You Scream, We Scream for the Study of Proteins

THE PARADIGM THROUGH which health care is researched and applied continues to grow in scope as it scales down to mere nanometers. Still in its infancy, the field of proteomics offers registered dietitian nutritionists (RDNs) a glimpse of a future focused on wellness, prevention, and individualized medicine. As part of a larger field of study encompassing genomics, metabolomics, and lipidomics, proteomics promises to ultimately expand health care access to a world of underserved patients, while providing researchers with new tools to fight disease.

Those in the field observe that not enough evidence-based research yet exists for RDNs to fully use some of these concepts in practice, but the principles at hand are guiding present study, making for ample research opportunity. An outgrowth of genomics, proteomics requires a basic understanding of genetics and involves fields from cancer treatment to hunger. The Academy of Nutrition and Dietetics' (Academy's) position on nutritional genomics suggests that RDNs interested in this area of science and practice should acquire a "basic competency in genetics as a foundation for understanding nutritional genomics; proficiency requires advanced knowledge and skills."[1] Staying abreast of new technologies, such as those used in proteomics, will be crucial for RDNs seeking to optimize their patients' health through nutrition science. A basic overview of the field quickly opens one's mind to the seemingly limitless possibilities, particularly those involving cancer research, such as are described in the present article. But given that the technologies enabling these studies can be used across the scope of health care, it's reasonable to expect great change in all areas of nutrition.

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THE STUDY OF PROTEINS

Proteomics is the study of proteins, in terms of expression, structure, and function.[1,2] The term proteome is derived from the word *protein*, which is expressed by a *genome*, and it refers to the sum total of proteins produced by an organism, similar to the way a genome refers to an entire set of genes.[2] Any given human might have more than 2 million proteins within its proteome, with each individual protein carrying out a different function, from catalyzing biochemical reactions and enzymes to defending the body against disease.[2] One goal within the field of proteomics is to develop a map of the human proteome—much like work underway as part of the Human Genome Project—that identifies novel protein families, interactions, and signaling pathways.[2] But whereas the human genome remains fairly constant throughout one's life, the proteome is in a constant state of dynamic flux, as individual proteins interact not only with one another, but with the environment and an individual's diet. Whereas the genome serves as a metaphorical blueprint for the body, the involved proteins are the building blocks and, as such, are decidedly impacted by environmental conditions. As Colleen Spees, PhD, RDN, LD, assistant professor of medical dietetics and health sciences in the College of Medicine at The Ohio State University, Columbus, and author of that school's first graduate course on nutritional genomics, observed, the diet is the most intimate and continuous interaction between a host and its environment during a lifetime.

Spees points out that the proteome changes constantly in response to thousands of intracellular and extracellular environmental signals, varying widely from times of good health to those of disease, and also in response to drug treatments. In this sense, proteomics runs parallel to genomics in that the latter begins with the gene and makes inferences about the gene's products, many of which are proteins. Conversely, proteomics begins with the functionally modified protein and works backward to find the gene responsible for its modification.[2]

Through rapidly developing technologies, researchers are thus able to target individual proteins and deduce their role within a given system, as well as determine what interactions caused them to behave in a particular manner. This paves the way for individualized, point-of-care screening processes. Recent work conducted by researchers at Johns Hopkins Medicine took this approach to Nepal and, while working with children there, demonstrated that levels of certain proteins in the bloodstream can be used to estimate levels of essential vitamins and minerals without direct testing for each individual nutritional factor.[3,4] This indirect method allowed researchers to simultaneously analyze the levels of five vitamins and minerals—vitamins A (retinol), D (25-hydroxyvitamin D), E (α-tocopherol), copper, and selenium—in 500 Nepalese children aged 6 to 8 years.[3,4] The ability to test for such nutrients en mass, with relatively small samples of serum, represents a breakthrough in terms of lowering cost and increasing access to health care screenings.

Micronutrient deficiencies are common in undernourished societies, yet remain inadequately assessed due to the complexity and cost of the existing assays. A plasma proteomics-based approach holds promise in quantifying multiple nutrient–protein associations that reflect biological function and nutritional status.[3,4]

Spees says the growing field of "-omics"—these fields were born in the late 1980s as outgrowths of the International Human Genome Project[5]—is still relatively young, but quickly gaining global attention. The applications for such testing strategies are

easily seen here in the United States as well, where one in six citizens lives in a state of poverty, Spees said, noting that this economic status is often characterized by hard choices such as having to choose between purchasing food and paying rent, utilities, and health care bills. These struggles alone can develop into, or worsen existing, mental and physical health problems, she pointed out. Given that food insecurity is often correlated with poor dietary habits, it stands to reason that these individuals would benefit from more-frequent health care assessments with which RDNs could more quickly identify problems. Cost of health care services remains a barrier; thus, the potential value in lowering cost and increasing access. In food-insecure populations, testing procedures, such as those conducted by the Johns Hopkins team, would allow for the detection of mild and moderate nutritional deficiencies at earlier stages and potentially lead to treatment before the problem becomes more severe.

"Extensive applications of these tools could equate to more accessible health screenings for the underserved, as well as earlier diagnosis of diseases for the public," Spees said. "Basically, the concepts are there and scientists are eager. What is lacking is the necessary funding to develop, implement, and adequately evaluate these tools for clinical use."

MATHEMATICAL MODELS AND MICROSCOPIC MANIPULATION

The technology enabling these kinds of tests is aimed at the subatomic level, and the field of proteomics has attracted more than nutrition experts. Engineers, chemists, and mathematicians are likewise taking work in their fields to new levels by examining proteins. Daniel Morris, Jr, PhD, professor of chemistry at Rose-Hulman Institute of Technology, explained that new devices are being created across the country for just this purpose. Morris' work in microfluidic devices, high-performance liquid chromotography, capillary electrophoresis, and the role of metal ion binding in oxidative DNA damage, led him to a sabbatical at West Virginia University in connection with Protea Biosciences, where he worked on a new tool with which to conduct multidimensional proteome analysis.[6,7] That work on microfluidic and

Know Your —Omics

- Proteomics: The study of protein expression and function.
- Nutrigenomics: The interactions between dietary components and the genome, and the resulting changes in proteins and other metabolites that affect gene expression.
- Metabolomics: Research concerned with the comprehensive characterization of the small molecule metabolites in biological systems.
- Lipidomics: The study of large-scale pathways and networks of cellular lipids in biological systems.
- Allergenomics: The comprehensive analysis of putative proteinous allergens by way of a proteomic strategy.
- Secretomics: A subset of proteomics, the study of all secreted proteins within a cell, tissue, or organism.