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NUTRIGENOMICS: ARE WE THERE YET?

I. Introduction

About fifteen years ago, after the conclusion of the Human Genome Project, [1] we realized that different people's genes are not the same (and the difference is hidden in the 0.1% of our DNA). And for some people, those genes allow them to eat whatever they want and still remain slim, while for some people different genes are responsible for an increased risk of getting a certain disease.

But what if our individual genetic makeup could be changed by the food that we eat? This question is at the heart of an emerging science called *nutrigenomics*. [2]

In particular, nutrigenomics studies how what we eat and drink influences our genes' behavior based on the fact that our genes respond differently to certain nutrients. It explores the interaction between the nutrients as well as dietary compounds and the human genome, all the way down at the molecular level. [3] There is significant proof that ***470** genes affect how nutrients are metabolized, and conjointly, nutrients affect how genes are expressed and regulated. [4] Understanding those connections and being able to predict our body's reaction to food without actually having to try it may lead to a great breakthrough in the areas of personalized nutrition and in treating several chronic diseases.

However, although extremely promising, this is a new and emerging area of science. This article explores whether nutrigenomics is ready to be integrated into the whole society. Does it, perhaps, still lack enough regulatory guidance? Could various medical risks and unresolved ethical concerns outweigh the possible positive effect and thus slow nutrigenomics down? What must potential users and customers be aware of?

II. Personalized nutrition recommendations

Those who are struggling with weight problems or are simply willing to maintain a healthy lifestyle and not gain weight have probably heard and implemented various types of diet recommendations from all types of sources. Paleo diet, Mediterranean diet, Ketogenic diet, Atkins diet, Japanese diet, Dukan diet, Raw Food Diet - these are the ones I can name without even having to look them up on the Internet and yes, I have tried them all. However, while a particular diet works for some people and, sometimes, even for most of the people, there are always outliers in the happy statistics, who tried so hard, but did not notice any improvement.

Partly this may be caused by the fact that modern diet recommendations use the “one size fits all” approach. [5] Nutrition and diet guidelines are typically based on large-scale research and do not take into account that very 0.1% of gene variant, which makes us all differ from each other. One of the advertisements for nutrigenomics testing suggested to regard old diet advice as

a paper map - the information is there, but it is truly hard to understand where *you* are in the picture. Therefore, nutrigenomics is like upgrading to Google Maps - it tells you exactly where you are, so you can faster get where you want to be.

With nutrigenomics, we might be able to analyze people's gene variants, predict how a certain diet can impact gene expression and stability, [6] and then create personalized nutrition plans. Applying those tailored personalized nutrition plans may result in normalizing our gene expression for the purpose of promoting good health, so that our body is at its best. [7] We may never again have to chew healthy broccoli bites unless we have solid genetic proof that those bites will benefit our health.

***471** For instance, although healthy fats such as avocado or olive oil have cleared their names and finally gotten approved by the scientific society, some people tend to gain rather than lose weight on a high-fat, 'healthy' diet. [8] Researchers Corella and Ordovas, who explored the correlation between variants of the APOA5 gene, lipid metabolism and body-mass index (BMI), found a scientific explanation. [9] For men and women in one of the study groups who had the same gene variant, that variant had a protective effect against increasing BMI while increasing the lipid intake. [10] Similarly, a person's gene variant may have a significant impact on how well said person absorbs nutrients like Vitamin D. [11] Thus, one can consume large amounts of Vitamin D-rich products such as salmon, and still require dietary supplement with Vitamin D, because their gene variant dictates such.

Another scientific role of nutrigenomics might be to examine trends in phenotypes for different populations of people far distanced from each other and to find the underlying gene-nutrient reason for this. [12] For example, while living in Russia I very rarely came across cases of lactose intolerance, while here in the US, however, it seems like a rather widespread condition. Statistics add that only about 5% of people of Northern European descent are lactose intolerant. [13] Now that most non-Europeans experience at least some level of lactose intolerance because they have two polymorphisms lacking the enzyme (lactase) required to break down this brown sugar, [14] it makes sense. Likewise, Asian populations are generally known to avoid drinking alcohol, thanks to low levels of alcohol dehydrogenase, an enzyme necessary to break down the alcohol. [15] In these areas especially, nutrigenomics give us hope to one-day be able to develop and implement public health measures for genetically identified groups and populations.

***472 III. Possible new treatment for chronic diseases**

According to the National Academies of Sciences, Engineering, and Medicine, nutrition-related chronic diseases cost the US economy about $1 trillion per year. [16] Might nutrigenomics help reduce these dramatic numbers?

Just as different people react differently to certain food because of their genes, so do people to certain medications. Currently, there is no way for doctors and patients to determine in advance whether a particular drug will cause an adverse reaction until such reactions manifest. There is a great expectation that with nutrigenomics, as doctors better understand how a patient's body handles nutrients, they will be able to better predict the potential effects of a particular drug without having to take the "wait and see" approach. [17]

Ben Van Ommen, director of the European Nutrigenomics Organization, suggests that all diseases can be grouped into four main groups based on imbalances in their processes: (1) inflammatory; (2) metabolic; (3) oxidative; and (4) psychological stress. [18] Jim Kaput, director of the newly established Division of Personalized Nutrition ***473** and Medicine at the FDA National Center for Toxicological Research, says that nutrigenomics represent a major effort to improve our understanding of the role of nutrition and genomic interactions in at least the first three of these areas. [19]

In particular, inflammation has been often linked to various diseases including cancer, cardiovascular disorders, metabolic disorders, [20] atherosclerosis, insulin resistance, and obesity. [21] Meanwhile, there is proof that several nutrients have the power to modulate gene expressions related to cancer inflammation. [22] As such, nutrigenomics may also play a crucial role in developments in potential cancer treatments.

