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Applying genomics to nutrition and lifestyle modification

Personalized nutrition aims to prevent the onset and development of chronic diseases by targeting dietary recommendations to an individual's genetic profile. Gene–diet interactions that affect metabolic pathways relevant to disease risk are continuously being uncovered. Discoveries in the field of nutrigenomics demonstrate that some individuals may benefit from adhering to different dietary guidelines than others, depending on their genotype. Certain industries have already begun to capitalize on the anticipation that knowledge of genomic information could help prevent the risk of developing diseases. Although disclosure of genetic information has been associated with the adoption of positive health-related behaviors under certain circumstances, the effect of providing gene-based dietary advice on motivating adherence to favorable dietary changes is largely unknown.

KEYWORDS: genetic testing ■ health behavior ■ nutrigenetics ■ nutrigenomics ■ personalized nutrition

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Variability between individuals in response to dietary intervention is a well-documented occurrence in nutrition research and practice [1]. The effect of diet modification on health-related markers such as blood cholesterol, body weight and blood pressure can differ significantly between individuals [2]. These differences partially account for the limited effectiveness of the current one-size-fits-all population-based model of nutritional guidance for health promotion. Factors such as age, sex, physical activity and smoking are known to affect one's response to diet, but the influence of genetics is becoming an increasingly important consideration. Nutrigenomics (or nutritional genomics) is the study of the relationship between genes and diet, and is used as an umbrella term for two complimentary approaches: how nutrients affect gene function and how genetic variation affects nutrient response [3]. The latter is referred to as nutrigenetics [4] and includes the study of how genetic variation affects food intake and eating behaviors, in addition to the biological response to nutrients and food bioactives [5,6]. Recent advances in nutrigenomics have shown that some individuals benefit more by following different dietary recommendations than others based on their individual genotype. This method of personalizing dietary recommendations based on 'responders' and 'nonresponders' is one of the primary goals of nutrigenomics. While the term 'personalization' refers to the delivery of information of high relevance to an individual and can be based on several factors such as phenotypes

and individual preferences, this review will focus only on the incorporation of an individual's personal genomic information. Personalized nutrition could be useful in both the prevention and treatment of chronic diseases by tailoring dietary advice and designing targeted dietary interventions to an individual's unique genetic profile; however, no studies have examined the effect of providing gene-based dietary advice on dietary intake behavior. This review will highlight the available evidence for personalized nutrition and summarize the literature that has investigated the effect of genomic information on health-related behaviors. Studies that provided subjects with their own genetic information and had follow-up assessments on health behavior outcomes are reviewed. Studies that did not provide subjects with real genetic information (i.e., analogue studies that ask subjects to imagine they are informed of a genetic test result) or studies that were cross-sectional in design are not included in this review.

Evidence for personalized nutrition

The concept of nutrigenomics has been around for some time, although the term is relatively new. One familiar example is lactose intolerance, which is a condition resulting from an inadequate production of the enzyme lactase in the small intestine due to genetic variation in the lactase gene [7]. Lactose intolerant individuals are unable to efficiently break down lactose, the primary milk sugar from dairy products. This can lead to gastrointestinal discomfort if lactose-containing

products are consumed. As a result, the dietary recommendation is to limit consumption of lactose-containing foods, choose lactose-free dairy products or use lactase supplements [8]. Another classic example of nutrigenomics is phenylketonuria (PKU), which is an inborn error of metabolism that results in reduced activity of the enzyme phenylalanine hydroxylase, which is needed to convert phenylalanine to tyrosine. Rare genetic variations in the phenylalanine hydroxylase gene are primarily responsible for the condition [9]. Individuals with PKU can develop neurological damage from excess phenylalanine [10] and are therefore advised to follow a low-phenylalanine diet for life [11]. Lactose intolerance and PKU are examples of gene–diet interactions that result from a single gene and involve a single dietary exposure. A major objective of nutrigenomics, however, is to identify gene–diet interactions that affect complex disorders that are polygenic in nature and involve a number of dietary exposures such as cardiovascular disease, Type 2 diabetes, obesity and cancers.

The main goal of nutrigenomics is to prevent the onset and progression of chronic disease through proper dietary advice. Research strategies employing nutrigenomics methodologies contribute to this goal by building upon the body of evidence that links nutrients to metabolic pathways relevant to disease outcomes. Furthermore, the incorporation of high-throughput ‘omics’ technologies into nutritional epidemiologic studies aims to improve the consistency of findings. Knowledge gained from current research in the field could lead to the development of personalized nutritional guidelines for individuals and specific subpopulations, which may ultimately reduce the burden of chronic disease.

Several significant findings in the field of nutrigenomics have paved a path towards personalized nutrition. For example, the relationship between coffee consumption and cardiovascular disease risk had been controversial for some time, due to inconsistent findings across studies. Applying a nutrigenomics framework to this area of study resulted in more consistent findings. A study examining the association between *CYP1A2* genotype, coffee intake and myocardial infarction found that carriers of the variant allele (‘slow’ caffeine metabolizers) were at an increased risk of myocardial infarction when consuming two or more cups of coffee per day [12]. A different study found that risk of hypertension associated with coffee intake also varies according to *CYP1A2* genotype, with carriers of the slow allele being at increased risk when

consuming one to three cups of coffee per day [13]. These results suggest that individuals carrying a slow allele should limit their consumption of caffeine, potentially to no more than two cups of coffee per day.

Another example comes from studies on the effects of genetic variation in vitamin C metabolism where individuals with either a *GSTM1* or *GSTT1* deletion polymorphism are at increased risk of vitamin C deficiency if they do not meet the recommended dietary allowance for vitamin C [14]. The recommended dietary allowance for vitamin C protects against serum ascorbic acid deficiency regardless of genotype, yet these results suggest that individuals with deletion genotypes for *GSTM1* or *GSTT1* could benefit from being particularly mindful of meeting the daily recommendation. Inadequate levels of serum ascorbic acid have been associated with several markers of cardiometabolic disease, including glucose homeostasis [15], high blood pressure [16,17], oxidative stress [18], high-sensitivity CRP [19] and indicators of obesity such as a higher BMI and waist:hip ratio [20,21].

