Australasian Wound & Tissue Repair Society

Pan Pacific Connective Tissues Societies Symposium Report

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This year the 2020 AWTRS conference was held in conjunction with the Pan Pacific Connective Tissue Societies Symposium 2020 and the scientific meeting of Matrix Biology Society of Australia and New Zealand. The symposium spanned three days, covering topics including Frontiers in Matrix Biology, Cancer and Metastasis, Therapies & Clinical Advances, Tissue Repair & Fibrosis, Frontiers in Cutaneous & Matrix Biology, Inflammation & Chronic Wounds, Frontiers in Cutaneous Biology and Regenerative Medicine & Stem Cells. We were fortunate to have guests call in from across the world, including Australia, Japan, New Zealand, Russia, Finland, Sweden and USA.

The conference started off with a session on Frontiers in Matrix Biology, introduced by Professor Tony Weiss (USyd). Professor Weiss spoke on 'Elastic molecules and accelerated tissue repair', describing the importance of Tropoelastin as a model system to emulate extracellular matrix interactions for development and tissue repair. Next was Zhenjun Deng (UWA) speaking on 'The Impact of Matrix Stiffness on Keloid and Normal Fibroblasts'. Deng studied the impact of matrix stiffness on fibroblast phenotype by culturing fibroblasts on a stiff coverslip at different stiffness level. The results shown that keloid fibroblasts showed high and stable YAP activation, which does not respond to increasing matrix stiffness, suggesting that keloid fibroblasts have lost the normal mechanism of mechanosensation. Michael Papanicolaou (Garvan) ('Mapping the Extracellular Matrix Through Breast Tumour Progression') spoke the mapping of the ECM through tumourigenesis using the Polyoma Middle-T (PyMT) mammary mouse tumour model, consisting of staged-tumours (early, mid, and late) and age-matched healthy mammary tissue. The study identified 113 differentially regulated matrisomal proteins clustering into 4 temporal profiles. Closing the long talks for the Frontiers in Matrix Biology session was Dr Fatemeh Karimi (UNSW) speaking on 'Nano-Scale Design of Cardiovascular Biomaterials'. Dr. Karimi studied the functionalized biomaterial surfaces for cell interaction by synthesising a polymer functionalized with integrin- and syndecanbinding ligands. Our rapid-fire presentations for the Frontiers in Matrix Biology session were Shouyuan Jiang (UNSW) (Bioengineered Domain V of human perlecan for enhanced angiogenesis), Hayley Stent (UOtago) (Does Fish Muscle Hold Secrets to Improving Muscle Regeneration?), Ian Peall (QUT) (Investigating HSPGs in neural lineage specification) and Louise Croizat-Viallet (UOtago) (Can the extracellular matrix composition impact preadipocyte functionality and healing capacity?).

Session 2, Cancer and Cancer Metastasis, was introduced by Associate Professor Tom Cox (Garvan), speaking on 'Matrix remodelling in solid tumour progression and metastasis'. Associate

Professor Cox studies how the matrix and matrix remodelling can promote and restrict tumour progression. He employed various approaches to characterize tumour matrix remodelling, including the development of new approaches to visualise the matrix, in order to study at the molecular level how it regulates cell behaviour, and develop new therapeutic approaches to disrupt tumour progression and spread. Next was Dr Brooke Pereira (Garvan) speaking on 'Quantitative proteomics reveals cancer cell genotype can drive matrisomal changes associated with aggressive disease in pancreatic ductal adenocarcinoma (PDAC)'. Dr Pereira aimed to use proteomics to dissect the matrisomal signatures of pancreatic tumours derived from the highly metastatic KPC and poorly metastatic KPfIC mouse models. Dr Sarah Boyle (UniSA) then spoke on 'Breast cancers reprogram stromal fibroblasts to promote tumour progression via remodelling of the microenvironment'. Dr Boyle focuses the role of Rho-rhock signalling pathway in breast cancer. Her findings strongly suggest that breast cancers in which ROCK is activated release signalling mediators that act on CAFs to enhance their cancer-promoting capacity. Following, Dr Laura Bray (QUT) ('Dissecting the role of tissue-specific cancer-associated fibroblasts in the prostate tumour microenvironment') used in vitro cancer models to understand the role of the tumour microenvironment in prostate cancer progression. Primary prostate endothelial and fibroblast cells (nonmalignant fibroblasts (NPFs) and CAFs) were used to study differential influences of these cell types on tumour angiogenesis and epithelial plasticity within a tissue-specific context. Finishing the long talks for the Cancer and Cancer Metastasis session was Elysse Filipe (Garvan), speaking on 'Matrix Stiffness alters Metastatic Potential of Breast Cancer Cells through Metabolic re-wiring'. Dr Filipe investigates the role of substrate stiffness and ECM composition on Triple Negative Breast Cancer (TNBC) behaviour both in vitro and in vivo. Our rapid fire talks for the session were presented by Shona Ritchie (Garvan) ('A multi-omics approach to dissect the impact of the cancer cell-derived ECM during pancreatic cancer tumourigenesis'), Lu Fu (UNSW) ('The effects of heparin conjugated cerium oxide nanoparticles on angiogenesis'), Thomas G. Molley, (UNSW) (Freeform Printing of Tumor Invasion Models within Cell-laden Microgel Matrices) and Amelia Parker (Garvan) (Extracellular Matrix Remodelling Defines Aggressive Non-Small Cell Lung Cancer).

