

Biomarkers: blazing trails to better therapies

Novartis scientists are working at the forefront of customized therapy to bring the right drug, at the right dose, to the right patient.



Charles Paulding (left) from NIBR and Sven Godtfredsen (right) from Development work together to turn a biomarker discovery into a potential diagnostic tool for patients.

In an atmosphere where pharmaceutical companies are under increasing pressure to provide innovative therapies with the most favorable benefit-risk profile possible, shifting from a “one size fits all” paradigm to a more personalized approach to healthcare becomes of paramount importance. Novartis has been committed to this next revolution in healthcare for years. Customized therapies based on an understanding of a patient’s unique genetic makeup and individual response to a medicine is the best way to bring the right drug, at the right dose, to the right patient. It is the intention of Novartis to be a leader in this patient-centric approach to medicine.

Biomarkers are key

An important component to this customized approach depends on finding and understanding biomarkers. These are measurable biological factors, such as gene activity, proteins, or chemical compounds that can indicate how a disease or therapy is progressing. For instance, the presence of an abnormal protein called Bcr-Abl is a biomarker for chronic myeloid leukemia (CML), a cancer of the blood and bone marrow. Because biomarkers are specific to a person’s individual makeup, they are able to aid in predicting responsiveness to drugs or the likelihood for side effects.

Researchers at the Novartis Institutes for BioMedical Research (NIBR) are helping increase the success rate of new therapies and expedite the drug development process through



A genome-wide human array enables highly powered studies to find biomarkers associated with drug response or drug-related adverse events in patients.

the use of biomarkers. “Biomarker research will help us develop our customized therapies strategy earlier in the drug development process. It provides an important tool in understanding which patients are going to benefit the most from our drugs,” explains Joanne Meyer, Head of Biomarker Development (BMD).

Finding unique biomarkers

“With the development of new technologies we are capable of discovering unique biomarkers that may ultimately have clinical utility for patients,” says Charles Paulding, Senior Group Head, Pharmacogenetic Analysis at NIBR BMD, whose group searches for genetic biomarkers involved in either drug response or drug-related adverse events.

For example, using data from clinical studies, scientists can compare how gene activity differs in a group of patients who responds to a drug versus a group which does not. If scientists have a suspicion of which genes are involved in patient response, they will look at a list of “candidate genes,” which can range from only a few genes to several hundred. When scientists don’t know where to look for a biomarker or they want to perform an unbiased search they conduct a genome-wide scan. With this data in hand, scientists can look for a specific genetic variation that correlates significantly with whether the drug worked or didn’t work in a particular group. This genetic variant can then be used as a biomarker.

This method also applies to finding biomarkers that can predict which patients are likely to

suffer from a serious side effect. A drug may go through rigorous clinical testing and make it to market only to have a rare side effect become apparent after being exposed to a much larger patient population.

Finding biomarkers related to these kinds of side effect profiles gives Novartis an advantage in more reliably assessing the benefit-risk balance of a drug through the development process. In fact, safety biomarkers developed at Novartis, such as KIM-1, a biomarker for kidney toxicity, have been offered to the United States Food and Drug Administration (FDA) to share with the pharmaceutical community to help all companies develop safer drugs. In this way, and with the full support of the health authorities, Novartis is becoming a leader.

From biomarker to diagnostic

“Finding the biomarker is just one challenge but there is also the challenge of using the information in a clinical setting and commercializing a diagnostic,” says Paulding. To address this challenge, it is essential for NIBR to optimally collaborate with Development who provides the clinical and safety expertise to turn a biomarker discovery into a diagnostic tool. Such a diagnostic tool can be a blood or urine test, for example, that a doctor could use to select a patient’s therapy so that the benefit is maximized and the risk is minimized.

“It is critical that development of drugs and diagnostics are fully integrated from the beginning,” says Sven Godtfredsen, Global Program Head, Atherosclerosis & Thrombosis and project collaborator at Novartis Pharma Development. “Scientifically, we’ve known that the genetic underpinnings for certain adverse events have a large impact with a small, specific group of patients. By coupling a diagnostic with a therapeutic, we will be able to improve the benefit-risk profile of a medicine for the great majority of patients. Ultimately, we will be able to more fully realize the goal of customized therapies and better meet patients’ needs.”

A proactive move

As biomarkers take the spotlight, both the FDA and the European Medicines Agency (EMA) have been encouraging biomarker research and have been discussing regulatory processes to handle the resulting data.

Novartis is committed to moving in this direction and has created a new business unit, Novartis Molecular Diagnostics, that is focused exclusively on innovative diagnostics based on the genetic profiles of individual patients. “We are moving proactively now because we recognize that the requirements of drug development,

regulatory approval and the marketplace are changing such that we need to be able to deliver this capability,” says David Epstein, President and CEO of Novartis Oncology and Molecular Diagnostics.

liveglossary

What are biomarkers?

- Biomarkers are measurable characteristics that indicate how a disease or therapy is progressing in patients.
- Biomarkers, for example, are high blood pressure, HIV viral concentration, proteins, and chemical compounds.
- Biomarkers can predict the safety and effectiveness of a drug.
- Finding innovative biomarkers is key to customized therapy.

livefacts

Molecular diagnostics at Novartis

Novartis Molecular Diagnostics will leverage the demonstrated strengths of Novartis in pharmaceutical research, development and commercialization to deliver significant value through two sets of products:

1. Companion diagnostics that help identify patients who are most likely to respond to specific treatments or experience side effects and to inform clinical decision-making related to those treatments
2. Stand-alone diagnostics that inform clinical decision-making and help improve diagnosis, prognosis and outcomes across the entire patient-care continuum, from initial diagnosis through the conclusion of treatment