April 15, 2017

Dear Regina,

Welcome to BioMarketing Insight's monthly newsletter.

We have a new look to our newsletter. Love to receive your feedback.

Last month I covered "Trumpcare vs. Obamacare - Repeal and Replace." If you missed last month's article, click here to read it. This month's newsletter will cover, Liquid Biopsy: Could This Be a Reality for Cancer Diagnosis and Treatment in the Future?

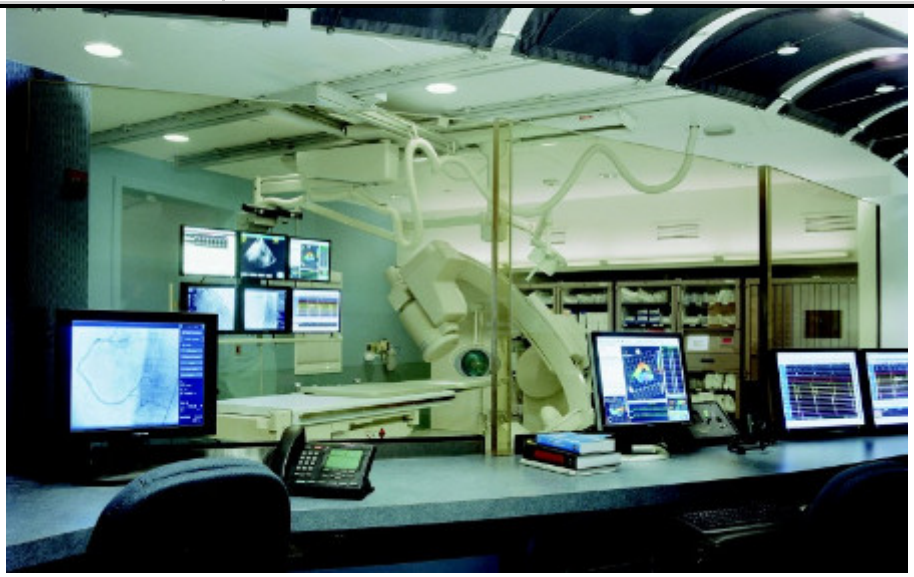
Read on to learn more about this topic and other current news. The next newsletter will be published in the new year on May 15th, 2017.

We encourage you to share this newsletter with your colleagues by using the social media icons below, or by simply forwarding this newsletter or use the link below. Should you or

Please email me, Regina Au, if you have any questions, comments, or suggestions.

Sincerely,
Regina Au
Principal, New Product Planning/
Strategic Commercial Consultant
BioMarketing Insight

Table of Contents



Developing a Product? Commercializing a Product?

If you are developing a product and have not conducted the business due diligence to determine commercial viability or success, contact me for an appointment. For successful commercial adoption of your product or looking to grow your business, contact me for an appointment.

For more information on our services, click on the links below:

Product Development
Market Development
Marketing Strategies

Top

Immunooncology: Can the Right Chimeric Antigen Receptors T-Cell

I am pleased to announce that my article on "Immunooncology: Can the Right Chimeric Antigen Receptors T-Cell (CAR-T) Design Be Made to Cure All Types of Cancers and Will It Be Covered?" has been published in Journal of Pharmaceutics. This article reviews the mechanism, design and administration of CAR-T cells, and whether payers will pay for this new technology. To read the article, click here.

Top

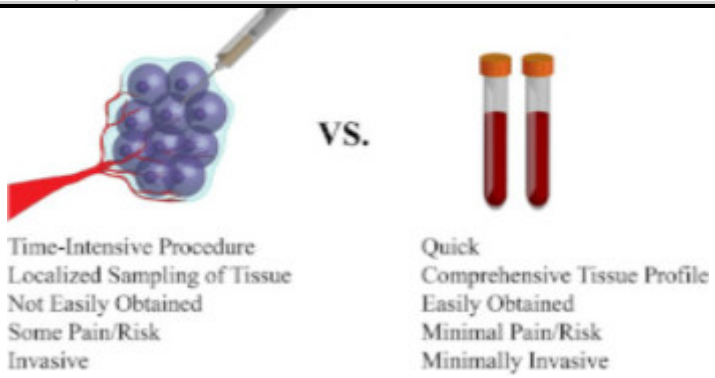
Save the Date: 5th Annual Medical Informatics World Conference - May 22-23, 2017

I am pleased to announce that I will chair the opening session, Perspective: Large Medical Centers in the Telehealth Integration and Implementation Track on Monday May 22, 2017 at 10:55 AM right after the Keynote Speakers.

