HOXC4

This gene belongs to the homeobox family of genes. The homeobox genes encode a highly conserved family of transcription factors that play an important role in morphogenesis in all multicellular organisms. Mammals possess four similar homeobox gene clusters, HOXA, HOXB, HOXC, and HOXD, which are located on different chromosomes and consist of 9 to 11 genes arranged in tandem. This gene, HOXC4, is one of several homeobox HOXC genes located in a cluster on chromosome 12. Three genes, HOXC5, HOXC4, and HOXC6, share a 5' non-coding exon. Transcripts may include the shared exon spliced to the gene-specific exons, or they may include only the gene-specific exons. Two alternatively spliced variants that encode the same protein have been described for HOXC4. Transcript variant one includes the shared exon, and transcript variant two includes only gene-specific exons.

Analysis of unique and powerful Utah genetic resources allowed the identification of 38 strong candidate Chiari malformation predisposition gene variants. These variants should be pursued in independent populations. One of the candidates, a rare HOXC4 variant, was identified in 2 high-risk CM pedigrees, with this variant possibly predisposing patients to a Chiari phenotype with craniocervical kyphosis [1].

1)
Brockmeyer DL, Cheshier SH, Stevens J, Facelli JC, Rowe K, Heiss JD, Musolf A, Viskochil DH, Allen-Brady KL, Cannon-Albright LA. A likely HOXC4 predisposition variant for Chiari malformations. J Neurosurg. 2022 Nov 25:1-9. doi: 10.3171/2022.10.JNS22956. Epub ahead of print. PMID: 36433874.