

PERSONALIZED NUTRITION-CURRENT TRENDS AND CHALLENGES

Tania MIREA (NICOLĂESCU)^{1,2}, Mona Elena POPA²

¹Administration of Hospitals and Medical Services Bucharest, Saint Catherine, 030167

²University of Agronomic Sciences and Veterinary Medicine Bucharest, Faculty of Biotechnology,
59 Boulevard Mărăști, 011464, Bucharest, Romania

Corresponding author email: nicolaescuanita@yahoo.com

Abstract

At present at national, European and international level, there is a real tendency for personalized nutrition, known to be that a food can have a positive effect for one person and negative for another and has emerged as an alternative to solving various health problems. Personalized diet recommendations are based on data on food habits and risk behaviours, physical characteristics and genetic profiling. The genetic code is similar for all people, the small variations that differentiate us can determine the effect, different responses of nutrients and how each individual metabolize food, as they interact with the genes. In the pioneering phase, the challenge is to opt out of global protocols in different conditions and paradigm shift. The nutrition of the future will be based on the identification and analysis of the genetic profile, and according to the existing data base, will be developed personalized therapeutic nutritional and pharmacological plans corresponding to the identified genetic profile. The purpose of this article is to capture the current level of knowledge about genetic factors that will allow for customized diet and broadening of the horizon of gene nutrition.

Key words: *personalized nutrition, genetic profile, genetic nutrition*

INTRODUCTION

The first definition about individual nutrition were mainly based on discussions about “genes”, frequently used as a synonym for personalized approach. The nutritional advice given according to the individual characteristics and behaviors is future, but it takes a lot of work to be able to make known key messages, which will lead to a change in the dietary preferences of people (Ordovas et al., 2018). Despite what has been said, this thought has been considered to encompass the notion of levels. Any of us comes into the world with a genetic dowry inherited from parents who adapted appetite, gives response to stimuli, chemical and biological transform food components and cause various diseases. Eating disorders are on the rise. Even if it is a big problem, we can say with certainty that most of the growth occurs due to the unhealthy diet based on already existing risk behaviors and we refer here to the consumption of alcohol, coffee or smoking. Conclusive clues accredit the idea that it is possible to be more secure in adopting an adequate lifestyle drug treatments to prevent illness in individuals predisposed to disease (Knowler et al., 2002). Personalized nutrition is being discussed because it is promising now and it will definitely

be the nutrition of the future. The purpose of this article is to bring information that gives another dimension to personalized nutrition: information about the reciprocal action of nutrients with the genome, about the different response of humans to interventions on eating habits, about how genes and their variants can influence absorption and metabolizing nutrients from diet. The diet involves, firstly, the balancing of some deficiencies existing in the nutritional processes of assimilation and dissimilation in the body through the food assembly, and secondly, through the appropriate nutritional processes, the ability to use the nutrients indispensable to an affected organism (Natea, 2008). We would like to present views from more recent or older works in the field of personalized nutrition, noting relevant issues that alter the particular response to lifestyle or eating habits. Because at the molecular level two identical conditions will not be encountered, each of them having a unique genetic profile, after identifying the particularities of the profile, personalized nutrition must be effective in prevention by specifying the predisposition to a certain disease because, the existence of a characteristic gene or some mutations, in most situations, this is the premise of a particular disease. If the genetic resource is to be expressed as a condition, it is

due to the interaction of the whole genome-environment-behavior (Fenech, 2007). Personalized nutrition should ultimately lead not only to prevention, but also to limiting the number of illnesses or reducing the suffering period compared to general nutritional recommendations. Once the genetic profile is identified, the condition can be treated by an individualized protocol so that it is necessary to select the nutrients according to their composition in the nutrients that defend the genome (Fenech, 2007).