Unfortunately, while cancer is the second leading cause of death in the United States,[23] existing methods of therapies available for patients are extremely costly, unsafe with numerous side effects, lack availability for the majority of patients, and significantly reduce patients' quality of life. Current cancer therapies are practically limited to surgery, radiation therapy, and chemotherapy - each of those bearing significant risks. Thus, nutrigenomics might be a great solution for this endeavor because it may let doctors modulate cancer metabolism through a safe and cost-effective nutritional intervention.[24] ***474** As many scientists observe, however, nutrigenomics in the field of cancer therapy still needs more research.[25]

In the field of cardiovascular (cardiometabolic) diseases, several lipid-responsive genes, namely, the peroxisome proliferator-activated receptor (PPAR) family, have proven to be directly affected by specific nutrients.[26] In addition to PPARs, other clear examples of gene-diet interaction in the medical field exist as of today. For example, the retinoic acid-responsive farnesoid X receptor and the oxysterol-responsive liver X receptor, which serve as nutrient regulators capable of altering atherosclerosis and diabetes risk.[27] Even though most of the studies have focused primarily on prevention of the cardiovascular diseases, there is great interest in developing research aimed at discovering gene-diet connections in secondary prevention to provide recommendations to patients who had already experienced cardiovascular events.[28]

IV. Reasons to be concerned

As great and innovative as it sounds, nutrigenomics gives rise to certain important considerations and concerns.

First, there are a number of ethical and legal issues intertwined. Nicholas Schork of the J. Craig Venter Institute (past chair of the planning committee for the 2006 National Academies workshop on nutrigenomics) explores how recent trends and new legislation in the biomedical sciences can serve as leverage in nutrition-based health care arena.[29] ***475** Specifically, the recently enacted 21st Century Cures Act may allow companies, under certain conditions, provide "data summaries" and "real-world evidence" rather than full clinic trial results.[30]

Similarly, the growing impact of big data, i.e. the use of information technology to identify patterns in massive amounts of data, may lead to uncertainty in physicians' determination of the ideal outcome of big data research. Thus, how should one define an optimal result? Should the individual outcome matter, or should you choose recommendations in order to make health care more cost-efficient for the society as a whole?[31] Corresponding questions are raised by I. Glenn Cohen et al, when they explore ethical concerns arising from the use of complex predictive analytics in health care.[32] Cohen notes, that in the modern era of predictive analytics and big data, physicians may be forced to make clinical decisions under the pressure of health care organizations.[33] As such, the optimal result and appropriate recommendation to the patient might be driven by financial and administrative incentives rather than old school patient's best interests.[34]

In addition, patients' autonomy might be unduly limited in the field of nutrigenomics. Respecting patients' autonomy means allowing people "to shape the basic ***476** course of their lives in line with their values and independent of the control of others."[35] For instance, many websites of companies that advertise nutritional genetic tests to consumers do not give any insight at all into how they derive their diet recommendations from consumers' DNA.[36] Instead, their disclaimers sections provide information that goes in direct controversy to what their advertisements say.[37] While those companies tend to rush into providing tailored nutritional recommendations, their disclaimers clearly state that genetics plays a very slight role in how the body responds to a diet.[38]

Furthermore, possible unauthorized or unanticipated third-party disclosure of the results of genetic tests also poses problems.[39] Who should have access to the results of nutrigenetic testing? May employers and insurance companies demand access to it once it is done? If so, may refusal to provide such information result in employment discrimination? May insurance companies leverage this information in order to increase their premiums for a particular client?

Finally, if the information reaches only the correct recipient, unrestricted access to nutrigenetic information, even to the customers themselves, may lead to dangerous problems of misunderstanding, misrepresentation and, therefore, identity issues, panic ***477** and even suicide. [40] Some of us may know that not all genetic information is dangerous - there are harmless genes responsible for a particular eye color or lactose intolerance that we discussed above. However, a lay person who received the test results may not be educated or qualified enough to understand the information contained therein. [41] Furthermore, if the individual does not interpret results correctly, he or she might fail to take required preventive measures, or, vice versa, jump into unnecessary or adverse medical decisions. [42]

Finally, another important question arises out of the fact that we share genes with our family members. As a mother, I can easily imagine myself struggling with deciding whether to continue testing my kids after I receive my results and thus, possibly, increase panic and spend big amount of money on unnecessary tests. Family history serves as an important tool to explore risks of hereditary diseases, [43] but may it, possibly, induce futile panic and anxiety with direct-to-consumer (and thus, easily accessible) genetic testing? Probably, yes.

