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Fruit Fly Study Digs Deeper Into Poorly Understood Details of Forming Embryos

Using fruit flies as a model to study embryo formation, scientists report in Nature Cell Biology that molecular breakdown of a protein called Bicoid is vital to normal head-to-tail patterning of the insect's offspring.

Published online by the journal Dec. 19, the study shows how Bicoid is targeted for molecular degradation by a newly identified protein the researchers named Fates-shifted (Fsd). Without the interaction between Bicoid and Fsd, fruit fly embryos are improperly formed and misshaped, according to scientists at Cincinnati Children's Hospital Medical Center.

The findings are another example of how genetic and molecular studies of embryonic development in fruit flies (known formally as *Drosophila melanogaster*) help inform medical research into human disease and birth defects? Over half of the genes known to cause disease in humans have a recognizable match in the fruit fly's genetic code.

"Although there is no direct medical impact, this study has critical relevance for medical research into birth defects," said Jun Ma, Ph.D., Senior Investigator and a Researcher in the Divisions of Biomedical Bioinformatics and Development Biology. "For tissues in the developing embryo to form properly, cells have to know what their proper locations are. This study looks at the location cues cells receive in early *Drosophila* embryos."

The cues are delivered through a process that scientists still don't completely understand. It's controlled by molecules called morphogens, which form concentration gradients along the head-to-tail axis, or other axes, of developing

embryos. Scientists think these gradients enable cells to know their locations when cells evaluate whether the chemical signals they receive are above or below specific threshold levels. The cells' knowledge of their locations leads them to choose different developmental paths and form distinct tissue types in embryos.

"There are really two sides of the morphogen problem," Dr. Ma explained. "The first is how such concentration gradients are formed in the first place, and the second is how cells respond to such gradients. Our current study looks into the first question at a molecular level."

Bicoid is a morphogen protein critical to fruit fly embryos in forming the head and thorax. The new findings suggest the protein's molecular breakdown is important for establishing a correct concentration gradient and the formation of appropriate tissues at their correct embryo locations.

Collaborating with Dr. Ma on the study is first author, Junbo Liu, Ph.D., a Researcher in the division of Biomedical Informatics. Funding support came from the National Institutes of Health and National Science Foundation.

Junbo Liu, Jun Ma. Fates-shifted is an F-box protein that targets Bicoid for degradation and regulates developmental fate determination in *Drosophila* embryos. *Nature Cell Biology*, 2010; DOI: 10.1038/ncb2141