Nutri-genetics and Nutri-genomics

Nutri-genetics and nutri-genomics are defined as knowing the efficiency of “genetic” transformations on hereditary nutritional challenges and biologically active nutrients in manifesting a functional nucleotide sequence (Simopoulos, 2010; Corella and Ordovas, 2009; Trujillo et al., 2006; Ferguson, 2009; Kaput, 2008; Ordovas and Corella, 2004). Harnessing the information about the genome, associated with wide-ranging omics techniques, has created the possibility of obtaining new information, which aims to achieve an efficient perception of nutrient-gene interference depending on genetic endowment, having as final aim the development of the processes individualized nutrition, to obtain that physical, mental and social well-being as well as disease prevention (Simopoulos, 2010; Corella and Ordovas, 2009; Trujillo et al., 2006; Ferguson, 2009; Kaput, 2008; Ordovas and Corella, 2004). The development of nutri-genetics bears a new nutritional paradigm, hinting at the possibility of personalizing the foods corresponding to the individual genetic structure. We hypothesize that in the next 25 years there will be a radical transformation of the technology that will encompass fields such as biotechnology, nanotechnology and genomics (Coronado et al., 2007). In the report of a special significance that resulted from research food-gene interference the condition of achieving intra and transgenerational effect is epigenetics (Jirtle and Skinner, 2007; Sharma et al., 2010). The accepted definition of epigenetics refers to researching the transformation of the function of inherited mitotic and/or meiotic genes that do not require remodeling in the DNA sequence (<https://ncbi.nlm.nih.gov/pubmed/11498582>) and

is epigenomics refers to the research of epigenetic transformations in a cell or the whole organism. Epigenetic transformations act on norm growth and development DNA methylation globally, plays a role in Nogenesis cells because, in many hypo- and hyper-methylation researches, DNA has been associated with cancer. Because nutrition can readily adjust biological chemistry directions by transforming the phenotypic effects of genes, the nutri-genomics domain has the potential to boost the knowledge of the interference between food and the epigenomics (chemical transformations at the level of DNA and histone proteins) in the development of human diseases (de Luca et al., 2017). Recent examples of the role of epigenetics have been encountered in obesity (Bordoni and Capozzi, 2014; Capozzi and Bordoni, 2013) and in the predisposition to develop type 2 diabetes. Nutri-genetics and nutri-genomics are based on several essential elements. First, nutrition can influence health outcomes, by directly harming gene expression in biochemical and energy transformations in organism biology. It may indirectly affect all genetic mutations either at the chromosomal level or at the base sequence level, and may further produce changes in quantitative determination and gene expression. Secondly, the effects of nutrition on the health of nutrients and their combinations (nutrients) are based on different hereditary genetic aspects which may change the absorption, biochemical and energy transformations of the nutrients. A deficiency or excess of nutrients can affect genome stability, cause mutations or gene grading contrary to normal rules, and gene expression may result in other phenotypes in different life stages. Good health results can be obtained if the nutritional needs are addressed on a personal level, taking into account the hereditary genetic profile, the acquired genetic characteristics, conditioned in turn by their lifestyle, traditions and eating habits, risk behaviors and health status. Of particular importance is to give better meaning to information from epidemiological and clinical epidemiological intervention studies regarding the impact on health of dietary factors that may help to revise recommendations for personalized nutrition (Ordovas and Corella, 2004; Simopoulos and Ordovas, 2004).

It is becoming easier for an individual's genome to be identified, to provide information on a broad spectrum of (single-nucleotide, polymorphism SNP, insertion-deletions, inversions, or variants of number of copies) in critical genes involved in metabolism, nutrients and pathways that require micronutrients as cofactors (Frazer et al., 2009).

Nutrigenomics is one of the most developed fields of research; includes studies on the impact of dietary components on genome functioning in terms of gene expression patterns and epigenetic modifications, such as DNA methylation and histone modifications (Bordoni and Gabbianelli, 2019). Most of the nutrigenomic research has been carried out on human nutrition and the effects of nutrients on the etiology of the disease (Reddy et al., 2018).

The purpose of nutrigenomic studies is to achieve personalized nutrition (Bouwman, 2008) considering who could use personalized nutritional products, associated tips and what are the limitations of providing potential users, provided extremely specific information about individual health risks and the benefits of specific habits. Nutrigenomics investigates the ways in which nutrients can act as chemical signals to influence gene expression, thereby altering protein synthesis and functioning of different metabolic pathways (Martinez, 2007). Nutrigenomics determines the effects of ingested nutrients and other dietary components on gene expression and regulation that is, they study diet-gene interaction to identify dietary components that have beneficial or harmful effects on health (German, 2005; Miggiano, 2006). Our genes include a myriad of hereditary alternatives that are aware of the transformations regarding nutrition some of them through poorly understood systems (van Ommen et al., 2017). It will also determine the nutritional needs based on the person's genetic makeup, the association between diet and chronic diseases, such as cancer, type 2 diabetes, obesity and cardiovascular disease (CVS) (Miggiano and DeSanctis, 2006).

