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Kidney cancer discovery could expand treatment options

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Oregon Health & Science University Knight Cancer Institute researchers uncovered a gene that may be the key to helping kidney cancer patients who don't respond to current therapies. This discovery could also provide a toolkit to identify patients who are most likely to benefit from drugs that block this gene from causing cancer cells to grow.

The OHSU study, published in the June 1 edition of *Science Translational Medicine*, identified a gene called Src that helps certain kidney cancers grow. Discovering that Src plays a role in kidney cancer could help in delivering more effective, individualized treatments to patients, said George Thomas, M.D., the study's senior author and a surgical pathologist at the OHSU Knight Cancer Institute.

The next step, Thomas said, is initiating clinical trials to test how these tumors respond to drugs already available and approved by the FDA.

There are many implications for the Src findings. Last year alone, kidney cancer accounted for about 58,000 new cases of cancer and 13,000 deaths in the United States. More than a quarter of these patients have metastatic disease when their cancer is discovered, and patients who are treated with surgery frequently relapse.

Currently, treatment of kidney cancer is primarily focused on blocking the formation of new blood vessels. While this strategy has been successful in the short term, it does not cure the patient and, more importantly, there are subgroups of patients who don't experience any

benefit from these drugs.

"Our preclinical tests found that cancer cells that have increased Src activity were more sensitive to dasatinib (Sprycel), an FDA-approved drug that inhibits Src, both in tissue culture and when grown as tumors in mice," Thomas said.

But there's also a kicker. Thomas and his colleagues developed a panel of clinical markers that could potentially select patients most likely to benefit from Src inhibitors.

Thomas credits the multidisciplinary approach for the study's success. The importance of Src was discovered because of a sophisticated mass spectrometry based assay, called a phospho-proteomics that analyzes activated proteins.

"We had hypothesized that phospho-proteomic screens could rapidly uncover proteins that could be targets for drugs, so that is why we pursued this line of research," Thomas said.

When the screening process suggested that the Src signaling network was activated, indicating that it was playing a role in the growth of cancer cells, it was a surprise. "Src was certainly was not on my radar," Thomas said.

The next step was to look at the role of Src expression in tumor tissues from patients who had previously had their kidney cancers removed.

"We found that patients with tumors expressing high levels of Src had worse survival rates than those patients whose tumors had weak expression of Src. This suggested to us that Src played a role in kidney cancer and that it was a therapeutic target worth exploring."

More information: "A HIF-Regulated VHL-PTP1B-Src Signaling Axis Identifies a Therapeutic Target in Renal Cell Carcinoma," *Science Translational Medicine* (2011).

Provided by Oregon Health & Science University