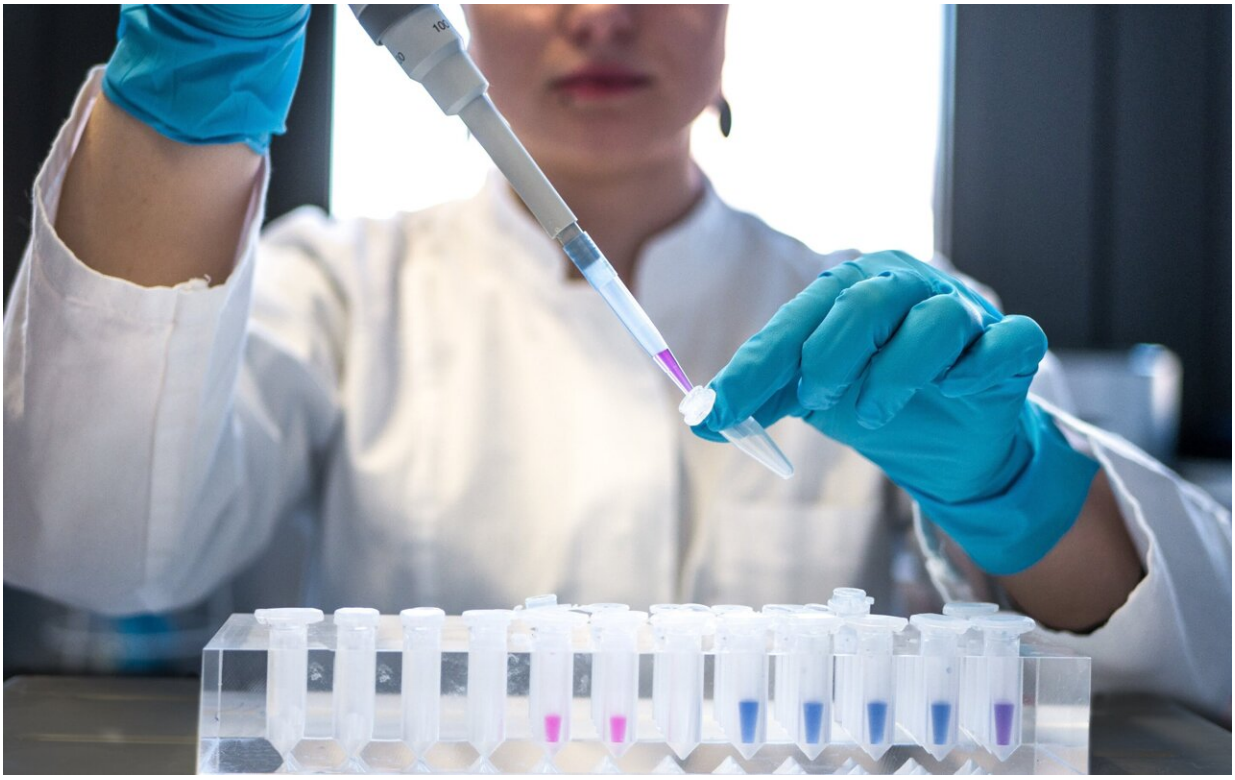
Sharing variant information to improve diagnosis

November 4 2022



Credit: Unsplash/CC0 Public Domain

A national platform for diagnostic laboratories to share genetic evidence and build consistent interpretations of that information is paving the way for more accurate diagnosis of patient conditions.

The variant hub and communication platform, Shariant, has been taken up by 11 laboratories in Australia, with more set to come on board in the next six months.

The project is an Australian Genomics initiative in collaboration with the Brisbane-based QIMR Berghofer Medical Research Institute and the Center for Cancer Biology, an SA Pathology and University of South Australia Alliance. A tool developed by the Center for Cancer Biology, VariantGrid, was the basis for developing the Shariant platform.

The Shariant story is described in the latest edition of the *American Journal of Human Genetics* where it reveals the complexities of interpreting the clinical data and the need for consistency.

Laboratories use information from external and internal sources to interpret if a variant is disease-causing, benign, or of uncertain clinical significance. Therefore, interpretation of variants can sometimes differ between laboratories, potentially leading to differences in clinical management advice between patients with the same variant.

One of the key outcomes of the project was establishing a process for laboratories to share knowledge about variant interpretations, and to promote consistent interpretation for newly discovered variants before a laboratory report is prepared.

"This is the first time a diagnostic laboratory in Australia has been able to share a classification with other laboratories, and reclassify a variant based on shared evidence," said Project Lead Professor Amanda Spurdle of QIMR Berghofer.

"By gradually standardizing interpretations nationally we can provide much more accurate diagnoses for patients irrespective of their location. Shariant now contains nearly 20,000 variant interpretations, and we

expect this number to increase markedly."

Shariant has also allowed Australian labs to share variant interpretations internationally, with a seven-fold increase in the number of variants submitted to the public database ClinVar from 2017 to August 2022—an increase largely enabled by the platform.

Clinical Geneticist Professor Zornitza Stark said sharing information between laboratories was key to improving test results: "It means that doctors can provide faster and more accurate diagnosis to patients."

"Shariant has massively scaled up data sharing between Australian laboratories and made it easy for us to contribute internationally," she said.

Professor Amanda Spurdle, project lead, said, "We know that Shariant information has led to a rapid genetic diagnosis and informed patient management of a critically ill child.

"We believe that the success of this project hinges on the flexibility of the Shariant hub to work with whatever knowledge system a laboratory is already using—the idea has always been to make sharing as easy as possible for laboratories.

"As another positive outcome, this project has provided a network where lab members can meet once a month to discuss, and find solutions to, all sorts of issues relating to challenges they face in their day-to-day work.

"This network has already led to many suggestions for additional features to further support laboratories, thereby leading to more genetic answers for patients and their families."

Hamish Scott, head of Department of Genetics & Molecular Pathology,

SA Pathology, said, "As the head of a diagnostic laboratory I have seen cases where patients from the same family were tested for the same mutation in different states, but where the diagnostic laboratories in those states arrived at different conclusions.

"It's not that one laboratory is wrong, but that with new and shared knowledge we can come to more informed conclusions.

"Shariant helps ensure that throughout Australia, and internationally, we know what other laboratories think and how to be consistent in the way the genetic information is interpreted and applied.

"Knowing if a variant seen in a genetic test is the cause of a patient or family's problem can be life saving and life changing. It may lead to effective or preventative treatment for a disease such as breast cancer, or enable families to have healthy children."

More information: Emma Tudini et al, Shariant platform: Enabling evidence sharing across Australian clinical genetic-testing laboratories to support variant interpretation, *The American Journal of Human Genetics* (2022). DOI: 10.1016/j.ajhg.2022.10.006

Provided by Australian Genomics