An introduction to nutrigenomics in clinical practice

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Presented by

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WHAT WE WILL COVER

- DNA and DNA synthesis
- Genes, gene expression and genetic variations
- Nutrigenomics in clinical practice

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What makes you, you?

Every cell in your body contains the instructions

- the recipe
- to make you

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The fundamentals

- The human genome contains ~3 billion bases with around 20,000 genes.
- A **gene** is a **segment of DNA** that contains instructions for building proteins
  - Proteins are complex molecules that trigger various biological actions to carry out life functions.
- The DNA double helix is made up of four bases
  - Adenine, Thymine, Guanine, and Cytosine

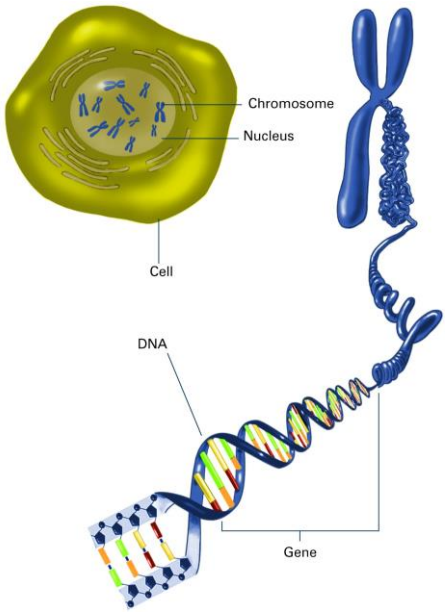

Image: National Institute of General Medical Sciences

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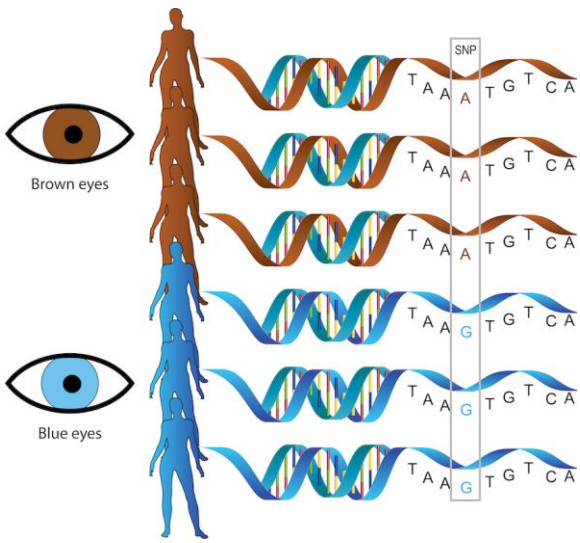
The genetic code

- Genes are the way that we inherit our characteristics.
- Our genetic code contains all of the **instructions** a cell needs to sustain itself
- 99% of human DNA is the same in all people.
- The order or sequence of these bases is as important as spelling a word or writing a sentence correctly.



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Gene expression

- Genes are turned into proteins through the steps transcription and translation.
- During transcription DNA is copied to RNA.
- The RNA code is then translated to an amino acid sequence.
- Amino acids attach to RNA according to which bases are present, and the resulting string of amino acids folds up into a protein.
- Proteins perform a wide range of functions and are required for the structure, function, and regulation of the body's cells, tissues, and organs.

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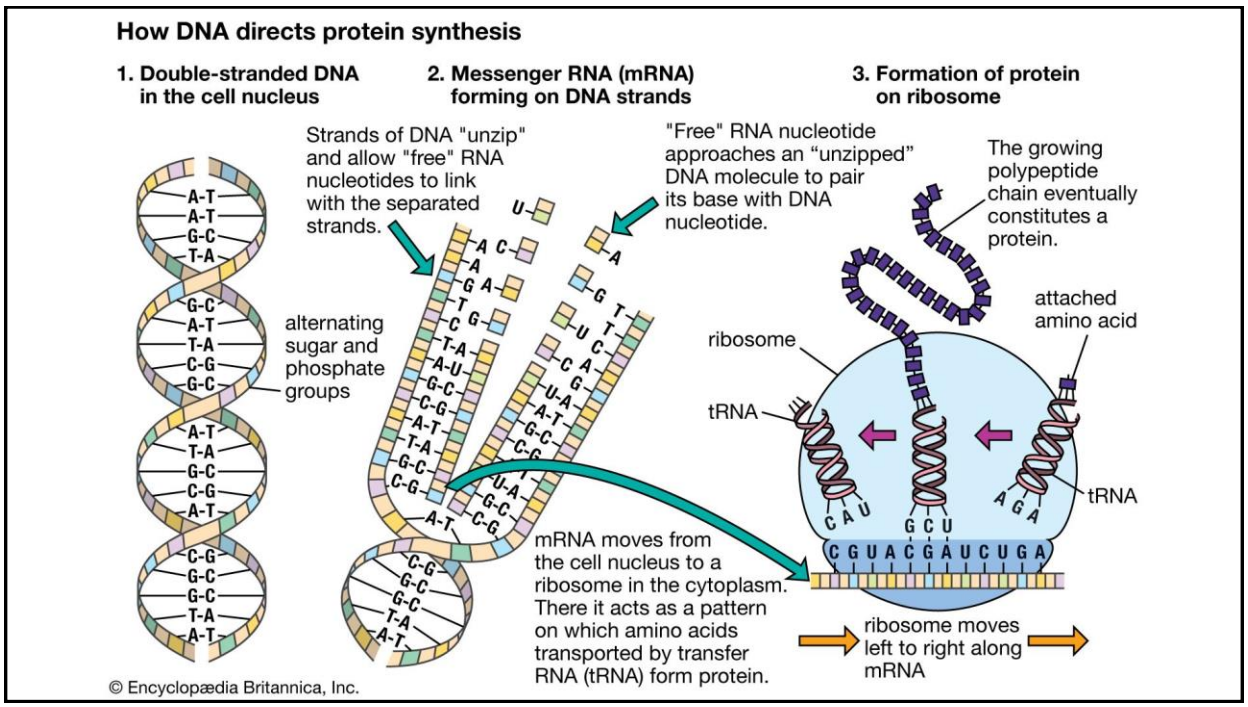

