Researchers find a new class of biomarkers to predict treatment outcomes in cancer patients

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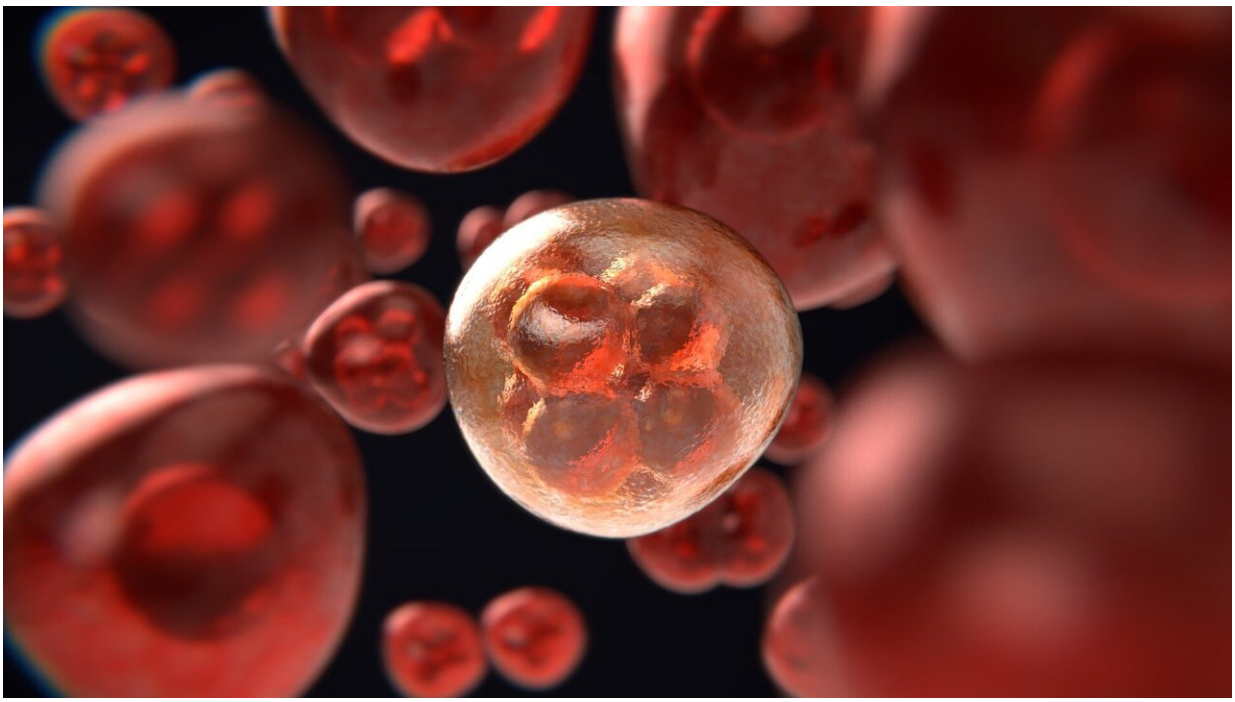

Cancer is the result of the uncontrolled division and spread of cells into surrounding tissue. Recently researchers have begun to focus on biomarkers as a source of information about different cancers, how they work in the body, and how they can be fought. Credit: Colin Behrens/Pixabay, CC0 Public Domain

One of the big reasons that cancer is difficult to treat is that patients

respond to treatments differently, and these differences can rarely be anticipated. In most cases, determining whether and how a patient will respond to any given therapy requires administering it to the patient and then waiting and watching. That is a lot of pressure for researchers and physicians and a lot of risk for cancer patients, and added expense.

If a patient's response were predictable, optimal therapies and regimens could be personalized, increasing the chances for success. This is why researchers have been focusing on identifying useful tumor biomarkers. Biomarkers are collections of biological molecules produced by a cancer patient's tumor that are intended to provide information on how it is formed, how it behaves, and, hopefully, how the patient will respond to a particular treatment.

