napuri, Cailu Lin, Christopher F. Pastore, Li-Yin Hung, Annabel Ferguson, Danielle Reed, and De'Broski R. Herbert
13	**A CASE SERIES OF CENTRAL CENTRIFUGAL CICATRICIAL ALOPECIA IN MEN** Tiaranesha Jackson, MPH, Yacine Sow, BA, Susan Taylor, MD, Temitayo Ogunleye
14	**NONCLASSICAL MONOCYTES SHOW HEART-HOMING PROFILE IN DRESS WITH CARDIAC INVOLVEMENT** Anna Kersh, MD, PhD, Satish Sati, PhD, Parker Jones, BS, Christina Murphy, BS, Amy Forrestell, MD, Thomas Leung, MD, PhD
15	**CHANGE IN DISEASE ACTIVITY NEEDED FOR MEANINGFUL CHANGE IN CUTANEOUS LUPUS BY PATIENT CHARACTERISTIC** Julianne Kleitsch, Rachita Pandya, Srita Chakka, Daisy Yan, Darosa Lim, DeAnna Diaz, Victoria P. Werth

16	**IMPAIRMENT OF H3K36 METHYLATION PROVOKES CELLULAR PLASTICITY TO DRIVE ABERRANT GLANDULAR FORMATION AND SQUAMOUS CARCINOGENESIS** Eun Kyung Ko, Amy Anderson, Jonathan Zou, Sijia Huang, Sohyun Cho, Faizan Alawi, Stephen Prouty, Vivian Lee, Kai Ge, John T. Seykora, Brian C. Capell
17	**IN VIVO FIELD CANCERIZATION AFTER LOSS OF NOTCH SIGNALING IN EPIDERMAL STEM CELLS** Paola Kuri, Sixia Huang, Lana Salloum, Hyunjin Bae, Maxwell Marshall, Stephen Prouty, Brian C. Capell, John Seykora & Panteleimon Rompolas
18	**FATE INDUCTION IN CD8 CHIMERIC ANTIGEN RECEPTOR T CELLS THROUGH ASYMMETRIC CELL DIVISION** Christoph T. Ellebrecht, Casey S. Lee, Andre R. Kelly, Corbett Berry, Sangwook Oh, Roddy S. O'Connor, Aimee S. Payne
19	**THE ROLE OF THE Y CHROMOSOME IN MELANOMA PATHOBIOLOGY AND THE MALE SEX BIAS** Ariana Majer, Paul Zhang, Todd Ridky
20	**EPIDERMAL EPITRANSCRIPTOMICS: METTL3 DEPENDENT M^6A REGULATES CHROMATIN MODIFYING ENZYMES** Alexandra M. Maldonado López, Sijia Huang, Gina Pacella, EunKyung Ko, Hui Shen, Julian Stoute, Amy Anderson, Fange (Kathy) Liu, Brian C. Capell
21	**BARRIERS TO CARE AND PREFERENCES FOR CARE PROVIDERS AMONG BLACK CHILDREN WITH ATOPIC DERMATITIS** Veda Nagubandi, Laura Bou Delgado, Andrea Bilger, Junko Takeshita
22	**MECHANOSENSITIVE PATHWAYS IN THE OCCLUDED WOUND-INDUCED HAIR NEOGENESIS MODEL OF REGENERATION** Allen S.W. Oak, Ying Zheng, Arben Nace, Ruifeng Yang, Jen-Chih Hsieh, Anisa Ray, and George Cotsarelis

23	**THE ROLE OF HISTONE DEMETHYLASE UTX IN EPIDERMAL HOMEOSTASIS** Gina N. Pacella, Carina A. D'souza, Alexandra Maldonado López, Lydia Bao, Amy Anderson, Brian C. Capell
24	**EVALUATION OF SKIN-SPECIFIC AND COMPOSITE OUTCOMES FOR MEASURING DERMATOMYOSITIS SKIN IMPROVEMENT IN THE LENABASUM PHASE 3 TRIAL** Rachita Pandya, BA, Julianne Kleitsch, BA, Joshua Dan, BA, Darosa Lim, MD, Barbara White, MD, Victoria P. Werth, MD
25	**SOX9 IS ESSENTIAL FOR CORNEAL EPITHELIAL MAINTENANCE** Gabriella Rice, Lisa Ohman, Pantelis Rompolas
26	**NOVEL FORMULATION FOR DELIVERY OF MINOXIDIL TO TREAT HAIR LOSS DISORDERS** Spencer Tuohy, Leo L. Wang, MD, PhD, George Cotsarelis, MD
27	**A NOVEL ASSESSMENT OF CARDIOVASCULAR HEALTH IN PEOPLE WITH PSORIASIS IN THE US: A CROSS-SECTIONAL STUDY** Sonia Wang, Daniel Shin[1], Tina Bhutani, Joel Gelfand
28	**MINING THE PIG SKIN MICROBIOME FOR ANTIMICROBIAL PRODUCTS** Monica Wei, Jasmine Walsh, Laurice Flowers, Simon Knight, Elizabeth Grice
29	**AN UNDERSTUDIED WOUND COMMENSAL BACTERIUM ACCELERATES DIABETIC WOUND HEALING BY BALANCING MATRIX METALLOPROTEINASE OVEREXPRESSION** Ellen White, Aayushi Uberoi, Jordan Ort, and Elizabeth Grice
30	**THE CURRENT STATE OF MANAGEMENT OF ATHEROSCLEROTIC CARDIOVASCULAR DISEASE RISK FACTORS IN DERMATOMYOSITIS (DM) PATIENTS** Megan Zhao, BA, Kevin Jon Williams, MD, Rui Feng, PhD, Victoria P Werth, MD



The Penn Academy of Skin Health (PASH) is a science outreach program targeting Philadelphia high school students. Sponsored by the SBDRC, PASH is currently in its 7th year. This year our Saturday Academy is running each Saturday in March, and we are excited to work with twelve aspiring skin biologists. All students who successfully complete the Saturday program are invited to apply for summer internships through the Program of Outreach, Education & Research (OER).

Today we are thrilled to welcome three former PASH students and 2022 OER interns back to Penn to present their summer research here at the 2023 SBDRC Scientific Symposium and Trainee Retreat. We hope you can take a few moments to meet with these aspiring young scientists to discuss their research.

PASH Poster Presentations

Name	School	Project Title	Lab PI	Direct Mentor
Jaylin Carter	CAPA High School	The Puzzle Pieces of PCR	Elizabeth Grice, PhD	Ellen White
Siani (Nabi) Elliott	Carver High School of Engineering and Science	Stem Cells and Their Use in Diabetes Research	Juan Alvarez, PhD	Juan Alvarez, PhD
Tszching Zhong	Northeast High School	Summer Intern in Dr. Seale's Lab	Patrick Seale, PhD	Rachel Stine, PhD

REDCap is a web application that can be used to build and manage online surveys and databases that doesn't require coding experience. While designed for clinical research, the versatility of REDCap allows it to be adopted for a variety of uses. This year the SBDRC is highlighting the substantial efforts of our REDCap team to streamline administrative efficiency and operations across the SBDRC and Departmental training program. The REDCap group has worked diligently and creatively to implement many new REDCap assignments across the department, and they will be presenting posters on three of these ground-breaking projects.

REDCap Poster Presentations

Team Member	Title & Authors
Nina Alfaro	NON-CONVENTIONAL USAGE OF REDCAP LEADS TO STREAMLINED MEMBERSHIP WORKFLOWS Maria Katerina C. Alfaro, MS; Vincent Zhao, Caitlin Cavarocchi, Donna Brennan-Crispi, PhD; Elizabeth Grice, PhD
Caitlin Cavarocchi	NOVEL USE OF REDCAP TO CAPTURE AND MANAGE T32 PROGRAM DATA Caitlin M. Cavarocchi, Vincent Zhao, Maria Katerina Alfaro, Donna Brennan-Crispi
Vincent Zhao	UTILIZING REDCAP TO IMPROVE OPERATIONAL WORKFLOW AND ORDER TRACKING FOR PENN SBDRC STAR SERVICES Vincent Zhao, Maria Katerina Alfaro, Caitlin Cavarocchi, Donna Brennan-Crispi

Oral Presentation

MRGPRA3 NEURONS SELECTIVELY CONTROL MYELOID-DERIVED IL-33 FOR IL-17 DEPENDENT CUTANEOUS IMMUNITY

Juan M. Inclan-Rico[1], Camila Napuri[1], Cailu Lin[2], Christopher F. Pastore[1], Li-Yin Hung[1], Annabel Ferguson[1], Danielle Reed[2], and De'Broski R. Herbert[1].

[1]Department of Pathobiology, School of Veterinary Medicine, University of Pennsylvania, Philadelphia, PA, USA
[2]Monell Chemical Senses Center, Philadelphia, PA, USA

Skin architecture contains diverse cell lineages that orchestrate organismal homeostasis, metabolic regulation, and host defense. However, the critical cytokine networks responsible for regulating skin biology under homeostasis and disease remain unclear. Interleukin 33 (IL-33) is a key regulatory cytokine thought primarily released by damaged epithelial, endothelial, and stromal cells, but it has been increasingly recognized that hematopoietic cells also release biologically relevant amounts IL-33. This study reveals that an itch-specific population of skin sensory neurons expressing MrgprA3 (A3) exert selective control over IL-33 production in myeloid antigen presenting cell (APC) subsets to initiate cutaneous inflammation. Data show that optogenetic activation of A3 neurons increases IL-17-expressing γδ T cell responses, drives epidermal thickening, and enhances resistance to the human helminth pathogen *Schistosoma mansoni* coincident with selective downmodulation of IL-33 production from myeloid cells, but not fibroblasts. This selective inhibition of IL-33 following neuron activation increases myeloid secretion of pro-inflammatory cytokines (e.g. IL-1β, IL-6, TNFα). Strikingly, mice genetically deficient for IL-33 specifically in CD11c+ cells spontaneously develop IL-23/IL-17-driven epidermal thickening, keratinocyte hyperplasia and resistance to percutaneous infection with *S. mansoni* relative to littermate controls. Single-cell RNA-seq, ATAC-seq, and immunoprofiling studies of antigen presenting cells from naïve mouse skin reveals that myeloid cell-intrinsic IL-33 shapes chromatin conformation that functionally restrains expression of IL-17-inducing cytokines (e.g. IL-1β, IL-6, and IL-23). Taken together, we propose a previously unappreciated neuroimmune circuit wherein itch-specific neurons can selectively suppress constitutively expressed IL-33 in tissue resident myeloid cells to rapidly unleash pro-inflammatory cytokine release for host immunity and keratinocyte turnover.