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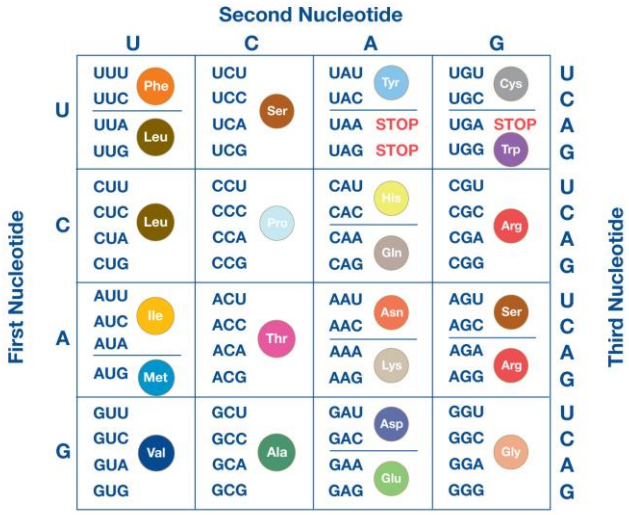
Amino acid codes

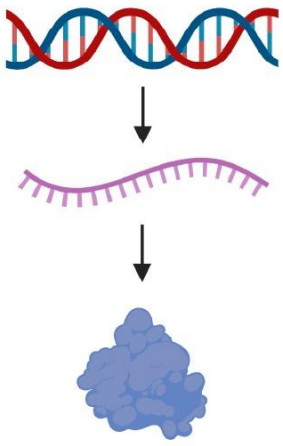


Smith, A. Nucleic acids to amino acids: DNA specifies protein. *Nature Education* (2008).

9

Variations in gene expression & protein function

- Genetic and epigenetic factors can alter gene expression and therefore protein function.
- Genetic factors include variations in the DNA sequence such as:
  - single nucleotide polymorphisms (SNPs)
  - deletions or insertions
  - copy number variants (CNV's)
  - mutations



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SNP – single nucleotide polymorphism

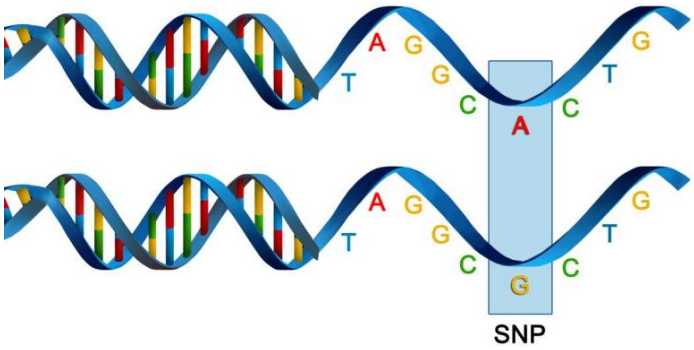

Image: https://www.genengnews.com

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Genetic variations – alleles

- An allele is an alternative version of a gene.
- SNPs have 2 alleles, for example
- MTHFR 677 **C** or **T**
- MTHFR 1298 **A** or **T**
- COMT 472 **G** or **A** (158 Val –Met)

