



Using biomarkers to improve health and disease outcomes

Part 3 of a 3-part series

By Maggie De Pano

The medical community has been moving steadily from the “one drug fits all” standard of drug discovery to a model of personalized and predictive medicine, which tailors therapy or the aggressiveness of a particular treatment option to a patient’s (or group of patients’) unique set of biological characteristics. Molecular biomarkers are playing a critical role in this shift.

Molecular biomarkers refer to specific alterations on the DNA, RNA, protein, or metabolite level that indicate inherent tendencies or signal more immediate changes in a person’s physiological state. Observed in blood or other tissue samples, biomarkers can help researchers re-define diseases into smaller sub-groups and acquire a better understanding of disease progression and treatment response.

Duke Medicine is among the most well-positioned institutions in the world to conduct biomarker research. Its investigators have access to diverse patient populations, potentially tens of thousands of biospecimens, and numerous experts in clinical and translational research, molecular and -omics discovery platforms, bioinformatics, assay development, and regulatory standards and requirements.

“Prior to recent developments at Duke that include the establishment of the DTMI and the initiation of the MURDOCK study, one would have concluded that it was virtually impossible to find all of these resources within any one institution, whether in academia or industry,” said Richard C. Becker, MD, professor of medicine in the divisions of cardiology and hematology and co-director of the DCRI’s Advanced Biomarkers Program. “However, we now possess the means, commitment, and vision to elevate biomarker science to the next level, translating fundamental science to drug development and, in time, safe and effective patient care.”

Despite these capabilities, however, many Duke researchers still navigate the biomarker development process on their own. “It’s a very one-off approach,” said L. Kristin Newby, MD, MHS, associate professor of cardiology and co-director of the DCRI’s Advanced Biomarkers Program. “It’s inefficient and leads to lost opportunities and lack of institutional memory, but perhaps most disappointing, this loner approach limits academic opportunities and collaborations beyond isolated study teams.”

Streamlining biomarker research

With these limitations in mind, the Duke Clinical Research Institute (DCRI) launched an advanced biomarkers program in 2007 to streamline biomarker research. The program is now part of the Biosignatures group, which also provides coordination, centralized operational support, and oversight to the eECG Core Laboratory¹ and the Cardiovascular Imaging Program².

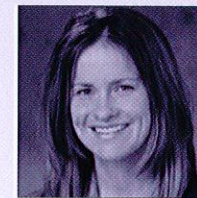
The biomarkers program provides a centralized yet flexible platform that helps investigators determine the clinical, technical, and/or operational resources they need to perform biomarker discovery, validation, and commercialization, and then connects them to those resources.

“Investigators have a very deep understanding of their areas of expertise, but no one understands all relevant expertise requirements,” said Terry Walker, PhD, director for Biomarker Sciences at the Duke Translational Research Institute (DTRI). “To give an analogy, if you’re building a house, you’d typically hire a contractor to interface with the sub-contractors that are experts at certain tasks. This makes the process easier and more efficient than if you were to navigate the entire process yourself. We serve that contractor-type role. We know what ‘tasks’ are important and we know where to find the experts and the resources needed to carry out those tasks.”

¹ Featured in the January/February 2009 issue of the DTMI Newsletter
² Featured in the November/December 2008 issue of the DTMI Newsletter

CMC-NorthEast is a regional 457-bed, non-profit medical center. As the primary healthcare provider in the county with more than 80 percent market share, it gives the MURDOCK study team access to patients through its hospital-based physicians as well as more than 200 providers in its physician network. It is also working to set up electronic medical records for its patients, which, after HIPAA (Health Insurance Portability and Accountability Act) and privacy issues have been addressed, will allow the team to follow up with study participants for decades.

The UNC Nutrition Research Institute (NRI) is studying why there are differences in people’s metabolism and nutrient requirements. Using recent advances in the sciences of nutrigenomics and metabolomics, the NRI is finding ways to use individually-targeted nutrition to enhance brain development, as well as to prevent or treat obesity, diabetes, and cancer. It is part of the world-renowned School of Public Health at the University of North Carolina in Chapel Hill.



“The success and promise of the MURDOCK study takes a partnership and depends upon the support of local residents, physicians, and other healthcare providers.”

— Ashley Dunham, PhD, MSPH, community health project leader of the study

Lakeside Primary Care provides essential health services to effectively prevent, manage, and treat a wide spectrum of health problems. These services include the management of acute and chronic medical problems, pediatric visits, women’s health, school, sports, and travel physicals, on-site diagnostic services, orthopaedic and sports medicine, minor surgery, and dermatology.

The MURDOCK study is helping its study sites by “supporting and encouraging some other research projects in which we are already involved, as well as addressing key health issues in our county and around the world,” said, Robert Kinney, MD, vice president for research at CMC-Northeast. It is also “directing patients who can potentially benefit from access to our services to where we are located,” added Phred Pilkington, DPA, chief executive officer and director of public health at the Cabarrus Health Alliance. Lastly, the MURDOCK study compensates sites for recruitment of each participant.

By partnering with a wide range of healthcare providers within the community, the MURDOCK study is able to reach a diverse population of residents, including the uninsured and underserved. This method allows the study’s designers to fulfill their original goal of creating a population-based registry and biorepository that accurately represents all the residents of Kannapolis and Cabarrus County rather than just those who have access to health care.

“The MURDOCK study is implementing a more thoughtful, broad-based recruitment effort than what you can expect from most trials and registries, which usually just target whomever they can,” said Pilkington. “Working with the public health alliance and the free clinic along with private practitioners not only engages the entire community, it also ensures that the study is representative of that community. It takes into consideration the multi-faceted and highly-integrated nature of health care.”

The MURDOCK study, to date:

The initial phase of the project—Horizon 1—has focused thus far on osteoarthritis, obesity, liver disease, and cardiovascular disease. The next wave of diseases to be studied will be announced soon.

Since the study’s inception, investigators have aggregated existing clinical data and generated molecular profiles from existing biological sample collections. The research teams are now analyzing these data for novel patterns and ‘signatures’ that may predict risk or response to therapy, and reveal underlying pathways with therapeutic potential.

The investigators will eventually validate their findings in prospective trials using the Horizon 1.5 community registry and biorepository, which will be mined for decades to come to answer questions related to the epidemiology and genomics of disease.

The MURDOCK study is often referred to as “the Framingham study of the molecular age,” but the planned registry is significantly larger than the registry which helped determine today’s standards for assessing cardiovascular disease risk. The Framingham study’s original cohort included only 5,200 subjects.

Furthermore, Horizon 1.5 allows for long-term follow up and will accommodate a random sample of 15,000 subjects to reduce selection bias and increase general applicability.

Finally, Horizon 1.5 is collecting and processing blood samples for DNA, RNA, serum, plasma, and urine, while other registry projects typically collect only one type of sample.

