

EXAMINING THE ROLE OF *Gbx1* IN SPINAL CORD DEVELOPMENT AND ITS CONTRIBUTION TO MAMMALIAN LOCOMOTION

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ABSTRACT

Animals explore their environment through locomotion. Motion is largely generated by the activity of neurons in the spinal cord. Genes expressed during embryonic development are essential for the formation of connections between spinal cord neurons that are responsible for producing movement. The murine *Gbx* genes, *Gbx1* and *Gbx2*, are transcription factors widely involved in central nervous system development. In the spinal cord, they are expressed in unique populations of developing spinal cord neurons. To examine the role of *Gbx1* in the developing spinal cord, we generated mice carrying a loss-of-function allele for *Gbx1* (*Gbx1*^{-/-}). By postnatal day 15, *Gbx1*^{-/-} mice begin to display a gross locomotive defect that specifically affects hindlimb walking gait. Molecular analysis of mutant embryos revealed premature termination of proprioceptive sensory afferents (1a afferents) in the dorsal spinal cord. In addition, a subset of ISL+ spinal motor neurons is eliminated by apoptosis, at mid-embryonic stages. Both observations persisted at postnatal stages. This study demonstrated a requirement for *Gbx1* for normal locomotor output. We also briefly assessed possible interaction of *Gbx1* with its family member *Gbx2* in spinal neuron development using *Gbx1*^{-/-}; *Gbx2*^{-/-} double knockout mutant embryos. Data from this study suggest that *Gbx* family members are required to maintain PAX2 interneuron cell fate in the dorsal spinal cord, but not functionally redundant for this shared function.