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CLINICAL NUTRITION RESEARCH

Review Article

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Direct-to-Consumer Genetic Testing in Korea: Current Status and Significance in Clinical Nutrition

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ABSTRACT

Direct-to-consumer genetic testing (DTC-GT) provides a means for consumers to gain insights into their genetic background and how it relates to their health without the involvement of medical institutions. In Korea, DTC-GT was introduced in 2016 in accordance with the legislation on Paragraph (3) 2 of Article 50 of the Bioethics and Safety Act. Only 12 genetic test items involving 46 genes were approved at first, but the approved items were expanded to 70 in November 2020. However, the genetic test items of DTC-GT services in Korea are still restricted to the wellness area, and access to disease risk related information is only permitted to medical institutions. Further, studies revealing the relationship between genotype differences and responses to nutrients, food components, or nutritional status are increasing, and this association appears to be robust for some genes. This strong association between genetic variations and nutrition suggests that DTC-GT can be used as an important tool by clinical nutritionists to gain insights into an individual's genetic susceptibilities and provide guidance on nutritional counseling and meal planning based on the patient's genetic information. This review summarized the history and current status of DTC-GT and investigated the relationship between genetic variations with associated phenotypic traits to clarify further the importance of DTC-GT in the field of clinical nutrition.

Keywords: Direct-to consumer screening and testing; Genetic variation; Nutrigenomics; Nutritionists; Clinical decision-making

INTRODUCTION

Direct-to-consumer genetic testing (DTC-GT) provides insights into the potential health effects of genetic variants without the involvement of a medical institution [1]. In parallel with the advancements in genomic medicine, DTC-GT became commercially available in the early 2000s [1-3]. In Korea, the public use of DTC-GT was legally approved in 2016 with the enactment of Paragraph (3) 2 of Article 50 of the Bioethics and Safety Act. DTC-GT services are allowed to provide a wide variety of information to consumers in countries such as the United States, Canada, and Japan, including their genetic risks for chronic disease and cancers, personal traits related to wellness, and ancestry information [1]. However, these services can exclusively provide wellness-associated information in Korea. The wellness components of DTC-GT include personal traits related to health or appearance such as body mass index, blood glucose, caffeine metabolism, and hair loss, among others.

There are approximately 7 million common single nucleotide polymorphisms (SNPs) with a minor allele frequency of at least 5% across the human population [4]. Among these SNPs, 50% occur in noncoding regions, 25% lead to missense mutations, and the remaining 25% are silent mutations (nonsynonymous SNPs) [5]. Many of these genetic variations are still under investigation to elucidate their specific functions. However, recent studies have identified strong associations between some genetic variations and nutrition-associated phenotypes such as dietary intake/requirements or nutritional status. Therefore, based on these robust gene-diet interactions, DTC-GT could be utilized in the field of clinical nutrition to provide personalized dietary counseling or meal planning based on the individual's genetic background.

Therefore, this review summarized the history and current status of DTC-GT in Korea as well as in other countries and investigated the associations between genetic variations and responses to nutrients or dietary factors to assess the applicability of genetic testing services in the field of clinical nutrition.

DTC-GT: DEFINITION, BACKGROUND, AND MARKETS

Definition of DTC-GT

DTC-GT is marketed directly to consumers without the involvement of a health care provider [6]. According to the Ministry of Health and Welfare Notice of Korea No. 2020-35, DTC-GT is defined as "a test that can be performed by a genetic testing institution other than a medical institution by collecting samples, testing, analyzing test results, and delivering test results directly to the consumers" [7]. DTC-GT services are generally utilized for three main reasons: 1) to provide insights into the consumer's identity (e.g., ancestry or paternity), 2) gain a gene-level assessment of disease risk to complement health care, or 3) curiosity-driven testing to achieve a better lifestyle [8].