An intriguing area of study that is rapidly expanding is the science of chemical senses and its relation to individual food preferences [6]. There is growing evidence that genetics plays a significant role in one’s detection of taste and smell, in turn affecting food preferences and dietary intake [22]. A study examining the role of genetic variation on sugar consumption found that a polymorphism in the *TAS1R2* gene (which encodes the sweet taste receptor) affects habitual consumption of sugars [23]. Individuals possessing a variant in the *TAS1R2* gene consumed more sugars than those without the genetic variant [23]. Although the mechanism for this variability in consumption is unknown, it is plausible that genetic variation in *TAS1R2* affects sweet taste perception which may play a role in an individual’s preference for sweet tasting foods. Knowing whether one is genetically predisposed to prefer sweet foods due to variation in taste receptor genes may assist in controlling the desire to consume such foods.

The role of genetic variation in salt-sensitive hypertension has also been explored [24,25]. One study found that hypertensive patients with a variant of the *ACE* gene had a significantly higher increase in blood pressure with high salt intake compared with those without the variant [24]. The prevalence of salt-sensitive hypertension, as determined by 24-h ambulatory mean blood pressure after high salt intake, was also significantly higher in patients with the *ACE*

variant [24]. The same results were observed when this sample size was increased from 50 patients to 71 patients, and additional genotypes were examined [25]. These results suggest that the *ACE* polymorphism may serve as a potential genetic marker of salt sensitivity. Informing an individual about his/her genetic susceptibility to salt-sensitive hypertension may motivate the adoption of behaviors, such as limiting dietary sodium intake, which could mitigate the chance of developing this condition later in life.

The evidence highlighted above demonstrates the ability to provide different dietary recommendations depending on genotype to target different health indicators, and several other examples of gene–diet interactions have been documented [26–34]. A potential outcome of personalized nutrition is a decrease in the prevalence of chronic diseases; however, this result is contingent upon adherence to the dietary recommendations. Disclosure of genetic information relating to disease risk has been shown to motivate the adoption of favorable health-related behaviors; however, the extent to which personalized nutrition is able to motivate individuals to make and adhere to dietary modifications is a key gap in the literature.

Disclosure of genetic information & health behavior change

Since the mapping of the human genome was completed, diagnostic tests that estimate an individual's risk of developing certain diseases based on genetic variants have been produced and used in clinical settings. Perhaps the most well-known tests of this nature are the *BRCA-1* and *BRCA-2* tests that detect mutations in genes that are known to increase the risk of breast and ovarian cancer development [35]. The ability for these tests to motivate favorable changes in health behaviors has been a subject of great interest to health researchers and behavioral scientists. A number of studies have evaluated the effects of providing genetic information related to genetic variants involved in hereditary breast, ovarian and colon cancers, on cancer screening behaviors. Genetic feedback of carrier status and cancer risk has been associated with improved screening behavior among those carrying an at-risk gene variant [36–41]. Regular cancer screenings are known to lead to earlier detection of cancer onset, which ultimately improves the prognosis of the disease [42].

In addition to cancer screening behavior, studies have also examined the effect of incorporating genetic testing information in smoking

cessation trials [43,44]. McBride *et al.* incorporated genetic susceptibility feedback to tobacco-related cancers into a smoking cessation program in a group of African–American smokers and compared cessation rates with a group that received a standard cessation intervention [43]. Participants in the genetic information group were counseled on their *GSTM1* genotype as previous studies have shown that individuals with lung cancer are more likely to have the *GSTM1* deletion genotype [45,46]. Smoking cessation was found to be greater in the group that received genetic information in the short-term (6 months following intervention), but not at the 12-month follow-up [43]. In a different study, Sanderson *et al.* examined the effect of *GSTM1* genetic test feedback on smokers' motivation to quit smoking. Those missing *GSTM1* reported a greater motivation to quit smoking compared with subjects with a functional *GSTM1*, and also smoked fewer cigarettes at 1-week follow-up [44]. These differences were not significant at 2-months follow-up [44].

The ineffectiveness of these trials to yield longer-term abstinence is not unique to these particular programs. Smoking relapse is a common occurrence among cessation programs that initially result in a reduction in or cessation of smoking, due to a variety of psychological and social factors [47]. A recent Cochrane review concluded that there is a lack of evidence to support the efficacy of any specific behavioral interventions aimed at preventing smoking relapse [47]; however, interventions of a complex psycho-educational nature, such as cognitive–behavioral coping skills training, have been effective in certain target groups [48], as well as postcessation treatment with pharmacological agents [49]. Cessation programs utilizing genetic information combined with more intensive behavioral therapy or pharmacological aid may result in increased rates of long-term smoking cessation.

Consultations with genetic information have also been used in weight loss interventions among obese individuals [50,51]. Conradt *et al.* found that incorporating genetic information about obesity into a weight loss consultation led to more realistic weight loss goals and greater satisfaction with a 5% weight loss. In addition, subjects with familial predisposition to obesity reported less self-blame about eating after receiving consultations with genetic information [50]. Rief *et al.* also found an improvement in negative mood in obese subjects with a family history of obesity when consultations included genetic information [51]. This is important as negative

thoughts and feelings about current weight have been shown to predict future weight gain [52]. Rief *et al.* also reported that subjects who received a consultation with genetic information of the etiology of obesity developed new insights about weight issues, suggesting the information was well received.

Pertinent to personalized nutrition, one study conducted in Greece evaluated the effect of personalized diets based on genetic information on weight loss among obese individuals who had a history of weight loss failures [53]. Individuals who opted for a commercial nutrigenetic screening test were given genotype-based weight loss recommendations and were compared with individuals who did not take the genetic test, but were following a weight loss diet [53]. There were no significant changes in BMI between the two groups in the first 100–300 days after the intervention; however, weight loss was more likely to be maintained in the nutrigenetic-tested subjects who were followed for more than 300 days [53]. Fasting blood glucose levels were also significantly improved among subjects who underwent nutrigenetic testing [53].

Additional studies examining genetic information and behavior have been related to Alzheimer's disease (AD) and familial hypercholesterolemia [54,55]. Chao *et al.* examined whether disclosure of *APOE* genotype altered health behavior among asymptomatic individuals at high risk for AD. It has been shown that first-degree family members and those carrying one or two copies of the *APOE* $\epsilon 4$ allele are at increased risk of developing AD [56,57]. Participants who learned they were $\epsilon 4$ -positive were significantly more likely to report AD-specific health behavior change, such as changing medication or vitamin use, 1-year after disclosure [54]. Adding a vitamin E supplement was the most common change [54]. Marteau *et al.* examined whether clinical diagnosis of familial hypercholesterolemia, as confirmed by a genetic mutation in the *LDLR* or *APOB* genes, affected patients' adherence to risk-reducing behaviors. Subjects with a mutation believed less strongly in the efficacy of diet in reducing cholesterol levels, but showed a trend in believing more strongly in the efficacy of medication [55].

