SINGAPORE INTERNATIONAL SKIN CONFERENCE

13 - 15 March 2024

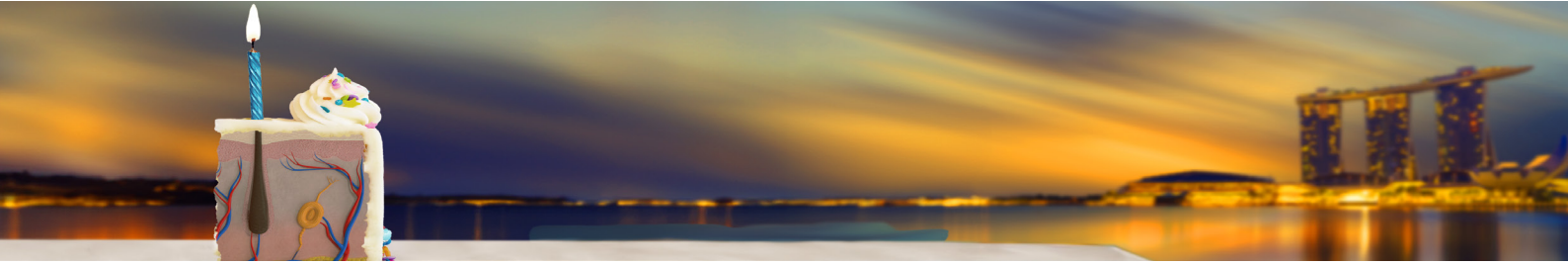
10 Years ANNIVERSARY

Poster Abstracts

SKIN RESEARCH SOCIETY (SINGAPORE)

SKIN RESEARCH INSTITUTE OF SINGAPORE
Leading Skin Health Innovation

WWW.SKINSOC.ORG.SG



P1

Enhancing epidermal re-pigmentation during phototherapy in Vitiligo

Gracia Goh[1,2], Jamien Lim[2], Joy Ng[1,2], Rachel Phua[1,2], Zoe Lim[1], Kenice Sim[1], Carlos Clavel[1,2]

*[1]Hair & Pigmentation Development, A*STAR Skin Research Labs (ASRL), Singapore; [2]Lee Kong Chian School of Medicine, Nanyang Technological University (NTU), Singapore*

Skin pigmentation disorders pose serious dermatological concerns and bring immense psychological burdens to individuals. Vitiligo is one such disorder and is resistant to various conventional treatments. The hair follicle bulge holds a stem cell (SC) population directly responsible for hair pigmentation, the melanocyte stem cells (MeSCs). MeSCs are an unpigmented quiescent population of SCs that control hair pigmentation by synthesizing and transporting melanin to matrix keratinocytes during anagen. UV-induced migration of hair follicle MeSCs can be achieved by phototherapy to trigger epidermal re-pigmentation. However, there is a clinical need for enhancing follicular re-pigmentation during phototherapy because the process is costly and requires repeated UV exposures. To unravel the possibility of enhancing treatment, we utilized in vitro models to study the role of BMP signalling in melanocyte function. Our preliminary data indicates that BMP4 decreases both melanin production and migration of melanocytes in vitro. Further, to determine its role in follicular re-pigmentation in vivo, we UV-induced melanocyte migration into the interfollicular epidermis in a mouse model. We found that MeSC-specific ablation of BMP4 enhances melanocyte migration and epidermal pigmentation. Moreover, to elucidate the molecular mechanism, we prospectively isolated MeSCs from our mouse model and performed whole transcriptome analysis, identifying several pigmentation and migration targets. Currently, we are using small molecules to regulate BMP signalling in vitro and in a novel vitiligo-like and epidermal-pigmented mouse model that is more relevant to human physiology. We believe our innovative strategy will guide us towards a novel therapeutic approach in pigmentation disorders like Vitiligo.

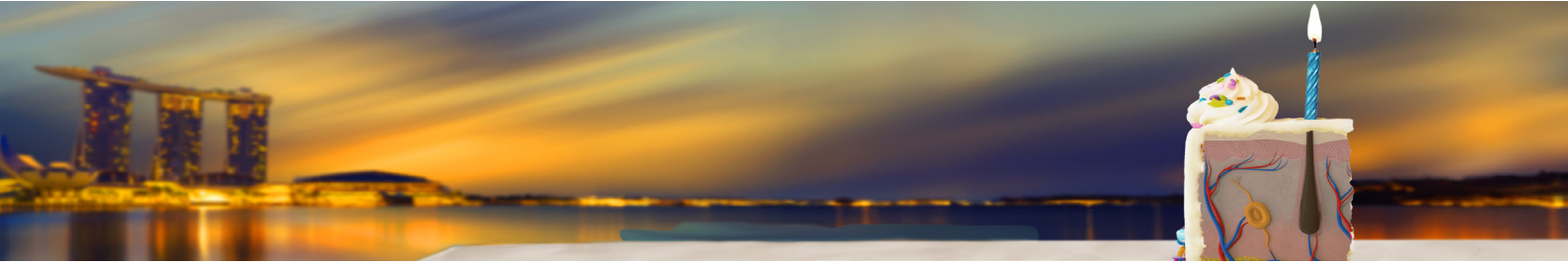
P2

The pursuit to understand skin ceramides' metabolism in atopic dermatitis: Workflow optimization for collection, extraction, and analysis of skin tape strips

Aliya Farissa Afandi[1], Sze Han Lee[1,2], Ray Putra Prajnamitra[1], James Chan[1,3]

*[1]A*STAR Skin Research Labs, Agency for Science, Technology and Research (A*STAR), Singapore; [2]Bioinformatics Institute, A*STAR, Singapore; [3]Singapore Institute of Food and Biotechnology Innovation, A*STAR, Singapore*

Skin ceramide abnormalities are a recognized hallmark of atopic dermatitis (AD), where both subclasses composition and acyl chain length can be altered. Such pathological changes suggest perturbation of biosynthetic or degradation pathways of ceramides in the skin of AD patients. Understanding ceramides' metabolism will yield clarity in the molecular mechanisms of AD and advance development of targeted therapeutics. In this study, we optimized a simple and non-invasive approach using tape stripping on skin to measure 500 ceramides across 20 subclasses via liquid chromatography–mass spectrometry (LC-MS). Several key enzymatic activities such as acid ceramidase and sphingomyelin deacylase were chosen to focus on the development of enzymatic assays for a juxtaposed analysis with the data obtained from LC-MS. From an inhouse pilot, comparison between two tape brands (D-Squame®, CorneoFix®) showed the latter to give a better sampling efficiency in terms of consistency, skin adherence and biomass yield. We optimized a comprehensive extraction method to obtain both free and protein-bound ceramides, the latter which are covalently bound to corneocyte surface proteins and are essential for skin barrier function. Our preliminary findings show that the subclasses of non-hydroxy-phytosphingosine (NP) and non-hydroxy-6-hydroxysphingosine (NH) are the most abundant in human skin, aligned with published literature. A prospective cohort of AD subjects (n=60) is currently in recruitment (Feb 2024 – Feb 2025, DSRB 2023/00890), which will reveal a detailed biochemical mapping of the ceramide pathway. In summary, our streamlined workflow is poised to elucidate human skin ceramides' metabolism and pathogenesis of AD.



