ASCO Abstract

Longitudinal Tracking of Necrotic Cell-Free DNA in Patients with Oncological Diseases

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Background: The presence of necrotic cell-free DNA (ncfDNA) has been shown to be elevated in cancer patients when compared to healthy individuals. Tracking the concentration of ncfDNA provides insight into tumor dynamics without the need to perform additional molecular characterization. Currently, protein biomarkers and imagining are relied upon for monitoring treatment; in addition, tissue biopsies provide only a static snapshot but do not address the adaptive, evolving nature of cancer. Biological Dynamics' AC Electrokinetic (ACE) technology is a rapid streamlined sample-to-answer approach to characterize the presence of ncfDNA in the blood without pre-processing or dilution. Paired with fluorescent microscopy and specific intercalating dyes or antibody labeling, the technology can quantify the isolated DNA. With this approach, a rapid assay has been developed that can track remission, stable, or progressive disease in multiple cancers

Methods: Plasma samples from cancer patients (ovarian, colorectal, lung and testicular) were collected in Lithium Heparin tubes and processed according to standard protocols. For the quantification of ncfDNA, the samples are loaded into the ACE system as well as two calibrators for the assay. The calibrators are physiological saline with spikes of high molecular weight DNA (> 500 bp) at a high and a low concentration. The microfluidics driven technique processes 250 µL of fluid in under 20 minutes. Limit of detection for capture is around 3 - 6 pg/µL when using specific intercalating dyes for dsDNA.

Levels of protein biomarkers (CA-125, CEA, CA 27.29 and CA 19-9) are measured in the TOSOH AIA-360 immunoassay from system according to manufacturer protocols.

Results: The presence of ncfDNA is confirmed in patients with local, regional, or distant diseases while healthy volunteers do not show the presence of the marker. By using the two calibrators within the same chip, the concentration of ncfDNA

can be determined and a longitudinal tracking allows for treatment response monitoring. The quantification of ncfDNA showed direct correlation with levels of protein biomarkers and with clinical annotation (remission, stable, or progressive disease).

Conclusions: Tracking of ncfDNA in a weekly or biweekly basis may be a helpful tool for treatment response / tumor burden monitoring. Doing so will allow for faster assessment of therapy efficacy and can be of aid for medical practitioners to decide a chance of treatment or discover drug resistance patterns.