Oral Presentation

FIBROBLASTS PROMOTE INCREASED CANNABINOID TYPE 2 RECEPTOR EXPRESSION AND INFLAMMATORY CYTOKINE PRODUCTION IN DERMATOMYOSITIS

DeAnna Diaz[1,2]; Muhammad M. Bashir[1,2]; Rohan Dhiman[1,2]; Avital Baniel [1,2]; Julianne Kleitsch[1,2]; Rachita Pandya[1,2]; Meena Sharma[1,2]; Thomas Vazquez[1,2]; Ming-Lin Liu[1,2]; Mariko Ogawa-Momohara[1,2]; Victoria P. Werth[1,2]

[1] Corporal Michael J. Crescenz VAMC, Philadelphia, PA
[2] Dermatology, U Penn, Philadelphia, PA

Dermatomyositis (DM) is a chronic, systemic autoimmune disease affecting the skin, muscle, and lungs. The activation of CB2R has been shown to reduce several, key proinflammatory cytokines implicated in DM. Our group has previously shown that CB2R expression was significantly increased in in DM skin compared to blood, possibly due to increased production of local inflammatory cytokines. CB2R stimulation alleviates inflammatory response by down-regulating the expression of TNF-α, IL31, IFN-γ, and type I interferon expression in the early stage of inflammation and reducing the infiltrated inflammatory cells. Having more CB2R on inflammatory cells will lead to enhanced effects of a CB2R agonist. We hypothesized that fibroblasts (FBs) in the skin may play an important role in upregulating CB2R on inflammatory cells within the skin. Therefore, we sought to examine the role of FBs in CB2R activation. DM PBMCs, which typically have minimal CB2R expression, were cultured with human FBs. We then utilized multiplexed flow cytometry to further analyze the expression of CB2R and inflammatory cytokines on 12 cell lineages. When comparing PBMCs cultured with and without FBs, cells cultured with FBs had a significant increase in CB2R expression in CD4+ T cells ($p<0.0001$), monocyte-derived dendritic cells (moDCs) ($p<0.0001$), classical Monocytes (CM) ($p<0.001$), and M1 Macrophages ($p <0.0001$). There was also a significant increase in inflammatory cells cytokines such as IFNβ, IFNγ, TNFα, IL31 and IL4 in CD4+ T cells, moDCs, CD11c+ myeloid dendritic cells, CM and CD68+ macrophages. These data suggest FBs play a role in increasing CB2R on inflammatory cells, as well as stimulate production of cytokines in DM skin. This suggests that drugs that activate CB2R, leading to downregulation of proinflammatory cytokines, may have enhanced efficacy in the skin due to FB-induced local upregulation of CB2R on inflammatory cells in the skin.

Oral Presentation

PRELIMINARY FINDINGS FROM THE PREVENTION OF CARDIOVASCULAR DISEASE AND MORTALITY IN PATIENTS WITH PSORIASIS OR PSORIATIC ARTHRITIS (CP3) STUDY

Aakriti Neopaney[1], Sonia Wang[1], Daniel Shin[1], Robert Fitzsimmons[1], Suzette Baez[1], April Armstrong[2], John Barbieri[3], Rinad Beidas[4], Michael Garshick[5], Nehal Mehta[6], Alexis Ogdie[1], Joel Gelfand[1]

[1]University of Pennsylvania, Philadelphia, PA, US
[2]University of Southern California, Los Angeles, CA, US
[3]Harvard Medical School, Boston, MA, US
[4]Northwestern University, Chicago, IL, US
[5]NYU Langone, New York, NY, US
[6]George Washington University, Washington DC, US

Psoriasis patients have an increased risk of cardiovascular disease (CVD) yet traditional CVD risk factors are under-identified and undertreated in this at-risk population, resulting in preventable morbidity and mortality. The Prevention of Cardiovascular Disease and Mortality in Patients with Psoriasis or Psoriatic Arthritis (CP3) study aims to narrow this evidence-to-practice gap through a novel, centralized care coordination (CC) model. In this model, a patient with psoriasis between the ages of 40 to 75 undergoes routine blood draw for lipids and takes up to 12 blood pressure (BP) measurements at home. A virtual care coordinator at the National Psoriasis Foundation uses the lab values and the average BP recording to calculate CVD risk based on the 2018 American Heart Association/American College of Cardiology (AHA/ACC) formula. Using AHA/ACC guidelines, the care coordinator then provides the patient with a guideline-based plan for lifestyle changes and medications that they are encouraged to discuss with a primary care provider. In a pilot of 85 participants from 11 clinicians at 4 sites, 43 (51%) were dermatology patients and 42 (49%) were rheumatology patients, 46 (54%) were female, 78 (92%) were white, 41 (48%) had a history of smoking, 25 (29%) had a history of depression, and 67 (79%) were on a biologic medication. The mean dermatology life quality index (DLQI), physician global assessment (PGA), and body surface area (BSA) were 3.5, 0.96, and 1.22%, respectively, and the mean psoriatic arthritis impact of disease (PSAID) score was 3.7, consistent with well-controlled psoriatic disease. In a questionnaire, more than 85% indicated that the CC model is acceptable, appropriate, or feasible. Out of 85 patients, 78 (92%) got lipid labs drawn, 71 (84%) completed at-home BP recordings, and 74 (87%) met with the care coordinator. 21 (25%) had undiagnosed, elevated CVD risk (i.e., risk ≥ 5%), and statins and BP medications were recommended for 21 (25%) and 28 (33%) patients, respectively. Overall, data from the CP3 pilot study demonstrates the feasibility and acceptability of a CC model in lowering CVD risk in psoriatic patients with a high prevalence of undertreated CVD risk factors.

Oral Presentation

MINORITIZED PATIENT RACE AND ETHNICITY ARE ASSOCIATED WITH POORER EXPERIENCES OF ACCESS TO DERMATOLOGIC CARE IN THE UNITED STATES

Jeromy W. Gotschall[1], Robert Fitzsimmons[1], Daniel B. Shin[1], Junko Takeshita[1,2]

[1] Department of Dermatology, Perelman School of Medicine at the University of Pennsylvania, Philadelphia, PA
[2] Department of Biostatistics, Epidemiology, and Informatics, Perelman School of Medicine at the University of Pennsylvania, Philadelphia, PA

The Press Ganey (PG) Outpatient Medical Practice Survey measures patients' experiences of health care, including access, in the U.S. Identifying differences in experiences of access to dermatologic care by patient race, ethnicity, and other sociodemographic characteristics is an important initial step in ensuring equitable healthcare delivery. We performed a cross-sectional analysis of PG surveys for adult outpatient dermatology visits within the University of Pennsylvania Health System from 2014-2017. The primary outcome was the maximum score for ability to schedule a timely appointment; secondary outcomes similarly included the remaining PG Access domain questions. Multivariable logistic regression was used to evaluate associations between patient sociodemographic factors and each outcome. The study included the first survey completed for 19,978 unique patients (mean [SD] age, 55.66 [16.36] years; 61.42% female patients [n=12,271]; 87.22% White patients [n=17,425]). Compared with White patients, Black (OR 0.81; 95% CI 0.71-0.92) and Asian (OR 0.62; 95% CI 0.58-0.66) patients had lower odds of reporting the maximum score for their ability to schedule a timely appointment. Interestingly, lower education level was associated with higher odds of reporting the maximum score for the primary outcome (up to high school or equivalent vs. more than 4-year college degree: OR 1.41, 95% CI 1.27-1.57); the same was true for Medicaid vs. commercial insurance (OR 1.29, 95% CI 1.12-1.51), suggesting differences in expectations of access to care by socioeconomic status. Associations with secondary outcomes were notable for the following: Hispanic patients (OR 0.79, 95% CI 0.63-1.00) and those whose primary language was not English (OR 0.67, 95% CI 0.46-0.99) had lower odds of reporting the maximum score for staff courtesy, compared to White and English-speaking patients, respectively, suggesting differences in experiences of communication and respect. Our findings underscore the need to improve experiences of access to dermatologic care among minoritized groups.

Oral Presentation

A TRANSIENT DERMAL NICHE AND DUAL EPIDERMAL PROGRAMS UNDERLIE SWEAT GLAND DEVELOPMENT

Heather L. Dingwall[1], Reiko R. Tomizawa[1], Adam Aharoni[1], Peng Hu[1,2], Qi Qiu[1], Blerina Kokalari[1], Serenity M. Martinez[1], Daniel Aldea[1], Meryl Mendoza[1], Hao Wu[1], Yana G. Kamberov[1]

[1]Dept. of Genetics, Perelman School of Medicine, Philadelphia, Pennsylvania, 19104
[2]Present address: College Fisheries and Life Sciences, Shanghai Ocean University, Shanghai, China

Eccrine glands are mammalian skin appendages indispensable for human thermoregulation. Like all skin-derived appendages, eccrine glands form from multipotent progenitors in the basal skin epidermis. How epidermal progenitors are progressively specialized to form eccrine glands and the extent to which extrinsic factors are required for this process are major outstanding questions. The absence of this information has blocked therapeutic efforts to regenerate eccrine glands for reconstructive skin repair. Herein, we applied single nucleus transcriptomics to compare the expression content of wildtype, eccrine-forming mouse skin to that of mice harboring a skin-specific disruption of *Engrailed 1 (En1)*, a transcription factor that promotes the formation of eccrine glands in both humans and mice. Using this targeted approach, we identify two, distinct epidermal transcriptomes in developing eccrine glands: one shared with hair follicles, and one that is *En1*-dependent and eccrine-specific. As development proceeds, we find that eccrine epidermal progenitors shift to favor the specialized transcriptome. We demonstrate that this process is dependent on the induction of a transient dermal niche that forms around each developing gland in humans and mice. Our study defines the major transcriptional transitions underlying eccrine identity in the epidermis and identifies the first dermal niche required for eccrine developmental progression. By uncovering these defining components of the eccrine developmental program, our findings set the stage for directed efforts to regenerate eccrine glands for comprehensive skin repair.

Oral Presentation

FERROPTOSIS ENHANCES EPIDERMAL CORNIFICATION THROUGH TRANSCRIPTIONAL AND METABOLIC REPROGRAMMING

Nina Kuprasertkul[1,2], Claudia Magahis[1], Shaun Egolf[1,2], Cory L. Simpson[3], Clementina Mesaros[4], Kathryn E. Wellen[2,5], Brian C. Capell[1,2]

[1]Department of Dermatology, University of Pennsylvania, Philadelphia, PA, United States
[2]Penn Epigenetics Institute, University of Pennsylvania, Philadelphia, PA, United States
[3]Deparment of Dermatology, University of Washington, Seattle, WA, United States
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Epidermal cornification is a unique process that requires complex changes in lipid metabolism and a non-apoptotic cell death to form the skin barrier. Dysregulation of cornification underlies the pathogenesis of numerous common skin diseases, ranging from psoriasis to cutaneous squamous cell carcinoma (cSCC), highlighting the need to understand the triggers for terminal cell death. Ferroptosis is a recently described form of regulated cell death gaining interest for its involvement in differentiation and carcinogenesis. It is defined by iron-dependent lethal lipid peroxide accumulation and imbalance of cellular redox homeostasis. However, the role ferroptosis plays in promoting epidermal differentiation, cornification, and the potential mitigation of cSCC remains elusive. Our lab has demonstrated that loss of a major tumor suppressor, MLL4, impairs epidermal differentiation and promotes neoplasia due to impaired ferroptotic signaling (Egolf et al., *Sci. Adv.* 2021). Here, we present further evidence that ferroptosis promotes cornification to govern epidermal cell fate. Utilizing RNA-sequencing and LC-MS lipidomics, we demonstrate that triggering ferroptosis in primary human keratinocytes upregulates endoplasmic reticulum (ER) stress signaling, cornified layer genes, and differentiation-associated ceramides. Further, inhibiting ferroptosis leads to disrupted cornification and significantly diminished expression of cornification genes, emphasizing a promising role for ferroptosis in enhancing cornification. We also demonstrate preliminary efficacy for ferroptosis inducers to selectively target cSCC cell lines. Overall, these studies provide insight into metabolic mechanisms governing epidermal cornification as well as open therapeutic avenues for regulating ferroptosis in cSCC.