Studies with reference to diet-gene interactions

According to various database searches, three levels of personalization are available to provide personalized nutrition (Gibney and Walsh,

2013; O'Donovan et al., 2017). The pan-European Food 4 Me study, the largest randomized controlled study recently illustrated, analyzed the performance of personalized nutrition (Celis-Morales et al., 2017). The study was conducted in seven European countries, was developed as a clinical study with the participation of 1600 individuals, divided into four intervention groups. The classification referred to dietary recommendations at the personal level as follows: - level 0 - control group that received non-personalized recommendations; level 1 - the group received individual recommendations based only on food intake; level 2 - the group received individual advice based on dietary intake and phenotype; level 3 - received individual recommendations based on dietary intake, phenotype and genotype. There was also a shift from individuals to groups of nutritional recommendations and they are called "stratified" or "adapted" (Ordovas et al., 2018). Other studies have investigated, how genes influence food preferences, affecting their signaling pathways rewards, or homeostatic energy (Garcia-Bailo et al., 2009). Developing a genetic basis for food tastes could provide the opportunity for the development of new nutritional products, targeting characteristic genotypes or ethnic population, and may explain the inconsistencies between studies related to foods with chronic disease (El-Soheily et al., 2007).

To date, the diversity of diet-gene interference analyzes has hampered the transposition of the purpose of analyzes into practical applications of the guidance based on personalized nutrition. The tests used indicate the precariousness of a patient with lactose and fructose intolerance or gluten intolerance. A conclusive sample is that the nutrient mutation 13910 C/T, is at a distance of about 14 kilo bases above the LCT lactase gene and controls lactase transcription. Substitution of thiamine with cytosine in this polymorphism allows permanent digestion of lactose at maturity (Enattah et al., 20020). In the diagnosis of hypolactasia, it was shown that C/T (13910) polymorphism with only a single protein component, with 13910 base pairs at the 5' end of lactase, is closely linked to lactase resistance and harms much of the statical collectivity, due to lactose intolerance (Rasinpera et al., 2004). In the study of celiac

disease, an appreciation of dietary applicability and the perception of celiac of dietitians could be made, especially in the village environment of Australia 2007-2014. Understandable impediments to appreciating a gluten-free diet, including restricted accessibility to dietitians or autonomy and limited prices of gluten-free preparations (Ludvigsson et al., 2014) or screening at phenylketonuria have allowed the use of nutritional advice based on genetic makeup (avoiding lactose by limiting the consumption of fresh milk, avoiding gluten and phenylalanine containing products for people at risk). CYP1A2 gene censor caffeine metabolism in coffee. Individuals carrying genetic variation C are at increased risk of myocardial infarction if they consume more than one cup of coffee per day, it is recommended to limit coffee consumption (<https://www.genetx.eu/>). The PLIN1 gene controls storage and the release of adipocyte fat. Female persons with the AT or GT haplotype have an increased risk of obesity. The FTO gene contributes to exercising control over hunger, hypothalamus, and eating preferences.

Efficiency of personalized nutrition in cancer

Cancer is a multi-step process in which gene expression, protein function and metabolite begin to function aberrantly (Franco and Reitsma, 2001). The risk of cancer development can be significantly increased if there is a gene-diet interaction (Nutrigenomics: <https://www.Diet.com>). Nutritional health depends on the interaction between the environmental aspects of supply, bioavailability, consumption and cohesion of dietary components, and genetically controlled aspects of digestion, absorption, distribution, transformation, storage, and excretion by proteins in the form of receptors, carriers, enzymes, and hormones (Berdanier and Hargrove, 1993; Castro and Towle, 1986; Rucker and Tinker, 1986; Williams et al., 1990). The ADH1 gene controls the metabolism of alcohol to acetic aldehyde, the ALDH2 gene controls the metabolism of acetic aldehyde to acetic acid. The two genetic variations in the same individual A (ADH1) and T (ALDH2) confer an increased risk of gastric cancer at an alcohol consumption greater than 5 g/day (<https://www.genetx.eu/>). The AGTT haplotype

is associated with an increased risk of gastric cancer (<https://www.genetx.eu/>). Personalized nutrition has traditionally been based on adapting food components according to personal needs and options. Today, this thinking has been reinforced by the use of highly successful ascending terminologies, in order to facilitate the knowledge of the molecular systems that are the foundation of a healthy state. This understanding would allow the adaptation of special dietary recommendations to suit the needs of the characteristic patient groups based on the identified genetic profile. The excellent evolution of nutrition directions on the most rigorous researches for the development of health requires a proper assessment of the bioaccessibility and cost-effectiveness of food components. To make these phenomena possible, credible explanations on the description of nutrients, their contributions and their consequences after application are indispensable.

