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Cloning and functional characterization of the zebrafish mutation belladonna

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Abstract

The zebrafish *belladonna (bel)* mutation was identified in a large-scale mutagenesis screen to identify genes involved in retino-tectal pathfinding in Tubingen, Germany. In *bel* mutants, after exiting the eye, retinal axons grow ipsilaterally instead of crossing the midline to form optic chiasm. *bel* mutants are semi-viable and live *bel* embryos at 5 days show a "dilated pupil" phenotype after which the mutation was named. Later work showed that *bel* mutants have functional eyes although the optokinetic response is reversed in the mutants. Previous work in our lab showed that most retinal axons in the mutants initially grow towards the midline but later turn ipsilaterally. Also, two major forebrain commissures, the anterior commissure (AC) and the post-optic commissure (POC) also failed to form in *bel* mutants. These studies showed that *bel* defects are restricted to forebrain. Detailed analysis of eye sections showed defects in *bel* eye morphology during embryonic and adult stages. Initial work also mapped the *bel* locus on chromosome 8 and finer mapping linked one z-marker on either side of *bel* locus (z24272 and z44909). ^ My dissertation project was to clone the *bel* gene and understand its role in forebrain patterning and axon guidance. I identified that *bel* locus encodes a zebrafish lim-homeodomain transcription factor, Lhx2. To further understand how *bel(lhx2)* might affect axon guidance, I first showed that *bel* mutants have subtle defects in forebrain patterning in the regions where axons cross the midline. I also showed that these forebrain patterning defects lead to defects in expression of proper cellular and

molecular axon guidance cues at the midline in *bel* mutants. Finally, I showed that *bel(lhx2)* is required for cell proliferation in the diencephalon. Thus my detailed analysis of *bel* mutants has revealed new roles for *lhx2* in diencephalon patterning and axon guidance. ^

Subject Area

Biology, Molecular|Biology, Neuroscience|Biology, Cell

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