I will also moderate a breakout discussion group on Monday afternoon entitled “Improving Health and Reducing Costs Through Traditional and Innovative Approaches to Coordinated Care and Patient Engagement."

Please join me at the Medical Informatics World conference as this event has become the critical meeting place for health IT executives and innovators, delivering the knowledge-sharing needed to continue improving patient care and outcomes. Click here to learn more about the conference. As my guest, you will receive a $200 discount off the registration fee with the key code “HITSPK1” when registering for this event. Offer is valid on new registrations and does not apply to workshop registration. To register, click here.

Top



Liquid Biopsy: Could This Be a Reality for Cancer Diagnosis and Treatment in the Future?

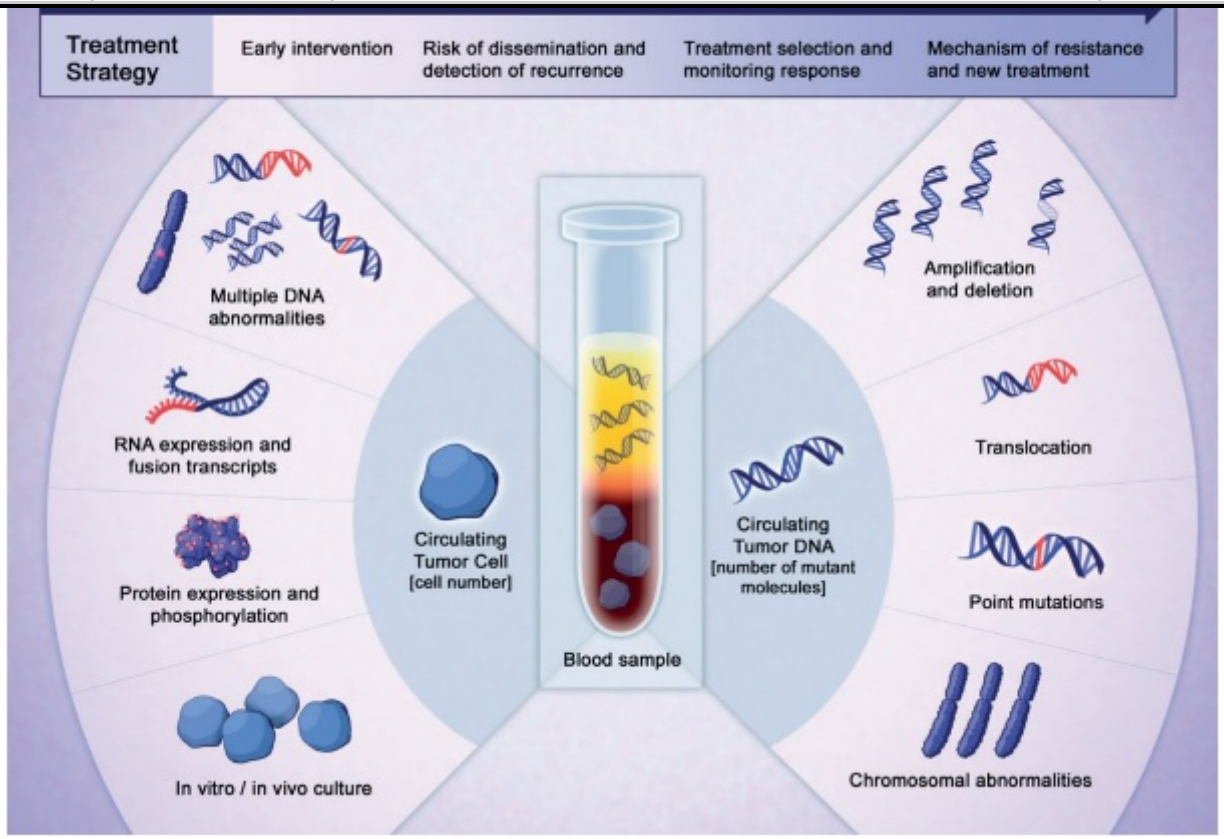
What is Liquid Biopsy?