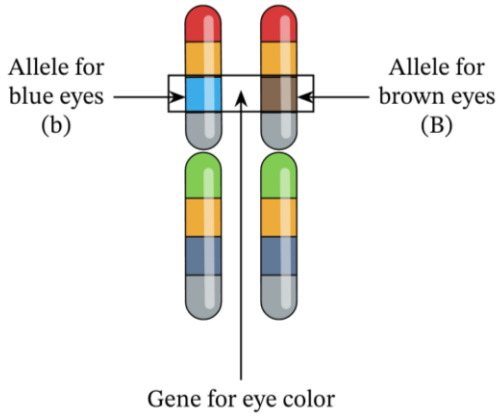

Image: Nagwa Education

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Genetic variations – genotype

- There are three possible genotypes:
  - Genotype 1 = bb (b from Mum, b from Dad)
  - Genotype 2 = bB (b from Mum, B from Dad)
  - Genotype 3 = BB (B from Mum, B from Dad)
- Genotypes are commonly referred to as:
  - Wild type (2 x major alleles e.g CC)
  - Heterozygous (major and minor e.g CT)
  - Homozygous (2 x minor alleles e.g TT)

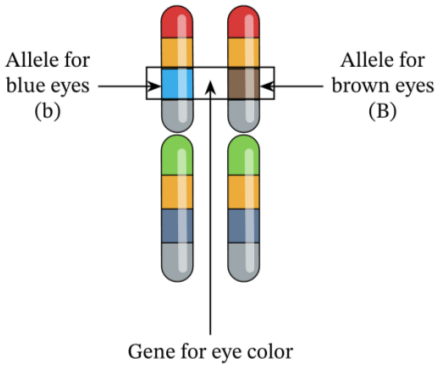

Image: Nagwa Education

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Example of genetic variation:

MTHFR 677 C ➡ T variation

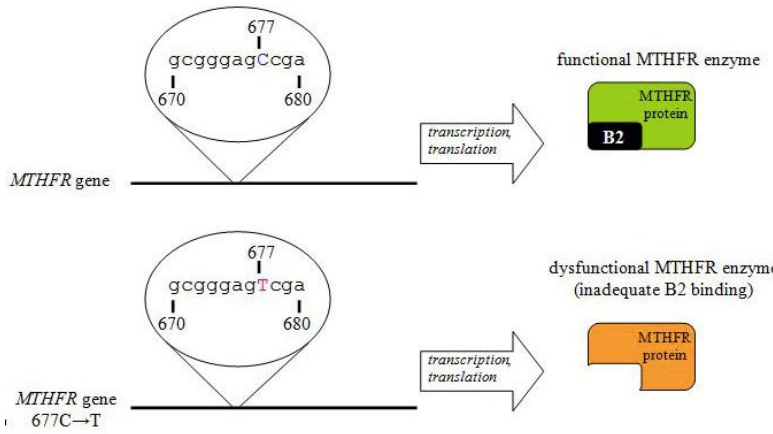

Image: http://www.nchpeg.org/nutrition/

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Review > Proc Nutr Soc. 2016 Aug;75(3):405-14. doi: 10.1017/S0029665116000197.
Epub 2016 May 12.

Riboflavin status, MTHFR genotype and blood pressure: current evidence and implications for personalised nutrition

E McAuley [1], H McNulty [1], C Hughes [1], J J Strain [1], M Ward [1]

Affiliations + expand

PMID: 27170501 DOI: 10.1017/S0029665116000197

Abstract

Clinical deficiency of the B-vitamin riboflavin (vitamin B2) is largely confined to developing countries; however accumulating evidence indicates that suboptimal riboflavin status is a widespread problem across the developed world. Few international data are available on riboflavin status as measured by the functional biomarker, erythrocyte glutathione reductase activation coefficient, considered to be the gold standard index. One important role of riboflavin in the form of flavin dinucleotide is as a co-factor for the folate-metabolising enzyme methylenetetrahydrofolate reductase (MTHFR). Homozygosity for the common C677T polymorphism in MTHFR, affecting over 10 % of the UK and Irish populations and up to 32 % of other populations worldwide, has been associated with an increased risk of CVD, and more recently with hypertension. This review will explore available studies reporting riboflavin status worldwide, the interaction of riboflavin with the MTHFR C677T polymorphism and the potential role of riboflavin in personalised nutrition. Evidence is accumulating for a novel role of riboflavin as an important modulator of blood pressure (BP) specifically in individuals with the MTHFR 677TT genotype, with results from a number of recent randomised controlled trials demonstrating that riboflavin supplementation can significantly reduce systolic BP by 5-13 mmHg in these genetically at risk adults. Studies are however required to investigate the BP-lowering effect of riboflavin in different populations and in response to doses higher than 1·6 mg/d. Furthermore, work focusing on the translation of this research to health professionals and patients is also required.