Oral Presentation

THE ROLE OF THE Y CHROMOSOME IN MELANOMA PATHOBIOLOGY AND THE MALE SEX BIAS

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Melanoma incidence and mortality are significantly higher in males than females. These sex differences are independent of melanoma stage and sex-related differences in environmental exposures and lifestyle behaviors, suggesting the melanoma sex bias is primarily driven by biological mechanisms that differ between the sexes. Interestingly, the Y chromosome is lost with age in peripheral blood cells, and this loss of the Y chromosome (LOY) in blood is associated with a four-fold increased risk of cancer and a three-fold decrease in cancer survival. Despite these associations between LOY and cancer, the functional significance of LOY is largely unexplored. Emerging data suggest the Y chromosome is lost in some solid tumors, but whether the Y chromosome is lost in melanoma was unknown. We found that the Y chromosome is lost in melanoma, with the frequency of both partial and complete loss increasing with melanoma stage and complete LOY occurring more frequently in metastases than primary lesions. The Y chromosome has 78 protein-coding genes, ten of which are ubiquitously expressed in all tissues, including melanocytes. Six of these genes are dysregulated in cancer, making them attractive candidates for genes that may mediate the pro-tumorigenic effects of LOY in melanoma. We therefore seek to determine whether any of these ten genes alter melanoma proliferation, malignancy, or tumorigenicity and thereby contribute to the melanoma sex bias.

REDCap Poster

NON-CONVENTIONAL USAGE OF REDCAP LEADS TO STREAMLINED MEMBERSHIP WORKFLOWS

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Research Electronic Data CAPture (REDCap) is a secure, web-based application primarily known for creating simple surveys and standalone databases within the context of research. Its user-friendly interface allows for the creation of projects, whilst negating the need for a formal programming background. Though, the application is flexible such that certain programming languages may be incorporated at a limited capacity to permit for increased functionality within and across projects. There were two primary objectives for this project: 1) To provide a medium for current and prospective SBDRC members alike to submit their current application materials and 2) To facilitate and standardize access to the SBDRC website. From the new member standpoint, the updated membership workflow through REDCap is a single-step process from application submission to website access. The internal process is a two-step process; however, it maximizes the number of completed applications and harmonizes the approved members and website access close to a 1:1 ratio. For internal housekeeping, we have leveraged REDCap to streamline membership workflows; we have created a centralized, up-to-date data repository for all SBDRC members which manages membership approvals, website access, and email contact list. This project is more readily able to track membership trends and members themselves, which is useful for reporting purposes within grant applications as well as keeping the SBDRC community connected as a whole. A potential future direction for this project is to incorporate its active member data as embedded visuals within the website.

REDCap Poster

NOVEL USE OF REDCAP TO CAPTURE AND MANAGE T32 PROGRAM DATA

Caitlin M. Cavarocchi[1], Vincent Zhao[1], Maria Katerina Alfaro [1], Donna Brennan-Crispi[1]

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Research Data Capture application (REDCap) is routinely used by academic institutions to organize, sort, and analyze data, typically for clinical research. However, with some innovative thinking, the versatility of REDCap allows its capabilities to be adapted for other uses. There is a growing need within the department to find concrete solutions to streamline departmental operations. For the T32 Training Program, it is critical to maintain accurate, longitudinal records of T32-appointed and associated fellows. A user-friendly interface is also essential to maximize self-reporting. We proposed that REDCap was well-suited for this purpose, and created multi-instrument project to collect and house the required data. Briefly, we create a record for each appointee from their application data (collected in another REDCap project) with instruments for all RPPRs and subsequent annual surveys that can be distributed using the REDCap automated invitations tool at varying timelines of their career. We also utilized repeatable instrument tool to collect information on multiple grants, publications, and presentations from each trainee in the program for the duration of their appointment and after. Thus, all the data/information for each trainee is housed in one project for easy reporting on detailed or broad information depending on the specific need. The implementation of this project has improved the workflow for the Grants Team within the department and saves time and effort by combining all required information in one area. In the future, we establish project dashboards for automated reporting and incorporate data collection from grant associated fellows for NIH reporting purposes. In summary, we have utilized REDCap in nonconventional ways, and by redefining common tools, have created a user-friendly interface and accurate record of current and past trainees in the Penn Derm T32 program.

REDCap Poster

UTILIZING REDCAP TO IMPROVE OPERATIONAL WORKFLOW AND ORDER TRACKING FOR PENN SBDRC STAR SERVICES

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Research Data Capture application (REDCap) is a web application widely used within the academic research community for collecting and housing data for clinical and/or research studies. REDCap is a user-friendly tool for researchers, allowing them to create and manage surveys, use real time data entry validation, and generate customizable reports from their databases without the use of programming. Leveraging this flexibility, we sought to improve the ordering, reporting, and invoicing processes for the SBDRC Resource Cores. Piloting this project with the Skin Translational Research (STaR) Core, we have effectively implemented a new ordering system with service modulization and improved internal tracking for reporting and invoicing. Service modulization was implemented by creating a unique survey for each core service and directs the requestor to their specific service using the survey queue feature in REDCap. The data from the order survey and core pricing are used to calculate estimated order totals which are summarized for the requestor. The information from these summaries are used to populate a separate review instrument that the service provider uses to note any changes to the request. Once the review is complete, that information is used to generate an order invoice form for the finance team. This process workflow of tracking orders as requested along with the modifications from service providers greatly enhances reporting and invoicing capabilities as all information is housed in the same database. Future directions include establishing functional project dashboards within the REDCap project that allow for real time data tracking and reporting for both NIH and financial reports. In summary, we harnessed REDCap's flexible functionality to improve the operational workflow of the STaR Core Services. As REDCap continues to improve, there will be many more innovative ways to utilize it for improving SBDRC operations.

Poster #1

ECTODYSPLASIN SIGNALING VIA XEDAR IS REQUIRED FOR MAMMARY GLAND MORPHOGENESIS

Abigail R. Wark[1], Daniel Aldea[2#], Reiko R. Tomizawa[1#], Blerina Kokalari[2], Bailey Warder[2], Yana G. Kamberov[2,3*]

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The Ectodysplasin A2 receptor (XEDAR), is a member of the tumor necrosis factor receptor subfamily and is a mediator of the Ectodysplasin (EDA) pathway. EDA signaling plays evolutionarily conserved roles in the development of the ectodermal appendage organ class that includes hair, eccrine sweat glands, and mammary glands. Loss of function mutations in *Eda*, which encodes the two major ligand isoforms, EDA-A1 and EDA-A2, result in X-linked hypohidrotic ectodermal dysplasia characterized by defects in two or more types of ectodermal appendages. EDA-A1 and EDA-A2 signal through the receptors EDAR and XEDAR, respectively. While the contributions of the EDA-A1/EDAR signaling pathway to EDA-dependent ectodermal appendage phenotypes have been extensively characterized, the significance of the EDA-A2/XEDAR branch of the pathway has remained obscure. Herein, we report the phenotypic consequences of disrupting the EDA-A2/XEDAR pathway on mammary gland differentiation and growth. Using a mouse *Xedar* knock-out model, we show that *Xedar* has a specific and temporally restricted role in promoting late pubertal growth and branching of the mammary epithelium that can be influenced by genetic background. Our findings are the first to implicate *Xedar* in ectodermal appendage development and suggest that the EDA-A2/XEDAR signaling axis contributes to the etiology of *EDA*-dependent mammary phenotypes.

Poster # 2

PROTEIN CARGO OF PLASMA-DERIVED EXTRACELLULAR VESICLES DRIVES INNATE MEDIATED INFLAMMATION IN DERMATOMYOSITIS

Avital Baniel[1,2], Mariko Momohara-Ogawa[1,2], Rachita Pandya[1,2], Julianne Kleitsch[1,2], Felix Chin[1,2], Ming-Lin Liu[1,2], Victoria P. Werth[1,2]

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Extracellular-vesicles (EVs) have been implicated in autoimmune disease pathogenesis. Plasma-derived DNA containing EVs have been shown to induce STING-mediated proinflammatory responses in dermatomyositis (DM), but their protein content is not well characterized.

We collected EVs from plasma of 16 DM patients and 5 controls and hypothesized their protein cargo may have a disease-specific profile. Protein profile was generated by mass spectrometry and differentially expressed proteins were assessed. Findings were used to train a machine learning model (random forest), which achieved 90% accuracy with AUC = 0.92 in correctly predicting disease state.

Sixty-seven proteins were uniquely detected in the patient cohort. Thirty-five proteins were significantly differentially expressed, of which 13 were upregulated and 22 downregulated. Over representation analysis found the unique and upregulated proteins enriched for myeloid mediated immunity, glutathione metabolism, nucleic acid synthesis and vesicle transport pathways. EVs were enriched with USP15, TMED2, STK4, ABCC1, PDMS14 and MMP8, all of which participate in induction of innate inflammatory cascades. Downregulated proteins were enriched for the classical and lectin complement pathways. The diminution of complement components in vesicles may reflect its abundance in target tissues but may also reflect host inability to circulate these molecules to damaged tissue, which in a chronic stage of disease may have a protective role. Finally, surfactant protein B was expressed almost exclusively in patients with lung disease, a finding that has been validated by ELISA in another patient cohort, rendering it a possible marker for pulmonary involvement. Taken together, proteins carried by EVs appear to be markers of DM, particularly pulmonary manifestations, and may have a role in inflammation in these patients and may indicate potential therapeutic targets.