P3

Unveiling the crucial roles of Plakophilin structural domains in desmosome localisation, integrity and disease pathogenesis

Beatrice Varanauskaite[1,2], Saba Notash[1], Judith Fülle[1], John Common[2], David Garrod1, Christoph Ballestrem[1]

*[1]Division of Cell Matrix Biology and Regenerative Medicine, The University of Manchester, United Kingdom; [2]A*STAR Skin Research Labs, Agency for Science, Technology and Research, Singapore*

Desmosomes are intercellular junctions that attach cells together, providing vital mechanical integrity within tissues and organs. The inner and outer structures of desmosomes are further linked by plakophilin. Due to constant exposures to mechanical stresses, organs such as the skin and heart rely greatly on desmosomes and plakophilin for structural integrity.
Therefore, mutations in plakophilin result in skin conditions and heart diseases such as epidermolysis bullosa and arrhythmogenic cardiomyopathy respectively, the latter leading to sudden cardiac death. Although truncating and missense mutations of plakophilin are identified, the exact mechanism of disease pathogenesis remains undefined. To better discern the role of plakophilin in health and disease, we generated multiple structural constructs of plakophilin. Here, we show that the N-terminus of plakophilin 2a is crucial not only for targeting plakophilin to desmosomes, but also required for the formation of the whole desmosomal complex. Interestingly, removal of the N-terminus led to a dominant negative effect resulting in a lack of desmosomes even in presence of endogenous plakophilin 2a.
Moreover, overexpression of full-length plakophilin 2a increased desmosomal areas at the cell borders compared to wild-type desmosomes. Removal of both N- and C-termini from plakophilin 2a reduced the dominant negative effect, suggesting that the C-terminus is involved in targeting plakophilin to desmosomes. Overall, these results have elucidated the differential importance of the respective main structural domains of plakophilin 2a in desmosome localisation. Further understanding of these functional parts will enable better prediction of disease pathogenic pathways caused by distinct mutational sites.

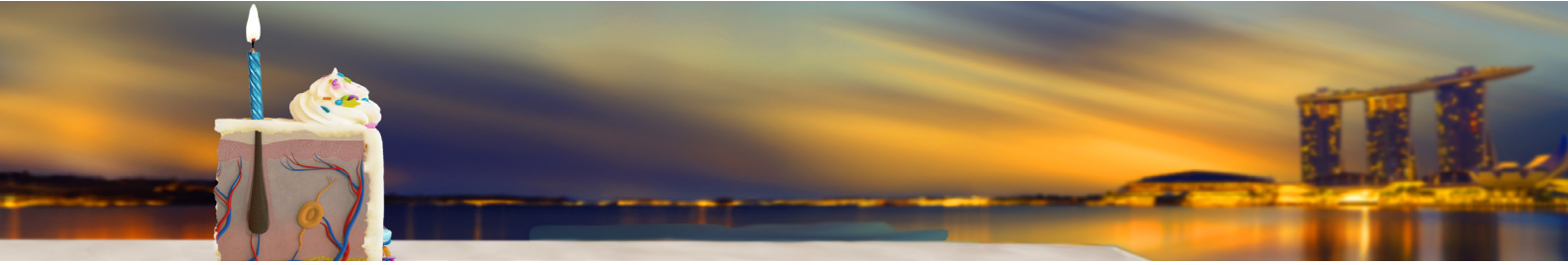
P4

Identification of Malassezia furfur Secreted Aspartyl Protease 2 (MfSAP2) in pityriasis versicolor and its role in corneodesmosin degradation

Wisely Chua[1], Yuanyuan He[i2], Li Fang Koh[3], Belle Lin Hwee Yap[3], Hui Ling Saw[1], Shirlyn Goh[1], Genevieve Ong[1], Thomas L. Dawson Jr.[3], Anthony O'Donoghue[4], John E. Common[3] and Hao Li[1,2]

*1Molecular Engineering Lab, Institute of Molecular and Cell Biology, Agency for Science Technology and Research, Singapore, 61 Biopolis Drive, Proteos, Singapore 138673; 2Department of Chemistry, National University of Singapore, 3 Science Drive 3, Singapore 117543; 3A*STAR Skin Research Labs (A*SRL), Agency for Science, Technology and Research (A*STAR), 8A Biomedical Grove, #06-06, Immunos, Singapore 138648; 4Skaggs School of Pharmacy and Pharmaceutical Sciences, University of California San Diego, La Jolla, California 92093, United States*

Malassezia is the dominant family of fungi residing on human skin and is associated with many dermatological conditions. Among these skin diseases, only pityriasis versicolor (PV) has definite etiological connections with Malassezia. In the hyper- or hypo-pigmented scales of PV patients, Malassezia is enriched in its hyphal form which is rarely present on healthy skin. How the hyphal form of Malassezia contributes to disease pathology in PV is unknown. In this study, we observed a distinct shift in the extracellular proteolytic activity when Malassezia furfur transitions from yeast to hyphae. We identified that the expression of the aspartyl protease MfSAP2 is dramatically upregulated at both the mRNA and protein level when M. furfur is in the mycelial form. We determined the substrate specificity of this protease and observed MfSAP2 can degrade key corneodesmosome proteins, which are intercellular adhesive proteins between corneocytes in the stratum corneum. In a 3D human skin model with MfSAP2 treatment, we observed clear degradation of corneodesmosin (CDSN), a component of the corneodesmosome. Taken together, our study demonstrates that a secreted protease is a key virulence factor associated with the hyphal form of M. furfur and is potentially involved in the disease pathogenesis of PV.



