



**CENTER FOR EMERGING
ISSUES IN SCIENCE**



Life Sciences Research Office

Report on:
THE FUTURE OF NUTRIGENOMICS

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**LIFE SCIENCES RESEARCH OFFICE, INC.
CENTER FOR EMERGING ISSUES IN SCIENCE REPORT ON:**

THE FUTURE OF NUTRIGENOMICS

Abstract:

The Center for Emerging Issues in Science (CEIS) is a think tank, established by the Life Sciences Research Office, Inc (LSRO) to determine which emerging scientific and technical advances will shift the business landscape and to consider the implications and challenges this new area of science will create for specific industries. Nutrigenomics, the science of how chemicals in food affect health by altering the expression and/or structure of an individual's genetic makeup, was chosen to be the premier emerging issue to be addressed by CEIS. LSRO assembled leading experts in science, technology, and business to consider the implications of nutrigenomics. The CEIS expert panel concluded that nutrigenomics will change the way that food, dietary supplement, and functional food companies do business because it will change the ways that individuals, scientists, and health care providers understand the effects of changes in diet on the individual. These changes will be realized in the context of personalized diets and personalized food and supplement products. The panel concluded that implementation of this technology will require new modes of interaction between agriculture, ingredient suppliers, food manufacturers, diagnostics makers, health care providers, and health insurance providers. The panel developed a framework to describe the interactions of various segments of industry in relation to nutrigenomic advances.

Introduction:

Arguably technological innovation is the trigger that initiates most scientific and business revolutions. New technologies open up new possibilities for scientific exploration, and scientists apply these technologies to build a new vision of the natural universe. Each of these visions is a paradigm and as these paradigms are codified and become part of the common understanding of the general (non-scientific) community, they are the landscape upon which commercial entities grow and succeed. Thus, business and science innovations are intimately linked and both are propelled by advances in technology.

Technologic and scientific advances are made daily, but only a few of these advances will trigger a scientific or business revolution. Examples of technologies that triggered revolutionary change include antibiotics, the internet, wireless communication, polymerase chain reaction (PCR), microchip arrays, freeze drying technology for foods, round-up ready soybeans, etc. Examples of technologies that had little or no impact include cold fusion, vitamin O, and mega doses of vitamin C. Predicting which are likely to trigger a shift in the landscape requires a firm grasp of the technologies, the current state of science, and of the affected industries. "These changes are not foreshadowed by

trends....These kinds of changes in the rules create new trends or dramatically alter trends already in place.”¹

It is difficult to accurately predict which of the many technologies will affect the landscape and by itself predicting change is not enough. Companies will need more information to react to the availability of a new technology. Understanding how a technology will play out, how it will impact their lives or industry and how to integrate it into their business plans can critically effect how well company management adapts to the changes. Management that anticipates how the new landscape will affect their ability to reach and deliver value to consumers will be able to position their companies to quickly adapt to it. Companies that anticipate change survive and thrive; those that only react to change fall behind and lose their competitive advantage.

LSRO, Inc and the Center for Emerging Issues in Sciences

LSRO is a non-profit company that provides objective, independent scientific analysis and advice to decision makers in industry and government. For over 40 years, LSRO has assembled panels of experts to evaluate and report on the state-of-the-science across the biological, clinical, agricultural, and environmental sciences (see WWW.LSRO.ORG). LSRO founded the Center for Emerging Issues in Science (CEIS) to act as a think tank to identify landscape-shifting emerging issues in science and technology and analyze the potential effects on science and industry. CEIS will assemble international experts in the emerging science areas and bring to bear LSRO’s considerable expertise in evaluating the state-of-the-science to help industry anticipate and adapt to the changing landscape.

