National Biomarker Development Alliance (NBDA)

Collaboratively creating the standards for end-to-end, evidence-based biomarker development processes

... to advance personalized medicine

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Current State of U.S. Health Care

U.S. health care costs are projected to increase from $2.7 trillion (2011) to $4.4 trillion (nearly 20 percent of the U.S. GDP) by 2020 (Centers for Medicare & Medicaid Services). The current "illness-focused" model of treating what is often late-stage disease is not sustainable. Due primarily to an aging population, the estimated economic burden of major diseases such as cancer ($280 billion in 2012[1]), Alzheimer's disease ($230 billion in 2013[2]), diabetes ($245 billion in 2012[3]), and cardiovascular disease ($312 billion in 2012[4]) are projected to increase significantly in the coming decade and beyond. This emerging reality could prove catastrophic to the U.S. economy. Biomarkers represent a real and achievable strategy to address this looming crisis by improving the accuracy of diagnosis, disease staging, and rationalization of treatment selection.
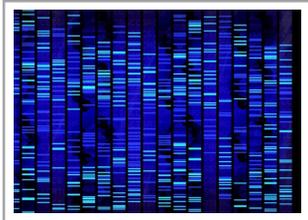
Biomarkers

Biomarkers are essentially biological signals. They are specific reproducible and measurable changes in disease-related (or normal) processes, or responses to therapy. Biomarkers take many forms, from physical representations (e.g., imaging) to biochemical measurements of changes in genes or proteins, or more complex changes in molecular pathways, referred to as "biosignatures."

Precision Medicine

The completion of the human genome project established the basis for sequencing an individual's genome. Today, 21st century genome sequencing is advancing rapidly to define genomic changes in most diseases. It is estimated that more than 1 million human genomes will be sequenced globally by the end of 2014,[5] with exponential future growth projected. The "biological signals" or biomarkers that represent these changes in genes, RNA, proteins, etc. are the foundation for molecularly based, precision medicine. These molecular alterations drive complex functional changes, and what were historically treated as single diseases are increasingly recognized as a number of different molecular subtypes. Precision medicine describes a new generation of biomarker-driven interventions—diagnostics, therapeutics, and preventives—specifically targeted to these molecular subtypes in a patient.

Biomarkers and Precision Medicine

The successful development of biomarkers is a prerequisite for, and the key to achieving, the promise of precision medicine for most diseases. Beyond disease diagnosis, treatment, and prevention, certain types of biomarkers can support disease prognosis, assignment to clinical trials, monitoring therapeutic response, disease risk prediction, and drug development.

The Biomarker Problem(s)

Although biomarker-driven precision medicine is a potentially transformative strategy, the development of validated biomarkers is unpredictable and currently fraught with failure. Despite advances in genomics, proteomics, and the molecular sciences, FDA approval of new protein biomarkers has been essentially the same since the early 1990s: less than 1.5 per year despite more than 1,500 submissions. Today, fewer than 100 biomarkers are routinely used in clinical practice. Moreover, the development of a new drug can take up to two decades and cost a billion dollars or more. While biomarkers are a key strategy for addressing many of these problems and advancing precision medicine, the field is plagued with a lack of rigor, problems of data reproducibility, and myriad other issues. Add to these obstacles the recent entry of advanced technologies such as whole-genome sequencing and a flood of non-FDA regulated laboratory developed tests, plus consumer genomes, and the problem seems almost irreducibly complex. However, one fact is clear: The most critical barrier, and ultimately the reason for failure of most biomarkers, is the lack of broadly accepted and applied standards-based, predictable, end-to-end systems for biomarker development. Solving this problem is the core of the NBDA mission.

> The NBDA was developed not just to relegate the current biomarker development processes to history, but also to serve as a working example of what convergence of purpose, scientific knowledge, and collaboration can accomplish.

The NBDA Is a "Big Idea"

The NBDA is a new nonprofit dedicated to assembling and/or creating the best practices, guidelines, standard operating procedures, etc. (NBDA standards) needed to advance biomarkers through each stage of biomarker development and make the information and knowledge publicly available.

The NBDA Model

Led by an experienced management team, the NBDA will work through networks of stakeholders from all sectors to integrate expertise and knowledge to address and remove barriers identified as critical for each module of biomarker development. Solutions will be in the form of evidence-based standards assembled and/or created through workshops, consensus conferences and transparent collaborative demonstration projects, and/or new research. The results will be available through the NBDA website, publications, tutorials, whitepapers, and public meetings. All of the NBDA's findings and recommended standards will be made available to the FDA and international regulators to inform current policy as appropriate. NBDA's goal is ultimately the implementation of predictable, transparent regulatory biomarker pathways.

Status of the NBDA

The NBDA concept has been nearly two years in development. To identify and understand specific barriers in biomarker development from discovery through translation into clinical trials and ultimately clinical practice, the NBDA sought expert planning input and analysis from local organizations including Arizona State University and others, as well as groups of experts working across all relevant sectors nationwide.

> The audacious goal of the NBDA in the future is to grant a "seal of excellence" for compliant biomarkers and biomarker developers.