It is clear that the disclosure of genetic information is able to motivate some favorable changes in a number of health-related behaviors. However, the genetic information used in the evidence summarized above was provided in clinical settings and, for the most part, was used as part of a research study. Personal genetic

information is currently easily obtainable, due to the rapid growth of the direct-to-consumer (DTC) genetic testing industry. The effect of genetic information obtained from a DTC source may be markedly different from the effect seen in a clinical or research setting and, therefore, studies that deliver genomic information in a manner more closely resembling a DTC method are needed to assess the impact of this industry on populations.

DTC genetic testing

DTC genetic tests claim to provide consumers with an analysis of either a select number of their genes, or a full-genome scan, that will reveal information about their ancestry, ability to metabolize nutrients and drugs, and risk for developing diseases [58]. One class of these genetic tests offers to provide personalized dietary advice based on an individual's DNA [59]. The DTC method of marketing facilitates the sales of these tests without involvement of a healthcare professional [60]. DTC genetic testing for disease susceptibility remains controversial, with opponents arguing that the tests currently possess limited value due to their questionable clinical validity and utility [61–63]. Critics note that predicted risk estimates will continue to change as new genetic variants are discovered, and thus risk calculations for disease based on currently known variants are premature [64,65]. Furthermore, environmental factors such as diet, smoking and physical activity can have a far greater impact on risk, but are often not considered when providing estimates of disease susceptibility. Another main criticism of most DTC genetic tests is that the corresponding advice is not genuinely personalized since the lifestyle recommendations are generally the same, regardless of genotype. Despite these criticisms, some propose that direct access to genetic information may motivate consumers to adopt favorable lifestyle behavioral changes that aim to prevent the onset and development of disease [66,67]. Therefore, a potential outcome of these genetic tests is a decrease in the prevalence of chronic diseases, such as cardiovascular disease, Type 2 diabetes and obesity, due to an increase in preventative measures through lifestyle modification such as adopting a healthier diet or increasing physical activity.

To date, only one study has examined the effect of genetic information obtained from a DTC genetic test on behavioral outcomes [68]. Subjects in this study purchased a commercially available DTC genetic test at a reduced price.

The test screens DNA for 23 different health conditions (e.g., Type 2 diabetes, heart disease, obesity and certain cancers) and provides estimates of one's risk for developing them over their lifetime. Prior to genetic testing, questionnaires were completed to measure initial health indicators and behaviors such as level of anxiety, dietary fat intake and time spent exercising. These questionnaires were repeated at a mean follow-up point of 6 months after the test results were disclosed and scores were compared to determine if the genetic information affected any outcome variable. No changes in scores were seen and the investigators concluded that the genetic information had no effect on the behavioral outcomes of interest.

This was the first study to evaluate the effect of DTC genetic test information on behavioral outcomes; however, the study had a number of limitations. Notably, the study did not include a control group, making it difficult to interpret the results. Furthermore, no truly personalized advice was provided to subjects who were found to be at greater risk of a condition. Therefore, these subjects may not have made changes to their diet or exercise patterns because they were not aware of what specific changes they should make that would mitigate their risk for the conditions.

Despite the null findings from Bloss *et al.* [68], there is evidence supporting the hypothesis that information from a DTC genetic test may result in lifestyle modification. A recent survey of readers of the journal *Nature* showed that 18% of respondents had their genomes analyzed in some way [69]. Of those 18%, 71% had the analysis performed by a commercial firm or company. Half of those who had undergone genetic testing reported learning of a health risk from the test results, and 27% reported changing their diet, lifestyle or medication use based on their genetic test results, despite not receiving specific recommendations to do so. These findings suggest that genetic information obtained from a DTC source could impact lifestyle behaviors.

Applications for nutrition

The finding that individuals report making changes to their diet following disclosure of DTC genetic test results for disease susceptibility merits further investigation. There is overwhelming evidence that cardiometabolic disease, including heart attack, stroke, heart failure, obesity and diabetes, is associated with a number of common, modifiable health behaviors, including diet [70]. Owing to the great deal of media

attention that the field of nutrition attracts, research findings relating diet and health are often translated to the public shortly after publication. However, dietary interventions aimed at reducing the risk of chronic disease have shown varying levels of effectiveness in clinical practice [71]. Poor compliance to dietary advice is commonly cited as an explanation for the ineffectiveness of these interventions to improve health outcomes. Biomarkers of nutritional exposure are often used in nutritional epidemiological studies to assess nutrient status, participants' adherence to assigned diets, and also to determine the validity of dietary intake questionnaires. Traditionally, surrogate indicators of nutritional intake have been measured individually from samples of urine (e.g., sodium, potassium, nitrogen) or blood (e.g., vitamins, carotenoids, fatty acids), although a great deal of interindividual variation exists between measurements [72]. This variability may be a result of genetic factors influencing an individual's response to various nutrients and may affect the utility of a biomarker to accurately reflect dietary exposure and adherence. Considering an individual's genotype when measuring nutritional biomarkers may improve the accuracy of assessing adherence to dietary advice. Furthermore, advances in the fields of proteomics and metabolomics offer new methods of quantitatively measuring several biomarkers or 'profiles' of an individual and relating them to nutritional patterns and exposures [73,74].

In addition to utilizing genomics and related technologies to improve assessment of nutritional exposures and dietary adherence, personalizing dietary advice by incorporating an individual's personal genomic information provides a unique opportunity to address issues of adherence and effectiveness of dietary interventions. As previously summarized, disclosure of genetic information related to disease risk can motivate individuals to adopt favorable health-related behaviors; however, the ability of genetic information to motivate changes in dietary habits has not been adequately explored.

A randomized controlled trial (NCT01353014) is currently exploring the effects of genotype-based dietary advice on dietary intake behavior [101]. Participants in the intervention (I) group receive a dietary advice report providing recommendations for daily intakes of caffeine, vitamin C, sugar and sodium based on genotypes for *CYP1A2* [12,13], *GSTM1* and *GSTT1* [14,75], *TASIR2* [23] and *ACE* [25], respectively. The reports were developed in collaboration

with Nutrigenomix, Inc. (Toronto, Canada), a company that is developing a nutrigenomics test kit for registered dietitians. The advice reports provide participants with their genotype for each gene, an explanation of what the genotype means in terms of the dietary component and a personalized recommendation for daily intake of the dietary component. Participants in the control (C) group receive general dietary recommendations from recognized health organizations for the same dietary components without genetic information. Dietary intakes and adherence are being assessed using a Toronto-modified Willett food frequency questionnaire (FFQ) that has been used previously in several studies demonstrating gene–diet interactions [30–32,76–78]. FFQs were collected at baseline, prior to intervention, and collected again at 3-month and 12-month follow-up points after the dietary advice reports were distributed. Changes in intake by the intervention group will be compared with the control group to determine the short- and long-term effect of gene-based dietary advice. Surveys are also being collected throughout the study to examine the perceptions of individuals toward genetic testing for personalized nutrition.

