

2012 Award Winner

Thor Thorsson, M.D.

Searching for the Genetic Origins of Heart Defects



Congenital heart defects are the most common type of birth defect, impacting about one in 100 live births. Babies born with severe defects such as hypoplastic left heart syndrome (HLHS) face the greatest risk. Advances in surgical and medical care—many of them pioneered here at Michigan—have greatly improved the outcomes for these vulnerable

patients, but research indicates that survival rates have plateaued in recent years. To make further improvements, many more questions must be answered about what causes these defects. 2011 Heart of a Champion award-winner Thor Thorsson is the right person to ask these questions, and Michigan is the right place to answer them.

The process of pinpointing specific genes responsible for these or any hereditary conditions is a complex one, requiring an understanding of gene sequencing technology, advanced mathematics and bioinformatics. But before Thorsson could put any of those tools to work, he had to find the right candidates to study. This too was no easy task. To begin, HLHS and related conditions are rare, accounting for no more than 20% of congenital heart defects. Another challenge: the study needed to focus on families with one or more affected siblings, but no other family history of defects. “Siblings with related conditions provide an ideal base for study,” notes Thorsson. “By identifying siblings with related heart abnormalities, we increase the likelihood that the defects occur because of a specific mutation or mutations, rather than by chance. Lightning doesn’t typically strike twice.”

Michigan proved the right place to find these rare subjects. Thorsson and his colleagues spent several years building a registry of information and genetic samples from patients operated on here. They identified several families in which two siblings have severe Left Ventricular Outflow Tract Obstructive, or LVOTO, a particular class of heart lesions. “Only a destination center like Michigan treats a large enough volume of these patients to make such an analysis possible,” Thorsson says.

As primary investigator, Thorsson has put together a ‘dream team’ to pull it off. Guidance in gene sequencing will be offered by two of the top experts in the field, U-M professors Friedhelm Hildebrandt, M.D., and Edgar Otto, Ph.D., who together have used a similar approach to identify the genes involved in certain renal disorders. Much of the computational work will take place in the Hildebrandt lab, utilizing technology called total exome capture and massively parallel sequencing. Once again, Michigan provided an unbeatable base of operations—the technology was developed by Drs. Hildebrandt and Otto here at the University.

Thorsson will also work closely with Mark Russell, M.D., Associate Professor of Pediatrics, an international expert in the genetic causes of heart disease. If successful in this step, they hope to conduct further studies of the gene or genes they find.

The study is a fine example of the kind of innovation and cross-collaboration Bo Schembechler wanted to reward with the Heart of a Champion Research Fund. “As an early-career investigator, it’s a thrill to have this project recognized and supported in such a big way,” says Thorsson. “We have lots of work ahead of us, but thanks in great part to this funding, I believe our chances of success are very high.”