Specifically, during the past year the NBDA brought together experts in think tanks and workshops to define a rational NBDA biomarker development concept(see below) and identify major barriers that negatively impact progress in each of the individual phases, or modules. In collaboration with these experts, the NBDA has analyzed each of the biomarker development modules and organized its initial work around four classes of biomarkers: genomic, proteomic, imaging, and complex or multicomponent biosignatures. Going forward, the NBDA will assemble and/or collaboratively create standards for biomarker discovery and development based on the clinical question, sample size and quality, technology platform standards, experimental/clinical trials design, data quality, and analysis. Four demonstration projects, representing the targeted biomarker classes, are in late-stage planning and will be launched in 2014.

Become an NBDA Partner/Collaborator

The NBDA faces a daunting challenge, but one that can and must be met. Failure will mean the fate of biomarker development and late-stage clinical trials will continue to be uncertain, the molecular diagnostics industry will remain an unattractive target for investors, and precision medicine will remain a theoretical ideal, but a largely unattainable vision for most patients. The NBDA illustrates the power of assembling and building knowledge through collaborative networks. Addressing this problem is not the FDA's responsibility. It falls to all of the stakeholders to solve. Contact us to become an NBDA Partner, Collaborator, and/or Supporter. Invest in the NBDA. Share knowledge, sponsor meetings—contribute as appropriate to your interests.
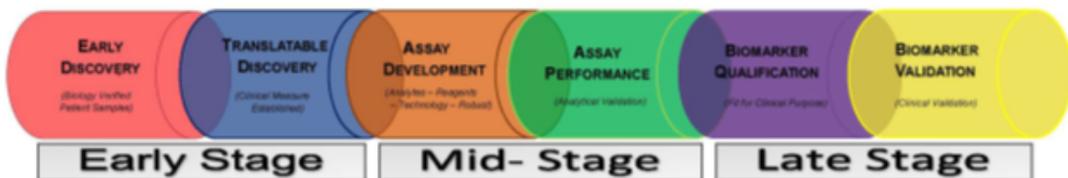
The NBDA's Biomarker Research and Development (R&D) Modules

[1]National Cancer Institute; [2]Alzheimer's Association; [3]American Diabetes Association; [4]American Heart Association; [5]National Human Genome Research Institute

The NBDA Leadership/Management Team

The NBDA team brings unprecedented experience and expertise in all aspects of biomarker discovery, development, regulatory science, and commercialization to achieve its mission. The team has deep experience in major large-scale scientific initiatives, biospecimen and biorepository research and development, bioinformatics and computational modeling, drug and diagnostics development, advanced technologies, and executive leadership. The management construct will operate at scale by building knowledge networks of experts from the full spectrum of biomarker communities. NBDA governance includes steering and scientific advisory committees and a local advisory council.

Anna D. Barker, Ph.D., director and president, works with the NBDA leadership team, external experts, and stakeholders to define the scope of targeted projects and programs for the alliance. She was formerly deputy director of the National Cancer Institute and served as founding co-chair of the NCI-FDA Interagency Task Force and founding co-chair of the Cancer Steering Committee of the FNIH Biomarkers Consortium. Prior to the NCI she served as a senior scientist and executive at Battelle Memorial Institute and subsequently co-founded a public biotechnology company engaged in biomarker development. She is co-director of Complex Adaptive Systems and professor in the School of Life Sciences at Arizona State University (ASU). She completed her M.A. and Ph.D. degrees at The Ohio State University.

Carolyn Compton, M.D., Ph.D., chief medical officer, collaborates with external biomarker experts to plan and execute specific programs and demonstration projects across the complex biomarker development continuum. She formerly served as CEO of Critical Path Institute, director of Biorepositories and Biospecimen Research for the NCI, and chair of the Department of Pathology at McGill University. She is a member of the Complex Adaptive Systems and professor in the School of Life Sciences at ASU. Dr. Compton received her M.D. and Ph.D. degrees from Harvard University.

George Poste, D.V.M., Ph.D., interim chief science officer, identifies key biomarker scientific and development problems and builds networks among relevant biomarker stakeholders to plan and implement solution strategies. He founded and developed the ASU Biodesign Institute and serves as co-director of Complex Adaptive Systems and Regents Professor at ASU. He was formerly chief science and technology officer and president, research and development, of SmithKline Beecham. Dr. Poste received his D.V.M., Ph.D., and D.Sc. degrees from the University of Bristol, U.K. He is a fellow of the Royal College of Pathologists and the U.K. Royal Society.

Kenneth Buetow, Ph.D., director of bioinformatics and data management, oversees development of the NBDA's foundational infrastructure and programs in bioinformatics, data management, and computational programs. He previously served as director of the Center for Biomedical Informatics and Information Technology for the NCI. He is director of the computational sciences and informatics program for Complex Adaptive Systems and professor in the School of Life Sciences at ASU. He received his Ph.D. degree in human genetics from the University of Pittsburgh.

Anne Marie Geary, administrative director, heads planning and implementation of workshops, think tanks, seminars, and all NBDA events. She also oversees the NBDA's financial and administrative programs and website. She previously served in senior administrative roles at Columbia University, including administrative director for the National Center for Disaster Preparedness, director of finance and administration for the Office of the Provost, director of recruitment for the Picker Center for Executive Education, program manager for the FDNY Officer's Management Institute, and assistant dean for curriculum and faculty affairs at the School of International and Public Affairs. Ms. Geary attended Syracuse University.

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