P5

Efficacy of dupilumab in palmoplantar pustulosis treatment highlights the role of Th2 inflammation

Yuxin Zheng[1,2], Xiaoyong Man[1], John Common[2]

*[1]Department of Dermatology, Second Affiliated Hospital, Zhejiang University School of Medicine, Hangzhou, Zhejiang, China; [2]A*STAR Skin Research Labs (A*SRL), Agency for Science, Technology and Research (A*STAR), Republic of Singapore.*

Background: Palmoplantar pustulosis (PPP) is a chronic, recurrent skin disorder characterized by sterile pustules and erythematous scaling on the palms and soles. PPP treatment is challenging for clinicians, and current small-molecule drugs and biologics have limited efficacy. The pathogenesis of PPP is related to Th2 specificity, and dupilumab has emerging therapeutic potential against PPP. Objective: The purpose of this study was to evaluate the serological characteristics of PPP patients and the efficacy and safety of dupilumab treatment. Methods: Ten PPP patients were treated with 300 mg dupilumab every 4 weeks after a 600 mg loading dose. PPPASI75 response rates were recorded after 16 weeks, and all patients were followed up with for at least 1 year. Furthermore, serum samples from 11 PPP, 15 atopic dermatitis, and 14 psoriasis patients and 19 healthy controls were analyzed using Olink® target 96 inflammation panel. Results: Nine of ten PPP patients achieved PPPASI75 with dupilumab at week 16, and no adverse events were reported. Based on Olink proteomics, CCL19, MCP-4, CCL11, and CXCL5 were increased in PPP patients' serum compared with healthy controls and the 'IL-17 signaling pathway' was enriched. Moreover, the serum biomarkers of PPP patients were similar to that of atopic dermatitis and psoriasis patients, although there were fewer similarities with the latter. Conclusion: Dupilumab showed efficacy and safety in PPP patients, potentially resulting from PPP patients' serum Th2 signatures and the similarities between PPP and atopic dermatitis.

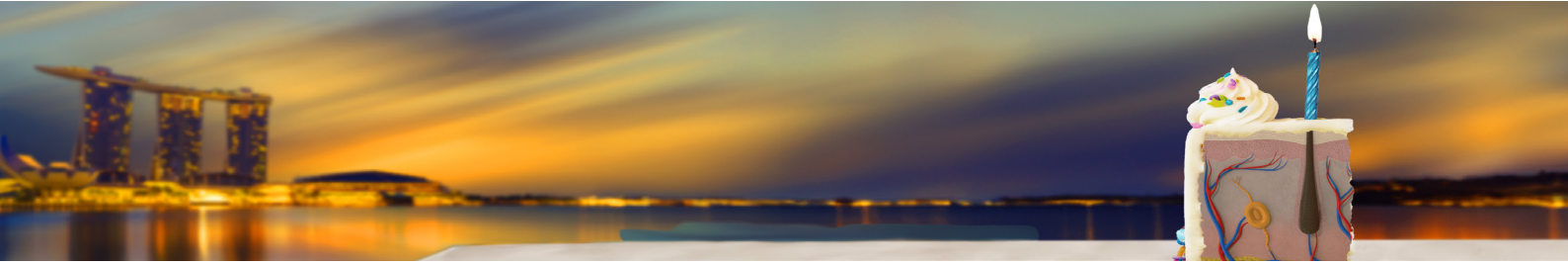
P6

RNAIssance in the art of healing chronic wounds

Kamaladasan Kalidasan[1], Gowtham Subramanian[1], Justin Chan[1], Shan Quah[1], Prabha Sampath[1,2]

*[1]A*STAR Skin Research Labs (A*SRL), Agency for Science, Technology and Research (A*STAR), 8A Biomedical Grove #06-06 Immunos, Singapore 138648; [2]Skin Research Institute of Singapore (SRIS), Singapore, 11 Mandalay Road #17-01 Clinical Sciences Building, Singapore 308232*

Diabetic foot ulcer (DFU) is one of the most common and devastating complications of diabetes. It is an escalating medical issue globally. Singapore has second highest rate of diabetics amongst developed nations, with an exceptionally high rate of amputations due to non-healing wounds. Chronic DFUs heal extremely slowly over weeks or months, and some patients never achieve wound healing. This delayed healing is a major health problem which can directly result in limb amputation and may even be life threatening in the absence of appropriate intervention. Unfortunately, there are currently no approved pharmacologic options available for treating DFUs. Accelerating wound healing in DFUs is essential to prevent complications such as infection and gangrene, which lead to amputations. Previously, we found a defective switch in chronic DFUs, which prevents wound healing. Herein, we found that downregulating miR-198 can support wound healing. Our objective is to develop a novel therapeutic strategy to enhance the efficacy of wound healing, mainly to arrest the progression of acute wounds to chronic non-healing wounds and subsequent amputation risk in diabetic patients.



P7

Uncovering the role of LINC complex proteins in skin

Krystle Joy Ng, Avinanda Banerjee, Fathima Rifkhana Shah Jahan, Jia Jun Ho, Yin Loon Lee, Brian Burke and Srikala Raghavan

*A*STAR Skin Research Lab (A*SRL), Singapore*

The Linker of Nucleoskeleton and Cytoskeleton (LINC) complex at the nuclear envelope (NE) comprise two protein families; The SUN (Sad1p, UNC-84) domain proteins (SUN1/2), that span the inner nuclear membrane and the KASH (Klarsicht/ANC-1/Syne Homology) domain proteins (nesprins) that span the outer nuclear membrane. The nesprins interact with various components of the cytoskeleton, including actin filaments and microtubules whereas the SUN proteins form a complex with nuclear lamins. The interaction between nesprins and SUN proteins connects the nucleoskeleton (nuclear lamina) to the cytoskeleton allowing for the transmission of forces and mechanical signals between the nucleus and the cytoplasm, which is crucial for cell migration, tissue development, and response to external mechanical cues. The constitutive loss of SUN1/2 is embryonic lethal. In order to understand the temporal role of these proteins we generated an inducible SUN 1/2 dKO system. To address our hypothesis, we generated primary keratinocyte lines from these SUN1/2 dKO mice as well as performed histological analysis on SUN1/2 dKO embryonic skin. Preliminary data suggests that the SUN1/2 dKO keratinocytes proliferated at a significantly slower rate. This was further corroborated with our NGS analysis performed on these lines where we observed a reduction in cell-cycle genes. Furthermore, our NGS analysis indicated an increase in differentiation-related genes suggestive of precocious epidermal differentiation.

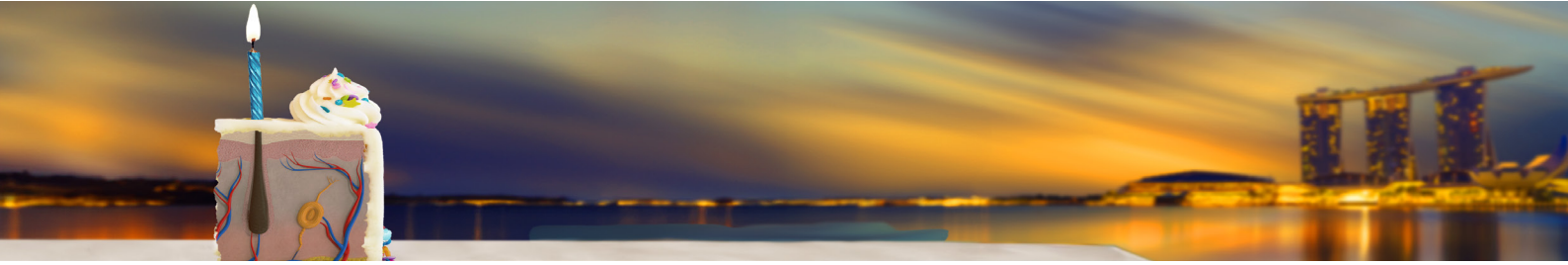
P8

Spatial metabolomics using MALDI mass spectrometry imaging: Workflow demonstration on rat dorsal root ganglion

