THE CENTRE OF RESEARCH EXCELLENCE FOR THE STUDY OF NAEVI
Naevi and Melanoma

- Number of naevi is the strongest risk predictor for melanoma
- Many melanomas arise adjacent to or within naevi
- Naevi are the most relevant simulators of melanoma
- Naevi are dynamic structures – “life of a lesion”
- ~ 80% of naevi harbour the same BRAF V600E mutation which characterise 50% of melanomas
28 year old male
2 melanomas to date;
2001 and 2008
Father had melanoma aged 52

INVOLUTING NAEVI

1) L palm 22/03/2010 15/11/2010 30/05/2011

2) Back 22/03/2010 15/11/2010 30/05/2011

EVOLUTING NAEVUS

3) Back 22/03/2011 15/11/2010 30/05/2011
Chief Investigators

- **CIA Prof H. Peter Soyer** brings dermato-oncology expertise, with special emphasis on advancing dermoscopy and dermato-pathology.
- **CIB Prof Adele Green** brings expertise in melanoma and skin cancer epidemiology as well as research methodology.
- **CIC Prof Joanne Aitken** brings expertise in melanoma early detection, and epidemiology, and will link the CRE with the community.
- **CID Prof Scott Menzies** knows the biological and morphological attributes of naevi, and can guide CRE staff in patent development.
- **CIE A/Prof Richard Sturm** brings expertise in molecular biology, gene expression and genetics. He brings laboratory research skills.
- **CIF Dr David Duffy** brings expertise in genetic epidemiology, particularly in relation to statistical analysis.
- **CIG Prof Monika Janda** brings behavioural research methods and qualitative analyses skills.
- **CIH A/Prof Tarl Prow** is the only biomedical engineer on this CRE and brings unique expertise in device manufacturing.
- **CII A/Prof Helmut Schaider** combines clinical and laboratory skills and will be a mentor linking expertise across programs.


Dr Victoria Atkinson, Medical Oncologist, Princess Alexandra Hospital, Brisbane

Professor Boris Bastian, Dermatopathologist, UCSF, San Francisco

Professor Clara Curiel-Lewandrowski, Dermatologist, University of Arizona, Tuscon

Professor Brian Gabrielli, Diamantina Institute, University of Queensland, Brisbane

Professor Allan Halpern, Chief, Dermatology Service, Memorial Sloan Kettering, New York

Professor Rainer Hofmann-Wellenhof, Dermatologist, University of Graz, Graz

Associate Professor Nadine Kasparian, Psychologist, University of New South Wales, Sydney

Associate Professor John Kelly, Dermatologists, The Victorian Melanoma Service, Melbourne

Associate Professor Lois Loescher, Behavioural Scientist, University of Arizona, Tuscon

Dr Graeme Walker, Carcinogenesis Laboratory, QIMR Berghofer Medical Research Institute, Brisbane
Main CRE Programs draw from the CRE core study
CRE Core Study

Study design: Prospective longitudinal population-based cohort study of the natural history of naevi in adults living in Brisbane. Participants followed for 3 years with 3D total body photography and dermoscopy, combined with genetic analysis to decipher;

• Average number of naevi (overall, >2mm, >5mm), average number of atypical naevi on each body site by sex and age

• Influence of phenotype and pigmentation/naevus genotype on the number and type of naevi by body site

• What changes in naevi number, size, and dermoscopic features occur over 3 years

• What naevi are being selected by participants for mobile telederomoscopy

• How well do molecular and genetic changes of in vivo and ex vivo microbiopsies reflect the histopathological outcomes
Automated Image Analysis by Naevus Size

Lesion Data

Group By: Area
Sort By: L* [Desc]
Location: Back Torso

Lesion #24-120

Lesion ID # 24-120
Location torso-back
Area 16.02 mm²
Major Axis Length 6.41 mm
Minor Axis Length 3.30 mm
Parameter 17.93 mm
Eccentricity 0.86
Levels 18.00
L* 46.07
a* 19.61
b* 25.72
Delta L* 21.98
Delta E* 24.48

Area: 6-10 mm²
Area: 4-6 mm²
Area: 2-3 mm²
Area: 1-2 mm²
Area: 14-24 mm²
Area: 8-12 mm²
Program I

Genetics and Epidemiology of Naevi

Study Design: A case-control study, including participants who have been diagnosed with melanoma in the past and non-melanoma controls.

