Good news! A team of twenty-one people, including some of the top geneticists and Chiari specialists in the US, discovered that there may be a genetic link specific to Chiari 1 Malformation. Researchers screened 71 Chiarians from 23 families and found two places in the pool of genetic information where certain test scores indicated there might be a gene that could cause Chiari. One of the two areas already is known to contain fibrillin-1, a gene linked to Marfan syndrome, that also has been linked to another disorder, Shprintzen-Goldberg syndrome, in which affected people are known to have Chiari malformations. Researchers are optimistic that further study of these two areas may lead to the discovery of the specific gene or genes that result in the development of Chiari.
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## Research Article

# Phenotypic definition of Chiari type I malformation coupled with high-density SNP genome screen shows significant evidence for linkage to regions on chromosomes 9 and 15†

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Chiari type I malformation • genome wide linkage screen • cranial morphology

Abstract

Chiari type I malformation (CMI; OMIM 118420) is narrowly defined when the tonsils of the cerebellum extend below the foramen magnum, leading to a variety of neurological symptoms. It is widely thought that a small posterior fossa (PF) volume, relative to the total cranial volume leads to a cramped cerebellum and herniation of the tonsils into the top of the spinal column. In a collection of magnetic resonance imagings (MRIs) from affected individuals and their family members, we measured correlations between ten cranial morphologies and estimated their heritability in these families. Correlations between bones delineating the PF and significant heritability of PF volume (0.955, $P = 0.003$) support the cramped PF theory and a genetic basis for this condition. In a collection of 23 families with 71 affected individuals, we performed a genome wide linkage screen of over 10,000 SNPs across the genome to identify regions of linkage to CMI. Two-point LOD scores on chromosome 15 reached 3.3 and multipoint scores in this region identified a 13 cM region with LOD scores over 1 (15q21.1-22.3). This region contains a biologically plausible gene for CMI, fibrillin-1, which is a major gene in Marfan syndrome and has been linked to Shprintzen-Goldberg syndrome, of which CMI is a distinguishing characteristic. Multipoint LOD scores on chromosome 9 maximized at 3.05, identifying a 40 cM region with LOD scores over 1 (9q21.33-33.1) and a tighter region with multipoint LOD scores over 2 that was only 8.5 cM. This linkage evidence supports a genetic role in Chiari malformation and justifies further exploration with fine mapping and investigation of candidate genes in these regions. 

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