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ResponderID: the future of predictive biomarker discovery is now

Genialis has created ResponderID, a machine-learning platform that unravels complex biological signatures from patient data to deliver next-generation biomarkers for diagnostic and drug development.

The promise of targeted cancer therapies relies on ensuring that they reach the right patients: those with the tumor-associated biological changes targeted by a given therapeutic. Achieving this goal requires finding biomarkers that capture the relevant biology, and which can reliably guide treatment decisions that lead to better patient outcomes. That's why Genialis is dedicated to developing next-generation biomarkers to realize the full potential of targeted therapies.

More than one million potential biomarkers have been identified, yet fewer than 50 have been cleared or approved by the US Food and Drug Administration for use in companion diagnostic devices. For many new targeted therapies—such as immune-checkpoint inhibitors that show powerful effects in some patients but little or no efficacy in others—there are just a few biomarkers available to inform treatment decisions, and they have limited power to predict how a patient will respond to a given drug.

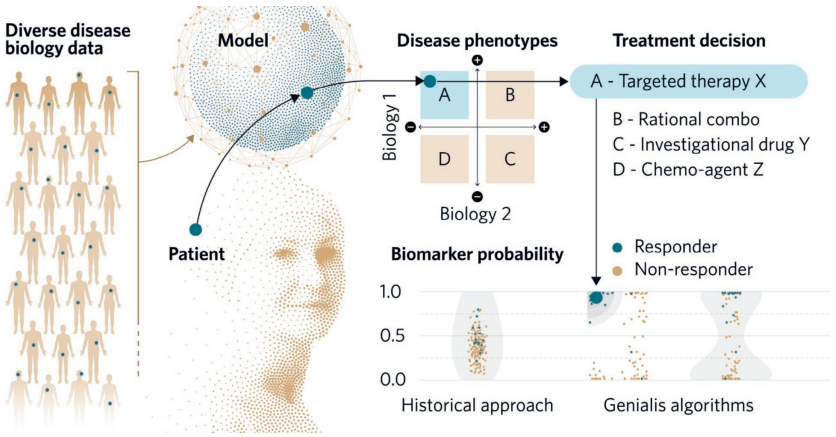

Fig. 1 | ResponderID. The people-first machine-learning platform for biomarker discovery.

Introducing ResponderID

For traditional biomarkers, the output is typically binary (for example, the presence or absence of a given mutation that causes a proteomic alteration) or a measure on a one-dimensional scale (for example, the level of a given analyte in a sample). Genialis' approach is different and embraces the full complexity of the biology driving cancer. ResponderID, Genialis' biomarker-discovery platform, draws on multi-modal datasets, such as RNA sequencing (RNA-seq) data, and employs machine learning (ML)/artificial intelligence (AI) to analyze changes in tens or hundreds of analytes relevant to disease pathology. The proprietary algorithms built into ResponderID identify patterns of RNA transcription that characterize the underlying biology of disease states, and the patient's likely response to therapeutics (Fig. 1). By probing the interactions of the underlying biologies of disease, ResponderID identifies multi-dimensional biomarkers that reflect complex disease phenotypes.

ResponderID is driven by the proprietary Genialis Expressions data engine that analyzes, annotates and harmonizes next-generation sequencing data and clinical metadata. These technologies are ideal not only for creating new, clinically useful diagnostic tools, but also for drug development programs.

In a notable application, Genialis worked with OncXerna Therapeutics to create the Xerna tumor microenvironment (TME) panel, a unique biomarker-driven diagnostic tool for informing treatment decisions in cancer. The Xerna TME panel classifies patient samples into one of four phenotypes based on the immune and angiogenic biologies of the TME.

The Xerna TME panel is an output of ResponderID. The model is an artificial neural network comprised of about 100 genes and takes RNAseq as the input. A key attribute of the ResponderID approach is that each phenotype class predicted by the model has an associated therapeutic hypothesis (Fig. 1). For example, in the case of the Xerna TME panel, the immune and angiogenic biological axes define a quadrant of four TME subtypes: 'angiogenic' (high angiogenic and low immune scores); 'immune suppressed' (high angiogenic and high immune scores); 'immune active' (low angiogenic and high immune scores); and 'immune desert' (low angiogenic and low immune scores). Each TME subtype is predicted to respond differently to drugs depending on their mechanism of action (MoA). TMEs with a predominantly angiogenic profile, for example, would be expected to respond better to drugs based on an anti-angiogenic MoA than an immune checkpoint inhibitor, and vice versa.

Collaborations and clinical trials

To date, ResponderID has been used to test the Xerna TME panel on real-world and clinical trial data from more than 15,000 patient samples representing 11 solid tumor types. Genialis, OncXerna and various other collaborators, such as Exact Sciences, Moffitt Cancer Center and Royal Marsden, have presented data demonstrating the Xerna TME panel's potential utility across numerous solid tumor types, based on retrospective analysis of six drugs (three approved and three investigational) with different targets and MOAs, and five different expression platforms. The Xerna TME panel is being developed as a companion diagnostic, as well as a laboratory-developed test (LDT) for clinical research and trial recruitment.

The Xerna use case demonstrates how Genialis' biology-first approach yields biomarkers that have pan-cancer potential and are applicable to entire classes of drugs rather than just single agents, thus increasing their utility for diagnostic and drug development applications. Further, these biomarkers aim to deliver a complete picture—identifying not just which class of drug is most suitable for a given patient, but also why that is based on the patient's tumor biology. This contrasts with other biomarkers that are either insufficiently predictive to be of much value in guiding treatment decisions, or only provide a yes/no recommendation, where the 'no' recommendations have few, if any, good options.

By providing deep insights into the biology of a patient's disease, ResponderID-generated biomarkers can ensure that clinical trials recruit patients most likely to respond well to the MoA of an investigational drug, increasing the likelihood of trial success. Genialis welcomes discussions with companies in both the diagnostic and pharma sectors about meeting their data-science and biomarker needs to ensure that every patient gets the best possible treatment, today and in the future.

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