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More about signaling pathway uncovered

Researchers at UT Southwestern have furthered the understanding of a critical signal pathway in regulating organ and system development, a finding that could eventually aid in preventing cancer formation.

The earliest cell divisions of fertilized eggs, in some higher organisms, result in cells called blastomeres, which can develop into entire tissues or organs. For example, one blastomere might generate all of the skeletal system, and another the entire intestine. This development is largely determined by the interaction of a few specific factors.

Dr. Rueyling Lin, assistant professor of molecular biology, and her colleagues who studied these interactions in worms called Caenorhabditis elegans reported their findings in the April 2 issue of the Cell.

“It surprises some people when they hear how relevant this little worm is to human development and medicine,” said Dr. Lin. “Fortunately, most of the basic processes that drive development in much more complicated animals are more easily studied in C. elegans, and we can take advantage of the very powerful tools that this system affords us.”

Among those factors is the Wnt signal pathway, a central mechanism regulating tissue development. When deregulated, the resulting malformations can cause cancerous cell and tumor formation, with certain tumors containing a mutation that improperly activates this pathway.

The UT Southwestern researchers studied and detailed a novel mechanism that regulates nuclear levels and activity of the terminal transcription factor in the Wnt signal pathway, showing that another signaling path way interacts with and affects the outcome of the Wnt signal.

Specifically, at the four-cell stage, one blastomere generates a Wnt signal detected by a neighboring blastomere called EMS. One EMS daughter cell then develops the worm endoderm, or gut, and the other daughter cell develops the mesoderm, predominantly muscle.

In the worms, Dr. Lin and her colleagues found that the nuclear level control of a specific protein or transcription factor is central to the mesoderm and endoderm fate specification caused by the Wnt signaling, as certain mutations led to both EMS blastomeres developing into either mesoderm or endoderm.

These findings provide a better understanding of the Wnt signaling pathway, whose specific components are targeted as possible sites for cancer treatment, said Dr. Lin.

“What we have learned about this important signaling pathway in the worm will be directly relevant to higher organisms, including humans,” she said. “Our challenge now is to determine exactly how Wnt signaling results in the different developmental fates observed between the two EMS daughters in the early embryo.”

Other UT Southwestern contributors to the Cell study were Miao-Chia Lo, student research assistant in molecular biology, and Rannan Odom, a third-year medical student.

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