Screening genes to predict who will respond badly to drugs

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Credit: Murdoch University

Research mapping genetic markers is being used to save lives at risk from a range of medical treatments, tests and vaccines.

All new medical treatments go through a stringent set of experiments, trials and approval processes before being passed for general use. However, adverse drug reactions caused by drug hypersensitivity

continue to be a significant problem in clinical practice today.

These serious and life-threatening reactions are driven by genetic factors and present both a physical and financial burden to patients, families and healthcare services around the world.

Professor Elizabeth Phillips is leading the Drug Hypersensitivity Research Group investigating genetics and mechanisms behind adverse reactions to find new ways of preventing, diagnosing and treating drug hypersensitivity.

The group has been instrumental in preventing fatal hypersensitivity in patients taking abacavir, a common drug used to treat HIV symptoms, after confirming the hypersensitivity was related to a specific gene.

"Through the design of innovative and inexpensive genetic testing assays, followed by blinded clinical trials, we demonstrated conclusively that abacavir hypersensitivity could be prevented across different races by screening for the HLA-B*57:01 gene," said Professor Phillips.

"Our research has provided a roadmap from discovery to translation of pre-prescription genetic screening into routine clinical practice to make prescription drugs safer."

Now, HIV patients around the globe are screened for the hypersensitivity gene prior to commencing abacavir treatment as part of routine HIV care.

Professor Phillips' research mapping genetic markers is now being applied to predict hypersensitivity to the antibiotic vancomycin, which is used to treat life-threatening resistant gram-positive bacterial infections.

The team have screened nearly 250,000 unique DNA samples to identify

genetic patterns between those who developed a drug reaction with eosinophilia and systemic symptoms (DRESS) when taking vancomycin. DRESS is a potentially serious complication when prolonged courses of antibiotics are given to patients.

"Our findings showed vancomycin-associated DRESS was strongly associated with HLA-A*32:01 which is present in almost seven percent of the Australian population," said Professor Phillips.

Professor Phillips and her team have now developed a simple and inexpensive "single allele" screening test for HLA-A*32:01 that can be set up in routine diagnostic laboratories for less than the cost required to perform a simple blood count.

The next phase of the study will mirror the approach taken to abacavir hypersensitivity and facilitate the translation of HLA-A*32:01 testing that will lead to safer use of vancomycin.

Professor Phillips reiterated that the development of rapid and inexpensive tests to identify the genes responsible for severe drug hypersensitivity syndromes is essential to improving the quality of clinical care available.

"Early diagnostic testing helps to prevent patient morbidity and mortality and avoids increasing costs of treatment or limiting options for future therapies for at-risk patients.

"These precision medicine approaches are improving patient safety and reducing unnecessary avoidance of other drugs, while most importantly, giving patients peace of mind about the safety of initiating and continuing treatment."

Provided by Murdoch University