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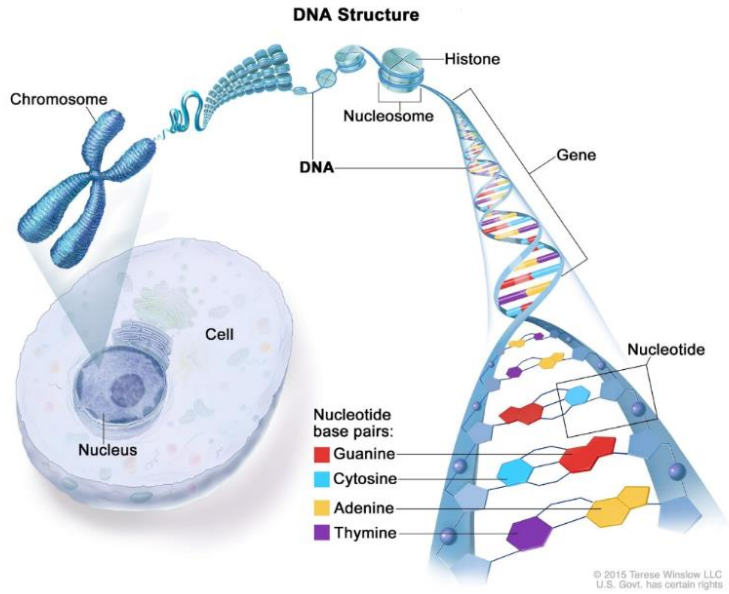
Recap



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Nutrigenomics

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Nutrigenomics

- The study of how diet and nutrient intake interacts with genes to impact health and performance. It includes nutrigenetics and nutrigenomics.

  - **Nutrigenetics** focuses on genetic variations (e.g SNPs) that can cause people to react differently to foods, specific nutrients, chemicals and lifestyle factors such as sleep or stress.
  - **Nutrigenomics** focuses on how diet or specific nutrients impact gene expression.

- These terms are often used interchangeably, currently the most common term used is nutrigenomics and this can be used to describe any area that focuses on the interaction between genes, nutrients, and health.

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Changes in gene expression & function

- Certain genotypes can alter protein function and increase the requirements of nutritional co-factors or increase the sensitivity foods, chemicals and environmental pollutants.
- Nutrigenomic testing usually involves SNP testing, but other genetic variations (such as deletions and CNVs) can be included.
- Many enzymes contain a cofactor/coenzyme that is necessary for the enzyme to function properly. This is important to know from a treatment perspective.
  - -Minerals (zinc, magnesium, iron, copper)
  - -Vitamins (B vitamins – FAD, NAD, methyl-cobalamin, pyridoxal 5'-phosphate)

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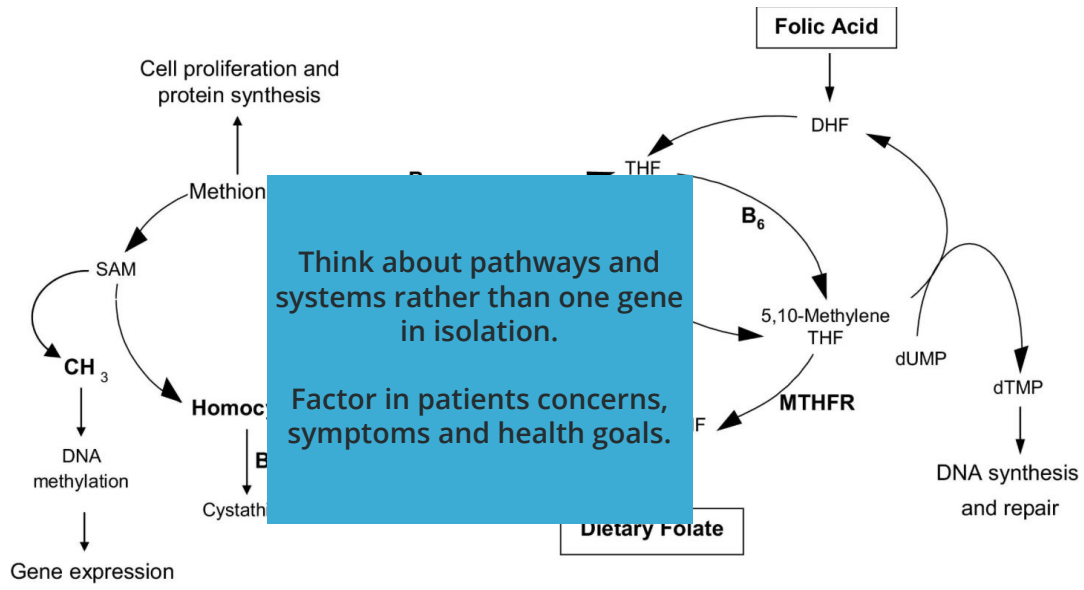

Furness, et al. American Journal of Obstetrics & Gynecology 2008

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J Matern Fetal Neonatal Med. 2020 Mar;33(5):752-757. doi: 10.1080/14767058.2018.1500546. Epub 2018 Sep 19.