Heather Tay[1], Sze Han Lee[1,2], Ray Putra Prajnamitra[1], James Chan[1,3]

*[1]A*STAR Skin Research Labs, Agency for Science, Technology and Research (A*STAR), Singapore; [2]Bioinformatics Institute, A*STAR, Singapore; [3]Singapore Institute of Food and Biotechnology Innovation, A*STAR, Singapore*

Spatial metabolomics is an emerging field focused on simultaneous measurement of hundreds of metabolites to yield their abundances and localization on solid specimens such as biopsies or skin tapes. This is enabled via several soft ionization techniques, such as desorption electrospray ionization (DESI) and matrix-assisted laser desorption/ionization (MALDI). MALDI is the most widespread technique, but matrix optimization is required for good metabolite coverage and image resolution. Here, we present a generalizable workflow for handling small tissue (20 – 100 µm) such as rat dorsal root ganglion (DRG). A 3-month-old Sprague-Dawley rat was euthanized, and DRGs from L4-6 were dissected and immediately embedded in gelatin and sodium carboxymethyl cellulose. Blocks were cut at 10 µm sections and mounted on glass slides. The matrices (2,5-dihydroxybenzoic acid and a-cyano-4-hydroxycinnamic acid) were evenly sprayed onto the slide with the HTX M5 sprayer. Finally, samples were acquired on a Waters SYNAPT XS in MALDI MS mode. In our study, we visualized over 700 features using a pixel size of 20 µm, where approximately 318 features are putatively identified with the Mouse Metabolome Database through Progenesis QI. This study demonstrates the feasibility of MALDI mass spectrometry to spatially visualize metabolites in small tissue sections. While analytical and computational challenges remain, opportunities to integrate complementary omics technologies make this an attractive tool to provide a new layer of metabolic insight into fundamental biology.



P9

Understanding the cross-talk between skin microbes and the host: Workflow optimisation for 13C-labelling of microbial metabolites

Ray Putra Prajnamitra[1]*, Puck Wee Chan[1]*, Sze Han Lee[1,2], James Chan[1,3]

*[1]A*STAR Skin Research Labs, Agency for Science, Technology and Research (A*STAR), Singapore; [2]Bioinformatics Institute, A*STAR, Singapore; [3]Singapore Institute of Food and Biotechnology Innovation, A*STAR, Singapore; * Equal contributions*

The skin microbiome plays a pivotal role in skin health and disease through metabolite production. In parallel, the human host also produces an intersecting set of metabolites. There is a lack of research to ascertain the proportion of influence on skin homeostasis between the host and microbes. To dissect this complex host-microbe relationship, we developed a workflow using unlabelled (^{12}C) and stable isotope labelling (^{13}C) to delineate host's and microbial metabolites respectively. A model commensal bacterium, *Micrococcus luteus,* was first cultured in an unlabelled ^{12}C-BioExpress medium to ensure compatibility, and later in uniformly labelled ^{13}C-BioExpress medium until major metabolites were fully labelled. Bacteria and spent medium were subjected to liquid chromatography-mass spectrometry analysis using a targeted method built from authentic standards (in-house, IROA® human/microbe libraries), and an untargeted method to identify partially labelled metabolites (isotopologues) resulting from host-microbial co-metabolism. A culture of *M. luteus* in ^{12}C-BioExpress over 48 hours yielded changes in 107 identified ^{12}C metabolites, including lipids, amino acids, indoles, and short-chain fatty acids. A subset of 14 ^{12}C-^{13}C metabolite pairs showed varying proportion of isotope labelling, reflecting gradual incorporation of ^{13}C. Nuclear magnetic resonance (NMR) is underway to confirm the incubation end point by quantifying changes in ^{13}C-NMR peak intensity. Subsequently, fully ^{13}C-labelled bacteria will be exposed to *in vitro* human skin to study host-microbe interactions. This workflow is useful to understand whether specific metabolites are produced by the host or microbes. It offers insights into microbiome research and development of novel therapeutic approaches to restore skin health.

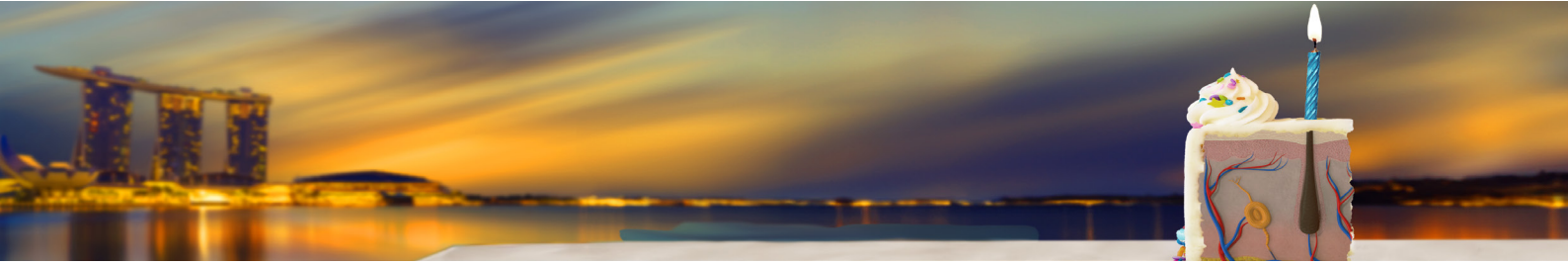
P10

Bioengineering approach for the design of magnetic bacterial cellulose membranes

Sundaravadanam Vishnu Vadanan[1], Rupali Reddy Pasula[1], Neel Joshi[2], Sierin Lim[1]

[1]School of Chemistry, Chemical Engineering and Biotechnology, Nanyang Technological University, Singapore; [2]Department of Chemistry and Chemical Biology, College of Science, Northeastern University, Boston, MA, USA

The significant role of biopolymers for biomedical applications has driven research into the development of novel products through innovative strategies. Bioinspired design methods enable the self-assembly of multifunctional biomaterials devoid of any structural disruption. As a proof of concept, we demonstrated two fundamental concepts that are engineering of functional materials based on magnetic bacterial cellulose (BC) membranes grown in the presence of amyloid-producing E. coli and its application in enhancing cell migration. BC produced by Gluconacetobacter species formed the skeletal framework and aided in entrapping recombinant E. coli bacteria. The recombinant E. coli contained genetic circuit that codes for amyloid proteins CsgA tagged with short functional m6A peptide domains, responsible for in situ magnetite nanoparticle nucleation. The injection of functional amyloid proteins into cellulose facilitated magnetite nanoparticle decoration across the matrix. Through this bioengineered design we achieved saturation magnetization of 40 emu g-1. The functional magnetic membranes demonstrated cytocompatibility and accelerated the process of wound healing by 40% in the presence of 10 mT static magnetic field.



