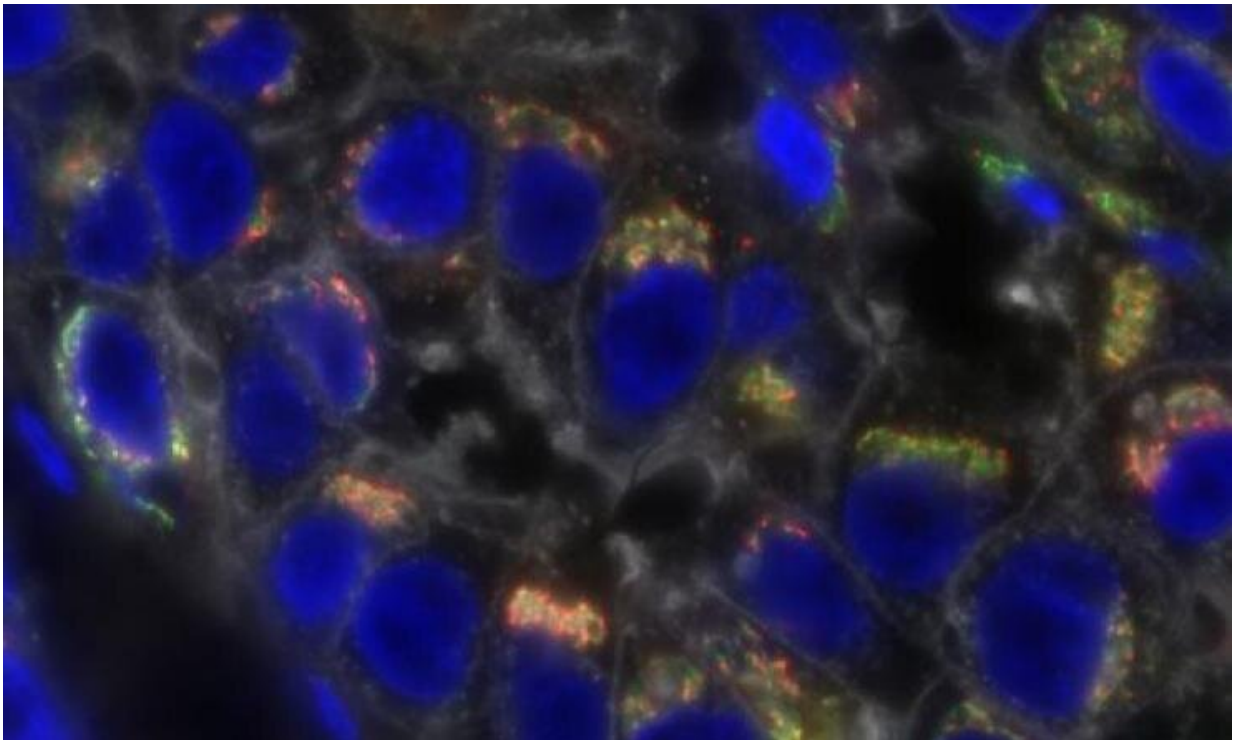


KIPA potentially predicts chemotherapy response in triple negative breast cancer

July 20 2023, by Molly Chiu



Cells of triple negative breast cancer. Credit: Baylor College of Medicine

Researchers at Baylor College of Medicine and collaborating institutions are developing a strategy to predict the response of triple negative breast cancer (TNBC) to chemotherapy, which would be a valuable tool for physicians deciding on the treatment with better probability of success on an individual basis. The study appears in *Cancer Research*

Communications.

"Multiple research innovations in cancer diagnostics are on display in this work," said co-corresponding author Dr. Matthew Ellis, member of the Lester and Sue Smith Breast Center and the Dan L Duncan Comprehensive Cancer at Baylor and also senior vice president of early oncology and oncology R&D at AstraZeneca.

The researchers used a laboratory assay called Kinase Inhibitor Pulldown Assay, or KIPA, to search for proteins they could target to control [tumor growth](#). They searched for these proteins in 43 frozen [tumor biopsies](#) that were part of the previous Clinical Proteomic Tumor Analysis Consortium (CPTAC)-TNBC study.

"Our initial goal was to find new ways to control TNBC growth, specifically by identifying and then inhibiting enzymes called [kinases](#) produced by the tumor to assist on its growth," said co-corresponding author Dr. Meenakshi Anurag, assistant professor of medicine at the Lester and Sue Smith Breast Center at Baylor. "Although our search for such kinases did not produce valuable candidates, it unexpectedly revealed an opportunity to improve the success of chemotherapy."

KIPA works by coating tiny beads with selective kinase inhibitors, then breaking down the cells in the [biopsy samples](#) and mixing them with the beads. Each kinase binds to its specific inhibitor, effectively separating it from other cell components, though some kinases can bind to multiple inhibitors. Then, the researchers collect and wash the beads, obtain the kinases and use mass spectrometry to identify each one of them.

"This approach did not reveal kinases we could potentially target to control these tumors' growth; however, the assay captured seven non-kinase proteins, specifically purine-binding proteins, that were enriched in tumors that completely responded to treatment," said first author

Junkai Wang, a graduate student working in the Ellis lab. "Further analyses showed that this seven-purine-binding protein signature predicted chemotherapy sensitivity and favorable clinical outcomes."

"The purine binding signature could help identify a subset of TNBC patients who should receive investigational therapy from the outset rather than an ineffective standard chemotherapy approach," Ellis said.

"Although originally KIPA was developed for the accurate quantification of druggable kinases, this paper demonstrates that its clinical utility extends beyond kinase quantification. With more clinical sample analysis, there is a great possibility that we will be able to identify additional signatures for many therapeutic strategies," said co-corresponding author Dr. Beom-Jun Kim, member of the Lester and Sue Smith Breast Center and the Dan L Duncan Comprehensive Cancer at Baylor and also associate director of diagnostic proteomics at AstraZeneca.

"We are excited about these findings, which we have validated in multiple TNBC cohorts," Anurag said. "In addition, KIPA offers other advantages: it produces results in a time-efficient manner and requires a much smaller tumor sample than other methods. The purine-binding protein signature we have identified has the potential to contribute to [clinical trials](#) designed to either escalate or de-escalate therapy by predicting the probability of chemotherapy success."

More information: Alexander B Saltzman et al, Kinase inhibitor pulldown assay identifies a chemotherapy response signature in triple negative breast cancer based on purine-binding proteins, *Cancer Research Communications* (2023). [DOI: 10.1158/2767-9764.CRC-22-0501](https://doi.org/10.1158/2767-9764.CRC-22-0501)

Provided by Baylor College of Medicine

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