Discovery offers hope for treating kidney cancer

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Kidney cancer is typically without symptoms until it has spread to other organs, when it is also the most difficult to treat. Newer chemotherapies show great promise for extending survival during later disease stages, but they can also be highly toxic.

In one of the first discoveries of its kind, UC Davis Cancer Center researchers have identified ways to block a cancer gene's own repair mechanism and, in so doing, help make chemotherapy for kidney cancer more effective and better tolerated. The outcome is published in the current issue of *Cancer Biology and Therapy*.

"Cancer cells are notorious in their ability to rapidly create copies of themselves. While the latest medications slow down that process, they do not tend to be curative and have many side effects," said Robert Weiss, a UC Davis professor of nephrology and chief of nephrology at the Sacramento VA Medical Center. "We wanted to find ways to help make chemotherapeutics as effective as possible at the lowest doses possible."

Newer medications work by destabilizing cancer cells at the DNA level, which reduces their ability to replicate. Knowing that the p21 gene has an important role in restoring cancer cell DNA and potentially circumventing the benefits of those treatments, Weiss sought to identify compounds that could interrupt this pathway.

The team tested thousands of compounds and 12 were found to bind to the recombinant protein p21. Additional tests showed that three of those

compounds decreased p21 expression, blocking kidney cancer cells' ability to mend and making them more responsive to DNA-damaging treatments.

"The results are very exciting, especially given how difficult kidney cancer has so far been to treat," Weiss said. "Our work offers hope that in the future these p21 inhibitors can be refined and used in concert with other conventional as well as novel cancer treatments to increase the comfort and life spans of patients with kidney cancer."

For future studies, Weiss will focus on the three candidate compounds to determine the lowest possible concentrations at which they remain effective and to further optimize their anti-cancer properties. He will then test those compounds with standard treatments in animal models and, ultimately, in human trials.

"The goal is to find new approaches to treating a cancer for which few options currently exist and make those approaches available in clinical settings as quickly as possible," he said.

Source: University of California - Davis - Health System