Our final session for day 1, Frontiers in Matrix Biology, started with four rapid-fire presentations by Dr Chloé Yeung (U Copenhagen) ('Day-to-night changes in expression of clock genes in human tendon indicate a conserved circadian clock'), Dr Shuji Mizumoto (Meijo U) ('A skeletal dysplasia with advanced bone age is caused by pathogenic variants in CSGALNACT1'), Dylan Ashton (Kolling Inst) ('The Effects of Decellularisation and Sterilisation on Kangaroo Xenograft Strength') and Ben Ventura (Kolling Inst) ('A comparative study of the degradation rate of lower limb tendons when exposed to bacterial collagenase'). The rapid-fire presentations were followed by two talks given by two exceptional researchers in the field of tissue engineering. The first, Dr Jelena Rnjak-Kovacina (UNSW) who reported her recent study on human recombinant perlecan domain V, which was found to promote angiogenesis in vitro and in vivo through potentiating FGF2 signalling via its glycosaminoglycan chains. Then, Dr Jiao Jiao Li from UTS focused on the treatment effect of mesenchymal stem cells (MSCs). In particular, she looked at how MSCs react in an in vitro model of a human osteoarthritic joint. Dr Jiao Jiao was the winner of ECR presentation from AWTRS and has also won the Bob Fraser New Investigator Award from MBSANZ. The session was then closed by our keynote speaker Professor Karl Kadler from the University of Manchester, who's studies were dedicated to how cells build tissues that are rich in collagen fibrils. His talk highlighted the regulation of collagen homeostasis. In particular, circadian clock regulates secretory pathway-resident proteins,

and procollagen-I synthesis is achieved during the night time while collagen fibril assembly is achieved during the daytime.

Day 2 started with the Therapies & Clinical Advances session, with a presentation by Dr Shenda Baker, president and CEO of Synedgen, speaking on 'Glycopolymer interactions with the glycocalyx to modulate innate immune responses after dermal injury'. This talk gave an interesting background into the research that founded Synedgen, with an insight into glycopolymer treatments for wound healing. Next was Hanif Haidari (UniSA), speaking on 'Antibiofilm efficacy of a multifunctional AgNP hydrogel for treatment of S.aureus infection in vivo with accelerated wound healing outcomes'. Hanif presented promising results on AgNP hydrogels in reducing infection, promoting wound closure and reducing cell toxicity. Kieran Lau (UNSW) was next, presenting data on 'Biofunctionalisation of gas-plasma modified silk biomaterials towards biomimetic vascular conduits'. Ending the Therapies & Clinical Advances long talks session was Dr Jessica Chitty (Garvan) presenting 'LOX family inhibition improves response to standard of care therapy in desmoplastic pancreatic cancer'. Results presented showed that PXS-5505 inhibits LOX activity from KPC cancer cells and CAFs. This session was ended with rapid fire talks from Aleksandra Butenko (Sechenov Uni) ('NO-containing gas flow accelerates wound healing by 7 days'), Kallyanashis Paul (Hudson Inst) ('Vaginal delivery of adult stem cells in Aloe vera-alginate hydrogel alleviates childbirth trauma in a rat model') and Xuan Huang (Targeting Syndecan-1 to Reduce Mammographic Density; Potential roles in Detection, Prevention and Therapy of Breast Cancer).

