ABSTRACTS
ASDR2026

7

Title: Inflammation-driven IL-1 signaling remodels epidermal stem cell compartments by suppressing Wnt activity

Authors: Hung Manh Phung[1,2], Ikuto Nishikawa[2,1], Nguyen Thi Kim Nguyen[1], Aiya K. Yesbolatova[2], Ahmed M. Hegazy[1,3], Tomson Kosasih[4,1], Jun Aoi[5], Satoshi Fukushima[5], Sho Hiroyasu[6], Hitoshi Takizawa[4], Aiko Sada[2,1]

[1]Laboratory of Skin Regeneration and Aging, International Research Center for Medical Sciences (IRCMS), Kumamoto University, Kumamoto, Japan
[2]Division of Skin Regeneration and Aging, Medical Institute of Bioregulation, Kyushu University, Fukuoka, Japan
[3]Zoology Department, Faculty of Science, Minia University, El-Minia, Egypt
[4]Laboratory of Stem Cell Stress, International Research Center for Medical Sciences (IRCMS), Kumamoto University, Kumamoto, Japan
[5]Department of Dermatology and Plastic Surgery, Faculty of Life Sciences, Kumamoto University, Kumamoto, Japan
[6]Department of Dermatology, Graduate School of Medicine, Osaka Metropolitan University, Osaka, Japan

Inflammation profoundly perturbs tissue homeostasis, yet how it reshapes epidermal stem cell heterogeneity remains poorly understood. Here, we investigated the impact of acute skin inflammation on epidermal stem cell compartments using a 12-O-tetradecanoylphorbol-13-acetate (TPA)-induced mouse model combined with lineage tracing of slow-cycling Dlx1+ and fast-cycling Slc1a3+ stem cell populations. Transcriptome analyses and functional perturbations, including IL-1α/β administration, transgenic induction of the IL-1 decoy receptor, and subcutaneous injection of Wnt ligands, were employed to dissect the underlying mechanisms. Lineage tracing in inflamed skin revealed that rather than exerting uniform effects, inflammation induced population-specific responses: slow-cycling Dlx1$^+$ stem cell clones persisted, while fast-cycling Slc1a3$^+$ clones declined through enhanced differentiation and lineage conversion. Notably, the reorganization of epidermal stem cell compartments was found to be reversible upon the resolution of inflammation. IL-1 signaling was both necessary and sufficient for this remodeling, as intradermal injection of IL-1α/β recapitulated compartment changes, while induction of the IL-1 decoy receptor preserved the epidermal stem cell compartments. Mechanistically, IL-1

suppressed canonical Wnt activity in both the mouse epidermis and human keratinocytes, and Wnt ligand administration restored the fast-cycling compartment *in vivo*. Together, these findings identify a reversible IL-1–Wnt axis that governs inflammation-induced reorganization of epidermal stem cell compartments, providing a mechanistic framework for epidermal stem cell plasticity and tissue remodeling.

8

Title: Pigmented Fungiform Papillae of the Tongue Across Three Generations: Implications for a Familial Pigmentary Phenotype

Authors: X. Hang[1,2], N. Ling[1,3]

[1]Mowbray Park Medical and Dermatology, Dermatology, East Brisbane, Queensland
[2]University of Queensland, Frazer Institute, Brisbane, Queensland
[3]Mater Misericordiae Health Service, Dermatology Department, South Brisbane, Queensland

Background: Pigmented fungiform papillae of the tongue (PFPT) is a benign mucosal pigmentary phenotype within the spectrum of melanocyte-associated pigmentation, most frequently observed in individuals with darker skin phototypes. While typically considered sporadic, emerging reports of familial cases raise the possibility of an underlying genetic or pigmentary regulatory mechanism, likely reflecting increased melanocyte activity and localised epithelial-melanocyte interactions within fungiform papillae. Recognition is clinically important, as PFPT may be misclassified as mucosal melanocytic pathology, including melanoma, leading to unnecessary investigation and patient anxiety.

Methodology: We describe a three-generation familial presentation of PFPT identified during dermatological assessment, with examination extended to affected relatives. A focused literature review was conducted using PubMed from inception to December 2025 to identify previously reported familial cases and evaluate patterns suggestive of heritable transmission.

Findings: The proband was a 31-year-old Fitzpatrick skin type VI female with asymptomatic pigmentation confined to the fungiform papillae. Similar findings were observed in her 71-year-old mother and 14-month-old daughter, while an additional child was unaffected. No associated mucocutaneous pigmentation or syndromic features were identified. Literature review identified 33 relevant articles, of which only three described familial PFPT (two mother-daughter pairs and one mother-son pair). No previously reported cases demonstrated involvement across three generations. Notably, all affected individuals in our case were female.

Conclusion: This report expands the limited literature on PFPT and supports a possible heritable component, with a pattern that may suggest sex-limited expression. These findings highlight PFPT as a recognisable pigmentary phenotype and raise the possibility of underlying melanocyte regulatory pathways. Recognition is important to avoid misclassification as melanocytic pathology and reduce unnecessary biopsy, particularly in patients with skin of colour. Further investigation into the biological and genetic basis of PFPT is warranted.

9

Title: Do commonly studied immunohistochemical biomarkers meaningfully stratify early-stage melanoma? Insights from a population-based cohort

Authors: X. Hang[1,2], D. C. Whiteman[1], C. M. Olsen[1], N. Pandeya[1], D. Lambie[2]

[1] QIMR Berghofer Medical Research Institute, Population Health, Brisbane, Queensland.
[2] University of Queensland, Frazer Institute, Brisbane, Queensland.

Background: Melanoma demonstrates biological heterogeneity not fully explained by conventional histopathologic features including Breslow thickness, mitotic rate and ulceration. This is particularly evident in early-stage disease, where prognostic uncertainty persists. Immunohistochemical (IHC) biomarkers, as tools readily implemented in routine pathology practice, have been proposed to improve risk stratification. However, their ability to distinguish biologically aggressive from less aggressive tumours remains uncertain.

Methodology: We evaluated three commonly studied IHC biomarkers (BRAF VE1, Ki67 and nestin) within the population-based QSkin Sun and Health Study. Incident invasive melanomas with available tumour tissue (n=165) underwent standardised IHC staining and digital quantification using QuPath. Associations between biomarker expression and demographic, phenotypic, genetic, clinical, histopathologic and host-related factors were evaluated using statistical analyses informed by causal modelling.

Findings: BRAF VE1 positivity was observed in 9% of tumours, reflecting detection of V600E-specific mutations within a predominantly thin melanoma cohort, and was associated with pigmentation-related phenotypes (darker skin colour, greater tanning ability and lower cumulative sun damage). Ki67 and nestin expression demonstrated marked inter-tumour heterogeneity and were associated with proliferative features (Breslow thickness and mitotic activity), but showed no independent associations with upstream host or environmental factors after adjustment. Neither PRS nor screening behaviour was associated with biomarker expression.

Conclusion: In this population-based cohort, selected IHC biomarkers demonstrated limited ability to discriminate biologically aggressive from less aggressive tumours, particularly in thin

melanomas. Ki67 and nestin primarily reflected tumour proliferative activity rather than adverse prognostic features, while BRAF VE1 positivity was more consistent with pigmentation phenotype and a low cumulative sun damage pathway than tumour aggressiveness. The absence of association with PRS and screening behaviour suggests these biomarkers predominantly reflect tumour-intrinsic biology rather than host susceptibility or detection patterns. These findings support the need for integrative approaches incorporating genomic, digital pathology and longitudinal data to more accurately define biologically meaningful melanoma subgroups.

10

Title: Methotrexate Toxicity in Dermatology: A Severe Mucocutaneous Presentation and Review of the Literature

Authors: Dr Isabella De'Ambrosis, Dr Amanda Godbolt

Methotrexate is a common systemic therapy in dermatology and is widely prescribed for inflammatory dermatoses. Despite its efficacy, methotrexate carries a narrow therapeutic index and a potentially life-threatening toxicity profile, particularly when dosing errors occur. Vigilant prescribing practices, patient education, and medication reconciliation are therefore essential.

We present the case of a 74-year-old man who presented to the Royal Brisbane and Women's Hospital with a two-week history of a severe mucocutaneous eruption. Clinical examination showed a widespread photoaggravated erythematous eruption with bullae with associated orogenital ulceration. His medical history was significant for psoriasis, for which he had been treated with Ixekizumab for the preceding two years. He was admitted with a provisional diagnosis of cutaneous lupus erythematosus. An extensive autoimmune work-up was unremarkable; however, laboratory investigations demonstrated profound neutropenia, thrombocytopenia, and leukopenia.

Further medication reconciliation revealed that the patient had inadvertently been taking 30mg methotrexate daily for the last 10 days. This medication had been prescribed three years earlier and remained within his medication pack. A diagnosis of methotrexate toxicity was made, and management included prompt cessation of methotrexate, folinic acid rescue in consultation with haematology, supportive care, and multidisciplinary input, resulting in clinical improvement.

This case highlights the severe and potentially fatal consequences of methotrexate toxicity and underscores the importance of meticulous patient education, clear dosing instructions, and regular medication review. This presentation will review the literature on methotrexate toxicity, outline common clinical presentations and risk factors, and discuss evidence-based approaches to diagnosis and management relevant to the general dermatologist.

11

Title: Grid-like facial granulomas following cosmetic procedures: a foreign body granulomatous reaction

Authors: S. Singh[c], J. Choi[2], R. Chan

[1] MD, Resident Medical Officer, Concord Repatriation General Hospital, Sydney, NSW
[2] Dermatology Consultant, Concord Repatriation General Hospital, Sydney, NSW
[3] Department of Anatomical Pathology and Electron Microscopy Unit, Concord Hospital, and Sydney University Medical School

Foreign body-associated granulomatous dermatitis is an increasingly recognised sequela of cosmetic procedures and may closely simulate inflammatory granulomatous dermatoses both clinically and histopathologically.

We describe a 56-year-old woman presenting with erythematous, monomorphic facial papules arranged in a striking, symmetrical grid-like distribution. A 3-mm punch biopsy demonstrated a flattened epidermis overlying well-formed, non-caseating dermal granulomas with an accompanying lymphocytic infiltrate. Polarised light microscopy revealed minute fragments of birefringent foreign material within the dermis. Further history identified prior microneedling and Q-switched laser therapy approximately six months prior to onset.

In the context of the distinctive patterned clinical distribution and histopathological findings, the features were most consistent with a foreign body-induced granulomatous reaction, likely related to prior cosmetic intervention.

This case highlights the importance of careful clinicopathological correlation and the use of polarised light microscopy in the evaluation of facial granulomatous eruptions, particularly in the setting of prior cosmetic procedures.

12

Title: Sesamin Induces MCL-1-Dependent Apoptosis in Activated T Cells and Ameliorates Experimental Atopic Dermatitis

Authors: Hee-Suk Park[1] and Hyun-Su Lee[1]

[1]Daegu Catholic University School of Medicine, Dept. of Physiology, Daegu, Republic of Korea.

Sesamin is a natural lignan derived from Sesamum indicum with reported anti-inflammatory and pro-apoptotic properties. However, whether sesamin modulates T cell-mediated inflammatory diseases and the molecular mechanisms involved remain unclear. In this study, we investigated the immunomodulatory effects of sesamin on activated T cells and its therapeutic potential in

atopic dermatitis. Sesamin markedly suppressed IL-2 expression, CD69 upregulation, and proliferation in activated human and murine T cells, while selectively inducing apoptosis in activated, but not resting, T cells. Molecular docking predicted that sesamin binds to the BH3-binding groove of MCL-1, a critical anti-apoptotic Bcl-2 family protein. This interaction was validated by pull-down and co-immunoprecipitation assays. Mechanistically, sesamin inhibited MCL-1 phosphorylation at Ser64 and disrupted MCL-1/Bak heterodimerization, leading to caspase-3 and caspase-8 cleavage and apoptotic T cell death. In a murine model of atopic dermatitis, oral administration of sesamin significantly ameliorated pathological skin symptoms, decreased Th2/Th17 cytokine expression, serum IgE levels, mast cell infiltration, and lymph node hypertrophy. These effects were accompanied by reduced MCL-1 activity and increased apoptosis in inflamed skin tissue. These findings reveal a previously unrecognized MCL-1-dependent mechanism by which sesamin selectively controls activated T cell survival and suggest that sesamin may represent a promising dietary-derived therapeutic approach for T cell-driven chronic inflammatory diseases, including atopic dermatitis.

13

Title: Epithelial NF-κB Shapes the Innate and Adaptive Immune Landscape and Coordinates IL-17 Immunity

Authors: Narayanan. D[1], Sim. S L[1] , Rudolph A Rupec[2], Kumari. S[1]

[1]Frazer Institute, The University of Queensland, Queensland, Australia
[2]Derma AG, Solothurn, Switzerland

Psoriasis affects 2 to 4% of the population across the world. GWAS studies have revealed that several genes regulated by the NF-κB pathway are implicated in the pre-disposition of psoriasis. However, the cell-type-specific role of NF-kB in initiating and sustaining inflammatory responses is not fully understood in the skin.

NF-κB activation in murine epithelial cells, achieved by inhibiting IκBα, an inhibitor of NF-κB, resulted in the development of progressive psoriasis-like skin lesions (hereafter referred to as IκBa^{E-KO} mice). The skin lesions were characterised by hyperkeratosis, immune cell infiltration, and an increase of pro-inflammatory cytokines, which reached severity by P7.

To elucidate how epithelial NF-κB coordinates the immune kinetics through the interaction between immune cells and cytokines, we dissected the myeloid and T cell landscape via multi-dimensional flow cytometry and analysed the gene expression using qPCR in the IκBα^{E-KO} mice skin. We found an increase in macrophage and monocyte populations that differentially express MHC II and Ly6C in the IκBα^{E-KO} mice. Additionally, an increase in IL-17a-producing γδ T cells was observed, which was accompanied by an elevated expression of IL-17a and IL-17f cytokines in the IκBα^{E-KO} mouse skin. To investigate the functional relevance of elevated IL-17a and f, we injected the IκBα^{E-KO} mice with their respective neutralisation antibodies for 7 days post-birth.

Interestingly, neutralization of IL-17a prevented and IL-17f ameliorated the skin phenotype of the IκBα^{E-KO} mice. We further analysed the local immune cell milieu and gene expression in the injected mice and observed a differential role of IL-17a and IL-17f in regulating inflammation in the IκBα^{E-KO} mice skin. These results demonstrate that epithelial NF-κB is sufficient to activate the IL-17-mediated skin pathogenesis, highlighting the key role of NF-κB in eliciting γδ T cells and IL-17 response in driving the skin pathology.

14

Title: Unique Role of an Ion Channel in Skin Homeostasis and Inflammation

Authors: Ye Mon Soe[1], Seen Ling Sim[1], Kiarash Khosrotehrani[1] and Snehlata Kumari[1]

1. The University of Queensland Frazer Institute, Brisbane, Australia

Skin homeostasis is regulated by a coordinated network of immune cells, non-immune cells and effector molecules (e.g., cytokines and chemokines), and immunomodulatory signalling pathways (e.g., NF-κB). Our previous studies have shown that epithelial cells are the key regulators of skin homeostasis and inflammation. Ion channels (IC) play a crucial role in maintaining skin homeostasis such as proliferation and differentiation in the epidermis, however, their role in skin epithelial cells is not fully understood. Here, we have focused on understanding the epithelial cell-specific role of an IC in the skin. We generated an epithelial-specific transgenic IC knockout mice using K14-Cre (hereafter named as IC^{E-KO}) and observed perinatal lethality in the IC^{E-KO} mice. We analysed the skin of the IC^{E-KO} mice and found architectural abnormalities at postnatal (P) day P1-P2. Specifically, the IC^{E-KO} mice skin was translucent compared to the littermate controls, and histological analysis revealed a thinner epidermis. Mechanistically, we found reduced expression of epidermal differentiation proteins, keratin 10, loricrin and filaggrin, which was accompanied by a mild defect in skin barrier integrity. IC^{E-KO} mice also showed an upregulation of NF-κB signalling pathways and pro-inflammatory cytokines and chemokines, as well as recruitment of immune cells. Collectively, we identified a unique role of a specific ion channel in the epithelial cells in integrating epidermal and dermal signals and simultaneously controlling skin development and inflammation, and hence, crucial to maintain skin homeostasis.

15

Title: One in Five Registry-Coded Melanomas Are Reclassified on Expert Review: Findings from the QSkin Cohort

Authors: X. Hang[1,2], Lambie. D [2,3,4], Brennan. T [4], Whiteman. D [1,2]

[1]QIMR Berghofer Medical Research Institute, Population Health, Brisbane, Queensland
[2]University of Queensland, Frazer Institute, Brisbane, Queensland

[3]Sullivan Nicolaides Pathology, Brisbane, Queensland
[4]Princess Alexandra Hospital, Pathology Queensland, Brisbane, Queensland

Background: Histopathologic diagnosis of melanocytic lesions is subject to interobserver variability, particularly for borderline and early lesions. Registry-based melanoma coding may differ from expert histopathologic assessment. The QSkin study is a population-based cohort of Australian adults (age 40-69) with linked histopathology and registry data. We aim to evaluate concordance for diagnosis and anatomical site between Queensland Cancer Registry (QCR) data and expert histopathologic review using an ACEMID-based framework.

Methods: Concordance in diagnostic and anatomical site codes for melanoma cases in the QSkin cohort (2010-2019) was assessed between QCR and expert histopathologic review. For the latter, we used a structured REDCap-based instrument, incorporating ACEMID (MPath-Dx2.0) framework and RCPA Invasive Melanoma Structured Reporting Protocol. H&E stained FFPE sections were independently reviewed by two histopathologists, with disagreements resolved by consensus. Anatomical site was harmonised by mapping QCR subsites to ICD categories (C443-C447) and compared with ACEMID coding using percentage agreement and Cohen's kappa (κ).

Results: After excluding incomplete cases, 1010 QCR-coded melanoma cases were analysed. Diagnostic discordance between QCR coding and expert review was 22.1% (n=223). Discordant lesions included QCR-coded as melanoma *in situ* (MIS) (n=94), invasive melanoma (n=98) and other melanoma subtypes (n=31), with invasive cases mainly superficial spreading melanoma. On expert review, these 223 lesions were reclassified from QCR-coded melanoma to 130 naevi (53 benign, 77 dysplastic), 32 atypical melanocytic proliferations and 61 indeterminate/non-diagnostic lesions. Among discordant lesions, 68% QCR-coded MIS were reclassified as benign naevi, invasive melanomas were reclassified to both benign (56%) and lower-grade lesions (44%), and other melanoma subtypes were reclassified to benign naevi (36%) and lower-grade lesions (64%). Anatomical site concordance between QCR coding and expert review was high (93.0%, κ=0.90).

Conclusion: A substantial proportion of registry-coded melanomas, particularly MIS and thin superficial spreading melanomas, were reclassified as non-melanoma on expert review, highlighting diagnostic variability and potential overdiagnosis in early lesions. Site recording remained highly concordant. These findings support the use of standardised frameworks such as MPath-Dx2.0 to improve diagnostic consistency.

16

Title: One in Five Registry-Coded Melanomas Are Reclassified: Predictors from the QSkin Cohort

Authors: X. Hang[1,2], Lambie. D [2,3,4], Brennan. T [4], Whiteman. D [1,2]

[1]QIMR Berghofer Medical Research Institute, Population Health, Brisbane, Queensland
[2]University of Queensland, Frazer Institute, Brisbane, Queensland
[3]Sullivan Nicolaides Pathology, Brisbane, Queensland
[4]Princess Alexandra Hospital, Pathology Queensland, Brisbane, Queensland

Background: Histopathologic diagnosis of melanocytic lesions is subject to interobserver variability, particularly for borderline lesions. Registry-coded melanoma may therefore differ from expert histopathologic assessment. While diagnostic discordance has been described, factors associated with reclassification remain unclear. We aimed to identify predictors of reclassification of Queensland Cancer Registry (QCR)-coded melanoma on independent expert review within the QSkin cohort.