P11

Targeting the epithelial-immune metabolic crosstalk to treat Psoriasis

Ryan Lim, Uttkarsh Ayyangar and Srikala Raghavan

*A*STAR Skin Research Labs, Agency for Science, Technology and Research (A*STAR), Singapore*

Psoriasis is a chronic inflammatory skin disease that results in a severe and rapid build-up of keratinocytes in the epidermis, causing significant scaling and inflammation in the skin. According to the Psoriasis Day consortium, 2-3% of the world population is afflicted with this condition. While studies have characterized the role of cytokines released by certain T cell subtypes from the adaptive immune system in exacerbating the psoriatic skin disease, much less is understood about the early signalling events of the innate immune system that crosstalk with the epidermis to contribute to this disease. By utilizing the mouse model of psoriasis-like dermatitis involving topical application of imiquimod, we delineate the involvement of innate immune cells such as macrophages that play an active and key role in initiating psoriasis. Strikingly, preliminary data using metabolomics and immunostaining also suggest a metabolic dysregulation that occurs in psoriasis-like dermatitis. We further demonstrated that the severity of this skin disease can be attenuated using intraperitoneal and topical administration of lactate transport inhibitor, Syrosingopine (SYRO). These results suggests that the psoriatic skin disease is potentially driven by an epidermal metabolic re-programming that drives inflammation and hyperproliferation in the skin.

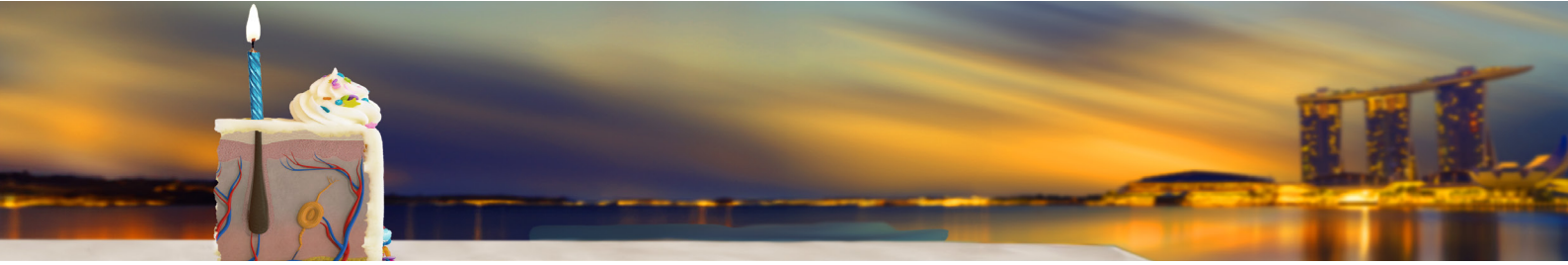
P12

Molecular regulation over metastasis in squamous cell carcinoma and its implications for drug discovery

Shan Quah, Ramisa Fariha Kabir, Prabha Sampath

*A*STAR Skin Research Labs, Agency for Science, Technology, and Research, Republic of Singapore*

Wound healing involves a finely-tuned, self-limiting series of cellular and molecular events orchestrated by transient activation of specific signalling pathways. Aberrant initiation of wound repair pathways where they are not required can cause cell behaviours favourable for cancer progression. The Follistatin-like 1 (FSTL1) transcript functions as a molecular switch regulating keratinocyte migration. It encodes two alternative products with opposite functions – the pro-migratory FSTL1 protein and the anti-migratory microRNA miR-198. Whilst the context-specific expression of these products is essential for coordinating epithelial wound repair, the switch is also hijacked by tumour cells to enhance their migration and invasion in squamous cell carcinoma (SCC). Here I will discuss regulatory pathways upstream of the miR-198/FSTL1 switch, events downstream of the switch that alter cell migratory behaviour, as well as how we are using this knowledge to develop anti-metastatic therapeutics through high-content drug library screening and downstream validation.



P13

Developing ‘diseased’ 3D in vitro human skin wound models to study the effect of therapeutics for chronic wounds

Priscilla L. K. Lim[1], Mandy Tan[1], Aishah Alimat[2], Joycelyn Lee[2], Alicia Yap[2], Declan Lunny[2], Cheong Ee Cherk[3], Joseph Lo[4], Carine Bonnard[1,2]

*[1]Model Development, A*STAR Skin Research Labs (A*SRL), Agency for Science, Technology and Research (A*STAR), Republic of Singapore; [2]Asian Skin Biobank, Skin Research Institute of Singapore (SRIS), A*STAR, Republic of Singapore; [3]Plastic, Reconstructive and Aesthetic Surgery, Tan Tock Seng Hospital (TTSH), Republic of Singapore; [4]Vascular Surgery, Woodlands Health (WH), Republic of Singapore*

To assess the effect of new therapeutics on wound repair and explore their underlying mechanisms, simplified 2D and 3D in vitro skin wound models are used. To simulate the pathophysiology of chronic wounds, animal models are well-recognized alternatives. However, none of the current models can fully recapitulate chronic wounds in humans, leading to failure of many clinical trials. We therefore aim to develop ‘diseased’ human skin models that mimic chronic wound context to validate our findings on acute wounds and establish an efficient platform to test new therapeutics for hard-to-heal wounds and investigate their mode of action. We are optimizing a well-established de-epidermized dermis-human skin equivalent (DED-HSE) wound model to recapitulate chronic wound environment following three main approaches: 1) incorporate ‘unhealthy’ skin cells and/or acellular dermis derived from patients with recalcitrant wounds, 2) modulate tissue culture systems by incorporating external ‘stress’ factors, and 3) validate our in vitro model by assessing their response to therapeutics. In collaboration with local surgeons, waste surgical skin tissues are collected from individuals undertaking plastic surgery and patients who undergo lower limb major amputations to prepare ‘healthy’ and ‘diseased’ DED-HSEs. Preliminary results showed great variability of wound re-epithelialization across different donors’ DEDs although the same control keratinocytes were used. Wound closure was significantly slower in ‘unhealthy’ DEDs compared to control, suggesting that the extra cellular matrix composition plays a central role in the re-epithelialization process. Upon validation, this platform will be used to assess new therapeutics and investigate their mode of action.

