New gene discovery for babies born with hole in the heart

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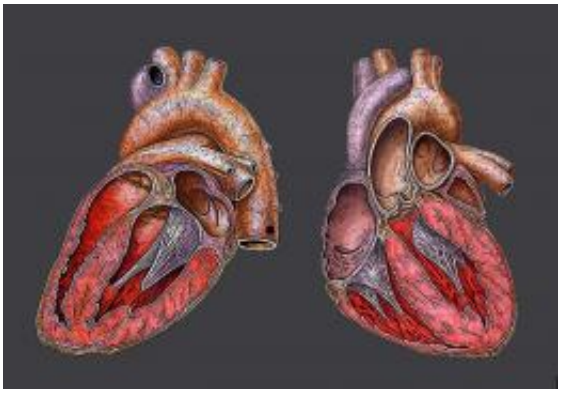

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(Medical Xpress)—A new gene associated with a form of congenital heart disease in newborn babies – known as "a hole in the heart" has been discovered by researchers.

British Heart Foundation (BHF) Professor Bernard Keavney, from The University of Manchester and Newcastle University, led the research which saw investigators from Newcastle, Nottingham, Oxford and Leicester universities in the UK, together with colleagues in Europe, Australia and Canada pool resources.

The discovery, published in *Nature Genetics* today, will help lead to better understanding of why some patients are born with the disorder.

Congenital heart disease (CHD) is the most common form of congenital malformation, occurring in seven in 1000 babies born and is one of the major causes of childhood death and illness. Most patients born with CHD now survive to adulthood, so identifying the responsible genes is important as experts attempt to provide individual-specific genetic counselling for these people. In about 20% of cases, a predisposing cause can be identified, for example Down's Syndrome, but in the remainder of patients, although genes are recognised to be important, scientists do not know the identity of these genes.

The study, funded by the BHF and the Wellcome Trust, looked at over 2,000 CHD patients and measured over 500,000 genetic markers which vary in the general population. The genetic markers in the patients were compared to the markers of over 5,600 people in good health who acted as a control group. The researchers found a relationship between a particular region of the human genome and risk of atrial septal defect (ASD) – a "hole" between the heart's blood-collecting chambers, which they went on to confirm in additional cases of atrial septal defect and healthy controls.

BHF Professor Keavney, Director of the Institute of Cardiovascular Sciences at The University of Manchester, said identifying a gene associated with one type of CHD was an important step forward. "We found that a common genetic variation near a gene called Msx1 was strongly associated with the risk of a particular type of CHD called atrial septal defect or hole in the heart," he said.

"ASD is one of the most common forms of congenital heart disease, and it carries a risk of heart failure and stroke. We estimated that around 10% of ASDs may be due to the gene we found. We can now work to find out how Msx1 and/or its neighbour genes affect the risk of ASD."

Researchers looked at all the major types of congenial heart disease

(CHD), but they did not find a genetic marker common in all types of CHD.

Professor Keavney added: "Our work also suggests that if we conduct larger studies we will be able to find genes that cause other types of CHD. Although we are not there yet, further studies may enable us to give better genetic counselling to high risk families. Also, when we identify genes important in the development of the heart because they have gone wrong, it helps us understand normal development better. Such an understanding is fundamental to any attempt to treat people with heart disease at any age – for example those suffering from heart failure – using regenerative medicine."

Dr Shannon Amoils, Senior Research Advisor at the BHF, which part-funded the study, said:

"We've made great strides in treating congenital heart disease; most babies born with a heart defect have a much brighter future now than they would have had in the 1960s when the BHF was founded. But we still need to fund much more research like this, to better understand the fundamental causes of congenital heart defects.

"These important results show how large collaborative studies are incredibly useful for uncovering the influence of our genes on congenital heart disease. As researchers continue to identify other associated genes, we will be able to better predict the chances of children being born with heart problems, and will also learn more about the underlying processes that can go wrong in the developing heart."

More information: Genome-wide association study of multiple congenital heart disease phenotypes identifies a susceptibility locus for atrial septal defect at chromosome 4p16, DOI: 10.1038/ng.2637

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