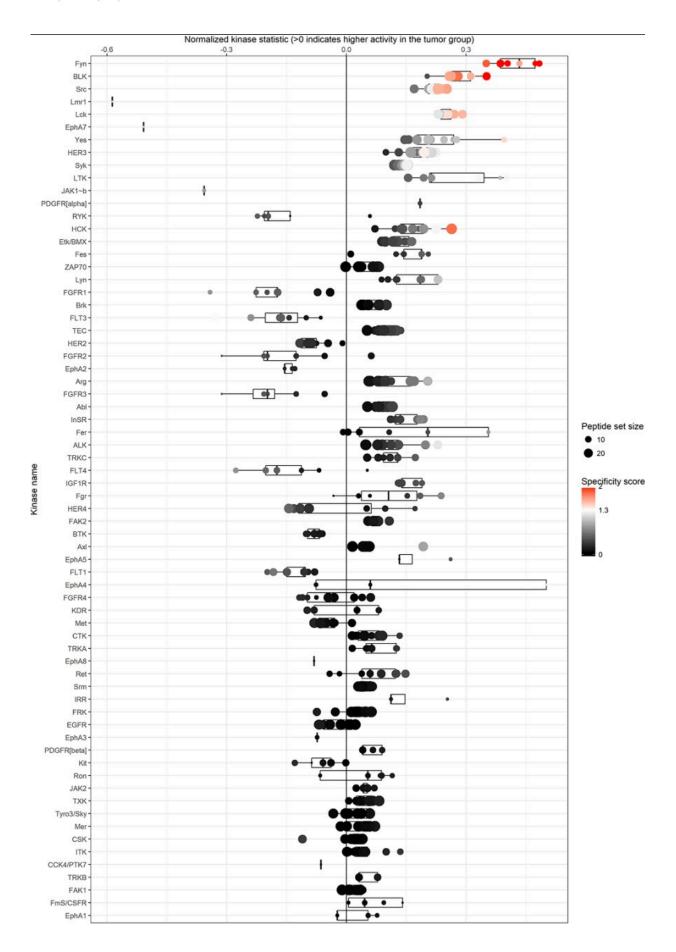


## Kinase activity in renal cell carcinoma, benign renal tissue and in response to tyrosine kinase inhibitors

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Upstream kinase analysis identifies kinases that might be responsible for the differences in phosphorylation profiles between normal and cancer tissue. Credit: Tahiri et al.

Kinase activity is frequently altered in renal cell carcinoma (RCC), and tyrosine kinase inhibitors (TKIs) are part of the standard treatment strategy in patients with metastatic disease. However, there are still no established biomarkers to predict clinical benefits of a specific TKI.

"Despite a number of new treatment options improving RCC patients' disease control rates and survival, the lack of useful biomarkers remains a major clinical concern," according to a new study published in *Oncotarget*.

"The aim of this study was to identify differences in PTK activity between normal and malignant kidney tissue obtained from the same patient, and to investigate the inhibitory effects of TKIs frequently used in the clinics: sunitinib, pazopanib, cabozantinib and tivozanib."

The results showed that 36 kinase substrates differ (FDR pathway exhibit high activity in renal cancer.

Furthermore, ex vivo treatment of clear cell RCC with TKIs revealed that pathways such as Rap1, Ras and PI3K pathways were strongly inhibited, whereas the neurotrophin pathway had increased activity upon TKI addition. Their assay showed that tivozanib and cabozantinib exhibited greater inhibitory effects on PTK activity compared to sunitinib and pazopanib, implying they might be better suitable as TKIs



for selected RCC patients.

"The results of our study contribute to better understanding of the changes in kinase activity in RCC tumor cells involved in fundamental oncogenic cellular processes and the ex vivo effect of TKIs. We found tivozanib and cabozantinib to be more potent TKIs in RCC samples than sunitinib or pazopanib. The next step will be to correlate the efficacy and toxicity in individual patients with their respective kinase activity of normal and malignant kidney tissue," say the researchers.

**More information:** Andliena Tahiri et al, Kinase activity profiling in renal cell carcinoma, benign renal tissue and in response to four different tyrosine kinase inhibitors, *Oncotarget* (2022). DOI: 10.18632/oncotarget.28257

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