Methods: We compared diagnostic and anatomic site codes for melanoma cases in the QSkin cohort (2010 to 31/12/2019) from two data sources: (1) QCR and (2) expert histopathologic review. For the latter, we used a structured REDCap-based instrument, incorporating the MPath-Dx2.0 framework and the RCPA Invasive Melanoma Structured Reporting Protocol. Reclassification from melanoma (melanoma *in situ* MIS or invasive) to non-melanoma was modelled as a binary outcome using multivariable logistic regression. Predictors included QCR diagnostic group (MIS vs invasive), anatomical site (head/neck, trunk, upper limb, lower limb), age and sex. Odds ratios (ORs) with 95% confidence intervals (CIs) were reported.

Results: Among 944 analysable cases, 60% were male with a median age of 65 years (IQR 59-69). Lesions were most commonly located on the trunk (37%) and upper limb (31%). 188 (20%) were reclassified as non-melanoma on expert review. In multivariable analysis, upper limb lesions were less likely to be reclassified than trunk lesions (OR 0.44, 95% CI 0.29-0.68, p=0.001). Increasing age was associated with a small reduction in odds of reclassification (OR 0.98 per year, 95% CI 0.96-1.00, p=0.05). Reclassification did not differ significantly by sex (OR 0.96, 95% CI 0.68-1.36) or QCR-coded MIS versus invasive melanoma (OR 1.30, 95% CI 0.93-1.82). In an exploratory model, reclassification was concentrated in diagnostically uncertain lesions.

Conclusion: Reclassification of registry-coded melanoma is not confined to MIS and is influenced by anatomical site and diagnostic uncertainty. Upper limb lesions were less likely to be

reclassified, while increasing age showed a modest association. These findings suggest diagnostic discordance reflects the inherent difficulty of borderline melanocytic lesions and highlight the need for cautious interpretation of registry-based melanoma data, particularly for early lesions, and wider adoption of standardised histopathologic classification frameworks.

17

Title: Abstract Title

Authors: Parvovirus B19 Infection Is Associated with Increased Risk of Autoimmune Blistering Diseases: A Global Large-Scale Propensity-Matched Cohort Study

H. Tseng[1,3], JW. Frew[1,3], DF. Murrell[2,3].

[1] Department of Dermatology, Liverpool Hospital, Sydney, New South Wales, Australia
[2] Department of Dermatology, St. George Hospital, Sydney, New South Wales, Australia
[3] School of Clinical Medicine, Faculty of Medicine and Health, UNSW Sydney, Australia

Background: Autoimmune blistering diseases (AIBDs), including pemphigus and bullous pemphigoid (BP), are associated with substantial morbidity and immunosuppressive burden. While their immunopathogenesis is well characterised, environmental and infectious triggers remain incompletely defined. Parvovirus B19 has been implicated in autoimmune phenomena; however, its association with AIBDs has not been systematically evaluated at scale.

Methods: We conducted a retrospective cohort study using the TriNetX global health research network. Parvovirus infection was defined by either ICD-10 code B34.3 or documented Parvovirus B19 IgM positivity (LOINC 5274-6), capturing both clinically diagnosed and serologically confirmed recent infection. Patients with parvovirus infection were propensity score matched 1:1 to unexposed controls (n = 97,719 per cohort) on demographics and relevant comorbidities. Outcomes included incident pemphigus, BP, and overall AIBDs. Hazard ratios (HRs) were calculated using Cox proportional hazards models with unlimited follow-up.

Results: Parvovirus infection was associated with a significantly increased risk of AIBDs. Specifically, exposure conferred a 104% increased risk of pemphigus (HR 2.04, p = 0.029), a 137% increased risk of BP (HR 2.37, p = 0.001), and a 55% increased risk of any AIBD (HR 1.55, p = 0.001). These associations were consistent across outcome definitions and following matching, supporting the validity of the findings.

Conclusion: Parvovirus B19 infection is associated with a significantly increased risk of subsequent AIBDs, including both pemphigus and BP. The consistency of this signal across disease subtypes suggests a broader role of infection-driven immune dysregulation rather than disease-specific mechanisms. These findings highlight a potential viral trigger in AIBD pathogenesis and warrant further mechanistic and prospective investigation.

18

Title: Cutaneous ageing in Asian skin: Loss of biomechanical resilience with preservation of epidermal architecture.

Authors: K.J. Ng[1,2], Ho J.J.[1,2], A.Y.L. Lim[1,2,3], Yew Y.W[2,3], S. Thng[2,3], Lin L[1,2], R.E.B Watson[1,2,3]

[1]A*STAR Skin Research Labs, A*STAR Singapore, Republic of Singapore
[2]Skin Research Institute of Singapore (SRIS), Republic of Singapore
[3]National Skin Centre, NHG Health Group, Republic of Singapore

Ageing is characterized by a progressive decline in physiological function and is influenced by both intrinsic genetic and extrinsic lifestyle and environmental factors. Our current understanding of cutaneous ageing has been derived from studies in predominantly Caucasian populations, with little to no studies performed on Asian skin. Our previous research has demonstrated that the structural organization of healthy, young skin is ethnicity-dependent, and that alterations in epidermal morphology in Caucasian subjects are closely associated with biomechanical decline.

Here we explore the consequences of ageing on biomechanical function and epidermal morphometry of the skin of healthy Singaporean participants of Chinese heritage (N=203; 21-76 years). Our data suggests that for photoprotected skin, a biomechanical transition occurs around 50 years of age, with significantly reduced elasticity (R2, R7; p=0.001) and an increase in "fatigue" parameters (R4, p=0.001; R6, p=0.0001; R9, p=0.01). By 70 years of age, the skins' biomechanical profile has fundamentally shifted from elastic to fatigue-prone (R10; p=0.05). Notably, histologic interrogation of intrinsically aged skin revealed no significant age-related differences in either epidermal thickness, dermal-epidermal junction (DEJ) convolution or *stratum corneum* thickness. At photoexposed sites, biomechanical decline was accelerated and was measurable around 40 years of age. Histologically, we observe a flattened DEJ (p=0.05) but with no alteration to the epidermal thickness or to the *stratum corneum*. This contrasts sharply to observations of Caucasian skin, where DEJ flattening and epidermal atrophy are well-documented features of ageing at both photoprotected and photoexposed body sites.

These findings suggest that the trajectory of intrinsic cutaneous ageing is ethnicity-dependent, highlighting the importance of including diverse ethnic populations in cutaneous ageing research.

19

Title: Bimekizumab impact on dichotomous IHS4 response levels over 3 years in moderate to severe HS: Results from BE HEARD EXT

Authors: Johannes S. Kern[1], Thrasyvoulos Tzellos[2–4], Dillon Mintoff[5], Kelsey R. van Straalen[6], Angelo V. Marzano[7,8], Koremasa Hayama[9], Vivian Y. Shi[10], Evelina van Ree[11], Bengt Hoepken[12], Nicola Tilt[13], Christopher J. Sayed[4,14].

[1]Monash University, School of Translational Medicine and Alfred Hospital, Department of Dermatology, Melbourne, Victoria, Australia; [2]Nordland Hospital Trust, Department of Dermatology, Bodø, Norway; [3]UiT – The Arctic University of Norway, Faculty of Health Sciences, Department of Clinical Medicine, Tromsø, Norway; [4]European Hidradenitis Suppurativa Foundation (EHSF) e.V., Dessau, Germany; [5]Mater Dei Hospital, Department of Dermatology, Msida, Malta; [6]Erasmus University Medical Center, Department of Dermatology, Rotterdam, The Netherlands; [7]Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Dermatology Unit, Milan, Italy; [8]Università degli Studi di Milano, Department of Pathophysiology and Transplantation, Milan, Italy; [9]Nihon University School of Medicine, Division of Cutaneous Science, Department of Dermatology, Tokyo, Japan; [10]University of Washington, Department of Dermatology, Seattle, Washington, USA; [11]UCB, Breda, The Netherlands; [12]UCB, Monheim, Germany; [13]UCB, Slough, UK; [14]University of North Carolina School of Medicine, Department of Dermatology, Chapel Hill, North Carolina, USA

Background: Hidradenitis suppurativa (HS) severity can be dynamically assessed using the International HS Severity Score System (IHS4). As a dichotomous outcome, IHS4-55 is a validated tool that allows for discrimination between active treatment and placebo, due to its association with a reduction in inflammatory lesion counts, including draining tunnels. Bimekizumab (BKZ) is a humanised IgG1 monoclonal antibody which selectively inhibits interleukin (IL)-17F in addition to IL-17A. In the pivotal phase 3 BE HEARD I&II trials and their open-label extension, BE HEARD EXT, BKZ led to clinical improvements in IHS4-55, IHS4-75, IHS4-90 and IHS4-100 in patients with moderate to severe HS, over 2 years.

Here, we report IHS4-55, IHS4-75, IHS4-90 and IHS4-100 responses over 3 years (148 weeks) from the BE HEARD I&II trials and BE HEARD EXT.

Methods: Data were pooled from the phase 3 BE HEARD I&II trials (NCT04242446/NCT04242498) and BE HEARD EXT (NCT04901195). Data are reported for patients randomised to BKZ from baseline in BE HEARD I&II who then entered BE HEARD EXT (BKZ Total). IHS4-55, IHS4-75, IHS4-90 and IHS4-100 responses were defined as ≥55%, ≥75%, ≥90% or ≥100% improvement in IHS4 total

score from baseline, respectively. Data are reported as observed case (OC) and analysed using a modified non-responder imputation (mNRI) over 3 years. For mNRI, patients discontinuing treatment due to lack of efficacy or treatment-related adverse events were considered non-responders; multiple imputation was used for other missing data.

Results: Of the 1,014 patients in BE HEARD I&II, 556 were randomised to BKZ at baseline, completed Year 1 (Week 48) and entered BE HEARD EXT. Of these, 367 patients in BE HEARD EXT completed a lesion count assessment at Year 3. At Year 1, 75.5%, 58.8%, 41.2% and 25.2% of patients in the BKZ Total group achieved IHS4-55, IHS4-75, IHS4-90 and IHS4-100 responses, respectively. Achievement of IHS4-55, IHS4-75, IHS4-90 and IHS4-100 response at Year 1 improved to Year 3 (OC). Similar trends were observed using mNRI methodology.

Conclusion: In conclusion, bimekizumab demonstrated clinically meaningful improvements at Year 1, as measured by IHS4-55 and the more stringent IHS4-75, IHS4-90 and IHS4-100 thresholds, and further improved over 3 years of treatment.

At Year 3, 40% of bimekizumab-treated patients achieved total resolution of inflammatory lesions, as measured by IHS4-100.

21

Title: A novel human immunomodulatory peptide as a candidate therapeutic for inflammatory skin diseases

Authors: A.S. Ashhurst[1], J. Rawlings[1], S. Stockdale[1], D. Ford[2,3], J.W.C Maxwell[2,3], A. Avila[1,4], D.M. McDonald[1,2], A. Tanaka[5], K.M. Bertram[4], C.C. Hanna[2], R.A. Ireland[1], S. Donnelly[5], A. Harman[4], R.J. Payne[2,3], S.N. Byrne[1].

[1]The University of Sydney, School of Medical Sciences, Faculty of Medicine and Health, Sydney NSW.
[2]The University of Sydney, School of Chemistry, Faculty of Science, Sydney NSW.
[3]The University of Sydney, Australian Research Council Centre of Excellence for Innovations in Peptide and Protein Science, Sydney NSW.
[4]The Westmead Institute for Medical Research, Sydney NSW.
[5]The University of Technology Sydney, School of Life Sciences, Faculty of Science, Sydney NSW.

Inflammatory skin diseases such as psoriasis and atopic dermatitis, which affect 2–6% and 8–15% of Australians respectively, represent a significant and growing health burden. Conventional steroidal and other frontline therapies are not consistently effective and may cause adverse effects, while biologics such as monoclonal antibodies are highly effective but often inaccessible due to cost. There remains a clear need for safe, cost-effective, and targeted therapies. We identified a novel role for a human peptide in suppressing inflammation. A modified, synthetically produced version of this peptide (called RP23) was developed to enhance manufacturability. In *in*

vivo murine models, subcutaneous RP23 injection significantly reduced disease severity in DNFB-induced contact hypersensitivity and imiquimod-induced psoriasis. Intradermal injection of RP23 into human skin explants reduced activation of dermal dendritic cells.

We consequently developed a series of topical formulations of the peptide designed for ease of use, that significantly suppressed psoriatic disease in mice when applied either prophylactically or therapeutically, and synergistically enhanced therapeutic efficacy of topical steroid use. Topical RP23 also reduced severity of disease in a murine model of atopic dermatitis (oxazolone-induced). Reductions in disease were isolated to the local area in which RP23 was delivered, unlike topical glucocorticoid or injected monoclonal antibody therapy, which caused systemic immune suppression. In psoriatic mice skin, RP23 reduced the number and proportion of neutrophils and dermal proinflammatory TCRgd T-cells, and reduced levels of IL-17, IL-12p40 and IL-6. Upon topical application to human skin explants, RP23 penetrated the stratum corneum and colocalised with HLA-DR cells in the epidermis and dermis. Confocal imaging of murine macrophages demonstrated that these cells readily take up RP23 via phagocytosis, with peptide co-localising in lysosomes. Culture of primary murine or human macrophages with RP23 led to reduced IL-12/23(p40) and IL-6 release after TLR-stimulation, highlighting direct immunomodulatory effects on myeloid cells, a key ongoing research interest. RP23 offers potential for development as a novel, locally acting peptide-based therapy for patients seeking improved management of inflammatory skin diseases.

24

Title: A tale of two dermatoses; morphoea and extra-genital lichen sclerosus in a single lesion.

Authors: Aalia Syed[1,2], Dédée F. Murrell[1,2], Zahra Asadi-Kani[3], Nasim Niknezhad[1,2],

Affiliations:
[1]University of New South Wales, Faculty of Medicine, Sydney, NSW
[2]St. George Hospital, Department of Dermatology, Sydney, NSW
[3]Danesh Pathobiology Laboratory, Department of Pathology, Tehran, Tehran Province

Background and significance: Morphoea and lichen sclerosus (LS) are chronic inflammatory dermatoses with distinct clinical and histopathological features. Their coexistence, particularly in extragenital disease, is increasingly recognised, but overlap within a single lesion is rare and has implications for management. We report a case of morphoea-extragenital LS overlap within a single truncal lesion, and a review of the literature.

Methods: A 62-year-old female presented with a five-year history of asymptomatic hyper- and hypopigmented truncal plaques, on a background of hyperthyroidism. Examination revealed hyperpigmented plaques on the back, and sclerotic and ivory-coloured plaques across the back and flanks. There was no genital involvement. A punch biopsy was obtained from the left flank for

histopathology. The patient was treated with narrowband ultraviolet B phototherapy three times weekly and 10mg oral methotrexate weekly. A search of PubMed and Embase databases was performed using the terms ("morphoea" OR "morphea" OR "localised scleroderma" OR "localized scleroderma") AND "extragenital lichen sclerosus". Articles were screened and critically appraised.

Major findings: Histopathology demonstrated overlapping features of LS (epidermal atrophy, hyperkeratosis and basal vacuolar change) and morphoea (dermal sclerosis with thickened collagen bundles, adnexal entrapment and lymphoplasmacytic infiltrate). Following 6 months of treatment, the patient showed significant clinical improvement, with repigmentation of hypopigmented plaques and softening of sclerotic lesions.

The literature search identified 48 articles encompassing 82 reported cases of overlapping disease. There was a female predominance (3:1) and truncal involvement was most frequent. Associations with lichen planus, systemic lupus erythematosus, bullous pemphigoid, primary biliary cirrhosis and eosinophilic fasciitis, were observed, suggestive of shared autoimmune mechanisms. LS-morphoea overlap was reported at sites of prior trauma (striae, surgical scars and injection sites), healed scars, as well as Blaschkoid and dermatomal distributions, likely reflecting the Koebner phenomenon, isotopic response and cutaneous mosaicism, respectively.

Conclusion: This case of morphoea and extragenital LS in a single lesion supports the hypothesis of a shared spectrum of localised sclerosing disorders. Histopathology is pivotal in the diagnosis of concomitant disease.

25

Title: International development and validation of a 5-point composite investigator global assessment scale for epidermolysis bullosa acquisita

Authors: Aalia Syed[1,2], Sera Sarsam[1,2], Aikaterini Patsatsi[3], Baoqi Yang[4], Kossara Drenovska[5], Angelo Marzano[6,7], Snejina Vassileva[5], Emiliano Antiga[8], Maryam Daneshpazhooh[9], Soner Uzun[10], Anisa Mosam[11,12], Avital Banial[13], Eli Sprecher[13], Nisha Chandran[14], Donna Culton[15], Dipankar De[16], Dario Didona[17], Ncoza Dlova[11], Pascal Joly[18], Johannes Kern[19], Yen Loo Lim[20,21], Hamidreza Mahmoudi[9], Aimee S. Payne[22], Marwah A Saleh[23], Elia Valeva[5], Jun Yamagami[24], Boaz Shulruf[1], Dédée F. Murrell[1,2]

Affiliations:

[1]University of New South Wales, Faculty of Medicine, Sydney, NSW

[2]St. George Hospital, Department of Dermatology, Sydney, NSW

[3]Aristotle University, Second Department of Dermatology, Thessaloniki, Central Macedonia

[4]Shandong First Medical University, Shandong Provincial Hospital for Skin Diseases, Taian, Shandong

[5]Aleksandrovska University Hospital, Department of Dermatology and Venereology, Sofia

[6]Fondazione IRCCS Ca 'Granda Ospedale Maggiore Policlinico, Dermatology Unit, Milan, Lombardy
[7]Università degli Studi Di Milano, Department of Pathophysiology and Transplantation Milan, Lombardy
[8]University of Florence, Section Dermatology, Florence, Tuscany
[9]Tehran University of Medical Sciences, Department of Dermatology, Tehran, Tehran Province
[10]Akdeniz University Faculty of Medicine, Department of Dermatology and Venereology, Antalya, Antalya Province
[11]University of Kwazulu-Natal, Department of Dermatology, Durban, KwaZulu-Natal
[12]Inkosi Albert Luthuli Central Hospital, Department of Dermatology, Durban, KwaZulu-Natal
[13]Tel Aviv Soura sky Medical Center, Division of Dermatology, Tel Aviv, Gush Dan
[14]National University Hospital, Division of Dermatology, Singapore
[15]University of North Carolina at Chapel Hill, Department of Dermatology, Chapel Hill, North Carolina
[16]Postgraduate Institute of Medical Education and Research, Department of Dermatology, Venereology and Leprology, Chandigarh, Punjab
[17]Philipps-Universität Marburg, Department of Dermatology and Allergology, Marburg, Hessen
[18]Rouen University Hospital, Department of Dermatology, Rouen, Normandy
[19]Monash University and Alfred Health, The School of Translational Medicine, Melbourne, VIC
[20]National Skin Centre, Immunodermatology Unit, Singapore
[21]Nanyang Technological University, Lee Kong Chian School of Medicine, Singapore
[22]Columbia University, Department of Dermatology, New York City, New York
[23]Cairo University, Faculty of Medicine, Cairo
[24]Tokyo Women's Medical University, Department of Dermatology, Tokyo

Background and significance: Epidermolysis bullosa acquisita (EBA) is a rare autoimmune blistering disease for which no validated Investigator Global Assessment (IGA) scale for severity assessment exists. The absence of an IGA, which is the Food and Drug Administration's (FDA's) preferred outcome measure, is significant as it hinders reliable disease assessment, treatment evaluation and clinical trial development. This study aimed to develop and validate a 5-point composite IGA scale for EBA (EBA-IGA) and assess the scale against existing scoring instruments; the EB Disease Activity and Scarring Index (EBDASI) and the EBA Disease Area Index (EBADAI). We hypothesised that the EBA-IGA would demonstrate excellent interrater reliability, intrarater reliability, and strong convergent validity with existing severity instruments.

Methods: Content and face validity of the EBA-IGA were established through international dermatologist and patient surveys. A multi-centre, image-based validation study was conducted using an initial de-identified photo set of 35 EBA patients independently scored by 24 international dermatologists with expertise in blistering diseases using the four instruments. Four weeks later, a second de-identified photo set, comprising 20 new EBA patients and 10 repeat EBA patients, was distributed to assess for intrarater reliability. Interrater and intrarater reliability

were statistically assessed using the intraclass correlation coefficients (ICC), and convergent construct validity was assessed using Pearson's correlation coefficient (r). ICCs greater than 0.9 were considered excellent.

