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CARDIAC RESEARCH INSTITUTE

MEDIA RELEASE

New Gene Abnormalities Identified that Cause Heart Malformations in Children

In breakthrough research, scientists from NSW have identified abnormalities (mutations) in a cardiac gene, *TBX20*, which are responsible for heart malformations in children. The mutations caused disease in multiple family members and for the worst mutation, the resulting heart disease was sometimes fatal. In some surviving adults, the mutation was associated with marked enlargement of the heart (dilated cardiomyopathy or DCM), a debilitating condition in which the heart enlarges and eventually fails.

The study was a major collaborative effort led by the Victor Chang Cardiac Research Institute (VCCRI) and involving The Children's Hospital at Westmead, St Vincent's Hospital, the Sydney Children's Hospital and The University of Sydney.

Researchers screened DNA from 352 people with congenital heart disease (CHD), donated by adults and children over several years. They found 2 mutations in individuals who also had a family history of CHD. Both mutations caused disruption of one of the two normal copies of the *TBX20* gene.

In the work, which was published this week in the prestigious American Journal of Human Genetics, it was found that 5% of affected people with a family history of CHD carried a *TBX20* mutation, suggesting that routine screening for *TBX20* mutations may be useful in patients who have inherited CHD. Knowledge about the gene mutation can help in counselling families and assist in the long-term management of affected individuals.

CHD is common and can be extremely debilitating. Investigations and interventions are often required in the first year of life, sometimes involving open heart surgery. Further surgery may be necessary later in life. For some, having CHD is a life long emotional and economic burden.

"Structural malformations of the heart (CHD) are present in approximately 5 in 100 live-born infants" explained Professor Richard Harvey of the VCCRI and the Sir Peter Finley Professor of Cardiac Research UNSW, head of the collaborative effort. "Unfortunately, at present only a small number of genes have been identified that cause CHD, and this limits our power to understand the more complex problem of dissecting the genetic basis of CHD in the vast majority of patients in which there is no family history of disease.

"*TBX20* is a member of the T-box family of genes that encode proteins that regulate how other sets of genes are turned on and off in the embryo. Several T-



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box genes are known to play important roles in heart formation. The work on *TBX20* is the first to link this gene to human disease.

A significant finding from the work was that some patients with *TBX20* mutations developed DCM, confirming initial findings in mice that also lacked the gene.

“In 50% of cases of DCM, the genetic cause of the disease is not known. Findings from our work suggest that mutations in regulatory genes like *TBX20* may be a more common cause of DCM than previously thought.”

“Our results highlight the need to examine other control genes of this sort in DCM families.”

As with any large genetic study, many patient samples needed to be collected.

“We started recruiting patients from St. Vincent’s Hospital to the study many years ago,” Professor Harvey explained. “This enabled us to begin forming a CHD DNA bank.” “Professor David Winlaw, a paediatric cardiac surgeon and Head of Kids Heart Research at The Children’s Hospital at Westmead enhanced our recruitment and gene sequencing effort. This is an expensive process, but in the coming years the DNA bank will be a wonderful resource for further unravelling the genetic basis of CHD.”

Established in 1994, the Victor Chang Cardiac Research Institute (VCCRI) is committed to excellence in research into heart disease and cardiovascular biology, cardiovascular research training, and facilitating the rapid application of research discoveries to patient care.

To donate to the Victor Chang Cardiac Research Institute call (02) 8382 3022 or visit www.victorchang.com.au

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