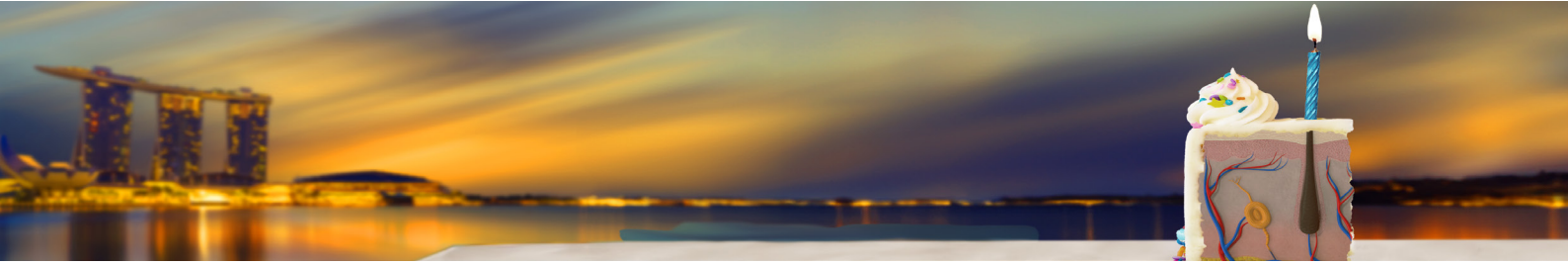
P14

using the Asian skin biobank resource to construct customized in vitro human skin models for research and product development

Yap Mei Yi Alicia1, Lee Xiang Yi Joycelyn[1], Siti Nur Aishah Binte Alimat[1], Lunny Patrick Declan[1,2], Tham Khek Chian2, Bonnard Carine[1,2]

*[1]Asian Skin Biobank, Skin Research Institute of Singapore (SRIS), Agency for Science, Technology and Research (A*STAR), Singapore; [2]A*STAR Skin Research Labs (A*SRL), Agency for Science, Technology and Research (A*STAR), Singapore*

The Asian Skin Biobank (ASB) is a core platform within the Skin Research Institute of Singapore (SRIS), that provides diverse human skin biospecimens to support the research community locally and abroad. The ASB has generated a unique collection of high-quality and safe-to-use primary skin cells, derived from different ethnic skin types (Chinese, Malay, Indian), body sites (solar UV-exposed vs unexposed), and age groups (from 4- to 81-year-old donors). The ASB uses this cell resource to develop customized in vitro models for fundamental-to-applied research activities. Beside the classic 2D cell cultures, the ASB reconstructs human epidermis, or full thickness pigmented skin, and provides ex vivo skin explants. These 3D skin models aid to study the mechanisms that drive skin health and diseases, ageing, and pigmentation, as well as to assess the efficacy of topical formulation on skin rejuvenation and repair. The de-epidermized dermis-human skin equivalent wound model is used to test the biocompatibility and efficacy of new wound healing therapeutics, including stem cell-derived secretome, peptides, and electrical stimulation. Together with academic and industry partners, the ASB contributes to the generation of more complex in vitro models, that include patients' derived cells, vascular system, and hair follicles.



P15

Quantitative severity assessment and monitoring of treatment response in inflammatory skin diseases: Structural and functional imaging markers with Multispectral Raster-Scanning Optoacoustic Mesoscopy (ms-RSOM)

Xiuting Li[1], Yik Weng Yew[2], Keertana Vinod Ram[1], Steven Tien Guan Thing[2], Dinish U.S[1], and Malini Olivo[1]

*[1]A*STAR Skin Research Labs (ASRL), Agency for Science, Technology and Research (A*STAR), 31 Biopolis Way, #05-01, Nanos Building, Singapore 138669; [2]National Skin Centre, Singapore*

Chronic inflammatory skin diseases, notably atopic dermatitis (AD) and psoriasis, pose substantial challenges in healthcare management, impacting patients' quality of life. Even seemingly healthy skin or non-lesional areas exhibit skin barrier defects and immune responses. The current semi-objective visual inspection for severity assessment may lack sensitivity to sub-clinical changes, emphasizing the need for a non-invasive, objective, and quantitative approach. Employing the ms-RSOM system with high resolution, we address this gap by providing structural and microvascular functional imaging metrics. This facilitates an in-depth exploration of the epidermal barrier impairment and intrinsic immune dysregulation balance in AD and psoriasis across different severities and treatment responses. Distinct metrics, including oxygen saturation, epidermis thickness, and total blood volume, extracted from ms-RSOM images enable quantitative analysis for objective delineation of morphological and physiological variations in diverse skin conditions. Our investigation, which also involved the assessment of treatment response in patients with AD and psoriasis following topical steroids treatment, underscores the potential of ms-RSOM derived functional and structural imaging metrics as objective markers. We anticipate the translation of these metrics into routine clinical settings, providing a diagnostic tool for the assessment of severity and the monitoring of treatment efficacy in inflammatory skin diseases such as AD and psoriasis.

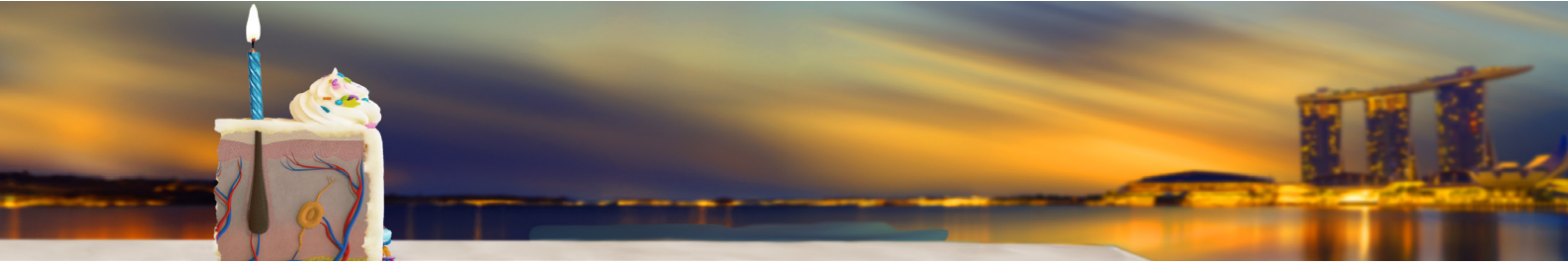
P16

Quinoa extracts mitigate skin photoaging

Christina Yan Ru Tan[1], Nursabrina Binte Mohammad Yusoff[1], Zen Lim[1], John Soon Yew Lim[1], Joseph Choon Wee Tan[2], Eng Shi Ong[2], Chen Huei Leo[2] and Sophie Bellanger[1]

*[1]A*STAR Skin Research Labs (A*SRL), Skin Research Institute of Singapore (SRIS), Agency for Science Technology and Research (A*STAR), Singapore; [2]Science, Math and Technology, Singapore University of Technology and Design (SUTD), Singapore*

