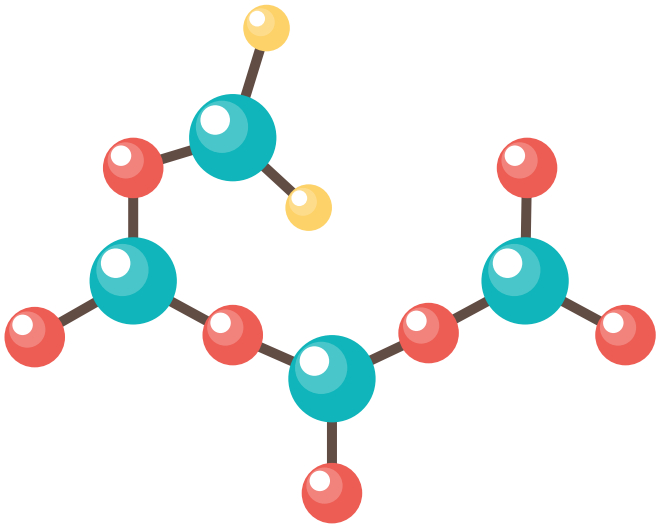
7 TIPS FOR CREATING A COMPETITIVE BIOMARKER DISCOVERY AND DEVELOPMENT PROGRAM



A biomarker is any molecule in the body that can be measured to assess health. Biomarker tests help doctors plan the best care by providing information on these molecular signs of health.

There is a huge amount of biomarker-related literature these days-probably a countless number in your specific field. What will make your program stand out?

We've synthesized some advice from experts in the field (see references below) into 7 critical strategies:

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1. Start with a good rationale

Will your biomarker provide information that will help change a patient's course of treatment? The risk for Alzheimer's disease can be assessed by examining the allele for ApoE, but if there are no preventative treatments available, a diagnostic test may not be very useful.

2. Put in place sound scientific strategies to drive the discovery and validation phase

Do you have a sound program in place to assess the validity of your biomarker? Unfortunately there are no gold standards used in the field for validation, but here are some things to address in your plan:

- **Statistical power** – Address the likelihood of attaining a large enough patient population and a large enough pool of specimens to conduct a meaningful assessment. Remember that factors like prevalence of the marker, tissue availability as well as access to information and clinical trial sites can make the identification and recruitment of patients difficult.
- **Access to broadly representative data** – Address the likelihood of large scale collaboration (and access to samples and data) outside of the boundaries of your institution, providing mechanisms for dealing with (the sometimes confounding) region- or institution-specific socio-ethical and legal norms.
- **Well-justified multi-modal data acquisition** – Measuring multi-modal signatures (e.g. point mutations, mRNA abundance, a particular splice-isoform, a protein, a protein domain, metabolite etc.) can mean the identification of a "composite biomarker" that's much more accurate than a single signature, but prioritize your portfolio carefully so your program does not morph into an expensive fishing expedition.
- **An accurate and appropriate assay** – Showcase data that support the reproducibility and accuracy of your biomarker measurement technology. For instance, is your assay able to definitively distinguish between a low frequency mutation and a sequencing error?
- **Well-defined protocols for sample processing** – Build into your study a clear protocol for how patients are consented and how samples are collected, handled, processed, transported and stored. Even small differences in the way specimens are treated can yield massive differences in a biomarker test result.
- **Standardized and robust data analysis workflows** – Put in place sophisticated data management and analytic systems that can demonstrably correlate the range of biomarker data with the specific event or outcome that is being studied.
- **Well-thought out clinical study design** – Ensure that the design of your study (e.g. a trial in biomarker-enriched populations vs. a non-restrictive trial) will generate a robust and appropriate dataset in the shortest amount of time and cost-effectively.

3. Demonstrate translational feasibility as early as possible

- **Anticipatory pharmaco-economic data points** – With an ultimate goal to reach routine adoption of your biomarker, build into your study data capture fields that can be analyzed to evaluate economic efficiency to the system.
- **Feasibility in the clinical setting** – Build into your study data capture fields to assess the usability and performance of your biomarker in the real-world setting. For instance, physiological, pharmacological and pathological features of patients (e.g. underlying comorbidities) can make the performance of the biomarker in the real world clinical setting more complex.

4. Choose commercialization and development partners strategically

Working with a drug company

- Diagnostics that result in targeted use of a comparatively well-reimbursed treatment can reduce revenue and/or profit margins of drugs that are already on the market. Going after a drug company as a co-development partner in this scenario may be challenging.
- Unlike the drug developer that can count on a lifetime of revenue from chronic treatment of a patient, the diagnostic developer only gets paid per test. The potential profits from a partnership are much higher for the drug developer but pharma companies can be hesitant to put up a comparatively higher R&D investment.

Working with a payor

- Payors such as insurance companies are interested in maximizing effectiveness of treatments (or preventative measures) to help minimize pay-outs. Even though this interest can at times conflict with the interests of a drug company with a reimbursed product, there are increasing examples of insurance companies and other payors providing support for biomarker R&D activities that may help facilitate cost-effective decision making down the line.

5. Chart out an anticipatory regulatory path

Biomarker tests are usually thought of as a diagnostic. Broadly speaking, the inventor of a biomarker can choose between two regulatory paths: Will you choose to sell a **diagnostic kit** (a packaged product) or will you sell the in-house performance of the test as a service (a **laboratory-developed test or an LDT**). In the United States, diagnostic kits must obtain pre-market regulatory clearance from the FDA. LDTs are not typically reviewed by the FDA but they are subject to the test performance standards of CLIA (Clinical Laboratory Improvement Amendments).

Note that the diagnostic kit route has not been the path of choice for most biomarker tests, perhaps because it is the costliest and most time-consuming option. However, meeting the high standards of a regulator like the FDA can go a long way toward convincing clinicians and payers of a test's validity and clinical utility. In comparison, more than 1000 biomarkers are currently offered as homebrew tests in central laboratories across the US with predictably smaller adoption rates.

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6. Outline a plan to educate clinicians, payers and patients

Make sure you have a plan in place to increase physician awareness and buy-in regarding the use of your biomarker once it is on the market. This could involve partnerships or parallel R&D programs to create visualization and communication tools aimed at educating docs about your test or traditional sales/marketing tactics (e.g. training groups, lab-specific educational materials, a dedicated sales force going to targeted clinical labs etc.).

7. Pre-conceive systems for post-market quality control

Think about how you will roll out and monitor the quality of your test to ensure it is robust in terms of accuracy, specificity and sensitivity, and that it handles consistently across multiple sites in the hands of multiple technicians.

Thanks to these great sources of information and insights:

"A Perspective on Challenges and Issues in Biomarker Development and Drug and Biomarker Codevelopment" by Sheila E. Taube et. al. 2009

"From Biomarkers to Diagnostics: The Road to Success" by Eric Groves, Quintiles, 2010

"Recent Trends in Biomarker Research and Development" by Timothy J. Hagen, 2012

"Personalized Medicine: The path Forward" by Smarth Kulkarni and Philip Ma, McKinsey & Company, 2013

"The Path to Routine Use of Genomic Biomarkers in the Cancer Clinic" by Paul C. Boutros, 2015

"Will Special Interests Derail The Future of Personalized Medicine" By Sujay Jadhav, GoBalto, 2017

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