

News About...

Chiari Type I Malformation Research

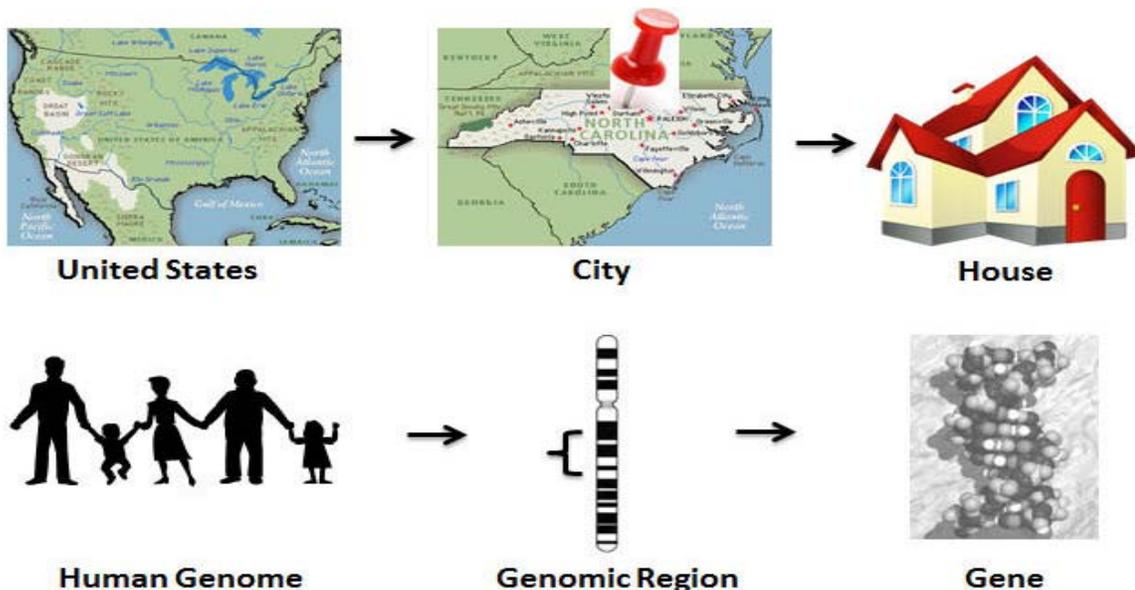
Spring 2012

Chiari Whole Genome Linkage Screen Completed

The human genome (all the DNA in a human) contains roughly 22,000 different genes. Genes can be thought of as instructions or recipes for how our bodies develop and function. Genetic disorders are caused by changes in a gene or genes, preventing the gene(s) from performing their proper function. Whole genome linkage analysis (a genome screen) is performed in an effort to locate specific regions of the genome that may contain genes that cause or contribute to Chiari Type 1 Malformation (CM1). A whole genome screen is a bit like searching the United States (the genome) for a single house (a gene) without an address. A

linkage screen allows us to identify the city (region) that the house is in and then we use other methods to locate the house.

We recently completed a whole genome linkage screen of 375 individuals in 67 CM1 multiplex families (families with two or more members diagnosed with CM1). We found several regions of interest and have already begun investigating candidate genes (genes we think may be involved in causing CM1) within these regions. One gene of particular interest is currently being sequenced (read) in individuals diagnosed with CM1 in order to find changes within the gene that are not found or rarely found in individuals without CM1.



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Chiari 1 and Zero Malformations

Chiari Type I Malformation (CM1) involves herniation of the lower part of the brain, called the cerebellar tonsils, through the opening at the bottom of the skull. Individuals with CM1 may or may not have syringomyelia (a fluid filled area in the spinal cord). Chiari Zero Malformation (CM0) on the other hand is defined as classic chiari symptoms and the presence of syringomyelia but no evidence of tonsillar herniation. In collaboration with Dr. Bermans Iskandar at the University of Wisconsin, Madison and others, we recently completed a small project which focused on a possible genetic link between CM1 and CM0, as well as further evaluated clinical similarities between the disorders. We identified five families in our study that contained at least one family member diagnosed with CM1 and one member diagnosed with CM0. In general, we found that relatives with CM1 and CM0 experienced similar symptoms and had similar head measurements on MRI. In addition to this study, there is increasing evidence which suggests that at least a portion of CM0 and CM1 may have the same cause. However, more research needs to be conducted in this area before any conclusions can be made.

Dura Expression Study Enrollment Completed

In 2010, Conquer Chiari, a non-profit organization dedicated to improving the experiences and outcomes of Chiari and Syringomyelia patients through education, awareness and research, awarded the Duke Center for Human Genetics a grant to further study the genetics of Chiari Type 1 Malformation (CM1). This funding was used towards research to identify subtypes of CM1 by looking at gene expression patterns (genes turned on and off) in

samples of blood and dura (the outmost layer covering the brain) from CM1 patients. Samples were collected by two neurosurgeons at Duke, Drs. Herbert Fuchs and Gerry Grant, from 70 patients between the ages of 10 months and 17 years undergoing decompression surgery for CM1. Clinical information consisting of medical records, head MRIs and symptoms was also



collected in hopes of matching gene expression patterns to clinical characteristics. Enrollment and sample collection lasted 20 months and was completed in October, 2011. The samples are currently being tested in the lab and we hope to have exciting results soon.

