Bench to Bassinet: Pediatric Cardiac Genomics Consortium

CHD GENES Newsletter

Welcome! This is the 3rd newsletter for the CHD GENES Study, a multicenter research study investigating the genetic causes of congenital heart disease (CHD). This study began in November 2010; since that time, we've enrolled over 12,000 individuals with CHD and almost 17,000 of their relatives. We wanted to take this opportunity to let you know what we've learned to date. Please visit our Bench to Bassinet website to learn more (https://benchtobassinet.com).

To our patients and families who participated in CHD GENES,

Thank you for helping us in our search for the causes of congenital heart disease

CHD genetics: progress and the road ahead

By Dr. Martina Brueckner and Nancy Cross (Yale University)

Since the CHD GENES study started 8 years ago, we have come a long way towards understanding the genetic cause of congenital heart disease (CHD). The most important thing we have learned is that we can identify a genetic cause for almost 40% of CHD. This breaks down as follows, the discoveries made by the CHD GENES Study:

- 12% of people with CHD have CHD due to an extra or missing copy of an entire chromosome. The most common example of this is Down Syndrome, where patients have an extra copy of chromosome 21. Other examples are found in girls with Turner Syndrome, who are missing a copy of the X chromosome.
- 10-15% have CHD due to an extra or missing piece of a chromosome. This is called a copy-number variation (CNV). CNVs can be either inherited from a parent or are new changes in the person with CHD. The new changes are called de-novo variation. There are CNVs that have been known to be an important contributor to CHD, such as a missing piece of chromosome 22 (DiGeorge Syndrome). **The CHD GENES work has identified many new CNVs that are important in CHD.**
- **Approximately 12% have CHD due to more subtle genetic changes, such as a change in just one letter of the genetic code. This has been a major finding from the CHD GENES Study.** Many of these are new changes (de-novo variations), and a small number are inherited from the parents. We have found that in families with inherited CHD, the type of CHD in the child can look similar, or quite different, from that found in the parents.

We are also beginning to learn what the specific genetic cause of CHD can mean for people with CHD. **One example is that we identified a group of genes, called chromatin modifier genes, that are important for development of both the heart and the brain**. People with CHD due to abnormal chromatin modifier genes are at higher risk for having problems such as learning disability, developmental delay and autism, and may benefit from early developmental interventions. Discovering the specific impact of the genetic causes of CHD on outcome, such as how well patients do

after surgery, will be one of the most important aspects of the CHD GENES study ahead of us. The big-picture goal of CHD GENES is to develop truly personalized care for CHD patients.

One of the most important things we have learned is that the genetic cause of CHD is very complicated. We now know that at least 400-500 of the 21,000 genes that make up the human genome can cause CHD. When things are this complicated, we can get answers only by looking at as many CHD patients as possible. Thanks to all of the CHD GENES participants (you!!) we have built the single largest source of information leading to a better understanding of CHD in the world. As of the writing of this newsletter, over 12,000 CHD patients and their families are participating in CHD GENES. These large numbers become more and more important as we work towards figuring out the genetic causes of the ½ of CHD for which we don't yet have an answer. Altogether, the study of CHD has come a long way, but we also have a long way to go. We look forward to working with all of the participating CHD GENES patients and families on the journey to better care and understanding of CHD.

A Personal Perspective

By Stephanie Pare (Boston Children's Hospital)

I have been a part of this study since early 2018, working as a research assistant at Boston Children's Hospital (BCH). People come from all over the world to be seen at BCH, and every person I meet and every story they share with me is going towards one goal: knowing more about congenital heart disease (CHD). It has been a very heartwarming experience to be able to meet such wonderful people who think beyond their own troubles and agree to participate in this research study. I see everyone from first time parents with newborns to parents with their adult children, and I always see the concern and love they have for their children going through an extremely stressful experience of a cardiac procedure.

My experience working on CHD GENES has given me the opportunity to hear the diverse stories of the many families who participate in our study. Through those stories, our consortium is also learning more and more about CHD. We thank you for being one of those families who was willing to take the time to share their story with us so that the future for children with CHD can be even brighter.

*****IMPORTANT*****

Help us to help <u>you</u> stay informed about the latest research findings from this study. Update your contact information by phoning or emailing your research center with your current contact information and the best way for us to reach you in the future.

The Bear Explosion

By Nancy Cross (Yale University)

Photo Credit: David Kosmin

As a research coordinator for the CHD GENES STUDY at the Yale University site, I continue to be amazed and touched by the wonderfully kind and generous families I meet who are affected by Congenital Heart Disease (CHD). In our 2015 newsletter, I shared a story about one such special family, who started the Bear Project at Yale New Haven's Children's Hospital Heart Center. The donor family conceived this idea as a means to increase awareness of CHD as well as inspire other families affected by CHD. Since 2014, they have purchased and donated Mended Heart Bummer Bears annually, which are beautiful teddy bears with a plastic zipper located on the chest revealing an embroidered heart with a white line (much like an incision). They attach their personal story and honor me with the pleasure of gifting these bears to children undergoing heart surgery. This generous and thoughtful act of kindness has touched the hearts of the families receiving the bears, helping them realize they are not alone and inspire hope for their child's recovery. Since then, several families touched by this gesture have also contributed to the Bear Project.

In 2017, I gifted a bear to an eight-year-old boy who was recovering from open heart surgery. Although he loved receiving the bear, he asked if I could save it for a child who might need it more! This past August, I learned from his mother that for his ninth birthday, in lieu of gifts, he asked family and friends "to open their hearts" and donate money so he could buy bears for other kids! He collected enough money to purchase 36 bears! He attached his own personnel inspirational story, in which he said his motto is "**If I can get through open heart surgery, I can get through anything**"! I can tell you I have been truly inspired by this young man's generosity and good will towards others - a wonderful role model at age nine. Thanks to his compassion and generosity, our bear population has exploded! When he came for his clinic visit, I gifted him with his own bear which he named "Zippy". Thank you to this amazing young man! And thank you to the donor family for their continued generosity and commitment to CHD, and to the other wonderfully generous families who have also contributed bears!

Find out about Congenital Heart Disease Awareness at https://mendedhearts.org/chd-awareness-week/

The Role of Genes in Neurodevelopmental and Brain Outcomes: A New Study

By Dr. Jane Newburger (Boston Children's Hospital)

Patients with congenital heart disease (CHD) have a high risk of neurological, developmental, and behavioral disorders. Research on how genetics may play a role in their learning abilities and behavior has great importance.

We are currently studying the role that genes play in neurodevelopmental and brain outcomes in people with CHD. This study is enrolling a portion of children and adults with CHD who took part in a previous research study (CHD GENES) that is looking at the genes that might be related to CHD. In this study, people with CHD will be tested to learn the strengths and weaknesses in their learning abilities (e.g., reading, writing, math), and those who are able will also have a brain MRI. They and their families also complete surveys. The results of these tests will be given to families after the testing. All testing and travel are free of charge, and, in addition, families will be paid a small amount to show our thanks for their time and effort. The in-person testing will provide rich information about neurocognitive function for use by patients, their families, and schools. The patients and families can also share the results of the testing with their physicians and schools. Finally, all results about the patients are kept confidential. To date, over 100 patients have enrolled or are scheduled to enroll in the study. Information sent out by mail, email, and text will invite even more patients and families to be a part of the study. By learning the genetic factors that affect development and brain structure, this study will improve prenatal screening and counseling, and treatments for people with CHD, including early detection of those who need specialized support services.

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