Stem cell and genetic editing may unlock treatments for heart disease

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Heart muscle diseases are a leading cause of disability and death in children and adults but the causes remain poorly understood. The genetic changes that cause heart muscle disease are in the early stages of discovery. Identifying the genetic cause of heart disease is crucial in improving understanding of these conditions and for developing new drugs and therapies.

Researchers at the Murdoch Childrens Research Institute (MCRI) using cutting edge genetic and stem cell technologies, have found new changes in a gene called ALPK3 that cause an enlarged heart, a disease known as hypertrophic cardiomyopathy. Researchers looked at one Australian family with inherited heart disease and used Next Generation DNA Sequencing to identify the changes in the ALPK3 gene that cause the disease.

The research, published in a leading cardiac research journal the *European Heart Journal* (EHJ), will increase understanding of how heart muscle functions and identify potential targets for the development of treatments for heart disease.

Dr David Elliott, joint lead author of the study says, "This study shows how we can now move quickly from the clinic to the laboratory in order to work out how genetic changes cause disease. This information will help us design new and better therapeutic options for children with heart disease."

Heart muscle diseases make it harder for the heart to pump blood around the body and can lead to heart failure.

Hypertrophic cardiomyopathy is one of the main types of heart muscle disease which can lead to an enlarged heart. By using stem cells, researchers were able to work out how a mutation in the ALPK3 gene causes an enlarged heart

The researchers discovered that heart muscle cells (called cardiomyocytes) with changes in ALPK3 are very poor at "talking" to their neighbouring cells adversely affecting the hearts ability to beat. The heart beat is disorganized and the heart muscle cannot generate enough force. This results in the heart being overworked and the muscle becoming enlarged.

Associate Professor Paul Lockhart, a genetics expert and joint lead author of the study says "Modern genetic methods are rapidly improving our ability to identify the genes that cause disease. In only about 50 per cent of cases is the genetic cause of hypertrophic cardiomyopathy known. This work identifies a new gene and by studying it we hope to identify other genes that cause the disease. Identifying these genes provides important information for the family and the care of the patient."

The results of this study will have a direct and immediate impact on diagnostic, counselling and clinical services offered to affected children and families. The identification and study of genes that cause disease improves our understanding of heart muscle function. In time, we hope that we can develop new drugs that improve this condition.

Stem cell drive cardiomyocytes - the red sections make the cell contract, the blue is the cell nucleus which has the entire DNA.

Provided by Murdoch Childrens Research Institute