More than that, nutrigenomics is often criticized for the lack of scientific evidence behind it. Cecile Janssens of Emory University performed an extensive research reviewing seven different companies' dietary recommendations based on genomic profiling. [44] Among other findings, Janssens discovered, for example, that profiles tested for heart health were based on genes usually associated with non-cardiovascular diseases. [45] Similarly, two of the five genes used to determine risk of bone disease are rather associated not with bone disease, but with Alzheimer's, asthma or another condition. [46] She ***478** concludes that, obviously, the field of nutrigenomics is not ready for its official debut yet. [47]

The scientific community is not unanimously on one side, however, claiming that nutrigenomics is still ripe. There is an opinion that DNA-based dietary advice has resulted in greater understanding of recommendations, greater interest in learning more and greater motivation to change eating habits. [48] In response to numerous statements about lack of evidence with nutrigenomic testing, El-Sohemy claims that, although the field is not without controversy, there are some good examples of proof that an individual's SNP [49] can modify the link between a dietary component and different health outcomes. [50] For instance, the risk of myocardial infarction associated with coffee intake depends on whether a person is a fast or slow metabolizer of the CYP1A2 genotype. [51] Likewise, there is evidence showing that a person's change in fat mass under a high protein diet depends on individual's FTO gene variant. Adding that “we need to eat today”, and we currently ***479** give dietary advice for health eating based on old science, he wondered how much more evidence do we need. [52]

V. Regulatory policy

Three federal agencies have the primary authority to regulate nutrigenomics, the Food and Drug Administration (FDA), Centers for Medicare and Medicaid Services (CMS) and the Federal Trade Commission (FTC). The regulation landscape is constantly evolving, and it is likely that more of the nutrigenomics industry will face greater oversight in the future. [53]

FDA regulates genetic testing kits and components sold to laboratories or other persons under the ‘medical device’ definition of the Federal Food, Drug and Cosmetic Act (FDCA). [54] Interestingly, FDA's power of authority only covers health-related tests, not “entertainment” applications or genetic testing (such as, for instance, test on what socks are good for your DNA or which wine do your genes prefer). [55] Although nutrigenomics, as a science, has been developing for years, the first direct-to-consumer genetic test was not cleared by the FDA until 2017 - that was the 23andMe's Genetic Health Risk test providing information on a person's predisposition to certain diseases. [56] The cleared test intended to provide information to help individuals make decisions about lifestyle choices or inform discussions with a health care professional. [57] It was cleared through a *de novo* premarket review pathway [58] and specifically excluded diagnostic testing due to higher risks associated with that type of testing.

***480** CMS regulates clinical laboratories conducting clinical genetic testing through its Clinical Laboratory Improvement Amendments [59] (CLIA) program. Under CLIA, CMS sets standards for laboratories that provide information about health-related conditions. [60] Although CLIA assures that genetic tests are analytically valid, CLIA does not ensure clinical validity or clinical utility of the genetic medical information. [61] Thus, the test could satisfy the analytical standard and still lack accuracy if there is not a string relationship between the genetic variant and the clinical manifestation of a disease. [62]

In addition to CLIA and FDA regulations, FTC regulates genetic testing companies who advertised false and misleading claims about their products. In particular, under the Federal Trade Commission Act (FTCA), [63] FTC prohibits unfair and deceptive trade practices, including false advertising. [64] As such, FTC's authority includes advertising claims for genetic testing product and services, advertising claims for food and data security practices concerning genetic test results and other personal consumer information. [65] An example of FTC's exercising its authority may be filing charges against Genelink, Inc. in January and against L'Oreal USA Inc. in June of 2014 for offering purported personalized genetic testing services. [66] There, Genelink and its subsidiary made claims that its nutritional products could help compensate for "disadvantaged" genes. [67]

Nutrigenomics testing companies do not stop at fighting with the FDA across the United States, however, and even actively engage in attempts to conquer foreign markets with lower standards and weaker regulations. Thus, while FDA's concerns about the safety of the direct-to-consumer genetic tests are not without merit, its attempts to slow the industry down might not succeed due to the rapidly growing market of internationally based sequencing firms. [68]

VI. Conclusion

For the reasons explained above, nutrigenomics seems to place itself in a gray area, heavily in need for additional research and time. Several ethical problems and scientific validity concerns remain unresolved; meanwhile the federal agencies fail to adequately protect the public from all the potential risks and dangers of implementing this theory in practice. Therefore, although great and inspiring promises are made, the response to those who pose the "are we there yet" question relating to nutrigenomics shall be the same as I give to my kids when we are travelling in a car, and we just started our journey: yes, we will get there, and no, we are not there yet.

Footnotes

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My gratitude goes to Prof. Barbara Evans, the Mary Ann & Lawrence E. Faust Professor of Law, for inspiring me and posing difficult questions. I dedicate this article to my 7-year-old son Maxim, who enjoys writing as much as I do, and who has already written a couple of great pieces. Go for it, Maxim!

1 *See* NAT'L HUMAN GENOME RESEARCH INST., *A Brief History of the Human Genome Project*, https://www.genome.gov/12011239/a-brief-history-of-the-human-genome-project (last updated Nov. 8, 2012).

