

New strategies to improve treatment and avert heart failure in children

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Structural and functional congenital cardiovascular abnormalities present at birth are the leading source of all congenital defects encountered in live births. Nearly half a million children in the United States have structural heart problems ranging in severity from relatively simple issues, such as small holes between chambers of the heart, to very severe malformations, including complete absence of one or more chambers or valves.

The April issue of the journal *Pediatric Cardiology* focuses on a recent meeting of pediatric cardiovascular experts from around the world who gathered at the Indiana University School of Medicine and Riley Hospital for Children for the second annual Riley Heart Center Symposium on Cardiac Development. The next Riley Health Center Symposium on Cardiac Development is scheduled for September.

The experts attending the most recent symposium presented novel basic science and clinical research approaches that strive to reach a common goal - to improve treatment of, and ultimately to rapidly identify and prevent, the congenital cardiovascular defects and the subsequent damage acquired after birth that ultimately results in heart failure.

The symposium focused on molecular mechanisms that implement the instructions embedded within DNA that enable cells to form a functional heart. The key proteins studied called transcription factors regulate how other genes are turned on and off in a complicated ballet that ultimately instructs a cell to become a cardiomyocyte and where to move and how



to function. When this dance goes a-rye, congenital heart defects are the unfortunate result.

"Although the process by which <u>transcription factors</u> regulate the expression of other gene products is well understood, how the many factors coordinate their functions to precisely define a cell's purpose is only now becoming possible to understand," said symposium coorganizer Anthony Firulli, Ph.D., professor of pediatrics and member of the Riley Heart Research Center.

"Indeed, when one considers the numerous different cell types that make up the heart and great vessels that are required to function in unison to pump blood throughout the body and that in every cell type there are complex combinatorial codes instructing each cell on how to function and how to communicate with their neighboring cells, it provides a complex challenge for heart researchers to understand," said Simon J. Conway Ph.D., professor of pediatrics and member of the Riley Heart Research Center, who co-organized the symposium.

Heart development is characterized by the differentiation, proliferation and movement of cardiac muscle cells which interact with extra cardiac tissues connecting the heart with the vasculature.

Dr. Firulli presented a comprehensive overview of the role that the Hand1 and Hand2 genes play during cardiogenesis, touching on interesting aspects of their overlapping functions. Dr. Conway presented data that directly tested whether the developing heart really requires both Hand1 and Hand2, and if one could be replaced by the other. These data from transgenic mouse models suggest that even though the Hand proteins are very similar in structure and may be expected to fulfill similar roles, Hand1 and Hand2 are independently required for the heart to develop normally.



A review of ideal imaging techniques for the most common complex congenital heart defects was presented by Tiffanie R. Johnson, M.D., associate professor of clinical pediatrics and co-director of the Pediatric/Congenital Cardiac MRI program at Riley Hospital. She discussed the best ways to diagnose and follow patients as they grow, both before and after surgical intervention. Dr. Johnson believes advances in imaging techniques will lead to higher quality and safer diagnostic imaging capabilities that will continue to be needed in the field of congenital heart disease.

It is the goal of the Riley Heart Center Symposia to establish strong communication between the basic and clinical research communities and ultimately establish collaborative projects to prevent the onset of congenital defects as well as heart failure in the young. The symposium faculty included leading clinical and basic scientists from the United States, United Kingdom and Germany.

The April issue of *Pediatric Cardiology* contains 16 studies presented at the symposium. This is the second issue of <u>Pediatric Cardiology</u> devoted to the innovative research presented at Riley Health Center Symposium. The first issue covered the inaugural gathering and was published in 2009.

Provided by Indiana University School of Medicine

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