It's a blood test that detects evidence of cancer in circulation or circulating tumor cells (CTC), as dying cancer cells are shed into a person's blood. This has generated a lot of excitement in the lab, but has not come to fruition in the clinic yet.

For cancer detection, the standard of care is tissue biopsies. However, "for most tumors, a tissue biopsy is quite challenging, in that it's costly, painful and potentially risky for the patient," explains Terence Friedlander, MD, from the Helen Diller Family Comprehensive Cancer Center at the University of California, San Francisco.

Currently, the only liquid biopsy to obtain US Food and Drug Administration (FDA) clearance is CellSearch Systems Technology, by Janssen Diagnostics, for use in the management of individuals or prognosis with metastatic breast cancer and with clearance subsequently expanded to include use in the management of individuals with metastatic prostate* and colorectal cancers.

Tumors are heterogeneous and tend to change over time, which makes them hard to detect. As a result of biomechanical and chemical cues, subsets of tumor cells die and others undergo reprogramming, allowing them to survive under adverse conditions, such as cell crowding, low tissue oxygenation, poor nutrient supply and influences from immune modulation. In metastasizing tumors, some cells develop the capacity to penetrate blood vessels, survive the shear forces of the bloodstream and travel to the bone marrow and distant sites, where a subset is capable of lodging, growing and triggering angiogenic switches in the relatively hostile foreign environment of other organs. For cells that have metastasized beyond their organ of origin, some remain dormant, resistant to adjuvant therapies, whereas others grow and seed new tumor foci that may not respond to cytotoxic drugs or targeted therapies.



Liquid assets. Learning how to isolate and interpret the clues that solid tumors leave in the blood and other fluids could transform the way we detect cancers, select treatments and monitor response. Source: Marc Beishon, Cancerworld.org and Reprinted from AACR.

Isolating and characterizing CTCs are challenging, given that many methods require sensitive collection and enrichment technology and technical challenges. CTCs are relatively rare and despite advances in next-generation sequencing, science has not advanced significantly. Therefore, tumor activity is being monitored through analyses of DNA isolated directly from blood. Even though the majority of circulating extracellular DNA is adsorbed to the surface of leukocytes or erythrocytes, a portion can be identified from plasma DNA or cell-free DNA (cfDNA). cfDNA comes from normal cells, including normal leukocytes that undergo apoptosis and cancer cells and therefore can be detected in healthy volunteers, patients with benign tumors and cancer patients. Circulating tumor DNA (ctDNA) is the portion of circulating DNA specifically derived from cancer cells and is present both unbound and bound to leukocytes and erythrocytes. Unbound ctDNA in the plasma is referred to as tumor-derived cfDNA.

Although the current FDA-approved liquid biopsy measures intact circulating tumor cells (CTC) to give a prognosis of overall survival, the potential predictive value of circulating tumor DNA (ctDNA, or tumor-derived cfDNA) is much more exciting, said Friedlander.

"Mutant DNA fragments are found at relatively high concentrations in the circulation of most patients with metastatic cancer and at lower but detectable concentrations in a substantial

This was evident in cases of breast, colon, pancreas and gastroesophageal tumors, where "detectable levels of ctDNA were present in 49% to 78% of patients with localized tumors and 86% to 100% of patients with metastatic tumors."

Dr. Diaz and his team evaluated 136 metastatic tumors in 14 different tumor types, and found that "most patients with stage III ovarian and liver cancers and metastatic cancers of the pancreas, bladder, colon, stomach, breast, liver, esophagus and head and neck, as well as neuroblastoma and melanoma, harbored detectable levels of ctDNA. In contrast, fewer than 50% of patients with medulloblastomas or metastatic cancers of the kidney, prostate, or thyroid and fewer than 10% of patients with gliomas, harbored detectable ctDNA."

In addition to offering clues about stage and spread, liquid biopsies can be used to monitor the effects of cancer treatment, giving an early warning about possible recurrence and offer clues to the reasons for treatment resistance.

"Predictive markers are better, because they help guide treatment decisions. In a sense, the ctDNA liquid biopsy allows us to understand specifically what kind of molecular changes are happening in the tumor in real time, which is a very big step beyond where CTCs are today, clinically." said Dr. Friedlander.