Introduction to DTC-GT

Since the completion of the human genome sequencing project in 2003, many companies offering genetic testing services have been established [9]. The emergence of DTC-GT was influenced by changes in the medical paradigm and the reduction of costs due to advances in genetic analysis technology. Based on the data collected from the National Human Genome Research Institute (NHGRI), the estimated cost of sequencing a whole human genome reached up to $150 million. However, this price had fallen below $1,500 by the end of 2015 and has more recently decreased to less than $1,000 in 2020 [10]. Accordingly, DTC-GT is now available at prices as low as approximately $100 [11]. In Korea, the primary legislation for the use of genomics in health is based on the Paragraph (3) 2 of Article 50 of the Bioethics and Safety Act, which was amended in 2015 to introduce the regulation of genetic treatment research. In 2016, the Ministry of Health and Welfare announced a plan to establish a large-scale biobank, a key infrastructure for precision medicine, and to allow non-medical institutions to directly conduct genetic testing for disease prevention [12].

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DTC-GT markets

According to the report by Global Market Insights, the global DTC-GT market size was valued at over $220 million in 2019 and is expected to exceed $3.4 billion by 2028 [13]. However, accurate statistics on the size of the domestic DTC-GT service market in Korea are not available. Both the DTC-GT market and industry have not been fully activated in Korea due to government regulations and policies [14].

CURRENT STATUS OF DTC-GT

Development of DTC-GT in Korea

According to the Notice Notification 2016-9 of the Ministry of Health and Welfare, which was enacted on June 30, 2016, DTC-GT was allowed to provide information regarding 12 items represented by 46 genes, including blood sugar, blood pressure, hair loss, and vitamin C metabolism (**Table 1**).

The Korean government is implementing cautious and stepwise approaches to allow a greater number of tests by establishing the DTC-GT service certification systems and regulatory sandbox. In February 2019, the Ministry of Health and Welfare promoted the DTC-GT service certification system to evaluate the accuracy and reliability of DTC-GT services and to use them as a basis for determining whether to expand the scope of the services in the future. The DTC-GT service certification system evaluates and certifies the quality and the appropriateness of DTC-GT services provided by DTC-GT companies by assessing 100 evaluation items. The first DTC-GT service certification was conducted from February 2019 to February 2020. Among the 12 items and 46 genes that were previously approved, the skin elasticity item was removed from the list due to a lack of scientific evidence. The Genetic Committee under the National Bioethics Review Committee reviewed scientific evidence that sufficiently verified and expanded the available test items from 11 to 56 in total (**Table 2**). The number of genetic test items was limited to 56 items, but the types of genes and SNPs for each item could be selected autonomously by the company [15]. The second DTC-GT service certification was conducted from March 2020 to February 2021. Through this initiative, the genetic test items that could be directly evaluated by genetic testing institutions other than medical institutions were expanded from 56 to up to 70 items (**Table 2**), and 8 recognized genetic testing institutions (Labgenomics, Macrogen, TeragenEtex, DNAlink, Medizen Humancare, Geninus, SCLHealthcare, and NGeneBio) were allowed to test up to 70 gene items. Additionally, it was specified that the provision of explanations and information

Table 1. Genetic test items that were approved for DTC-GT in 2016 (12 test items and 46 genes)

#	Test items (number of genes)	Genes
1	BMI (3)	*FTO*, *MC4R*, *BDNF*
2	Triglycerides concentration (8)	*GCKR*, *DOCK7*, *ANGPTL3*, *BAZ1B*, *TBL2*, *MLXIPL*, *LOC105375745*, *TRIB1*
3	Cholesterol (8)	*CELSR2*, *SORT1*, *HMGCR*, *ABO*, *ABCA1*, *MYL2*, *LIPG*, *CETP*
4	Blood sugar (8)	*CDKN2A/B*, *G6PC2*, *GCK*, *GCKR*, *GLIS3*, *MTNR1B*, *DGKB-TMEM195*, *SLC30A8*
5	Blood pressure (8)	*NPR3*, *ATP2B1*, *NT5C2*, *CSK*, *HECTD4*, *GUCY1A3*, *CYP17A1*, *FGF5*
6	Pigmentation (2)	*OCA2*, *MC1R*
7	Hair loss (3)	*chr20p11 (rs1160312*, *rs2180439)*, *IL2RA*, *HLA-DQB1*
8	Hair thickness (1)	*EDAR*
9	Skin aging (1)	*AGER*
10	Skin elasticity (1)	*MMP1*
11	Vitamin C concentration (1)	*SLC23A1 (SVCT1)*
12	Caffeine metabolism (2)	*AHR*, *CYP1A1*, *CYP1A2*

DTC-GT, direct-to-consumer genetic testing; BMI, body mass index.

