MedicalXpress

Controlling for size may also prevent cancer

September 20 2007

Scientists at Johns Hopkins recently discovered that a chemical chain reaction that controls organ size in animals ranging from insects to humans could mean the difference between normal growth and cancer. The study, published in the Sept. 21 issue of *Cell*, describes how organs can grow uncontrollably huge and become cancerous when this chain reaction is perturbed.

“This chain reaction, a domino-like chain of events we call the Hippo pathway, adds a single chemical group on a protein nicknamed Yap,” says lead author Duojia Pan, Ph.D., associate professor of molecular biology and genetics. “The good news is that maybe all organ growth can be reduced to this one chemical event on the Yap protein — but the better news is that we potentially have a new target for cancer therapy.”

Pan and colleagues previously had discovered in fruit flies that too much Yap supercharges growth-inducing genes and causes organs to overgrow.

In the new study designed to see if the same effect occurred in mammals, the research team genetically altered mice to make high levels of Yap protein, but only in liver cells. These animals’ livers grew to be five times the size of a normal mouse liver and often were dotted with large tumors.

“We were totally amazed,” says Pan. “Five times is just a huge effect.” When the researchers next looked at a variety of human cancer cells, they found that 20 percent to 30 percent contained increased levels of Yap. “We think it might be the extra Yap in these cells contributing to

their cancerous growth," says Pan.

Yap, like most proteins, exists in more than one form, in this case two, one with and one without a chemical phosphate tag attached. Such tags can dramatically alter what proteins do in the body.

When the Hopkins team engineered the cells to stop or slow growth, Yap in those cells has its phosphate attached and moves from the nucleus—the brain center of the cell—into the main body of cells, or cytoplasm.

"A drug that somehow turns off Yap might also stop cancer cells from growing," says Pan, "and manipulating the Hippo pathway could provide a way to grow organs to a pre-determined size for transplantation."

Source: Johns Hopkins Medical Institutions