Tuning in on cellular communication in the fruit fly

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In their ongoing study of the processes involved in embryonic development in fruit flies, researchers at WPI's Life Sciences and Bioengineering Center at Gateway Park have identified the function of a protein that sticks out of the embryonic cell membrane like an antenna and processes signals needed for the flies' wings to develop properly.

After fertilization, cells must send and receive signals that instruct them how and when to specialize and build all the tissues that comprise the adult organism. This requires a complex system of communication, both within each cell and among cells. The WPI team focused on one portion of that network known as the bone morphogenetic protein (BMP) pathway, in the fruit fly (Drosophila melanogaster) and reported their findings in the paper "Kekkon5 is an extracellular regulator of BMP signaling," published in the Feb. 1, 2009, edition of the journal *Developmental Biology*.

"The BMP pathway is very important for embryonic development, not only in fruit flies, but in vertebrates as well," said Joseph Duffy, PhD., associate professor of biology and biotechnology at WPI and lead author of the paper. "What we've identified is a new component of that pathway."

A cellular pathway is like a series of links in a chain that transmit signals to prompt specific actions within a cell. The BMP pathway directs the development of many tissue types in animals, including muscles, bones and the nervous system. In fruit flies, the pathway sends the signals that

direct proper wing formation.

Many links along the BMP pathway within a cell are well-characterized, but how the pathway works from one cell to another as the embryo develops is less clear. In the current study, Duffy's team focused on a protein called Kekkon5 (Kek5), which extends through the cell membrane, much like an antenna extends from a mobile phone to send and receive signals. Duffy's team found that when they disrupted the Kek5 protein in developing fruit flies their wings would not grow properly. Conversely, when Duffy's team engineered fruit fly cells to have too many copies of Kek5, the wings grew with defects. "It was pretty clear that Kek5 was regulating the BMP pathway, and that was an exciting observation," Duffy said.

The recent work on Kek5 follows earlier studies in the Duffy lab that revealed a related protein, Kek1, regulates the Epidermal Growth Factor (EGF) pathway, which is another important developmental pathway. Problems with the BMP and EGF pathways are implicated in cancer, bone disorders, heart disease, and neurodegenerative diseases. Developing compounds that can regulate or repair these pathways is an active area of therapeutic research.

By exploring the role of Keks and related proteins in fruit flies and other model systems, Duffy hopes to glean new knowledge that may, one day, have an impact on human health. "The fruit fly is an excellent model system to study basic biologic processes," Duffy said. "Then, as we understand how these proteins function in the fly, we can use that knowledge to help us explore similar processes in humans."

More information: *Dev Biol.* 2009 Feb 1; 326(1):36-46.

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