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Table 2. Genetic test items allowed for DTC-GT that were added after the 1st and 2nd DTC-GT certification systems

Classification	First approved items ('16.6) (12 items)	Items added after the 1st DTC-GT certification system ('20.2) (56 items in total)	Items added after the 2nd DTC-GT certification system ('20.11) (70 items in total)
Nutrients	Vitamin C concentration	Vitamin D concentration Coenzyme Q10 concentration Magnesium concentration Zinc concentration Iron storage and concentration Calcium concentration Potassium concentration Arginine concentration Fatty acid concentration	Vitamin A concentration Vitamin B6 concentration Vitamin B12 concentration Vitamin E concentration Vitamin K concentration Tyrosine concentration Betaine concentration Selenium concentration Lutein & Zeaxanthin concentration
Exercise		Muscle fitness Muscle development ability Grip force Suitability for aerobic exercise Ability for short-distance running Ability to recover after exercise Suitability for endurance exercise Risk of ankle injury	
Skin/Hair	Pigmentation Hair thickness Skin aging Skin elasticity (Removed through the first certification project) Hair loss	Freckles Acne Tanning after sun exposure Skin inflammation Stretch mark/keratin Alopecia areata	
Dietary habits		Appetite Satiety Sensitivity for salty taste Sensitivity for bitter taste Sensitivity for sweet taste	
Personal traits	Caffeine metabolism	Alcohol metabolism Wine preference Alcohol dependence Nicotine metabolism Caffeine dependence Morning or night person Sleep habits/time Alcohol flush Insomnia Pain sensitivity	
Healthcare	Triglyceride concentration Cholesterol BMI Blood pressure Blood sugar	Susceptibility to degenerative arthritis Motion sickness Obesity Uric acid Percentage of body fat	Bone mass Abdominal obesity (hip-waist ratio) Weight loss effect after exercise Possibility of weight recovery after weight loss
Lineage		Ancestry	

DTC-GT, direct-to-consumer genetic testing; BMI, body mass index.

were under the responsibility of the genetic testing agency, in addition to sample collection, analysis of samples, interpretation of data, and delivery of test results. Through the introduction of this certification system, the reliability and accountability of DTC-GT services can be strengthened. The third pilot project for the DTC-GT service certification system was started in April 2021 and is still underway.

Genetic information on disease susceptibility can be provided only through medical institutions in Korea. In February 2019, the Ministry of Health and Welfare introduced a regulatory sandbox into the DTC-GT. A regulatory sandbox is a system that allows innovative technologies in their early stages of development to be implemented without regulations. Four companies selected as regulatory sandbox operators were allowed to conduct DTC-GT for research purposes. Specifically, these companies were allowed to examine genetic variants associated with 13 diseases (e.g., chronic diseases, stroke, and cancers) and wellness

Table 3. Outline of regulatory sandbox projects regarding DTC-GT conducted by four companies

