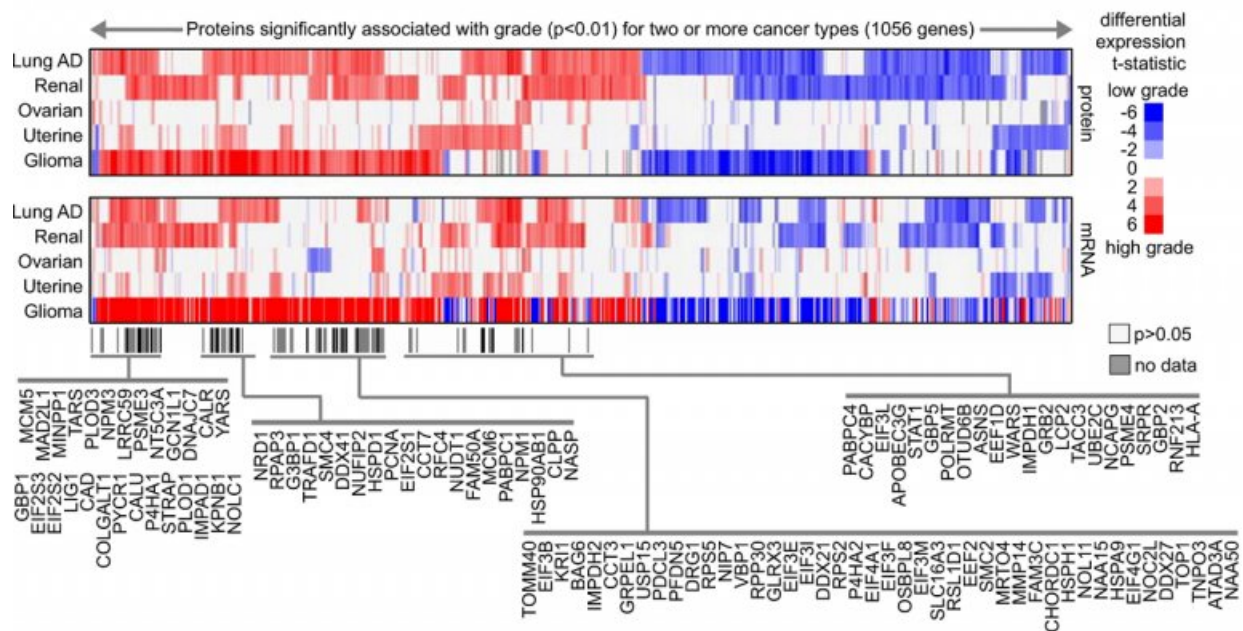


Proteomics analysis identifies potential drug targets for aggressive human cancers

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Proteins shared among the cancer type-specific grade comparing higher grade versus lower grade (red, higher expression with higher grade; white, not significant with $p > 0.05$). Credit: [Monsivais, et al/Oncogene, 2021](#)

Researchers at Baylor College of Medicine show that analysis of the proteomics, or all the protein data, from aggressive human cancers is a useful approach to identify potential novel therapeutic targets. They report in the journal *Oncogene*, the identification of "proteomic signatures" that are associated with clinical measures of aggressive

disease for each of the seven cancer types studied. Some signatures were shared between different types of cancer and included cellular pathways of altered metabolism. Importantly, experimental results provided proof-of-concept that their proteomics analysis approach is a valuable strategy to identify potential therapeutic targets.

"There are two notable aspects of this study. One is that we explored the proteomic landscape of [cancer](#) looking for proteins that were expressed in association with aggressive forms of cancer," said co-corresponding author Dr. Chad Creighton, professor of medicine and co-director of Cancer Bioinformatics at the Dan L Duncan Comprehensive Cancer Center at Baylor. "We analyzed protein data that included tens of thousands of proteins from about 800 tumors including seven different [cancer types](#)—breast, colon, lung, renal, ovarian, uterine and pediatric glioma—made available by the Clinical Proteomic Tumor Analysis Consortium (CPTAC) mass-spectrometry-based proteomics datasets."

Computational analysis for the CPTAC datasets identified proteomic signatures associated with aggressive forms of cancer. These signatures pointed at altered cellular pathways that might be driving aggressive cancer behavior and could represent novel therapeutic targets. Each cancer type showed a distinctive proteomic [signature](#) for its aggressive form. Interestingly, some signatures were common to different types of cancer.

The other aspect of this study was to provide proof-of-concept that the proteomic analysis was a useful strategy to identify drivers of aggressive disease that could potentially be manipulated to control cancer growth.

"That's exactly what we were able to do with this new, very powerful dataset," said co-corresponding author Dr. Diana Monsivais, assistant professor of pathology and immunology at Baylor. "We focused on the uterine cancer data for which the computational analysis identified

alterations in a number of proteins that were associated with aggressive cancer. We selected [protein kinases](#), enzymes that would represent stronger candidates for therapeutics."

Of hundreds of initial candidates, the researchers selected four kinases for functional studies in uterine cancer cell lines. They found that the kinases not only were expressed in the uterine cancer cells lines, but also that manipulating the expression of some of the kinases reduced the survival or the ability to migrate for some uterine cancer cells. Cell migration is a property of cancer cells that allows them to spread cancer to other tissues.

This work is the result of a productive collaboration between two Baylor centers, the Dan L Duncan Comprehensive Cancer Center and the Center for Drug Discovery.

"Chad conducted this wonderful analysis on new CPTAC datasets and was interested in validating it in a human cancer. He approached us about performing functional studies to determine whether some proteins could translate to new targets for endometrial cancer," Monsivais said.

"Our experiments provided proof-of-concept that proteomics [analysis](#) is a useful strategy not only to better understand what drives cancer, but to identify new ways to control it or eliminate it."

"Historically, researchers have only been generating transcriptomic data (the messenger RNA (mRNA) that is translated into protein). Looking at the protein data itself, which is made available by the CPTAC, enables researchers to extract a new layer of information from these cancers," Creighton said. "In this study, we compared mRNA and protein signatures and, although in many cases they overlapped, about half the proteins in the [proteomic](#) signatures were not included in the corresponding mRNA signature, suggesting the need to include both mRNA and [protein](#) data in cancer studies."

More information: Diana Monsivais et al, Mass-spectrometry-based proteomic correlates of grade and stage reveal pathways and kinases associated with aggressive human cancers, *Oncogene* (2021). [DOI: 10.1038/s41388-021-01681-0](https://doi.org/10.1038/s41388-021-01681-0)

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