Aims:

• Study associations between clinical and dermoscopic phenotype (globular & reticular pattern) and genotype

• Determine the contribution of novel candidate pigmentation and naevogenic genes to naevus count, morphology and dermoscopic patterns

• Provide information to allow the development of risk prediction models for melanoma based on pigmentation and naevogenic phenotype

• Perform whole exome sequencing of up to 30 melanoma patients and 30 controls to search for genetic polymorphisms associated with contrasting naevus phenotype traits.
Brisbane Naevus Morphology Study (BNMS) 2011 to 2016

**AIM**

600 CMM cases or Family History

vs

600 control subjects

\[ N = 1200 \]

Interim analysis of survey at 3 years

240 CMM cases + 76 Family History

256 control subjects

Total with phenotype + genotype \[ N = 572 \]
Genotyping platforms

**Sanger Sequencing**
MC1R Genotyping

**Sequenom and Taqman**
based SNP Genotyping
IRF4 and MITF

**Whole Exome Sequencing**

**Illumina CoreExome**
500,000 SNPs

Figure 1: HumanCoreExome-24 BeadChip

The HumanCoreExome-24 BeadChip enables informative genotyping of tag SNP and exome-focused markers across diverse world populations, delivering high-quality data that can be used in various downstream applications.
Program II

Consumer facilitated naevi monitoring

Study Design: Provide participants with instructions and dermatoscope iPhone attachments to conduct skin self-examinations every 3 months for a period of 3 years (part of Core Study).

Aims:

• Create evidence for how we can best support consumers in the detection of transforming naevi, using the latest technological developments.

• Evaluate if mobile teledermoscopy used in skin self-examinations improve participants’ sensitivity and specificity for identifying naevi requiring clinical management

• Decipher if repeated mobile teledermoscopy improves sensitivity further

• Measure consistency between dermatologists’ tele-diagnoses and whether concordance is dependent on years of practice

• Establish what cognitive processes are used when people choose naevi they think require management by a doctor
Device Market – FotoFinder Handyscope
Combining expert knowledge and machine learning:
no missed melanomas

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<th>Histopathologic Diagnosis</th>
<th>HPS evaluation</th>
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Molecular and Genetic Properties of Changing Naevi

Study design: An observational study to examine the natural history and molecular properties of naevi in advanced melanoma patients undergoing treatment over a one year period using dermoscopy, 3D full body photography and molecular analysis of excised naevi.

Aims:

• Ascertain how rapidly naevi are changing in Stage III and IV melanoma patients undergoing treatment, and which germline/somatic genotypes predict these changes?

• Determine if involuting and/or growing naevi are clinical markers of response to treatment.

• Identify differences in the somatic genotype associated with changeable naevi

• Define distinct epigenetic profiles attributable to changeable naevi and how this relates to dermoscopic and histopathologic naevus types
BRAF<sup>V600E</sup> mutation status in involuting and stable nevi upon BRAF± MEK treatment
McClenahan P et al.
JAMA Dermatology 2014
Involuting naevi are possessing BRAF^{V600E} mutation, whereas stable naevi do not possess the BRAF^{V600E} mutation.
Transfer of Knowledge

- National/International practice and policy guidelines
- Technology advances and patents
- CRE professional developmental activities
- CRE website and SoMe
- CRE white book
Melanoma Detection and Treatment in the Near Future
SAVE THE DATE!

MELANOMA 2017

A joint meeting of the 9th World Congress of Melanoma & 14th International Congress of the Society for Melanoma Research
18–21 October 2017, Brisbane Australia