BioMarker Strategies
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BioMarker STRATEGIES

Personalizing drug development and treatment with live cells

BioMarker Strategies has developed an innovative approach to enable more accurate prediction of patient response to targeted treatments for solid tumors.

The evolution of personalized medicine is changing the way oncologists diagnose and treat cancer. Approximately half of all compounds currently in development are molecularly targeted drugs. The pharmaceutical industry is also rapidly moving beyond the development of single-target agents guided by single-biomarker tests, toward the development of drugs and drug combinations with complex mechanisms of action that will benefit from pathway-based diagnostics derived from an increasing understanding of the complex signal transduction network of living cells.

Currently available biomarker tests for solid tumors primarily rely on dead, fixed tissue samples. Tests based on these static samples can reveal relevant mutations and guide general therapeutic approaches, but are generally not useful for understanding mechanisms of acquired resistance. For this reason, they are not optimally predictive of individual tumor response to targeted treatments.

> "Our mission is to help make personalized medicine more of a reality"
>
> Jerry Parrott, President & CEO

BioMarker Strategies has developed a system that has the potential to usher in a new era in which live, unfixed solid tumor tissue can be routinely and rapidly analyzed, in contrast to the current reliance on primarily dead, fixed tissue samples that provide limited insight into the biological complexity of solid tumor cells. The company's patented SnapPath Cancer Diagnostics System enables the use of predictive tests that guide targeted drug development and treatment selection for patients with solid tumor malignancies. "Our mission is to help make personalized medicine more of a reality for these patients," said BioMarker Strategies' president and CEO Jerry Parrott.

Live cells improve predictions

SnapPath is the only diagnostics system that can generate purified populations of live solid tumor cells from live, unfixed samples in an automated and standardized manner. The system preserves the molecular integrity of these living cells for ex vivo exposure to targeted therapies. This enables the generation of highly predictive biomarker tests, known as PathMAP Functional Signaling Profiles.

"The dynamic information available only from live cells is required to understand initial responses and the acquired resistance that too often develops in the treatment of cancer," said Parrott. "This understanding is necessary for accurate prediction of individual response to targeted treatment of solid tumors."

SnapPath is unique in its ability to automate and standardize functional ex vivo profiling to capture the dynamic and predictive signaling information available only from live solid tumor cells. Ex vivo biomarkers are dynamic molecular markers, such as phosphoproteins, that are evoked from live tumor cells after removal from the patient. Unlike static biomarkers, which are detected from formalin-fixed, paraffin-embedded tumor samples, ex vivo biomarkers enable true functional testing of cancer cells and can reveal important elements of tumor cell biology, including signal transduction circuitry.

"Much of the early work in ex vivo biomarkers was pioneered in leukemia and lymphoma," said Parrott. "Our groundbreaking live tumor testing platform extends this work to solid tumors and enables a new class of biomarkers, potentially including ex vivo-based companion diagnostics."

Fast, automated and versatile

SnapPath is a highly customizable, automated, fluidics-based system. It consists of a compact benchtop instrument and a single-use cartridge (**Fig. 1**). The system generates purified populations of live solid tumor cells from a fine-needle aspiration biopsy, surgical excision or other live, unfixed tumor tissue sample. SnapPath is compatible with any solid tumor for which live tissue samples are available.

The process begins with the loading of live tissue samples onto the single-use cartridge, which is then snapped into place on the SnapPath instrument. The automated process takes as little as 30 minutes and involves five steps: dispersion, enrichment, distribution, modulation and stabilization.

In the dispersion step, the live solid tumor tissue samples are mechanically disaggregated into smaller, more homogeneous populations of living solid tumor cells. Following disaggregation, non-tumor cells such as red blood cells and white blood cells are removed from the sample using antibody-coated magnetic beads, thereby enriching the tumor-cell population to facilitate downstream molecular analysis. The live cells are then distributed via automated fluidics into multiple test chambers for ex vivo modulation.

Following distribution into test wells on the cartridge, the live solid tumor cells are modulated by exposure to targeted therapies to evoke new biomarkers. The last automated step involves stabilization of the modulated live cells using the technique appropriate to the analytical method of choice. The SnapPath system is agnostic to the type of analytical technology used.

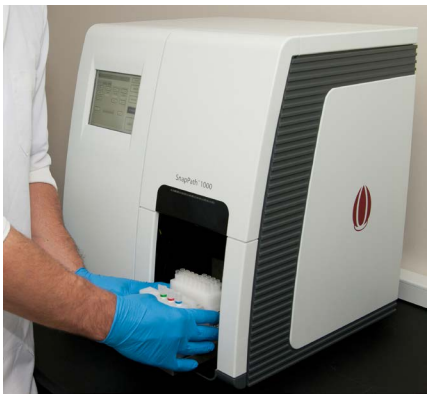

Fig. 1 | The SnapPath Cancer Diagnostics System. The system enables the use of predictive tests that guide targeted drug development and treatment selection for patients with solid tumor cancers. Patents covering the SnapPath system have been granted in the United States, Europe, Australia, Canada, Hong Kong, Japan and Korea.

An algorithm is then applied to the off-platform analytical result, yielding a Functional Signaling Profile, which provides predictive information about drug response and resistance that cannot be obtained through DNA-based or RNA-based analysis of dead fixed-tissue samples.

"The SnapPath system is ideally suited to assess response to targeted drugs in development for solid tumor cancers in preclinical studies involving patient-derived xenografts and other model systems, and in early clinical studies to assess pharmacodynamic changes in the solid tumors of individual patients," said Parrott. "Our business development efforts are directed toward providing research services to companies developing targeted therapies for these patients. We expect to enter into our first commercial research services agreements in 2018."

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