2 Kissairis Munoz, *Nutrigenomics: Does Food Influence How Our Genes Behave?* DR. AXE, https://draxe.com/nutrigenomics (last updated Nov. 15, 2017); *see* David Castle, *Genomic Nutritional Profiling: Innovation and Regulation in Nutrigenomics*, 9 MINN. J.L. SCI. & TECH. 37 (2008) (discussing regulatory challenges given nutrigenomics is a relatively new field); *see, e.g.*, Michelle D. Irick, Comment, *Age of an Information Revolution: The Direct-to-Consumer Genetic Testing Industry and the Need for a Holistic Regulatory Approach*, 49 SAN DIEGO L. REV. 279 (2012) (discussing the regulatory challenges of consumer-wide access to genetic testing services). The concept of tailoring on

a human-by-human basis also runs into other regulatory challenges, for example, a lack of a complete and coherent set of standards regulating the resultant overflow of information. *Id.*

3 Allison Webster, *In the Know About Nutrigenomics,* FOOD INSIGHT, https://www.foodinsight.org/what-is-nutrigenomics-diet-health (last updated Jan. 31, 2018); *see also* Ruan Elliot & Teng Jin Ong*, Science, Medicine, and the Future: Nutritional Genomics*, 324 BRIT. MED. J. 1438 (2002) (discussing the procedure of and challenges toward conducting nutrigenomic research).

4 *Cf.* William E. Evans & Julie A. Johnson, *Pharmacogenomics: The Inherited Basis for Interindividual Differences in Drug Response*, 2 ANN. REV. GENOMICS & HUM. GENETICS 9, 10-11 (detailing how drug metabolizing enzymes in humans cause changes in the effects of the drug).

5 *See* Munoz, *supra* note 2 ("Diet recommendations will no longer be 'one size fits all"').

6 *See* Jing X. Kang, *The Coming of Age of Nutrigenetics and Nutrigenomics*, KARGER (June 2012), https://www.karger.com/Article/Pdf/339375 (describing nutrigenomics as a method for normalizing gene expression).

7 Macaela Mackenzie, *What Is Nutrigenomics and Can It Improve Your Diet?*, SHAPE (Jan. 9, 2018), http://shape.com/healthy-eating/diet-tups/what-is-nutrigenomics; *see* Moul Dey, *Molecular Nutrition, Nutrigenomics and Health Promotion*: *A Long Road Ahead*, 1 J. FOOD NUTRITION DISORDER 1, 1 (2012) (discussing nutrigenomics' potential to lead dietary intervention strategies). These intervention strategies are for "restoring health and fitness and preventing disease. *Id.*

8 *See Feeding Your DNA*: *The Science Behind Nutrigenomics*, ORIG3N (May 15, 2018), https://orig3n.com/blog/feeding-your-dna-the-science-behind-nutrigenomics/ ("[W]hile avocado and olive oil have gained popularity ... due to their labeling as 'healthy fats,' these foods may not be the best fit for an individual with certain fat processing gene result due to their impact on weight."); *see also* Bàrbara Reynés et al., *Peripheral Blood Cells, a Transcriptomic Tool in Nutrigenomic and Obesity Studies: Current State of the Art*, 17 COMPREHENSIVE REV. FOOD SCI. FOOD SAFETY 1006, 1006-07 (2018) (discussing gene expression in blood cells in relation to body weight control).

9 Dolores Corella & Jose M. Ordovas, *Single Nucleotide Polymorphisms that Influence Lipid Metabolism: Interaction with Dietary Factors*, 25 ANN. REV. NUTRITION 341, 348 (2005) (examining gene-diet interactions involving lipid metabolism - some are insensitive to dietary intervention).

10 *Id.* at 375.

11 *See* Mackenzie, *supra* text accompanying note 7 (eating Vitamin D rich foods can still require taking a supplement depending on a person's genetics).

12 *See generally* Richard S. Spielman et al., *Common Genetic Variants Account for Differences in Gene Expression Among Ethnic Groups*, 39 NATURE GENETICS 226 (2007) (noting that differences in gene expression phenotypes between populations have not been examined before).

13 *See generally* U.S. NAT'L LIBR. MED., *Lactose intolerance*, GENETICS HOME REFERENCE (Feb. 19, 2019), https://ghr.nlm.nih.gov/condition/lactose-intolerance#sourcesforpage (noting that rates of lactose intolerance are lowest in populations dependent on unfermented milk products).

14 *See* David Castle, *Genomic Nutritional Profiling: Innovation and Regulation in Nutrigenomics*, 9MINN. J.L. SCI. & TECH. 37, 44 (2008) (noting Asian populations have low levels of alcohol dehydrogenase, the enzyme required to break down alcohol).