Chiari Study Enrollment Update

We have collected DNA samples from 1,350 individuals in 277 families from across the United States. Of these 277 families, 217 families (78%) are multiplex families, meaning there are two or more individuals diagnosed with Chiari Type 1 Malformation (CM1) in the family. The other 60 (22%) are singleton families, meaning there is only one individual diagnosed with CM1 in the family.

Thank you to anyone who contributed a sample since 1994 when the study began. Research toward a better understanding of the causes of CM1 would not be possible without your help. We continue to enroll additional families with two or more members diagnosed with CM1.

Chiari Malformation and Ehlers Danlos Syndrome

Ehlers Danlos Syndrome (EDS) is a group of inherited connective tissue disorders caused by gene changes that disrupt collagen function, the material that provides strength and structure to skin, bone, blood vessels and internal organs. There are several different types of EDS, each with its own associated symptoms. Researchers have noticed that some individuals with Chiari Type 1 Malformation (CM1) also have EDS (typically Hypermobility Type). EDS is characterized by hypermobility (the ability to touch the thumb to the forearm, bend fingers back more than 90 degrees, hyperextend elbows and knees and place palms of the hands flat to the floor with



legs straight), chronic joint pain, joint and hip dislocations, soft velvety skin and easy bruising.

We have enrolled 22 families with both CM1 and a documented diagnosis of EDS, though we suspect many more of our participants may have EDS but are undiagnosed. EDS is best diagnosed by a medical geneticist. More information about EDS can be found at www.ehlersdanlosnetwork.org. We hope to look further into the relationship between CM1 and EDS in the coming years.

Chiari Researchers Come Together

Conquer Chiari Research Conference

In November 2010, Conquer Chiari in partnership with the Chiari and Syringomyelia Foundation (CSF) held their bi-annual research conference in Chicago, Illinois. Over 40 Chiari researchers and neurosurgeons gathered to discuss their research. Many outstanding presentations were given over a two day period. Presentations covered a wide range of topics, including syrinx formation, tethered cord, symptoms, cognitive function, disease mechanisms, and surgical techniques. The Duke Chiari research team, represented by Dr. Simon Gregory and graduate student Christina Markunas presented the genetics of Chiari malformation. It was a wonderful experience for all attendees and a good chance for researchers to share and discuss ideas. Presentations from the conference were recorded by Conquer Chiari and can be found on their website (<http://www.conquerchiari.org>).

ASAP's Chiari and Syringomyelia Conference

In July 2011, the American Syringomyelia & Chiari Alliance Project (ASAP) held their annual Chiari and



Dr. Gregory presenting research findings

Syringomyelia Conference in Denver, Colorado. The meeting was aimed at raising awareness of Chiari and

to provide individuals with Chiari and their families an update in the current knowledge of Chiari symptoms, treatments and research. The meeting which was attended by over 50 advocates over the four days was a tremendous success, both scientifically and socially. Dr. Simon Gregory spoke about the genetic basis of Chiari malformations in the context of the human genome, sequence variation and genetic risk. The 2012 ASAP annual meeting will be held July 18-21 in Arlington, Virginia.

Keep Us Updated

Please keep us in mind when important changes happen in your family. We would like to know if there are any major changes in the health status of family members, such as if another family member is diagnosed with Chiari.

Also, if you should move, please give us your updated contact information. You may give us your updates by calling us at **919-684-0655** or toll-free at **1-877-825-1694** or by sending an email to **chiari@chg.duhs.duke.edu**. Thank you!

Follow us on Facebook

For periodic updates on Chiari research being conducted at the Duke Center for Human Genetics “like” us on Facebook at:

<http://www.facebook.com/pages/Chiari-Type-1-Malformation-Study-at-Duke-University-Medical-Center/258936470795236>

Who Pays for Research?

Conducting genetic research studies is painstaking and expensive work that relies on funding support from both public and private sources. Over the years the Duke CHG team has been awarded research funds or grants from the National Institute of Neurological Disorders and Stroke (NINDS), Conquer Chiari, the American Syringomyelia & Chiari Alliance Project (ASAP), the Chiari & Syringomyelia Foundation (CSF), and from private donors whose lives have been touched by Chiari malformation.

We are often asked if we can accept donations to support the Chiari research, sometimes in memory of a loved one who has passed away. The answer is yes, and these donations are very much appreciated! If you or someone you know would like to make a gift, the Center for Human Genetics has created the Duke CHG Chiari Research Fund. To make a financial gift to Chiari research, you may visit the secure web site of the gift records office at www.giftrecords.duke.edu and click on “Make a Gift Now!” and then “Make a Credit Card Gift.” Under Additional/Other Designations make sure to type in Center for Human Genetics Chiari Fund. Or you can send your tax-deductible donation to the address below:

**Duke Center for Human Genetics
Chiari Research Fund
Box 3445
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