ASSC Australian Skin and Skin Cancer Research Centre

SCIENTIFIC MEETING 13 OCTOBER 2016

Session 1: ASSC Enabling Grant Scheme Winners

Title: Research evaluation of the Princess Alexandra Hospital Transplant Clinic: pilot study

Investigators: Professor Adele Green, Associate Professor Kiarash Khosrotehrani, Associate Professor Scott Campbell, Associate Professor Nicole Isbel, Associate Professor Louisa Gordon & Dr Anthony Griffin

Associate Professor Louise Gordon
Team Head, Health Economics
QIMR Berghofer Medical Research Institute

Associate Professor Nicole Isbel
Nephrologist
Princess Alexandra Hospital

Over 15,000 surviving organ transplants recipients (OTRs) live in Australia with numbers rising as transplant rates increase. The combined incidence of squamous cell carcinoma (SCC) & basal cell carcinoma (BCC) in OTRs is some 30 times higher than the general population. Keratinocyte cancers and melanoma in OTRs are caused by sun exposure (specifically ultraviolet radiation) and immunosuppression. Skin cancer morbidity and mortality rise steeply with age and duration of immunosuppression. Immunosuppression is vital for graft viability, so sun protection measures (hat, clothing, sunscreen use) are the mainstay of primary prevention.

Despite leading the world in skin cancer prevention, Australia fares poorly in controlling skin cancer in OTRs. In view of this deficiency, the Princess Alexandra Hospital (PAH) recently established a Transplant Skin Clinic (TSC) with a small clinical staff, for dedicated management of skin cancer in very-high-risk OTRs. Evidence to sustain this pioneering initiative is vital and hence we propose a research and evaluation arm of the TSC to capture numbers of patients seen, monitor details of all skin cancers treated, and document primary prevention efforts. With this seeding grant we will pilot this innovative clinical research.

Significance:

The potential benefits of the new multidisciplinary TSC must be evaluated in its real-world setting because:

1) Without it, Organ Transplant Recipients (OTRs) spend too much time in serial specialist-clinics. As well as convenience for OTRs and staff, the TSC eliminates intrinsic waiting times in the sequence (eg, up to 1- to 2-year waiting times for some OTRs referred to PAH Dermatology OPD).

2) It meets the desperate need to detect skin cancers in OTRs very early: SCCs in OTRs are many and aggressive, and large SCCs are difficult and costly to treat with high recurrence rate. We will monitor pattern of SCC severity before and after TSC commencement.

3) Primary prevention of SCC is effective in adults at high risk and inexpensive. Skin cancer in OTRs is preventable by regular practice of multiple recommended primary prevention measures including long sleeves, hats and sunscreen use.

4) Avoided or reduced health care services for skin cancer and actinic keratoses via a TSC potentially brings cost savings, even in the short-term.

Title: Pre-clinical development of antigen specific immunotherapy and strategies to overcome regulation in cutaneous malignant melanoma

Investigators: Professor Riccardo Dolcetti, Professor Ranjeny Thomas, Dr Kelli MacDonald & Dr Andreas Möller

Professor Riccardo Dolcetti MD
Research Chair min Medicine
The University of Queensland Diamantina Institute

The proposal brings together clinician scientists, oncologists, basic and translational immunologists with highly complementary expertise to provide the preclinical proof of concept of a novel immunotherapy combination with enhanced efficacy and dissect the complex role of the immunosuppressive regulatory network. We expect that the results obtained by the UQDI-QIMR team allow the joint application to National and International Agencies to further support this project on cutaneous melanoma immunology and immunotherapy. This with the final goal to exploit our preclinical findings through the activation of a phase I/II clinical trial of combination immunotherapy. Results obtained by this joint proposal will provide the proof of concept and the rationale supporting a rapid translation of the proposed immunotherapeutic combination in the human setting within the frames of a specific clinical trial. If successful, the results obtained would lead to a significantly improvement in the response rates currently obtainable in advanced melanoma patients with schedules including immune checkpoint inhibitors.