The association of parental methylenetetrahydrofolate reductase polymorphisms (*MTHFR* 677C > T and 1298A > C) and fetal loss: a case-control study in South Australia

Britt J P Kos [1,2], Shalem Y Leemaqz [1], Catherine D McCormack [3], Prabha H Andraweera [1], Denise L Furness [1], Claire T Roberts [1], Gustaaf A Dekker [1,2]

Affiliations + expand

PMID: 30001659 DOI: 10.1080/14767058.2018.1500546

Abstract

Objective: To determine the association between parental MTHFR 677C > T (RS1801133) and 1298A > C (RS1801131), and fetal loss (FL).**Design:** Case-control study.**Setting:** Department of Obstetrics and Gynecology, Lyell McEwin Hospital (LMH), and the Women's and Children's Hospital (WCH) in Adelaide, Australia.**Patients:** A total of 222 couples with FL and 988 couples with uncomplicated pregnancies.**Measurements:** The main outcomes were FL and hyperhomocysteinemia (HHcy). All couples were tested for MTHFR 677C > T and 1298A > C. Fasting homocysteine was measured in the women with FL.**Results:** The main finding was a significant difference between the FL group and controls in couples with ≥4 abnormal alleles compared to <4 [p=.0232, OR 1.9 (95% CI 1.1-3.3)]. None of the couples with FL had zero abnormal alleles (both parents 677CC/1298 AA). However, this was also rare amongst the controls. Maternal carriage of both 677C > T and the 1298A > C polymorphisms was similar between the FL group and controls. The prevalence of paternal 677TT/1298AA and 677CC/1298AC was significantly higher in the FL group compared with controls. HHcy was significantly more common in the FL group compared with controls.**Conclusion:** The presence of parental MTHFR 677C > T and 1298A > C is associated with FL. The association between maternal MTHFR genotypes with FL is less pronounced than in previously published articles investigating first trimester miscarriages. Maternal HHcy is a significant risk factor for FL.

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Nutrigenomics and MTHFR

- MTHFR and other methylation related genes can impact folate and homocysteine levels, methylation and associated health conditions:
  - Fertility and pregnancy health
  - Mood, mental health and cognitive decline conditions
  - Cardiovascular health
  - Cancers
- The gene is not the cause, but increases risk for health disorders.
- Gene interactions with dietary and environmental factors cause biochemical and cellular changes, resulting in dysfunction.

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Nutrigenomics in clinical practice

- Not all genetic variations cause a change in protein function or have health implications.
- Some SNPs have a high impact, some have no impact, and others have small to modest impacts that may have cumulative value when combined with other SNPs.
- Consider the testing company you use.
- Nutrigenomics is based on the interaction of our genes and our environment (not just nutrient intake)
- Nutrigenomics is not intended to diagnose or cure any medical condition, therefore it fits within the scope of most healthcare practitioners.

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Genetic testing in practice

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Genetics and personalised medicine

- Molecular science has made huge advances to benefit personalised medicine
  - Human Genome project – 1990 - 2003 sequenced the human genome
  - International HapMap project – Identified tag SNPs
  - GWAS - Genome-wide set of SNPs in large cohorts
- Genetic testing is expected to become a routine part of patient care in the future
  - Personalised or Precision medicine
- The various types of genetic testing currently used can be categorised into
  - Clinical Genetics
  - Pharmacogenomics
  - Nutrigenomics

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Clinical genetics

- Clinical Genetics is the medical specialty that provides a **diagnostic** service and genetic counselling for individuals or families with, or at risk of, conditions which may have a genetic basis.
- Genetic disorders include:
  - Chromosomal abnormalities, which cause birth defects, intellectual disability and/or reproductive problems.
  - Single gene disorders such as cystic fibrosis, muscular dystrophy, Huntington's disease and sickle cell disease.
  - Familial cancer and cancer-prone syndromes such as inherited breast or colorectal cancer.
- This service is provided by clinical geneticists (medical doctors) and genetic counsellors who are trained specifically in this field.

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Pharmacogenomics

- Pharmacogenomics tests genes that metabolise pharmaceuticals and drugs.
- A person's genetic make-up can impact drug toxicity and efficacy.
- Testing has the potential to avoid potential adverse events or toxicity, increase clinical efficacy and reduce ineffective medical care.
- Ethnicity is a concern in this field – most studies are based on those with European ancestry.
- This service is best delivered by trained medical doctors who prescribe pharmaceuticals or pharmacists who administer these medications.