Company (approval date)	Project name and additional allowed test items	Region/period/subject
Macrogen (2019.2)	App-based customized health promotion service through DTC genome analysis, 13 additional diseases were allowed. · Diseases (8): coronary artery disease, hypertension, atrial fibrillation, stroke, type-2 diabetes, osteoarthritis, macular degeneration, and Parkinson's disease · Cancer (5): prostate cancer, colorectal cancer, stomach cancer, lung cancer, and liver cancer	Incheon Economic Free Zone/2 years/2,000 adults
TheragenEtex (2019.9)	Management service for obesity and nutrition based on DTC-GT, 24 additional items were allowed. · Obesity management (6): appetite control, fat metabolism, inflammation, sugar metabolism, energy consumption, stress · Nutrition management (18): Coenzyme Q10, magnesium, zinc, calcium, iron, selenium, vitamins A, B, D, E, and K, lutein, L-carnitine, tyrosine, betaine, omega-3 and 6, and phytoestrogen	Seoul/18 months/1,200 adults
Medizen Humancare (2019.9)	Prediction of exercise performance based on DTC-GT, 13 additional items were allowed. · Exercise performance (13): muscle development, grip force, endurance, heart rate resilience, fracture risk, injury risk, weight control (obesity), stress sensitivity, agility, athletic activity, biorhythm, multifunctional performance, and motor sensitivity	Metropolitan area/2 years/3,000 adults
DNAlink (2019.9)	Validation of usefulness and risk of DTC-GT, 32 additional items were allowed. · Cancers (6): colorectal cancer, lung cancer, stomach cancer, liver cancer, thyroid cancer, and prostate cancer · Diseases (14): coronary artery disease, arterial fibrillation, stroke, intracranial aneurysm, type 2 diabetes, Parkinson's disease, macular degeneration, chronic kidney disease, nonalcoholic fatty liver, hypertension, esophageal reflux, chronic obstructive pulmonary disease, osteoarthritis, and hyperlipidemia · Wellness (12): antioxidant capacity, inflammatory system, vitamin A, B, D, E, fatty acids, magnesium, exercise effect, weight control, nicotine dependence, and alcohol dependence	Gwangju/2 years/2,000 adults

DTC-GT, direct-to-consumer genetic testing.

for two years after deliberation by the Bioethics Committee (**Table 3**). Although the pilot studies conducted by the companies are still in progress, DTC-GT can be utilized for overall health management if the study results prove that DTC-GT can contribute to the prevention and diagnosis of diseases, as well as the identification of personal traits.

Current status and limitations of DTC-GT in Korea

In Korea, DTC-GT services are confined to health and beauty care products, and the number of DTC-GT services is relatively limited. Approximately 52 companies are currently providing DTC-GT services in Korea, but the total number of DTC-GT services reported to the Ministry of Health and Welfare was less than 10,000 in 2018, whereas in 2020 more than 10 million services were provided by 23andMe, a popular US-based DTC-GT service [16]. **Table 4** summarizes the currently available DTC-GT service products developed and used in Korea.

Despite the usefulness and popularity of DTC-GT, consumers should be aware of the potential risks and limitations of DTC-GT [17]. The genetic variations included in DTC-GT may facilitate the estimation of phenotypic traits; however, many conditions are affected by the interplay of various factors including genetic, lifestyle, and environmental factors. Therefore, the results predicted in the test may differ from the individual's current conditions. Results from DTC-GT should not be the sole basis of any type of medical decision-making and should always be discussed with health professionals for an appropriate interpretation of the results [18]. Furthermore, although the number of genetic test items for DTC-GT is limited, there are no regulations on the type of genes and genetic variations that can be used for each item. Therefore, the results of genetic testing are bound to depend on the technical expertise and know-how of the company. The number and type of genes being analyzed, interpretation method (algorithm), and reference database of the analyzed genotypes differ from company to company, and therefore the results may vary among different service providers. However, this information is often not transparently disclosed to the consumers.

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Table 4. DTC-GT services provided by companies in Korea