Nutrigenomics

The first charge assigned to CEIS was to address the consequences of the genomics/informatics revolution, in particular to assess the emerging area of nutrigenomics. Nutrigenomics is the science of how bioactive chemicals in foods and supplements alter the molecular expression and/or structure of an individual’s genetic makeup. The excitement about nutrigenomics comes from a growing awareness of the potential for modifications of food or diet to support health and reduce the risk of diet-related diseases. Thus, by identifying individual genetic predispositions for chronic diseases and the potential for individual response to dietary intervention, these diseases may be effectively prevented by proper dietary intake. Nutrigenomics brings together the science of bioinformatics, nutrition, molecular biology, genomics, epidemiology, and molecular medicine. We are using the term nutrigenomics to encompass the fields of genomics, epigenomics, post-translational modifications, proteomics, and metabolomics. CEIS convened a group of experts² in science, technology, and business to explore nutrigenomics and to brainstorm the challenges this new area of science will create, especially in the area of personalized nutrition, diets, and supplements. The conclusions and recommendations of this expert panel are summarized herein.

¹Joel Arthur Barker, *Future Edge: Discovering the New Paradigms of Success*, William Morrow and Company, New York, NY, 1992.

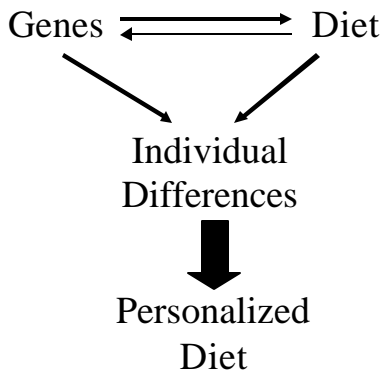
² The Expert Panel member biographies may be found in the appendix.

The great success of the 20th century was identifying the essential nutrients and their deficiencies. This allowed for differential diagnosis of deficiency and universal recommendations. Nutritional advice and public health recommendations are made on a population-wide basis, based on statistical norms. The advantages of this process are in the simplicity of the recommendations and the success can be measured in decreased deficiency-disease incidence and increased lifespan. However, viewing the benefits of diet as solely preventing nutrient deficiency is much too limiting; diet plays a wider role in either promoting health or preventing disease.

It is apparent that one size does not fit all. Thus, as we have become aware of the limitations of population-wide advice such as the food guide pyramid, second generation approaches have proliferated with pyramids tailored for children, the elderly, ethnic groups, vegetarians, etc. Although these attempts are steps in the right direction, they do not take full advantage of the breakthroughs in biomedical science.

Fortuitously, this realization has come at a time of great expansion of knowledge, the genomics/informatics revolution. The achievement of sequencing the genome has spurred efforts to characterize the proteome (the proteins expressed by the genome), the metabolome (the metabolic entities present in a cell, tissue, organ, organism, and species that are produced during different states of health and disease), the epigenome (DNA modifications that alter genome function but do not change DNA sequence), and other post-translational modifications that influence gene expression. The great challenge of the 21st century will be to integrate this scientific understanding and provide diet, lifestyle, and drug recommendations to the individual to maintain health and prevent diseases rather than simply develop diagnostics and drugs to identify and attempt to cure them once they have emerged.

What will all this information mean to science, to industry, and to the individual? The sum total of this knowledge will be a better understanding of the influence of inheritance and environment on individual health and performance. We will better understand what role diet and environment play on gene expression and what limitations gene expression imposes on an individual's responses. This opens the opportunity to have personalized medicine and personalized nutrition (Figure 1).



We have begun to assemble the capabilities to profile (genomic, epigenomic, proteomic, metabolomic) each individual. Using these profiles we can understand which drug will be effective, what levels might be toxic, whether they should be eating a low carbohydrate diet, whether the standard nutritional advice will be effective or counter-effective, or whether they have special nutrient requirements. This information can allow healthcare professionals to provide personalized advice and avoid the inherent inadequacies of population-based recommendations. This goes far beyond the level of the new personalized food guide pyramid, which is inherently still population-based advice, and will bring health-promoting guidance down to the level of the individual. We have already begun to see Internet-based companies providing individual genomic profiles and advice optimized for that profile. The current version of these services may be more fluff than substance, but if it is properly developed by reliable and competent companies and based on sound scientific data, it holds great potential to reshape the industry.

