Regulation of cancer-causing protein could lead to new therapeutic targets

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Researchers with the Cincinnati Cancer Center (CCC) and the University of Cincinnati (UC) Cancer Institute have discovered a new regulation for the cancer-causing protein KRas which may help with the development of targeted therapies for patients with a KRas mutation.

Atsuo Sasaki, PhD, a member of the CCC, the UC Cancer Institute and the UC Brain Tumor Center as well as an assistant professor in the division of hematology oncology within the department of internal medicine, is the principal investigator on the study, which is published in the Dec. 13, 2013, online edition of the *Journal of Biological Chemistry*.

He says pharmacologic targeting of KRas as a cancer therapy has been challenging.

"The mutation of a KRas gene is an essential step in the development of many cancers," Sasaki says. "In fact, the KRas mutation is present in more than 90 percent of patients with pancreatic cancer, and other research has shown that lung and colon cancers have prevalent mutations of this gene as well.

"Researchers in academia and industry have been trying to target KRas pharmaceutically for many years without significant success. In this study, we took a unique approach. We use a social amoeboid—a powerful model system to study Ras signaling and look at the KRas regulation."

To do this, researchers introduced the oncogenic KRas gene into the social amoeboid and compared its regulation to that of a normal KRas gene.

"We discovered that the cell has a system to recognize the oncogenic KRas and break it down," he says. "This clearance system led to ubiquitination on oncogenic KRas—which means it is being chopped and trashed.

"With this knowledge, we could increase the clearance of mutated KRas from cancer cells; next steps include finding the gene or protein that starts this process. With this additional piece of the puzzle, we're one step closer to finding a targeted therapy for various cancer types that harbor KRas mutations."

Provided by University of Cincinnati Academic Health Center