

Specific inhibition of autophagy may represent a new concept for treatment of kidney cancer

April 16 2012

New research at the University of Cincinnati (UC) suggests that kidney cancer growth depends on autophagy, a complex process that can provide cells with nutrients from intracellular sources. Researchers say in certain circumstances autophagy can protect tumor cells from chemotherapy, allowing them to survive for long periods of time in a hidden, dormant, metastatic state.

In this newly published data, researchers identify two distinct autophagy regulated pathways downstream from the von Hippel-Lindau [tumor suppressor gene](#), or VHL. This specific tumor suppressor is lost in the majority of renal [cell carcinomas](#).

UC researchers report these findings in the April 16, 2012, issue of *Cancer Cell*.

Maria Czyzyk-Krzeska, MD, PHD, corresponding author of the study, says the discoveries could guide researchers to more effective treatment approaches for kidney cancer, particularly metastatic disease, based on knowledge of these specific autophagic processes. UC collaborators in this study include David Plas, PhD, assistant professor of cancer and cell biology, and Jarek Meller, PhD, associate professor of environmental health.

"VHL has emerged as a master controller of access to intracellular

nutrients through autophagy and to extracellular nutrients through formation of blood vessels. Our work shows that there are different autophagic programs—pro-and anti-oncogenic. Drugs that inhibit the final stages of autophagy non-specifically, such as derivatives of chloroquine, may not be as beneficial as hoped," explains Czyzyk-Krzeska, a professor of cancer and cell biology at the UC College of Medicine and researcher with the UC Cancer Institute.

She says the challenge is to understand the molecular mechanisms of these diverse autophagic pathways and identify targets that are specific to the pro-oncogenic pathway but not affecting tumor-suppressing pathways.

"Current drugs for metastatic kidney cancer target angiogenesis—blocking the formation of blood vessels that feed the tumor—but they typically only increase survival by a matter of months," says Czyzyk-Krzeska. "We hope this new body of evidence can help pave a new path to more effective treatment options for this disease."

According to the American Cancer Society, incidence rates of [kidney cancer](#) are increasing steadily by 2 to 3 percent each year. The disease is curable when it is identified early and isolated to the kidney. Treatment options for metastatic disease are limited.

Provided by University of Cincinnati Academic Health Center

Citation: Specific inhibition of autophagy may represent a new concept for treatment of kidney cancer (2012, April 16) retrieved 19 April 2024 from <https://medicalxpress.com/news/2012-04-specific-inhibition-autophagy-concept-treatment.html>

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