Company	Services	Available test items	
		Product name	Test items (number of items)
TheragenEtex	GeneStyle	GeneStyle Wellness 70+	· Nutrients (21), healthcare (16), skin/hair (13), exercise (8), dietary habits (12), personal traits (7)
		GeneStyle Health Nutrition 41	<Health>: healthcare (15), dietary habits/sleep habits (5) <Nutrition>: nutrients (21)
		GeneStyle Beauty Fitness 32	<Beauty>: skin/hair (13) <Fitness>: healthcare (6), dietary habits/sleep habits (5), exercise (8)
		GeneStyle Diet 29	<Diet>: healthcare (14), dietary habits/sleep habits (5), personal traits (2), exercise (8)
		GeneStyle Me	· Lineage (Ancestry)
		GeneStyle Inner Healthcare + Outfit Beautycare	· Healthcare (5), personal traits (1), skin/hair (4), nutrients (1)
		GeneStyle Inner Healthcare	· Healthcare (5), personal traits (1)
		GeneStyle Outfit Beautycare	· Skin/hair (4), nutrients (1)
Macrogen	My Genomestory	My Genomestory The Plus	· Nutrients (20), exercise (8), skin/hair (11), dietary habits (5), personal traits (12), healthcare (14)
Medizen Humancare	MELEHY	MELTHY Balance 3	· Healthcare (3)
		MELTHY Balance 5	· Healthcare (4), personal traits (1)
		MELTHY Skin 4	· Nutrients (1), skin (3)
		MELTHY Skin 6	· Nutrients (1), skin/hair (5)
		MELTHY Full 12	· Nutrients (1), skin/hair (5), healthcare (5), personal traits (1)
Eone Diagnomics	gene2me	i-Happy	· Healthcare (4), nutrients (1), personal traits (1)
		e-Happy	· Healthcare (1), skin/hair (5)
DNAlink	DNA GPS	myDNA	· Nutrients (12), exercise (8), skin (9), personal traits (15), obesity (8), metabolism (6)
		myDNA Beauty	· Nutrients (1), skin (5)
		myDNA Health	· Nutrients (1), obesity (1), metabolism (4), personal traits (1)
		myDNA Beauty & Health	· Nutrients (1), obesity (1), metabolism (4), skin (5), personal traits (1)

DTC-GT, direct-to-consumer genetic testing.

Current status of DTC-GT in other countries

Although many companies provide DTC-GT services in the United States, 23andMe is the leading and by far the most popular individual genome analysis service and DTC-GT provider [19]. Since its establishment in 2006, 23andMe has grown rapidly, lowering the cost of genetic testing from $1,000 at the time of its establishment to $99 in 2013. Further, 23andMe analyzes 254 items related to disease risk, drug sensitivity, wellness, and ancestry [1,20]. However, in November of 2013, 23andMe received an order from the US Food and Drug Administration (FDA) to suspend its service because its accuracy and safety were not verified [21]. Eventually, 23andMe announced that only ancestry analysis services would be provided, but the company continued to develop DTC-based services even after receiving the suspension order from the FDA. As a result, 36 genetic diseases including cystic fibrosis and sickle cell anemia were approved for testing in February 2015, and 10 additional diseases such as Parkinson's disease and Alzheimer's dementia were approved in April 2017 [22].

There are no legal regulations on DTC-GT in many other countries including the UK, Canada, and Japan. Many tests advertised and sold via the internet in these countries have not undergone clinical evaluation. In Japan, for example, diverse services are provided through various companies without strict legal regulations on DTC-GT analysis [23]. A total of 112 organizations in Japan reportedly provide analysis services for more than 360 test items including disease risk, health management, and personal traits. Further, there is no need to request approval from the Japanese government when establishing a genetic testing company, and various test items provided to consumers are independently selected by the company.

APPLICATION OF DTC-GT FOR CLINICAL NUTRITION

Genetic variations associated with nutrient intake responses or dietary factors

Nutrigenetics is defined as the study of the differential response to specific nutrients based on genetic variations [24-28]. Several genes and alleles have been found to affect the absorption, utilization, and intake of nutrients or dietary components [25,29]. **Table 5** summarizes genetic variations that are known to affect the response to various macronutrients, vitamins, and minerals. The *FTO* gene is known to play an important role in metabolism and is linked to body weight and body mass index (BMI) [29-31]. Some nutrients such as protein, saturated fatty acids (SFAs), and polyunsaturated fatty acids (PUFAs) may

