FOUNDATION FOR THE National Institutes of Health

The Biomarkers Consortium

Advancing Medical Science

BACKGROUNDER

The Foundation for the National Institutes of Health (FNIH), the Food and Drug Administration (FDA), the National Institutes of Health (NIH), and the Pharmaceutical Research and Manufacturers of America (PhRMA) have announced the launch of The Biomarkers Consortium, a public-private research partnership. The consortium will discover, develop, and qualify new biological markers to support new drug development, preventive medicine, and medical diagnostics. Results from consortium projects will be broadly available to researchers worldwide.

Biomarkers are molecular, biological, or physical characteristics that indicate a specific, underlying physiologic state. Biomarkers can be used to identify risk for disease, to make a diagnosis, to assess severity and identify the organs that are involved, and to guide treatment. Biomarkers can also be used in research—clinical studies to assess whether a drug is safe and effective as well as studies to learn more about health and disease. Moreover, biomarkers can help the FDA judge whether drugs are safe and effective at treating disease.

Cholesterol is perhaps the most well known biomarker and is an indicator of cardiovascular health. Other biomarkers include blood sugar, various metabolites, and proteins, plus physical measurements such as temperature and blood pressure, and medical imaging. Every lab test or X-ray doctors order is a marker of what is going on with their patients, showing whether they are healthy, sick, getting better, or getting worse. These examples are only the tip of the biomarker iceberg.

Biological biomarkers for HIV/AIDS include viral load (the number of free virus particles in the blood) and the count of CD4-positive immune system cells. Fasting blood sugar and hemoglobin A1c, a protein that indicates a patient's blood sugar history, are established biomarkers for diabetes treatments.

The Human Genome Project and subsequent proteomics research have generated thousands of potential molecular biomarkers that include genes, proteins, and metabolites. Analysis of these biomolecules has led to new scientific disciplines that indicate an underlying biological state or response (say, to a treatment) by profiling panels of biomarkers.

Increasingly, researchers are appreciating the value of medical imaging as a biomarker. The consortium's first project will be to qualify fluorodeoxyglucose positron emission tomography (FDG-PET) as a biomarker for how cancer responds to treatment. FDG-PET measures glucose uptake by tumors using a radioactive form of fluorine incorporated in a sugar molecule. Tissues that accumulate radioactive glucose are visible through positron emission tomography (PET), an imaging method to detect gamma rays.

Researchers believe that FDG-PET could become a tool for gauging a cancer patient's response to chemotherapy or radiation by accurately measuring tumor metabolism. Physicians will thereby rapidly know whether the tumor is responding to therapy or when to switch therapies to provide the best chance for curing or managing the cancer. FDG-PET can also assist clinical research and drug development, by helping to assess a study subject's response to investigational drugs.

Initially, the consortium will focus its FDG-PET efforts on non-Hodgkin's lymphoma and lung cancer. Non-Hodgkin's lymphoma strikes over 55,000 Americans each year and kills close to 20,000 according to the National Cancer Institute. Lung cancer makes up 13 percent of all cancer cases in the United States. More than 170,000 individuals are diagnosed with lung cancer each year, and close to that number die from the disease. Although it was once thought to almost exclusively be caused by smoking, approximately 13 percent of lung cancer patients have never smoked.

Drug development

Biomarkers are integral to all stages in the process of drug development and, thus, improving understanding of them will have a profound impact on the length of time required, the rate of success, and costs of discovering and developing new medicines. Biomarkers are often used as an initial measuring stick to aid in the selection drug candidates that are more likely to succeed in later stages of development. More understanding of these biomarkers can help improve the rates of success by enabling correct decisions to be made earlier and avoiding expenditure of significant resources and time on candidate drugs that would be eliminated. Biomarkers can help scientists design clinical studies by provided endpoints for measuring an investigational drug's safety or efficacy.

In some cases, biomarkers can also compress the drug development timeline, by several years, by providing an early indicator of treatment effects. For example, in contrast to the average drug development time of eight to ten years, approval of the use of CD4 and viral load biomarkers in HIV/AIDS clinical development led to introduction of an entire class of life-saving antiviral drugs in as little as 3.5 years. Biomarkers can also provide an early indication of a safety issue, or can be used to pinpoint suitable patient populations before the clinical trial begins. This would have the twofold benefit of recruiting high responders for purposes of demonstrating safety and efficacy, as well as eliminating those patients who may be prone to experiencing side effects or adverse drug reactions. Biomarkers can thus play a crucial role in the drug developers' efforts to discover the right treatment for the right patient at the right time.

To be useful in healthcare, biomarkers must be associated in some way to clinical outcome, which requires that biomarkers correlate strongly with currently applied outcome measures (tumor shrinkage, prolonged survival, etc.). These validation studies require a high level of cooperation and coordination between biologists, chemists, clinical researchers, and biomedical engineers. The consortium will foster that environment of cooperation.

Biomarkers are widely viewed as essential for developing tomorrow's treatments, but they also play a role in the re-evaluation of treatment guidelines for existing drugs. For example, biomarkers can help researchers identify which drugs are working for specific patients or patient populations, and uncover or predict drug combination interactions, both beneficial and harmful, that were previously unknown.

Personalized medicine

Biomarkers are one of several key tools in medical science's quest for personalized medicine, or the right treatment at the right time for the right patient. Biomarkers help identify patients who will respond to drugs, as well as individuals who are likely to suffer serious side effects.

Personalized medicine usually involves a test followed by treatment. The breast cancer drug Herceptin is an example of a personalized treatment. Before being treated with Herceptin, women diagnosed with breast cancer undergo a blood test to determine if they will respond to the drug. If the test is positive, they receive Herceptin; if not, they may select from more traditional surgery, chemotherapy, and/or radiation.

Biomarkers take decades to discover and develop into reliable indicators of biological events and phenomena inside a human body. The consortium expects to compress research and development of new biomarkers into a timescale of years, by pooling the efforts across all sectors in the healthcare research and development ecosystem, assembling world-class expertise in chemistry, biology, and clinical medicine, and focusing on important public health needs that can be addressed through biomarkers.

Interdisciplinary approach to streamline adoption

Because biomarkers are so widely applicable to basic biomedical research and drug development, they have generated broad interest from both public and private sectors. The NIH, the U.S. Food and Drug Administration, the Centers for Medicare & Medicaid Services (CMS), and the pharmaceutical, biotechnology, diagnostics, and medical device industries have long recognized the need for interdisciplinary efforts to discover, identify, and validate biomarkers. The Biomarkers Consortium plans to coordinate efforts and harmonize protocols towards biomarker development, thus streamlining the build-up of knowledge on a biomarker that is necessary to support adoption by the medical, scientific, regulatory, and industrial communities.

All of the founding consortium members share a common mission to improve human health. All partners intend to work together to accelerate progress in promising areas of research—either disease-specific or broader scientific areas—and by sharing each sector's complementary insights, perspectives, and priorities. The consortium will initiate projects that address significant public health needs and are most likely to benefit from leveraging the competencies its members and associate research groups. The consortium will assemble teams of experts from across research and development sectors, both public and private, to develop a comprehensive approach for each category of significant biomarker interest, and encourage public and private investment in the most promising projects that will benefit most from public-private partnership.

The Foundation for NIH will manage The Biomarkers Consortium under direction of the consortium executive committee, with guidance from leading scientists within and outside the member organizations, plus input from a public representative and funding partners. The foundation actively seeks additional funding partners to both help support the consortium's operational activities and for individual research projects, each of which has the potential to emerge as a distinct scientific initiative under the consortium's administrative umbrella.

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