Study reveals major genetic differences between blood and tissue cells

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(PhysOrg.com) -- Research by a group of Montreal scientists calls into question one of the most basic assumptions of human genetics: that when it comes to DNA, every cell in the body is essentially identical to every other cell. Their results appear in the July issue of the journal *Human Mutation*.

This discovery may undercut the rationale behind numerous large-scale genetic studies conducted over the last 15 years, studies which were supposed to isolate the causes of scores of human diseases.

Except for cancer, samples of diseased tissueare difficult or even impossible to take from living patients. Thus, the vast majority of genetic samples used in large-scale studies come in the form of blood. However, if it turns out that blood and tissue cells do not match genetically, these ambitious and expensive genome-wide association studies may prove to have been essentially flawed from the outset.

This discovery sprang from an investigaton into the underlying genetic causes of abdominal aortic aneurysms (AAA) led by Dr. Morris Schweitzer, Dr. Bruce Gottlieb, Dr. Lorraine Chalifour and colleagues at McGill University and the affiliated Lady Davis Institute for Medical Research at Montreal's Jewish General Hospital. The researchers focused on BAK, a gene that controls cell death.

What they found surprised them.

AAA is one of the rare vascular diseases where tissue samples are removed as part of patient therapy. When they compared them, the researchers discovered major differences between BAK genes in blood cells and tissue cells coming from the same individuals, with the suspected disease "trigger" residing only in the tissue. Moreover, the same differences were later evident in samples derived from healthy individuals.

"In multi-factorial diseases other than cancer, usually we can only look at the blood," explained Gottlieb, a geneticist with McGill's Centre for Translational Research in Cancer. "Traditionally when we have looked for genetic risk factors for, say, heart disease, we have assumed that the blood will tell us what's happening in the tissue. It now seems this is simply not the case."

"From a genetic perspective, therapeutic implications aside, the observation that not all cells are the same is extremely important. That's

the bottom line," he added. "Genome-wide association studies were introduced with enormous hype several years ago, and people expected tremendous breakthroughs. They were going to draw blood samples from thousands or hundreds of thousands of individuals, and find the genes responsible for disease.

"Unfortunately, the reality of these studies has been very disappointing, and our discovery certainly could explain at least one of the reasons why."

AAA is a localized widening and weakening of the abdominal aorta, and primarily affects elderly caucasian men who smoke, have high blood pressure and high cholesterol levels. It often has no symptoms, but can lead to aortic ruptures which are fatal in 90 per cent of cases.

If the mutations discovered in the tissue cells actually predispose for AAA, they present an ideal target for new therapies, and may have even wider therapeutic implications.

"This will probably have repercussions for vascular disease in general," said Schweitzer, of McGill's Department of Medicine. "We have not yet looked at coronary or cerebral arteries, but I would suspect that this mutation may be present across the board."

Schweitzer is optimistic that this discovery may lead to new treatments for vascular disease in the near to medium term.

"The timeline might be five to 10 years," he said. "We have to do in-vitro cell culture experiments first, prove it in an animal model, and then develop a molecule or protein which will affect the mutated gene product. This is the first step, but it's an important step."

Source: McGill University (news : web)