The global cosmeceutical market has been growing rapidly in recent years, driven by various factors such as the rising prevalence of skin photoageing, and the increasing demand for natural products devoid of synthetic chemicals, which offer both cosmetic and therapeutical benefits. Quinoa (Chenopodium quinoa) has become a popular ingredient in skincare due to its anti-oxidant and anti-inflammatory properties. However, its efficacy at preventing photoageing, and the underlying molecular mechanisms, remain unclear. Hence, this study aims to explore the potential anti-ageing effects of quinoa extracts in human primary keratinocytes (HPKs). White quinoa extracts, obtained using a pressurised hot water “green” extraction method, were found to contain several bioactive compounds (e.g., catechin and p-coumaric acid), and to exert anti-oxidant activities in vitro. Subsequently, HPKs exposed to UV radiation were co-treated with these quinoa extracts (0.05 mg/mL). RNA sequencing showed that quinoa extracts caused the overexpression of 849 and the repression of 1465 genes in UV-irradiated HPKs as compared to HPK exposed to UV without the extracts. Gene ontology enrichment analysis revealed that overexpressed and repressed genes were associated with protein biosynthesis/trafficking processes and extracellular matrix/structure organization, respectively. Furthermore, 3D organotypic skin models showed that quinoa extracts prevented UV-induced senescence, characterized by the maintenance of Lamin B1 levels in the upper layers, while the UV-exposed 3D controls showed a decrease. In conclusion, quinoa extracts prevent UV-induced premature senescence, suggesting their potential at preventing photo-ageing.



P17

Refining tumor boundary with automated image segmentation in photoacoustic imaging

Valerie Teo Xinhui[1], Li Xiuting[1], Amalina Binte Ebrahim Attia[2], Sai Yee Chuah[3], Kwa Cheng Yi[3], Tan Wan Ling[3], Bi Renzhe[1], Dinish U.S[1], Steven Tien Guan Thng[3], and Malini Olivo[1]

*[1]A*STAR Skin Research Labs (A*SRL), Singapore; [2]Biomedical Research Council (BMRC), Agency for Science, Technology and Research (A*STAR), Singapore; [3]National Skin Centre, Singapore*

Tumor boundary determination is crucial in oncological diagnostics, with methods like histopathology commonly used. However, these methods have drawbacks, including invasiveness, and limited spatial representation. Moreover, subjective interpretation of histopathological images introduces variability among observers and potentially leading to inconsistent tumor boundary delineation. Despite imaging advancements, there remains a persistent challenge in resolution, depth penetration, and contrast, hindering their clinical effectiveness. To address these issues, the photoacoustic imaging method, Multispectral Optoacoustic Tomography (MSOT) emerges as a promising non-invasive solution offering high isotropic resolution (80 µm), deep tissue penetration (10 mm), and contrast-enhanced imaging for dermatology. By capturing chromophore signals, MSOT generates a detailed 3D spatial map of tumors. Extraction of tumor features using Gray-Level Co-occurrence Matrix (GLCM), evaluates texture, patterns, and pixel intensity relationships within tumors, enhancing our understanding of their composition and heterogeneity. Functional characteristics of chromophores offer insights into tumor oxygenation levels and metabolic demands. Incorporating an automated level-set image segmentation technique enhances the precision of tumor boundary delineation by discerning tumor boundaries from adjacent healthy tissue through differences in optoacoustic signals. This robust segmentation facilitates precise measurement of tumor dimensions, assisting in preoperative mapping and surgical planning. Validation against histology ensures the dependability of these measurements, enabling clinicians to optimize treatments while safeguarding healthy tissue and cosmetic outcomes. The combination of tumor analysis and automated segmentation provides a comprehensive insight into the morphology and metabolic activity of various tumor lesions images via photoacoustic methods, facilitating improved patient outcomes in oncological management and revolutionizing diagnostics and treatment strategies.

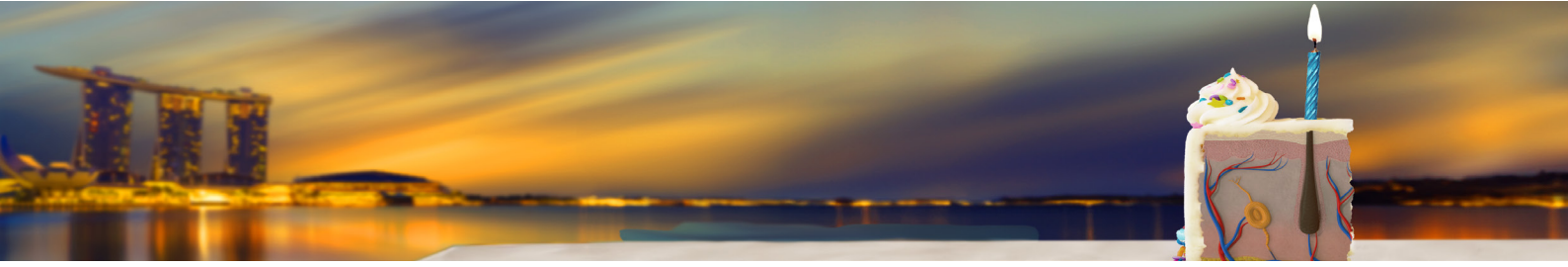
P18

E2 nanocage stabilized pickering emulsion delivery system

Chase Chow and Sierin Lim*

School of Chemistry, Chemical Engineering and Biotechnology, Nanyang Technological University, 70 Nanyang Dr., Singapore

Emulsions are colloidal mixtures of two or more immiscible liquids that consist of droplets in one phase dispersed within another continuous phase. This is a thermodynamically unstable system that undergoes phase separation over-time. Emulsion stability is improved by surfactants that reduce interfacial surface-tension. However, commercially available emulsions utilize synthetically produced surfactants which may cause unwanted side-effects. Pickering Emulsions, where solid particles act as stabilizers, have drawn attention in recent years for applications in cosmetics. Inorganic nanoparticles like silica and clay are all widely used as commercially available emulsifiers but have similar drawbacks to synthetic surfactants. Thus, the use of organic particles such as protein nanoparticles has been explored. Furthermore, cosmetic research has also emphasized the need to deliver hydrophobic compounds, which have low bioavailability and absorption. Encapsulation of such compounds in Pickering emulsions using bioderived stabilizers may provide a desirable alternative as novel formulations for active ingredients. In this work, we explore the potential of E2 protein nanocages as bioactive vehicles and Pickering emulsifiers. E2 protein nanocages are derived from pyruvate dehydrogenase multi-enzyme complex of Geobacillus stearothermophilus. Its amphiphilicity and well-defined structure make it a promising candidate for stabilizing emulsions. We are developing an E2 nanocage-stabilized Pickering emulsion delivery system and exploring the roles of surface activity of the protein nanocage in stabilizing the emulsion. Our study has shown that hydrophobic surface modifications enhance emulsion stability at lower pH while cysteine mutations within the inner cavity increase thermal stability and improve emulsification at neutral to basic pH. More work on exploring the compatibility between the nanocage and bioactive cargos are being explored.



