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# Nutragenomics: Nexus of Value for the Nutraceutical Industry

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"The field of nutragenomics, which examines the relationship between genes and food, promises to explain why some people who gobble up cheeseburgers and french fries stay trim while others battle the bulge."[1]

Nutragenomics, more specifically and less "tongue in cheek," is a discipline that attempts to explain how nutrients, or common dietary chemicals, affect one's health by altering gene expression. Basic tenets of the discipline include the following:

- Common dietary chemicals act on the human genome, directly or indirectly, to alter gene expression or structure.
- Under certain circumstances and in some individuals, diet can be a serious risk factor for a number of diseases.
- Some diet-regulated genes (and their normal, common variants) are susceptibility genes and likely play a role in the onset, incidence, progression, and/or severity of chronic diseases.
- The degree to which diet influences the balance between healthy and disease states may depend on an individual's genetic makeup.
- Dietary intervention based on knowledge of nutritional requirement, nutrition status, and genotype (i.e., "individualized nutrition") can be used to prevent, mitigate, or cure chronic disease.[2]

One reason that nutragenomics currently is receiving substantial attention is that the necessary science to monitor gene expression finally has been developed. Instruments and analytical tools, such as those surrounding the Affymetrix GENECHIP®,[3] allow for the monitoring of specific gene expression from experimental samples obtained from humans and other biological systems. By accurately controlling input to such biological systems (e.g., nutrients), how gene expression varies with input can be measured. Where the function of a particular gene, or set of genes, is understood, one can correlate what one eats with a particular and measurable biological outcome. The outcome may be related to a known disease.

Another reason why nutragenomics is receiving attention may involve recent reports in peer-reviewed journals that show interesting relationships between minerals and beneficial effects in animal models. For instance, Emma Guns et al. have shown that cesium chloride potentiates the effect of certain chemotherapeutic compounds when co-administered.[4] The cesium chloride supposedly impacts tumor responsiveness through modulating the animal's pH, a systemic effect that could alter gene expression.

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## Regulatory Impact

In the short term, the largest regulatory impact of nutragenomics could relate to the labeling of dietary supplements. The Dietary Supplement Health and Education Act (DSHEA) of 1994[5] provides for the inclusion of "structure/function claims" on such labels. The claims, or statements, may "(1) describ[e] the role of a nutrient or dietary ingredient intended to affect the structure or function of the human body or behavior, (2) characteriz[e] the documented mechanism by which a nutrient or dietary ingredient acts to maintain such a structure or function, or (3) describ[e] general well-being resulting from the consumption of a nutrient or dietary ingredient."[6]

Structure/function claims are not subject to regulatory preapproval by the Food and Drug Administration (FDA) and the postmarketing requirements are minimal. Where such a claim is made, the supplement manufacturer must notify FDA within 30 days of commercial launch. Furthermore, the manufacturer must include the following disclaimer on the supplement label: "This statement has not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease."[7]

Accordingly, one should expect to see dietary supplement labels emerging that point to the supplement's effect on gene expression. Statements such as "This supplement increases the expression of the BRCA1 and BRCA2 genes." speak to a mechanism by which the supplement affects the functioning of a human body. The statement appears factual—assuming it is based on controlled, statistically significant experiments—and purely scientific, but to an individual who knows that BRCA1 is breast cancer gene 1 and BRCA2 is breast cancer gene 2, and that functioning of the genes is correlated with an absence of breast cancer, the statement speaks volumes beyond cold fact.

## Intellectual Property Impact

Nutragenomics should substantially affect patenting strategies in the supplement area as well. Where a combination of ingredients in a supplement has been described or specific portions of the included ingredients have been disclosed, one still may be able to obtain patent protection on a combination slightly different from that previously presented. Practitioners sometimes refer to such inventions as "selection inventions." Out of all of the possible combinations, the inventor has selected the one that provides optimal results.

There is at least one catch with respect to selection inventions. If one is doing nothing more than optimizing ratios of ingredients for a known supplement type in relation to a well-understood parameter (e.g., dissolution rate), then the U.S. Patent & Trademark Office likely will find the optimized ration obvious. The key to patentability in this situation is discovering a new "result-effective variable"[8] (i.e., a parameter that has not been recognized previously as related to the subject combination). Gene expression should be such a variable in most cases because nutragenomics is a developing field.

With technologies such as the GENECHIP®, shifts in gene expression in animal models as the ration of dietary supplement ingredients is varied can be monitored. Where there is a correlation with either the inhibition of gene expression of a gene reasonably related to disease production, or potentiation of gene expression of a gene reasonably related to disease prevention, the odds associated with obtaining patent protection increase dramatically.

Based on this discussion, it is apparent that the discipline of nutragenomics is poised to add significant value to the nutraceutical industry. Structure/function claims that appear on dietary supplement labels may incorporate nutragenomic information, which may be appealing to consumers. New intellectual property positions will emerge based on correlations between supplement composition and gene expression. In both cases, greater support will flow to an important and rapidly growing commercial space. ⚠

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1 *A Better Diet Through Nutrition?*, Wall St. J., Mar. 1, 2005, at D6.

2 J. Kaput, *Diet Disease Gene Interactions*, 20 Nutrition 26-31 (2004).

3 For further information on Affymetrix's GENECHIP®, see Affymetrix, GENECHIP® Arrays, http://www.affymetrix.com/products/arrays/index.affx (last visited June 13, 2006).

4 *See* Emma Guns et al., *pH Modulation Using CsCl Enhances Therapeutic Effects of Vitamin D in LNCaP Tumor Bearing Mice*, 64 Prostate 316 (2005).

5 Pub. L. No. 103-417, 108 Stat. 4325.

6 Council for Agricultural Science and Technology (CAST), Issue Paper 24, at 6-7 (Oct. 2005), *available at* http://www.cast-science.org/cast/src/cast_publications.php.

7 *Id.* at 7 (quoting DSHEA (Congress 1994)).

8 *See* USPTO, Manual of Patent Examining Procedure (MPEP) 2144.05 (8th ed. 2001, rev. 2005), *available at* http://www.uspto.gov/web/offices/pac/mpep/index.html.