Dennis Lo, MD at Chinese University of Hong Kong, is well known for being the first to show that a fetus sheds bits of its DNA into the bloodstream of its mother in 1997, that led to a much safer, simpler screening test for Down syndrome. Dr. Lo has worked for nearly 20 years on a “liquid biopsy” technique to detect liver and other cancers very early on, before symptoms arise, by sequencing the DNA in a few drops of a person’s blood.

Liquid Biopsy Studies

Dr. Lo's hospital is involved in two of the largest studies to prove that DNA analysis can also act as a screening test. The researchers are following a thousand people with hepatitis B to see if the DNA test can spot liver tumors before an ultrasound can. For the time being, the cost of the DNA test being used on people at risk for liver cancer is still too expensive for routine use.

A larger study on nasopharyngeal carcinoma involving the upper part of the throat, which is rare, is nevertheless predominant in men in South China. These men have a one in 60 chance of contracting it in their lifetimes. This cancer appears to be linked to consuming salted fish, genetics among Chinese ethnicity and the Epstein-Barr virus. The test Lo developed identifies viral DNA that dying cancer cells release into the bloodstream or plasma.

The study will recruit 20,000 healthy middle-aged men from Hong Kong. The study has already screened 10,000 men and has identified 17 cases of cancer—13 of which were stage 1, or the

symptoms, such as a mass in the neck, the typical survival rate is less than 70%. “They (are)… a time bomb waiting to go off,...” says Lo. Every man in South China should be screened, as “we believe it will save lives.”

A recently published prospective, single-center study evaluated three blood-based biomarkers, cfDNA, CA15-3 and CTCs, in women with progressive metastatic breast cancer confirmed by radiologic imaging. The concentration of cfDNA was shown not only to be the most sensitive biomarker, but also to detect disease progression five months earlier than documented by imaging.

In addition to screening for cancer, liquid biopsies could help those people already diagnosed with cancer and in need of treatment. Doctors would be able to pick a drug determined by the specific DNA mutation identified to that specific type of cancer, since cancer comes in many forms. Dr. Lo believes he’s close with nasopharyngeal cancer. “If you can screen and prognosticate in very common cancer types, that is the time when it will go mainstream,” says Lo.

Researchers at the University of California, Los Angeles believe their liquid biopsy test can detect early-stage cancer in blood samples using a computer software program to analyze specific molecular patterns in cancer DNA. They claim their program can not only detect tumor DNA, but also identify what type of cancer it is.

The scientists built their program on epigenetic patterns known as “methylation,” which are common in cancer. Methylation patterns differ from one tumor to another, making it possible to build “molecular footprints” of cancers emanating from specific tissues, such as those in the lung or liver, says Jasmine Zhou, a professor at UCLA.

“We also compiled the same 'molecular footprint' for non-cancerous samples, so we had a baseline footprint to compare the cancer samples against,” Zhou said in a press release. “These markers can be used to deconvolute the DNA found freely in the blood into tumor DNA and non-tumor DNA."

The UCLA team tested blood samples from 29 patients with liver cancer,12 with lung cancer and 5 with breast tumors. Their program was able to detect early-stage cancers with 80% accuracy.

Commercial interest in liquid biopsies has recently started to explode. Eric Topol, a professor of genomics at the Scripps Research Institute, predicted that this technology applied to cancer and other diseases, will become the “stethoscope for the next 200 years.” Jay Flatley, CEO of Illumina, the San Diego company that builds fast gene-sequencing machines, told investors that the market for such tests could be worth at least $40 billion. Calling the technology “perhaps the most exciting breakthrough” in cancer diagnostics, Flatley said his company would begin offering researchers a liquid-biopsy test kit to facilitate the search for signs of cancer.

