Decapentaplegic

Decapentaplegic (Dpp) is a key morphogen involved in the development of the fruit fly *Drosophila melanogaster*. It is known to be necessary for the correct patterning of the fifteen imaginal discs, which are tissues that will become limbs and other organs and structures in the adult fly. It has also been suggested that Dpp plays a role in regulating the growth and size of tissues. Flies with mutations in decapentaplegic fail to form these structures correctly, hence the name (*decapenta-*, fifteen, *-plegic*, paralysis). Dpp is the Drosophila homolog of the vertebrate bone morphogenetic proteins (BMPs), which are members of the TGF-β superfamily, a class of proteins that are often associated with their own specific signaling pathway. Studies of Dpp in Drosophila have led to greater understanding of the function and importance of their homologs in vertebrates like humans.

Function in *Drosophila*

Dpp is a classic morphogen, which means that it is present in a spatial concentration gradient in the tissues where it is found, and its presence as a gradient gives it functional meaning in how it affects development. The most studied tissue in which Dpp is found is the wing. In the wing, Dpp is strongly expressed in a narrow stripe of cells down the middle of the wing where the tissue marks the border between the anterior and posterior sides. Dpp diffuses from this stripe towards the edges of the tissue, forming a gradient as expected of a morphogen.

Signaling pathway

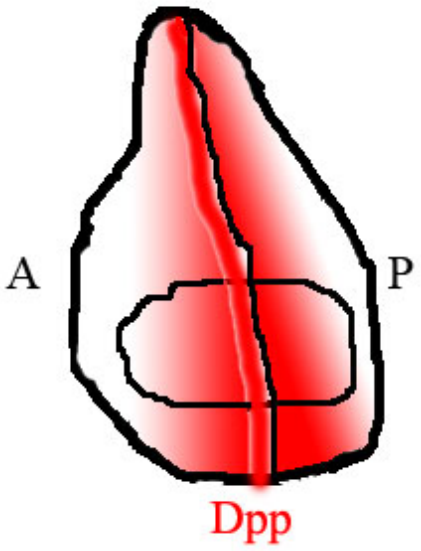
Dpp, like its vertebrate homologs, is a signaling molecule. In Drosophila, the receptor for Dpp is formed by two proteins, Thickveins (Tkv) and Punt.[1] Like Dpp itself, Tkv and Punt are highly similar to homologs in other species. When a cell receives a Dpp signal, the receptors are able to activate an intracellular protein called mothers against dpp (mad) by phosphorylation. The initial discovery of mad in Drosophila paved the way for later experiments that identified the responder to TGF-β signaling in vertebrates, called SMADs.[2] Activated Mad is able to bind to DNA and act as a transcription factor to affect the expression of different genes in response to Dpp signaling. Genes activated by Dpp signaling include optomotor blind (omb) and spalt, and activity of these genes are often used as indicators of Dpp signaling in experiments. Another gene with a more complicated regulatory interaction with Dpp is brinker. Brinker is a transcription factor that represses the activation targets of Dpp, so in order to turn on these genes Dpp must repress brinker as well as activate the other targets.[3]

Morphogen

In the fly wing, the posterior and anterior halves of the tissue are populated by different kinds of cells that express different genes. Cells in the posterior but not the anterior all express the transcription factor Engrailed (En). One of the genes activated by En is hedgehog (hh), a signaling factor. Hedgehog signaling instructs neighboring cells to express Dpp, but Dpp expression is also repressed by En. The result is that Dpp is only produced in a narrow stripe of cells immediately adjacent to but not within the posterior half of the tissue.[4] Dpp produced at this anterior/posterior border then diffuses out to the edges of the tissue, forming a spatial concentration gradient.

By reading their position along the gradient of Dpp, cells in the wing are able to determine their location relative to the anterior/posterior border, and they behave and develop accordingly.

It is possible that it is not actually the diffusion and gradient of Dpp that patterns tissues, but instead cells that receive Dpp signal instruct their neighbors on what to be, and those cells in turn signal their neighbors in a cascade through the tissue. Several experiments have been done to disprove this hypothesis and establish that it is actually the gradient of actual Dpp molecules that are responsible for patterning.



A cartoon illustrating the distribution of Dpp, shown in red, in the wing disc. Dpp is produced in a stripe just anterior of the anterior/posterior border and diffuses out to the edges of the tissue.

Mutant forms of the Dpp receptor Tkv exist that behave as if they are receiving high amounts of Dpp signal even in the absence of Dpp. Cells that contain this mutant receptor behave as if they are in an environment of high Dpp such as the area near the stripe of cells producing Dpp. By generating small patches of these cells in different parts of the wing tissue, investigators were able to distinguish how Dpp acts to pattern the tissue. If cells that receive Dpp signal instruct their neighbors in a cascade, then additional tissue patterning centers should appear at the sites of the mutant cells that seem to receive high Dpp signaling but do not produce any Dpp themselves. However, if the physical presence of Dpp is necessary, then the cells near the mutants should not be affected at all. Experiments found the second case to be true, indicating that Dpp is acting like a morphogen.[5]

The common way to assess differences in tissue patterning in the fly wing is to look at the pattern of veins in the wing. In flies where the ability of Dpp to diffuse through the tissue is impaired, the positioning of the veins is shifted from that in normal flies, and the wing is generally smaller.[6]

Dpp has also been proposed as a regulator of tissue growth and size, a classic problem in development. A problem common to organisms with multicellular organs that must grow from an initial size is how to know when to stop growing after the appropriate size is reached. Since Dpp is present in a gradient, it is conceivable that the slope of the gradient could be the measurement by which a tissue determines how large it is. If the amount of Dpp at the source is fixed and the amount at the edge of the tissue is zero, then the steepness of the gradient will decrease as the size of the tissue and the distance between the source and the edge increase. Experiments where an artificially steep gradient of Dpp is induced in wing tissue resulted in significantly increased amounts of cell proliferation, lending support to the steepness hypothesis.[7]

Role in molluscs

dpp is also found in molluscs, where it plays a key role in shell formation by controlling the shape of the conch. In bivalves, it is expressed until the protoconch has taken on the required shape, after which point its expression ceases.[8] It is also associated with shell formation in gastropods,[9] with an asymmetric distribution that may be associated with their coiling: shell growth appears to be inhibited where *dpp* is expressed.[10]

External links

- *Drosophila decapentaplegic* - The Interactive Fly [11]
- MeSH *decapentaplegic+protein,+Drosophila* [12]

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