BioFluidica

LiquidScan™ Oncology Applications

Liquid biopsy is a high-value source of important diagnostically relevant biomarkers with information to improve disease outcomes for patients in addition to biopsies obtained through surgery or needle biopsies. Liquid biopsy biomarkers have three main origins, cell-free circulating nucleic acids cfDNA (including circulating tumor DNA; ctDNA), extracellular vesicles (exosomes), circulating cells (including circulating tumor cells; CTC). After many years of technical challenges, liquid biopsy is now moving rapidly from research into clinical applications (Alix-Panabières and Pantel, 2021, doi.org/10.1158/2159-8290.CD-20-1311). Cell-free DNA (cfDNA) has delivered on some early promise with fast turn-around times and reduced costs to better serve patient health with some critical diagnostic tests. Not all clinical conditions however lend themselves to diagnosis, testing, or even screening by cfDNA-based testing. There is a clear need to be able to further explore the blood milieu for the presence of diagnosable biomarkers with a "next-generation liquid biopsy".

Enter BioFluidica and the potential that microfluidics provides liquid biopsy.

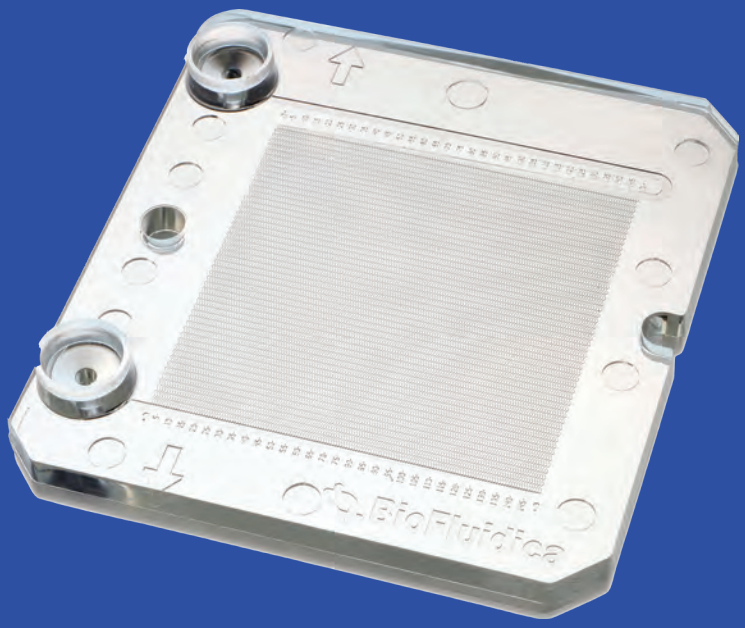
> Highly Efficient Circulating Tumor Cell Isolation from Whole Blood and Label-Free Enumeration Using Polymer-Based Microfluidics with an Integrated Conductivity Sensor | doi.org/10.1021/ja8015022

The approach provided by BioFluidica LiquidScan™ is predicated on the ability to prepare a plastic microchannel liquid device (microfluidic chip) with chemistry directed against specific biomarkers present in the liquid biopsy (e.g. blood, saliva, urine). For example, if a specific biomarker is projected from a CTC, the microfluidic chip can be prepared to capture the CTC from blood allowing extraneous cells to be washed away (see the above-referenced paper for the first description). The same approach can be used to isolate specific exosomes from blood plasma. In addition, being able to isolate and enrich rare cells from blood using LiquidScan broadens the application of liquid biopsy to prenatal screening. A recent example is described in the Prenatal Diagnosis December 2021 cover article seen below.

