

Bringing Together Institutions and Individuals in Kannapolis, North Carolina, for Discoveries That Make the World Healthier

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As you enter the town of Kannapolis, North Carolina, a billboard reads, "Historians will no longer differ on when the modern scientific age began." This is a bold statement from a historic mill town that, just 7 short years ago, was the site of the largest single-day layoff in North Carolina history. Today, that same site has undergone a phoenix-like transformation and is evolving into a global epicenter of nutrition and health care research. The claim on the billboard becomes understandable once you arrive at the North Carolina Research Campus (NCRC); this is the new home of numerous academic, government, and industry researchers and the David H. Murdock Research Institute (DHMRI). The collective goal of the NCRC is to apply an approach grounded in integrated systems biology to the development of tomorrow's healthier, more nutritional foods; improved lifestyle behavior; and targeted therapeutics.

There have been dramatic scientific advances over the past 50 years. Nevertheless, numerous global challenges continue to face the scientific and human health community, including the declining ability of the pharmaceutical industry to address global health requirements, the growing incidence of obesity and childhood diabetes in the developed world, and shortages of locally produced food in the developing world. Together, these issues have led to the number one health and economic issue facing the world today: hunger and proper nutrition. It is estimated that over 1 billion people were poorly fed in 2009, representing a startling increase from an estimated 870 million individuals who were undernourished in 1970 (Figure 1).

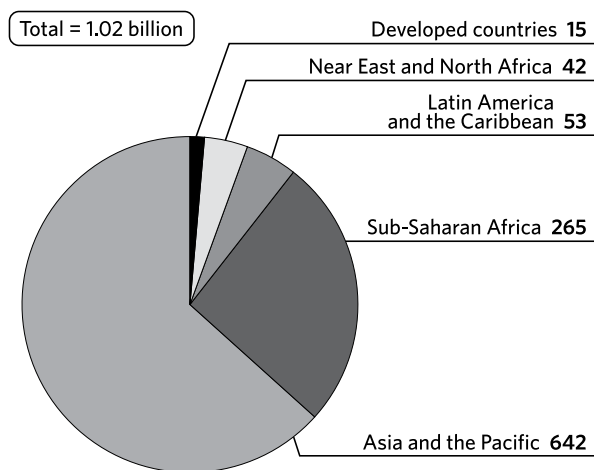
To help reverse this rapid decline in the quality of nutrition worldwide, the biotechnology industry has had a significant impact on crop productivity, but much more remains to be accomplished. Technological advances have helped improve knowledge of the traits needed to improve yields per acre and have increased the nutritional and health value of food crops.

Scientists have been able to use modern research tools to begin the task of identifying bioactive materials in plants that not only have basic nutritional value but also provide therapeutic benefits for the prevention and treatment of human diseases. However, researchers are just beginning to understand how biotechnology can change the way in which

specialty crops can impact human health. While advances in technology and informatics over the last decade have increased knowledge of the relationship between food crops and human health, new tools in understanding the role of proteins and metabolites can now be coupled to genetic data that provide increased understanding and improvement of human health benefits from plant nutrients.

On the drug-development front, the explosion of knowledge generated by the revolution in genetics and biomedical science has not translated as rapidly as initially hoped into breakthrough advances for disease prevention, treatment, and general health improvement. For example, the acceleration of therapeutic discoveries fueled by advances in genetic research over the past decade has been disappointing. The number of novel, first-in-class drug and biologics applications (including those with nutritional and functional-food claims) to the Food and Drug Administration (FDA) has actually declined over the past 10 years, while development costs have soared. Increased costs are driven, in part, by a high failure rate of key studies at the proof-of-concept stage, which bridge preclinical and clinical research. Much of this

Figure 1.
Worldwide Levels of Undernourishment in 2009, by Region



Note. Data are millions of people [1].

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is due to the reductionist approaches that were fueled by the ability to mine the human genome for "targets." Knowledge of gene targets without an appreciation of environmental and physiological factors has not led to new therapies. A deeper understanding of human physiology and pathophysiology is needed to decrease these failure rates.

Although the problem is multifaceted, there is a strong consensus that the discovery-to-development gap has grown wider from a lack of emphasis on product-focused translational applications in pivotal areas such as genomics, epigenomics, proteomics, metabolomics, and bioinformatics. This has led to the growing integration of academia, technology, agriculture, and biopharmaceutical industries in an attempt to address some of these challenges. Simultaneously, several national governments have initiated and distributed large "strategic plans," including the National Institutes of Health (NIH) *Roadmap*. Mindful of the impact of these deficiencies, the FDA developed its Critical Path Initiative to stimulate and facilitate a national effort to modernize the scientific process through which potential drugs, biological products (which could include functional foods and supplements), and medical devices are transformed from the discovery or proof-of-concept phase into therapeutic products. As underscored by the FDA, a redesigned and invigorated enterprise of discovery and product development science could generate new methods to investigate the biological mechanisms of disease and more accurately predict the clinical efficacy and safety of emerging therapeutics. However, although applauded by industry and academia, the Critical Path Initiative has not thus far generated sufficient momentum to accelerate progress in translational medicine. This consideration does not just pertain to new drug therapies as traditionally defined, but the same approaches can be applied to an understanding of nutrition and how this can be used to improve human health.

