Novel RNA gene expression signatures advancing companion diagnostics for cancer

RNA-based complementary and companion diagnostics could identify more patients able to receive clinical benefit from cancer therapeutics and increase response rates. Employing its expertise in RNA gene signatures, GeneCentric is developing these novel diagnostics through strategic partnerships with biopharma and diagnostics companies.

Innovative therapeutic approaches, such as immune or targeted therapies, have revolutionized patient care, but only a subset of all cancer patients have realized dramatic improvements in long-term survival, partially due to a lack of precise tools to select the most appropriate therapy for the patient. At the same time, many promising cancer therapeutics fail in late-stage clinical studies even though there are pronounced effects seen in a subset of study participants, suggesting greater success may lie in improved diagnostics for treatment selection.

GeneCentric recognized the limitations of the existing treatment selection approaches, such as DNA mutational analysis. Building on the pioneering work of its academic co-founders, including Charles Perou (co-inventor of the Prosigna breast cancer test), GeneCentric has become the leader in RNA bioinformatics technology to develop next-generation RNA-based signatures and diagnostics. Through this, GeneCentric has established strategic partnerships to develop and commercialize its novel tests to address the limitations of the current diagnostic approaches.

“While DNA testing has produced many precision medicine solutions, this doesn’t necessarily mean the DNA mutation is the oncogenic driver of tumor activation,” said Michael Milburn, President and CEO of GeneCentric. “DNA mutations don’t fully account for the downstream complexity leading to tumor response, and some patients without a known mutation of interest have responded to a targeted therapy.”

For example, studies have shown that patients with the BRAF V600 mutation have vastly different response rates to vemurafenib therapy: patients with the BRAF V600 mutation have a 5% response rate, whereas patients with colorectal cancer with the same mutation who received the same treatment had a response rate of only 5%.

“DNA is more of a signpost that a patient will respond to a drug, while RNA is comparable to a high-resolution GPS map. We’re developing RNA-based tests to uniquely provide a dynamic range for how well a patient is going to respond to a particular therapy,” said Milburn.

RNA diagnostics better reflect the phenotype or inherent expressed traits of a tumor, including genetic drivers and the immune environment. A diagnostic that incorporates these diverse aspects of the tumor yields higher fidelity in response prediction and can result in a larger population of patients that better responds to a drug.

RNA expression signatures allow for improved patient selection of new and existing targeted and immuno-oncology therapeutics. The signatures are also leveraged for identifying other cancer types harboring the same activated pathway that may be sensitive to the therapy.

**Development pipeline**

GeneCentric’s platform leverages extensive, publicly available gene expression datasets, along with the company’s proprietary datasets and machine learning, to develop robust gene signatures that predict drug response but are also built with an eye towards clinical development. GeneCentric’s broad pipeline of novel RNA signatures stems from its proprietary RNA-based Tumor and Immune Microenvironment (rT(I)ME) Explorer platform. The process en route to a CDx is depicted in figure 1. The rT(I)ME Explorer platform also provides insight to address the increased interest in combining small molecule-targeted therapies with immuno-oncology agents or multiple agents.

With its extensive pipeline of RNA-based predictive response signatures for cancer therapeutics, GeneCentric works collaboratively with biopharmaceutical partners to advance cancer programs from pre-clinical stage through commercialization.

**The rT(I)ME Explorer platform, combined with GeneCentric’s deep tumor biology and clinical knowledge, can be applied at all stages of cancer drug development: discovery and translational research, clinical evaluation, commercialization, repositioning clinical-stage compounds and identifying new indications for existing drugs.**

- Targeted therapy predictive response gene signatures: provide a more complete measure of sensitive tumors compared to DNA alterations.
- Immunotherapy predictive response gene signatures: capture a more complete picture of immune response than existing markers.
- Rational combination strategies guided by gene signatures: sharpen/design combination strategies.
- Fit-for-purpose real world evidence cohorts: drive and accelerate clinical trial assay prototype development with exceptionally curated real world evidence studies.
- Signature-guided indication expansion: leverage the gene signature for the lead indication to find other suitable indications.

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