Poster # 3

A CROSS-SECTIONAL GOOGLE TRENDS ANALYSIS OF ONLINE SEARCHES AMONG US SPANISH SPEAKERS WITH DERMATOLOGIC CONCERNS

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BACKGROUND: In the US, 40% of Spanish speakers (16 million people) have limited English proficiency.[1] However, only 7% of dermatologists are readily identifiable as Spanish-speaking, making language a formidable barrier to equitable dermatologic care.[2] In addition, online dermatologic health information in Spanish is scarce, available among only 18% of US academic dermatology departmental websites, and 24% of major US-based dermatology organizations and patient resource websites.[2,3]
PURPOSE: We aim to understand the interests of Spanish speakers with limited English proficiency Sp-LEP) in dermatologic health information by identifying online search engine keyword phrases (KP) in Spanish and assessing the differences in the temporal search trends of common dermatologic topics.
METHODS: In this cross-sectional analysis, we compared five prevalent dermatologic concerns: acne, dry skin, dark spots, hair loss, and nail fungus.[4] Under the premise that Sp-LEP primarily search the internet in their native language, we utilized "Google Keyword Planner," a search engine optimization (SEO) tool, to identify five relevant KP in Spanish for each topic (based on SEO average monthly searches and competition). Each KP was then queried in "Google Trends" to extract monthly "search volume index" (SVI)—a normalized value (min.-max.=0-100) of the proportion of searches for a KP during a select period.[5] To ensure a reliable comparison of KP, all SVI data was extracted on the same date for the same region (US).[6] We used the mean monthly SVI per KP to identify the KP per topic with the greatest search interest. Differences in the mean monthly SVI per topic were compared using a generalized estimated equation with Gaussian estimation and exchangeable correlation. We set our significance level at P<.05 and performed all analyses using Stata v.17.
RESULTS: Among US Google searches made between January 1, 2010 - December 31, 2020, four out of 25 KP did not yield an SVI. Per topic, the KP with the highest mean monthly SVI were: "*espinillas"* (blemishes); *"piel seca"* (dry skin); *"manchas cara"* (face spots); *"caída de pelo"* (hair loss); *"remedios caseros para hongos"* (home remedies for fungus). Among Spanish speakers, the topic of dark spots had significantly more search interest than acne (*R, 3.29;* 95% CI, 0.85, 5.72); dry skin (*R, 13.32;* 95% CI, 10.88, 15.75); hair loss (*R,* 4.02; 95% CI, 1.59, 6.45); and nail fungus (*R,* 15.80; 95% CI, 13.36, 18.23). Compared to dry skin, the topics acne (*R*, 10.03; 95% CI, 7.59, 12.46) and hair loss (*R*, 9.30; 95% CI, 6.86, 11.73) had significantly greater search interest. The topic of nail fungus had significantly less search interest than acne (*R,* -12.51*;* 95% CI -14.94, -10.07); dry skin (*R,* -2.48*;* 95% CI -4.91, -0.04)); dark spots (*R,* -15.80; 95% CI, -18.23, -13.36); and hair loss (*R,* -11.77; 95% CI, -14.22, -9.34).
CONCLUSION: Our findings suggest that US Sp-LEP are most interested in information on dark spots, that colloquial phrases may be preferred over formal translations, and that cultural humility is needed when translating dermatologic patient information. Dermatology departments and organizations can use readily accessible search data and SEO tools to evaluate what topics are of greatest interest to Spanish-speaking populations. This critical information can guide dermatologic institutions in providing timely and culturally sensitive dermatologic health information to better target outreach efforts, optimize equitable patient care, promote language inclusivity, and meet the needs of Spanish-speaking patients.

Poster # 4

ASSOCIATION OF CHRONIC GRAFT-VERSUS-HOST DISEASE CLINICAL SUBTYPE WITH HEALTH-RELATED QUALITY OF LIFE AND SYMPTOM BURDEN: A COHORT STUDY

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Significance: Cutaneous chronic graft-versus-host disease (cGVHD) is a debilitating complication of allogeneic hematopoietic cell transplantation and is associated with increased mortality.
Objective: The purpose of this study was to assess health-related quality of life (HRQOL) and symptom burden in a large multicenter cohort of patients with cutaneous cGVHD requiring systemic immunosuppression.
Methods: The Chronic GVHD Consortium collects socio-demographic and transplant characteristics, clinical severity assessments, and patient-reported outcome measures at cGVHD diagnosis and every 3-6 months thereafter at 10 academic medical centers across the United States. Using generalized estimating equations, we evaluated whether epidermal, sclerotic, or combination types of cutaneous cGVHD differentially impact HRQOL (FACT-BMT) and symptom burden (Lee Symptom Scale Skin Subscale) over time with cGVHD. Using linear mixed effects models, we also evaluated the association between patient-reported outcomes (FACT-BMT, Lee Symptom Scale) and clinical severity (NIH Skin Score).
Results: Of 436 patients with cutaneous cGVHD, 229 (52.5%) presented with epidermal disease, 131 (30.0%) with sclerotic disease, and 76 (17.4%) with combination epidermal and sclerotic disease. Patients with sclerotic and combination disease were more likely to have undergone myeloablative conditioning (p=0.007), develop cGVHD later after transplant (p<0.001), and have extra-cutaneous involvement (p=0.006). Overall, median baseline FACT-BMT score was 106 (IQR 90,120) and median baseline Lee Symptom Scale Skin Subscale score was 25 (IQR 10,40) demonstrating significant impairment. On average, sclerosis was associated with lower FACT-BMT scores compared to epidermal disease throughout the study period after adjusting for confounders (-6.0, 95% CI -11.7, -0.3, p=0.038). Combination disease was associated with higher symptom burden compared to epidermal disease (Lee Symptom Scale Subscale 9.1, 95% CI 4.2, 13.9, p<0.001) but there was no difference in symptom burden between sclerotic and epidermal disease. For every point increase in NIH Skin Score (0-3), there was a decrease in FACT-BMT (-1.9, 95% CI -2.6, -1.1, p<0.001) and increase in Lee Symptom Scale Skin Subscale (7.5, 95% CI 6.7,8.4. p<0.001), however, the change in FACT-BMT did not meet the clinically meaningful difference (score change of 7).
Conclusions: Clinical type of cutaneous cGVHD impacts longitudinal HRQOL and symptom burden in cGVHD. Patients with sclerotic and combination disease experience greatest impairment, and differences persist despite time on treatment. Patient-reported outcomes should be incorporated into patient management and future trials.

Poster # 5

FITZPATRICK SKIN TYPE GROUP 1/2 BASELINE CHARACTERISTICS FOR THE LITE STUDY

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The Light Treatment Effectiveness (LITE) Study, is a randomized pragmatic trial comparing the effectiveness of home versus office based narrow band UVB phototherapy for the treatment of psoriasis (NCT03726489). The co-primary end points are measured at week 12 and include the Physician Global Assessment (PGA) and Dermatology Life Quality Index (DLQI). Funded by the Patient Centered Outcomes Research Institute, the LITE Study is developed to be patient centered and is uniquely designed to have equal representation across all Fitzpatrick skin types (stratified into groups 1/2, 3/4, and 5/6). The study aims to increase access to phototherapy and change the paradigm towards trials that reflect real-world clinical practice. Enrollment for skin types 1/2 (n=350) was completed in July 2022 while the other skin type groups remain open for enrollment. Baseline characteristics were analyzed for skin type group 1/2; they had a mean age of 49 years (SD 16, Range 12-85), 42% male, a mean BMI of 30 (SD 7, Med 28), have had psoriasis on average 15 years and 20% with psoriatic arthritis. 83% reported attending some college or above, 52% indicated they had full-time employment, 18% retired and the remainder had various part time or no work. At the decision time to begin phototherapy the mean DLQI was 12, PGA 2.7 (SD 0.83, Med 2.9) and BSA 13% (SD 16.49, Range 2-90%) where 76% had plaque psoriasis, 11% guttate, and 12% both. Location of psoriasis was primarily on legs (90%), arms (84%), and trunk (78%). 39% reported a history of biologic or oral systemic use and 42% a history of phototherapy with 7% of patients currently on a biologic and 4% on an oral systemic. 71% reported at least one comorbidity, 14% indicated anxiety or depression, and 8% had a history of internal malignancy. Skin type group 1/2 estimated that they would spend approximately 59 minutes travelling to and from their treatment and had a mean copay of $19.75. For a full 12 week course of phototherapy, 3 times/week, the estimated burden of office treatment would be nearly 36 hours of travel and $711 in co-pays. Patients with psoriasis who pursue phototherapy treatment in real-world standard care have a very high subjective and objective burden of disease as well as major barriers in accessing office phototherapy.

Poster # 6

MERGED AND HARMONIZED IMAGING MASS CYTOMETRY DATASETS REVEAL NEW FINDINGS FROM LENABASUM-TREATED DERMATOMYOSITIS SKIN FROM PHASE 3 DETERMINE TRIAL

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Single-cell study has the potential to reveal single-cell phenotypes and markers that can be used as targets for precision medicine in diseases such as cancer and autoimmune disorders. In the same way that the Human Genome Project attempted to compile sequencing data to profile different diseases, single-cell is attempting to phenotype every cell in the human body with the goal of using this information to develop targeted therapies as well as biomarkers predictive of disease and treatment response. The field of single-cells has received backing from large organizations such as the Chan Zuckerberg Human Cell Atlas (HCA) program and the Knut and Allice Wallenberg Foundation's Human Protein Atlas (HPA). Along with the NIH Accelerating Medicine Partnership (AMP) and the NIH Human BioMolecular Atlas Program (HuBMAP), the field of single cell is a multi-billion dollar global effort on par with the Human Genome project. With the advent of large troves of single cell data on the horizon, it's becoming more important now than ever to develop computational tools to analyze highly multidimensional single cell sequencing and protein marker data. Imaging mass cytometry is a technique routinely performed by our lab that allows for the measurement of up to 40 protein markers in a single cell. Here we used two batch correction algorithms, one for merging imaging mass cytometry data across time/different panels and the other for merging data across patients (harmonization) to combine two imaging mass cytometry datasets acquired from dermatomyositis skin (n=25 patients) from the phase 3 DETERMINE trial. The batch corrected, merged data was then subjected to three cytometry-based clustering algorithms, and the highest performing algorithm (as determined by cluster sizes, inter-algorithm agreement and biological sensibility) was selected for downstream analysis. The clustering algorithm most suitable for our dataset used shared nearest neighbor (SNN) clustering combined with harmony integration. The algorithm identified 9 immune cell populations, with the most dominant cell populations being macrophages (CD68+CD14+CD16+) and dendritic cells (BDCA2+CD11c+ as well as CD11c+HLADR+). The BDCA2+CD11c+ dendritic cell population along with endothelial cells (CD31+) appeared to be the most upregulated in interferons (alpha/beta) as well as cytokines traditionally expressed by T-lymphocytes (IL4/IFNy/IL17). No changes in cell populations were observed prior and post treatment with Lenabasum, which was in line with the negative findings from the trial, however, reduction in the BDCA2+CD11c+ dendritic cell population along with CD45+ cells was observed in the single Lenabasum responder (CDASI 17 to 11) pre- vs. post treatment.

Poster # 7

AGE-DEPENDENT UPREGULATION OF CHEMOKINE CCL11 IN SKIN FIBROBLASTS IS ESSENTIAL FOR HOMEOSTATIC SUBCUTANEOUS ADIPOGENESIS

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Background: Fibroblasts are the most abundant mesenchymal cells in the dermis and are known for their role in extracellular matrix synthesis. Recent advances have provided insight into unexpected immunomodulatory properties of skin fibroblasts during homeostasis and in diseased conditions. Here, we hypothesized that immuno-regulatory secretome by cutaneous fibroblasts is age-dependent and tested if CCL11, a chemokine expressed largely by fibroblasts, is necessary for physiologic skin development during perinatal growth.

