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Scanning for cancer genomic changes in plasma: towards an era of personalized blood-based tumor markers

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Guest:
Professor Allen Chan is a chemical pathologist working in the Chinese University of Hong Kong.

Bob Barrett: This is the podcast from *Clinical Chemistry*. I am Bob Barrett.

The analysis of circulating cell-free tumor DNA has considerable potential for the detention and monitoring of cancers. Substantial effort has been made to identify cancer associated genetic changes that might be suitable for use as new tumor markers. However, only a few of these genetic markers have been translated into clinical use.

In a prospective article appearing in the November 2013 issue of *Clinical Chemistry,* Professor Allen Chan of the Chinese University of Hong Kong provides insight into this issue. He is our guest in this podcast.

Dr. Chan, in your article you raise the issue of individualized tumor markers. What are the advantages of such personalized tumor DNA markers compared with conventional tumor markers?

Dr. Allen Chan: So conventional tumor markers, most of those markers are proteins or glycoproteins, but only a limited subtype of cancers would secrete these substances, like the cancer-specific proteins or glycoproteins. So only a few types of cancers we have suitable detectable tumor markers in blood.

But for personalized molecular tumor markers, in sense virtually all tumors would carry some mutations or genetic changes. Therefore, if we tried hard enough, we would be able to find at least a few to hundreds of suitable markers for each individual cancer. So this can be a generic approach and can be applied to all cancer patients and also all subtypes of cancers.

Bob Barrett: What are some of the technical challenges for the development of personalized molecular tumor markers?

Dr. Allen Chan: To develop these methods first we need to indentify the specific cancer changes in the tumor tissues so that we can develop these specific changes into suitable tumor markers. But to identify these specific changes, it is technically challenging, because there are only a few hundreds or few thousands of genetic changes in each tumor, and over the whole genome there are three billions of nucleotides.

So to find these few hundreds to a few thousands of changes, we need to screen the whole genome for these changes. And also we need tumor tissues to identify these cancer specific changes, because most of these changes are having mutations and they are not recurrent in different cancer patients.

Bob Barrett: As of right now, Doctor, what are the most useful applications of personalized circulating molecular tumor markers?

Dr. Allen Chan: So for the detection of these personalized molecular tumor markers, first we need to get hold of the tumor tissues to identify the specific changes, and the most important applications of these markers would be the monitoring of the progress of the cancer after curative intense treatment. In most patients after they received curative intense treatment, they would ask a similar question, that is, whether the cancer is going to come back or whether I am cured? So in that case these personalized tumor markers would be very useful to answer these questions.

Now, what are the specific genetic changes in the tumor tissues? So after the treatment, if we can still detect considerable amount of these cancer-specific changes in the blood of these patients, then we know that not all the tumor tissues are removed during the treatment and then we can deduce that there are some residual cancer cells inside the patient and the probability of having a disease recurrence is very high.

In contrast, if we do not find any cancer-specific changes in the blood of the patients after the treatment, then we can assume that most of these cancer cells have been removed. So it would indicate that there is a lower probability of disease recurrence in the future.

Bob Barrett: Well, in addition to the monitoring of the disease progression and treatment response, can these individualized tumor markers be used for the screening of early cancers?

Dr. Allen Chan: As I have mentioned, for the detection of these personalized tumor markers, we need to get hold of the tumors to

identify the specific changes in the tumor tissues so as to develop them into the personalized tumor markers.

But for screening, because when we screen a large population, we assume that most of these people do not have cancer. Therefore, we would not have the tumor tissues of these people to develop the personalized tumor markers.

But in a recent study we have demonstrated that we can detect in the plasma without getting hold of the tumor tissues, we can detect the tumor, cancer-associated copy number changes in the plasma. And those changes detected in the plasma are identical to those observed in the tumor tissues.

In this case if we monitor or if we detect any copy number changes or chromosomal aberration, then we don't need the tumor tissues, and we can deduce from the plasma what is happening in the tissues.

So it is possible to use personalized markers for screening purpose.

Bob Barrett: Well finally, Doctor, do you think that molecular tumor markers will find their way into routine clinical use in the next five years? And if so, what are some of the major hurdles for the early adopters?

Dr. Allen Chan: I think the most important consideration of adopting these personalized molecular markers for routine clinical use is still the cost. Because we need to sequence the tumor tissues or plasma to a very high sequencing coverage to identify these patient-specific markers, at present it is still very costly to sequence the whole genome to identify these changes.

But we know that the sequencing cost, especially the cost for next generation sequencing, is dropping very rapidly. So we think that the cost hurdle would become less significant in the coming years.

So I am very optimistic that these approaches can be applied in routine clinical diagnostics.

Bob Barrett: Professor Allen Chan is a chemical pathologist working in the Chinese University of Hong Kong. His major research interest is the development of new diagnostic tests for prenatal diagnosis and cancer detection based on the analysis if circulating cell-free DNA. He has been our guest in this podcast from *Clinical Chemistry.*

I am Bob Barrett. Thanks for listening!