> Identification of fetal aneuploidy with dual-probe fluorescence in situ hybridization analysis in circulating trophoblasts after enrichment using a high-sensitivity microfluidic platform – doi.org/10.1002/uog.23586

The BioFluidica LiquidScan platform was developed over the last ten years and is now offered as a commercial product for research labs. BioFluidica LiquidScan consists of:

- ✔ LiquidScan STARlet™* with LiquidScan microfluidic chip processing module and LiquidScan software
- ✔ LiquidScan reagent plate
- ✔ LiquidScan blood collection tube (BCT)
- ✔ LiquidScan sinusoidal chips – for rare cell enrichment
- ✔ LiquidScan pillar chips – for exosome enrichment



The BioFluidica LiquidScan chip, the heart of the system, is a one-time-use test-specific microfluidic device. From 1 to 8 chips can be processed simultaneously on the platform controlled to run autonomously by LiquidScan software. In a sample with five million white blood cells and five billion red blood cells, only one viable CTC may be present, yet BioFluidica LiquidScan can capture and isolate it, based on the specificity and affinity of the chip surface chemistry. Recovery and purity for the chip technology are unprecedented, reaching over 95% and 80%, respectively. Elution of the cells and exosomes from the chip is performed such that the isolated material is fully compatible with downstream molecular and immunochemical analyses, as required for specific assays.

BioFluidica used Acute Myeloid Leukemia (AML) as a trial showing the system can be used to longitudinally track any patient and search for signs of relapse following therapeutic intervention. Since the instrument uses a standard blood draw, there is no need for a bone marrow biopsy and the accompanying discomfort to the patient. This allows for more frequent testing which can be particularly important for acute-based diseases, such as AML, and other acute leukemic diseases, such as Multiple Myeloma (MM) or Acute Lymphoid Leukemia (ALL). BioFluidica-associated automated hardware also supplies a workflow conducive to clinical implementation by operators with limited training in the art.

*STARlet and STAR are trademarks of Hamilton® Company.

Described in representative publications below are clinical applications using LiquidScan for disease management:

a. Molecular subtyping of breast cancer patients using EVs

b. Tracking response to therapy (PARC inhibitors) for pancreatic ductal adenocarcinoma (PDAC) patients using divergent subtypes of circulating tumor cells

c. Early detection of ovarian cancer (screening test) using EVs and the necessary hardware

d. Detection of relapse from minimum residual disease (MRD) for children with acute lymphoblastic leukemia using circulating leukemia cells found in blood

Selected Downstream Applications after biomarker enrichment using the LiquidScan system as described in peer-reviewed publications:

Myeloma (Immunostaining; PCR/LCR; FISH)
Isolation of circulating plasma cells from blood of patients diagnosed with clonal plasma cell disorders using cell selection microfluidics – DOI: 10.1039/c7ib00183e

Ovarian, Colorectal, Prostate, Breast, Pancreatic (NGS; qPCR; LDR, Capillary Electrophoresis)
Discrete microfluidics for the isolation of circulating tumor cell subpopulations targeting fibroblast activation protein alpha and epithelial cell adhesion molecule
DOI: 10.1038/s41698-017-0028-8

Acute Myeloid Leukemia (Immunophenotyping)
Microfluidics for the detection of minimal residual disease in acute myeloid leukemia patients using circulating leukemic cells selected from blood – DOI: 10.1039/c5an01836f

Pancreatic (Sequencing)
Circulating Tumor Cells as a Biomarker of Response to Treatment in Patient-Derived Xenograft Mouse Models of Pancreatic Adenocarcinoma – DOI: 10.1371/journal.pone.0089474

Modular microsystem for the isolation, enumeration, and phenotyping of circulating tumor cells in patients with pancreatic cancer – DOI: 10.1021/ac401720k

ABOUT

BioFluidica, Inc. is a privately held liquid biopsy instrument company with headquarters and commercial development operations in the heart of the San Diego biotechnology region with R&D operations in Lawrence, Kansas. BioFluidica was incorporated in 2013 with the mission to innovate technology and processes to overcome the technical challenges that hindered the large-scale application of liquid biopsy, especially the use of information-rich rare circulating cells and exosomes for clinical use.

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