Materials and methods: Publicly available scRNA-seq dataset (GSE189210, GSE183031, GSE172226) were pooled, and fibroblast subsets were categorized as neonatal (P0) or adolescent (P22 and P28) for downstream analysis using Seurat package. Among fibroblast transcriptome, CCL11 upregulation was most notable, which was validated using FACS followed by RT-qPCR and RNAscope. To determine biological significance, $CCL11^{null}$ mice were generated, and skin specimens were compared to control mice at P3 and P28 of age. As CCL11 is a potent eosinophil attractant, we also examined skin specimens of eosinophil-depleted dblGATA1 mice histologically at P3 and P28. Animal studies were carried out with N=4-6 mice each, and statistical significance was determined at $p<0.05$ by one-way ANOVA and T-test.

Results: Bioinformatics analysis demonstrated that CCL11 transcripts were highly upregulated in the fibroblasts of adolescent mice compared to that of P0 mice. CCL11 was minimally expressed in other cell types in both age groups. Further validation experiments in vivo showed that CCL11 mRNA was highly expressed in PDGFR+ sorted cells from P15 skin, compared to P3 skin. RNAscope analysis confirmed age-dependent expression of CCL11, which was largely localized to the dermal layer. CCL11 knockout mice showed a significant reduction in subcutaneous adipose layer width, suggesting a role in regulating adipogenesis in developing skin. Despite the well-known function of CCL11 for recruiting eosinophils, mice that lack eosinophils (dblGATA2) did not present with a similar defect in the subcutaneous adipose layer, implicating an indirect role for CCL11 that is not eosinophil dependent.

Conclusion: Our data demonstrate an unexpected role for CCL11 expression by the fibroblasts that is necessary for homeostatic adipogenesis during perinatal growth. This may have clinical implications for potential role of cutaneous fibroblasts in skin disorders that have pediatric propensity.

Poster # 8

LENABASUM AND ITS INTERACTION WITH DERMATOMYOSITIS LEUKOCYTE SIGNALING PATHWAYS

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Dermatomyositis (DM) continues to be a challenging disease to manage as current treatments fall short for many patients. Lenabasum is a potent CB2R agonist and has shown promise in alleviating DM symptoms. Curiously, some patients have shown strong positive response to Lenabasum treatment while others had no response. Previous research has shown that responders tend to have higher amounts of CB2R expression in whole blood and skin samples compared to non-responders, highlighting an important difference in the disease signaling pathways of these patient populations. Additionally, it has been shown that Lenabasum binds and activates PPARg. To investigate this further, we are analyzing the expression and activity of PPAR and the role of TLR4, STING, and TBK1 in the inflammatory signaling pathway in DM leukocytes. The PPAR pathway is investigated by staining for p-PPAR and analyzing via flow cytometry. A combination of Lenabasum and inhibitors for CB2R, PPAR, TLR4, STING, and TBK1 were used in cultures of PBMCs and Whole Blood isolated from DM patients. Results using PBMCs has shown high median percent p-PPAR positivity in certain cell types with CD4 at 93.8% (SD= 23.6%), CD8 at 84.4% (SD= 24.2%), NK T at 90.9% (SD= 13.0%), NK at 91.2% (SD= 20.5%), and CD19 at 98.7% (SD= 22.9%). MoDCs, cM, iM, and ncM p-PPAR staining shows a range from high to low level of positivity, while other cell types showed low median percent positivity with M1 at 3.5% (SD= 29.4%) , M2 at 19.4% (SD= 15.6%), pDC at 10.4% (SD= 20.1%), and cDC at 14.2% (SD= 5.5%). These cells were also stained for IFN-b, IFN-g, and NFK as markers for inflammatory activity. The results of this study will aid in uncovering the mechanisms behind the response to a CB2R agonist and allow clinicians to better understand the heterogeneity of cellular signaling and response that can account for variability of clinical response.

Poster # 9

HUMANS ARE A DOG'S BEST FRIEND: ENHANCING CANINE CART WITH HUMAN CAR DOMAINS

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CD19-targeted chimeric antigen receptor T (CART) cells have transformed cancer therapy by inducing durable remissions of otherwise refractory B cell cancers, raising hope that cellular immunotherapies can similarly induce cures of B cell-mediated autoimmune diseases. Dogs develop spontaneous B cell cancers and autoimmune diseases, including the autoantibody-mediated skin blistering disease pemphigus, which is the most common IgG-mediated disease in dogs and has similar pathophysiology as human pemphigus. Dogs therefore present an opportunity to assess CART immunotherapy in a relatively outbred model of spontaneously-occurring autoimmune disease. A first-in-canine trial has shown that anti-CD20 CARTs exert selective pressure on CD20-expressing B cell lymphomas, although robust cytolytic activity, expansion, and engraftment have not yet been observed in canine CART trials. We thus sought to rationally optimize CART design to improve the translational value of dogs as a model for preclinical evaluation of cellular immunotherapies for autoimmune disease. We first examined the metabolic response to anti-CD3/anti-CD28 bead activation in primary canine and human T cells, representing the first step of CART manufacturing, using real-time cell metabolic profiling. Canine T cells exhibited a delay in glycolytic induction and a reduction in overall glycolytic metabolism relative to human T cells. We next sought to determine whether the mechanism for the observed glycolytic defects was due to defective glucose uptake using a fluorescent glucose analog, 2-NBDG. Canine T cells activated with anti-CD3/anti-CD28 beads demonstrated reduced glucose uptake relative to anti-CD3/anti-CD28 bead-activated human T cells. However, activation with phorbol 12-myristate 13-acetate and ionomycin significantly augmented glucose uptake in both canine and human T cells without a corresponding enhancement in glycolysis, indicating that glucose uptake does not limit glycolytic activity in dog T cells. Because human CART effector function is linked to a glycolytic state, we anticipated that the defects in glycolytic activity after activation would correlate with impaired cytotoxic effector function. As predicted, canine CARTs expressing a canine CD137z cytoplasmic domain demonstrated poor cytotoxic activity upon initial target cell encounter, which was in part rescued through expression of canine CD28z or human CD137z domains. Surprisingly, inclusion of human CD137z conferred the greatest prolonged cytolytic activity in dog CART, which will be further explored to determine whether the sustained activity is due to human CD137 and/or human CD3z domains. Despite differences in cytolytic activity, all canine CARTs demonstrated a terminally differentiated, exhausted immunophenotype after repetitive target cell restimulation. Collectively, these data suggest that strategies to combat exhaustion and enhance glycolytic capacity will improve the in vivo function and therapeutic potential of canine CART technology.

Poster # 10

MICROBIAL AND IMMUNE ENVIRONMENTAL STATES ARE TRANSMITTED VIA TRANSGENERATIONAL EPIGENETIC INHERITANCE

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The commensal microbiota mediates skin barrier integrity and function via its effects on other microbes and host cells of the skin. Sebum is a critical component of the skin's chemical barrier and a powerful determinant of skin microbiota composition. To investigate the relationship between the microbiota and sebaceous gland activity, we studied sebum secretion in germ-free (GF) mice. Compared to specific pathogen-free (SPF) control mice, sebum release in GF mice was reduced by 50%. Microbial colonization of adult or neonatal GF mice did not rescue this defect. Furthermore, natural breeding or *in vitro* fertilization of gametes from GF and SPF mice (GFxSPF) yielded progeny with defective sebum release in the F_1 and the majority of the F_2 and F_3 generations, suggesting microbially-induced epigenetic transgenerational inheritance. Since small non-coding RNAs (ncRNAs) of sperm can act as epigenetic factors that modify gene expression of resulting embryos, we profiled ncRNA of GF and SPF gametes. GF gametes had a distinct small ncRNA landscape compared to SPF gametes, suggesting candidate ncRNAs that underlie transmission of the sebum phenotype. Similar to GF mice, RAG knockout (KO) mice, which lack T and B cells, displayed 50% reduction in sebum secretion and gave rise to F_1 heterozygous mice (KOxWT) with reduced sebum release and F_2 mice (HetxHet) with a sebum defect in a portion of mice, regardless of genotype. Small ncRNA profiles of RAG KO sperm were highly analogous to GF sperm, suggesting that the two processes are connected. These findings reveal that the environment of previous generations has a lasting impact on skin integrity, where both the microbiota and immune system induce epigenetic changes in the germline, to transgenerationally promote skin barrier function. These observations have important implications for human health as they suggest that perturbing our current microbiota, such as via antibiotics, may have lasting impacts on the health of our offspring.

Poster #11

TUMOR AND TME COMPARTMENT-SPECIFIC SPATIAL TRANSCRIPTOMICS IN SCCIS

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This study defined the *in situ* transcriptomics of cellular subsets in the epidermis and dermis of lesional and perilesional skin in squamous cell carcinoma *in situ* (SCCIS), in an attempt to identify novel prognostic and therapeutic biomarkers. SCCIS from organ transplant patients was examined, as these patients are 65-250 times more likely to develop cSCC and have an 8-fold increased risk of developing metastatic disease compared to immunocompetent cSCC patients. The nanoString GeoMx Digital Spatial Profiler was used to interrogate the whole transcriptome of lesional and perilesional epidermal (CK+) and dermal (CD68+, CD45+ and SYTO13+) cellular subsets in 34 SCCIS specimens from 12 immunosuppressed, solid organ transplant patients and 17 immunocompetent patients without organ transplant. 664 unique transcriptomic libraries were collected from these two cohorts of specimens. Gene set enrichment analysis and differential expression analysis identified enriched genes (average: 2,939 and 1,295, FDR<0.05) and gene pathways (average: 379 and 398, FDR<0.05) in the lesional vs perilesional epidermis and dermis, respectively. Expected upregulation of Cell Cycle, DNA Replication, nucleotide metabolism and Kinase signaling was seen in the lesional epidermis along with downregulation of Hedgehog signaling. Ubiquitin conjugating enzymes were upregulated including *NEURL1B,* which inhibits Notch signaling. Inter-cohort variabilities indicate biologic differences in the immunosuppressed patient population. These include downregulation of CXC chemokine signaling including CXCL9 and other immunoregulatory molecules such as MHC class II clusters in the immunosuppressed cohort. These data provide insights into the spatial transcriptomic landscape of cellular subcompartments in SCCIS. While identifying putative novel mechanisms underlying disease biology including post-translational downregulation of Notch and immunoregulatory differences that may contribute to the propensity for disease progression in immunosuppressed patients.

