Scientists detect lymphoma relapse by monitoring cell-free tumor DNA

20 April 2015, by Krista Conger

Circulating tumor DNA in the blood of patients treated for non-Hodgkin lymphoma can be used to identify those who are relapsing earlier, and with greater accuracy, than conventional monitoring, according to a study by researchers at the School of Medicine.

The finding is important because it will allow clinicians to quickly identify patients who need additional treatment. It also further validates the use of circulating tumor DNA as a means to detect or monitor cancers.

"Diffuse large B-cell lymphoma is the most common blood cancer," said Ash Alizadeh, MD, PhD, an assistant professor of medicine and a member of Stanford's Cancer Institute. "This disease is curable in most patients, but a significant minority of these patients will relapse. Right now we don't have a good way to identify those who fall into this category."

The current standard for detecting the cancer in these patients is imaging with combined PET and CT scans. However, imaging is limited by its specificity; not every positive PET scan means a patient has truly relapsed.

A paper describing the new research was published April 16 in *Blood*. Alizadeh is the senior author, and postdoctoral scholar David Kurtz, MD, and former postdoctoral scholar Michael Green, PhD, share lead authorship.

The researchers studied 75 patients diagnosed with diffuse large B cell lymphoma. They identified the DNA sequence unique to each patient's tumor and then used high-throughput sequencing to look for the sequence in the patient's blood, both in the plasma (the straw-colored, cell-free liquid in which blood and immune cells circulate), and in the patient's circulating immune cells.

The researchers found that, in patients known to be relapsing, they could reliably detect the tumor DNA in the plasma. In contrast, when they examined the circulating cells in the blood they could detect the disease in only 30 percent of the relapsing patients. They then compared their plasma-based method with PET/CT scans. Studying patients who would go on to relapse, they found their new method identified all patients at the time of their relapse, and often was able to detect disease prior to relapse. Furthermore, the test was positive only in those patients who truly had relapsed. In contrast, a positive PET/CT scan was correct only 56 percent of the time.

Alizadeh cautions that it's not yet possible to identify the unique cancer-specific DNA sequence in every patient. About 20 to 30 percent don't have enough circulating tumor DNA to do so. "This is all about sharpening the tool," Alizadeh said, "but the specificity of this new approach is very promising."

Provided by Stanford University Medical Center