We then moved onto the Tissue Repair & Fibrosis session, which was introduced by Professor Shuhei Yamada (Meijo Uni) speaking on 'Congenital Disorders Caused by Defects in Biosynthesis of Glycosaminoglycans'. Following was Dr Samantha Stehbens (UQ) speaking on '+TIP-dependent Tuning of Microtubule Mechanical Flexibility Protects Cells Navigating Confined Environments'. Within this talk, we saw some fantastic live microscopy, showing CLASP depleted cells could not resist mechanical load via microtubules which resulted in cells exploding. Next was Professor Cory Xian (UniSA) speaking on 'Enhanced Bone Morphogenetic Protein Signalling Causes Injury Site Bony Repair and Adjacent Uninjured Region Hypertrophic Change in the Injured Growth Plate Cartilage'. Results showed that over activation of BMP signalling at injured growth plates caused bony repair and increased hypertrophy and uninjured regions. Finishing the long talks for the Tissue Repair & Fibrosis session was Akaiti James (UWA) speaking on 'Fibroblast heterogeneity within keloid scars: functional studies of subpopulations'. Our rapid talks for this session were presented by Anna Trengove (UMelb) ('Adhesive bioink for improved cartilage repair'), Clare Bandy (Harry Perkins Inst) ('Circadian rhythm disruptions in wound healing after trauma'), Subhajit Konar (U Auckland) ('Role of matrix stiffness in tendon health and disease') and Samantha Hefferan (Kolling Inst) ('Histological Variations in Human Tendons').

The Frontiers in Cutaneous & Matrix Biology started off with a fantastic presentation by the Barry Preston Award winner – Professor Chris Parish. This talk gave an excellent presentation on Professor Parish's work and love of a lifetime – Heparanase and heparan sulfate. They found that heparanase inhibitor PI-88 decreased the ability of heparanase to degrade blood vessel wall and stop tumour cells from migrating through the basement membrane. Further, his presentation focussed on cloning heparanase, developing heparanase assays, and pushing the heparanse inhitor PI-88 through clinical trials. Following we had great rapid fire presentations from Dr Audrey Wang (A*STAR) ('Identification and Quantification of Senescent Cells In UV-induced Skin Pathologies'), Michael Yang

(UMelb) ('Decellularized extracellular matrices on substrates of variable stiffness improve mesenchymal stromal cell function and phenotype') and Parinaz Ahangar (UniSA) ('Therapeutic potential of Multipotent adult progenitor cells secretome for cutaneous wound treatment') who was also the winner of the AWTRS ECR best speaker and AWTRS Young Investigator Award. Next up was Dr. Anna Guller from the University of NSW, discussing her work on the role of ECM in cancer colonization of organs. Her work presentation focussed on how they used metastatic triple negative breast cancer cells in various ECM architectures of various organs, and they noticed that metastasis of cancer cells in secondary organs are organ specific, suggesting that ECM affects the growth, invasion and drug response of these cancer cells. Our first keynote speaker for the evening was Associate Professor Sara Wichstrom. Her work focusses on stem cells in their niches, and specifically affects the renewal capabilities of these stem cells. She discussed that aged stem cells have a reduced regeneration activation, but that this can be restored in a "younger" niche, suggesting that specific ECM components contribute to stem cell renewal activation. The final keynote speaker was Dr Patricia Rousselle from CRNS from the University of Lyon, France. She discussed that during wound healing, the keratinocytes at wound edge transition from a static to motile phase. These basal keratinocytes change morphology to a "front-rear" polarity for directed migration into the wound site, and this is facilitated by MMPs, specifically MMP9 and MMP14.

Starting our first session (Inflammation & Chronic Wounds) of our final day off, was our keynote speaker, Associate Professor Jennifer Flegg from the University of Melbourne where she discussed her group's work in using mathematical modelling to predict and guide biomedical research into wound healing. Specifically, she presented her work where she investigated the effect of hyperbaric oxygen therapy (HBOT) on the healing process of non-healing diabetic wounds. Next up, Zahra Lotfollahi from the University of Adelaide discussed her work on diabetic foot ulcers (DFU) and the wound healing process. More specifically how they used good cholesterol, high density lipoproteins (HDL) to improve the slow healing process of DFU. They found that topical rHDL increases the rate of wound closure, and this is due to the rHDL being successfully taken up into the wound and macrophages compared to a PBS control. Dr Cindy Shu from the Kolling Institute continued our session of Inflammation and Chronic wounds. Her work focusses on osteoarthritis (OA), and in her presentation she used a 10 week old male C57/BL6 Chloe mouse model to investigate how MMP resistance in aggrecan worsen PA cartilage pathology. She found that with histopathology, the Chloe model showed increased chondrocyte hypertrophy, proteoglycan loss and structural damage in the medial meniscus, however this increased pathology (compared to WT) was not attributed to altered behaviour responses and synovial inflammatory responses. Masters student Nicole Garcia from Alfred Health presented her work in comparing how autologous (FTSG) and synthetic (BTM) skin grafts promote wound healing. She hypothesised that skin grafts contribute to wound healing by modulating the inflammatory response, and that synthetic skin grafts contribute to wound repair in a similar way. Dr Brooke Farrugia from the University of Melbourne was our final full-length presentation for the morning. She presented her work into Mast cells and what affects the activation of their secretory granules. She found that within mammalians, Hyaluronidase, HAYL1 and HAYL4 digests chondroitin sulfate in a similar way as condroitinase ABC (in bacteria), which leads to this release of secretory granules. To end this morning's session, we had four fantastic student rapid fire presentations from Dr Patrick Haubruck (Kolling Institute) ('Evaluating the role of pro-inflammatory T-cell and macrophage subsets as part of the cellular immune response during the onset and development of posttraumatic osteoarthritis in mice.'), Savannah Aitcheson (QUT) ('Predicting