Major findings: For interrater reliability, the ICCs for overall scores were: EBA-IGA 0.979, EBDASI 0.969 and EBADAI 0.962. For intrarater reliability, the ICCs for overall scores were: EBA-IGA 0.931, EBDASI 0.890 and EBADAI 0.891. The EBA-IGA demonstrated a very strong positive correlation with the EBADAI ($r = 0.829$, $p<0.001$) and a strong positive correlation with the EBDASI ($r = 0.755$, $p<0.001$). The EBADAI was very strongly positively correlated with the EBDASI ($r = 0.837$, $p<0.001$).

Conclusion: The EBA-IGA demonstrated excellent interrater and intrarater reliability, as well as strong-to-very-strong convergent validity, indicating its utility in FDA-compliant clinical trials. Together, the EBA-IGA, EBDASI and EBADAI are complementary instruments for harmonising disease assessment in clinical practice and trial settings.

26

Title: Trial in progress: a phase 3 randomized study of low-dose intralesional cemiplimab versus primary surgery for patients with early-stage cutaneous squamous cell carcinoma (CLEAR CSCC)

Authors: *Michael R. Migden,[1] Sherrif Ibrahim,[2] John Strasswimmer,[3] Nathalie Zeitouni,[4] Greg J. Goodman,[5,6] Kiarash Khosrotehrani,[7,8] Pablo Fernández-Peñas,[9,10] John Frew,[11] Kurt Gebauer,[12] Suk-Young Yoo,[13] Frank A. Seebach,[13] Israel Lowy,[13] Sabina Sandigursky,[13] Matthew G. Fury[13]*

[1]The University of Texas MD Anderson Cancer Center, Departments of Dermatology and Head and Neck Surgery, Houston, TX, USA
[2]Rochester Dermatologic Surgery, Department of Dermatology, Victor, NY, USA
[3]Dermatology Associates of the Palm Beaches, Dermatology & Mohs Surgery, Delray Beach, FL, USA
[4]Medical Dermatology Specialists, Division of Dermatology, Phoenix, AZ, USA
[5]Monash University, Faculty of Medicine, Nursing and Health Sciences, Clayton, VIC, Australia
[6]University College London, Faculty of Medical Sciences, London, United Kingdom
[7]The University of Queensland, Frazer Institute, Faculty of Health, Medicine and Behavioural Sciences, Woolloongabba, QLD, Australia
[8]Princess Alexandra Hospital, Department of Dermatology, Woolloongabba, QLD, Australia;
[9]Westmead Hospital, Department of Dermatology, Westmead, NSW, Australia
[10]The University of Sydney, Sydney Medical School, Sydney, NSW, Australia
[11]University of New South Wales, School of Clinical Sydney, NSW, Australia
[12]Fremantle Dermatology, Dermatology Department, Fremantle, WA, Australia
[13]Regeneron Pharmaceuticals, Inc., Tarrytown, NY, USA

Introduction: Cemiplimab 350 mg administered intravenously every 3 weeks is approved in the US and several other countries for the treatment of adult patients with metastatic or locally advanced cutaneous squamous cell carcinoma (CSCC) who are not candidates for curative surgery

or curative radiation. Surgery is the standard of care for early-stage CSCC; however, for patients who prefer non-surgical management of early-stage CSCC, low-dose intralesional (IL) cemiplimab has demonstrated promising clinical activity in a pilot study (NCT03889912). The purpose of this study (NCT06585410) is to determine the noninferiority of IL cemiplimab versus primary surgery, along with its safety, tolerability, and efficacy in patients with early-stage CSCC.

Methods: In this phase 3, randomized, open-label, multicenter study, approximately 369 patients with early-stage CSCC will be randomized 2:1 to cemiplimab (5 mg IL every week for 6 weeks) versus primary surgery. Key inclusion criteria include: patients aged ≥18 years; a histologically confirmed invasive CSCC target lesion that is amenable to curative surgery as determined by size ≥1.0 cm and ≤2.0 cm (longest diameter) located in the head and neck, hand, or pre-tibial surface; Eastern Cooperative Oncology Group (ECOG) performance status ≤1; and adequate hepatic, renal, and bone marrow function. Key exclusion criteria include target lesion of keratoacanthoma, autoimmune disease requiring treatment with systemic autoimmune suppressants, concurrent or prior solid tumor or hematologic malignancy (except for protocol-allowed exceptions), and a history of solid organ transplant. Patients will be followed for approximately 3 years. The primary objective is to assess the non-inferiority of IL cemiplimab versus primary surgery by event-free survival. Secondary objectives include safety, tolerability, longest diameter of surgical defect after resection in both arms, and composite complete response in the experimental arm. This study is currently recruiting. Enrollment is planned at study sites across North America and Australia.

28

Title: Use of 5% Imiquimod Cream to Successfully Treat Extra-mammary Paget Disease in a 75-Year-Old Man, A Case Report.

Authors: Zahra Almosawy[1], Peter Fergin[2,]

[1] Resident, Department of Dermatology, Monash Health, Clayton, Vic, Australia
[2] Dermatologist, Department of Dermatology, Monash Health, Clayton, Vic Australia

Extra-mammary Paget Disease (EMPD) is a rare and slow growing skin-cancer of apocrine-rich tissue. Traditionally, wide-local excision has been used to treat the disease; but this is not without complications. Imiquimod cream is a topical immune response modulator. There is emerging literature supporting its efficacy in treating EMPD. This report details the use of imiquimod cream for the clearance of EMPD in two different body sites.

The 75-year-old male patient originally had an eruption in his right axilla for 5 years. EMPD was eventually diagnosed on skin-biopsy. The region was treated successfully with wide local excision and sentinel node removal. One year and a half later, he presented with a persistent eruption in the left inguinal region. Histopathology confirmed EMPD in this additional site. Two surgical excisions failed to achieve clearance of the rash. The latter attempt was complicated by wound dehiscence. A further biopsy, performed eighteen-months later, confirmed persistent EMPD. An

additional, ill-defined, atrophic site on the right scrotum also demonstrated EMPD on histopathology. Reluctant to pursue further surgery, the patient sought alternative therapy. A trial of imiquimod 5% cream was implemented. The cream was applied daily for three months. On review twelve-months later, the left inguinal and right scrotal areas remained clinically clear of EMPD.

Conclusion: This case illustrates the role of imiquimod cream as a promising adjuvant or alternative therapy for EMPD. Considering the sensitive anatomical sites and older age group typically affected, topical therapy may be a particular option in selected patients.

29

Title: Patch Testing Outcomes and Diagnostic Yield in a Tertiary Dermatology Service: A Six-Month Retrospective Review

Authors: NKM. Yoong[1], L. Ly[1,2,3], FYX, Lai[1,3], C. Higgins[1,3].

[1] Monash Health, Dept. of Dermatology, Clayton VIC.
[2] Eastern Health, Dept. of Dermatology, Box Hill VIC.
[3] Skin Health Institute, Dept. of Dermatology, Carlton VIC.

Background
Patch testing is central to the diagnosis of allergic contact dermatitis (ACD). This study reviewed patients attending a tertiary patch testing clinic over six months to quantify test completion, diagnostic yield and clinical outcomes.

Methods: A retrospective chart review was conducted at a public tertiary dermatology service. Data analysed included patient demographics, history of atopic dermatitis (AD), dermatitis distribution, reported exposures and patch testing results. Analyses were descriptive. Fisher's exact test was used to compare rates of positive patch test reactions between patients with and without AD.

Results: Forty-five patients were referred to the patch testing clinic during the study period; of these, 23 underwent patch testing. Dermatitis most commonly involved the face or eyelids (13/23) and hands/palms (8/23). Reported exposures were related to cosmetics, hair products, glove use, wet work and detergents. Among these, 16 demonstrated at least one positive reaction and 6 had no reactions. One patient discontinued testing due to severe eczema flare that precluded interpretation. Of the remaining patients who did not complete testing within the review period, the majority had rescheduled appointments, with patch application pending beyond six months. Four patients repeatedly failed to attend and were subsequently discharged.

Metals, fragrances and preservatives were the most common allergen groups; nickel was the single most frequent allergen. Positive reactions were less frequent in patients with AD compared with those without AD, though this difference was not statistically significant (p = 0.33). A diagnosis of ACD was documented in six patients and irritant contact dermatitis in three.

Conclusion: As the only adult public patch testing clinic in Victoria, this service managed a substantial referral volume under conditions of high demand. Among patients who completed patch testing, diagnostic yield was high, with metals, fragrances, and preservatives most commonly implicated. These findings affirm the strong clinical value of patch testing in routine dermatological practice. The six-month review period represents a limitation of this study, as a proportion of referrals remained pending at the time of analysis. Longer-term follow-up would better capture overall completion rates and diagnostic outcomes. Nonetheless, these findings highlight opportunities to further support timely diagnosis of allergic.

30

Title: Time-Dependent Dynamics of Norepinephrine and Beta-Adrenergic Blockade on CD8+ T-Cell Cytotoxicity in Melanoma

Authors: Thuy Luong[1,2], Cindy Tseng[1], Natalie Teh[2,3], Robyn Saw[2,3,4], Diona Damian[2,3,4], G. Greg Neely[5], Jess Tiffen[1], J. Guy Lyons[1,2,3]

[1]Centenary Institute, The University of Sydney, [2]Sydney Medical School, The University of Sydney, [3]Department of Dermatology, The University of Sydney at Royal Prince Alfred Hospital, [4]Melanoma Institute Australia, [5]School of Life Sciences, The University of Sydney.

Background: Adrenergic signaling, primarily through norepinephrine (NE), is increasingly recognized as a regulator of anti-tumor immunity and the tumor microenvironment. However, its time-dependent effects on CD8+ T-cell-mediated cytotoxicity, and the impact of beta-adrenergic blockade on this process, remain incompletely understood.

Methods: Human A375 melanoma cells and primary CD8+ T cells (post-expansion purity 95%) were cultured for 7 days under matched conditions with vehicle, 10 uM NE, NE plus beta-blockers (1 uM propranolol and 0.2 uM SR59230A), or beta-blockers alone before co-culture. During the 24-hour pre-T-cell phase, melanoma behavior was monitored by Cell Index (CI). After CD8+ T-cell addition, data were normalized to the post-seeding baseline and tracked in a real-time impedance assay at effector-to-target (E:T) ratios of 20:1, 10:1, and 1:1. Cumulative CI burden was analyzed by two-way ANOVA, and kinetics were assessed using one-phase decay modeling.

Results: During the pre-T-cell phase, NE increased melanoma CI relative to vehicle, consistent with enhanced adhesion/proliferation, whereas beta-blocker monotherapy showed no significant difference. After T-cell addition, distinct time- and E:T-dependent effects emerged. At 20:1 and 10:1, CI rapidly declined within 2 and 5 hours, respectively. In both settings, two-way ANOVA and

kinetic modeling showed higher CI in the NE plus beta-blocker group than in the NE-only group, consistent with reduced early tumor control. At 1:1, no significant difference between NE and the combination group was detected during the first 5 hours by either analysis. However, over 30 hours, the combination group showed greater CI reduction than NE alone, indicating a delayed effect under lower T-cell pressure. Notably, beta-blocker monotherapy did not significantly alter cumulative CI burden by ANOVA, but kinetic analysis showed a faster CI increase than vehicle.

Conclusions: Adrenergic modulation of melanoma-CD8+ T-cell interactions is strongly time- and E:T-dependent. NE promoted melanoma growth-related behavior before T-cell addition, while NE plus beta-blockade impaired early tumor control at high E:T ratios but was associated with greater CI reduction during prolonged co-culture at 1:1. Beta-blockade alone showed no overall benefit and may exert unfavorable kinetic effects.

31

Title: Altered immunophenotype may explain the persistence of psoriasis on the lower legs after highly effective biological therapy

Authors: Ali Azimi[1,2,3,4], Juneau Middleton[2,3,4], Lauren Faul[1,2,3], Vivienne Speirs[2] & Pablo Fernandez-Penas[1,2,3]

[1.] Westmead Clinical School, Faculty of Medicine and Health, The University of Sydney, Westmead, New South Wales, 2145, Australia
[2.] Department of Dermatology, Westmead Hospital, Westmead, New South Wales, 2145, Australia
[3.] Centre for Cancer Research, The Westmead Institute for Medical Research, The University of Sydney, Westmead, New South Wales, 2145, Australia
[4.] School of Medical Sciences, Faculty of Medicine and Health, The University of Sydney, Westmead, New South Wales, 2145, Australia

Background: Psoriasis is a chronic, immune-mediated inflammatory skin disease with significant variability in treatment response across different anatomical sites. While biologics have revolutionised psoriasis management, a strong resistance to this therapy in lower-leg (LL) versus non-lower-leg (NLL) lesions suggests underlying molecular differences driving recalcitrance.

Objectives: This study compares the proteome of LL and NLL psoriasis to identify molecular mechanisms that may explain this difference.

Methods: A total of 75 non-invasive biopsies were collected from 25 patients at the Department of Dermatology, Westmead Hospital, Australia. Tape stripping was used to collect samples from LL and NLL psoriatic lesions, as well as normal skin (NS). Proteins were extracted and prepared before their identification and quantification using a data-independent acquisition mass

spectrometry-based proteomics. Statistical and bioinformatic analysis were performed to identify differentially abundant proteins and pathways altered between the lesion sites.

Results: A total of 4,587 unique protein groups were identified across all samples. Differential abundance analysis revealed a trend of downregulated proteins related to innate immune defence in LL lesions. Pathway analysis predicted a strong link to a weakened antimicrobial barrier through downregulation of antimicrobial peptides, and revealed potential additional mechanisms behind psoriatic inflammation, distinct from the traditional IL-23/Th17 pathway in the LL.

Conclusion: Overall, this study proposed novel mechanisms contributing to the recalcitrant nature of LL psoriasis, revealing proteomic signatures that drive persistent inflammation and keratinocyte differentiation. By identifying key deficiencies in innate immune defence and alternative inflammatory pathways, this research may inform the development of site-specific therapeutic strategies to improve outcomes for patients with challenging LL psoriatic lesions.

32

Title: Proteogenomic Detection of Melanoma-Associated Mutations by Mass Spectrometry-Based Proteomics

Authors: Ali Azimi[1,2,3], Mitchell Stark[4], and Pablo Fernandez-Penas[1,2,3]

[1.] Westmead Clinical School, Faculty of Medicine and Health, The University of Sydney, Westmead, New South Wales, 2145, Australia
[2.] Centre for Cancer Research, The Westmead Institute for Medical Research, The University of Sydney, Westmead, New South Wales, 2145, Australia
[3.] Department of Dermatology, Westmead Hospital, Westmead, New South Wales, 2145, Australia
[4.] Frazer Institute, The University of Queensland, Dermatology Research Centre, Brisbane, QLD, Australia

Introduction: Detection of genetic mutations is widely used for tumour diagnosis and classification. However, genomic testing identifies DNA-level alterations irrespective of their translational status, is relatively costly, and may require prolonged turnaround times. On the other hand, proteomics offers a functional alternative by detecting protein products of mutated genes, thereby confirming the translation of genomic alterations.

Materials and Methods: In this study, we investigate the feasibility of proteomic-based mutation detection using four human melanoma cell lines: PT101, PT111, PT129, and SK-MEL-28. Gene mutation profiles for the cell lines were used to computationally generate customised mutation-augmented protein reference libraries. These libraries incorporated missense mutation–derived protein sequences alongside orthogonal positive and negative control peptides. Matched high-resolution liquid chromatography-tandem mass spectrometry (LC–MS/MS) proteomic datasets

for the cell lines were searched against the customised reference library to identify mutation-specific peptides.

Results: Using a stringent threshold of ≥3 peptide-spectrum matches (PSMs), we identified 83, 55, 168, and 48 unique mutation-derived peptides in PT101, PT111, PT129, and SK-MEL-28, respectively. Positive control peptides were consistently detected across all samples (>55% detection), whereas no negative control peptides were identified, supporting analytical sensitivity and specificity.

Conclusion: In conclusion, this study demonstrates proof-of-concept that genetic mutations can be detected directly at the protein level using mutation-informed proteogenomic libraries. This approach provides confirmation of translated mutations and represents a scalable and potentially cost-effective complementary strategy to genomic testing in melanoma and other malignancies.

33

Title: "Minicircle DNA-derived melanocortin peptides enhance melanogenesis via MC1R signalling in murine melanoma cells"

Authors: GN. Robinson[1], RJ. Pickering[1], C. Tikellis[1], A. Sharma[1], MA. Zuniga-Gutierrez[1], M. Bose[1], ME. Cooper[1] & MC. Thomas[1].

[1]Monash University, Department of Diabetes, Melbourne VIC.

Background: Melanocortin 1 receptor (MC1R) signalling is known to play a key role in inducing pigmentation formation in melanocytes. This pilot study project presents a novel way of overexpressing melanogenesis-promoting peptides via minicircle DNA vector to explore mechanisms behind pigmentation. Minicircle DNA is a form of next-generation gene therapy that consists of small circular plasmids with their bacterial elements removed, leading to a greater transfection efficiency and less potential immunologic reactions.

Methods: Chinese Hamster Ovary (CHO) cells were transfected with melanocortin-encoded (alpha melanocyte stimulating hormone and two amino acid substituted gamma melanocyte stimulating hormone variants) minicircle DNA with a secretory tag. Media was collected after 48 hours and applied to B16F10 murine melanoma cells. Melanin absorbance assays were performed to quantify melanin production and oxidative stress was measured via RT-PCR.

Results: B16F10 cells treated with conditioned media from melanocortin encoded minicircle DNA transfected CHO cells showed a significant increase in melanin versus controls.

Inhibitors of melanogenesis reduced this effect.

Oxidative stress was found to be lower in melanocortin peptide treated groups via induction of Nrf2, a master regulator of antioxidant response and Hmox-1, a regulator of oxidative stress-induced cytoprotection.

Conclusion: Minicircle DNA-derived melanocortin peptides can increase melanogenesis *in vitro* and they have an antioxidant effect on cells. This is the first study demonstrating melanocortins produced from minicircle DNA. This pilot study supports further mechanistic research into the role of MC1R, cAMP and oxidative stress pathway signalling in pigmentation. Future research utilising this *in vitro* technique could highlight potential targets in pigmentary skin disease.

34

Title: Glossed over: the increasing importance of ultraviolet-cured gel nail polish in allergic contact dermatitis

Authors: Aalia Syed[1,2], Brandon Tan[1,2], Dédée F. Murrell[1,2]

Affiliations:

[1]University of New South Wales, Faculty of Medicine, Sydney, NSW

[2]St. George Hospital, Department of Dermatology, Sydney, NSW

Background and significance: Allergic contact dermatitis (ACD) is a rare, but increasingly recognised complication of gel nail polish (GNP) use. Hydroxypropyl methacrylate (HPMA) is a potent sensitiser capable of inducing type IV hypersensitivity reactions, particularly due to incomplete curing, which results in inadequate polymerisation and residual monomer exposure. We report a case of rapid-onset, extensive ACD following a single at-home use of HPMA-containing GNP in a 46-year-old woman with pre-existing palmar dyshidrotic eczema.

Methods: Clinical evaluation included detailed exposure history, physical examination and laboratory investigations. Diagnosis was made based on temporal association with GNP use and known allergen exposure. Management was considered and involved oral prednisone 25mg daily, cetirizine 10mg twice daily, and daily wet dressings with mometasone furoate 0.1%, tapered over two weeks.

Major findings:

The patient developed an acute, multifocal vesiculopapular eruption involving the hands, lips, face and neck within 24 hours of at-home GNP use. Prodromal periungual burning occurred six hours post-application, prompting removal of the product, followed by the onset of widespread vesicles and erythematous papules, severe pruritus and paraesthesia. There were no alternative identifiable exposures. Her history was notable for chronic palmar dyshidrotic eczema and nickel contact allergy. Examination demonstrated a multifocal eczematous eruption over the dorsal hands, neck, postauricular, forehead and perioral skin. Vital signs were normal. Laboratory findings revealed mild eosinophilia (0.81×10^9/L) and a mildly elevated C-reactive protein (7 mg/L). Marked clinical improvement was observed at six weeks post-treatment.

These findings are consistent with existing literature, including a 2022 systematic review of 62 cases of GNP-induced ACD, in which HPMA was the most commonly implicated allergen (90.7%).