Preliminary findings from this study have recently been published [79]. Briefly, dietary recommendations based on genotype were reported to be more understandable than general dietary recommendations (93% agree [I] vs 78% agree [C]; $p = 0.009$) and were also reported to be more useful (88% agree [I] vs 72% agree [C]; $p = 0.02$). Participants reported that they would not be uncomfortable learning about their own genetic information. Consistent with this, participants in the intervention group did not express discomfort in learning about their genetics and were more likely to report enjoyment in learning about the dietary recommendations they were given (96% agree [I] vs 72% agree [C]; $p < 0.0001$), as well as a greater desire to know more about the recommendations (95% agree [I] vs 76% agree [C]; $p < 0.0001$). The FFQ analysis to investigate changes in dietary intake is currently underway, yet initial survey results demonstrate an appreciable difference in the way gene-based dietary advice is valued in comparison to general dietary advice [79]. Genetic tests for personalized nutrition may, therefore, be more valuable than those based solely on disease risk predictions.

Issues for consideration

A new era of genomic medicine is upon us. The potential for genomics technologies to

personalize prevention and treatment of disease is apparent and certain industries are already putting these advancements to commercial use. While current available evidence shows some benefit of disclosing genetic information related to disease risk, results should be considered cautiously as additional scientific questions have yet to be investigated in more detail. The field of genomics is relatively new and constantly changing. As new findings are discovered, it is likely that current estimates for disease risk or personalized advice for nutrition will be affected and may require updating. Additional factors, such as the gut microbiome and its interaction with the host genome, could impact response to nutrition as well and should be considered in future work.

Many ethical considerations regarding the use, access and storage of genomic information are being debated [80,81]. The DTC genetic testing industry is currently largely unregulated, although significant measures are being taken to regulate the market in certain jurisdictions [82]. In addition, concerns have been raised over the consumer's ability to accurately recall and interpret the meaning of the test results, given that no healthcare professional involvement is required [83]. Coupled with this concern is the recent finding that the literacy demands and quality of informational content across DTC genetic testing websites have been shown to vary and users may struggle to find and understand the important information on the sites [84]. A recent study examined understanding of genetic susceptibility test results among individuals who underwent free genetic testing for eight common health conditions [85]. More than 80% of the participants ($n = 199$) correctly recalled their test results 10 days after receiving them and were unlikely to interpret the results as deterministic of health outcomes at the 3-month follow-up assessment. A subset of the participants who had lower educational status and were members of ethnic minority groups reported a more deterministic interpretation of the results and were more confused by the information. This finding suggests that certain target groups may benefit from a consultation with a healthcare professional before and after genetic testing to ensure that the information is not misinterpreted. Furthermore, consumer attitudes toward genetic testing and personalized nutrition must be well understood to ensure that emerging technologies are successfully integrated into commercial use. A survey conducted among European consumers reported that 66% of individuals would be willing to undergo genetic testing and 27% to

follow a personalized diet [86]. Of note, individuals who were aware that they had health problems associated with the metabolic syndrome were more favorable toward nutrigenomic intervention [86]. In addition, a study assessing consumer acceptance of personalized nutrition found that acceptance was enhanced when consumers were able to make their genetic profile available free by their own choice, and if the products of testing provided an advantage to the consumer and could be easily implemented into daily routines [87]. Key areas to address in future studies include individual perceptions toward the acquisition and storage of genomic information, as well as opinions of the most trusted sources of delivery (i.e., healthcare professionals, research institutes, or DTC companies).

In addition to considering ethical, social and consumer questions, research geared at examining the effect of applying genomics for lifestyle modification would benefit from an investigation of behavioral change theories. Three major theories exist: the social cognitive theory, the theory of planned behavior and the transtheoretical model [88]. These theories have been applied to interventions aimed at improving physical activity patterns [89,90], mental health status [91] and addictive behaviors [92], as well as eating behavior [93,94]. Including assessments of stages of behavior change will inform researchers and clinicians of what barriers are present that may prevent an individual from adopting a favorable health behavior, and what strategies could assist in overcoming those barriers. Indeed, the National Human Genome Research Institute has recently highlighted the need to investigate the use of genomic information to improve behavior change interventions as part of its 2011 strategic vision for the future of genomics research [95]. Stemming from this, behavioral scientists have taken an interest in the relationship between genetic variation involved in adherence behaviors and intervention outcomes (e.g., dopaminergic rewards associated with eating behavior [96]) in order to further our understanding of the individual characteristics that predict the likelihood of a successful lifestyle intervention [97].

Conclusion

Advances in genomics offer many novel avenues toward personalized medicine. Personalized nutrition is one such application that holds much potential to deliver tailored dietary recommendations to individuals and subpopulations that can effectively prevent and manage the development

of chronic diseases. The extent to which personalized nutrition is able to motivate individuals to adopt healthier dietary habits is currently being investigated, yet remains a topic of intense interest and will play a significant role in determining strategies for designing and implementing successful lifestyle interventions in the future.

Future perspective

There is growing recognition amongst researchers, healthcare professionals and consumers that the one-size-fits-all population-based model of nutritional guidance for health promotion is inefficient and often ineffective. Research in nutrigenomics has shed light on the role of human genetic variation within a population and its ability to explain why some individuals respond differently than others to the same foods and beverages consumed. This area of research is revolutionizing the science of nutrition and we envisage there will be a strong demand for diagnostic kits that can provide this kind of personalized information in the near future. A tangible output of this research will be the commercialization of genetic tests for personalized nutrition. Unlike existing genetic tests that have been fraught with difficulties because of their questionable ability to accurately predict disease risk, the tests for personalized nutrition will be much more reliable and beneficial because the predicted phenotype will be based on dietary responsiveness, which is much more consistent and robust than gene-disease association studies. This information is likely to be delivered by a qualified healthcare professional, such as a registered dietitian, in order to ensure appropriate communication of test results to the consumer, as well as handling and storage of the genetic information. Collaborations with various partners, such as dietetics associations and public health agencies, will be essential to integrate personalized nutrition into clinical use in the near future.