Future practical implications of nutrigenetics and nutrigenomics

Nutrigenetics and nutrigenomics are fundamental aspects in establishing the effect of personalized nutrition on health, and the incidence of nutrients can be assessed objectively and as widely as possible, using human techniques. Four 'omic' domains of agriculture (agronomics) and nutrition (nutrigenomics, nutriproteomics, nutrimetabolomics) have been evoked as effective processes for understanding the diversity of relationships between individuals as a solution to environmental exposure to food (Ozdemir and Kolker, 2016). Progress in 'omic' techniques is constantly shifting the different way of responding to the same lifestyle treatment, to reality. Even if they are attached to the decisive analytical challenges, precisely the exact adaptation of the multiomic research and the introduction of the means and the computerized data banks, will facilitate the reproduction of the clinical results, in positive individual feeding procedures (Braconi et al., 2018). Genetic dowry, way of life and eating habits can exert an influence on personal nutritional needs and depending on the geographical area, the existing social-economic status, religion and traditions. The transposition

of these knowledge into valid recommendations following the identification of the genetic profile at the individual level is used in a few circumstances (phenylketonuria or galactosemia), because the genetic profile is overwhelming on any other factor. Accessibility based on valid studies is the only way that can guarantee that the information provided by nutrigenetics and nutrigenomics are applied accordingly. In Romania, personalized nutrition as a trend, is more at the level of research and very little transposition into practice. The challenge is to transform the knowledge we have into working tools that, individually applied, contribute to the physical and mental well-being we all want. Of course, identifying the genetic profile also raises ethical issues. But as long as this information / knowledge remains within the boundaries of confidentiality and will be used only and only for the restoration and consolidation of health, while respecting the right to image, dignity and personal life, as regulated in national and European law, the benefit is huge. Although few nucleotide sequences have been observed that have the consequence of cancer genesis, there is no well-which greatly diminishes their life expectancy. Cancer and its treatment alter the nutritional status of the patients by altering the metabolic function and by decreasing the dietary contribution (Shahmoradi et al., 2009; Trabal et al., 2006). Studies have shown that under nutrition is a psychological evidence of a predisposition to disease in developed cancer, and it is therefore possible that it has a great significance (Gupta et al., 2005). It is therefore imperative that future studies be conducted to come up with personal nutrition solutions in these situations as well.

CONCLUSIONS

Deciphering gene – nutrient - disease interference will be difficult. Currently, tests are being carried out and nutritional recommendations are applied in practice to avoid lactose, this being the specific carbohydrate, which represents about 90% of the total milk carbohydrates and avoiding gluten (a protein that favors gluten intolerance, currently undiagnosed) by eliminating noodles, not bakery and pasta product. The introduction of high-value standard bring the feeling of

tranquility and confidence of those suffering, transforming health care into a true art. Based on the valid clear evidence of a predisposition to a particular disease, we hope that personalized nutritional will be optional in a first phase in the care plan, and the conclusions of future research will go beyond the option indispensable health certainty. Many research is crediting the idea of paradigm shift due to the fact that there are specific treatment option and diets depending on the individual genetic profile, so as to give up global treatments, the same for everyone and to apply differentially. Many research is crediting the idea of paradigm shift due to the fact that there are specific treatment options and diets depending on the individual genetic profile, so that global treatments, the same for all, and differentially applied, are given up.

