Immunotherapy may be the most promising development in cancer treatment in the last decade, but so far it is only effective for about 30 percent of patients. Testing for biomarkers can sometimes predict which patients will benefit, but current tests do not provide absolute proof of how a patient will respond.

“While many patients derive remarkable benefit from immunotherapy, it fails to help many others,” said Abhijit Patel, MD, PhD, Associate Professor of Therapeutic Radiobiology, “so these patients waste time when they could have been receiving some other therapy instead. There’s a lot of interest in developing biomarkers that can predict response, but the biomarkers we have aren’t correct as often as we would like them to be.”

The stakes are high. What if a patient for whom immunotherapy could be lifesaving gets disqualified from the treatment? What if a patient tests positive for the biomarker but doesn’t receive it because of a falsely negative biomarker test? Or, immunotherapy could be lifesaving gets disqualified from the treatment, before a scan could detect shrinkage, a tumor can actually look worse. That can be confusing. Do we continue the therapy or do we wait another month or two to see if it shrinks? The scans aren’t giving us clear-cut data that we do other therapies, so immunotherapy presents a unique challenge in monitoring and predicting response.”

Since scans can’t reliably detect the early effects of immunotherapy, Dr. Patel and a team of scientists at Yale began looking for blood biomarkers that could. They settled on circulating tumor DNA (ctDNA), a byproduct of dying cancer cells shed by a tumor into the bloodstream. They theorized that measuring changes in ctDNA could provide a quicker and more reliable assessment of immunotherapy efficacy than CT scans because the amount of ctDNA in the blood reflects how many cancer cells are dying. To test this idea, they studied a group of patients with non-small cell lung cancer who were receiving immunotherapy, and published their eye-opening findings last year [2018] in Clinical Cancer Research. They began looking for blood biomarkers that could detect early-stage lung cancer, which kills an estimated 154,000 Americans each year.

“The impact of this, if it works, could be tremendous,” said Dr. Patel. “It’s widely known that if you detect most types of cancer early, outcomes will improve, because you can surgically remove or eradicate all of the cancer cells and have a higher probability of achieving a cure.”

He expects his multidisciplinary group to have made substantial progress toward a lung cancer early detection test within the five-year period of the grant, but his ultimate goal is a “pan-cancer assay” that could detect early-stage cancers of all types through a blood test that looks for ctDNA, sometimes called a “liquid biopsy.” The theory is that ctDNA contains evidence of mutations specific to each tumor, evidence not typically found in healthy people. If ctDNA was detected, said Dr. Patel, imagining this future, “You could say, ‘This patient very likely has cancer, but the three most likely cancers are X, Y, or Z,’ then you could do a CT scan or an MRI to further diagnose. Such early detection could save countless lives.”

In September 2018, Dr. Patel and a multidisciplinary team from Yale, Harvard, Rice, and Microsoft Research received a $2.6 million grant from the National Institute of Health to develop an assay that will use ctDNA-mining to detect early-stage lung cancer, which kills an estimated 154,000 Americans each year.

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“We eventually saw substantial shrinkage of their tumors on scans, and these patients benefitted from immunotherapy for a much longer duration.” Conversely, measuring ctDNA also offered an early indication of when immunotherapy was not working.

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