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Executive summary

Background

- Variability between individuals in response to dietary intervention is well documented in nutrition research and practice and partially accounts for the limited effectiveness of the current one-size-fits-all population-based model of nutritional guidance for health promotion.
- Personalized nutrition could be useful in both the prevention and treatment of chronic diseases by tailoring dietary advice and designing targeted dietary interventions to an individual's unique genetic profile.

Evidence for personalized nutrition

- Gene–diet interactions that affect metabolic pathways relevant to disease risk are continuously being uncovered and offer new insights into personalizing dietary recommendations according to genotype.
- Applying a nutrigenomics framework to nutritional epidemiological studies has resulted in more consistent findings relating diet and markers of health.
- The relationship between coffee consumption and cardiovascular disease risk is one example of findings that have been clarified by taking genotype into account.

Disclosure of genetic information & health behavior change

- Since the mapping of the human genome was completed, diagnostic tests that estimate an individual's risk of developing certain diseases based on genetic variants have been produced and used in clinical settings.
- Disclosure of results from these tests has been shown to motivate favorable changes in health behaviors under particular circumstances, such as increasing cancer screenings and affecting vitamin and medication use.

Direct-to-consumer genetic testing

- Diagnostic tests that predict disease susceptibility have also been produced for commercial use. The marketing and distribution of these tests has been highly controversial, due to their questionable clinical validity and utility.
- Critics argue that the use of these tests to estimate disease risk is premature, while proponents note that direct access to genetic information may result in favorable lifestyle modifications that could reduce the risk of developing chronic diseases.
- Very few studies have examined the effect of direct-to-consumer (DTC) genetic test information on health behaviors.

Applications for nutrition

- A recent survey demonstrated that a proportion of individuals who had undergone genetic testing for disease susceptibility, mostly by means of a DTC genetic testing company, reported making changes to their diets and lifestyles despite not being given specific recommendations to do so.
- When informed of a health risk, diet is one of the first modifiable lifestyle factors that is taken into consideration.
- Genetic testing for personalized nutrition will be much more reliable and beneficial than disease-susceptibility tests because the predicted phenotype is based on dietary responsiveness, which is much more consistent and robust than gene–disease association studies.

Issues for consideration

- Issues of communication such as health literacy and healthcare professional involvement are important factors that can affect the way results from genetic tests are interpreted and applied. Furthermore, ethical issues surrounding the DTC genetic testing industry, such as privacy and regulatory standards, are currently being debated.
- Theories of behavior change may be important to consider when investigating the utility of genetic testing for lifestyle modification.

Conclusion

- Personalized nutrition holds much potential to deliver tailored dietary recommendations to individuals and subpopulations that can effectively prevent and manage the development of chronic diseases. The extent to which personalized nutrition is able to motivate individuals to adopt healthier dietary habits is currently being investigated.
- In the future, genetic tests for personalized nutrition will be in demand and qualified healthcare professionals, such as registered dietitians, will likely be the providers of this service.

References

Papers of special note have been highlighted as:

- of interest
- of considerable interest

- 1 Ordovas JM. Genotype–phenotype associations: modulation by diet and obesity. *Obesity (Silver Spring)* 16(Suppl. 3), S40–S46 (2008).
- 2 Ordovas JM, Kaput J, Corella D. Nutrition in the genomics era: cardiovascular disease risk and the Mediterranean diet. *Mol. Nut. Food Res.* 51(10), 1293–1299 (2007).
- 3 Cahill LE, El-Soehmy A. Nutrigenomics: a possible road to personalized nutrition. In: *Comprehensive Biotechnology* (Volume 4, 2nd Edition). Moo-Young M (Ed.). Elsevier, Amsterdam, The Netherlands, 703–712 (2011).
- 4 El-Soehmy A. Nutrigenetics. *Forum Nut.* 60, 25–30 (2007).
- 5 Eny KM, El-Soehmy A. The genetic determinants of ingestive behaviour: sensory, energy homeostasis and food reward aspects of ingestive behaviour. In: *Obesity Prevention: the Role of Brain and Society on Individual Behavior*. Dube L, Bechara AD, Dagher A *et al* (Eds). Elsevier, London, UK, 149–160 (2010).
- 6 Garcia-Bailo B, Toguri C, Eny KM, El-Soehmy A. Genetic variation in taste and its influence on food selection. *OMICS* 13(1), 69–80 (2009).
- 7 Swallow DM. Genetics of lactase persistence and lactose intolerance. *Annu. Rev. Genet.* 37, 197–219 (2003).
- 8 Swagerty DL Jr, Walling AD, Klein RM. Lactose intolerance. *Am. Fam. Physician* 65(9), 1845–1850 (2002).