The sensitisation rate of HPMA is 1% amongst methacrylate-exposed populations. There has been a growing number of occupational and non-occupational cases of methacrylate-induced ACD, corresponding with the trend towards affordable and convenient do-it-yourself (DIY) beauty.

Conclusion: This case highlights the potential for severe, rapid-onset ACD following a single use of at-home GNP, underscoring the need for greater consumer awareness and stricter regulation of DIY methacrylate-containing nail products.

35

Title: Non-lytic necroptotic signaling drives keratinocyte differentiation and delays wound repair via Ca^{2+}-dependent mechanisms

Authors: Yingxue He [1,2], Holly Anderton[1,2], Natasha Silke[1,2], John Silke[1,2]

[1] The Walter and Eliza Hall Institute for Medical Research, Parkville, Melbourne, VIC 3050, Australia
[2] Department of Medical Biology, University of Melbourne, Parkville, VIC 3050, Australia

Necroptosis is best known as a lytic, proinflammatory cell-death pathway mediated by RIPK3 and MLKL. Lytic forms of cell death, such as necroptosis, amplify inflammation, either supporting effective tissue defense or exacerbating an already inflamed environment. Efficient wound repair requires rapid resolution of inflammation; however, damaged skin represents a trigger-rich environment for necroptotic signaling, creating an unresolved paradox.

We found that mice deficient in the key necroptotic mediators, RIPK3 or MLKL, exhibit significantly enhanced epidermal repair across multiple murine models, including following excision wounding. By day 6 post-excision, knockout mice display markedly reduced wound areas compared to wild-type controls. Importantly, this pro-repair phenotype is preserved in epidermis-specific MLKL knockout mice, supporting a keratinocyte-intrinsic role for necroptosis in regulating skin regeneration. Surprisingly, rather than a consequence of inflammatory cell death, we found that MLKL activation in WT keratinocytes induces differentiation and membrane repair rather than cell lysis.

In immortalised human keratinocytes, TSI-induced activation of necroptotic signalling induces rapid Ca^{2+} flux, originating from both intracellular stores and extracellular sources, promoting terminal differentiation rather than cell lysis, evidenced by increased expression of differentiation markers. This Ca^{2+} signaling also engages ESCRT-III-mediated membrane repair. These effects are absent in MLKL-deficient cells, confirming pathway specificity. Consistently, MLKL wild-type keratinocytes exhibit reduced proliferative capacity compared to knockout cells in both 2D

cultures and 3D human skin equivalents. Together, these findings reveal a non-lethal mode of necroptotic signaling.

This adaptive, non-lytic signaling preserves barrier integrity but delays re-epithelialisation. Our findings redefine epidermal necroptosis as a stress-responsive program that modulates keratinocyte fate. Transient inhibition of this pathway may enhance regeneration following barrier disruption without compromising immune defence, positioning necroptosis as a tenable mechanism balancing tissue repair and inflammation.

37

Title: A Mechanistic Case Analysis of Dupilumab in Dual-Therapy Refractory Pemphigoid Gestationis

Authors: Ahmed Abid[1], Ali Abid[2,3], Kelvin Truong[1,2], Jing Jing Li[4], Paul Weller[2]

[1]The University of Sydney, Faculty of Medicine and Health, Sydney, NSW
[2]Liverpool Hospital, Department of Dermatology, Sydney, NSW
[3]University of New South Wales, South-West Sydney Clinical School, Sydney, NSW
[4]Liverpool Hospital, Department of Anatomical Pathology, Sydney, NSW

Pemphigoid gestationis (PG) is a rare autoimmune blistering disorder of pregnancy characterised by autoantibodies directed against BP180. The disease is thought to involve a predominantly eosinophilic, Th2-skewed inflammatory response, with IL-4 and IL-13 acting as key cytokine drivers. While systemic corticosteroids remain the first-line therapy for PG, refractory cases highlight the need for more targeted immunomodulatory approaches. Dupilumab, a monoclonal antibody that inhibits IL-4 and IL-13 signalling via blockade of the IL-4 receptor α subunit, directly targets this Th2 axis and therefore represents a mechanistically rational therapeutic option in PG.

In assessing the effectiveness of the proposed treatment, we present the case of a 31-year-old G4P3 woman with recurrent PG presenting at 15 weeks gestation with pruritic urticarial plaques and bullae involving the abdomen, intermammary region, and upper limb. Initial management with oral prednisone (up to 0.5 mg/kg) was ineffective, and escalation to combination therapy with cyclosporine (3 mg/kg/day) failed to achieve disease control after 4 weeks, with progression of lesions and severe pruritus impairing quality of life. Dupilumab was commenced at 25 weeks gestation (600 mg loading dose followed by 300 mg fortnightly) alongside existing therapy.

A rapid clinical response was observed within 48 hours, with marked reduction in pruritus and cessation of new blister formation. This enabled tapering of corticosteroids and discontinuation of cyclosporine, with sustained remission following cessation of therapy postpartum. No neonatal blistering was observed. The pregnancy was complicated by preterm premature rupture of membranes and preterm delivery; however, multiple confounding factors limited attribution to dupilumab.

This case supports a pathogenic role for Th2-mediated inflammation in PG and demonstrates the clinical efficacy of targeting this pathway. By inhibiting IL-4 and IL-13 signalling, dupilumab likely attenuates eosinophilic inflammation, pruritus, and downstream tissue damage. These findings support consideration of dupilumab as a targeted, steroid-sparing therapy in refractory PG and highlight the need for further studies to define its role in management.

39

Title: UVB exposure drives a tumour-permissive epithelial–immune microenvironment that promotes early cSCC development

Authors: Chenhao Zhou[1], Edwige Roy[1], Jack Galbraith[1], Ho Yi Wong [1], Yung-Ching Kao[1], Katie Lee[1], Samuel X. Tan[1,4], Nicholas M. Muller[1, 4], Janin Chandra[1], Graeme Walker[1], Mitchell S. Stark[1], Quan Nguyen[3], Kiarash Khosrotehrani[1,4]

[1] The University of Queensland, Frazer Institute, Dermatology Research Centre, Experimental Dermatology Group, Brisbane, Australia
[3]QIMR Berghofer Medical Research Institute, Brisbane, Australia
[4]Department of Dermatology, Princess Alexandra Hospital, Brisbane, Australia

Chronic ultraviolet B (UVB) exposure is one of the major risk factors for developing cutaneous squamous cell carcinoma (cSCC). However, the early cellular and molecular events that govern tumour initiation remain incompletely understood. Here, we performed an integrated single-cell transcriptomic analysis of human UV-exposed and UV-protected skin, actinic keratoses (AK), and cSCC lesions, complemented by spatial transcriptomics and a mouse model of chronic low-dose UVB exposure.

UV-exposed skin exhibited a marked shift in epidermal composition, characterised by an increased basal-to-differentiated keratinocytes (KC) ratio and expansion of a highly proliferative basal KC population. These cells displayed enrichment of cell cycle-associated transcriptional programs, including YBX1, RUNX1 and STAT3, and were conserved across UV-exposed skin, AK and cSCC, suggesting a persistent proliferative epithelial state during disease progression. However, despite their stem-supportive features, these KCs retained differentiation-associated signatures and lacked canonical cancer stem cell markers, indicating a transcriptional configuration that is not fully tumour-initiating.

In parallel, UV exposure broadly reprogrammed KC transcriptional profiles, including downregulation of epithelial differentiation, cell-cell adhesion and immune regulatory pathways. Importantly, these findings indicate that the majority of KCs primarily function as modulators of

the UV-exposed skin microenvironment rather than serving as direct cells of origin for SSC. Consistent with this, ligand-receptor analysis revealed extensive remodelling of epithelial-immune crosstalk, including impaired IL34-CSF1R signalling associated with reduced Langerhans cell maturation, and enrichment of immunoregulatory T cell populations such as Tregs and NKT cells. These changes were accompanied by increased immune checkpoint and cytokine signalling interactions across epithelial and immune compartments.

Together, our findings define a UV-induced tissue ecosystem in which proliferative keratinocyte states and coordinated immune remodelling act in concert to create a tumour-permissive microenvironment. This work provides a framework for distinguishing tumour-initiating processes from adaptive field effects and highlight actionable epithelial-immune signalling pathways, including IL34-CSF1R and immunoregulatory networks, as potential targets for early intervention to prevent or limit cSCC development.

40

Title: Proteomic Profiling of Benign and Dysplastic Nevi Using a Non-Invasive Scarless Biopsy Approach

Authors: Fatemeh Mehdikhani [1,2,3], Rachel Teh [1,2,3], Zhaoxiang Cai [4], Victoria Mar [5,6], Peter Soyer [7,8], Monika Janda [9], Pablo Fernandez-Penas [1, 2,3], Ali Azimi [1,2,3]

[1.]Westmead Clinical School, Faculty of Medicine and Health, The University of Sydney, Westmead, New South Wales, 2145, Australia
[2.]Centre for Cancer Research, The Westmead Institute for Medical Research, The University of Sydney, Westmead, New South Wales, 2145, Australia
[3.]Department of Dermatology, Westmead Hospital, Westmead, New South Wales, 2145, Australia
[4.]ProCan, Children's Medical Research Institute, Faculty of Medicine and Health, the University of Sydney, Westmead, NSW, Australia
[5.]School of Public Health and Preventative Medicine, Monash University, Melbourne, Victoria, Australia
[6.]Victorian Melanoma Service, Alfred Health, Melbourne, Victoria, Australia
[7.]Frazer Institute, The University of Queensland, Dermatology Research Centre, Brisbane, QLD, Australia
[8.]Department of Dermatology, Princess Alexandra Hospital, Brisbane, QLD, Australia
[9.]Centre for Health Services Research, Faculty of Medicine, The University of Queensland, Brisbane, QLD, Australia

Background: Melanoma may arise from pre-malignant lesions, benign and dysplastic nevi. Distinguishing between these lesions is critical for improved patient outcome. Histopathology remains the gold standard, but it is invasive and may not always distinguish between these lesions. Therefore, this study aims to apply a non-invasive scarless biopsy technique (tape stripping) combined with proteomics to identify protein biomarkers distinguishing between benign and dysplastic nevi.

Materials and Methods: Scarless biopsy using tape stripping was used to collect samples from patients with benign (n=46) and dysplastic nevi (n=49) attending dermatology clinics at Westmead, Alfred and Princess Alexandra Hospitals. Proteins from the samples were analyzed by data-independent acquisition liquid chromatography–mass spectrometry (DIA LC–MS), followed by data processing and molecular pathway analysis.

Results: Participant characteristics were similar: age (benign: 60.2 ± 12.8 vs dysplastic: 55.9 ± 15.4 years; p = 0.14) and sex distribution (benign vs dysplastic: female 56.5% vs 53.1%, male 43.5% vs 46.9%; p = 0.89). A total of 4,065 proteins were identified. Principal component analysis showed limited separation (PC1: 15.5%, PC2: 9.1%). Differential abundance analysis identified 13 significantly altered proteins (adj. P value < 0.05, |logFC| ≥ 0.5), including C16orf89 and RBBP6. Biological function analysis indicated enrichment of cancer-related processes and protein metabolism in dysplastic nevi, with inhibition of RNA processing, cell viability, and migration, and activation of extracellular matrix organization and tissue remodeling. Molecular pathway analysis showed strong inhibition of EIF2AK4 (GCN2)-mediated amino acid response and translation-related pathways, with suppression of RNA processing and oxidative stress response (NRF2), and activation of extracellular matrix remodeling pathways. Upstream regulator analysis showed inhibition of MYC family members and MLXIPL, with activation of LARP1 and FMR1. Inhibition of NFE2L2 (NRF2) with activation of SOD2 and TXNIP indicated dysregulated oxidative and metabolic stress responses in dysplastic nevi.

Conclusion: This study highlights the potential of non-invasive scarless biopsy combined with proteomics to identify biomarkers like C16orf89 and RBBP6 for distinguishing benign and dysplastic nevi. Dysplastic transformation involves targeted protein synthesis and metabolic changes, warranting further investigation.

41

Title: Ultraviolet Mutational Signature 7 as Definitive Evidence of Cutaneous Origin in a Rare Case of Metastatic Basal Cell Carcinoma

Authors: A. Susanto[1], C. Mahon[1], C. Cooper[1], T. Liu[1].

[1]Queensland Health, Brisbane, QLD.

Background and Significance: Metastatic basal cell carcinoma (BCC) is exceptionally rare and typically arises from large or high-risk primary tumours. Distinguishing metastatic BCC from primary basaloid squamous cell carcinoma (SCC) of the lung is often challenging due to substantial overlap in histopathology and immunohistochemistry. Genomic mutational signatures offer a valuable adjunct when conventional methods are inconclusive.

Basic Methodologies: We report a man in his 50s who developed two incidentally detected pulmonary nodules six years after complete excision of two small low-risk cutaneous BCCs. His

diagnostic evaluation included CT-guided core needle biopsy, left lower lobectomy and lingulectomy, whole lesion histopathology and immunohistochemistry, and whole exome sequencing with mutational signature analysis. Recurrence risk and long-term outcomes were assessed through dermatology follow-up.

Major Findings: Initial biopsy favoured a diagnosis of primary basaloid SCC, with p40 positivity and TTF-1 negativity. While histopathology of resected specimens demonstrated basaloid nests with peripheral palisading, this could not reliably differentiate metastatic BCC from primary basaloid SCC. The presence of dual pulmonary nodules strengthened suspicion for metastatic BCC, consistent with known patterns of haematogenous dissemination. Whole exome sequencing revealed UV mutational signature 7, a hallmark of cutaneous carcinogenesis incompatible with primary lung cancer, thus confirming metastatic BCC. All lymph nodes were negative. Three years post-resection, the patient remains disease-free on biannual PET/CT surveillance, with mild chronic dyspnoea, good functional recovery, and no further cutaneous BCCs found on dermatologic review.

Concluding Statement: This case illustrates the potential for metastatic BCC to arise even from small, apparently low-risk lesions, and mimick primary lung carcinoma. Conventional histopathology and immunohistochemistry may be insufficient to determine tumour origin in such cases. UV mutational signature analysis provides decisive diagnostic clarity and should be considered when evaluating basaloid pulmonary tumours in patients with any prior history of BCC. As a diagnostic adjunct of increasing importance, genomic sequencing may in future be incorporated into standard diagnostic pathways and thereby prevent misclassification, refine risk stratification, and guide precise, targeted therapies.

42

Title: Agminated Spitz naevi arising within a congenital naevus spilus: a diagnostic challenge in a paediatric patient.

Authors: M. Noda[1], M. Zureigat[2], M. Formby[3]

[1] Illawarra Shoalhaven Local Health District, Wollongong, New South Wales, Australia
[2] Flinders Street Dermatology, Wollongong, New South Wales, Australia
[3] Southern.IML Pathology, Wollongong, New South Wales, Australia

Agminated Spitz naevi arising within a congenital naevus spilus are exceptionally rare and may clinically and dermoscopically mimic melanoma, posing a significant diagnostic challenge. Accurate differentiation is critical given the potential consequences of misdiagnosis, particularly in paediatric populations.

We report a case of a four-year-old girl presenting with multiple rapidly developing papules within a congenital naevus spilus on the dorsum of the hand. Clinical examination revealed three pink-

red papules measuring 3-4 mm within a speckled hyperpigmented patch. Dermoscopy demonstrated symmetrical, homogenous pink lesions with dotted vessels. A punch biopsy was performed for diagnostic clarification.

Histopathological examination showed nests of epithelioid and spindle melanocytes within minimal pigmentation and no dysplastic of malignant features, consistent with Spitz naevi. No features suggestive of spitzoid melanoma were identified. The clinical and histopathological findings supported a diagnosis of agminated Spitz naevi arising within a congenital naevus spilus.

This case highlights the diagnostic complexity of spitzoid lesions, particularly when occurring in atypical patters such as amination within naevus spilus. Despite the rarity of melanoma in prepubescent children, overlapping clinical and dermoscopic features necessitate histopathological confirmation. Careful clinicopathologic correlation remains essential, with emerging immunohistochemical and molecular tools offering potential adjunctive value in diagnostically challenging cases.

43

Title: A Novel *De Novo* KRT6A Splice-Site Variant in Pachyonychia Congenita: Atypical Phenotype and 17-Year Diagnostic Journey

Authors: E. Sisson[1 2], Edel O'Toole[3], D.F. Murrell[1 2]

[1] Department of Dermatology, St George Hosptial, Sydney NSW
[2] University of New South Wales, Department of Dermatology, Sydney NSW
[3] Queen Mary University of London, UK

Background and Significance: Pachyonychia congenita (PC) is a rare autosomal dominant genodermatosis caused by pathogenic variants in keratin genes including *KRT6A*, typically characterised by hypertrophic nail dystrophy, palmoplantar keratoderma, and severe plantar pain. Nail involvement occurs in >97% of *KRT6A*-associated PC, making its absence distinctly uncommon. Of 274 *KRT6A* variants in ClinVar, only 8 involve splice sites, with none previously described at the c.817-2 acceptor site. Reporting novel variants is essential for improving genotype–phenotype correlations and enabling earlier diagnosis.

Methodologies: We report an 17-year longitudinal clinical case with detailed phenotyping and molecular investigation. Investigations included serial dermatologic assessment, histopathology, and next-generation sequencing (NGS) with Sanger sequencing confirmation. Family segregation testing was performed. Variants were classified per American College of Medical Genetics and Genomics criteria.

Major Findings: A female patient was first referred at age 3 for suspected epidermolysis bullosa after blistering on her feet, with early keratoderma, oral leukokeratosis and hoarseness. Neonatal nail dystrophy resolved in infancy and did not recur. Contemporaneous documentation indicated

that its absence reduced diagnostic suspicion for PC, reflecting reliance on classical phenotypic features. Histopathology did not support EB. At age 10, a clinical geneticist proposed focal non-epidermolytic palmoplantar keratoderma; genetic testing was deferred due to cost. She re-presented at age 15 with debilitating plantar pain requiring 3-weekly podiatric debridement. At age 17, comprehensive NGS identified a heterozygous *KRT6A* splice-site variant (NM_005554.4:c.817-2A>G), absent from population databases, classified as likely pathogenic, and confirmed *de novo*.

Concluding Statement: This is the first clinical description of *KRT6A* c.817-2A>G, the only variant at this ClinVar position across 274 *KRT6A* submissions. Despite nail dystrophy present in >97% of *KRT6A*-associated cases, its absence contributed to an 17-year diagnostic delay, demonstrating how reliance on classical features may obscure atypical presentations. This case also illustrates how advances over 17 years from targeted histopathology to accessible comprehensive NGS have transformed the diagnostic landscape for rare genodermatoses, exemplifying the translational impact of genomic science on clinical diagnosis.

44

Title: Proteomic Insights into the Effectiveness of Cryotherapy and Topical Treatments for Actinic Keratosis

Authors: L. Faul[1], I. Dixit[2, 3], A. Azimi[2], S. Cai[4], P. Fernandez-Penas[2, 3]

[1]Westmead Institute of Medical Research
[2]The University of Sydney
[3]Westmead Hospital
[4] ProCan, Children's Medical Research Institute

Aim: Actinic keratoses (AKs) are common premalignant keratinocytic skin lesions managed with lesion-directed cryotherapy or field-directed topical 5-fluorouracil (5-FU). Comparative molecular responses within treated epidermis are incompletely characterised. We compared pre- and post-treatment tape-striped proteomic changes following cryotherapy versus topical 5-FU.

Method: In a comparative observational study, paired tape-striped samples were collected from patients with AK lesions before and after treatment with cryotherapy (max evaluable pairs n=20) or topical 5-FU (max evaluable pairs n=13). Proteins were identified and quantified using liquid chromatography–mass spectrometry-based proteomics. Then, paired differential protein abundance was analysed using limma with Benjamini–Hochberg false discovery rate (FDR). Pathway enrichment was assessed using pre-ranked GSEA across GO Biological Process, KEGG, Reactome and Hallmark gene sets; significance was defined as FDR $q<0.25$.

