BNMS: Genetic association of naevi morphology and melanoma
Study Populations available to the CRE

**BERNS** = Brisbane Electoral Roll Naevus Study, CRE core study n=150

**BTNS** = Brisbane Twin Naevus Study; n>3,000 (QIMR-B controls 23,724 individuals unaffected by CMM)

**BNMS** = Brisbane Naevus Morphology Study, n=1,200

**BMPMNS** = Brisbane Multiple Primary Melanoma Naevus Study, n=100

**BAMNS** = Brisbane Advanced Melanoma Naevus Study n=80

**BLTNS** = Brisbane Lung Transplant Naevus Study n=90

**Nambour trial** = Trial of Sunscreen for Melanoma Prevention n=1,626

**MST** = QSkin Melanoma Screening Trial n>60,000
What are naevi and how do they arise?
Effect of naevogenesis susceptibility genes and phenotypic correlation with dermoscopic characteristics of naevi

**Hypotheses:**

- **MC1R** variant alleles will have a major influence on innate melanocytic naevus morphology.
- Variation in other pigmentation genes such as **TYR**, which are modifiers of melanoma risk, may influence melanocytic naevus colour and morphology.
- Genes that have recently been recognised to influence naevus count including **IRF4, MTAP** and **PLA2G6** may also influence naevus morphology.
- Genes that regulate melanocytic cell function such as **MITF** will also act to modify naevus count and/or morphology.
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 Dec 2013 with phenotype + genotype N = 572

Recruited as of April 2016 N > 1100
Naevi classified by size, profile, colour and dermoscopic naevus pattern

13,587 melanocytic naevi
>5mm

Globular
15.6%

Reticular
21.9%

Homogeneous/
Nonspecific
62.5%
Total body naevus count by body-site and sex

Female vs Male
Collection of saliva for genetic analysis

Assess pigmentation using Spectrophotometer

Assess freckling density on face, hand & shoulders

Documentation of patient demographics, sun exposure background, personal and family skin cancer / naevi history, medications

Photographic documentation of eye colour
Phenotypic Characteristics of BNMS

Naevus count vs Sex

Freckling score vs Melanoma

Skin Reflectance vs Sex

Skin Reflectance vs Melanoma

NaN

Facultative

Male Female

Facultative

Male Female

P***

CMM FH+ Control

CMM FH+ Control
Naevus Count vs Melanoma

**Total**

- Naevi > 5mm
- CMM  |  FH+  | Control
- P***

**Reticular**

- Naevi > 5mm
- CMM  |  FH+  | Control

**Globular**

- Naevi > 5mm
- CMM  |  FH+  | Control

**Nonspecific**

- Naevi > 5mm
- CMM  |  FH+  | Control
Genotyping platforms

Sanger Sequencing
MC1R Genotyping

Sequenom and Taqman based SNP Genotyping

Whole Exome Sequencing (WES)

Illumina CoreExome
500,000 SNPs

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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.
### Candidate genes and SNPs associated with CMM in BNMS

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### CDKN2A carriers identified by Whole Exome Sequence (WES) Analysis

Arch Dermatol Res  
DOI 10.1007/s00403-015-1582-y

**CONCISE COMMUNICATION**

High incidence of primary melanomas in an *MC1R RHC* homozygote/CDKN2A mutant genotype patient

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