- 9 Dilella AG, Kwok SC, Ledley FD, Marvit J, Woo SL. Molecular structure and polymorphic map of the human phenylalanine hydroxylase gene. *Biochemistry* 25(4), 743–749 (1986).
- 10 Surtees R, Blau N. The neurochemistry of phenylketonuria. *Eur. J. Pediatr.* 159(Suppl. 2), S109–S113 (2000).
- 11 National Institutes of Health Consensus Development Panel. National Institutes of Health Consensus Development Conference statement: phenylketonuria: screening and management. *Pediatrics* 108, 972–982 (2001).
- 12 Cornelis MC, El-Sohehy A, Kabagambe EK, Campos H. Coffee, *CYP1A2* genotype, and risk of myocardial infarction. *JAMA* 295(10), 1135–1141 (2006).
- **First study to identify *CYP1A2* genotype as a modifier of coffee consumption and cardiovascular disease risk.**
- 13 Palatini P, Ceolotto G, Ragazzo F *et al.* *CYP1A2* genotype modifies the association between coffee intake and the risk of hypertension. *J. Hypertens.* 27(8), 1594–1601 (2009).
- 14 Cahill LE, Fontaine-Bisson B, El-Sohehy A. Functional genetic variants of glutathione *S*-transferase protect against serum ascorbic acid deficiency. *Am. J. Clin. Nutr.* 90(5), 1411–1417 (2009).
- 15 Paolisso G, D'amore A, Balbi V *et al.* Plasma vitamin C affects glucose homeostasis in healthy subjects and in non-insulin-dependent diabetics. *Am. J. Physiol.* 266(2 Pt 1), e261–e268 (1994).
- 16 Moran JP, Cohen L, Greene JM *et al.* Plasma ascorbic acid concentrations relate inversely to blood pressure in human subjects. *Am. J. Clin. Nutr.* 57(2), 213–217 (1993).
- 17 Toohey L, Harris MA, Allen KG, Melby CL. Plasma ascorbic acid concentrations are related to cardiovascular risk factors in African-Americans. *J. Nutr.* 126(1), 121–128 (1996).
- 18 Johnston CS, Dancho CL, Strong GM. Orange juice ingestion and supplemental vitamin C are equally effective at reducing plasma lipid peroxidation in healthy adult women. *J. Am. Coll. Nutr.* 22(6), 519–523 (2003).
- 19 Ford ES, Liu S, Mannino DM, Giles WH, Smith SJ. C-reactive protein concentration and concentrations of blood vitamins, carotenoids, and selenium among United States adults. *Eur. J. Clin. Nutr.* 57(9), 1157–1163 (2003).
- 20 Canoy D, Wareham N, Welch A *et al.* Plasma ascorbic acid concentrations and fat distribution in 19,068 British men and women in the European Prospective Investigation into Cancer and Nutrition Norfolk cohort study. *Am. J. Clin. Nutr.* 82(6), 1203–1209 (2005).
- 21 Johnston CS, Beezhold BL, Mostow B, Swan PD. Plasma vitamin C is inversely related to body mass index and waist circumference but not to plasma adiponectin in nonsmoking adults. *J. Nutr.* 137(7), 1757–1762 (2007).
- 22 Reed DR, Knaapila A. Genetics of taste and smell poisons and pleasures. *Prog. Mol. Biol. Transl. Sci.* 94, 213–240 (2010).
- 23 Eny KM, Wolever TM, Corey PN, El-Sohehy A. Genetic variation in *TAS1R2* (Ile191Val) is associated with consumption of sugars in overweight and obese individuals in 2 distinct populations. *Am. J. Clin. Nutr.* 92(6), 1501–1510 (2010).
- 24 Giner V, Poch E, Bragulat E *et al.* Renin-angiotensin system genetic polymorphisms and salt sensitivity in essential hypertension. *Hypertension* 35(1 Pt 2), 512–517 (2000).
- 25 Poch E, Gonzalez D, Giner V, Bragulat E, Coca A, De La Sierra A. Molecular basis of salt sensitivity in human hypertension. Evaluation of renin-angiotensin-aldosterone system gene polymorphisms. *Hypertension* 38(5), 1204–1209 (2001).
- 26 Corella D, Peloso G, Arnett DK *et al.* *APOA2*, dietary fat, and body mass index: replication of a gene-diet interaction in 3 independent populations. *Arch. Intern. Med.* 169(20), 1897–1906 (2009).
- 27 Cornelis MC, Qi L, Kraft P, Hu FB. *TCF7L2*, dietary carbohydrate, and risk of Type 2 diabetes in US women. *Am. J. Clin. Nutr.* 89(4), 1256–1262 (2009).
- 28 Ferguson JF, Phillips CM, McMonagle J *et al.* *NOS3* gene polymorphisms are associated with risk markers of cardiovascular disease, and interact with ω-3 polyunsaturated fatty acids. *Atherosclerosis* 211(2), 539–544 (2010).
- 29 Solis C, Veenema K, Ivanov AA *et al.* Folate intake at RDA levels is inadequate for Mexican American men with the methylenetetrahydrofolate reductase 677TT genotype. *J. Nutr.* 138(1), 67–72 (2008).
- 30 Fontaine-Bisson B, Wolever TM, Connelly PW, Corey PN, El-Sohehy A. NF-κB –94Ins/Del ATTG polymorphism modifies the association between dietary polyunsaturated fatty acids and HDL-cholesterol in two distinct populations. *Atherosclerosis* 204(2), 465–470 (2009).
- 31 Eny KM, Wolever TM, Fontaine-Bisson B, El-Sohehy A. Genetic variant in the glucose transporter type 2 is associated with higher intakes of sugars in two distinct populations. *Physiol. Genomics* 33(3), 355–360 (2008).
- 32 Eny KM, Corey PN, El-Sohehy A. Dopamine D2 receptor genotype (C957T) and habitual consumption of sugars in a free-living population of men and women. *J. Nutrigenet. Nutrigenomics* 2(4–5), 235–242 (2009).
- 33 Cornelis MC, El-Sohehy A, Campos H. *GSTT1* genotype modifies the association between cruciferous vegetable intake and the risk of myocardial infarction. *Am. J. Clin. Nutr.* 86(3), 752–758 (2007).
- 34 Cuda C, Garcia-Bailo B, Karmali M, El-Sohehy A, Badawi A. A common polymorphism near the interleukin-6 gene modifies the association between dietary fat intake and insulin sensitivity. *J. Inflamm. Res.* 5, 1–6 (2012).
- 35 Ford D, Easton DF. The genetics of breast and ovarian cancer. *Br. J. Cancer* 72(4), 805–812 (1995).
- 36 Kinney AY, Simonsen SE, Baty BJ *et al.* Risk reduction behaviors and provider communication following genetic counseling and *BRCA1* mutation testing in an African American kindred. *J. Genet. Couns.* 15(4), 293–305 (2006).
- 37 Watson M, Foster C, Eeles R *et al.* Psychosocial impact of breast/ovarian (*BRCA1/2*) cancer-predictive genetic testing in a UK multi-centre clinical cohort. *Br. J. Cancer* 91(10), 1787–1794 (2004).
- 38 Claes E, Denayer L, Evers-Kiebooms G *et al.* Predictive testing for hereditary nonpolyposis colorectal cancer: subjective perception regarding colorectal and endometrial cancer, distress, and health-related behavior at one year post-test. *Genet. Test* 9(1), 54–65 (2005).
- 39 Collins V, Meiser B, Gaff C, St John DJ, Halliday J. Screening and preventive behaviors one year after predictive genetic testing for hereditary nonpolyposis colorectal carcinoma. *Cancer* 104(2), 273–281 (2005).
- 40 Hadley DW, Jenkins JF, Dimond E, de Carvalho M, Kirsch I, Palmer CG. Colon cancer screening practices after genetic counseling and testing for hereditary nonpolyposis colorectal cancer. *J. Clin. Oncol.* 22(1), 39–44 (2004).
- 41 Halbert CH, Lynch H, Lynch J *et al.* Colon cancer screening practices following genetic testing for hereditary nonpolyposis colon cancer (HNPCC) mutations. *Arch. Intern. Med.* 164(17), 1881–1887 (2004).
- 42 Etzioni R, Urban N, Ramsey S *et al.* The case for early detection. *Nat. Rev. Cancer* 3(4), 243–252 (2003).
- 43 McBride CM, Bepler G, Lipkus IM *et al.* Incorporating genetic susceptibility feedback into a smoking cessation program for African-American smokers with low income. *Cancer Epidemiol. Biomarkers Prev.* 11(6), 521–528 (2002).