Results: Cryotherapy produced limited single-protein change, with 5/3492 proteins significantly altered (FDR<0.05; 4 upregulated, 1 downregulated), including

increased ITIH3, LRG1 and TMPRSS11E, and decreased CYTH1. Despite this, GSEA identified 450 significant gene sets, including enrichment of Lysosome (NES 2.71) and ECM degradation (NES 2.10) with depletion of translation programs (cap-dependent translation initiation, NES −2.53). Topical 5-FU induced broader disruption, with 150/3556 proteins significantly altered (130 upregulated, 20 downregulated), including complement/coagulation and inflammatory proteins (e.g., C1R, CFI, C4BPA, PLG, MPO, ELANE). GSEA identified 683 significant gene sets, including enrichment of complement and coagulation cascades (NES 2.66) and depletion of translation initiation pathways (translation initiation complex formation, NES −3.07).

Conclusion: Tape-strip proteomics demonstrates that both therapies shift the AK surface proteome toward innate immune activation and tissue remodelling with concurrent suppression of ribosome/translation programs. The molecular response is substantially stronger following topical 5-FU, consistent with a pronounced inflammatory field reaction, supporting tape-strip proteomics for mechanistic assessment and biomarker discovery in AK management.

45

Title: Assessing the feasibility of PLA_2 as a therapeutic target in NMSC

Authors: Su Y. Tan[1], Maria G. Elias[1,2], Jasmine M. Zhou[2,3], Mila Sajinovic[1,2,3], Kieran F. Scott[1], Albert S. Mellick[2,3]

[1]School of Medicine, Faculty of Health, Western Sydney University, Campbelltown, NSW, Australia
[2]Ingham Institute for Applied Medical Research, Department of Medical Oncology, Liverpool, NSW, Australia
[3]Nepean Clinical School, Faculty of Medicine and Health, University of Sydney, Kingswood, NSW, Australia

Background: Non-melanoma skin cancer (NMSC) is often overlooked as a benign skin condition due to its slow progression, often causing delayed diagnosis and treatment. Its characteristic of being an aggressive malignancy urges the need for a treatment plan that allows a better prognosis and overall survival. Phospholipase A_2 (PLA_2), an enzyme, has been demonstrated to play a role in NMSC proliferation and metastasis. However, the feasibility of PLA_2 being a therapeutic target remains unclear. We aimed to evaluate the effect of Kesonotide (C2), a PLA_2 inhibitor, on squamous cell carcinoma (SCC) cell lines in cancer progression and determine the expression pattern for PLA_2.

Methods: SCC and keratinocyte (KC) cell lines were used to analyse the cytotoxicity of C2. Cell viability was evaluated using an MTS assay following 72 hours of incubation. A scratch assay was performed on the cell lines, and the wound width was measured every 4 hours over 72 hours

using Incucyte imaging. PLA_2 expression in these cell lines was then determined using immunofluorescence with confocal microscopy following PLA_2 antibody staining.

Outcomes: All eight cell lines demonstrated sensitivity C2, with cell viability reducing to 10-40% at 300 μM concentration and an IC_{50} range of 63 to 900 μM with MTS. At 100 and 200 μM concentrations, treated cells showed significantly greater wound widths in comparison to control cells at 72 hours, demonstrating reduced growth capacity. PLA_2 expression was strongly expressed in KC cell lines in comparison to SCC cell lines.

Conclusions: The C2 drug demonstrated an inhibitory effect on NMSC cell viability and growth, which supports the hypothesis that it is a potential therapeutic agent. The differential expression of PLA_2 suggests it may also play a role in tumour progression, which highlights a potential direction for future research.

46

Title: Defense or Dysregulation? The *Streptococcus pyogenes* Immunopeptidome in Health and Disease

Authors: Runqiu Song [1], Shanzou Chung [1], Nathan P. Croft [1], Prithvi Raj Munday [1], Joshua Osowicki [2,3,4], Hannah R. Frost [2], Natalie Caltabiano [2], Danika L. Hill [5], Melanie R. Neeland [3,6], Shivanthan Shanthikumar [3,6,7], Eric Levi [6,8,9], Karen Davies [9], Andrew C. Steer [3,6,10], Anthony W. Purcell [1], Asolina Braun [1]

[1] Department of Biochemistry and Molecular Biology, Infection and Immunity Program, Biomedicine Discovery Institute, Monash University, Melbourne, VIC, 3800, Australia
[2] Tropical Diseases Research Group, Murdoch Children's Research Institute, Melbourne, VIC, 3052, Australia
[3] Department of Paediatrics, University of Melbourne, Melbourne, VIC, Australia
[4] Infectious Diseases Unit, Royal Children's Hospital Melbourne, Melbourne, VIC, 3052, Australia
[5] Department of Immunology, Monash University, 89 Commercial Rd, Melbourne, VIC, 3004, Australia
[6] Infection, Immunity and Global Health Theme, Murdoch Children's Research Institute, Parkville, VIC, 3052, Australia.
[7] Respiratory and Sleep Medicine, Royal Children's Hospital, Parkville, VIC, 3052, Australia.
[8] Department of Medical Biology, University of Melbourne, Parkville, VIC, 3050, Australia.
[9] Otolaryngology, Royal Children's Hospital, Parkville, VIC, 3052, Australia.
[10] Department of Infectious Diseases, Royal Children's Hospital Melbourne, Parkville, VIC, 3052, Australia.

Human leukocyte antigens (HLA) present peptide antigens (collectively termed the immunopeptidome) to T cells and are central to antimicrobial immunity. *Streptococcus pyogenes* is associated with pharyngitis, impetigo and psoriasis. *S. pyogenes* triggered psoriasis risk is significantly increased among individuals carrying HLA-C*06:02, and pharyngeal *S. pyogenes* infection can drive the expansion of skin-homing T cells, linking tonsillar immunity to skin

inflammation. First, to map the broader *S. pyogenes* antigen repertoire, we analysed the immunopeptidome of 13 *S. pyogenes*-colonised tonsils, and using tandem mass spectrometry identified 47 *S. pyogenes*-derived peptides presented across various HLA allotypes. Secondly, to specifically define the HLA-C*06:02-restricted immunopeptidome, we exposed HLA-C*06:02+ cells to live or heat-inactivated *S. pyogenes* and identified 63 *S. pyogenes* peptides that were predicted to bind this allele. Of these, 39 showed sequence similarity to human peptides (78–89% homology), supporting our hypothesis that such peptides may contribute to tolerance breakdown and the psoriasis pathogenesis following *S. pyogenes* infection via a mechanism known as molecular mimicry. We then tested CD8+ T cell responses to candidate peptides using HLA-C*06:02+ PBMCs from psoriasis patients and healthy donors. Responses were observed to peptide pools, and ongoing work is deconvoluting these responses at the level of individual peptides. Overall, our study defines the human- and *S. pyogenes*-derived tonsillar immunopeptidome and identifies candidate *S. pyogenes* antigens relevant to skin disease. These findings will support safer *S. pyogenes* vaccine design by potentially reducing the risk of cross-reactivity linked to psoriasis and by defining potential links with autoimmune sequelae.

47

Title: Three dimensional total body photography identifies cutaneous phenotypes associated with late-onset invasive melanoma risk

Authors: Sam Kahler [1 2], Clare Primiero [1], Adam Mothershaw [1], Dilki Jayasinghe [3], Chantal Rutjes [1], Brigid Betz-Stablein [1], Monika Janda [1 3], H Peter Soyer [1 2], Aideen McInerney-Leo [1]

Affiliations

[1.] Frazer Institute, The University of Queensland, Dermatology Research Centre, Brisbane, QLD, Australia.

[2.] Department of Dermatology, Princess Alexandra Hospital, Brisbane, QLD, Australia.

[3.] Centre for Health Services Research, The University of Queensland, Brisbane, Faculty of Medicine, QLD, Australia.

Aims: High naevus counts and UV photodamage are strong melanoma risk factors. Three-dimensional (3D) total body photography (TBP) and artificial intelligence (AI) allow for the automated extraction of detailed, site-specific distributions of naevi and photodamage. This study combined 3D-TBP, AI, and unsupervised clustering in a high-risk cohort to identify distinct phenotypic patterns associated with melanoma.

Methods: Melanoma-affected individuals (diagnosed >50 years) underwent 3D-TBP (n=117). Photodamage and naevus counts were assessed using density-based spatial clustering of applications with noise (DBSCAN) to identify body-site dependent phenotypic patterns. Melanoma prevalence relative to phenotypic pattern was evaluated using population prevalence ratios (PPR).

Results: Four phenotypic patterns of increasing severity were identified: moderate v-neck photodamage with few (median=38) naevi (24%), moderate generalised photodamage with several (median=155) naevi (27%), moderate v-neck photodamage with many (median=203) naevi (17%), and severe generalised photodamage with few (median=37) naevi (32%). No individuals had severe photodamage and several-many naevi. Participants in the mildest phenotypic pattern were least likely to be affected with invasive melanomas (PPR:1.51, 95%CI:1.01–2.26), whereas the severe pattern was more likely to be affected by multiple invasive melanomas (PPR:2.00, 95%CI:1.06–3.77). The prevalence of MiS was consistent across patterns. Melanoma was more likely at sites of large naevi (>5mm, $p<0.05$) in moderate photodamage patterns, but were independent of naevi in severe photodamage patterns. From a control cohort unaffected by melanoma (n=114), only 18 (16%) matched to a high-risk phenotypic pattern.

Conclusions: 3D-TBP phenotyping of a high-risk, older Australian cohort revealed four distinct phenotypic patterns associated with invasive melanoma risk, that were uncommon in melanoma-unaffected controls. Specifically, invasive melanoma risk was greatest in severe photodamage phenotypes, and increased alongside naevus count moderate photodamage phenotypes. Thus, comprehensive phenotypes may be predictive for the diagnosis and site of invasive melanoma, to assist with nuanced risk stratification and customised surveillance.

48

Title: Systemic and Topical Retinoids for Primary and Secondary Chemoprevention of Non-melanoma Skin Cancer in High-risk Populations: an Updated Systematic Review

Authors: Bomin Ko[1], Hyun Jae Nam[1], Vinod Gopalan[1]

[1]School of Medicine, Griffith University, Gold Coast Campus, Southport, QLD.

With the rising global burden of skin cancer, particularly in high-risk populations, there is a growing need for effective chemopreventive strategies. This systematic review synthesises the latest clinical evidence on systemic and topical retinoids for the primary and secondary prevention of non-melanoma skin cancer (NMSC) across high-risk populations, including individuals with genetic cancer-predisposition syndromes, solid organ transplant recipients (SOTRs), patients with prior NMSC, and those with therapy-induced keratinocyte carcinoma risk.

Method: The systematic review was conducted according to PRISMA guidelines and identified all relevant papers meeting predefined inclusion criteria through a search of Embase, with publications spanning from 1981 to 2024.

Result: Across high-risk populations, retinoids were evaluated for primary chemoprevention of NMSCs (35 studies) and for secondary chemoprevention, including the prevention and treatment of actinic keratoses (AK) (20 studies). In genetic cancer-predisposition syndromes, systemic isotretinoin was associated with a reduction in NMSC incidence. Among SOTRs, acitretin was the

most frequently studied agent and demonstrated a relatively consistent reduction in SCC, with limited effect on BCC. In contrast, the majority of RCTs in patients with prior NMSC showed no meaningful chemopreventive benefit, while studies evaluating AK in this population similarly showed no consistent benefit. Therapy-induced high-risk cohorts demonstrated reduced SCC risk with acitretin. Topical retinoids showed limited efficacy as monotherapy for primary chemoprevention but appeared more beneficial for AK and when used in combination with systemic retinoids. Adverse effects and post-discontinuation rebound were common with systemic retinoids.

Conclusion: Although systemic retinoids demonstrated efficacy for both primary and secondary chemoprevention of NMSC, their clinical utility is limited by uncertainty regarding optimal agent selection, dosing, treatment duration, and discontinuation strategies, particularly in the context of cumulative toxicity and frequent post-discontinuation rebound. Combination strategies integrating better-tolerated topical retinoids with more effective systemic regimens may help optimise efficacy while improving tolerability. Future large-scale, well-designed RCTs with enhanced monitoring and long-term surveillance are needed to define durable, patient-centred chemopreventive strategies.

49

Title: Why are thick melanomas lethal? Immune exclusion underpins recurrence in primary melanoma

Authors: Tan SX[1, 2], Muller NM[1, 2], Kao YC[1], Zhou C[1], Xiong Z[3], Gavanescu D[1], Roy E[1], Whiteman D[3], Lambie D[2], Soyer HP[1, 2], Stark M[1], Nguyen Q[3], Khosrotehrani K[1, 2]

[1]Frazer Institute, University of Queensland, Dermatology Research Centre, Brisbane, Australia
[2]Department of Dermatology, Princess Alexandra Hospital, Brisbane, Australia
[3]QIMR Berghofer Medical Research Institute, Brisbane, Australia

Melanoma staging is guided by two opposing paradigms: the biology-informed Clark level, which stratifies melanoma by its level of invasion into distinct anatomic compartments; and the clinically pragmatic Breslow thickness, which measures the distance, in millimetres, from the epidermal surface to the deepest tumour cell.

Despite forgoing the anatomic contexture of Clark level, Breslow thickness is more predictive of outcome, and it is Breslow thickness that underlies staging in the modern melanoma clinic. However, it is not clear why Breslow thickness is so associated with recurrence and mortality; tumour behaviour should hold no regard for the metric system. Compounding this, it is unclear from the literature how thin and thick tumours differ at all.

In this translational dermatopathology study, we performed computer vision and spatial RNA sequencing to study the relationship between Breslow thickness and recurrence from the whole-slide diagnostic biopsies of 185 Queensland patients with primary melanoma (Stage IA-IIB). We applied organization metrics, first developed in the geological and ecological sciences, to quantify the developmental trajectory of melanoma: from junctional Pagetoid spread and focal nesting in thin melanomas to dense tumour sheets in thick melanomas. Notably, while thin melanomas maintained strong contact with local lymphocytes (p: 0.001) and blood vessels (p: 0.019), thick melanomas cultivated an 'immune-cold' niche characterized by absent lymphocyte infiltration (p: 0.001), high oxygen demand (p: 0.013), and invasive-state phenotypic switching (p: 0.007). On survival analyses, these thickness-related phenotypes mediated the relationship between Breslow thickness and recurrence (median follow-up 7 years)

Notably, in the 51 patients with thin melanoma (Breslow thickness ≤1mm), we identified a subset of tumours expressing thickness-related phenotypes despite their early-stage disease. These immune-cold thin melanomas were associated with increased disease-specific mortality (HR: 2.71; 95% CI: 1.33-5.50; p: 0.006), with an estimated case fatality rate commensurate with much thicker melanoma. High-risk thin melanomas deviate from the standard developmental trajectory, and pending prospective validation may be appropriate candidates for enhanced surveillance or even systemic immunotherapy.

50

Title: Machine Learning–Assisted Detection of Circulating Tumour Cells for Cutaneous Squamous Cell Carcinoma in Epidermolysis Bullosa

Authors: Jasmine M. Zhou[1,3,5,6], Midhun Shyam[2], Chen (Amy) Wang[1,3,5,6], Fiaz R. Chowdhury[3], Steven Thomas[2,3], Mila Sajinovic[1,3,4], Monavvar Andarva[3,4], Kieran F. Scott[4], Ali Azimi[5], Guy Lyons[6], Paul de Souza[1], Albert S. Mellick[1,2,3]

[1]Nepean Clinical School, Faculty of Medicine and Health, University of Sydney, Kingswood, NSW, Australia
[2]South Western Emergency Research Institute, Department of Emergency, Liverpool Hospital, Liverpool, NSW, Australia
[3]Ingham Institute for Applied Medical Research, Department of Medical Oncology, Liverpool, NSW, Australia
[4]School of Medicine, Faculty of Health, Western Sydney University, Campbelltown, NSW, Australia
[5]Centre for Cancer Research, The Westmead Institute for Medical Research, The University of Sydney, Westmead, NSW, Australia
[6]Centre for Cancer Innovations, Centenary Institute, The University of Sydney, Camperdown, NSW, Australia

Cutaneous squamous cell carcinoma (cSCC) is the second most common skin cancer and can be fatal if diagnosis is delayed, particularly in high-risk groups such as the elderly,

immunocompromised, and patients with recessive dystrophic epidermolysis bullosa (RDEB). RDEB, caused by mutations in type VII collagen, leads to extreme skin fragility, making conventional biopsies invasive and often unsuitable. Liquid biopsy, through the detection of circulating tumour cells (CTCs), presents a minimally invasive alternative. This study evaluates the feasibility of CTC enrichment using the ScreenCell® filtration system and the application of machine learning for improved diagnostic accuracy.

Blood samples spiked with cancer cells (RDEB- and non-RDEB–derived) were processed using the ScreenCell® filtration system. Captured cells were fixed and stained with monoclonal antibodies targeting cytokeratin (CK), CD45, and chondroitin sulfate proteoglycan 4. Confocal fluorescence microscopy was used to identify putative CTCs. A machine learning algorithm was developed and trained using CK-positive cells as the reference standard, supported by an optimised object selection protocol.

Reproducible and efficient CTC enrichment was achieved using the filtration system in mock blood samples. A standardised workflow for CK-positive CTC detection enabled the generation of a robust training dataset. Preliminary analyses demonstrated accurate identification of CTCs based on morphological and fluorescence features, including size, shape, and signal intensity, supporting the feasibility of machine learning–assisted classification.

This study demonstrates the potential of a minimally invasive, blood-based diagnostic approach for cSCC. The integration of CTC enrichment with machine learning may enable earlier detection, reduce reliance on invasive biopsies, and improve diagnostic efficiency in high-risk populations. Further validation in clinical cohorts is required to assess diagnostic performance and clinical applicability.

52

Title: Treatment Preferences for Alopecia

Authors: V. Azzi[1*], A. Dhruv*, C. Chew[2]

[1]University Notre Dame, School of Medicine, Sydney, New South Wales
[2] Monash University, Faculty of Medicine, Nursing and Health Sciences, Clayton, Victoria, Australia.
*Co-first authors

Alopecia is a common condition associated with significant psychological morbidity, impacting self-esteem, social functioning and overall wellbeing. The most prevalent forms, androgenetic alopecia and alopecia areata, are chronic conditions that often require long-term pharmacological

management. Given that treatment efficacy may take several months to become apparent, patient adherence is critical and may be influenced by treatment preferences, including route of administration. There is limited research examining preferred routes of administration and factors prioritised when selecting treatment for alopecia.

This study aimed to identify preferred routes of administration for alopecia treatments among individuals with and without self-reported hair loss as well as the factors prioritised when selecting treatment, to inform patient-centred management strategies. A cross-sectional mixed-methods survey was distributed via REDCap, using snowball and convenience sampling, to 82 participants. Preferences for treatment route (topical, oral, sublingual, injectable) were analysed using the Friedman test with Dunn's post-hoc comparisons, with significance set at p less than 0.01.

Oral administration was the most preferred overall, followed by topical, sublingual, and injectable routes. There was no statistically significant difference between topical and oral preferences. However, both topical and oral routes were significantly preferred over injectable administration (p less than 0.0001). No statistically significant differences in route preferences were observed between participants with and without self- reported alopecia. Efficacy was the highest-ranked factor participants would consider when selecting a treatment, followed by side effects, with route of administration and contraindications of medication (including pregnancy safety) ranked equally third.

These findings suggest that non-invasive routes of administration are strongly preferred regardless of lived experience of alopecia. Importantly, treatment efficacy appears to be the primary driver of decision-making, with practical considerations playing a secondary role. Incorporating patient preferences into treatment selection may improve adherence and long-term outcomes, with potential applicability to other chronic conditions requiring sustained pharmacological therapy.

53

Title: Understanding the impacts of prolonged UV exposure on Melanoma Recurrence and Long-term Survival

Authors: Danielle Gavanescu[1], Samuel X Tan [1, 3] Nicholas M Muller[1,3], Léa Dousset[1], Lena A von Schuckmann[2,3], Kiarash Khosrotehrani[1,2,3]

[1]The University of Queensland, Frazer Institute, Dermatology Research Centre, Woolloongabba, QLD, Australia
[2]Queensland Melanoma Project, Princess Alexandra Hospital, The University of Queensland, Woolloongabba, QLD, Australia
[3]Princess Alexandra Hospital, Department of Dermatology, Woolloongabba, QLD, Australia

Introduction: Exposure to ultraviolet (UV) radiation is a well-established modifiable risk factor for the initial development of cutaneous melanoma. However, its role in melanoma progression after diagnosis is less clear. Melanoma recurrence, defined as local, regional, or distant return of the original cancer, is distinct from the development of a new primary melanoma or separate lesion. Identifying factors associated with patients at high-risk recurrence may help guide surveillance or management strategies, ultimately improving survival.
Methods: Occupational sun exposure since leaving school was self-reported as mainly indoors, both indoors and outdoors, or mainly outdoors. Adjusted Cox proportional hazards models assessed associations with recurrence and Fine-Gray competing risk models examined melanoma-specific mortality. Participants were followed for a minimum of 7 years, with all recurrences recorded.