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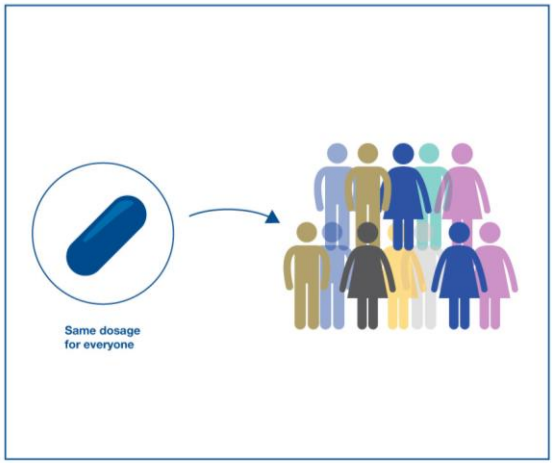
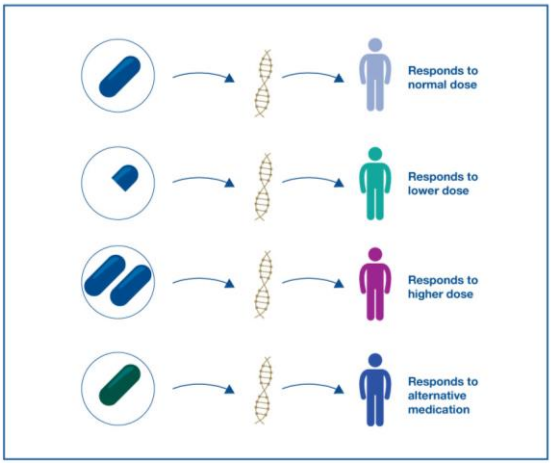
Genetic testing and personalised health





https://acola.org.au "The future of precision medicine"

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Nutrigenomics – diet and lifestyle choices

- The field of nutrigenomics examines how gene expression, diet and lifestyle interact to influence health and/or disease risk.
- Testing is offered
  - via Health care practitioners
  - Direct-to-Consumer (DTC) testing companies
- DTC genetic tests are marketed and sold directly to consumers, and do not require the assistance of a health care provider to obtain or interpret.
  - Health reports are not provided
  - Generally designed for ancestry information

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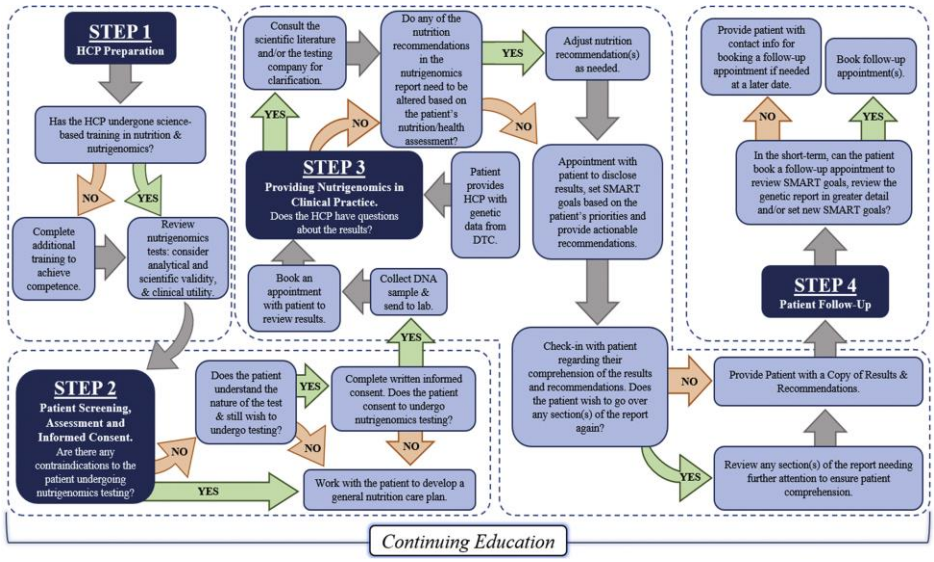
Nutrigenomics care map



Horne JR, et al. Guiding Global Best Practice in Personalized Nutrition Based on Genetics: The Development of a Nutrigenomics Care Map. J Acad Nutr Diet. 2022

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Terminology

Clinical genetics: Medical specialty which provides a diagnostic service and genetic counselling.

Pharmacogenomics: Used to predict how an individual will respond to certain medications.

Nutrigenomics (Nutritional genomics): The broad term including nutrigenetics and nutrigenomics, which describes how nutrients impact on gene expression.

Nutrigenetics: The interaction of genetic variations (SNPs) and nutritional intake and how this influences health and disease risk.

General concept: Used to determine susceptibility for health risks and optimise diet and lifestyle.

Epigenetics*:* Refers to gene expression without changing the DNA sequence.

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Clinical evidence, benefits & limitations of nutrigenomics

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Challenges in the health system

•The challenges people face in relation to their health and wellbeing are different, and what works for some may not work for others.

•In addition, statistics clearly show that obesity, chronic disease, and complex disorders are increasing at an alarming rate.

•Patients are now looking for evidence-based, personalised recommendations that result in long term health and well-being.

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Where does the evidence lie?