Table 5. Genetic variations associated with responses to nutrient intake

Gene (rs number)	Variants	Function	Dietary factor	Phenotypic traits
FTO gene (rs1558902/rs9939609)	T;A	Plays a key role in metabolism and is linked to weight and BMI	Protein/SFA:PUFA	Individuals with an A allele of the *FTO* gene (gene variant rs1558902) who consumed a high-protein diet were more likely to have a higher BMI and an increased risk of obesity compared to TT allele carriers [32-34]. Additionally, people carrying an A allele of the *FTO* gene had a higher risk of obesity compared to TT homozygotes when SFA intake was high and PUFA intake was low [35].
BCMO1 gene (rs11645428)	G;A	Encodes a gene that is a key enzyme in the conversion of beta-carotene to vitamin A	Vitamin A	Individuals carrying the GG genotype do not efficiently convert dietary provitamin A carotenoids into the active forms of vitamin A and may have a higher risk of vitamin A deficiency [38].
CYP2R1 gene (rs10741657)	A;G	Encodes the enzyme 25-hydroxylase related with vitamin D activation and is associated with vitamin D binding and transport to tissues	Vitamin D	Participants with the GG or GA genotype of *CYP2R1* (rs10741657) have an increased risk of low levels of 25(OH) D_3 [39-41].
GSTT1 gene	Ins/Del	Involved in vitamin C utilization through glutathione S-transferase enzymes	Vitamin C	Individuals with the *GSTT1* Del/Del genotype are at higher risk of serum ascorbic acid deficiency when consuming less than the RDA of vitamin C compared to those with the Ins allele [37].
FUT2 gene (rs602662)	G;A	Involved in vitamin B12 cell transport and absorption	Vitamin B12	Carriers of the G alleles possess a higher risk of low vitamin B12 serum levels when they consumed diets with low bioavailable sources of vitamin B12 compared to AA genotype carriers [42].
GC gene (rs7041 and rs4588)	A;C and G;T	Encodes a protein that binds to vitamin D and transports it to target tissues	Calcium	Individuals homozygous for the G allele of rs7041 and the C allele of rs4588 have an increased fracture risk compared to other genotypes when they consumed a low-calcium diet (< 1.09 g/day) [43].
MTHFR gene (rs1801133)	C677T	Produces the enzyme methylenetetrahydrofolate reductase (*MTHFR*), which is involved in the conversion of 5, 10-methylenetetrahydrofolate to 5-methyltetrahydrofolate	Folate	Individuals carrying the T allele have a higher risk of low serum folate levels due to a lower MTHFR enzymatic activity [44]. *MTHFR* gene mutations are associated with neural tube defects, vascular disease, and hyperhomocysteinemia [45,46].
HFE gene (rs1800562)	G;A	Encodes a membrane protein that is similar to MHC class-I protein and is associated with beta2-microglobulin, which in turn are associated with iron absorption regulation by modulating the interaction between transferrin receptor and transferrin	Iron	Individuals with the AA genotype of the *HFE* gene rs1800562 are associated with a higher risk of hemochromatosis compared to those with the G allele [47].
TMPRSS6 gene (rs4820268), *TF* gene (rs7385804), and *TFR2* gene (rs3811647)	G;A, C;A, and G;C	Involved in the regulation of the expression of hepcidin, a peptide hormone that modulates iron absorption	Iron	Individuals carrying the GG genotype in the *TMPRSS6* gene have an increased risk of low hemoglobin and transferrin saturation compared to those with the A allele [48-50]. Individuals with the AA genotype of the *TF* gene tended to have a higher risk of elevated transferrin and low ferritin compared to those carrying the C allele [50,51]. Polymorphisms in the *TFR2* gene can affect red blood cell count, hematocrit, and mean corpuscular volume, and individuals homozygous for the CC genotype have a higher risk of low serum levels [50].

BMI, body mass index; SFA, saturated fatty acid; PUFA, polyunsaturated fatty acid; RDA, recommended dietary allowance.

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also alleviate genetic predispositions associated with a higher BMI and body weight [32-35]. The A allele of the *FTO* gene (gene variant rs9939609) has been linked to an increased risk of obesity and higher BMI when individuals consume high-protein diets compared to individuals exhibiting the TT genotype [32-34]. Further, people with the A allele of the *FTO* gene had a higher obesity risk compared to the TT homozygotes when saturated fatty acid intake was high and polyunsaturated fatty acid intake was low [35]. Moreover, the *GSTT1* gene polymorphism is a well-known genetic variation associated with serum vitamin C levels. The *GSTT1* gene is involved in the utilization of vitamin C via the glutathione S-transferase enzyme [36]. Individuals with the *GSTT1* Del/Del genotype are at increased risk of vitamin C deficiency when they consume less than the recommended dietary allowance (RDA) of vitamin C, whereas those with the Ins allele do not exhibit these risks [37].

