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# Neural tube closure depends on expression of Grainyhead-like 3 in multiple tissues

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**Abstract**

Failure of neural tube closure leads to neural tube defects (NTDs), common congenital abnormalities in humans. Among the genes whose loss of function causes NTDs in mice, Grainyhead-like3 (*Grhl3*) is essential for spinal neural tube closure, with null mutants exhibiting fully penetrant spina bifida. During spinal neurulation *Grhl3* is initially expressed in the surface (non-neural) ectoderm, subsequently in the neuroepithelial component of the neural folds and at the node-streak border, and finally in the hindgut endoderm. Here, we show that endoderm-specific knockout of *Grhl3* causes late-arising spinal NTDs, preceded by increased ventral curvature of the caudal region which was shown previously to suppress closure of the spinal neural folds. This finding supports the hypothesis that diminished *Grhl3* expression in the hindgut is the cause of spinal NTDs in the *curly tail* hypomorphic *Grhl3* allele . Complete loss of Grhl3 function produces a more severe phenotype, however, in which closure fails earlier in neurulation, before the stage of onset of expression in the hindgut of wild-type embryos. This implicates additional tissues and NTD mechanisms in *Grhl3* null embryos. Conditional knockout of *Grhl3* in the neural plate and node-streak border has minimal effect on closure, suggesting that abnormal function of surface ectoderm, where Grhl3 transcripts are first detected, is primarily responsible for early failure of spinal neurulation in *Grhl3* null embryos.

Keywords: Neural tube defects, grainyhead, spina bifida, curly tail, mouse embryo

## *Introduction*

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