- There is an abundance of research investigating SNPs with nutrients, dietary factors and health related outcomes – cell culture, cohort studies and GWAS.
- First nutrigenomics RCT published in 2012 - concluded that dietary recommendations based on genotype were more useful than general dietary recommendations. (Nielsen, El-Sohemy. Genes Nutr. 2012)
- The largest RCT to include nutrigenomics date is the Food4me trial: 2017 publication indicated personalised nutrition provided better outcomes but genetics didn't enhance the results. (Celis-Morales C, et al. Int J Epidemiol. 2017)
- 2021 paper showed that key genes linked to fat metabolism (APOE, TCF7L2) may be more effective at helping people reduce discretionary foods, therefore genetics may enhance long term dietary results. (Livingstone, K. et al. Int J Behav Nutr Phys Act 2021)

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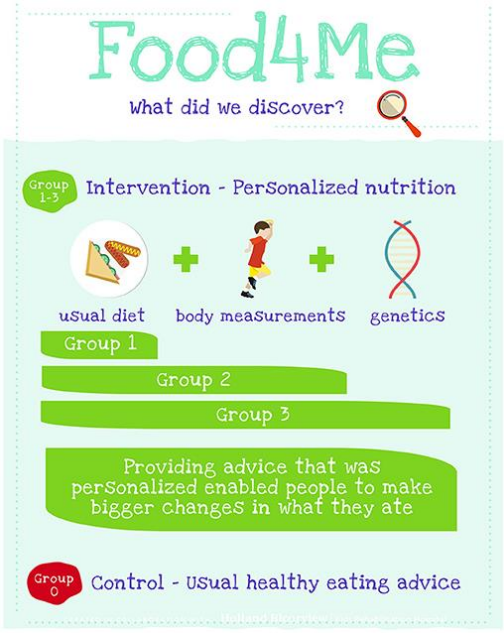

https://kids.frontiersin.org/articles/10.3389/frym.2022.71874

- A total of 5,562 participants (63.2 % females) were screened online over 12-months.
  - 1,607 met the inclusion criteria and were recruited randomised to one of the four intervention groups.
- The intervention trail went for 6 months and was delivered online.
- Recruited participants from every decade of adult life.
- Results showed that personalised nutrition advice helped people to make bigger improvements in their diets than non-personalised advice and other studies have discovered this (Jinnette R, et al. Adv Nutr. 2021).

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> BMJ Nutr Prev Health. 2020 May 21;3(1):49-59. doi: 10.1136/bmjnph-2020-000073. eCollection 2020.

Enhanced long-term dietary change and adherence in a nutrigenomics-guided lifestyle interv compared to a population-based (GLB/DP intervention for weight management: res the NOW randomised controlled trial

Justine Horne [1 2], Jason Gilliland [3 4 5 6 7 8], Colleen O'Connor [7 9], Jamie Si Janet Madill [7 9]

Affiliations + expand

PMID: 33235971 PMCID: PMC7664486 DOI: 10.1136/bmjnph-2020-000073
Free PMC article

Abstract

Background: Adherence to nutritional guidelines for chronic disease preventio remains a challenge in clinical practice. Innovative strategies are needed to help behaviour change.

Objective: The objective of this study was to determine if a nutrigenomics-guid intervention programme could be used to motivate greater dietary adherence a intake short-term, moderate-term and long-term compared to the gold-standa weight management intervention (Group Lifestyle Balance (GLB)/Diabetes Preve (DPP)).

Design: The Nutrigenomics, Overweight/Obesity, and Weight Management (NOW) randomised controlled trial is a pragmatic, parallel-group, superiority clinical trial (n=140), which was conducted at the East Elgin Family Health Team (EEFHT). GLB weight management groups were prerandomised 1:1 to receive either the standard GLB programme or a modified GLB+nutrigenomics (GLB+NGx) programme. Three 24-hour recalls were collected at baseline, 3, 6 and 12 months using the validated multiple pass method. Research assistants collecting the three 24-hour recalls were blinded to the participants' group assignments. Statistical analyses included split plot analyses of variance (ANOVAs), two-way ANOVAs, binary logistic regression, χ^2 and Fisher's exact tests. Using the Theory of Planned Behaviour as guidance, key confounding factors of behaviour change were considered in the analyses. This study was registered with clinicaltrials.gov (NCT03015012).

Results: Only the GLB+NGx group significantly reduced their total fat intake from baseline to 12-month follow-up (from 36.0%±4.8% kcal to 30.2%±8.7% kcal, p=0.02). Long-term dietary adherence to total fat and saturated fat guidelines was also significantly (p<0.05) greater in the GLB+NGx group compared to the standard GLB group.

Conclusions: Weight management interventions guided by nutrigenomics can motivate long-term improvements in dietary fat intake above and beyond gold-standard population-based interventions.