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Title: Immune contexture of transforming naevi

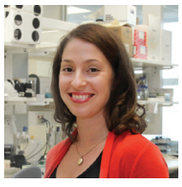
Investigators: Professor Mark Smyth, Professor Rajiv Khanna, Dr Michele Teng, Associate Professor Rick Sturm, Professor Brian Gabrielli, Dr Mitchell Stark, Associate Professor Helmut Schaider

Professor Mark Smyth
Senior Scientist
Immunology in Cancer and Infection
QIMR Berghofer Medical Research Institute

The ability to conduct multiplex immunohistochemistry (IHC) profiling of a bank of naevus tissue that has been diagnostically examined, together with the availability of genotypically characterized (germline and somatic mutations) matched naevus cell cultures and naevus tissue sections provides a unique resource to investigate the immune context of benign and transforming naevi. The hypotheses and aims complement and intersect these two groups. Despite advances in our knowledge concerning the diagnosis of naevi it is still not known how well clinical screening with the naked eye or imaging techniques, combined with genetics, predicts risk of developing melanoma. This study will utilise various genetic analyses combined with immunological characteristics on the basis of clinically and dermoscopically well defined naevi to help identify a diagnostic improvement in naevus transformation. We will generate new data by exploring the immune context of different types of naevi, generating more naevi cultures, and comparing this data in the same lesions with germline and somatic markers of early transformation.

Title: The feasibility of circulating tumour DNA as an alternative to biopsy for mutational characterisation in Stage III melanoma patients

Investigators: Professor Andrew Barbour, Dr Nicola Waddell & Dr Lauren Aoude



Dr Lauren Aoude PhD
NHMRC Research Fellow
Surgical Oncology Group
Faculty of Medicine
The University of Queensland

This project aims to determine to what extent circulating tumour DNA can be used to elucidate the genomic profile of melanoma in Stage III patients. A blood test for determining the mutation load or tumour genomic heterogeneity in tumours from melanoma patients has the potential to change melanoma management. Determination of mutation load or tumour genomic heterogeneity is complex, requiring specialised skills and access to samples. In this proposal we bring together a clinician, a bioinformatician and a melanoma researcher, who have the expertise to undertake the work. An important outcome of this project would be to determine whether sequencing of cfDNA could be performed on stage IV patients where it is not possible to sequence the tumour tissue directly. This could allow patients with unresectable high-risk stage 1118/C or stage IV disease to be treated with a personalised medicine approach in an appropriate time frame as the window for treatment of late-stage patients may be as little as a few months. Furthermore, if tumours can be characterised in stage III, a treatment plan may be developed before the patients reach stage IV so that treatment can be implemented as soon as transition occurs and there is no delay in their therapy.

Title: Epigenetic modifiers as novel targets for therapy in melanoma

Investigators: Associate Professor Jason Lee, Associate Professor Helmut Schaider, Professor Frank Gannon, Prof Nick Hayward, Dr Fares Al-Ejeh & Dr Victoria Atkinson

Associate Professor Jason Lee
QIMR Berghofer International Research Fellow
QIMR Berghofer Medical Research Institute

Associate Professor Helmut Schaider
Professor of Dermatology
Dermatology Research Centre,
The University of Queensland

This will be the first comprehensive study assessing the efficacy of epigenetic enzyme inhibitors in melanoma. This project will identify gene signatures associated with aggressive nature of melanoma that can be directly utilized in the clinic for the stratification of patient before standard or novel treatment. This will impact on the molecular understanding of how recurrent and metastatic melanoma is driven by epigenetic changes and identify a panel of markers important in aggressive progression. NanoString platform designed for clinical diagnostics (FDA-approved) will permit direct translation into novel biomarkers of epigenetically driven-melanoma and novel melanoma therapeutics.