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Characterizing DRG axon phenotypes in a novel *Lfng* mutant

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Abstract

During embryonic development, structures such as the vertebral column, ribs, trunk muscles, and meninges arise from blocks of mesoderm called somites that surround the neural tube, a precursor to the central nervous system. Precise regulation of the Notch signaling pathway is required for establishing somite boundaries and patterning. Mutations in *Lunatic Fringe* (*Lfng*), a fucose-specific beta 1,3-N acetyltransferase that regulates Notch signaling, results in abnormal spacing of the somites and their derivatives, resulting in stereotypical skeletal malformations and spondylocostal dysostosis, a recessive disorder that results in malformations of the vertebral column and ribs resulting in shortened trunks and respiratory difficulties.

In a forward genetic screen for genes involved in peripheral nervous system development, we isolated a line with a mutation in *Lfng* ($Lfng^{C20R}$). In addition to skeletal malformations, $Lfng^{C20R}$ mutants display abnormal axonal branching of dorsal root ganglion (DRG) neurons. DRGs convey sensory information from the periphery into the spinal cord, where neurons in the dorsal horn process sensory information. Currently, it is unknown how *Lfng* mutations affect the development of the primary somatosensory circuit.

In the present study, we sought to understand how DRG axon branching is affected throughout development and whether specific subtypes of DRG neurons are affected in $Lfng^{C20R}$ mutants. We also examined whether the axon guidance phenotype is DRG-autonomous or due to alterations in the surrounding environment. To test the hypothesis that the phenotype is DRG-autonomous, we measured axon growth and fasciculation in neuronal explants cultured from control and $Lfng^{C20R}$ mutants. Preliminary data demonstrated that axon growth and fasciculation did not differ between mutants and controls, suggesting that the axon branching phenotype may originate from the surrounding environment. One possible explanation is that the development of the spinal meninges is abnormal in $Lfng^{C20R}$ mutants, which will be investigated in future studies.