The expert panel embraced this view of a personalized, health-promoting future, then identified and prioritized many areas of nutrition that are ripe for this type of approach, developed a multi-partner model that will allow industry to take advantage of this approach, and identified the challenges to bring it to fruition. After an extensive review of the evidence for individual responsiveness to dietary intervention, the expert panel was convinced we are on the cusp of a business revolution. Some of the expert panel conclusions/recommendations are included below:

- There is already evidence for consumer demand for personalized information, as long as consumers feel they have control of the information. The “worried, wealthy well” will likely be the early adopters of personalized dietary advice and personalized products; other consumer segments will follow. The future industrial leaders will be those companies that are capable of simultaneously making those personalized foods preferred. This type of product will support higher margins than conventional functional foods.
- There is good evidence that nutritional intervention at the earliest possible points in the life cycle, e.g. during pre-pregnancy, pregnancy, early infancy, etc, will have profound effects on long term health. Epigenetic and other post-translational mechanisms are the wave of the future; however the implications of life-long effects of dietary choices particularly early in life could drive rapid adoption of certain segments of the consumer population to dietary choices that are a reflection of that heightened nutritional susceptibility of early childhood.
- Companies will NOT have to manufacture hundreds of different products tailored to each type of individual. The panel described a business model for personalized dietary products as an analogy to a shoe store. Rather than custom fitting shoes to each individual customer, as is possible with the luxury sector, the mass market is designed to produce and sell a limited number of stock products nonetheless ‘tailored’ to various customer needs and preferences. Ultimately the number of products may

increase and diversify as medical science discovers further nutrigenomic capacities and production advances combine to provide a wider range of products and thus the best fit for the customer's needs.

- Personalized diet will require a strong diagnostics component. The diagnostic technology sector is already available but needs refinement to accurately identify the health status of the healthy and thus be more consumer-friendly. As well as being critical to determining each individual's needs, diagnostics will be important in providing the customer feedback about efficacy. Positive reinforcement and a sense of accomplishment has been a critical fault of many health promotion/disease prevention programs. Compliance and consumer interest wanes over time without it.
- This new personalized dietary advice will likely be mediated through some sort of health care provider (HCP) or other trusted source. The HCP will help interpret the diagnostic results, suggest personalized dietary advice, and provide monitoring feedback. It is unlikely that this HCP will be a physician, but perhaps pharmacists, nurses, dietitians or trained paraprofessionals will fill the need. One model is a company like Pharmica that has begun selling healthy foods and supplements and training pharmacists to become advisers. Health maintenance organizations (HMOs) could also be involved as HCP and could even sell the products as one of their services. HMOs could wrap this into their existent health promotion efforts and attract the worried, wealthy well as clientele.
- Personalized diet will only work if it is based on sound science. The dietary supplement and health food industry has heightened consumer wariness about reliability of claims and product performance. A new business paradigm based on validated personal assessment such as envisioned herein will not be based on promise, but on actual personal demonstrations of efficacy and hence will not be extremely susceptible to bad press and consumer backlash.
- Personalized diet will depend on a strong bioinformatics component. Most of these technologies are already available but will require serious commitment to development and refinement to be fully operational. Analyzing the entire genome or metabolome of an individual will currently overwhelm the available informatics capabilities. Moreover, the manifold single nucleotide polymorphisms (SNP), metabolic markers, etc have yet to be completely identified and correlated with individual health status and disease susceptibility. However, subsets of the data are available and could be made into actionable recommendations now. We are close to implementing valuable personalized health promotion advice. Refinements and future development will include more markers, integrate more information, and identify more potentially susceptible health outcomes.
- Not all products will be immediately amenable to this personalized diet approach. Consumer acceptance in the short term will presumably depend on the proper choice of product that has consumer 'permission' to be individualized (orange juice , probiotics drinks, etc)

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- Not all health and physiologic targets have enough data at present to benefit from the new health-care paradigm/approach. The expert panel reviewed and prioritized health outcomes and bioactive substances. Health and physiologic endpoints that are best positioned to take off include cardiovascular disease, cancer (prostate, colon, and breast), type II diabetes, taste acuity, and inflammation. Next in line are lactose intolerance, obesity, taste reception, immune diseases, and allergies. Also meriting consideration for health promotion through nutrigenomics are dementia, Alzheimer's disease and other memory and cognition disorders, macular degeneration and cataracts, osteoarthritis, muscle atrophy, and gut function.
- No one company or industry will be able to get their nutrigenomic products off the ground alone. Marketplace success will require cooperation and communication among various industrial segments, though it is not certain how different segments will contribute. The expert panel developed a couple of models for implementation. These include participation of food producers, food manufacturers, dietary supplement manufacturers, diagnostic companies, health care providers, HMOs or health insurance companies, and venture capital or other investors. Similarly, scientific advances of the required knowledge will need the integration of different scientific expertise and the creation of scientific consortia to develop these emerging concepts into a mature field.

