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Cancer Genome Scanning in Plasma

Detection of Tumor-Associated Copy Number Aberrations, Single-Nucleotide Variants, and Tumoral Heterogeneity by Massively Parallel Sequencing

Author: Dennis Lo // **Date:** JAN.3.2013 // **Source:** Clinical Chemistry

Topics: Analytical Techniques and Applications, Informatics, Pathophysiology and Organ Systems, Emerging Technology, Sequencing, Genomics/Proteomics/ Metabolomics/ Pharmacogenomics, Cancer

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Article

K.C.A. Chan, P. Jiang, Y.W.L. Zheng, G.J.W. Liao, H. Sun, J. Wong, S.S.N. Siu, W.C. Chan, S. L. Chan, A.T.C. Chan, P.B.S. Lai, R.W.K. Chiu, and Y.M.D. Lo. *Cancer Genome Scanning in Plasma: Detection of Tumor- Associated Copy Number Aberrations, Single-Nucleotide Variants, and Tumoral Heterogeneity by Massively Parallel Sequencing.* Clin Chem 2013;59:211.

Guest

Dr. Dennis Lo is the Director of the Li Ka Shing Institute of Health

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Bob Barrett:
This is a podcast from *Clinical Chemistry*, sponsored by the Department of Laboratory Medicine at Boston Children's Hospital. I am Bob Barrett.

The presence of tumor derived DNA circulating in the plasma of cancer patients has offered exciting opportunities for the detection and monitoring of various types of cancers. In the January 2013 issue of *Clinical Chemistry*, Dr. Dennis Lo and his colleagues in Hong Kong have applied their massively parallel sequencing approach to cancer genome scanning. Dr. Lo is our guest in this podcast.

Doctor, please describe the background work that has led to your paper?

Dennis Lo:
In previous work we have worked in the area of noninvasive prenatal diagnosis in which we show that by randomly sequencing the plasma DNA of a pregnant woman, we can deduce the fetal genome and to see if the fetus is suffering from a variety of chromosomal abnormalities.

So we wondered that due to the similarity between a fetus living inside a pregnant woman and a cancer growing in a patient whether we can use a similar approach to profile the cancer genome, so this has led to the current work.

Bob Barrett:
What's the most important advance reported in this paper and how does it differ from other work that you have reported in *Clinical Chemistry*?

Dennis Lo:
So the most important advance is that we have shown for the first time that by randomly sequencing a cancer patient's plasma, we can work out on a genome-wide level tumor associated genetic abrasions.

For example, we can profile copy number abrasions and single-nucleotide mutations across the whole of tumor genome just by analyzing a blood sample from a patient. And this is different from

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level the major of those genomic abrasions, we can also measure their concentration. And so in other words, we can measure the concentration of tumor DNA in a particular sample. And then we can monitor the change of that concentration over time, to try to use it for monitoring of the patient's response to treatment and possibly for prognostication purposes as well.

And we have also shown that this technology can be applied to very complex oncologic scenarios. For example, we have studied a patient with BRCA1 mutation who has a breast cancer and bilateral ovarian cancer. And then we have shown that by using this random sequencing of the patient's plasma, we can monitor the progress of those individual cancers, the contribution of those different cancers into the blood plasma.

And furthermore, in the case of the patient with multiple cancers, we have even shown that mutations released by individual clones of the ovarian cancer can be separately tracked in the patient's plasma. So it suggests that this approach can be used to stop the tumoral heterogeneity, which is an emerging and rather hot field in the cancer area.

Bob Barrett:
Dr. Lo, what were the main difficulties that you encountered during this study?

Dennis Lo:
Because we are doing very deep sequencing, so we generate a lot of sequencing data, so the main difficulties that we have encountered while doing this work is basically how to handle the massive amount of sequencing data.

But luckily we have a very good bioinformatics team who have helped us to do this and we have also got to develop a lot of new algorithms to try to apply sequencing data to look at things like to measure the tumor DNA concentration in plasma and to look at tumoral heterogeneity.

Bob Barrett:
What is the main clinical implication of your work?

Dennis Lo:

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Dennis Lo:
So we are now going for follow-up work to validate our data on a large scale to see the general applicability of these approaches to different tumor types and to multiple patients.

Bob Barrett:
Dr. Dennis Lo is the Director of the Li Ka Shing Institute of Health Sciences and Professor of Medicine and Chemical Pathology at The Chinese University of Hong Kong. He has been our guest in this podcast from *Clinical Chemistry*. I am Bob Barrett. Thanks for listening.

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