THE *C. ELEGANS* LISSENCEPHALY (LIS1)-LIKE GENE *LIS-1* IS REQUIRED FOR EMBRYONIC DEVELOPMENT

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In the human disease lissencephaly, abnormal neuronal migration during brain development leads to reduced cerebral convolutions. Afflicted patients suffer epilepsy and mental retardation. The most common cause of lissencephaly is haploinsufficiency of the gene LIS1. The predicted *C. elegans* LIS-1 protein is 58% identical to human LIS1. We have isolated two deletion alleles of *lis-1*, one that removes 1465 bp, including predicted exons 4-5, and one that removes 2019 bp, including predicted exons 4-6. These 2 alleles fail to complement.

Deletion homozygotes are Unc, Egl, and Mel. Progeny of deletion homozygotes appear to arrest at the 50-100 cell stage and contain enlarged, heterogeneous, asymmetrically distributed nuclei. We have analyzed the cell biological basis of the defects in embryonic development and in egg-laying. A translational *lis-1::gfp* fusion gene driven by the worm *lis-1* promoter is expressed in multiple tissue types in transgenic worms; expression in the nervous system is restricted to a subset of neurons. We are now attempting to confirm this expression pattern using antibody staining. To test whether the human and worm genes are orthologous, we are attempting to rescue the phenotype of the worm deletion mutants with the human LIS1 cDNA driven by either the heat-shock or the endogenous *lis-1* promoters.

We are seeking *lis-1* interactors both by screening for suppressors of the *lis-1* Mel phenotype and by testing candidate genes. An F1 screen of ~10,000 haploid genomes failed to yield suppressors of the *lis-1* Mel phenotype. We now plan to extend this screen to the F2 generation.