15 *See id.* at 44. One useful approach to nutrigenomics is to identify phenotypes in vastly different and far removed populations in order to link that phenotype to certain gene-nutrient causes. *Id.* This method is designed so scientists can establish statistically significant correlations to allow them to predict measurable outcomes based on the presence of certain nutrients. *Id.*

16 NAT'L ACAD. OF SCI., ENG'G, & MED., NUTRIGENOMICS AND THE FUTURE OF NUTRITION: PROCEEDINGS OF A WORKSHOP - IN BRIEF, 9 (2018), https://www.nap.edu/read/25049/chapter/1. Although much of the interest in applying nutrigenomics is to attempt to lower nutrition related chronic disease costs, the author notes that most chronic disease is in low-income populations, which are the least likely populations to benefit from this kind of study. *Id.* This is due to the enormity in over-nutrition of low-income populations. *Id.*

17 Christina Tarantola, *Medicinal Food: How Nutrigenomics Is Shaping Our Health,* PHARMACY TIMES (Apr. 17, 2018), http://www.pharmacytimes.com/contributor/christina-tarantola/2018/04/medicinal-food-how-nutrigenomics-is-shaping-our-health (noting possibility of adverse interactions between certain types of diets and medication regimens). "Diet, and medication recommendations will no longer be 'one size fits all'. Understanding their nutrition profiles will help patients avoid adverse reactions and find the individual plans that work for their bodies." *Id.*

18 *See* M. Nathaniel Mead, *Nutrigenomics: The Genome-Food Interface,*115 ENVTL. HEALTH PERSPECTIVES A582 (2007), https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2137135/pdf/ehp0115-a00582.pdf (describing diseases stem from one of four stressors from genetic predispositions); Yun-Zi Liu, et al., *Inflammation: The Common Pathway of Stress-Related Diseases*, FRONTIERS HUMAN NEUROSCIENCE, June 2017, at 316-1, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5476783/pdf/fnhum-11-00316.pdf (defining stress and the evolution of stress influencing diseases). "Stress is a state of threatened homeostasis provoked by a psychological, environmental, or physiological stressor." *Id.* Inflammation is known as "the crucial response to microbe invasion or tissue injury to keep maintenance of tissue homeostasis." *Id.* (explaining how inflammation plays pivotal role in the progression and/or onset of stress-related diseases). Metabolic stress is linked to the development of cardiovascular disease; whereas, oxidative stress is an imbalance occurring from overproduced reactive oxygen or a shortage of antioxidants. *Id. See also* So-Won Chung, et al., *The Association Between Oxidative Stress and Metabolic Syndrome in Adults*, 34 KOREAN J. FAM. MED. 420 (2013), https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3856284/pdf/kjfm-34-420.pdf (defining the different stressors and explaining metabolic stress is linked to cardiovascular disease). Oxidative stress is associated with the development of metabolic stress. *Id.* Psychological stress is caused by an individual perceiving that environmental demands tax or exceed one's adaptive capacity. *Id.* Sheldon Cohen et al., *Psychological Stress and Disease* 298 JAMA, 1685-87, (2007), https://jamanetwork.com/journals/jama/article-abstract/209083 (discussing how this stress contributes to diseases including clinical depression, cardiovascular disease, HIV/AIDS, and cancer).

19 *See* Chung et al., *supra* note 18 (focusing discussion on inflammatory, metabolic, oxidative factors and how these stressors caused diseases of civilization).

20 *See* Kang, *supra note* 6. Listing the different diseases linked to inflammation suggesting the environment is having an adverse effect on nutrition which in turn is leading to a global health crisis in chronic disease. *Id. See also* Beatrice Godard & T. Hurlimann, *Nutrigenomics for Global Health: Ethical Challenges for Underserved Populations*, 7 CURRENT PHARMACOGENOMICS & PERSONALIZED MED., 205, 205 (2009) https://core.ac.uk/download/pdf/55647023.pdf. "Many chronic diseases are multifactorial and social and environmental determinants of health are worth emphasizing as genetic/genomic factors." *Id.* at 208.

21 Jane F. Ferguson et al., *Nutrigenomics, the Microbiome, and Gene-Environment Interactions: New Directions in Cardiovascular Disease Research, Prevention, and Treatment*, 9 GENOMIC & PRECISION MED. 291 (2016). Cardiometabolic diseases play an active role in the existence of inflammation in a body, like obesity. *Id.* Low grade systemic inflammation that plays a large role in the issue. *Id.*

22 Jing X. Kang, *Nutrigenomics and Cancer Therapy*, J. NUTRIGENET NUTRIGENOMICS (2013). Inflammation, angiogenesis, and proliferation are certain types of nutrients that may be used in gene expressions related to cancer. *Id.* The ability to modulate the metabolic pathways is a step in the right direction in the biology of cancer which will hopefully lead to developments in cancer research. *Id.*

23 *See Leading Causes of Death*, CENTERS FOR DISEASE CONTROL & PREVENTION (last updated Mar. 17, 2017), https://www.cdc.gov/nchs/fastats/leading-causes-of-death.htm. Out of a list of the ten top causes of death in 2016, cancer ranked number two behind heart disease. *Id.* Cancer was the cause of death of roughly 598,038 people in the United States. *Id.*

24 *See supra* note 22 and accompanying text; *see also* M. Nathaniel Mead, *Nutrigenomics: The Genome-Food Interface*, 115 NAT'L INST. ENVTL HEALTH SCI. A582 (2007). Researchers believe we will see important contributions from the study of nutrigenomics. *Id.* at A587. Nutrigenomics will be used for the prevention of many common diseases such as: obesity, diabetes, cardiovascular disease, cancer, inflammatory disorders, age-related cognitive disorders, visual function, and many vitamin deficiency disorders. *Id. See generally* Lydia Afman and Michael Muller, *Nutrigenomics: From Molecular Nutrition to Prevention of Diseases*, 106 J. AM. DIETETIC ASS'N 569, 572-73 (2006) (explaining a major focus of nutrition research is on prevention of chronic diseases).