Existing biomarkers have led to tests with encouraging but limited reliability

One of the most significant recent advances in cancer treatment has been immune checkpoint inhibitor, or ICI, therapies. ICIs work by blocking checkpoint proteins from binding with partner proteins long enough to allow T cells in the body to kill off cancer cells. This is important because, in all types of cancer, the immune system is tricked by the tumor into turning off, allowing the cancer to grow. Unfortunately, most cancer patients do not respond to these drugs; identifying who will benefit and who will not is critical.

Our research on ICI treatment prediction is not the first of its kind. Previous work has already led to tests with encouraging results for predicting how tumors will respond to ICI therapies. However, these earlier tests had one or more limitations, including modest accuracy, limited patient applications, and elaborate protocols. Notably, no earlier tests have predicted adverse events.

Lung cancer is the leading cause of cancer deaths and we're looking for a solution

Our team chose to initially focus our studies on lung cancer because it is the leading cause of cancer deaths globally. More than 2 million people are diagnosed with lung cancer each year and another 2 million more die, including many receiving treatments.

ICIs are now frontline therapies against lung cancer. They have proven to be seemingly miracle drugs for some, yet carry significant downsides such as very high costs, risk of serious adverse side effects, and importantly, low patient response rates. That's the big problem we wanted, and still want, to solve: how to treat cancer with ICIs more effectively, at low cost, and with fewer, or no, adverse events.

Current research revealed a new class of biomarkers for predicting treatment outcomes

The Calviri team has discovered a new class of biomarkers for predicting these treatment responses and adverse events. In a study recently published in the *Journal of Translational Medicine*, we demonstrated the biomarkers' utility for predicting outcomes in lung cancer patients following ICI therapy regimens.

Our research started with blood samples drawn from 74 patients diagnosed with advanced lung cancer. Following the blood draws, these patients received anti-PD-L1 or anti-PD-1 immunotherapy, either with or without chemotherapy. Combining these data, we developed a blood-based, or liquid biopsy, test that predicted post-treatment tumor responses and adverse events in these patients with an accuracy rate between 90% and 100%.

This new test is based on blood-based biomarkers called anti-frameshift peptide antibodies, or anti-FSP antibodies. We discovered that tumors produce an enormous number of mistakes during RNA processing, such as splicing, that are translated into variant, out-of-frame peptides. These frameshift peptides are highly immunogenic—they cause an immune response—and raise antibodies that we can easily detect in our tests.

This is exciting news because the information these biomarkers hold could help us develop improved or orthogonal testing to predict how any tumor will respond to cancer treatments. Since our test is conducted with a very small amount of blood in a simple assay, it will be inexpensive and broadly applicable. We intend to enable physicians to accurately predict therapy outcomes and make optimally safe and effective treatment recommendations for each patient.

These newly discovered biomarkers could have implications beyond lung cancer

Although our team was studying lung cancer, this research and its outcomes are not limited to this single type of cancer. The new biomarkers we discovered have implications for many types of cancers that do not usually respond to ICI therapies. Brain cancer, for example, overall has a very low ICI response rate. Consequently, brain cancer patients are not offered ICIs, even though a subset of them would have responded. A simple test using anti-FSP biomarkers could identify these patients to physicians, enabling them to offer treatment and save lives.

Conclusion

Even though this study represents the first step in predicting outcomes for immunotherapy, it is a major step in the right direction. Our next goal is to collect and analyze data from a larger sample and use that

information to further develop this new technology. Importantly, we are focusing on broadening the scope so we both address specific needs in lung cancer treatment and evaluate its potential use in treating other cancers and chronic diseases.

This story is part of Science X Dialog, where researchers can report findings from their published research articles. Visit this page for information about ScienceX Dialog and how to participate.

More information: Luhui Shen et al, Predicting response and toxicity to immune checkpoint inhibitors in lung cancer using antibodies to frameshift neoantigens, *Journal of Translational Medicine* (2023). DOI: 10.1186/s12967-023-04172-w

Dr. Kathryn Sykes, PhD, is a co-founder and VP Research and Product Development at Calviri—a leading biotech developer of promising new vaccines against cancer and aging-associated diseases. She is an expert with more than 20 years of experience in the development of molecular and chemical technologies to support the immune system and promote healthful longevity in humans. She received her bachelor of science degree in biology and economics at Duke University and her PhD in biochemistry at Duke University Medical Center.