Hereditary Cancer Whole Genome Sequencing Project to Identify Pathogenic Germline Variants

Aimee Davidson1,2, Uwe Dreses2, Felicity Newell1, Helen Mar Fan1, Emma Tudini1, Lambros Koufarisiotis1, Stephen Kazakoff1, Georgina Holway1, Amy McCarr-Reed1, Olga Kondrashova1, Katia Nones1, Dylan Glubb1, Oliver Holmes1, Conrad Leonard1, Scott Wood1, Christina Xu1, John Pearson1, Nicola Poplawski1, Paul James6, Gillian Mitchell7, Robyn Ward2,8,9, Amanda Spurdle1, Nic Waddell1

1QIMR Berghofer, 2Faculty of Medicine, UQ, 3Genetic Health Queensland, RBWH, 4Faculty of Medicine, Centre for Clinical Research, UQ, 5Adult Genetics Unit, RAH, 6Parkville Familial Cancer Centre, Peter MacCallum Cancer Centre, 7Sir Peter MacCallum Cancer Centre, Department of Oncology, UnMelb, 8Faculty of Medicine, UNSW, 9Faculty of Medicine and Health, USYD

Hereditary Cancer Predisposition Syndromes (HCPS) are genetic disorders in which cancer causing germline variants are inherited.

Our project aims to assess whether the adoption of whole genome sequencing into routine clinical practice is: useful, safe, cost efficient and if the necessary infrastructure is in place.

This will be assessed by sequencing the germline whole genomes of 190 individuals with suspected hereditary cancer for which previous genetic testing had been uninformative.

Primary endpoint has been reached for 138 participants.

- 53% had no variants reported
- 47% had variants reported

The causal variant was identified in ~4% of participants, with potentially associated variant/s identified in a further ~23% of participants

Novel variants have been identified in genes including: FH, DICER1, BRCA2, BAP1 and APC

Changes to clinical management for participants and family members have included: increased surveillance, risk-reducing surgery, prophylactic medication

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Future research directions

- Segregation and functional analysis to evaluate variants of uncertain significance
- Expanded analysis e.g. explore regulatory genetic elements, to identify additional likely causal variants
- Health economics analysis
- Submission to Medical Services Advisory Committee (MSAC)