complications in people with Type 1 and Type 2 Diabetes'), Adriana Zanca (UniMelb) ('Multicellular computational model of collective cell migration with an irregular free boundary') and Justin Farrell (Kolling Inst) ('Establishing a novel activated Th0/joint-tissue co-culture system to investigate osteoarthritis pathogenesis')

Before the next session started, we had a wonderful sponsor talk given by Dale Edwick from ConvaTec. His study was focused on using novel technology electrical stimulation to treat acute minor burn injuries. The Frontiers in Cutaneous Biology officially started with a talk from our keynote speaker Winthrop Professor Fiona Wood, who is a Plastic Surgeon dedicated to burn care, trauma and scar reconstruction. Her talk discussed the complexities of translating skin regeneration strategies into clinical practice based on her experience of developing spray-on skin using patient cells. During this journey, she emphasised the importance of shifting from scar repair to a regenerative repair of skin. The success of this regeneration process is affected by multiple factors such as cell type and source, point of care, tissue integration, vascularisation, and innervation. The first invited talk from Associate Professor Pritinder Kaur discussed the heterogeneity of dermal pericytes and their potential contribution to wound healing. In particular, they have identified CD45-CD49abri pericyte and hypothesised that the subpopulations of this pericyte fraction might have different roles in promoting epidermal renewal. Next, we had a talk from Zoe West, the winner of the best student oral presentation from AWTRS. Chronic wound healing is associated with an increased number of macrophages at the wound site, which migration replies on the matrix metalloproteinase 14 (MMP14) to degrade ECM. Following Zoe, Dr Oliver Dreesen from Agency for Science, Technology and Research (A*STAR) in Singapore gave a talk about unravelling molecular mechanism(s) that trigger premature ageing in progeria. Using a doxycycline-inducible system to regulate mutant progerin and single-cell immunofluorescence microscopy, they found that introducing progerin can cause the cascade of premature senescence in fibroblasts. This talk was followed by three amazing rapid-fire presentations. First, Caitlin Berry-Kilgour (U Otago) ('Assessment of a bioactive hydrogel to improve healing and reduce scarring in a murine skin model.'), Huan Ting Ong (Ear Science Inst) ('Hypoxic regulation of wound healing activity from adipose-derived mesenchymal stem cells: Identifying wound healing targets using Ligand-Receptor Interactome') and Helen Cao (U Otago) ('Role of subcutaneous adipose tissue in surgical wound healing').

The third and last session of the PPCTS symposium certainly continued the theme of exciting, novel and interesting scientific research. The topic of the session was "regenerative medicine and stem cells". Firstly, the rapid fire presentations covered research in areas of vascular grafting (Ziyu Wang), 'disease-in-a-dish' collagen models (Jinia Lilianty), prevention of fibrotic scar development (Alexey Fayzullin) and activation and differentiation of skeletal myoblasts (Osvaldo Contreras). The second part of the session was heavily based around the development of new models of tissue for research. Firstly, Professor Shireen Lamande gave an interesting talk around her lab's work in stem cell differentiation protocols to model human skeletal development and disease. Next, invited speaker Dr Andrew Cox gave insight into his model for liver regeneration with particular interest in the role of Nrf2 in this process. Lastly, invited speaker Dr Yu Suk Choi presented his novel approach to 3D stem cell cultivation using hydrogel, specifically looking at the optimisation of stiffness and pore size for replication of endogenous conditions.

The meeting was closed with the announcement of the lucky award winners. These include:

Young Investigator Award - Parinaz Ahangar

AWTRS Award Winners

- ECR Presentation – Dr Jiao-Jiao Li
- Student Presentation - Zoe West
- Student Rapid Fire - Parinaz Ahangar
- Student Rapid Fire Runner Up - Helen Cao

MBSANZ Award Winners

- Barry Preston Award - Professor Chris Parish
- Bob Fraser New Investigator Award: Dr. Jiao Jiao Li
- Dennis Lowther student award - Shona Ritchie

As Professor John Whitelock put it, there is no word for “goodbye” in the languages of the traditional owners of the land that the meeting was virtually held from. Thus, the meeting was left on a “see you next time”.