New genetic marker identified for aortic aneurysm risk

A new genetic marker for increased risk of abdominal aortic aneurysm (AAA) has been identified through a large multinational collaborative research project in which an HRC funded University of Otago research group played a major role.

Co-directors of the Vascular Research Group, Professor Andre van Rij and Associate Professor Greg Jones, headed the New Zealand branch of the Iceland led study of over 40,000 people across a dozen countries.

AAA, which often goes undiagnosed, involves the large blood vessel that carries blood to the abdomen, pelvis and legs becoming abnormally large or ballooning outward. It is found in seven per cent of New Zealand men over the age of 60 and if the aneurysm ruptures it leads to death in 40-80 per cent of cases.

Associate Professor Jones says the common variant in a gene known as *DAB2IP* is only the third genetic marker for AAA to be conclusively identified and validated.

"So there's not been a lot. We're also involved in a study looking at myocardial infarction and that is getting up to 23 markers now. This marker is interesting because it was originally found to be associated with prostate cancer. And that's interesting because we know that prostate cancer is a male cancer and abdominal aortic aneurysm has a strong male component, more than other vascular diseases."

In prostate cancer it appears this gene gets switched off and allows the prostate tumour to keep growing. But in AAA it seems to get switched on and sends the cell into apoptosis, or programmed cell death, causing the wall of the aorta to erode and thin. Associate Professor Jones says it creates a new biological target to stop the growth of the aneurysm.

"The best way to treat it is to stop it from growing. You can identify people very easily using screening when they have a small aneurysm and all you can really do is sit and watch them grow until they get to a size where the risk of them bursting is so high you have to operate, which isn't ideal." He says genome-wide studies such as this help them find these never thought of before targets.

The Otago group's contribution to the study included screening the initial list of possible candidate genes and then using their own genome-wide association scan to test and validate the DAB2IP candidate gene.

Professor Andre van Rij and Associate Professor Greg Jones

Key words:

- Genetic marker, abdominal aortic aneurysm, prostate cancer, myocardial infarction

Aims of this research:

- To identify genetic markers for increased risk of abdominal aortic aneurysm
- To also look at biomarkers which may assist with identifying early aneurysms

They now have a cohort of about 1,300 patients with aneurysms and 1,000 elderly controls. Using HRC funding they have been able to build up a genetic genome wide set of samples involving over 1,200 participants made up of 600 people with AAA and a matching group of 600 controls, which is a critical resource that is of interest to international collaborators.

The Otago/Southland cohort is good for this type of research because it is relatively homogenous, reducing genetic differences that could turn out to be related to ethnicity, and also has a quality group of controls that has been screened for aneurysms, greatly reducing the degree of false negatives.

"It is a large resource, so if we make an observation about AAA we can test whether it is relevant to coronary artery disease, cartoid disease etc, with our other cohorts."

They are now looking for biomarkers related to the latest discovery which may help identify those with early aneurysms.

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