25 Praveen Sharma & Shaleindra Dwiledi, *Nutrigenomics and Nutrigenetics: New Insight in Disease Prevention and Cure*, IND. J. CLIN. BIOCHEM (Oct.-Dec. 2017), https://link.springer.com/article/10.1007/s12291-017-0699-5; *see also* M. Nathaniel Mead, *supra* note 24 at A584 (discussing the need for more scientific study into genome-protective nutrients); Carol Potera, *Nutrigenomics. Diet and DNA*, 112 ENVTL HEALTH PERSPECTIVES A404 (2004) (summarizing research advances in nutrigenomics). The Center of Excellence for Nutritional Genomics was established in 2003 to coordinate nutrigenomics studies among participating institutions. *Id.* With a $6.5 million grant, twenty-five experts from four participating institutions, the group will explore how different foods interact with genes. *Id.* Across the Atlantic, the European Nutrigenomics Organization was formed shortly after in 2004. *Id.* Twenty-two scientists from ten European countries will receive €17.3 million over six years from the European Union to develop new technologies, improve model systems, and advance nutritional bioinformatics. *Id. See generally* Afman and Muller *supra* note 24 (indicating research limitations on nutrigenomics).

26 *See* Ferguson et al., *supra* note 21.

27 *See id.*

28 *See id.*

29 *See* NAT'L ACAD. OF SCI., ENG'G, & MED., *supra* note 16. Schork also opined that recent changes in FDA, such as the 21st Century Cures Act, will bear on how one can make claims about nutritional interventions in the future. *Id.* The act will allow companies to provide "data summaries" and "real-world evidence" instead of full clinical trial results to the FDA in order to accelerate medical product development. *Id.* Schork also identified key questions to consider when leveraging new trends and new legislations:
What is being tailored to what? For example, is a gross diet being tailored to an individual's genotype? Or, are more refined recommendations (e.g., nutrients, supplements) being tailored to a complex profile based on not just genetic, but also biomarker and other information about an individual? At what level should nutrition recommendations be operating? Is personalized, or individual, nutrition the best approach, or would a stratified approach be better (i.e., with individuals clustered into groups based on how they respond to particular dietary interventions)?
Id. at 7.

30 *See id.* at 7 (summarizing Nicholas Shork's commentary on the 21st Century Cures Act).

31 *See id.* (discussing the paradox of whether individual results benefit society as a whole).

32 *See* I. Glenn Cohen et al., *The Legal and Ethical Concerns that Arise from Using Complex Predictive Analytics in Health Care*, 33 HEALTH AFFAIRS 1139, 1139-47 (2014). "Predictive analytics, or the use of electronic algorithms to forecast future events in real time, makes it possible to harness the power of big data to improve the health of patients and lower the cost of health care. However, this opportunity raises policy, ethical, and legal challenges." *Id.* at 1139.

33 *Id.* "[P]redictive analytics models make treatment recommendations that are designed to improve overall health outcomes in a population, and these recommendations may conflict with physicians' ethical obligations to act in the best interests of individual patients." *Id.*

34 *Id.* at 1146-47. "It may seem to patients that the treating physician is no longer exercising clinical judgment and acting in their best interests." *Id. See* Arnold J. Rosoff, *On Being a Physician in the Electronic Age: Peering into the Mists at Point-&-Click Medicine*, 46 ST. LOUIS U. L.J. 111, 120 (2002).

The physician chooses what sources to turn to and what information to use in his or her decision-making process. It is the physician's educated discretion that finds, filters, and focuses these inputs for the benefit of the patient; thus, it is appropriately the physician's exercise of that discretion that is the focus of the legal inquiry. *Id.* at 120; *see also* Susan M. Ridgely and Michael D. Greenberg, *Too many Alerts, too much Liability: Sorting Through the Malpractice Implications of Drug-Drug Interaction Clinical Decision Support,* 5 ST. LOUIS U. J. HEALTH L. & POL'Y 257, 266-67 (2011) (explaining that courts assume physicians primarily rely on their own judgment when determining liability).

35 Ruth R. Faden, et al., *An Ethics Framework for a Learning Health Care System: A Departure from Traditional Research Ethics and Clinical Ethics*, 43 HASTINGS CTR. REP. S16, S20 (2013). Advances in technology could mean that "[n]ot all health care decisions are likely to be attached to a significant autonomy interest of individual patients, and deference of the wrong sort can constitute a moral failure ...." *Id.*

36 *See* NAT'L ACAD. OF SCI., ENG'G, & MED., *supra* note 16, at 7. Autonomy is required for individuals to make an education decision on their own and it is believed that "there is not enough evidence yet to offer these [diet recommendation] tests online." *Id. See also* Timothy Caulfield, *The Obesity Gene and the (Misplaced) Search for a Personalized Approach to our Weight Gain Problems*, 5 WAKE FOREST J.L. & POL'Y 125, 133 (2015). "The material available on the [direct-to-consumer] websites provides little to explain how ... their service resolve these issues or why ... their services will be effective." *Id.*; NUTRIGENOMIX, FAQ, https://www.nutrigenomix.com/faq (last visited Mar. 10, 2019) (stating health care professionals will create dietary plans based on genetic profile without insight into how).