- 44 Sanderson SC, Humphries SE, Hubbard C, Hughes E, Jarvis MJ, Wardle J. Psychological and behavioural impact of genetic testing smokers for lung cancer risk: a Phase II exploratory trial. *J. Health Psychol.* 13(4), 481–494 (2008).
- 45 McWilliams JE, Sanderson BJ, Harris EL, Richert-Boe KE, Henner WD. Glutathione S-transferase M1 (GSTM1) deficiency and lung cancer risk. *Cancer Epidemiol. Biomarkers Prev.* 4(6), 589–594 (1995).
- 46 Bartsch H, Rojas M, Nair U, Nair J, Alexandrov K. Genetic cancer susceptibility and DNA adducts: studies in smokers, tobacco chewers, and coke oven workers. *Cancer Detect Prev.* 23(6), 445–453 (1999).
- 47 Hajek P, Stead LF, West R, Jarvis M, Lancaster T. Relapse prevention interventions for smoking cessation. *Cochrane Database Syst. Rev.* (1), CD003999 (2009).
- 48 Song F, Huttunen-Lenz M, Holland R. Effectiveness of complex psycho-educational interventions for smoking relapse prevention: an exploratory meta-analysis. *J. Public Health (Oxf.)*. 32(3), 350–359 (2010).
- 49 Tonstad S, Tonnesen P, Hajek P *et al.* Effect of maintenance therapy with varenicline on smoking cessation: a randomized controlled trial. *JAMA* 296(1), 64–71 (2006).
- 50 Conrads M, Dierk JM, Schlumberger P *et al.* A consultation with genetic information about obesity decreases self-blame about eating and leads to realistic weight loss goals in obese individuals. *J. Psychosom. Res.* 66(4), 287–295 (2009).
- 51 Rief W, Conrads M, Dierk JM *et al.* Is information on genetic determinants of obesity helpful or harmful for obese people? – a randomized clinical trial. *J. Gen. Intern. Med.* 22(11), 1553–1559 (2007).
- 52 Burk-Braxton CL. Is shame a factor in overweight relapse? *Diss. Abstr. Int. B Sci. Eng.* 57, 4052 (1996).
- 53 Arkadianos I, Valdes AM, Marinos E, Florou A, Gill RD, Grimaldi KA. Improved weight management using genetic information to personalize a calorie controlled diet. *Nutr. J.* 6, 29 (2007).
- 54 Chao S, Roberts JS, Marteau TM, Silliman R, Cupples LA, Green RC. Health behavior changes after genetic risk assessment for Alzheimer disease: the REVEAL Study. *Alzheimer Dis. Assoc. Disord.* 22(1), 94–97 (2008).
- 55 Marteau T, Senior V, Humphries SE *et al.* Psychological impact of genetic testing for familial hypercholesterolemia within a previously aware population: a randomized controlled trial. *Am. J. Med. Genet. A* 128A(3), 285–293 (2004).
- 56 Farrer LA, Cupples LA, Haines JL *et al.* Effects of age, sex, and ethnicity on the association between apolipoprotein E genotype and Alzheimer disease. A meta-analysis. *APOE and Alzheimer Disease Meta Analysis Consortium. JAMA* 278(16), 1349–1356 (1997).
- 57 Green RC, Cupples LA, Go R *et al.* Risk of dementia among white and African American relatives of patients with Alzheimer disease. *JAMA* 287(3), 329–336 (2002).
- 58 Janssens AC, Van Duijn CM. An epidemiological perspective on the future of direct-to-consumer personal genome testing. *Investig. Genet.* 1(1), 10 (2010).
- 59 Sterling R. The on-line promotion and sale of nutrigenomic services. *Genet. Med.* 10(11), 784–796 (2008).
- 60 Norrgard K. DTC genetic testing for diabetes, breast cancer, heart disease and paternity. *Nat. Educ.* 1(1), (2008).
- 61 Burke W. Clinical validity and clinical utility of genetic tests. *Curr. Protoc. Hum. Genet.* Chapter 9, Unit 9.15 (2009).
- 62 Eng C, Sharp RR. Bioethical and clinical dilemmas of direct-to-consumer personal genomic testing: the problem of misattributed equivalence. *Sci. Transl. Med.* 2(17), 17cm15 (2010).
- 63 Caulfield T, Ries NM, Ray PN, Shuman C, Wilson B. Direct-to-consumer genetic testing: good, bad or benign? *Clin. Genet.* 9(6–7), 48–50 (2010).
- 64 Janssens AC, Wilde AA, Van Langen IM. The sense and nonsense of direct-to-consumer genetic testing for cardiovascular disease. *Neth. Heart J.* 19(2), 85–88 (2011).
- 65 Mihaescu R, Van Hoek M, Sijbrands EJ *et al.* Evaluation of risk prediction updates from commercial genome-wide scans. *Genet. Med.* 11(8), 588–594 (2009).
- 66 Bloss CS, Darst BF, Topol EJ, Schork NJ. Direct-to-consumer personalized genomic testing. *Hum. Mol. Genet.* 20(R2), R132–R141 (2011).
- 67 McBride CM, Koehly LM, Sanderson SC, Kaphingst KA. The behavioral response to personalized genetic information: will genetic risk profiles motivate individuals and families to choose more healthful behaviors? *Annu. Rev. Public Health* 31, 89–103 (2010).
- **Review of studies that have investigated the effect of genetic information on health behaviors.**
- 68 Bloss CS, Schork NJ, Topol EJ. Effect of direct-to-consumer genomewide profiling to assess disease risk. *N. Engl. J. Med.* 364(6), 524–534 (2011).
- **The first study to investigate the effect of direct-to-consumer genetic test results on specific health behavior outcomes.**
- 69 Maher B. *Nature* readers flirt with personal genomics. *Nature* 478, 19 (2011).
- **Survey reporting that individuals make changes to their diet and lifestyle following disclosure of genetic test results, mostly obtained from a direct-to-consumer company.**
- 70 Parekh S, Vandelanotte C, King D, Boyle FM. Design and baseline characteristics of the 10 Small Steps Study: a randomised controlled trial of an intervention to promote healthy behaviour using a lifestyle score and personalised feedback. *BMC Public Health* 12, 179 (2012).
- 71 Desroches S, Lapointe A, Ratte S, Gravel K, Legare F, Thirsk J. Interventions to enhance adherence to dietary advice for preventing and managing chronic diseases in adults: a study protocol. *BMC Public Health* 11, 111 (2011).
- 72 Jenab M, Slimani N, Bictash M, Ferrari P, Bingham SA. Biomarkers in nutritional epidemiology: applications, needs and new horizons. *Hum. Genet.* 125(5–6), 507–525 (2009).
- 73 Fuchs D, Winkelmann I, Johnson IT, Mariman E, Wenzel U, Daniel H. Proteomics in nutrition research: principles, technologies and applications. *Br. J. Nutr.* 94(3), 302–314 (2005).
- 74 Rezzi S, Ramadan Z, Fay LB, Kochhar S. Nutritional metabonomics: applications and perspectives. *J. Proteome. Res.* 6(2), 513–525 (2007).
- 75 Horská A, Mislanová C, Bonassi S, Ceppi M, Volkovová K, Dusínská M. Vitamin C levels in blood are influenced by polymorphisms in glutathione S-transferases. *Eur. J. Nutr.* 50(6), 437–446 (2010).
- 76 Cahill LE, El-Sohemy A. Vitamin C transporter gene polymorphisms, dietary vitamin C and serum ascorbic acid. *J. Nutrigenet. Nutrigenomics* 2(6), 292–301 (2009).
- 77 Cahill LE, El-Sohemy A. Haptoglobin genotype modifies the association between dietary vitamin C and serum ascorbic acid deficiency. *Am. J. Clin. Nutr.* 92(6), 1494–1500 (2010).
- 78 Fontaine-Bisson B, El-Sohemy A. Genetic polymorphisms of tumor necrosis factor- α modify the association between dietary polyunsaturated fatty acids and plasma high-density lipoprotein-cholesterol concentrations in a population of young adults. *J. Nutrigenet. Nutrigenomics* 1(5), 215–223 (2008).