REFERENCES

- Berdanier, C. D., Hargrove, J. L., Hargrove, J. L., eds. (1993). *Nutrition and Expression*. Boca Raton, FL: CRC Press Publishing House.
- Bland, J.S., Minich, D.M., Eck, B.M. (2017). A systems medicine approach: Translating emerging sciences into individualized wellness. *Advances in Medicine*, 5.
- Bordon, I. L., Gabbianelli, R. (2019) Primers on nutrigenetics and nutri(epi)genomics: origins and development of precision nutrition. *Biochimie*, 160, 156-171.
- Bordoni, A., Capozzi, F. (2014) Foodomics for healthy nutrition. *Current Opinion in Clinical Nutrition and Metabolic Care*, 17, 418-424.
- Bouwman, L. I. (2008). *Personalized nutrition advice, an everyday-life perspective; thesis*, Wageningen University.
- Braconi, D., Bernardini, G., Millucci, L., Santuci, A. (2018). Foodomics for human health: Current status and perspectives. *Expert Review of Proteomics*, 15, 153-164.
- Capozzi, F., Bordoni, A. (2013). Foodomics: A new comprehensive approach to food and nutrition. *Genes & Nutrition*, 8, 1-4.
- Carter, H. B., Walsh, P. C., Landis, P., Epstein, J. I. (2002). Expectant management of non-palpable prostate cancer with curative intent preliminary results. *J. Urol.*, 167, 1231-1234.
- Castro, C. E., Towle, H. C. (1986). *Nutrient – genomics interaction*. Fed. Proc., 45, 2382.
- Celis-Morales, C., Livingstone, K., Marsaux, C. F. M., Macready, A. L., Fallaize, R., O'Donovan, C. B., et al. (2017). Effect of personalized nutrition on health-related behaviour change. Evidence from the Food4Me European randomized controlled trial. *International Journal of Epidemiology*, 46, 578-588.
- Corella, D., Ordovas, J. M. (2009). Nutrigenomics in cardiovascular medicine. *Circ Cardiovasc Genet.*, 2, 637-651.