Table 6 summarizes genetic variations known to impact the response to food components. Caffeine is the active compound in coffee, one of the most widely consumed beverages worldwide. This compound has been investigated in numerous studies to elucidate its effect on the association between *CYP1A2* gene variants and phenotypic traits. Individuals with the C allele of the *GYP1A2* gene (gene variant rs762551) are considered slow metabolizers and tend to have an increased risk of hypertension, myocardial infarction, and elevated blood pressure when they consume more than 200 mg of caffeine per day, whereas AA homozygotes do not have these risks [52-55].

Significance of DTC-GT in clinical nutrition

DTC-GT can motivate consumers to participate more actively in overall health management and may play an important role in the implementation of personalized clinical nutrition [60,61]. Clinical dietitians can use DTC-GT to provide nutritional counseling and meal planning based on the genetic background of their patients. This information can provide the clinician with important insights regarding the individual's genetic susceptibilities and dietary factors that can increase the risk of disease.

Nevertheless, extensive research on gene-diet interactions is still required. Further, to avoid misuse and protect the public, nutrigenetic advice should be grounded in clear evidence

Table 6. Genetic variations associated with responses to food components

Gene (rs number)	Variants	Function	Dietary factor	Phenotypic traits
CYP1A2 gene (rs762551)	C;A	Encodes the CYP1A2 liver enzyme, which is a member of the cytochrome P450 superfamily that catalyzes various reactions associated with drug metabolism and synthesis of cholesterol, steroids, and other lipids; metabolizes caffeine; serves as a biomarker of fast or slow metabolism	Caffeine	Individuals carrying the C allele of the *CYP1A2* gene (rs762551), who are considered slow metabolizers, have an increased risk of hypertension, myocardial infarction, elevated blood pressure, and pre-diabetes when they consume more than 200 mg of caffeine per day, whereas people possessing the AA genotype (fast metabolizers) do not carry these risks [52-55].
TAS1R2 gene	Ile19Val	Encodes the sweet taste receptor 2 protein subunits, T1R2, which is specifically required to perceive sweet tastes	Sugar	Val carriers of the *TAS1R2* gene tended to consume fewer sugars in comparison with those homozygous for the Ile allele [56].
ACE gene	Ins/Del	Encodes an enzyme that catalyzes the conversion of angiotensin I to angiotensin II, a potent vasopressor and aldosterone-stimulating peptide that controls fluid-electrolyte balance and blood pressure	Sodium	Individuals with ID and DD genotypes of the *ACE* gene are associated with a higher blood pressure during a high-Na+ diet compared to those with II genotype [57,58]
LCT gene (rs4988235)	G;A	Encodes enzymes that belong to the glycosyl hydrolase 1 family, which has lactase activity; polymorphisms in the *LCT* gene are related to lactase persistence	Lactose	Individuals carrying the C allele are associated with an increased risk of suboptimal plasma 25(OH)D concentration compared to those with the TT genotype. Particularly, carriers with the CC genotype are prone to lactose intolerance, which is associated with a low plasma 25(OH)D concentration [59].

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based on a cautious and valid assessment resulting from the outcomes of many nutrigenetic studies [44]. Additionally, dietitians and healthcare professionals should be qualified and skilled in this rapidly evolving field [62].

CONCLUSIONS

This study reviewed the history and current status of DTC-GT in Korea and discussed the relationship between genotype differences and associated phenotypic traits, particularly those linked to dietary intake. Several studies that evaluated gene-diet interactions have revealed that the associations between genotype differences and responses to nutrients and dietary factors are robust for some genes. This suggests that genetic testing can be implemented in clinical nutrition, thus providing dietitians with crucial insights on genetic susceptibility and allowing them to provide personalized counseling and meal planning based on this genetic information. Nevertheless, more studies on gene-diet interactions are needed to accumulate comprehensive scientific evidence and promote the use of DTC-GT in the field of personalized clinical nutrition.

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