The Next Steps

CEIS will reconvene the expert panel to expand on this analysis and consider detailed implications and challenges for one or more of the most promising health outcomes as identified in the first meeting. The panel will be expanded to ensure coverage of the various aspects of science, business, regulation, and investment.

Select sponsors will be invited to become subscribers to this service. Subscribers will be invited to attend the meeting and to receive the final report. Attendance to this meeting will be limited and initially only subscribers will have access to the outcome of the meeting. Ultimately, a summary of the CEIS report may be published by LSRO.

APPENDIX

BIOGRAPHIES OF EXPERT PANEL FOR NUTRIGENOMICS MEETING

Steven Clarke is Director of Science Research, McNeil Nutritionals, New Brunswick, New Jersey. He served as Chairman, Department of Human Ecology, The University of Texas-Austin; M.M. Love Chair of Nutritional, Cellular and Molecular Sciences, University of Texas at Austin (1995-2002); Director of the Nutrition Consortium for Colorado State University and University of Colorado Health Sciences Center; and, Assistant Professor, Department of Food Science and Nutrition, Ohio State University.

His honors include, Department of Human Ecology Outstanding Research Award (2000); Outstanding Alumni Award, Department of Food Science and Human Nutrition, Michigan State University (1997); and Outstanding Paper, “Regulatory of gene expression by polyunsaturated fats”, American Oil Chemist Society (1992). He also served on the Editorial Board of the Journal of Nutrition and participates in several Nutrition Center Advisory Committees. He organized many symposia and meetings on nutrient-gene interactions; served as the Industry Liaison Committee member for the American Society for Nutritional Sciences; and advised several companies including AstraZeneca and Galileo Labs. He published more than 150 book chapters, reviews and journal articles on nutrition, gene expression, and molecular methodologies.

Bruce German is a professor in the Department of Food Science and Technology, University of California, Davis. He has published more than 200 documents. He belongs to the American Society of Nutritional Science and the Institute of Food Technologies. He served as Chair of the ILSI Functional Foods Biomarkers Task Force and the Steering Committee of the European Union Concerted Action PASSCLAIM to establish the criteria for claims on foods.

He held several academic positions since 1984 as Postdoctoral Research Associate, Cornell University; Assistant Professor, Associate Professor and Professor at the University of California, Davis. He headed the Molecular and Metabolic Regulation Group, Nestlé Research Centre, Lausanne, Switzerland. His awards and honors include: John E. Kinsella Endowed Chair, University of California, Davis (1998); Visser Visiting Professor, Wageningen University (2001); Trout Visiting Scholar Michigan State University (1999); and Mention D’Honneur Du Jury, Academi Morim, France (1995).

John Finley is Chief Technology Officer at A.M. Todd, Montgomeryville, PA. From 1999 to 2004, Dr. Finley had been serving as a fellow at Kraft Foods. From 1983 to 1999, Dr. Finley held a number of senior positions at Monsanto and Nabisco. Dr. Finley was appointed as an Advisor to Sepragen on February 4, 2000. He has led several major research projects including the safety evaluation and GRAS petition for SALATRIM. Dr. Finley is associate editor of the *Journal of Agricultural and Food Chemistry*. He has been instrumental in developing two International Congresses to standardize methods to assess activity of antioxidants in foods and their bioactivity.

Randy Jirtle is Professor of Radiation Oncology and Associate Professor of Pathology, at Duke University Medical Center, NC. His laboratory investigates the evolution and regulation of imprinted genes involved in human behavioral diseases and cancer. Professor Jirtle received his Bachelors degree in Nuclear Engineering, and his Masters Degree and Ph.D. in Radiation Biology from University of Wisconsin-Madison.