Poster #12

MRGPRA3 NEURONS SELECTIVELY CONTROL MYELOID-DERIVED IL-33 FOR IL-17 DEPENDENT CUTANEOUS IMMUNITY

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Skin architecture contains diverse cell lineages that orchestrate organismal homeostasis, metabolic regulation, and host defense. However, the critical cytokine networks responsible for regulating skin biology under homeostasis and disease remain unclear. Interleukin 33 (IL-33) is a key regulatory cytokine thought primarily released by damaged epithelial, endothelial, and stromal cells, but it has been increasingly recognized that hematopoietic cells also release biologically relevant amounts IL-33. This study reveals that an itch-specific population of skin sensory neurons expressing MrgprA3 (A3) exert selective control over IL-33 production in myeloid antigen presenting cell (APC) subsets to initiate cutaneous inflammation. Data show that optogenetic activation of A3 neurons increases IL-17-expressing γδ T cell responses, drives epidermal thickening, and enhances resistance to the human helminth pathogen *Schistosoma mansoni* coincident with selective downmodulation of IL-33 production from myeloid cells, but not fibroblasts. This selective inhibition of IL-33 following neuron activation increases myeloid secretion of pro-inflammatory cytokines (e.g. IL-1β, IL-6, TNFα). Strikingly, mice genetically deficient for IL-33 specifically in CD11c+ cells spontaneously develop IL-23/IL-17-driven epidermal thickening, keratinocyte hyperplasia and resistance to percutaneous infection with *S. mansoni* relative to littermate controls. Single-cell RNA-seq, ATAC-seq, and immunoprofiling studies of antigen presenting cells from naïve mouse skin reveals that myeloid cell-intrinsic IL-33 shapes chromatin conformation that functionally restrains expression of IL-17-inducing cytokines (e.g. IL-1β, IL-6, and IL-23). Taken together, we propose a previously unappreciated neuroimmune circuit wherein itch-specific neurons can selectively suppress constitutively expressed IL-33 in tissue resident myeloid cells to rapidly unleash pro-inflammatory cytokine release for host immunity and keratinocyte turnover.

Poster # 13

A CASE SERIES OF CENTRAL CENTRIFUGAL CICATRICIAL ALOPECIA IN MEN

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Introduction: Central centrifugal cicatricial alopecia (CCCA) is a form of scarring alopecia seen primarily in Black women. The etiology of CCCA is unknown, but an association with PADI3 genetic mutation, type II diabetes mellitus (T2DM), and bacterial infections have been suggested. [1–3] There are few published cases of this disorder in men.[4–6] The purpose of this study was to investigate the demographics, pathology reports, and medical histories of male patients with CCCA with the hypothesis that these features may differ from women with the disorder.

Methods: This was a retrospective chart review of cases of biopsy-confirmed CCCA seen in outpatient clinics at the University of Pennsylvania Department of Dermatology between 2012 and 2022.

Results: In total, 108 men were diagnosed with unspecified scarring alopecia at our facility, 17 of which had a scalp biopsy and clinical findings consistent with CCCA. The average age was 43 years. Most patients (88.2%) were Black or African American and presented with the classic variant of CCCA. However, we observed 8 cases with an atypical presentation of CCCA. 76.5% of our study patients were symptomatic, with pruritus as the most prevalent reported symptom. We identified 29.4% of patients with overlap of CCCA and another hair disorder. None of the patients had diagnosis of T2DM, but 3/17 had latent tuberculosis.

Conclusions: While there are some similarities between men and women with CCCA, comorbidities may be distinct. We posit that different presentations may support the under diagnosis we suspect among males with CCCA.

Poster # 14

NONCLASSICAL MONOCYTES SHOW HEART-HOMING PROFILE IN DRESS WITH CARDIAC INVOLVEMENT

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Drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome is a severe multisystem drug reaction that manifests with fever, rash, eosinophilia and internal organ injury. Cardiac involvement is rare in DRESS, although when present is often a delayed manifestation that increases mortality (45%). We present a case of a young, previously healthy woman who developed DRESS syndrome after a two-week course of minocycline. She subsequently developed renal and cardiac DRESS which presented with acute renal failure requiring dialysis and severe biventricular dysfunction, arrhythmia, and myocarditis, respectively. The patient's skin and cardiac symptoms recrudesced upon tapering of her oral steroid. Single cell RNA sequencing of PBMCs isolated from time of recrudescence as well as a post-symptomatic/stable timepoint was performed and compared to healthy control PBMCs.

We identified a population of CD16+ "nonclassical" monocytes that were decreased in the DRESS patient's blood during her flare and hypothesized these cells were playing a role in her pathology. Receptor-ligand signaling analysis showed enrichment of the CCR2/CCL2 signaling pathway in these DRESS monocytes at the symptomatic timepoint whereas those from healthy controls had no significant CCR2 expression. CCL2-induced monocyte migration was confirmed with in vitro migration assays. As the CCL2/CCR2 axis has been shown to recruit classical CD14+ monocytes to cardiac tissue after injury to modulate inflammation, we conclude CCR2+CD16+ inflammatory monocytes are cardiac-homing and contributing to pathogenesis in cardiac DRESS. We additionally show enrichment of JAK/STAT signaling within the monocyte population in our DRESS patient compared to healthy controls. The patient has since been started on JAK-inhibitor therapy (tofacitinib) and is clinically improving. Post-treatment analysis is pending.

Poster # 15

CHANGE IN DISEASE ACTIVITY NEEDED FOR MEANINGFUL CHANGE IN CUTANEOUS LUPUS BY PATIENT CHARACTERISTIC

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Cutaneous lupus erythematosus (CLE) is an autoimmune skin disease that can occur with or without systemic involvement. CLE has a profound impact on patients, causing physical and psychological distress and severely impaired quality of life (QoL). The Cutaneous Lupus Erythematosus Disease Area and Severity Index (CLASI) is a validated tool that quantifies disease severity in CLE by measuring both activity (CLASI-A) and damage. The CLASI-A has been correlated to improvement in QoL, measured by the Skindex-29. In this study we aim to define the improvement needed in CLASI-A score to predict meaningful improvement by patient characteristic.

We performed a retrospective study of 568 patients within the University of Pennsylvania Longitudinal Lupus Cohort. We included patients with an initial CLASI-A score of ≥ 4 who also had complete CLASI-A and Skindex-29 scores for the initial and a subsequent visit. Linear regression models were used to calculate the relationship between the difference and percent difference in CLASI-A scores and Skindex-29 subscale scores for the two visits. Meaningful improvement in QoL was defined as a respective 9.38-point in the Emotions subscale of Skindex-29, and a 7.37-point change in the Symptoms subscale of Skindex-29.

Of 194 patients included, 161 (83%) were female, 125 (64.4%) were White, 51 (26.3%) were Black and 8 (4.1%) were Asian. Predominant CLE subtype included 104 (53.6%) with discoid lupus erythematosus (DLE), 59 (30.4%) with subacute CLE (SCLE), 10 (5.2%) with acute CLE, and 20 (10.8%) with other subtypes. Ninety-three (47.9%) were diagnosed with CLE <5 years prior to their initial visit and 101 (52.1%) were diagnosed ≥ 5 years prior. The change and percent change in CLASI-A needed for meaningful improvement in the Emotions subscale was 9.2 and 69.5% for White patients, 4.9 and 47.1% for Black patients, 5.7 and 48.1% for DLE patients, 11.1 and 69.0% for SCLE patients, 8.6 and 51.8% for patients diagnosed <5 years prior, and 6.3 and 63.4% for patients diagnosed ≥5 years prior. The change and percent change in CLASI-A needed for meaningful improvement in the Symptoms subscale was 6.9 and 55.4% for White patients, 4.5 and 47.6% for Black patients, 7.5 and 71.6% for DLE patients, 6.5 and 43.1% for SCLE patients, 6.8 and 53.0% for patients diagnosed <5 years prior, and 5.9 and 61.9% for patients diagnosed ≥5 years prior.

Our findings suggest that Black patients may require smaller changes in CLASI-A score to reflect meaningful change in Emotions compared to White patients. Similarly, DLE patients may require smaller CLASI-A changes for meaningful change in Emotions compared to SCLE patients. CLASI-A changes needed for meaningful change in Symptoms were similar regardless of characteristic.

Poster # 16

IMPAIRMENT OF H3K36 METHYLATION PROVOKES CELLULAR PLASTICITY TO DRIVE ABERRANT GLANDULAR FORMATION AND SQUAMOUS CARCINOGENESIS

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Epigenetic dysregulation is pervasive in cancer, frequently impairing normal tissue development and differentiation[1]. Beyond alterations in histone modifying enzymes, “oncohistone” mutations have been described across a variety of cancers[2-4], although the *in vivo* effects and underlying mechanisms behind these observations have not been well-studied and remain unclear. Here, by inducing the *in vivo* expression of histone H3.3 carrying a lysine to methionine (K to M) mutation at position 36 (H3K36M) in self-renewing stratifying epithelial tissues, we show that the H3K36M oncohistone dramatically disrupts normal epithelial differentiation, leading to extensive tissue dysplasia characterized by a significant increase in mitotic, proliferative basal stem cells. Furthermore, this differentiation blockade promotes increased cellular plasticity and enrichment of alternate cell fates, and in particular the aberrant generation of excessive glandular tissue including both hypertrophic salivary, sebaceous, and meibomian glands. Upon carcinogen stress, H3K36M mice display markedly enhanced squamous tumorigenesis. These aberrant phenotypic and gene expression manifestations are associated with global loss of H3K36me2 and concomitant gain of H3K27me3. Collectively, these results have revealed a previously unknown critical role for H3K36 methylation in both the *in vivo* maintenance of proper epithelial cell fate decisions and the prevention of squamous carcinogenesis. Additionally, they suggest that H3K36 methylation modulation may offer new avenues for the regulation of numerous common disorders driven by over- or under-active glandular function

Poster # 17

IN VIVO FIELD CANCERIZATION AFTER LOSS OF NOTCH SIGNALING IN EPIDERMAL STEM CELLS

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Skin carcinogenesis is a common phenomenon; however, the effects of the initial mutagenic hits on the activity of individual keratinocytes have not been fully resolved in vivo. In this study we recapitulate these very early mutational events in a genetic mouse model and analyze the behavior of keratinocytes that carry them by single cell lineage tracing and live imaging. Our results provide direct evidence of a field-cancerization phenomenon. Based on this, cells that carry mutations which are not sufficient to drive tumor growth, such as those in Notch related genes expand their clonal progeny without immediately disrupting the tissue physiology or directly leading to tumorigenesis. Consequently, these mutant cells can linger in the skin and thus accumulate additional mutations until a sufficient number or combination of mutations triggers the conversion of unremarkable skin to hyperplasia, actinic keratosis, squamous cell carcinoma in situ (SCCIS) and eventually squamous cell carcinoma (SCC). Normal keratinocytes on the other hand, compete neutrally with each other without a growth advantage and therefore more likely to terminally differentiate, effectively eliminating any mutations in the collective skin genome when they are eventually shed from the epidermis. In conclusion our data support a paradigm of carcinogenesis that does not rely on driver mutations and uncovers events that may precede tumor growth initiation but that may be essential for this critical step to occur.