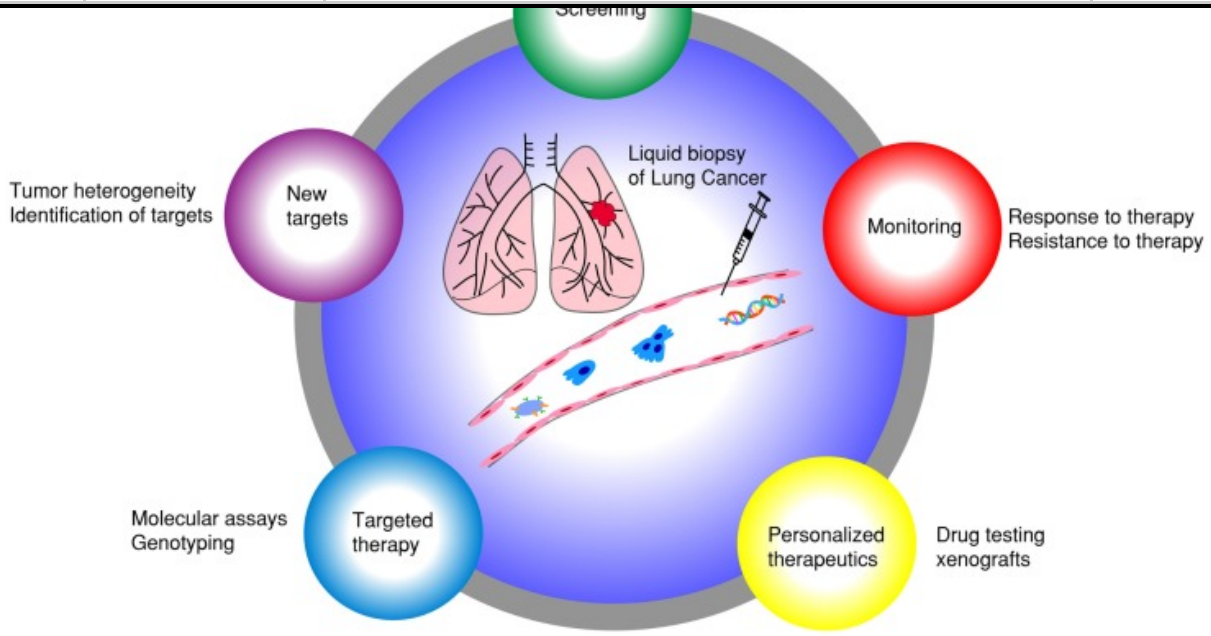
$100 million in 2016 from Bill Gates, Bezos Expeditions and other high-profile investors.

Top

Closing Thoughts

The etiology of cancer is very complicated and no two cancers are the same, even if it's the same type of cancer today, or tomorrow, or even in siblings. Cancer cells are very smart and able to survive under the harshest conditions, while hiding from detection by imaging and cancer treatment.

Liquid biopsy will become the test of the future, able to diagnose cancer early on and even before the cancer shows up on imaging, as reported in this article. A noninvasive liquid biopsy test is much preferred over an invasive tissue biopsy because it is less costly, painful and risky for the patient. Liquid biopsy allows the opportunity to take serial samples in order to monitor tumor genomic changes in real time, since tissue biopsy is just a snap shot in time. This will allow clinicians to ensure that the therapy they have selected, based on a particular molecular target, remains relevant and allows them to observe the emergence of any resistance.



The possible application of liquid biopsy are the following, as depicted by the image above by Zhang, Zhou et al., University of Michigan

1. Early detection of cancer
2. Identify the type of cancer
3. Identify the stage of cancer
4. Identify how aggressive the cancer is
5. Identify which drug is the best to treat the cancer
6. Monitor for early signs of resistance or re-occurrence

Researchers are not there yet, but they have come a long way since CTCs were being studied. But before we get there, as Dr. Giuseppe Curigliano from the European Institute of Oncology in Milan, Italy stated at the 2014 European Society for Medical Oncology, standardization will be a key factor in ensuring consistency between centers and in determining its clinical success. He believes it is crucial that we standardize the assays used to evaluate cfDNA and define the optimum sampling specimen (i.e. serum or plasma). Standardization should be across the board: blood collection, processing, storage and DNA extraction, quantification, analysis and reporting of data. It also needs to be a cost-effective analysis, able to accurately identify the genes known to be recurrently mutated in each tumor. By developing standardized methodologies for cfDNA analysis and validation through large prospective clinical studies, the liquid biopsy approach will no doubt be incorporated into the clinical management of cancer patients.

Top

free to contact me at 781-935-1462 or regina@biomarketinginsight.com.