- Coronado, M., Vega, S., Gutierrez, R., Diaz, G. (2007). A new paradigm in health: Nutrigenetics. *Nutrition clinics*, 10, 116-125.
- de Luca, A., Hankard, R., Borys, J. M., Sinnett, D., Marcil, V., Levy, E., (2017). Nutriepigenomics and malnutrition. *Epigenomics*, 9, 893-917.
- Enattah, N.S., Sahi, T., Savilahti, E., Terwilliger, J.D., Peltonen, L., Jarvela, I., (2002). Identification of a variant associated with adult-type hypolactasia. *Nature Genetics*, 30(2), 233-237
- El-Sohemy, A., Stewart, L., Khataan, N., et al. (2007). Nutrigenomics of taste – impact on food preference and food production. *Forum of Nutrition*, 176-182.
- Fenech, M. (2007). Nutrigenomics – The Genome. *Food Interface*.
- Ferguson, L. R. (2009). Nutrigenomics approaches to functional food. *J. Am. Diet. Assoc.*, 109, 452-458.
- Franco, R. F, Reitsma, P. H. (2001). Gene polymorphisms of the hemostatis system and risc of arterial thrombotic disease. *Br. J. Haematol.*, 115, 491-506.
- Frazier, K.A., Murray, S. S., Schork, N. J., Topo, I. E.J (2009). Human genetic variation and its contribution to complex traits. *Nat Rev Genet.*, 10, 241 – 251.
- Garcia-Bailo, B., Toguri, C., Eny, K.M., El-Sohemy, A. (2009). Genetic variation in taste and its influence on food selection. *OMICS*, 13, 69-80.
- German, J. B. (2005). Genetic dietetic: nutrigenomics announces the future of dietary practice. *J Am Diet Assoc.*, 530-531.
- Gibney, M., Wals, M. C. (2013). The future direction of personalised nutrition: My diet, my phenotype, my genes. *Proceeding of the Nutrition Society*, 72, 219-225.
- Gupta, D., Lis, C.G., Granick, J., Gruntsch, J. F., Vashi, P. G. (2006). Lammersfeld CA: Malnutrition was associated with poor quality of life in colorectal cancer: a retrospective analysis. *J Clin Epidemiol.*, 59, 704-700.
- Jirtle, R.L., Skinner, M.K. (2007). Environmental epigenomics and disease susceptibility. *Nat Rev Genet.*, 8, 253-262.
- Kaput, J. (2008) Nutrigenomics research for personalized nutrition and medicine. *Curr Opin Biotechnol.*, 19, 110-120.
- Knowler, W., Barrett-Connor, E., Fowler, S., Hamman, R., Lachin, J., Walker, E., et al. (2002). Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. *New England Journal of Medicine*, 346, 393-403.
- Kohlmeier, M., De Caterina, R., Ferguson, L. R., Gorman, U., Allayee, H., Prasad, C., et al. (2016). Guide and position of the International Society of Nutrigenetics/Nutrigenomics on personalized nutrition: Part 2 – Ethics, challenges and endeavors of precision nutrition. *Journal of Nutrigenetics and Nutrigenomics*, 9, 28-46.
- Ludvigsson, J. F., Bai, J. C., Biagi, F., Card, T. R., Ciacci, C., Ciclitira, P. J., Verde, P.H.R., Hadjivassiliou, M., Holdaway, A., van Heel, D. A. et al. (2014). Diagnosis and treatment of adult celiac disease: Guides from *British Society of Gastroenterology*. *Gut.*, 63, 1210-1228.
- Martinez, E. (2007). Nutritional genomics. *New nutrition Nutr Clin Med.*, 1 (2), 73-86.
- Miggiano, G. A., De Sanctis. (2006) Nutritional genomics: towards a personalized diet; US National Library of Medicine, National Institutes of Health. *Clin Ter.*, 157 (4), 355-361.
- Natea, C.N. (2008). *Nutrition and diet. Theoretical and practical aspect*. Sibiu, RO: Lucian Blaga University Publishing House.
- Ozdemir, V., Kolker, E. (2016). Precision Nutrition 4.0: A big data and ethics foresight analysis–Convergence of agrigenomics, nutrigenomics, and nutrimentalomics. *OMICS: A Journal of Integrative Biology*, 20, 69-75.
- Ordovas, J.M., Corella, D. (2004). *Nutritional genomics. Annu Rev Genomics Hum Genet.*, 5, 71-118.
- Ordovas, J. M., Ferguson, L.R., Tai, E.S., Mathers, J.C. (2018) Personalised nutrition and health. *The British Medical Journal*, 361.
- Popescu, A. (2017). Personalized nutrition: the solution of the future. *Galenus Magazine*, 05, 1-2 (Accessed: 25 february 2020).
- Rasinpera, H., Savilahti, E., Enattah, N. S., Koukkanen, M., Totterman, N., Lindahl, H., Jarvela, I., Lkolho, K.L. (2004). A genetics test which can be used to diagnose adult-type hypolactasia in children. *Gut.*, 53, 1571-1576.
- Reddy, V.S., Palika, R., Ismail, A., Pullakhandam, R., Reddy, G. (2018). Nutrigenomics opportunities & challenges for public health nutrition. *Indian J Med Rev.*, 148, 632-641.
- Rucker, R., Tinker, D. (1986). The role of nutrition and gene expression. A fertile field for the application of molecular biology. *Journal of Nutrition*, 116, 177-189.
- Shahmoradi, N., Kandiah, M., Peng, L.S. (2009). Impact of nutritional status on the quality of life advanced cancer patients in hospice home care. *Asian Pac Journal Cancer Prev.*, 10, 1003-1009.
- Sharma, S., Kelly, T.K, Jones, P.A. (2010). Epigenetics in cancer. *Carcinogenesis*, 31, 27-36.
- Simopoulos, A. P. (2010). Nutrigenetics/ nutrigenomics. *Annual Rev Public Health*, 31, 53-68.
- Simopoulos, A.P., Ordovas, J. M. (2004). Nutrigenetics and Nutrigenomics. *World Rev. Nutr.*, 93.
- Trabal, J., Leyes, P., Forga, M.T., Hervas, S. (2006). Quality of life, dietary intake and nutritional status assessment in hospital admitted cancer patients. *Nutr Hosp.*, 21, 505-510.
- Trujillo, E., Davis, C., Milner, J. (2006). Nutrigenomics, proteomics, metabolomics, and the practice of dietetics. *Am Diet Assoc.*, 106, 403-441.
- van Ommen, B., van den Broek, T., de Hoogh, L., van Erk, M., van Smmeren, E., Rouhani-Rankouni., T., et al (2017). System biology of personalized nutrition. *Nutrition Review*, 75, 579-599.
- Williams, R. R., Hunt, S.C., Hasstedt, S. J., Hopkins, P.N., Wu, U., et al. (1990). Genetics and nutrition. *World Rev. Nutr. Diet.*, 63, 116-130.
- *** www.advancednutrigenomic.com, 27, 28, 56-57, 62
- *** Genes, genetics, and epigenetics: <https://www.ncbi.nlm.nih.gov/pubmed/11498582>
- *** <https://doi.org/10.1016/j.biochi.2019.03.006>
- *** Nutrigenomics: <https://www.Diect.com>
- *** <https://dx.doi.org/10.1155/2017/1718957>
- *** <https://doi.org/10.1136/bmj.k2173>