Melbourne Genomics
Health Alliance

Global knowledge. Individual care.

Investigating new genomic technologies in clinical care

Background

Genomic sequencing methods continue to evolve in research, but these new methods are often not ready for use in clinical care.

To enable patients to access innovative genomic sequencing methods, diagnostic and bioinformatics experts must gain knowledge and experience with new horizon technologies. The lessons from this experience can then inform decision-making and planning for bringing innovative technologies to clinical reality.

Thus, the Melbourne Genomics New Technology Project was established (running 2017 to 2018).

Project description and activities

The objective: to apply state-of-the-art diagnostic approaches in clinical care.

The New Technology Project considered the readiness for clinical use of a range of new genomic technologies. One was selected to determine its diagnostic potential to make a difference in real-world patient care: Chromium linked reads with whole genome sequencing.

Chromium technology has the potential to provide information about disease-causing structural changes in genes that cannot be detected through accredited genomic testing methods currently used in Australia.

Sixteen patients whose molecular diagnosis was known but not fully resolved (using currently available clinical genomic methods) agreed to have chromium technology applied to their samples. The Australian Genome Research Facility performed this Chromium sequencing. A collaborative effort from clinical bioinformatics specialists across the Melbourne Genomics members enabled all 16 cases to be analysed and Chromium technology evaluated.

The Melbourne Genomics Health Alliance members involved were: the Australian Genome Research Facility, the Peter MacCallum Cancer Centre, Monash Health, Murdoch Children's Research Institute (Victorian Clinical Genetics Services), The University of Melbourne and WEHI.

Outcomes

The project showed that Chromium technology can reveal hidden causes of disease, providing more accurate bioinformatic resolution of the genome. The technology was able to definitively uncover the true complexity of known causal genetic variants not detectable using current clinical genomic testing approaches, and patient diagnoses were able to be made.

The organisations involved gained first-hand experience of working with a new technology: the challenges of innovating together, the system changes that might need to be considered and a better understanding of the effort required – relative to the benefits that could be realised.

Lessons learnt

- No single technology can currently address all the technical challenges of accurately sequencing the entire genome – particularly within the clinical setting. Diagnostic laboratories were able to gain

a better understanding of the trade-offs between traditional sequencing, Chromium and other emerging sequencing technologies.

- The type of complex variants readily detected were not those anticipated, demonstrating the value of prototyping prior to implementation.
- Whole genome sequencing using Chromium technology potentially provides better clinical value than standard whole genome sequencing, and the data generated has higher value for research.
- Chromium technology is best suited to high-quality DNA taken from patient blood samples. It is not suited to DNA taken from dried blood spots or from mouth/cheek swabs.
- The infrastructure is already in place to offer Chromium technology; laboratories could immediately undertake a 'light touch' implementation. However, the full potential of this technology will require further bioinformatics development and improvements in supporting software.
- If undertaken by a single organisation, this project would have been less robust and taken longer due to: limited resources of clinical laboratories; lack of access to the wide variety of cases included; and relatively limited bioinformatics, scientific and clinical expertise.
- A pathway for investigation of new technologies – from research to diagnostic use – is needed. Among the Melbourne Genomics members, this could be achieved by establishing New Technology Flagships, including testing of prospective cases and dedicated resources for bioinformatics, software, and evaluation.

Impact

This project provided a world-leading investigation into the potential to move Chromium linked reads technology from research to the clinical laboratory. Results were presented at a National Linked Reads Symposium in July 2018.

The specific experience with Chromium technology provides evidence to guide future decision-making and a practical time-frame for implementation of this technology into clinical testing. It also opened opportunities for future collaboration with the technology supplier.

Project team

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