Arnold Kahn currently serves as Treasurer and member of LSRO's Board of Directors, representing the affiliated American Society for Bone and Mineral Research. He is a Professor in the Department of Cell and Tissue Biology, University of California at San Francisco, where he is a member of the graduate program in Biomedical Sciences and Oral Biology and the Longevity Consortium. He also serves as an associate editor of the Journal of Gerontology. He is the author of more than 110 scientific papers. The Hebrew University in Jerusalem honored him with the Cabakoff (2002) and the Lady Davis (1996) Visiting Professor awards. He served as Secretary/Treasurer of the American Society for Bone and Mineral Research (1991-1994; re-elected 1995-1997) and as Vice Chair and Chair of the Gordon Conference on Bones and Teeth (1985-1986).

Mitchell Kanter is Director of Nutrition/ Director of Venturing at Cargill Food Technology Development Center, Wayzata, MN. Dr Kanter has held previous positions with Quaker Oats Company where he served in various capacities, including Director of the Gatorade Sports Science Institute, and Director of the Quaker Oats Health Institute. Prior to joining Cargill in 2000, Dr. Kanter served as the Director of Nutrition Science for the General Mills Company in Minneapolis, MN. Dr. Kanter received his Bachelors degree in Health Education from Queens College in New York City, Master Degrees in Exercise Physiology and Nutrition (Queens College) and his Ph.D. in Physiology from The Ohio State University.

Gilbert Leveille manages Leveille Associates. He is Past President, the Charles Valentine Riley Memorial Foundation and serves on its Board of Directors. He belongs to many professional organizations, including the Institute of Food Technologists (President, 1983-84), the American Society of Nutritional Sciences (President, 1988), the American Society of Clinical Nutrition, and the American Chemical Society. He participates in many professional symposia, lectures widely, has several patents and has published more than 300 scientific papers and books including *Nutrients in Foods* in 1983 and *The Setpoint Diet*, a New York Times non-fiction best seller, in 1985. He was Vice President of Technology, Food and System Design at Cargill, Inc. and also served as Cargill's Director of the Food Technology Development Center for North America. Dr. Leveille currently serves as Senior Consultant for Cargill, Inc.

Jose M Ordovas is Professor of Nutrition and a Senior Scientist with the USDA Human Nutrition Research Center on Aging (HNRC) at Tufts University in Boston, Massachusetts where he also is Director of the Nutrition and Genomics Laboratory, HNRC. His major research interests focus on the genetic factors predisposing to cardiovascular disease and their interaction with the environment and behavioral factors

with special emphasis on diet and more specifically the different effects of n-6 and n-3 fatty acids. Professor Ordovas completed his undergraduate work in chemistry, his graduate work in biochemistry, and received his doctorate in biochemistry from the University of Zaragoza, Spain.

Tim Osborne is Professor and Chair of Molecular Biology and Biochemistry at the University of California, Irvine. His research program is focused on the regulation of cholesterol and fatty acid metabolism in higher animals, with a focus on regulation of the genes that encode strategically positioned proteins involved in biosynthesis, uptake, and efflux/secretion of cholesterol and fatty acids. Professor Osborne received his Bachelors from UC, Santa Barbara and his Ph.D. from UC, Los Angeles.

Terry Quill currently serves as a member of LSRO's Board of Directors, representing the affiliated International Society of Regulatory Toxicology and Pharmacology. He is a toxicologist, attorney, and a Partner in Washington, DC office of Duane Morris, where he provides legal counseling and litigation services regarding environmental and regulatory issues. His practice focuses on the legal and technical matters associated with potential human and environmental exposures to toxic substances. He is experienced in environmental and toxic tort litigation, administrative hearings and appellate challenges to rulemakings. He also is a Past-President of the International Society of Regulatory Toxicology and Pharmacology and Chair of the American Bar Association Special Committee on Science and Technology.

Ann Rose founded ViCro, a consortium of professionals credentialed in the disciplines required for biomedical translational research, i.e. development research required to establish a clinical proof-of-concept, where she is Principal and CEO. Founded in 1998, the Company assists biopharmaceutical companies and academic institutions in evaluating preclinical work on their biomedical inventions for clinical testing. ViCro files the IND's and conducts the Phase I/IIa clinical trials.