Poster # 18

FATE INDUCTION IN CD8 CHIMERIC ANTIGEN RECEPTOR T CELLS THROUGH ASYMMETRIC CELL DIVISION

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Chimeric antigen receptor T-cell (CART) therapy has led to lasting remissions in hematologic cancers and autoimmune diseases including systemic lupus. Long-lived memory CARTs predict better clinical response, but mechanisms for CART differentiation after activation remain unclear. Here, we show that activated human CARTs undergo asymmetric cell division to impose distinct fates upon first-division daughter cells. We use a novel protein-protein interaction dependent molecular labeling technique to label target-engaged CAR molecules and sort first division proximal and distal daughter CARTs for single-cell surface proteomic and transcriptional profiling; metabolic profiling; and assessment of *in vitro* and *in vivo* cytotoxic function. Target-engaged CAR molecules aggregate on proximal first-division daughter cells and induce asymmetry between proximal and distal daughter cells in surface proteome, transcriptional profile, and metabolic program. Proximal daughter cells enrich in the surface protein levels for CD25 and Notch1; upregulate *MYC* and *MTORC1* target genes; upregulate a core transcription factor set promoting proliferation (E2F7), apoptosis (TP73), and effector differentiation (YBX1); and demonstrate increased metabolic activity largely supported by glycolysis, consistent with proximal daughter cell activation and differentiation toward a terminal effector cell fate. In contrast, distal daughter cells enrich in the surface protein levels for CD45RA and CD5; upregulate genes such as *CCR7*, *IL7R*, and *KLF2*; upregulate a core transcription factor set promoting quiescence (STAT1) and restraining effector cell expansion (FLI1); and employ an oxidative phosphorylation-predominant metabolic profile indicative of distal daughter cell differentiation toward a memory cell fate. RNA velocity analysis reveals that proximal and distal daughter cells demonstrate diverging cell fate trajectories and that both uneven distribution of pre-existing transcripts and changes in transcriptional regulation establish transcriptional asymmetry between proximal and distal daughter cells. Consistent with their memory T cell fate, distal daughter T cells exhibit superior engraftment capability compared to proximal daughter T cells ($p < 0.05$). Surprisingly, despite their memory phenotypes and *in vivo* functional longevity, first-division distal daughter cells also transiently exhibit potent cytolytic activity, resulting in superior long-term leukemic control ($p < 0.01$). These studies establish asymmetric cell division as a framework for studying mechanisms of human CAR T cell differentiation and improving therapeutic outcomes.

Poster # 19

THE ROLE OF THE Y CHROMOSOME IN MELANOMA PATHOBIOLOGY AND THE MALE SEX BIAS

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Melanoma incidence and mortality are significantly higher in males than females. These sex differences are independent of melanoma stage and sex-related differences in environmental exposures and lifestyle behaviors, suggesting the melanoma sex bias is primarily driven by biological mechanisms that differ between the sexes. Interestingly, the Y chromosome is lost with age in peripheral blood cells, and this loss of the Y chromosome (LOY) in blood is associated with a four-fold increased risk of cancer and a three-fold decrease in cancer survival. Despite these associations between LOY and cancer, the functional significance of LOY is largely unexplored. Emerging data suggest the Y chromosome is lost in some solid tumors, but whether the Y chromosome is lost in melanoma was unknown. We found that the Y chromosome is lost in melanoma, with the frequency of both partial and complete loss increasing with melanoma stage and complete LOY occurring more frequently in metastases than primary lesions. The Y chromosome has 78 protein-coding genes, ten of which are ubiquitously expressed in all tissues, including melanocytes. Six of these genes are dysregulated in cancer, making them attractive candidates for genes that may mediate the pro-tumorigenic effects of LOY in melanoma. We therefore seek to determine whether any of these ten genes alter melanoma proliferation, malignancy, or tumorigenicity and thereby contribute to the melanoma sex bias.

Poster # 20

EPIDERMAL EPITRANSCRIPTOMICS: METTL3 DEPENDENT M^{6}A REGULATES CHROMATIN MODIFYING ENZYMES

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The balance between epidermal stemness and differentiation requires regulated spatiotemporal changes of gene expression. One emerging area of gene regulation is that of epitranscriptomics (RNA epigenetics), which offers an additional layer of gene regulation in a spatiotemporal- and signal-dependent manner. However, its significance in healthy and diseased epidermis is poorly understood. N^6-methyladenosine (m^{6}A) is the most abundant internal mRNA modification in eukaryotes and is found to facilitate rapid transcriptome turnover during cell differentiation to maintain homeostasis. Its deposition on nascent pre-mRNA is carried out by a multicomponent writer complex that consists of catalytic subunit METTL3. To understand the role of METTL3 in the epidermis, we created mice with an epidermis-specific knockout of *Mettl3* (Krt14-Cre; Mettl3 fl/fl). These mice displayed a dramatic epithelial phenotype marked by the absence of hair, altered epidermal differentiation dynamics, as well as an oral epithelium that was notable for a lack of filiform papillae and oral ulcerations. Consistent with these changes, transcriptional profiling by RNA-seq demonstrated a loss of expression of basement membrane transcripts along with concomitant upregulation of keratinocyte differentiation and chromatin modifier transcripts. Additionally, m^{6}A-seq analysis in normal human keratinocytes reveal that these chromatin modifiers lose their m^{6}A peaks with knockdown of METTL3. Due to all this evidence, we suggest the epitranscriptomic mechanism that the loss of the METTL3-m^{6}A epitranscriptome promotes upregulation of chromatin modifiers by increasing their mRNA half-life and enhancing their transcripts' translation. This upregulation of chromatin modifiers, and thus histone modifications, in turn deregulate proper epidermal development and differentiation.

Poster # 21

BARRIERS TO CARE AND PREFERENCES FOR CARE PROVIDERS AMONG BLACK CHILDREN WITH ATOPIC DERMATITIS

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Black children are more likely to see a primary doctor or go to the emergency room (ER) and less likely to see a dermatologist for their atopic dermatitis (AD) than White children. We aimed to understand the barriers to routine outpatient care and reasons for specific healthcare use patterns for AD among Black children. We performed semi-structured interviews of 13 adult caregivers of Black children with AD who did not have ready access to a dermatologist or went to the ER frequently. Interviews were independently coded by three members of the research team using a grounded theory approach and NVivo software. Median (interquartile range, IQR) ages of the caregivers and children were 38 (31, 48.5) years and 7 (6, 12.5) years, respectively; 84.6% and 61.5% were female, respectively. Median (IQR) duration of AD among the children was 6.4 (2.5, 11.3) years; 53.8% had moderate-to-severe AD. Barriers to seeking care included long distance to a healthcare facility, the need to take time off school or work, transportation challenges, and long wait times for appointments. The main facilitator for accessing care was online or phone access to an on-call provider. Many caregivers preferred going to their child's pediatrician for care because they valued the established, long-term relationship. While dermatologists were recognized for providing more specialized care, they were also viewed as being less accessible due to long wait times for appointments and, for some, not accepting of all insurance. Others viewed dermatologists as a last resort. Perceptions of the ER were mixed. Some caregivers preferred the ER because it provided quicker access to care; others did not like the ER due to long wait times and lack of a personal touch. Our study provides new insight about barriers to care and perceptions of different health care options among caregivers of Black children with AD that can inform interventions to optimize healthcare use and improve outcomes for childhood AD.

Poster # 22

MECHANOSENSITIVE PATHWAYS IN THE OCCLUDED WOUND-INDUCED HAIR NEOGENESIS MODEL OF REGENERATION

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Occlusive dressings are commonly utilized in clinical settings to manage acute wounds, but the effect of wound occlusion on regeneration is poorly understood. Furthermore, some clinical evidence from wounds with high regenerative capacity suggests a negative impact. To investigate the impact of occlusion on regeneration, we used the murine wound-induced hair neogenesis (WIHN) model which is defined by Wnt-dependent hair follicle regeneration in large, full-thickness wounds. Interestingly, occluding wounds with commonly used dressings (*e.g.* film and hydrocolloid) for three days between post-wound days 0-7 completely inhibited WIHN.

During post-wound days 0-7, occlusion increased mechanotransduction (a fibrosis-promoting pathway sensitive to mechanical stimuli), triggered TGF-β2 expression without affecting TGF-β1 or TGF-β3 levels, and reduced canonical Wnt signaling. The spatial rigidity gradient in open wounds provides the necessary symmetry breaking for WIHN, and we determined the tissue rigidity of wounds on scab detachment day using atomic force microscopy. Occluded wounds lacked a spatial rigidity gradient and had uniform tissue rigidity across the wound center and periphery.

Blocking mechanotransduction in occluded wounds partially restored WIHN by re-establishing the spatial rigidity gradient and normalizing TGF-β2 expression. Transgenic mice (*Axin2*$^{LacZ/LacZ}$) with enhanced Wnt signaling were immune to the disruption of tissue mechanics caused by occlusion and displayed WIHN in occluded wounds. Our findings show that Wnt signaling directly attenuated mechanotransduction in epidermal keratinocytes, but not in dermal fibroblasts. These results from the WIHN model suggest that occlusion elicits mechanotransduction to support fibrosis over regeneration, and Wnt signaling is critical for breaking the symmetry of tissue mechanics necessary for WIHN.

Poster # 23

THE ROLE OF HISTONE DEMETHYLASE UTX IN EPIDERMAL HOMEOSTASIS

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Carefully coordinated transcriptional changes are imperative for keratinocyte differentiation and epidermal barrier maintenance. Epigenetic histone modifiers play a critical role in this process evident by their high mutation rate in carcinogenesis, with the histone demethylase *UTX (KDM6A)* being one of the most frequent. Found on the X chromosome, UTX is one of the few genes to escape X inactivation and functions as a major enhancer regulator. UTX establishes the active enhancer landscape through its histone demethylase activity as well as its ability to complex with other activating histone modifiers. UTY, the Y-linked paralog of UTX, retains minimal catalytic function but can potentially compensate for UTX loss by other mechanisms. This may account for some of the sex specific differences that have been observed in the risk and severity of several different cancers. Despite its importance in other tissues throughout the body and its high mutational rate in cutaneous carcinomas, there is virtually no understanding of how it functions during epidermal homeostasis. To address these questions, we have generated mice with epidermal specific deletions of *Utx*. Interestingly, these mice present with a sex-biased phenotype showing no significant change in Utx knockout males or heterozygous females, but *Utx* knockout female mice display regions of epidermal hyperplasia, an expanded K14 basal layer, reduced hair follicle size, enlarged sebaceous glands, and increased immune invasion in the skin when compared to littermate controls. Retinoic acid signaling is downregulated in the epidermis of Utx KO mice supported by reduction of Crabp2 and Ppard protein levels in the skin. Utx loss also leads to a more severe psoriatic phenotype in imiquimod treated female mice. Taken together, these data suggest that UTX is critical to maintain epidermal homeostasis and proper gene expression, and when lost leads to abnormal development and higher cancer risk.