P19

Remodelling of the dermal-epidermal junction occurs in intrinsically aged Far East Asian skin without significant epidermal atrophy

Zoe Lim[1], Declan P Lunny[1,2], Carine Bonnard[1,2], Abigail K Langton[3] and Rachel E B Watson[1,2]

*[1]A*STAR Skin Research Labs (A*SRL), Singapore; [2]Skin Research Institute of Singapore (SRIS), Singapore; [3]Centre for Dermatology Research, Manchester Academic Health Science Centre, The University of Manchester and Salford Royal NHS Foundation Trust, Manchester, United Kingdom*

Ageing is characterized by a gradual decline in physiological function and is influenced by both intrinsic genetic and extrinsic lifestyle and environmental factors. However, much of our knowledge of cutaneous ageing comes from the study of Caucasian populations. We have previously shown that the organization of young healthy skin is ethnicity-dependent and that altered epidermal morphology in Caucasian volunteers correlates with loss of skin's biomechanical function. In this study, we have used epidermal morphometry to determine whether parameters associated with intrinsic skin ageing in Caucasian skin are also observed in Far East Asian subjects. Skin samples were obtained from the Asian Skin Biobank and stained with haematoxylin & eosin prior to image analysis for dermal-epidermal junction (DEJ) convolution and measurement of epidermal thickness. Weigert's resorcin fuchsin stain revealed that all samples were photoprotected, with no evidence of solar elastosis. Comparison study showed that neither the DEJ convolution nor epidermal thickness were impacted by geographic ancestry. However, a significant flattening of the DEJ was observed between young and aged samples ($P<0.01$). Interestingly, no significant difference in epidermal thickness was observed as a function of age. Whilst intrinsically aged Asian skin undergoes the same flattening of the DEJ as is seen in Caucasian populations, epidermal thickness does not significantly alter; this is in stark contrast to intrinsically aged Caucasian skin, where epidermal atrophy is observed. Hence, trajectory of intrinsic cutaneous ageing may be ethnicity-dependent, providing further evidence that studies of ethnic skin are necessary.

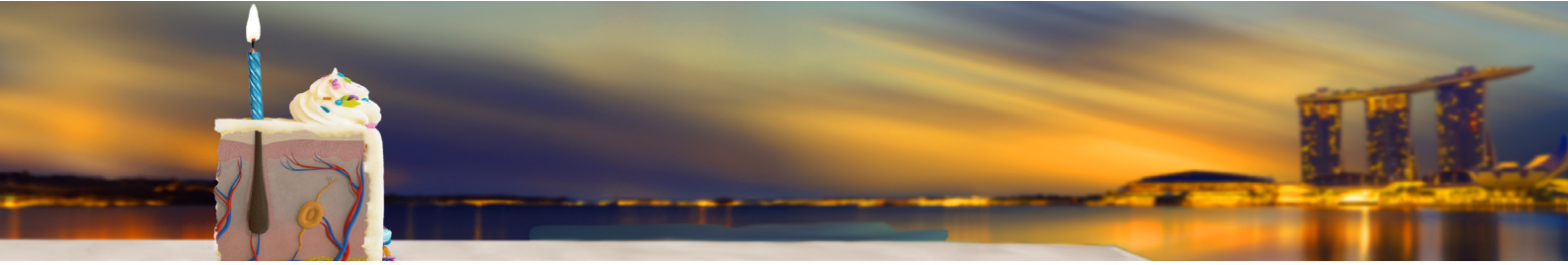
P20

Inducing fate changes at the hair follicle stem cell niche in mouse model

Zoe Lim[1] and Carlos Clavel[1,2]

*[1]A*STAR Skin Research Labs (A*SRL), Singapore; [2]Lee Kong Chian School of Medicine, Nanyang Technological University, Singapore*

Self-renewal and differentiation of stem cells are tightly orchestrated by signals within their niche. Signaling alterations within the hair follicle stem cell (HFSC) will impact the niche and alter its fate. Premature senescence of the dermal papilla (DP) has been identified as a key player in androgenetic alopecia (AGA) and senescent alopecia but the mechanistic link between senescence and the loss of the hair induction capacity remains elusive. Using genetic tools, we developed an oncogene-induced senescence mouse model to conditionally trigger senescence and fate alterations within the HFSC niche. Interestingly, our mutant mice failed to regenerate hair and shared histological features resembling human AGA like hair miniaturization and enlarged multi-lobular sebaceous glands. To further study this fate switch, we performed lineage tracing experiments which revealed that HFSC migrated out of their niche and consequently acquired senescence-associated secretory phenotype (SASP). Additionally, using a novel senescence marker, Lamin B1, we identified and characterized the senescent cell populations at the protein level. Our data show low Lamin B1 expression in non-proliferative senescent cells. However, cells adjacent to the senescent cells are highly proliferative. Hence, suggesting that senescent cells are indirectly contributing to the differentiation and enlargement of the sebaceous glands' cells. Finally, we corroborate our findings by using senolytic drugs to rescue the mutant phenotype. Interestingly, Lamin B1, cellular proliferation and other SASP makers are being restored. And importantly, hair regeneration in mutant mice is partially recovered. Identifying the mechanism responsible for the loss of hair induction will allow for the development of different translational programs for pharmaceutical therapies.



P21

Comparative analysis of Sequential Patch and D-Squame Tape Disc for skin gene expression analysis

Sija Sajibu, Siu Ling Wong, Oliver Worsley, Albert Dashi

Sequential Pte Ltd

Skin biopsies are considered ideal for measuring mRNA expression, but their invasive nature limits their widespread application. In contrast, tape stripping offers a simple yet robust and non-invasive alternative. However, collecting measurable amounts of RNA from skin tapes presents challenges. To address this, we compared the effectiveness of the Sequential Patch and D-Squame tape disc in collecting total RNA through skin tape stripping method. Twenty D-Squame discs were applied to the right forearm, and twenty Sequential patches, sized as D-Squame discs, to the left forearm of a healthy individual. Samples from the 2nd to 10th tapes and the 11th to 20th tapes were pooled for RNA extraction, cDNA synthesis, and quantitative PCR. Our results demonstrate that the Sequential patch outperforms the D-Squame tape disc in detecting skin epidermal and dermal markers. With the Sequential patch, we successfully detected all five highly expressed genes (18S, ACTB, FLG, IL-8, KRT-10) in both the 2nd to 10th and 11th to 20th tapes. Notably, the 18S RNA transcripts were detected at 17.1 cycles in the 2nd to 10th tapes and at 22.3 cycles in the 11th to 20th tapes. Conversely, in the D-Squame tape disc samples, all target genes except 18S (2nd to 10th tapes: 39 cycles; 11th – 20th tapes: 39.8 cycles) were undetectable. In addition, we also observed less inflammation and redness with Sequential patch. In summary, the Sequential Patch offers a promising alternative to DSquame discs for skin gene expression analysis for future research and clinical use.