To confront and provide an innovative approach to these ever-increasing global health issues and to provide global leadership to the emerging paradigm shift in the application of a transdisciplinary systems approach, the DHMRI was established as a nonprofit research institute, built from the ground up, to provide superior-quality laboratory services and developmental tools to scientists on the NCRC and to off-campus researchers from academic, government, and industry sectors beyond the boundaries of the NCRC. As the flagship of the NCRC, the \$100 million state-of-the-art DHMRI occupies over 110,000 square feet of space and provides remarkably well-equipped laboratories that bring together a variety of disciplines under one roof. Furthermore, the DHMRI has hired highly qualified scientists to lead investigative efforts. The growing number of research partners on the NCRC include the University of North Carolina (UNC)-Chapel Hill, UNC-Charlotte, Duke University, North Carolina State University, Appalachian State University, North Carolina A&T, North Carolina Central University, UNC-Greensboro, the US Department of Agriculture, Dole

Foods, Monsanto, LabCorp, the Immune Tolerance Institute, and Carl Zeiss Microimaging. Additional partners are under discussion and will be announced soon.

The research strategy of the DHMRI calls for an integrated, transdisciplinary systems approach intent on understanding pathophysiologic characteristics at the target cellular, tissue, and organ levels in plants, animals, and humans to better understand the systemic integration of the environment and genetics. To exploit recent enhancements in technology, the DHMRI has developed an integrated approach in areas critical to driving this transdisciplinary approach, including genomics, proteomics, metabolomics, light microscopy, histochemistry, transgenics, and nuclear magnetic resonance. To anticipate and meet the demands of its research partners, the DHMRI offers a portfolio of stand-alone and combined products and services.

As part of the critical path initiative of the DHMRI and its partners, it is the belief that the identification and use of traits and biomarkers will increase dramatically and change the way in which agriculture, food, pharmaceuticals, and other biotechnology enterprises, including those at academic institutions and private corporations, understand and contribute to human health and development and the economic viability of related projects and products. For example, in drug discovery and development, the use of well-positioned and validated biomarkers has the potential to shorten development times, reduce costs, and decrease failure rates during clinical development and to guide more-informed patient selection for targeted therapies, all of which lie within the scope of the emerging field of companion diagnostics.

Of the many research projects underway at the DHMRI, 2 significant programs that illustrate the transdisciplinary approaches mentioned above are the MURDOCK study (available at: <http://www.murdock-study.com>) and the Center for Critical Path Research in Immunology (CCPRI).

The MURDOCK study, which is under the leadership of the Duke Translational Medicine Institute, is gaining international attention as a leader in next-generation efforts to reclassify disease through the use of so-called omic technologies (eg, genomics and proteomics) and electronic health records. The study is guided by a multitiered approach that includes retrospective analysis, clinical studies, and a long-term longitudinal phase. Its plans and objectives are to understand the mechanisms of disease and, on the basis of these findings, to discover and develop useful biomarkers, diagnostic tests, and therapeutics that guide the next generation of prevention and intervention strategies. In this far-reaching study design, each component stretches toward incremental knowledge that will illuminate the next horizon of inquiry.

Research partners in this study include Cabarrus Health Alliance, Carolinas Medical Center, the North Carolina Biotechnology Center, Rowan Cabarrus Community College, the UNC Nutrition Research Center, and the DHMRI. The

MURDOCK study has an ultimate enrollment goal of 50,000 patients, and with 3,200 patients already enrolled in the first year, it is well on its way to reaching this milestone.

By capitalizing on these assets, the MURDOCK study could catalyze a cycle that will use molecular techniques, generate and test clinical hypotheses, aggregate and disseminate new knowledge for clinical practice and disease prevention, stimulate novel mechanistic theory and discovery, elucidate and test novel prevention or intervention strategies, discover and evaluate new therapies, and promote wellness in a way that will consolidate emerging knowledge, strengthen the global population and the health care system, and unburden economies.

Located within the DHMRI, the CCPRI serves a unique role at the intersection of academia, government, and industry. Through a collaboration between the Immune Tolerance Institute and the University of California at San Francisco, and with funding, in large part, from the NIH, the CCPRI expects to facilitate the development of diagnostic tests and drugs for a wide range of disease conditions, including allergy, asthma, autoimmune diseases, cancer, cardiovascular disease, immunodeficiency, infectious diseases, and immune challenges following organ and tissue transplantation.

The goal of the CCPRI is to provide a one-stop solution for analysis of the immune system's role in disease by integrat-

ing advanced technology platforms in cellular, proteomic, genomic, and bioinformatic analyses. These platforms are deployed to perform multiple cellular and molecular assays on specimens obtained from patients during clinical trials of emerging therapeutics. The mechanistic data that are generated from these assays are analyzed in parallel with clinical safety and efficacy data by using advanced bioinformatics approaches that leverage new insights at the nexus of emerging life-science and information technologies. The correlation of mechanistic and clinical data will identify high-value biomarkers predictive of the course of a disease, the likelihood of response to an individual drug or biologic, as well as drug efficacy and safety. Such biomarkers will serve to more effectively guide drug development and match patients with therapies that provide them the greatest benefit.

There is no argument that the health care issues facing the world are complex and require a new paradigm of discovery, analysis, and deployment. It is recognized that the answer will not come from a single entity, but through a collaborative effort between academia, industry, and government that relies on a transdisciplinary technological approach. The NCRC intends to be a global leader in providing tomorrow's health care solutions by bringing together institutions and individuals for discoveries that will make the world healthier. NCMJ

REFERENCE

1. Food and Agriculture Organization of the United Nations. Undernourishment around the world. In: *The State of Food Insecurity in the World: Economic Crises—Impacts and Lessons Learned*. [ftp://ftp.fao.org/docrep/fao/012/i0876e/i0876e02.pdf](http://ftp.fao.org/docrep/fao/012/i0876e/i0876e02.pdf). Published 2009. Accessed December 14, 2010.