Results: Participants with mainly outdoor occupations (n=124) had a significantly higher risk of recurrence than those with mainly indoor occupations (n=252) (aHR 1.81, 95% CI 1.09-3.02; P=0.02). Among participants with recurrence (n=190), the mean time from diagnosis to recurrence was 32.7 months (SD 26.8), with no significant difference between exposure groups. Compared with mainly indoor occupations, mainly outdoor occupations were also associated with increased melanoma-specific mortality (sHR 2.64, 95% CI 1.28-5.43). Mixed exposure showed a similar direction of effect but was not statistically significant.

Conclusion: Greater occupational UV exposure was associated with increased risks of melanoma recurrence and melanoma-specific mortality in our cohort. Looking beyond traditional prognostic factors such as Breslow thickness, ulceration, and mitotic rate, could facilitate our understanding of why two patients with comparable disease at diagnosis may have different recurrence risks or survival trajectories.

54

Title: Precision diagnostics for early melanoma detection using spatial biology and AI-guided image analysis

Authors: Y-C. Kao[1], S. Tan[1], X. Tan[2], H. Oey[1], K.J. Lee[1], T. Vallius[3,4,8], R. Pelletier[3,4], A. Causer[2], C. Zhou[1], D.J Smit[1], J. O'Neill[1], A. Xiong[2], B. O'Brien[5], A. Collins[5], P. K Sorger[3,4,8], H.P. Soyer[1,6], K. Khosrotehrani[1,6], Q. Nguyen[2,7] and M.S. Stark[1]

[1]Frazer Institute, The University of Queensland, Dermatology Research Centre, Brisbane, QLD 4102, Australia
[2]QIMR Medical Research Institute, Queensland, Australia
[3]Laboratory of Systems Pharmacology, Harvard Program in Therapeutic Science, Harvard Medical School, 200 Longwood Avenue, Boston, MA 02115
[4]Ludwig Center at Harvard
[5]Sullivan Nicolaides Pathology, Brisbane, Australia
[6]Department of Dermatology, Princess Alexandra Hospital, Brisbane, Queensland, Australia

[7]Institute for Molecular Bioscience, the University of Queensland, Saint Lucia, Queensland, Australia
[8]Department of Systems Biology, Harvard Medical School, 200 Longwood Avenue, Boston, MA 02115.

Accurate diagnosis of melanoma is particularly challenging, as malignant lesions often resemble benign naevi. The gold standard for diagnosing melanocytic lesions relies on the examination of morphological cell features using hematoxylin and eosin (H&E) stained tissue samples. This process is often subject to variability, lacking the sensitivity to precisely define cell types with a high degree of accuracy. This project aims to overcome histopathological limitations by accurately defining transcriptional cell states, indicative of invasive potential, in benign and malignant lesions. We propose that this will enable more precise definitions of true melanomas in a sea of benign or indolent lesions, constituting the bulk of excised lesions sent for diagnosis. To identify these "hidden" cell states, we performed spatially resolved whole transcriptome profiling (Visium) of whole lesions using a progression series of samples (n=75) ranging from healthy skin, naevi (benign and low to high grade dysplastic naevi), melanoma *in situ*, T1a melanomas, and melanoma arising from pre-existing naevi. To enable deconvolution of Visium 'spots', we performed scRNA sequencing on healthy skin, naevi and thin melanomas, to determine marker genes specific to each cell type. This analysis revealed a change of melanocyte cell states along melanoma progression, from conventional naevus to T1a melanomas. We further identified naevus and melanoma-specific signatures which can be spatially resolved, enabling classification of lesions as "benign" or "malignant", as well as identifying previously hidden regions of malignant potential. We also performed single cell resolved transcriptomic and proteomic platforms to validate the spatial expression of benign and malignant genes, and to finely characterise immune cell populations within the tumour microenvironment. Additionally, all specimens have been assessed for a panel of 361 cancer genes, facilitating a comprehensive characterization of the mutational profile driving melanoma progression. By integrating the molecular data with spatial gene expression analysis, we have developed an innovative deep learning model that enhances diagnostic precision for melanoma based on H&E-stained slides. Together, we have defined melanocyte cell states across melanoma progression and uncovered key tumour–microenvironment interactions. We envision these data will permit AI-guided diagnosis to accurately delineate benign and malignant melanocytic lesions.

55

Title: Gaps and Opportunities from whole exome sequencing Australia's first hidradenitis suppurativa cohort

Authors: Keywords: Hidradenitis suppurativa, genetics, variants, hereditary, familial, Australia

Authors:
Ellie J Maas[1], Sam Kahler[1,2], Snehlata Kumari[1], Kiarash Khosrotehrani[2,3], *Erin McMeniman[2], *Aideen M McInerney-Leo[1]
*Joint senior authorship
Affiliations:

[1]Frazer Institute, The University of Queensland, Dermatology Research Centre, Brisbane, Australia
[2]Department of Dermatology, Princess Alexandra Hospital, Brisbane, Queensland, Australia
[3]Dermatology Research Centre, Experimental Dermatology Group, Frazer Institute, The University of Queensland, Brisbane, Australia

Aim: Hidradenitis suppurativa (HS) is a chronic inflammatory skin disease associated with substantial morbidity, yet its genetic architecture remains incompletely characterised. Delayed clinical recognition (7–10 years) and a paucity of large-scale genomic studies have limited understanding of genetic risk, particularly across diverse populations. This study aimed 1) to synthesise reported HS-associated genetic variants, assess their pathogenicity, inheritance patterns, and ancestry representation, and 2) conduct a pilot study to characterise the genetic landscape of Australia's first HS cohort using whole-exome sequencing (WES).

Method: Firstly, a scoping review of the literature (2010–2025) identified 401 manuscripts, of which 42 met inclusion criteria. Extracted data included reported genes and variants, familial versus sporadic cases, in-silico pathogenicity classification, and ancestry. Secondly, 96 patients with clinically diagnosed HS were recruited through Queensland's first dedicated HS clinic at Princess Alexandra Hospital, Brisbane. Participants consented to WES, with sequencing and bioinformatic analysis performed at QIMR Berghofer Medical Research Institute.

Results: Across published studies, 129 HS-associated variants were reported across 22 genes, with variants in γ-secretase complex genes comprising 46% of findings. Only 57 variants were classified as pathogenic or likely pathogenic using in-silico tools. Ancestry representation was heavily skewed toward East Asian and European populations, with no reported Australian or New Zealand cohorts. In the Australian pilot cohort, three multigenerational families with extensive HS history were identified and pedigrees documented by a genetic counsellor. The cohort was predominantly of white European ancestry, reflecting causal gene patterns detailed in the literature.

Conclusions: HS genetics remains an evolving and unevenly characterised field, constrained by delayed diagnosis and limited ancestral diversity. Establishing inclusive, well-phenotyped cohorts and leveraging emerging registry infrastructure are essential steps toward equitable precision dermatology for HS.

57

Title: Fields of *BRAF*^{V600E}-mutant melanocytes are present in non-lesional skin and enriched near naevi and prior melanoma sites

Authors: Katie J. Lee[1], Yung-Ching Kao[1], Amanda Jiang[2], Anastasia Prokofyeva[2], Lisa N. Tom[1], Kasturee Jagirdar[1], Darren J. Smit[1], Harald M. Oey[1], Jean-Marie Tan[1], Stephen A. Ainger[1], Nancy Huang[1], Zewen Kelvin Tuong[1], Stacey Andersen[3], Anne Senabouth[4], Joseph E. Powell[4], Duncan Lambie[5], Helmut Schaider[1], H. Peter Soyer[1], Richard A. Sturm[1], Alana L. Welm[2], Douglas Grossman[2], Robert L. Judson-Torres[2], and Mitchell S. Stark[1].

[1]The University of Queensland, Frazer Institute, Brisbane, QLD, Australia
[2]University of Utah Health Sciences Center, Huntsman Cancer Institute, Salt Lake City, UT, USA
[3]The University of Queensland, Institute for Molecular Bioscience, Brisbane, QLD, Australia
[4]Garvan Institute of Medical Research, Sydney, NSW, Australia
[5]Sullivan Nicolaides Pathology, Brisbane, QLD, Australia

The *BRAF*^{V600E} mutation is a major driver of naevus and melanoma formation, and while UVR exposure is the major environmental driver of melanoma, *BRAF*^{V600E} is not a UV-generated mutation. In addition, melanoma screening currently focuses on naevus surveillance, but ~70% of melanomas arise from clinically normal skin with no precursor lesions. We hypothesised that *BRAF*^{V600E} mutation could also be present in non-lesional, clinically healthy skin as a hidden field of tumour-precursor cells.

We examined *BRAF*^{V600E} mutation in 97 clinically and histologically healthy non-lesional skin samples from Australian high-risk melanoma patients with droplet digital PCR (ddPCR), immunohistochemistry, and single cell RNA sequencing. The samples included skin adjacent to a naevus or prior melanoma site, similarly-photodamaged skin 5cm from the melanoma site ("proximal") and photoprotected skin distant from lesions. We also examined 11 low-risk neonatal foreskin-derived melanoblasts.

BRAF^{V600E} mutation was 50% more frequent in skin adjacent to melanocytic lesions (naevi 75% of samples; melanoma sites 78%) compared to proximal and distant photoprotected sites (both 53%; $p = 0.04$). The fields of *BRAF*^{V600E} were also up to 20-fold denser adjacent to melanocytic lesions. There were no significant differences between sites with different grades of clinical photodamage. Single cell RNA-Seq analysis of one naevus-perilesional skin pair confirmed that the cells expressing *BRAF*^{V600E} were melanocytes and had a *BRAF*^{V600E}-induced growth arrest transcriptional

profile. In addition, we detected *BRAF*^{V600E} mutation in one of 11 neonatal foreskin-derived melanoblast cell lines.

Apparently healthy skin in high-risk melanoma patients contains a reservoir of melanocytes bearing oncogene mutations, challenging the current assumption that such mutations will always develop into a tumour. We cannot currently say whether these denser fields of mutated melanocytes preceded or followed their adjacent melanocytic lesions, but their existence suggests that melanoma may be a field-based phenomenon similar to squamous cell carcinoma. Identifying these genetically-primed melanocytes may allow mapping of melanoma-prone skin or targeting them with topical treatments, allowing us to prevent a melanoma from developing at all.

58

Title: Leprosy in Disguise: A Case of Chronic Treatment Refractory Dermatosis

Authors: Yuyang Liu[1,2], Shu Zhe Cheah[1]

[1.] Princess Alexandra Hospital, Metro South Health, Brisbane, QLD, Australia
[2.] University of Queensland, Frazer Institute, Brisbane, Australia

Background: Leprosy (Hansen disease) is a chronic granulomatous infection caused by *Mycobacterium leprae,* predominantly affecting skin and peripheral nerves. Diagnosis is often delayed in non-endemic setting due to its heterogenous clinical presentation and ability to mimic inflammatory dermatoses. This case highlights the diagnostic challenges of leprosy presenting in a non-endemic setting.

Case Presentation: We report a case of a 26-year-old female from Philippines presented with acute osteomyelitis of the right thumb, developing one week post kitchen burn injury. During admission, an incidental widespread eruption was observed. Patient described 18-month history of a progressive rash, initially involving the left hand before becoming generalised. Previous dermatological assessment and treatment including potent topical corticosteroids and systemic methotrexate had yielded minimal response.

Examination demonstrated extensive annular erythematous plaques with raised borders involving approximately 50% body surface area, predominantly over the trunk. Neurological examination revealed patchy glove and stocking sensory disturbance with reduced pin prick sensation to the mid upper arm. Initial differential diagnoses included sarcoidosis, lupus erythematosus, and leprosy**.**

Management and Outcome:
Skin biopsies demonstrated non-necrotizing tuberculoid granulomas throughout the dermis. Polymerase chain reaction testing detected *M. leprae* DNA, confirming leprosy within the tuberculoid spectrum. Patient was commenced on recommended multidrug therapy with

rifampicin, dapsone, and clofazimine with good tolerance. She remains under multidisciplinary follow-up, with improvement in cutaneous disease and no progression of neurological symptoms.

Conclusion: This case highlights the diagnostic challenges posed by leprosy in non-endemic settings, where clinical suspicion is often low and presentations may be atypical. As migrations and international travel increase, clinicians in low incidence countries should maintain vigilance for imported infectious diseases such as leprosy. Chronic, treatment refractory dermatoses accompanied by sensory deficits should prompt consideration to enable timely diagnosis and prevent long term neurological sequelae and improve patient outcome

59

Title: Can AI See Me? Part II: A Systematic Review of Artificial Intelligence for Diagnosing Inflammatory Skin Conditions in Skin of Colour Populations

Authors: Yuyang Liu[1,3], Tabrez Sheriff[1], H. Peter Soyer[1,2,3], Brigid Betz-Stablein[2], Clare A Primiero[2]

[1]The University of Queensland, Faculty of Medicine, Brisbane, Australia
[2]Frazer Institute, The University of Queensland, Dermatology Research Centre, Brisbane, Australia
[3]Department of Dermatology, Princess Alexandra Hospital, Brisbane, Australia

Background: Artificial intelligence (AI) systems in dermatology have largely focused on skin conditions using datasets dominated by lighter skin types. Inflammatory skin diseases are common globally and often present differently in people with skin of colour (SOC), contributing to diagnostic delays and inequities in care.

Objective: The aim of this study was to systematically review the technique, quality, accuracy, and implications of studies using image-based AI models developed in SOC populations for the diagnosis of inflammatory skin conditions.

Methods: A systematic review was conducted in accordance with PRISMA guidelines, with protocol registration on PROSPERO. PubMed was searched (March 2021, updated 2025) for studies applying AI to image-based classification of inflammatory skin disorders in SOC populations. Eligible studies included clinical or dermoscopic images derived from predominantly SOC cohorts or countries with predominantly non-European ancestry. Study quality was assessed using the CLEAR Derm Consensus Guidelines.

Results: Forty eligible articles were identified. Most studies evaluated psoriasis (n=20), eczema/atopic dermatitis (n=16), acne (n=13), seborrheic dermatitis (n=8), and rosacea (n=3). Cohorts were primarily from China and India, with limited representation of African, Hispanic/Latino, or Fitzpatrick V–VI populations. Several multiclass models (e.g. specific diagnosis) reported accuracy above 85%, while some binary models (e.g. disease present or absent) achieved

sensitivity and specificity approaching 100% for psoriasis detection. Broad multi-disease models also demonstrated promising performance, including accuracies of 94.8% and 98.1% in selected studies. Reader studies (n=16) suggested AI achieved similar or superior diagnostic accuracy to dermatologists in several settings, and consistently outperformed non-experts. However, quality assessment revealed frequent deficiencies in reporting of bias, class balance, external validation, and clinical implementation pathways.

Conclusions: AI models demonstrate promising diagnostic performance for common inflammatory skin diseases in SOC populations, but current evidence is limited by inadequate dataset diversity, lack of transparency, and insufficient external validation. Standardised reporting and inclusion of diverse skin tones are essential to ensure equitable clinical translation of AI tools in dermatology.

60

Title: Managing Cutaneous Adverse Events in Cancer Care: An 18-Month Review of a Rapid-Access Oncodermatology Clinic

Authors: Yuyang Liu[1, 2], Samuel X. Tan[1, 2], Nicholas M. Muller[1, 2], Xiaohua Shen[1], Celine Lee[1], Yit Nah Lau[1], Victoria Atkinson [3], Rahul Ladwa[3], Emma-Anne Karlsen[1, 2], Kiarash Khosrotehrani[1, 2]

Affiliations

[1]Princess Alexandra Hospital, Department of Dermatology, Brisbane, Australia
[2]University of Queensland, Frazer Institute, Brisbane, Australia
[3]Princess Alexandra Hospital, Department of Medical Oncology, Brisbane, Australia

Background: Cutaneous adverse events (CAEs) are common complications affecting up to half of patients receiving anti-cancer therapies. CAEs can significantly impair quality of life, increase systemic corticosteroid exposure, cause treatment interruption or even cessation. Given their prevalence, inter-specialty collaboration between oncology and dermatology teams, or oncodermatology, has the potential to improve management of CAEs and support delivery of anti-cancer therapies.

Methods: A retrospective review was conducted on patients referred to a rapid access oncodermatology clinic at a tertiary hospital in Brisbane, Australia, over an 18-month period. Demographics, cancer type, anti-cancer therapy, CAE morphology and severity, treatments, corticosteroid use, clinical outcomes, and treatment continuity were analysed.

Results: A total of 142 patients were included (median age 66 years; 51% female), most commonly with melanoma (18%), breast cancer (16%), lung cancer (14%), and lymphoma (10%). Anti-PD-1 monotherapy (28%), chemotherapy (16%), and combination immunotherapy (11%) were the most frequent causative treatments. CAEs were graded as Grade 1 (33%), Grade 2 (37%), and Grade 3 (20%); 10% of referrals were unrelated to therapy. Common presentations included

eczematous (18%), lichenoid (13%), morbilliform (11%), and acneiform (9%) eruptions, as well as immunotherapy-associated pruritus (8%). Management through oncodermatology clinic prioritised supportive and topical therapies. Only 9% of patients required systemic corticosteroids overall, with majority being Grade 3 CAEs. Targeted therapies, including dupilumab, were successfully used as steroid sparing agents in selected severe cases. At three months, 88% of CAEs had completely (59%) or partially (29%) resolved. Anti-cancer therapy cessation due to CAEs was uncommon and occurred in only 14% of Grade 3 cases.

Conclusions: Rapid access oncodermatology represents a practical and reproducible approach to cutaneous toxicity care. It facilitates accurate diagnosis, reduces avoidable systemic corticosteroid use, supports steroid-sparing targeted therapies, and enhances treatment continuity in selected patients with high-grade CAEs through toxicity grade reduction or achievement of clinical resolution.

61

Title: Beneath the Surface of Hidradenitis Suppurativa: Histopathological Patterns Across 197 Surgically Deroofed Specimens

Authors: Yuyang Liu[1,2], Timothy J. Liu[1,2], Duncan Lambie[3], Luke Watson[4], Erin K. McMeniman[2]

Affiliations
[1] Dermatology Research Centre, Frazer Institute, The University of Queensland, Brisbane, QLD, Australia
[2] Department of Dermatology, Princess Alexandra Hospital, Metro South Health, Brisbane, QLD, Australia
[3] Department of Anatomical Pathology, Princess Alexandra Hospital, Pathology Queensland, Brisbane, QLD, Australia
[4] Department of Plastics and Reconstructive Surgery, Princess Alexandra Hospital, Metro South Health, Brisbane, QLD

Background: Hidradenitis suppurativa (HS) is a chronic autoinflammatory condition characterised by recurrent painful nodules and abscesses in intertriginous sites such as axillae, groin and buttocks. HS diagnosis relies on clinical assessment and is frequently delayed, with the average timeframe between first manifestation of symptoms to formal diagnosis been 7-10 years. Given there is sparse literature to provide codified descriptions of the histopathology of HS. The present study aims to characterise and quantitate the histopathological features of HS lesions, thereby contributing to early diagnosis, better treatment and patient outcomes.

Methods: A retrospective audit was conducted on deroofed lesions from hidradenitis suppurativa (HS) patients at a public specialist oncodermatology service in Brisbane, Australia. Each deroofing specimen underwent histological examination by a clinical dermatopathologist, and histological

features were defined and coded accordingly recorded using predefined categories including sinus tract, follicular, inflammatory, apocrine, and miscellaneous features.

