

Molecular subtypes of advanced kidney cancer matter for treatment response

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A combination of immunotherapy and targeted therapies show promise in managing metastatic renal cell carcinoma (RCC), the most common form of kidney cancer that makes up 90% of all cases. However,



accurately predicting responses to these treatments remains a significant challenge.

A new study <u>published</u> April 4 in *Cancer Cell* was led by Yale Cancer Center researchers, who collaborated with investigators nationally to differentiate the molecular subgroups of RCC tumors to better understand how their makeup might affect treatment responses. The study builds upon a clinical trial that identified seven distinct molecular subtypes with unique biological characteristics.

"The motivation for this study is really what we see in the clinic—we have patients with the exact same diagnosis of clear cell <u>kidney cancer</u> who received the same therapy but have dramatically different outcomes," said the study's senior author Dr. David Braun, who is a member of Yale Cancer Center and an assistant professor of medicine (<u>medical oncology</u>) at Yale School of Medicine.

"We know there is tremendous biological diversity between tumors, and we sought to understand whether we could leverage classic machine learning approaches to classify different subtypes of clear cell kidney cancer and whether those subtypes impact the likelihood of responding to therapy."

Researchers analyzed <u>clinical data</u> from 734 patients and used an <u>artificial intelligence</u> (AI) machine learning tool to search for predictive capabilities of these molecular subtypes in the setting of standard, FDA-approved treatments for clear cell kidney cancer.

With the help of AI, researchers were able to determine the distinct biological states for each molecular subtype. They also found that some patients had a different response to the immunotherapy based on their molecular subtype. However, Braun is cautious about whether molecular subtypes can guide treatment.



"We can use this machine learning approach to understand the subtypes of kidney cancer," said Braun, who also is a Louis Goodman and Alfred Gilman Yale Scholar. "But we still cannot say one treatment is better depending on the subtype you have—subtypes of clear cell kidney cancer appeared to have benefit from the use of immune checkpoint inhibition, a type of targeted therapy treatment.

"As a kidney cancer community, we need to investigate these molecular subtypes prospectively in <u>clinical trials</u> to determine whether specific subtypes benefit from certain therapies or not."

More information: Renée Maria Saliby et al, Impact of renal cell carcinoma molecular subtypes on immunotherapy and targeted therapy outcomes, *Cancer Cell* (2024). DOI: 10.1016/j.ccell.2024.03.002

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