- 79 Nielsen DE, El-Sohemy A. A randomized trial of genetic information for personalized nutrition. *Genes Nutr*. doi:10.1007/s12263-012-0290-x (2012) (Epub ahead of print).
- **First study to investigate perceptions of personalized nutrition among individuals who received gene-based dietary advice.**
- 80 Nordgren A. Neither as harmful as feared by critics nor as empowering as promised by providers: risk information offered direct to consumer by personal genomics companies. *J. Community Genet*. doi:10.1007/s12687-012-0094-0 (2012) (Epub ahead of print).
- 81 Hawkins AK, Ho A. Genetic counseling and the ethical issues around direct to consumer genetic testing. *J. Genet. Couns.* 21(3), 367–373 (2012).
- 82 McGuire AL, Evans BJ, Caulfield T, Burke W. Science and regulation. Regulating direct-to-consumer personal genome testing. *Science* 330(6001), 181–182 (2010).
- 83 Leighton JW, Valverde K, Bernhardt BA. The general public's understanding and perception of direct-to-consumer genetic test results. *Public Health Genomics* 15(1), 11–21 (2011).
- 84 Lachance CR, Erby LA, Ford BM, Allen VC Jr, Kaphingst KA. Informational content, literacy demands, and usability of websites offering health-related genetic tests directly to consumers. *Genet. Med.* 12(5), 304–312 (2010).
- 85 Kaphingst KA, McBride CM, Wade C *et al.* Patients' understanding of and responses to multiplex genetic susceptibility test results. *Genet. Med.* doi:10.1038/gim.2012.22 (2012) (Epub ahead of print).
- **First study to investigate understanding of genetic test results among individuals who underwent genetic susceptibility testing.**
- 86 Stewart-Knox BJ, Bunting BP, Gilpin S *et al.* Attitudes toward genetic testing and personalised nutrition in a representative sample of European consumers. *Br. J. Nutr.* 101(7), 982–989 (2009).
- 87 Ronteltap A, Van Trijp JCM, Renes RJ. Consumer acceptance of nutrigenomics-based personalised nutrition. *Br. J. Nutr.* 101(1), 132–144 (2009).
- 88 Glanz K, Rimer BK, Viswanath K. Theory, research, and practice in health behavior and health education. In: *Health Behavior and Health Education: Theory Research and Practice (4th Edition)*. Glanz K, Rimer BK, Viswanath K (Eds). Jossey-Bass, CA, USA, 23–38 (2008).
- 89 Tavares LS, Plotnikoff RC, Loucaides C. Social-cognitive theories for predicting physical activity behaviours of employed women with and without young children. *Psychol. Health Med.* 14(2), 129–142 (2009).
- 90 Kirk A, De Feo P. Strategies to enhance compliance to physical activity for patients with insulin resistance. *Appl. Physiol. Nutr. Metab.* 32(3), 549–556 (2007).
- 91 Baker R, Reddish S, Robertson N, Hearnshaw H, Jones B. Randomised controlled trial of tailored strategies to implement guidelines for the management of patients with depression in general practice. *Br. J. Gen. Pract.* 51(470), 737–741 (2001).
- 92 Webb TL, Sniehotta FF, Michie S. Using theories of behaviour change to inform interventions for addictive behaviours. *Addiction* 105(11), 1879–1892 (2010).
- 93 Horwath CC. Applying the transtheoretical model to eating behaviour change: challenges and opportunities. *Nutr. Res. Rev.* 12(2), 281–317 (1999).
- 94 Anderson AS. How to implement dietary changes to prevent the development of metabolic syndrome. *Br. J. Nutr.* 83(Suppl. 1), S165–S168 (2000).
- 95 Green ED, Guyer MS. Charting a course for genomic medicine from base pairs to bedside. *Nature* 470(7333), 204–213 (2011).
- **Perspective from the National Human Genome Research Institute on the future of genomic medicine.**
- 96 Stice E, Dagher A. Genetic variation in dopaminergic reward in humans. *Forum Nut.* 63, 176–185 (2010).
- 97 McBride CM, Bryan AD, Bray MS, Swan GE, Green ED. Health behavior change: can genomics improve behavioral adherence? *Am. J. Public Health* 102(3), 401–405 (2012).
- **Commentary on the ability of genomic information to improve adherence to behavior change interventions.**
- **Website**
- 101 Genetic Information and Dietary Intake Behaviour. <http://clinicaltrials.gov/ct2/show/NCT01353014>