Results: Among 197 specimens, lesions most frequently involved the axillae (41%), groin (22%), and buttocks (11%). Documented Hurley staging included 8% stage I, 33% stage II, and 38% stage III disease, with staging unavailable for 20% of specimens. The most common sinus tract findings were keratinised epidermally lined sinus tracts (54%) and horizontally oriented sinus tracts (42%). Follicular occlusion (32%) and interfollicular epithelial hyperplasia (13%) were the most frequent follicular features. Common inflammatory findings included fibrosis (70%) and lymphocytic infiltrates (70%). Several features, including compound hair structures, foreign body reactions, and deep abscess formation, were more frequently observed in Hurley stage II and III specimens, suggesting increasing histopathological complexity with disease progression.

Conclusions: This study provides a quantitative overview of the histopathological spectrum of HS using surgically derived deroofing specimens. The findings support a model in which early follicular pathology is followed by progressive inflammatory and structural changes as disease advances. Increasing histopathological complexity in more advanced disease likely reflects repeated follicular rupture, chronic inflammation, and tissue remodelling.

62

Title: Understanding the immune cell interactions with Herpes simplex virus in initial infection in human foreskin

Authors: Naomi R. Truong [1,2,4], Jacinta B. Smith [1,2], Blake Johnson[1,2], Jason J. Herbert[1,2], Hafsa Rana[1,2], Dona R. Sirimanne[1,3], Andrew N. Harman[1,3,4], Najla Nasr[1,3,4], Kirstie M. Bertram[1,2], Kerrie J. Sandgren[1,2,4], and Anthony L. Cunningham[1,2,4]

[1] The Westmead Institute for Medical Research, Westmead, NSW, 2145, Australia
[2] Faculty of Medicine and Health, The University of Sydney, Westmead, NSW, 2145
[3] School of Medical Sciences, Faculty of Medicine and Health, University of Sydney
[4] Sydney Infectious Diseases Institute (Sydney ID), University of Sydney

Herpes Simplex Virus (HSV) is sexually transmitted through the anogenital epithelium to infect keratinocytes, Langerhans cells (LCs) and dendritic cells (DCs). We developed a human inner foreskin explant model using microarray patches (MAPs) to introduce the virus and found that microtrauma was essential to establish viral infection beyond the superficial layers of the epithelium. Using this model, combined with intraepidermal nerve (IENF) labelling by PGP9.5, we found that HSV-1 (detected by RNAscope) directly interacted with IENFs 24 hours post infection (h.p.i.). Thus, there is only a narrow time window for prophylactic strategies to target HSV before it establishes lifelong latency in the nervous system. When HSV-1 infects human LCs and epidermal (Epi-) DCs, both cell types undergo apoptosis. HSV-infected LCs migrate to the dermis, clustering with dermal type 1 conventional DCs (cDC1s) and macrophages, which phagocytose LC

fragments containing HSV antigen- a “viral antigen relay”. However, the role of dermal cDC2s in interactions with HSV-infected LCs and Epi-DCs is unknown. We analysed dermal DC clusters with HSV-infected LCs by cyclic immunofluorescence (IF). At 24 h.p.i. there were significantly more cDC2s clustering in the dermis beneath areas of epidermal HSV-1 infection than in regions far from infection. We analysed cell clusters in the upper dermis beneath foci of infection and found 19% of these cell clusters contained LCs. Of these, 77% also contained cDC2s and 23% contained cDC1s. LCs were not observed in the occasional small clusters in regions far from HSV foci or in mock samples. To extend our understanding of the initial immune response to HSV infection and the viral relay, we are performing spatial multiomics, including automated multiplex IF and spatial transcriptomics on HSV-infected foreskin explants compared with rare herpes lesion biopsies obtained from penile skin, foreskin and vulva. Significance: The stimulation of both primary CD8+ and CD4+ T cell responses are necessary for viral clearance. A comprehensive understanding of the immune cells involved in response to HSV infection in human tissue, including those that facilitate stimulation of both T cell subsets and the establishment of resident memory T (T_{RM}) cells, is critical for designing vaccine candidates that successfully elicit these responses.

63

Title: The role of the skin microenvironment in suppressing cutaneous squamous cell carcinoma initiation.

Authors: Natasha Kolesnikoff[1], Michael S. Samuel[1].

[1]Centre for Cancer Biology, Adelaide University, Adelaide, South Australia

The tumour microenvironment (TME) encompasses all non-malignant components of a tumour mass, including stromal fibroblasts, vasculature, immune cells, and the extracellular matrix (ECM). My research focus is to understand the role of the TME in the initiation of cutaneous squamous cell carcinoma (cSCC). One established route of cSCC initiation is by malignant transformation of resident stem cells of the hair follicle to yield cancer stem cells. My data show that alteration in the ECM surrounding the stem cell niche triggers mechano-transduction signalling which may modulate the number of hair follicle cells that exhibit stem-like features. Co-opting Paget’s *seed and soil* hypothesis to primary cancers, we hypothesise that cSCC tumour initiation may be modulated by a permissive TME, including the ECM (soil), by alteration in the number of cells susceptible to oncogenic transformation (seed), thereby resulting in more frequent initiation events. In a complementary study using cutaneous chemical carcinogenesis mouse model, we observe that deletion of an ECM-modulating protease leads to reduced immune cell surveillance, increased collagen content with altered organisation, and expanded dermal fibroblast populations. Together, these changes lead to a higher number of initiated cutaneous tumours. These data suggest that the protease has a protective role during the earliest stages of tumour development. These data all support the hypothesis that whilst the cells of the TME have not

undergone oncogenic transformation, they have context-dependent driver or suppressor roles in the initiation and progression of primary cutaneous tumours.

64

Title: Environmentally stressed drug-naive melanoma cells share a molecular signature with drug-tolerant and drug-resistant cells

Authors: Shahla Asgharzadeh Kangachar[1], Farzana Ahmed[1], Abdullah Al Emran[1], Nicholas Matigian[2], Glen M. Boyle[3], Quan Nguyen[3,4], Helmut Schaider[1], Nikolas K. Haass[1]

[1]Frazer Institute, The University of Queensland, Brisbane, QLD, Australia;
[2]Queensland Cyber Infrastructure Foundation Ltd (QCIF), Brisbane, QLD, Australia;
[3]QIMR Berghofer Medical Research Institute, Brisbane, QLD, Australia;
[4]Division of Genetics and Genomics, Institute for Molecular Bioscience, The University of Queensland, Brisbane, QLD, Australia

Melanoma drug resistance, driven predominantly by dynamic heterogeneity, prevails in slow-cycling rather than proliferating tumour cells. We analyzed the transcriptome of 3D melanoma spheroids, where the inner cell-layers are slow-cycling while the outer cell-layers remain proliferating. The differentially expressed genes (DEGs) and pathways affecting the spheroid cell cycle (inner vs. outer cells, IVO) were correlated with drug-sensitive vs. drug-tolerant (TVS) and drug-resistant (RVS) melanoma. IVO shared 14.7% (192 genes) of their upregulated and 36.6% (357 genes) of their downregulated DEGs with the TVS group, and 9.2% (120 genes) and 15.8% (154 genes) with the RVS group. The number of shared enriched pathways in IVO vs. TVS was higher than IVO vs. RVS. In addition, hsa-miR-4497 is the only miRNA that is dysregulated significantly in all three experimental conditions. Our comparative analysis of hsa-miR-4497 target genes revealed it plays a key role in all three different experimental groups through distinct but overlapping mechanisms. We speculate that hsa-miR-4497 drives both inner and drug-tolerant cells to exhibit early adaptive responses to stress. Although through regulation of different genes in inner and resistant cells, the genes affected by hsa-miR-4497 exhibit long-term adaptive processes that involve a strategic reallocation of resources to enhance survival under prolonged adverse conditions. Also, adaptation of inner cells to hypoxia mirrors stable resistance (RVS), which focuses on maintaining critical survival pathways and reducing cell migration and invasion. In conclusion, environmentally stressed inner cells revealed gene expression patterns more similar to drug-induced early persister than irreversibly drug-resistant cells.

65

Title: Modulating Melanoma TIME (Tumour Immune Microenvironment) to Improve Immune Cell Infiltration

Authors: Yimeng Guan[1], Daniel Chan[1], Satoru Sugihara[2], Alexis de Sa Ribeiro Do Bonfim Melo[1], Alexander Browning[3], Gency Gunasingh[1], Loredana Spoerri[1], Janin Chandra[1], Fernando Guimaraes[1], Nikolas K. Haass[1]

[1] The University of Queensland, Frazer Institute, Brisbane, QLD, Australia,
[2] Okayama University, Department of Dermatology, Okayama, Japan,
[3] University of Melbourne, School of Mathematics and Statistics, Melbourne, VIC

Microphthalmia-associated transcription factor (MITF) is a key player in melanoma phenotype switching between proliferative and invasive states. We showed previously that MITF regulates phenotypic melanoma heterogeneity through changing extracellular matrix (ECM) composition and tumour microarchitecture. ROCK (Rho kinase) inhibition mimics the MITF-high phenotype by generating a loose spheroid architecture and a wider distribution of proliferating cells and thus a smaller G1-arrested core.

We hypothesise that MITF-upregulation or ROCK inhibition regulate immune cell infiltration through changed ECM structure.

We show that MITF-upregulation or ROCK inhibition affect immune cell infiltration in a cell line-dependent manner. The spatial distribution pattern of PBMCs infiltrating into spheroids matched the pattern of ECM fiber organization, suggesting that ECM structure, regulated by MITF expression and ROCK activity, plays a critical role in PBMC penetration.

Notably, PBMCs preferentially targeted proliferating cells. ROCK inhibition boosted PBMC activity regarding eliminating proliferating melanoma cells in the spheroid periphery. Natural Killer (NK) cells are likely responsible for the melanoma cell death, given the short duration of the experiment, which precludes T cell activation. Indeed, NK cell cytotoxicity in 2D culture resulted in an increase in cell death, indicating that NK cells were responsible for the melanoma cell elimination.

Given the melanoma cell death in PBMC-infiltrated groups primarily emerged in the peripheral zone, which was occupied by proliferating cells, we further sought to understand why NK cells specifically targeted the proliferating peripheral cell population. By investigating NK cell activation and inhibitory ligands in both melanoma subpopulations, we found that proliferative melanoma cells produced more MICA/B, a critical activation ligand for NK cells.

In summary, dormant cells are often responsible for melanoma relapse, which is a challenge for current clinical treatments. We propose that ROCKi will increase the total number of immune-

sensitive proliferating cells and allow for a better innate immune response, suggesting a potential combination with immune checkpoint inhibitors.

66

Title: Systemic Immune Correlates of Cutaneous Immune Related Adverse Events in Patients Receiving Immune Checkpoint Inhibitors

Authors: Yuyang Liu[1,2], Huang Wang[2], Emma-Anne Karlsen[1,2], Euan Walpole[3], Lea Dousset[2], Janin Chandra[2,4], Kiarash Khosrotehrani[1,2,4]

Affiliations

[1]Princess Alexandra Hospital, Department of Dermatology, Brisbane, Australia
[2]The University of Queensland, Faculty of Health, Medicine and Behavioural Science, Frazer Institute, Brisbane, Australia
[3]Princess Alexandra Hospital, Department of Medical Oncology, Brisbane, Australia
[4]Dermatology Research Centre, The University of Queesland, Brisbane, Australia

Background: Cutaneous immune-related adverse events (cirAEs) are the most common toxic effects associated with immune checkpoint inhibitors (ICIs). Despite its prevalence, the baseline immune features associated with cirAE development remain unclear. This study characterizes the incidence, severity, and outcomes of cirAEs in ICI-treated patients and investigates baseline peripheral immune features associated with the development of immune-related adverse events (irAEs) with a specific focus on cutaneous toxicity.

Methods: We performed a secondary analysis of clinical and biospecimen data from immunotherapy-naïve solid cancer patients initiating ICI at a tertiary centre in Brisbane, between August 2021 and February 2023.

Baseline peripheral blood samples underwent immunophenotyping and proteomic profiling. Primary outcomes included the incidence, severity, and phenotype of cirAEs and their associations with baseline immune profiles. Correlations with treatment response and survival were also assessed.

Results: Among 82 patients, 58 (51%) developed an irAE and 31 (27%) specifically developed a cirAE. Most cirAEs were mild, with grade 1 reactions occurring in 84% of patients. Patients with irAEs, particularly cirAEs, demonstrated higher treatment response rates and improved survival compared with those without irAEs ($p<0.05$). Baseline demographic and disease characteristics were similar across groups, and multivariable analysis showed no significant associations between cirAE development and ICI agent, age, sex, body mass index and ethnicity ($p>0.05$). Baseline immune profiling revealed differences in T-cell and dendritic cell subsets between patients with and without irAEs. Lymphocyte activation gene-3 (LAG-3) expressing immune subsets were

consistently higher in patients without irAEs, suggesting a more immunoregulatory baseline immune state.

Conclusion: cirAEs were common, predominantly mild, and associated with improved treatment response and survival. Baseline clinical characteristics did not predict cirAE development, whereas patterns of immune cell composition and inhibitory checkpoint expression suggest that toxicity risk may be influenced by the balance between immune activation and regulation. These findings support the concept that cirAEs represent a clinically accessible marker of effective immune engagement and highlight the potential future role of baseline immune profiling in toxicity risk stratification.

67

Title: Pigmentation Delta: Change from Innate to Facultative Pigmentation as an Objective Marker of Photodamage Risk

Authors: A. Susanto[1,2], S. Kahler[1,2], C. Primiero[1].

[1]Frazer Institute, Dermatology Resarch Centre, The University of Queensland, Brisbane, Queensland, Australia.
[2]Department of Dermatology, Princess Alexandra Hospital, Brisbane, Queensland, Australia.

Background: The Fitzpatrick scale is widely used to estimate sun sensitivity and skin cancer risk, however it relies on subjective interpretation and performs poorly in darker skin tones. Objective pigmentation metrics such as melanin index (MI), individual typology angle (ITA) and CIE L* quantify skin colour precisely but do not capture how an individual responds to ultraviolet (UV) exposure. This study evaluated whether pigmentation delta, the within-person contrast between innate and facultative pigmentation, acts as a novel, objective marker of UV susceptibility and early pre-malignant change, outperforming Fitzpatrick type.

Methods: Participants (n=151) from the Australian SPAI cohort completed questionnaires on Fitzpatrick type, ancestry, sun exposure history, tanning behaviours, and UV-response traits. Innate and facultative pigmentation (MI, ITA, CIE L*) were measured at standardised axilla and forearm sites using spectrophotometry and colorimetry. Photodamage was graded using the Glogau wrinkle scale and a structured forearm photoaging assessment. Pigmentation deltas were calculated for all metrics (MI used a relative difference). Regression analyses examined associations between Fitzpatrick type, innate pigmentation, and pigmentation delta with UV-response traits and early photodamage, adjusting for age, sex, and sun exposure behaviours.

Results: Fitzpatrick type correlated more strongly with innate pigmentation ($r=0.41$-0.59; $p<0.001$) than with UV-response traits ($r=0.28$-0.41; $p<0.001$), indicating it primarily reflects baseline skin colour rather than UV susceptibility. Fitzpatrick type was minimally associated with photodamage ($R^2=0.04$, $p=0.01$; significant for superficial actinic keratoses only). In contrast,

pigmentation deltas showed significant associations with early photodamage: Δ ITA with superficial actinic keratoses (R^2=0.03, p=0.03), ΔCIE L* and ΔMI with wrinkles (R^2=0.07, p=0.001; R^2=0.04, p=0.02), and all pigmentation deltas with hypochromia count (ΔMI: R^2=0.05, p=0.003; ΔITA: R^2=0.11, p<0.001; ΔCIE L*: R^2=0.09, p<0.001).

Conclusion: Pigmentation delta reflects an individualised, dynamic measure of UV-induced skin response not captured by Fitzpatrick type. Its stronger associations with early photodamage and pre-malignant changes support pigmentation delta as a promising objective marker of UV susceptibility with potential applications in risk stratification and improving equity in dermatological artificial intelligence.

68

Title: Novel serum autoantibodies against ATRX, a component of PML nuclear bodies, in dermatomyositis

Authors: Y. Yamashita[1], H. Kanoh[2, 3], Y. Muro[1], S. Kamiya[1], E. Noda[1], N. Akashi[1], H. Koizumi[1, 4], M. Ogawa-Momohara[1], T. Takeichi[1], M. Akiyama[1, 5].

[1]Nagoya University, Dept. of Dermatology, Nagoya, Japan.
[2]Gifu University, Dept. of Dermatology, Gifu, Japan.
[3]Gifu Municipal Hospital, Dept. of Dermatology, Gifu, Japan.
[4]Toyota Memorial Hospital, Dept. of Dermatology, Toyota, Japan.
[5]Shin-yurigaoka General Hospital, Dept. of Dermatology, Kawasaki, Japan.

Idiopathic inflammatory myopathy (IIM) is a systemic autoimmune disorder that affects the skeletal muscles, skin, and various other organs. Myositis-specific autoantibodies (MSAs) are associated with IIM classification and disease prognosis, but 24.8% of adults and 55.9% of juveniles with IIM are negative for MSAs. We experienced a unique case of juvenile dermatomyositis (JDM) with autoantibodies against alpha thalassemia/mental retardation syndrome X-linked (ATRX), which is one component of promyelocytic leukaemia nuclear bodies (PML-NBs), in clinic. To investigate the relationship between IIM and autoantibodies against PML-NBs, we measured the autoantibodies against some components of PML-NBs, such as anti-ATRX, anti-Sp100 and anti-NXP-2 antibodies, in our cohort.

Our cohort consists of 1,252 sera from various diseases and conditions. Anti-ATRX antibodies were detected by double immunofluorescence staining, our in-house ELISA and immunoprecipitation using ATRX recombinant protein produced by *in vitro* translation/transcription system. Anti-Sp100 antibodies were analyzed by ELISA according to the manufacturer's instructions. Anti-NXP-2 antibodies were examined by our previously reported methods.

Anti-NXP-2 antibodies were detected in 10 serum samples, although anti-ATRX antibodies were detected only in one adult female IIM patient. She was an amyopathic dermatomyositis (DM)

patient. She developed diffuse large B-cell lymphoma around the time she was diagnosed with cancer-associated DM (CADM). Anti-Sp100 antibodies were found in two patients, one with Sjögren's disease and the other with eosinophilic fasciitis, neither of whom had features of primary biliary cholangitis often associated with anti-Sp100 antibodies. There was no coexistence of anti-NXP-2 and anti-ATRX or anti-Sp100 antibodies in our cohort. Notably, anti-ATRX antibodies were detected in the JDM and the CADM patients, just as they are detected as a feature in patients with anti-NXP-2 antibodies, which are widely known to be MSAs.

This study might pave the way to uncovering novel aspects of autoimmunity targeting various components of PML-NBs in DM, and suggests that ATRX may be associated with the pathogenesis of DM.

69

Title: Ammonium persulfate as a leading cause of vulval contact dermatitis

Authors: Lily Rath[1,2], Jonathan J Peek[1,2], Lynda Spelman[1,2]

[1.]Gabba Dermatology, Woolloongabba, Queensland, Australia
[2.]Veracity Clinical Research, Woolloongabba, Queensland, Australia

Aim: Vulval irritation and pruritus can be debilitating, affecting an estimated 5-10% of women. This figure is thought to be underreported due to social stigma and perceived embarrassment. This study aimed to identify key allergens in patients with suspected vulvar contact dermatitis at a single dermatology centre.

Method: A retrospective audit of patients referred for persistent vulval irritation to a specialist dermatology outpatient clinic was conducted between 2018 and 2025, focusing on cases of suspected allergic contact dermatitis. Patch testing was performed on 40 patients using the Australian Baseline Series (60 allergens) with additional testing of the patient's personal care products in 77.5% of patients. Results were read according to International Contact Dermatitis Research group criteria at days 3 and 5 to 4 and 5 depending on patient availability. Descriptive statistics were used to analyse patch test results, with allergen reactivity expressed as frequencies and percentages.

Results: Patch testing results were obtained from forty females (age range 12-65) with persistent vulval irritation and suspected allergic contact dermatitis. Positive patch tests occurred in 97.5% of patients. A history of atopy was present in 62.5% of patients. Ammonium persulfate was the most common allergen, affecting 60% of patients. Other frequently implicated allergens included hydroperoxides of limonene (52.5%), nickel sulfate (50%) and potassium dichromate (35%). Personal product testing revealed 66.9% positive reactions, with shower wash products (78.9%) and shampoos (64.3%) most frequently implicated.

