Protein can help cells or cause cancer, researcher finds

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A Purdue University scientist has discovered a key process in cell growth that can lead to the formation of tumors.

Xiaoqi Liu, an assistant professor of biochemistry, found that an overabundance of the polo-like kinase 1, or Plk1, molecule during cell growth, as well as a shortage of the p53 molecule, will lead to tumor formation. Studies in Liu's laboratory showed that the Plk1 molecule indirectly attacks p53 in a process called ubiquitination.

"This provides the mechanism for how p53 loses its function in cancer cells," said Liu, whose work was published in the early online publication of the Journal of Biological Chemistry. "If we understand how the cancer forms, then we can create a more useful therapeutic approach to treating that cancer."

During cell growth, Plk1 uses its protein kinase activity called phosphorylation, which consists of adding a phosphate group to a protein called Topors. Topors binds itself to p53 molecules during the ubiquitination process. Phosphorylation is basically an instruction from Plk1 to increase its ubiquitination activity, which kills p53 molecules.

Liu said p53 could be thought of as a protective force. When Topors kills off that force, Plk1 becomes stronger, allowing the cells to become cancerous.

"We're trying to understand how p53 is regulated. We want to keep p53

as normal as possible," Liu said. "In about 50 percent of cancers, p53 had lost its function, and there was too much Plk1. Since Plk1 is overexpressed in cancers, it is a cancer therapy target."

Topors can also carry out a function called sumoylation, in which Topors binds to p53 molecules and creates more p53. Liu was able to force cells in his lab to go through the ubiquitination or sumoylation process to show how p53 molecules were affected.

Liu said it is unknown why the Plk1 molecule chooses to initiate ubiquitination over sumoylation.

Researchers from Sichuan University in China and faculty in the Department of Basic Medical Sciences at Purdue collaborated with Liu on the research. The work was funded through a Howard Temin Award from the National Institutes of Health.

Liu said the next step in the research is to test different Plk1 inhibitors to see how they affect the phosphorylation process.

Source: Purdue University (news : web)