37 *See* NAT'L ACAD. OF SCI., ENG'G, & MED., *supra* note 16, at 7. These discrepancies create a place for ethical principles to play a role, especially with the companies fostering good intentions and autonomy. *Id.* In the future, companies are asked to communicate in a more respectful manner with their consumers regarding the "prematurity of genetically personalized nutrition recommendations." *Id.*

38 *See id.* at 7. There are many questions to be asked when creating nutritional strategies for individuals, one of those being what type of approach, personalized, individual, or stratified, should be used to provide the best recommendations. *Id. See also* Caitlin Ostroff, *Your DNA, your Diet: How Nutrition Is Being Personalized*, WALL STREET J. (Aug. 30, 2018), https://www.wsj.com/articles/your-dna-your-diet-how-nutrition-is-being-personalized-1535641259. Research fellows from Australia are skeptical "of whether there's currently enough data to draw straw conclusions and recommendations solely from a person's DNA, as some companies do." *Id.*

39 Gabrielle Kohlmeier, *The Risky Business of Lifestyle Genetic Testing: Protecting Against Harmful Disclosure of Genetic Information*, UCLA J.L. & TECH. 5 (2007). Discrimination, by employers, insurance companies or even family members, is one of the greatest concerns. *Id.* The individual may not intend for the results to be shared with specific parties. *Id.* If the results are shared with unintended parties, the parties have the capability to react how they chose which leaves room for discrimination against not only the individual customer, but blood relatives. *Id.*

40 *Id.* at 19. The customer themselves may be placed in a position to lie or face potential discrimination because they either do not want to share their results, or they are willing to share them but would face the ramifications of other's opinions. *Id.* Family ties may become strained because family members do not want to know this specific information, but they inadvertently find out from another blood relative who was curious. *Kohlmeimer*, *supra* note 39.

41 *Id.* at 18. Although much of genetic information is harmless if shared, there is a large number of genetic variants being tested and correlations of a particular genetic variants are being discovered. *Id.* There is no way for one to know whether the information will remain "innocuous or will be imputed meaning making it dangerous." *Id.*

42 *See generally* Sarah F. Sunderman, *The Need for Regulations of Direct-to-Consumer Genetic Testing in the United States: Assessing and Applying the German Policy Model*, 12WASH. U. GLOBAL STUD. L. REV. 357 (2013).

43 *See* Martin Kohlmeier, et al., *Guide and Position of the International Society of Nutrigenetics/Nutrigenomics on Personalized Nutrition: Part 2 - Ethics, Challenges and Endeavors of Precision Nutrition*, 9 J. NUTRIGENETICS NUTRIGENOMICS 28-46 (2016) (discussing the influence of individual genetic variations and predisposition to diseases).

44 *See* NAT'L ACAD. OF SCI., ENG'G, & MED., *supra* note 16.

45 *See id.* at 7 (stating large discrepancy between companies' advertisement claims to what their disclaimers reveal); *see also* Lynnette R. Ferguson & Nishi Karunasinghe, *Nutrigenetics, Nutrigenomics, and Selenium*, FRONTIERS GENETICS (Apr. 25, 2011), https://www.frontiersin.org/articles/10.3389/fgene.2011.00015/full. There has been a number of flaws and inconsistencies in data generated by nutrigenomics studies. *Id.* Nutrigenomics studies need improvements and consistency in their study designs. *Id.* "[I]nternational collaborations agreed study design and analytical methods, alongside new generation genomics technologies will be essential to take the field to the next plateau and begin to release its real potential." *Id.*

46 *See* NAT'L ACAD. OF SCI., ENG'G, & MED., *supra* note 16, at 6. Furthermore, findings included that "almost half of the 56 genes tested by the companies had not been subject to meta-analyses of gene-disease associations ...." *Id. See also* David Castle & Nola M. Ries, *Ethical, Legal and Social Issues in Nutrigenomics: The Challenges of Regulating Service Delivery and Building Health Professional Capacity*, 622 MUTATION RESEARCH 138, 140 (2007), http://citeseerx.ist.psu.edu/viewdoc/download?doi=10.1.1.568.2060&rep=rep1&type=pdf. The United States Government Accountability Office ("GAO") attempted to test the scientific legitimacy of nutrigenomics, and the results they received mislead consumers as they made "health-related predictions that are medically unproven." *Id.* Additionally, the report found that some companies sold expensive supplemental pills, that they claimed were unique to individual's DNA composition, but in reality the pills were not unique. *Id.*