Conclusions: Ammonium persulfate emerged as the leading allergen in this cohort, primarily from cosmetic hair products, a finding not widely reported in international literature. These results highlight the need for detailed exposure history and consideration of region-specific allergen patterns in the management of vulvar dermatitis in Australian practice.

70

Title: Novel rescue therapy for steroid-refractory drug eruption with overlying pustular psoriasis/AGEP: combination ciclosporin and bimekizumab

Authors: Lily Rath[1,2], Jim Muir[1,2], Daman Langguth[3]

[1]Mater Hospital, Department of Dermatology, Brisbane, QLD
[2]University of Queensland, Brisbane, QLD
[3]Sullivan Nicolaides Pathology, Department of Immunology, Brisbane, QLD

Background: Drug reactions commonly manifest on the skin. A severe cutaneous adverse reaction (SCAR) is a term used to describe skin reactions that require prompt recognition and discontinuation of the most likely culprit drug to decrease both morbidity and mortality.

Case: A 60-year-old male with a background of psoriasis, hypertension, anxiety and hypercholesterolaemia presented to the emergency department with a six-week history of a progressive generalised psoriasiform eruption following consumption of liver detox tablets containing milk thistle amongst other medications including a dose increase of atorvastatin approximately 8 weeks prior. The patient developed skin pain and took further medications including semaglutide, cefalexin and celecoxib which was followed by appearance of widespread pustules and progression of his psoriasiform plaques. Initial histopathology was consistent with a lichenoid drug reaction. The patient became febrile with markedly deranged liver function tests and a rising CRP prompting multidisciplinary review. All of his medications were withheld and prednisolone 50mg daily was administered for a week before starting apremilast. The eruption continued to progress to erythroderma and worsening liver function test (LFT) derangement.

Further cutaneous biopsies demonstrated subcorneal pustules with epidermal neutrophilic exocytosis and mild epidermal hyperplasia, with a moderate superficial dermal perivascular to interstitial lymphocytic infiltrate with dispersed neutrophils and scattered eosinophils, dermal papillary oedema and red cell extravasation, favouring acute generalised exanthematous

pustulosis (AGEP). Although pustular psoriasis remained a differential, there was only limited parakeratosis, underdeveloped psoriasiform hyperplasia, only mildly prominent dermal papillary vascularity and eosinophils were seen. A diagnosis of drug eruption with overlying psoriasis/AGEP was suspected. Apremilast was commenced, however on day 6, the patient developed a peripheral eosinophilia and it was ceased. The patient was hypertensive with erythrodermic disseminated sterile subcorneal pustules and widespread desquamation. Following multidisciplinary review, a liver biopsy was performed, and infectious and autoimmune causes were deemed unlikely. The LFT derangement was likely secondary to systemic inflammation. Ciclosporin and bimekizumab were commenced alongside an antihypertensive from a different class to his prior antihypertensives. Clinically meaningful improvement was observed within 24 hours, with near-complete pustule clearance by day four. CRP and liver function tests improved in subsequent days. Prednisolone has been successfully weaned to 20mg daily.

Conclusion: This case demonstrates a rapid and dramatic response to combination ciclosporin and bimekizumab in a steroid-refractory drug eruption. AGEP is associated with elevated IL-17 levels, which stimulate keratinocytes to produce IL-8, the latter acting as a chemokine-like mobilising agent for neutrophils. The dual inhibition of IL-17A and IL-17F by bimekizumab offers a mechanistically rational approach in this AGEP-like drug eruption. The ciclosporin helped reduce the systemic inflammation. To our knowledge, this is the first reported use of a combination of bimekizumab and ciclosporin in this clinical context. Further evaluation of IL-17AF blockade in AGEP is warranted.

71

Title: Photoprotection in Australia: Bridging Photobiological Mechanisms and Public Health Practice in the World's Highest UV-Burdened Environment

Authors: Matthew Chen[1 2], Katie M. Dixon[1].

[1]School of Medical Sciences, Faculty of Medicine and Health, The University of Sydney, Sydney, NSW, Australia.
[2]Sydney Medical School, Faculty of Medicine and Health, The University of Sydney, Sydney, NSW, Australia.

Ultraviolet radiation (UVR) remains the driving environmental cause of skin carcinogenesis, photoageing, and immunological dysregulation. Despite extensive mechanistic understanding of UVR-induced molecular damage, contemporary photoprotection strategies remain anchored to erythema-based protection metrics that predominantly reflect UVB exposure and incompletely capture UVA-mediated oxidative and immunological injury. There is therefore a critical need to reframe photoprotection around mechanistic, multi-pathway UVR damage models integrated with realistic behavioural and environmental exposure patterns to facilitate effective skin cancer prevention.

A narrative literature review was conducted across photobiological, dermatological, and public health domains, to synthesise contemporary evidence in UVR photobiology to evaluate the adequacy of current photoprotective paradigms, with a focus on the Australian context where skin cancer incidence is among the highest globally. Current photoprotective strategies, including sunscreens, protective clothing, behavioural interventions, and regulatory frameworks, were critically assessed alongside epidemiological and compliance data, with particular attention to SPF based limitations and UVA protection inconsistencies. The current literature demonstrates that while existing interventions reduce acute erythema and non-melanoma skin cancer risk, significant gaps persist in protection against UVA-mediated oxidative damage, immunomodulation, and usage effectiveness. The insufficient application of sunscreen, behavioural non-compliance, and sociocultural normalisation of tanning further reduce population-level efficacy. Emerging strategies, including DNA repair enzyme formulations, oral photoprotective agents, and photostable broad-spectrum filters, are promising but remain insufficiently validated for population scale implementation.

This review concludes that next generation photoprotection must shift toward mechanistically informed, spectrum complete, and behaviourally realistic strategies. Australia represents a key translational setting in which integrated policy, education, and innovation could redefine global standards in UVR risk mitigation especially as a country burdened with the highest melanoma rates globally.

72

Title: Double trouble: How Herpes Simplex Virus promotes HIV in Genital Tissue

Authors: *Dona Sirimanne[1,2], *Hafsa Rana[1,3], Kirstie Bertram[1,3], Najla Nasr[1,2], Kerrie Sandgren[1,3,4], ØAnthony Cunningham[1,3,4] and ØNaomi Truong[1,3,4]

[1]Centre for Virus Research, The Westmead Institute for Medical Research; Westmead, Australia. [2]School of Medical Sciences, Faculty of Medicine and Health, The University of Sydney; Sydney, Australia [3]Faculty of Medicine and Health, The University of Sydney, Westmead, Australia. [4]Sydney Infectious Diseases Institute (SydneyID), The University of Sydney; Sydney, Australia

*Co-first authors, ØCo-last authors

Herpes Simplex Virus (HSV) amplifies HIV acquisition 3-5-fold, yet the immunological mechanisms underlying coinfection are not well understood. HSV-infected human epidermal Langerhans cells (LCs) and Epidermal (Epi-) DCs migrate to the dermis and cluster with dermal DCs, which phagocytose apoptotic LC fragments containing HSV for antigen presentation and stimulation of a primary T cell response to HSV (as demonstrated in mice) - a “viral antigen relay”. Meanwhile HSV infection recruits CD4+ T cells to the dermis, the target cell of HIV. We set up human anogenital explant infection models in which microarray patches (MAPs) coated in HSV are used

for virus delivery - mimicking the clinically relevant microtrauma required for sexual transmission. Cyclic immunofluorescence microscopy with RNAscope and high parameter multiplex imaging have been optimised to simultaneously identify HSV infected LCs and Epi-DCs, interacting with subsets of dermal DCs and CD4+ T cells. Using our model optimised with a new iteration MAP, we successfully visualised HSV-infected LC migration to the dermis in HSV-1 infection within inner foreskin. It was hypothesised that all anogenital tissues would be infectible by HSV due to their minimal stratum corneum, however unlike foreskin, vaginal mucosal samples lacked infection, and only single-cell infection was visible in cervix, correlating with clinical observations of genital herpes lesions: in males, inner foreskin and penile shaft are common sites, while in females, vulva, labia and perineum are common sites, while vaginal lesions are not observed. We are profiling the expression of the HSV-entry receptor nectin-1 and cornified envelope proteins in foreskin compared to vagina and labia to correlate their expression with susceptibility to infection. Preliminary data in vaginal mucosa compared to foreskin indicates that nectin-1 is predominant in basal layers in vagina however present throughout the epithelium in foreskin. To determine whether HIV hijacks the viral relay to traffic to and infect dermal CD4+ T cells, we are also extending studies of inner foreskin to coinfection with HIV, by topically applying HIV infection via a cloning cylinder following HSV infection. Given the explicit epidemiological link between HSV and HIV, determining the interactions underlying early coinfection in various anogenital tissue types will help to define the immune pathways that may be targeted in the development of an HSV prophylactic vaccine.

73

Title: Deciphering the complex pathways in Lentigo Maligna through Proteomics in scarless biopsy

Authors: R. Ruiz Araujo [1], A. Azimi[1,2,3], R. Teh[1,3], L. Faul[1,2,3] & P. Fernandez-Penas[1,2,3]

[1.] Department of Dermatology, Westmead Hospital, Westmead, New South Wales, 2145, Australia

[2.] Centre for Cancer Research, The Westmead Institute for Medical Research, The University of Sydney, Westmead, New South Wales, 2145, Australia

[3.] Westmead Clinical School, Faculty of Medicine and Health, The University of Sydney, Westmead, New South Wales, 2145, Australia

Lentigo maligna (LM) is a common subtype of melanoma in situ arising on chronically sun-damaged (CSD) skin. Diagnosis and management rely on morphological assessment, including clinical examination, reflectance confocal microscopy (RCM), and histopathology. These methods can be challenging because LM often has subtle features and may be difficult to distinguish from adjacent CSD skin. Molecular studies may provide complementary information to improve diagnostic precision and management. However, research on LM is limited, and no studies have examined its proteomic profile or compared it with surrounding skin to identify altered pathways.

Methods: A scarless biopsy technique was used in which superficial layers of the stratum corneum were sequentially removed using adhesive discs, followed by protein extraction and quantification with liquid chromatography–mass spectrometry (LC-MS/MS). The study included 42 adults with clinically and histologically confirmed LM attending the Dermatology Clinic at Westmead Hospital between 2021 and 2024. RCM was performed to map lesions and guide sampling from three regions: LM centre, LM edge, and adjacent normal skin. Participants then underwent surgical excision with histological confirmation of residual LM , margins and normal skin . Differential abundance analysis compared protein expression between regions. Ingenuity Pathway Analysis (IPA) identified disrupted biological pathways.

Results: No statistically significant differentially abundant proteins were identified between groups. However, pathway analysis comparing LM centre with normal skin suggested activation of carcinogenesis-related pathways involving metabolism, epithelial integrity, immune and inflammatory signalling, stress responses, and regulation of tumour cell migration. In contrast, LM edge compared with surrounding skin showed enrichment of pathways related to apoptosis and immune cell responses.

Conclusion: This discovery proteomic study provides preliminary evidence of molecular differences between LM, lesion edge, and surrounding skin. Although no individual proteins reached significance, pathway-level findings suggest biologically relevant alterations that may improve understanding of LM pathogenesis and help future research.

74

Title: Changes in Microbial Composition in Actinic Keratosis after Topical Application of *Cutibacterium acnes* D1 over Two Weeks: A Placebo-controlled, Randomised, Double-blinded Pilot Study.

Authors: Jacoba Bromfield1*, Julian Zaugg2*, Francois Brillet3,4, Annika Krueger1, Charlotte Cox1, Nadeem Khan3, Bernhard Paetzold3, Philip Hugenholtz2#, Ian H. Frazer1#, Kiarash Khosrotehrani1,5,6,4#, Janin Chandra1,6#

[1]Frazer Institute, Faculty of Health, Medicine and Behavioural Science, The University of Queensland, Woolloongabba, QLD 4102, Australia
[2]Australian Centre for Ecogenomics, School of Chemistry and Molecular Biosciences, The University of Queensland, St Lucia, QLD 4067, Australia
3S-Biomedic NV, 9052 Gent Belgium
[4]Department of Medicine and Life Sciences, Universitat Pompeu Fabra, Barcelona, Spain
[5]Department of Dermatology, Princess Alexandra Hospital, Woolloongabba, QLD 4102, Australia.
[6]Dermatology Research Centre, The University of Queensland, Brisbane, QLD 4102, Australia

Actinic keratosis (AK) is a premalignant precursor of cutaneous squamous cell carcinomas (cSCC). Recent studies have demonstrated that AK and cSCC are often in a state of microbial dysbiosis,

characterised by an enrichment of staphylococcal species, such as Staphylococcus aureus, and a decrease of Cutibacterium acnes. Molecular research supports that S. aureus may be a microbial contributor of AK to cSCC progression. This interventional, randomised, placebo-controlled clinical trial explored the use of a topical live biotherapy containing C. acnes for AK lesions, assessing its capacity to shift or rebalance the microbial profile and reduce Staphylococcus abundance. Here, we demonstrate that 14 days of topical application of C. acnes strain D1 can modulate the microbiome of AK lesions for a minimum of 120–180 days. Staphylococcus relative abundance was decreased after C. acnes application and remained lower than at pre-treatment level. Treatment further led to broad long-term (120–180 days) changes in microbial composition, including increased microbial diversity, and reduced relative abundance of Staphylococcus. Interestingly, the same effects were observed on the non-lesional photodamaged skin of the opposite arm of participants that was not intentionally treated, suggesting that the local application of C. acnes may benefit distant skin regions too via physical carry-over. This demonstrates a potential for C. acnes to act as a topical live biotherapy to restore eubiosis on AK lesions and non-lesional photodamaged skin.

76

Title: Retrospective analysis of basal cell carcinoma growth using serial dermoscopic imaging

Authors: Joe Beaird, Sam Kahler, Ellie Maas, Clare Primiero, H. Peter Soyer, Aideen McInernery-Leo

Introduction: Basal cell carcinoma (BCC) is the most common skin malignancy worldwide. Despite its high prevalence, the growth rate of BCC remains largely understudied, as lesions are typically excised shortly after clinical diagnosis. This pilot study aimed to investigate changes in BCC surface area over time using retrospective serial dermoscopic imaging from the Australian Centre of Excellence in Melanoma Imaging and Diagnosis Cohort Study.

Methods: Dermoscopic images of 10 clinically diagnosed BCCs from 9 participants were analyzed using ImageJ software to estimate lesion growth over time. Due to variable imaging intervals between patients, lesion growth was standardized by calculating absolute and relative monthly changes in surface area. Results: Of the 10 lesions analyzed, 7/10 (70%) demonstrated growth rates ,0.5 mm¬≤/month, with these lesions exhibiting a mean surface area increase of 7.7% per month. One lesion (10%) demonstrated minimal growth (0.15 mm¬≤/month), while 2/10 lesions (20%) remained stable or decreased slightly in size. BBC histologic subtypes included nodular (3/10), superficial (3/10), infiltrative (3/10), and pigmented (1/10). All superficial and infiltrative lesions increased in size, as did 2/3 nodular lesions. The single pigmented lesion demonstrated slight regression.

Conclusion: This pilot study suggests that most BCCs demonstrate measurable longitudinal growth on serial dermoscopic imaging. Further investigation in a larger cohort is warranted to better characterize subtype-specific growth patterns and assess potential implications for clinical monitoring and management.

78

Title: Cost-utility of sirolimus in the treatment of vascular malformations

Authors: Grace X Li, Deshan F Sebaratnam

Aims: Although there is a growing body of evidence supporting the mTOR inhibitor sirolimus as an effective treatment for specific vascular anomalies, its use remains off-label and is not currently subsidised by the Australian government. This study evaluated the cost-effectiveness of sirolimus for vascular malformations from the perspective of the Australian healthcare sector.

Methods: A simulated cohort of adults aged ,18 years with slow-flow vascular malformations requiring treatment was modelled. Patients were either initiated on sirolimus 1 mg daily or received supportive care. Health state utility values were obtained from published literature, and cost data were sourced from hospital pharmacies and public reimbursement schedules. Outcomes included costs, quality-adjusted life-years (QALYs), and the incremental cost effectiveness ratio (ICER). One-way and probabilistic sensitivity analyses were conducted to assess parameter uncertainty, using TreeAge Pro Healthcare.

Results: Over a one-year time horizon, sirolimus was associated with an additional cost of A$2,833 and a gain of 0.08 QALYs compared with supportive care, resulting in an ICER of A$35,410 per QALY gained. One-way sensitivity analysis demonstrated that the ICER was most sensitive to utility values and drug cost. Probabilistic sensitivity analysis showed sirolimus was cost effective in 55.1% of 10,000 Monte Carlo simulations. Conclusion: At a willingness-to-pay threshold of A$50,000 per QALY, these findings suggest sirolimus is likely to be a cost-effective treatment option for vascular malformations in the Australian healthcare setting.

79

Title: A Mechanistic Case Analysis of Dupilumab in Dual-Therapy Refractory Pemphigoid Gestationis

Authors: Ahmed Abid,[1] Ali Abid,[2,3] Kelvin Truong,[1,2] Jing Jing Li, [4] Paul Weller[2]

[1]Faculty of Medicine and Health, University of Sydney, NSW
[2]Department of Dermatology, Liverpool Hospital, Sydney, NSW
[3]School of Clinical Medicine, University of New South Wales, Sydney, NSW
[4]Department of Anatomical Pathology, Liverpool Hospital, Sydney, NSW

Pemphigoid gestationis (PG) is a rare autoimmune blistering disorder of pregnancy characterised by autoantibodies directed against BP180. The disease is thought to involve a predominantly eosinophilic, Th2-skewed inflammatory response, with IL-4 and IL-13 acting as key cytokine drivers.

While systemic corticosteroids remain the first-line therapy for PG, refractory cases highlight the need for more targeted immunomodulatory approaches. Dupilumab, a monoclonal antibody that inhibits IL-4 and IL-13 signalling via blockade of the IL-4 receptor α subunit, directly targets this Th2 axis and therefore represents a mechanistically rational therapeutic option in PG.

In assessing the effectiveness of the proposed treatment, we present the case of a 31-year-old G4P3 woman with recurrent PG presenting at 15 weeks gestation with pruritic urticarial plaques and bullae involving the abdomen, intermammary region, and upper limb. Initial management with oral prednisone (up to 0.5 mg/kg) was ineffective, and escalation to combination therapy with cyclosporine (3 mg/kg/day) failed to achieve disease control after 4 weeks, with progression of lesions and severe pruritus impairing quality of life. Dupilumab was commenced at 25 weeks gestation (600 mg loading dose followed by 300 mg fortnightly) alongside existing therapy. A rapid clinical response was observed within 48 hours, with marked reduction in pruritus and cessation of new blister formation. This enabled tapering of corticosteroids and discontinuation of cyclosporine, with sustained remission following cessation of therapy postpartum. No neonatal blistering was observed. The pregnancy was complicated by preterm premature rupture of membranes and preterm delivery; however, multiple confounding factors limited attribution to dupilumab.

This case supports a pathogenic role for Th2-mediated inflammation in PG and demonstrates the clinical efficacy of targeting this pathway. By inhibiting IL-4 and IL-13 signalling, dupilumab likely attenuates eosinophilic inflammation, pruritus, and downstream tissue damage. These findings

support consideration of dupilumab as a targeted, steroid-sparing therapy in refractory PG and highlight the need for further studies to define its role in management.

80

Title: Frisson, ÄëTriggered Piloerection as a Novel Non, Äëpharmacological Strategy to Modulate Itch and Pain Pathways.

Authors: Max Wu, BMedSci (Hons), MD4; Geoffrey Lee, MBBS, DPhil (Oxon), FACD

Chronic pruritus affects up to one in five individuals and causes morbidity comparable to chronic pain, yet current therapies remain limited and often poorly tolerated. Frisson, elicited by music, film, or ASMR, produces piloerection with robust autonomic and limbic activation. Emerging evidence suggests that frisson, Äërelated piloerection engages central circuits overlapping itch and pain networks, activating endogenous gating mechanisms that suppress pruriception. We synthesise cross, Äëspecies data supporting this concept and propose an integrated model in which frisson, Äëevoked piloerection recruits spinal inhibitory and reward circuits to down, Äëweight itch salience. This framework highlights frisson, Äëbased interventions as a low, Äërisk, non, Äëpharmacological tertiary adjunct for refractory pruritus.