Genetic predictors could guide heart disease treatment

For University of Otago, Christchurch, researcher Associate Professor Vicky Cameron, the results of her group's recent research into heart disease related gene variations has turned out to have personal implications.

Working under the HRC funded *Neurohumoral and Genetic Prediction and Protection in Heart Disease* programme directed by Professor Mark Richards, she has been examining a region on chromosome 9 that has been identified as something of a risk "hotspot".

Rapid advances in gene testing technology called genome-wide association studies allow scientists to check for thousands of gene variants across the genome at once, rather than simply testing a variant at a time. They are then able to see which of those genetic variants stand out as being more frequent in people who develop heart disease than those who do not.

Using this technology, several small changes in the DNA code from the chromosome 9 area have been identified as good predictors of a higher risk of heart disease. Associate Professor Cameron knows that she, along with around a quarter of the New Zealand population, has received copies of the most frequently found "hot spot" gene from both her parents. She and her team have taken that gene variant and other so-called top hits from the genome wide association studies and used their cohort of 2,000 heart disease patients, and healthy controls, to see if it affects outcome and prognosis for people who have heart disease.

Their results, published in *Circulation: Cardiovascular Genetics*, showed that although patients carrying that genetic variant were a couple of years younger when they developed their heart disease, their outcome was no different or no worse after they had developed heart disease. "There may have been risk factors for developing heart disease but we've shown they don't affect your outcome. It's kind of reassuring that this top hit, identified in genome wide association studies internationally, isn't a death knell for those who develop heart disease."

They were also able to replicate the findings in a separate patient group from an earlier study.

Associate Professor Cameron says genetic markers could eventually be used by clinicians to help guide treatment for people with heart disease. "When people come into hospital it has been difficult to tell whether they are going to be coming out of hospital in two weeks' time, and digging in their vegetable garden, or whether they are someone who is going to continue to go downhill and eventually get heart failure. Our group has been looking at markers for predicting those that need to be treated much more intensively to give them much better survival and those that will only need fairly minimal treatment or management."

She says they want to understand why people who have apparently similar risk profiles actually have very different clinical outcomes. "We've explored associations with over 60 different genetic variants, looking at when you combine particular profiles of genetic variants do you see particularly significant effects on outcomes? What we are finding is that risk factors like that hot spot isn't a predictor for subsequent bad outcome but there are genetic profiles for these heart hormones which are predictive."

Associate Professor Cameron says thanks to the generosity of their heart disease patients, they have an invaluable resource of over 2,000 cardiac patients.

Associate Professor Vicky Cameron (fourth from left) and the research team

Key words:

- Heart disease, gene variations, chromosomes, gene testing, DNA, genetic markers

Aims of this research:

- To research heart disease related gene variations, and establish which genetic variants are more frequent in people who develop heart disease

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