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New findings may help patients with deadly kidney cancer

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Van Andel Research Institute (VARI) researchers have found a way to reverse resistance to sunitinib, a treatment that is currently the first line of defense against clear cell renal cell carcinoma (ccRCC), a deadly form of kidney cancer. Most patients who show a positive response to sunitinib develop a resistance to the drug after one year of treatment.

Kidney cancer is among the 10 most common cancers in both men and women, striking nearly 50,000 Americans in 2009 and killing more than 11,000. Renal cell carcinoma (RCC) accounts for 9 out of 10 kidney cancers, and ccRCC is the most common subtype, accounting for 8 out of 10 RCC cases.

"The research from Dr. Teh's (VARI) group is a critical step forward in understanding the mechanisms of response and resistance to the new standard of care therapies in renal cell carcinoma such as sunitinib," said Brian Rini, MD, Solid Tumor Oncology, Cleveland Clinic Taussig Cancer Institute.

Sunitinib received FDA approval in 2006 and is a standard of care for both ccRCC and gastrointestinal stromal tumors. The drug is being investigated as a possible therapy for other cancers, including breast cancer, colorectal cancer, and non-small cell lung cancer.

Researchers found that ccRCC tumor cells that had developed a resistance to sunitinib had increased secretion of the protein interleukin-8 (IL-8). Administering sunitinib and IL-8 neutralizing

antibodies re-sensitized tumors to sunitinib treatment. Researchers also found that IL-8 may serve as a useful biomarker to predict patients' response to sunitinib treatment.

"The development of ccRCC resistance to sunitinib treatment is of major clinical concern," said VARI Distinguished Scientific Investigator Bin Tean Teh, M.D., Ph.D., whose laboratory published its findings in this month's issue of Cancer Research. "It is now of critical importance to validate these findings in the clinical setting."

Another study from Teh's laboratory also published in *Cancer Research* this month looked into exactly how sunitinib works. The study found that the treatment does not target tumor cells, but rather the tumor's blood supply.

"Understanding how sunitinib works should have important implications for the improved treatment of ccRCC and perhaps other cancers as well," said VARI Postdoctoral Fellow Dan Huang, Ph.D., lead author of both studies.

"These insights will help build upon recent advances to extend clinical benefits to more patients with metastatic kidney cancer," said Dr. Rini.

Provided by Van Andel Research Institute

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