Poster # 24

EVALUATION OF SKIN-SPECIFIC AND COMPOSITE OUTCOMES FOR MEASURING DERMATOMYOSITIS SKIN IMPROVEMENT IN THE LENABASUM PHASE 3 TRIAL

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Dermatomyositis (DM) is a heterogeneous, autoimmune disease with skin and muscle involvement. There have been few industry-sponsored DM trials, with most of them focused on muscle improvement. Skin involvement is a cardinal symptom of DM, requiring an understanding of which outcome measure best discriminates across a range of skin improvement. We evaluated skin-specific and composite outcome measures: CDASI-Activity (CDASI-A), Investigator's Global Assessment (IGA), and Total Improvement Scores (TIS), from the DM lenabasum phase 3 trial. Our study population included both amyopathic (n=18) and classic subtypes (n=151). We assessed physician-reported degrees of improvement in skin disease activity and corresponding mean changes in CDASI-A, IGA, and TIS scores from baseline, at weeks 28 and 52. Of note, physician-reported improvement was defined as 1) no vs yes improvement and 2) if yes, slight vs moderate vs major improvement. Mean changes for no, slight, moderate, and major improvement in CDASI-A include: -1.9; -5.5, -8.6, -17.1 (Week 28) and 0.5; -6.2; -13.4; -17.5 (Week 52). Mean changes in IGA include: -0.2; -0.4; -0.6; -1.3 (Week 28) and -0.6; -0.8; -1.0; -1.7 (Week 52). Mean TIS scores include: 13.1; 26.3; 34.6; 50.8 (Week 28) and 19.7; 36.4; 45.1; 46.2 (Week 52). At each timepoint, mean changes in CDASI-A increased with each degree of improvement, with most step changes associated with statistically significant greater improvement than the previous degree ($p < 0.05$). IGA mean changes reflected a 1.3-1.7 point change corresponding to major improvement, and could only discriminate between no vs yes improvement. Mean TIS scores increased for each degree of improvement but displayed trends of plateauing, and could only discriminate among degrees of improvement ($p < 0.05$) at the Week 28 timepoint. Mean score change for slight improvement represents the minimal clinically significant change. This value is close to a 5-point change for CDASI-A, which is consistent with previous research. For IGA, this value is less than a 1-point change and is smaller than the currently used 2-point change threshold for meaningful change. In TIS, this value is 26-36-points, which is greater than the currently used 20-point threshold for slight improvement. This study is a novel assessment of the CDASI-A, IGA, and TIS outcomes from the investigator's perspective in the largest DM study, and suggests preferential use of CDASI-A scores for measuring the range of skin disease improvement in future DM trials.

Poster # 25

SOX9 IS ESSENTIAL FOR CORNEAL EPITHELIAL MAINTENANCE

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Many tissues, especially those that are under constant demand to be replenished, such as barrier epithelia, rely on tissue-resident stem cells for their maintenance. Stem cells reside in specialized niches, or microenvironments. In some tissues, this stem cell niche is organized in such a way that they are physically separated from the terminally differentiating progeny. Such a tissue organization often raises the question: how are stem cells and their activity regulated across a tissue to achieve homeostasis? To answer this question, our lab uses the corneal epithelium as a model system. The corneal epithelium has a unique organization in that the stem cells that maintain the tissue reside in the periphery of the tissue in a compartment known as the limbus. Through single-cell transcriptomics and live-imaging approaches, we identified the transcription factor, SOX9, and determined its expression in the limbal niche. When we deleted *Sox9* from the corneas of adult mice, we found that loss of *Sox9* lead to hyperproliferation in the limbus and epithelium as well as abnormal differentiation and cell growth at the central cornea. Based on this work, we propose that SOX9 is required for Notch-Dependent Differentiation of Corneal Stem cells.

Poster # 26

NOVEL FORMULATION FOR DELIVERY OF MINOXIDIL TO TREAT HAIR LOSS DISORDERS

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Please attend poster session for further information

Poster # 27

A NOVEL ASSESSMENT OF CARDIOVASCULAR HEALTH IN PEOPLE WITH PSORIASIS IN THE US: A CROSS-SECTIONAL STUDY

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Psoriasis is associated with cardiovascular (CV) disease; however, few studies have analyzed aggregated holistic markers of cardiovascular health (CVH) in psoriasis patients. We analyzed the new American Heart Association scoring system for quantifying CVH called Life's Essential 8 (LE8) score which uses data for 8 CV risk factors (BMI, blood pressure, blood sugar, physical activity, sleep, diet, cholesterol, and smoking) to provide a continuous CVH score ranging from 0 (worst) to 100 (best) points. A cross-sectional study was conducted using the National Health and Nutrition Examination Survey (NHANES), a US population-based study, in adults with (n=523) or without (n=18,139) self-reported psoriasis from 2005-2006 and 2009-2014. Controlling for age, self-reported gender and race/ethnicity, and socioeconomic status, survey-adjusted logistic regressions showed lower prevalence of better LE8 scores (≥80/100 points) (OR 0.68 [95% CI 0.48, 0.96], p=0.03) in psoriasis patients compared to non-psoriasis patients. This difference was mostly driven by worse BMI component scores in patients with psoriasis (survey-adjusted difference of -4.72 [95% CI -8.27, -1.17], p=0.01). There was also a trend toward worse scores in psoriasis patients for 6 other risk factors (blood pressure, cholesterol, blood sugar, physical activity, sleep, smoking) with the largest differences seen for blood pressure, physical activity, and smoking, though these were not statistically significant. Comparing people with moderate or severe psoriasis (BSA>3%) to people with mild psoriasis or people with no psoriasis, overall scores and 6 out of 8 risk factors (BMI, blood pressure, blood sugar, physical activity, sleep, diet) were worse, though these differences were not statistically significant possibly due to small sample size. This study is the first to analyze the LE8 score in psoriasis patients, showing that overall CVH is worse in patients with psoriasis.

Poster # 28

MINING THE PIG SKIN MICROBIOME FOR ANTIMICROBIAL PRODUCTS

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Methicillin resistant *Staphylococcus aureus* (MRSA) is a leading cause of infections by antibiotic resistant organisms in the US, with the skin being the most common site of infection. MRSA colonization of skin and nasal passages further contributes to spread of MRSA within the community. There is a therefore a growing need for new antibiotics against drug resistant pathogens such as MRSA. One potential source of novel antibiotics against MRSA is the skin microbiome, which can be colonized by MRSA and is an unmined source of natural products. We hypothesized that the skin microbiome might be enriched for bacteria capable of competitive interactions against MRSA. Using pigs as a model organism, our lab screened the skin microbiome and identified 30 unique bacterial species that inhibited MRSA via a modified disk diffusion assay. We further find that the novel skin commensal *Desemzia incerta* can inhibit the growth of MRSA through a secreted antimicrobial molecule that can be isolated from cell-free supernatant. This antimicrobial activity fails to pass through a 50kDA molecular weight cutoff filter and is lost after digestion with proteases, suggesting that the active antimicrobial molecule is a protein. Analysis of the *D. incerta* genome shows little homology to known antimicrobial genes clusters, suggesting a novel antimicrobial molecule. We developed a protein purification strategy that combines centrifugal filtration, liquid chromatography, and comparative proteomics to identify 27 candidate proteins potentially related to the observed antibiotic activity. Of particular interest is a peptidoglycan hydrolase homologue, which has been previously proposed to have antimicrobial properties. Finally, we find that *D. incerta* colonization reduces MRSA colonization efficiency by 60% in a murine skin model. Further efforts will focus on narrowing our candidate protein list, examining the antibiotic mechanism of action, and exploring porcine models of skin colonization.

Poster # 29

AN UNDERSTUDIED WOUND COMMENSAL BACTERIUM ACCELERATES DIABETIC WOUND HEALING BY BALANCING MATRIX METALLOPROTEINASE OVEREXPRESSION

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An untapped therapeutic target for chronic wounds is the skin microbiota. Thus far, chronic wound treatments have focused on eliminating pathogenic microbes, such as *Staphylococcus aureus*, that are known to delay healing. However, it is not well understood how non-pathogenic bacterial colonization modulates wound healing, and if any colonizing bacteria confer a beneficial response. To initiate such an investigation, our lab performed culture-based and metagenomic analysis of non-infected diabetic foot ulcers. We identified a surprisingly prevalent wound inhabitant, *Alcaligenes faecalis*. Though detected in many chronic wounds, little is known about this species. We found that treating murine diabetic wounds with *A. faecalis* accelerates wound closure compared to control ($p = 0.015$). Furthermore, *A. faecalis* promotes diabetic keratinocyte migration *in vitro* and a 3-fold increase in proliferation *in vivo.* These keratinocyte behaviors are necessary for re-epithelialization, a critical step in early healing. Thus, the central goal of this study is to identify mechanisms by which *A. faecalis* mediates accelerated re-epithelialization. Towards this goal, we performed RNA-sequencing on *A. faecalis*-treated wounds. We discovered that *A. faecalis* reduces overexpression of matrix metalloproteinases (MMPs) during early healing. Overactivation of MMPs contributes to impaired re-epithelialization in diabetic healing. Furthermore, treating wounds with the pathogen *S. aureus* leads to delayed healing and increased MMP expression. We also found that protease sensitive, sterile supernatant of *A. faecalis*, rather than bacterial-cell surface molecules, promotes keratinocyte production of healing-associated cytokines. These results support a model wherein *A. faecalis* secretes a protein that improves re-epithelialization by balancing MMP expression. This work uncovers host mechanisms of bacterial-driven healing, as well as a microbial product capable of tuning the host wounding response.

Poster # 30

THE CURRENT STATE OF MANAGEMENT OF ATHEROSCLEROTIC CARDIOVASCULAR DISEASE RISK FACTORS IN DERMATOMYOSITIS (DM) PATIENTS

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Patients with dermatomyositis (DM) are at a heightened risk for clinical events, chiefly heart attacks and strokes, caused by atherosclerotic cardiovascular disease (ASCVD). To address this problem, we recently proposed new guidelines for categorization of levels of risk for future ASCVD events specifically in DM patients, with corresponding recommendations for management of conventional therapeutic targets, chiefly hypercholesteremia, hypertension, smoking, prediabetes, and diabetes mellitus (Keyes et al. 2021). Here, we assessed current management of ASCVD event risk in an established longitudinal cohort of DM patients at UPenn (DM-ASCVD Cohort, n=70). 94.3% (66/70 patients) had a primary care physician. By the newly proposed guidelines, low-density lipoprotein (LDL) cholesterol levels were above goal for 52.9% (9/17) of DM patients classified at High Risk for an ASCVD event, 78.0% (32/41) of DM patients classified at Very High Risk, and 66.7% (8/12) of DM patients classified at Extreme Risk). Despite established approaches to manage statin-associated muscle symptoms (Keyes et al. 2021), LDL-lowering remains an issue for DM patients. Of 48 DM patients with hypertension, 41.7% (20/48) were not on any anti-hypertensive medications, and another 41.7% (20/48) were undertreated, meaning on medications yet still ≥130/80. Regarding smoking, only one patient in our DM-ASCVD Cohort (1.4%) is a current smoker, and 31.43% (22/70) are former smokers. Of the six DM patients with prediabetes, 5/6 (83.3%) had documentation of lifestyle counseling in their charts, but none had an active prescription for metformin. Of the 12 DM patients with diabetes in our Cohort, only one (8.3%) was not well-managed, defined by a glycated hemoglobin >7%. We conclude that DM patients are undermanaged for conventional therapeutic targets to reduce ASCVD event risk, particularly hypercholesteremia and hypertension. Efforts are underway to investigate impediments to guideline-based care, to allow rational strategies to improve the management of ASCVD event risk in DM patients.