Researchers find molecule that kills kidney cancer cells

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Kidney cancer patients generally have one option for beating their disease: surgery to remove the organ.

But that could change, thanks to a new molecule found by Stanford University School of Medicine researchers that kills kidney cancer cells. Ideally, the researchers said, a drug created from this molecule would help fight the life-threatening disease while leaving patients' kidneys intact.

"You now have a potential means of going after a disease that's been difficult to treat," said Amato Giaccia, PhD, professor and director of radiation oncology and radiation biology at the medical school. His findings will be published in the journal *Cancer Cell* on July 8.

Giaccia said his lab focused on renal cell carcinoma, or kidney cancer, because there is no known cure for it short of removing a damaged kidney from a patient's body. "There is no effective chemotherapy to treat renal cell carcinoma," said Giaccia, also a researcher at the Stanford Cancer Center. "Patients still succumb."

Almost 54,400 people in the United States will be diagnosed with kidney cancer this year, and about 13,000 will die from the disease, according to the American Cancer Society. Radiotherapy, a powerful weapon used to fight cancer, has also proven to be ineffective in killing kidney cancer, in contrast to other types of cancer, Giaccia said.

This new research could lead to a treatment to save patients from losing one of their two kidneys. The organs are responsible for filtering blood, controlling blood pressure and preventing anemia, among other tasks.

Giaccia's work focuses on the von Hippel-Lindau tumor suppressor gene, or VHL gene, which normally slows tumor growth in humans but does not work in 75 percent of kidney tumor cells. Giaccia's team searched for a small molecule that would kill cancer cells when this VHL gene is broken. They found their weapon in a molecule called STF-62247.

While STF-62247 is toxic to kidney cancer, it is generally harmless to most other cells in the human body, as they carry a working VHL gene, Giaccia said.

As an added benefit, Giaccia said, patients treated with STF-62247 should not suffer some of chemotherapy's infamous side effects, like nausea and hair loss, because STF-62247 is not toxic to the entire body.

Clinical trials could begin "in the next couple years," Giaccia said.

Stanford co-author and postdoctoral fellow Denise A. Chan, PhD, said she believed the new findings could affect how all types of cancer are treated in the future.

This study is one of the first to identify a trait unique to a certain form of cancer - in this case, kidney cancer's deficient VHL gene - and exploit it to defeat the disease, Chan said. She predicted other scientists soon would follow suit, looking for characteristics in other cancers that also could be manipulated.

Researchers' motivation could be twofold, the study's authors said: to find cures for deadly cancers, and to rein in the debilitating side effects

caused by many current cancer treatments.

"These results can be extended far beyond kidney cancer," Chan said.

The findings also speak well for Stanford's High-Throughput BioScience Center, which opened in 2004. The results of this study are some of the first using the center's equipment.

The high-throughput equipment at Stanford can analyze thousands of molecules for their cytotoxicity at the same time, allowing researchers like those in Giaccia's lab to search for hidden genes and molecules that previously would have been quite laborious to find.

Without the center, "This work would not have been possible," said Stanford co-author Patrick Sutphin, MD. The findings have special significance for Sutphin, who worked with the Stanford team before moving on to his internship in medicine at Massachusetts General Hospital in Boston. In 1995, when Sutphin was a sophomore in college, his grandfather was diagnosed with kidney cancer and died three months later, he said.

The experience of losing his grandfather to kidney cancer helped motivate Sutphin to study the disease. His hope, Sutphin said, "is that one day our collective research will result in new drugs that are more effective than traditional drugs, and without the toxic side effects."

Source: Stanford University