47 *See* NAT'L ACAD. OF SCI., ENG'G, & MED., *supra* note 16, at 7 (providing people with more relevant scientific studies on how companies make recommendations from consumers' DNA); *see also* David Castle, *Genomic Nutritional Profiling: Innovation and Regulation in Nutrigenomics*, 9 MINN. J.L. SCI. & TECH. 37, 46 (2008). Voicing the concerns that nutrigenomics targeted population is premature and problematic because not enough information is known about disease susceptibility genes. *Id. See* Steven Novella, *Nutrigenomics-Not Ready for Prime Time*, SCIENCE-BASED MED. (Jan. 2, 2013), https://sciencebasedmedicine.org/nutrigenomics-not-ready-for-prime-time/. Nutrigenomics is one example of using medical science to promote new treatments that are not ready for clinical application. *Id.* "[Nutrigenomics] is a legitimate field of research, and the current quackery is likely to taint the reputation of what in the future might be a promising approach." *Id.* Researchers in this space said that there is a huge gap between what is actually known about nutrition genomics and what companies in the nutrigenomics space are claiming they can offer people. *See* Julia Belluz, *"Personalized Nutrition" Isn't Going to Solve Our Diet Problems*, VOX (Feb. 20, 2018, 11:20 AM), https://www.vox.com/2016/11/2/13453434/personalized-diet-nutrition-dna. *Id.*

48 *See* Daiva E. Nielsen & Ahmed El-Sohemy, *A Randomized Trial of Genetic Information for Personalized Nutrition*, 7 GENES NUTRITION 559 (2012).

49 *See* NAT'L ACAD. OF SCI., ENG'G, & MED., *supra* note 16, at 5 (noting coffee consumption as example that can carry different risks for heart attacks among people).

50 *See* Nielsen & El-Sohemy, *supra* note 48 (noting that test subjects enjoyed learning about their genetics and of recommended diets); NAT'L ACAD. OF SCI., ENG'G, & MED., *supra* note 16, at 5 (referencing that knowing how metabolisms factor into a diet can help mitigate certain health risks).

51 *See* NAT'L ACAD. OF SCI., ENG'G, & MED., *supra* note 16, at 5. Research has shown that intake of coffee was related to an elevated risk of nonfatal myocardial infarction only among persons with slow caffeine metabolism. *Id.*; *see also* Zainab Shateri and Kurosh Djafarian, *Coffee Consumption and Coronary Heart Diseases: A Mini-Review*, J. CLINICAL NUTRITION & DIET. at 1-3 (Jan. 25, 2016).

52 *See* Ahmed El-Sohemy, *Is Genetic Testing for Personalized Nutrition Ready for Prime Time?*, NUTRIGENOMIX (2017), http://www.nationalacademies.org/hmd/~/media/Files/Activity%20Files/Nutrition/FoodForum/Dec%202017%20meeting/Presentations/07%20Ahmed%20ElSohemy.pdf.

53 *See* NAT'L HUMAN GENOME RESEARCH INST., *Regulation of Genetic Tests* (Jan. 17, 2018), https://www.genome.gov/10002335/regulation-of-genetic-tests/; *see also* Kohlmeier et al., *supra* note 43. "Legal regulation

remains insufficient, with genetic test guidelines still in development in many countries. Progress is, however, being made." *Id.* at 35. It is unclear which legal instruments may apply to any specific personalized nutrition offering. *Id.* at 36.

54 *See* 21 U.S.C. § 360c (2018) (classifying medical devices for varying levels of regulation); 21 U.S.C. § 360e (2018) (outlining the FDA's requirements and procedures for obtaining premarket approval for medical devices); 21 C.F.R. § 866.5950 (2018) (identifying FDA regulatory requirements for genetic health risk assessment systems).

55 NAT'L ACAD. OF SCI., ENG'G, & MED., *supra* note 16, at 7 (summarizing proceedings comments of Sarah Roller regarding federal regulation of genetic testing).

56 *See* Press Release, Food and Drug Admin., FDA Allows Marketing of First Direct-to-Consumer Tests That Provide Genetic Risk Information for Certain Conditions (Apr. 6, 2017), https://www.fda.gov/newsevents/newsroom/pressannouncements/ucm551185.htm. "The 23andMe GHR tests work by isolating DNA from a saliva sample, which is then tested for more than 500,000 genetic variants. The presence or absence of some of these variants is associated with an increased risk for developing any one of ... 10 diseases or conditions." *Id.*

57 *See id.* (explaining how health care professionals help individuals incorporate nutrition after learning about their predispositions to diseases).

58 *See* Elias Mallis, *De Novo Program*, U.S. FOOD & DRUG ADMIN., https://www.fda.gov/downloads/training/cdrhlearn/ucm421766.pdf (last modified Nov. 4, 2014). De novo is a classification process by which the United States Food and Drug Administration sorts new health devices that have not previously been classified. *Id.* All devices classified as de novo must have low-to-moderate-risks that are not substantially equivalent to an already legally marketed device. *Id.*

59 42 C.F.R. § 493.1253 (2003).

60 Chelsea Weiermiller, *The Future of Direct-to-Consumer Genetic Testing: Regulation and Innovation*, 16 N.C. J.L. & TECH, ONLINE 137 (Jan. 2014).

61 Kayte Spector-Bagdady & Elizabeth Pike, *Consuming Genomics: Regulating Direct-to-Consumer Genetic and Genomic Information*, 92 NEB. L. REV. 677, 689 (2014).

62 *Id.*

63 15 U.S.C. §§ 41-58 (2018).

64 15 U.S.C. §§ 45, 52 (2018).

65 *See* NAT'L ACAD. OF SCI., ENG'G, & MED., *supra* note 16.

66 Weiermiller, *supra* note 60.

67 *Id.*

68 *Id.*

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