

New protein discovery links to cancer research

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A Simon Fraser University graduate student's collaboration with her thesis supervisor on how a particular type of protein controls the growth of another protein could advance cancer research.

Their findings have just been published in the online July 26 issue of [Current Biology](#).

Esther Verheyen, an SFU professor of [molecular biology](#) and biochemistry, has helped her Master's of Science student Joanna Chen uncover how Hipk can be manipulated to stop Yorkie from causing tissue overgrowth in flies.

Hipk is a protein kinase — a type of enzyme that controls the activity of other proteins by depositing a phosphate residue on them.

Yorkie, known as Yap in humans, is another type of protein that induces the overgrowth of cell tissue in the eyes, legs and wings of flies. High levels of Yap are often found in human tumours.

In experiments on the fruit fly *Drosophila*, Verheyen and Chen first found that Hipk could cause overgrowths similar to those found on tissue with too much Yorkie.

The researchers then genetically generated flies in which there was a higher concentration of Yorkie but a lower concentration of Hipk present than normal in their organ and limb tissues.

"When we did that," says Chen, "Yorkie could not cause overgrowths anymore. We were able to show this need for Hipk to be present in a number of different fly tissues, such as the eyes, legs and wings."

"We found that Hipk could add a phosphate residue on Yorkie and we thought this might explain how Hipk could disrupt Yorkie's ability to cause an overgrowth," adds Verheyen. "This is a very common and reversible method of regulating protein activity, and, as a result, many essential developmental processes."

"Next we tested a mutant form of Hipk that had lost its ability to add phosphates to Yorkie," says Verheyen. "This form of Hipk could no longer prompt Yorkie to trigger cell proliferation or do anything to regulate cell growth."

"Hipk is the first discovery of a [protein kinase](#) that regulates Yorkie by stimulating its cell proliferation ability. All other known [protein](#) kinases either directly inhibit or block Yorkie from working."

Chen and Verheyen say their discovery is generating a lot of excitement in the molecular biology science community. "We have identified a factor that in flies is required for even overly active Yorkie to trigger overgrowth," explains Chen, who graduated in June. She begins working as a research assistant at the Vancouver Prostate Centre in August.

"By analogy, perhaps the human form of Hipk is needed in cells for overly active Yap (human form of Yorkie) to induce tumours. So if we can inhibit or reduce Hipk activity, it would allow us to prevent overgrowths and possibly cancer caused by excessive Yap in humans."

The two are now checking to see if this new cell growth regulation mechanism they've discovered is conserved across different species, including mice, which have similar Hipk proteins to humans.

More information: Homeodomain-Interacting Protein Kinase Regulates Yorkie Activity to Promote Tissue Growth, *Current Biology*.

Provided by Simon Fraser University

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