

Accepted Manuscript

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PII: S0378-1119(17)30904-6
DOI: doi:[10.1016/j.gene.2017.10.058](https://doi.org/10.1016/j.gene.2017.10.058)
Reference: GENE 42279

To appear in: *Gene*
Received date: 27 July 2017
Revised date: 2 October 2017
Accepted date: 20 October 2017

Please cite this article as: Gary R. Kunkel, Jessica A. Tracy, Frank L. Jalufka, Arne C. Lekven , CHD8short, a naturally-occurring truncated form of a chromatin remodeler lacking the helicase domain, is a potent transcriptional coregulator. The address for the corresponding author was captured as affiliation for all authors. Please check if appropriate. *Gene*(2017), doi:[10.1016/j.gene.2017.10.058](https://doi.org/10.1016/j.gene.2017.10.058)

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CHD8short, a naturally-occurring truncated form of a chromatin remodeler lacking the helicase domain, is a potent transcriptional coregulator

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Abstract

Chromodomain-Helicase-DNA binding protein 8 (CHD8) is a member of a large family of eukaryotic ATP-dependent chromatin remodeling complexes. Loss of function alleles of human chd8 are correlated with autism spectrum disorder. The CHD subfamily members contain a tandem pair of chromodomains that are adjacent to a centrally located Snf2-like helicase domain. An alternatively spliced variant mRNA of CHD8 was identified years ago in mammals that encodes a truncated form of the protein, called Duplin, that lacks the helicase domain and everything else in the carboxyl direction. We are using zebrafish to explore the functions of CHD8, especially the truncated form that we refer to as CHD8short (CHD8S). The mRNA for CHD8S is expressed differentially during embryonic development. Using a PCR assay we detected expression of putative zebrafish chd8s mRNA that is barely detectable during early embryogenesis (shield stage at 6h), but increases markedly soon thereafter at 80-90% epiboly (9h) and bud stages (10h), with a return to low levels in 16-somite (17h) and 24 hpf embryos. Except

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