Researchers at the University of California, Davis, believe it may be possible to attack <u>renal</u> <u>cell carcinoma (RCC)</u> in a whole new way.

In a report recently published in the journal *Cancer Research* they indicate that they were able to use a sophisticated combination of proteomics and metabolomics to show how RCC reprograms its metabolism and evades the immune system.

The study may be of particular interest because it found that cancer grade has a major impact on this reprogramming.

"We now say if a patient has a grade 3 tumor then it goes better with this therapy. It has been a one size fits all," said study investigator Robert Weiss, MD, who is a professor of nephrology and internal medicine at University of California, Davis, and chief of nephrology at the VA Northern California Health System in Sacramento, CA. "The clinical implications are that we may be able to impact those pathways that have been programmed."

Dr. Weiss said RCC reprograms its environment to minimize the immune response. He and his colleagues made these discoveries by combining proteomics with metabolomics. The proteomic analyses examined how RCC affects levels of different proteins.

The metabolomic studies performed a similar task with metabolites. "Genomics had been around for a while, but the metabolomics is pretty new. Each one has its own holes, but when you combine them you get a pretty powerful picture," Dr. Weiss said in an interview with *Cancer Therapy Advisor*.

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He said by combining metabolomics and proteomics it was possible to come up with a "unified

field theory" to look at the metabolites in cancer.

The proteomic analysis showed how RCC increases an enzyme that breaks down the amino acid tryptophan. In turn, the metabolomics studies flagged that tryptophan metabolites suppress the immune system.

A similar story unfolded with glutamine. By manipulating this amino acid, kidney cancer appeared to remove reactive oxygen species (ROS), a key immune system weapon that would usually help destroy the cancer.

Overall, the researchers found that the glutamine metabolism pathway acts to inhibit ROS and tryptophan catabolism is associated with immune suppression. The work points to new therapeutic targets involving the tryptophan and glutamine pathways.
