Is specter a mutation in the cell cycle gene cyclin B1?

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ABSTRACT

Progression through cell division is controlled by genes that regulate the cell cycle. As of now, the way embryos control cell division is regulated on one recessive mutation. Herein, we elucidate that as a cell cycle disruption or loss of activity in the cell cycle is often considered to be involved in cancer pathways. Thus, we show that the specter mutation is a cell division mutant that causes mitotic abnormalities and later becomes developmentally arrested at about 20 hours of development. We mapped the spr mutation to an interval on linkage group 5, which includes the cyclin B1 gene. Cyclin B1 is essential for the control of the G2 to M transition of the cell cycle. Sequencing spr mutant mRNA showed that there is a nonsense mutation (C597T) in exon 2 of cyclin B1 gene. We hypothesize that the spr mutation is caused by a non-functional cyclin B1 protein: cell cycle progression and developmental abnormalities are seen as soon as maternal cyclin B1 mRNA is depleted. In situ hybridization of cyclin B1 revealed that the expression is greatly reduced in the mutant embryos at the 10-somite stage. Sycos Green staining of DNA showed nuclear fragmentation in the mutants at the 15-somite stage. Phospho histone H3 antibody staining showed that fewer cells enter mitosis in the mutants compared to the wild type embryos, and that neural stem cells do not migrate properly to the midline to divide. In situ hybridization of a marker for neural precursors revealed that there are fewer neural precursors in the spr mutant at the 15-somite stage. This is consistent with the observation that the neural precursors, the neural retina, and the spinal interneurons, showed that there were also fewer neural precursors in the mutant compared to the WT at the 15-somite stage. Caspase-3 antibody staining revealed that a wider-scale apoptosis in the spr mutant occurs as early as 10 somite in the brain and spinal area that first has an optical transparency, and correlates with further development. Thus, morphological changes described in spr mutant can be explained by the mutation in the cell cycle gene and cyclin B1 seems like a really good candidate. We are now using mRNA injections to test if we can rescue the mutant, part of the proof that the specter phenotype is caused by a mutation in cyclin B1 gene.

RESULTS

Are cells dying in the central nervous system in spr by apoptosis?

It seems so. Sequencing data reveals a nonsense mutation early in exon 2 of the cyclin B1 gene on linkage group 5. It is likely that there is no expression of cyclin B1 in later somite stages.

CONCLUSION

Morphological changes described in spr mutant can be explained by the mutation in the cell cycle gene and cyclin B1 seems like a really good candidate

FUTURE DIRECTIONS

- Confirm that the spr phenotype results from a disruption in cyclin B1 by rescuing the mutant with injections of WT cyclin B1 mRNA. By knocking down cyclin B1 mRNA by antisense oligonucleotide and CRISPR-Cas system.
- Determine at what stage in the cell cycle and what kind of cells are affected by a loss of cyclin B1.

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