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

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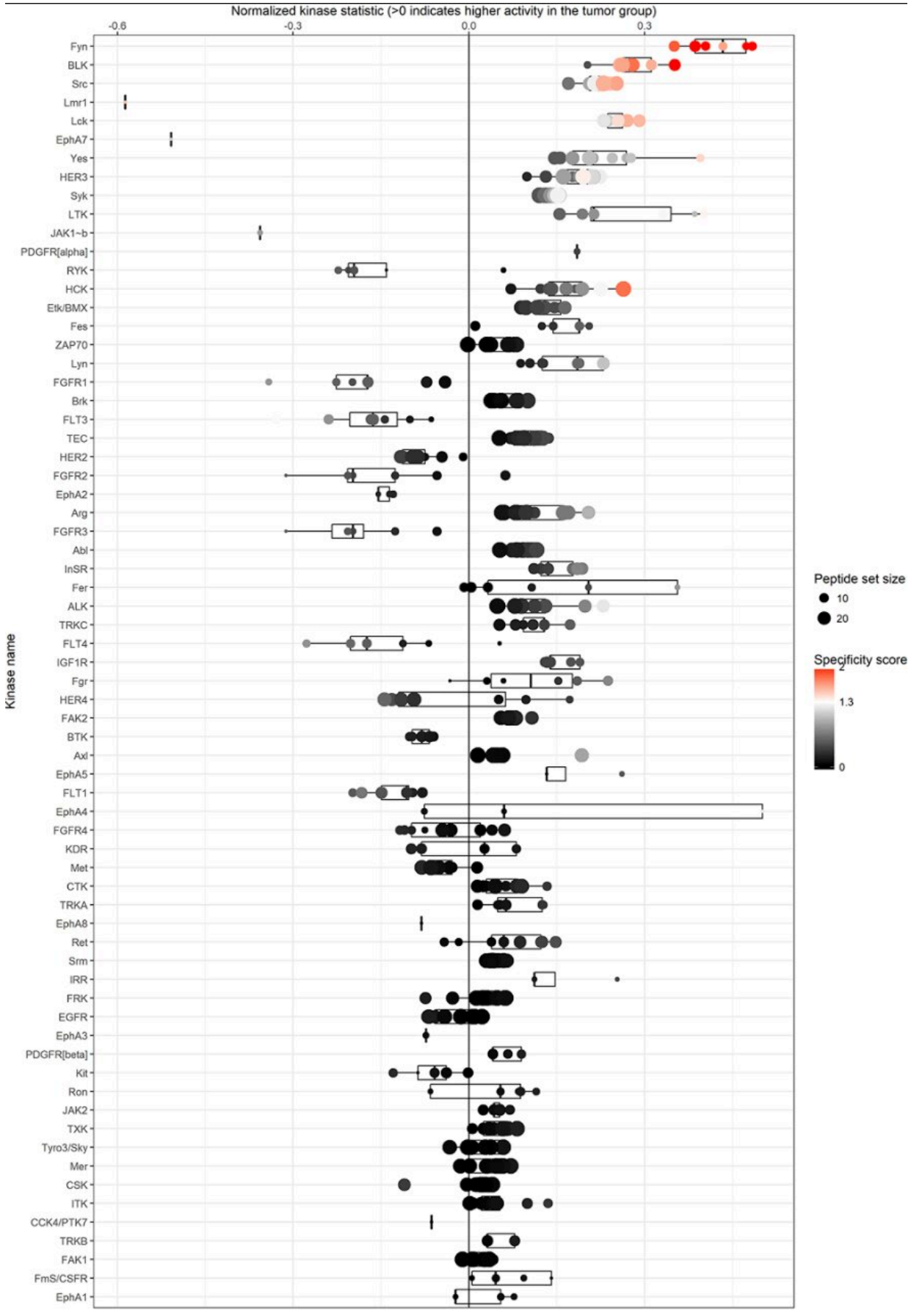
Normalized kinase statistic (>0 indicates higher activity in the tumor group)
-0.6
-0.3
0.0
0.3
Kinase name
Fyn
BLK
Src
Lmr1
Lck
EphA7
Yes
HER3
Syk
LTK
JAK1~b
PDGFR[alpha]
RYK
HCK
Etk/BMX
Fes
ZAP70
Lyn
FGFR1
Brk
FLT3
TEC
HER2
FGFR2
EphA2
Arg
FGFR3
Abl
InSR
Fer
ALK
TRKC
FLT4
IGF1R
Fgr
HER4
FAK2
BTK
Axl
EphA5
FLT1
EphA4
FGFR4
KDR
Met
CTK
TRKA
EphA8
Ret
Srm
IRR
FRK
EGFR
EphA3
PDGFR[beta]
Kit
Ron
JAK2
TXK
Tyro3/Sky
Mer
CSK
ITK
CCK4/PTK7
TRKB
FAK1
FmS/CSFR
EphA1
Peptide set size
10
20
Specificity score
2
1.3
0

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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