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Benefits

- DNA testing through a healthcare practitioner - **improved patient compliance**.
- Research shows that delivering dietary, nutrient and lifestyle advice with DNA testing can improve compliance and individuals are more likely to make long term changes.
- Can help to pinpoint where to start in the patient's wellness journey.
- Help practitioners choose particular forms of nutrients or compounds
- DNA testing can also act as a screening tool, directing practitioners to key areas or pathways that may require further testing, such as vitamin D levels or methylation markers.
- Can be offered to a wide range of patients and provides a unique service.
- The test does not need to be repeated.

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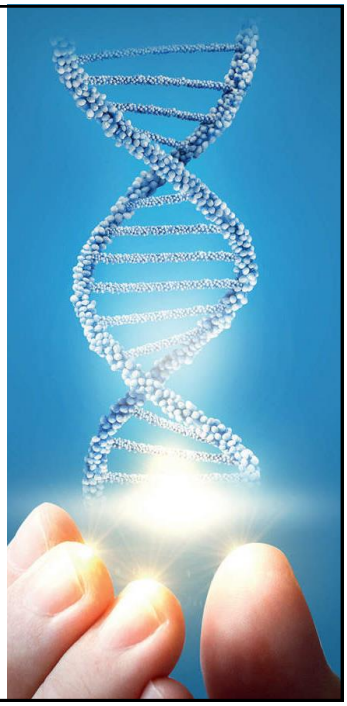
Limitations

- Single gene testing has limited value (this is different for clinical genetics and pharmacogenomics).
- Cost, training and preparation is required.
  - Look for testing company that offers support.
- Requires longer consults.
- Results do not help with dosage of supplements.
- Genes should not be looked at in isolation.
  - Questionnaires, symptoms, biochemical markers
- Check lab accreditations, if the report is backed by science and user friendly.



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Summary

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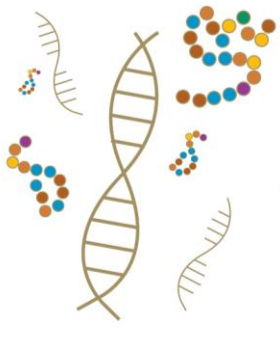
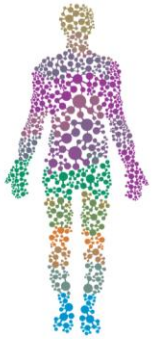


GENOMICS
Our genes can suggest what diseases we might be prediposed to, but it's an incomplete picture of human health.



PHENOTYPE
A snapshot of the current state of health that can be used to prevent, diagnose and treat disease or improve health.

LIFESTYLE / ENVIRONMENT
External factors like diet, excercise, medications, microbiota and even where we live influence our metabolic state

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Summary

- The field of nutrigenomics is evolving and advancing quickly with improved technology and consumer interest.
- More than 99% of the human genome is identical among all people, therefore it is less than 1% of our DNA that makes us different and unique.

  -These differences have a profound impact on our looks (physical traits), behaviour, susceptibility to health and disease as well as the way we react to food, chemicals and exercise.
- Nutrigenomics and genetic testing allows for a targeted approach to identify specific metabolic pathways, systems and key genes that may require nutritional support or lifestyle interventions to optimise health.
- High demand for practitioners to be able to order and deliver DNA test results.

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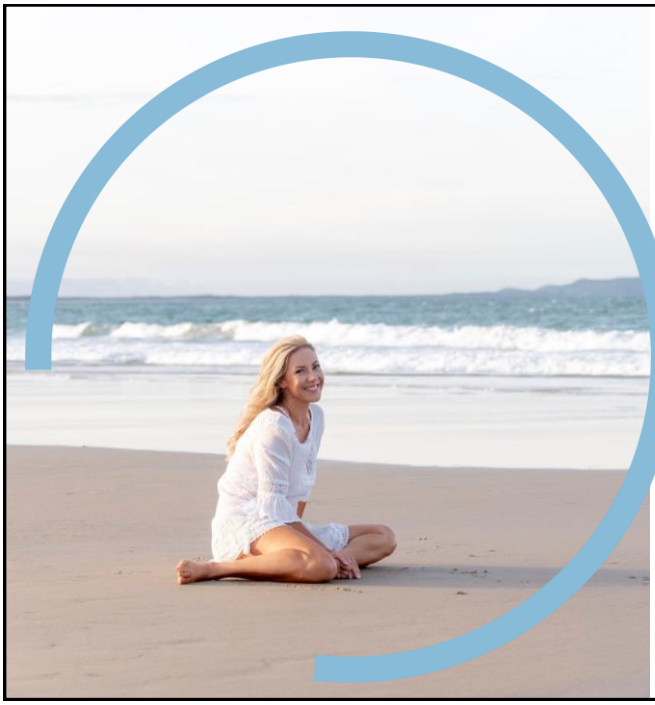

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Thank you
Question time

info@genenutrition.com

https://drdenisefurness.com.au

https://www.facebook.com/groups/yourgenesandnutritioncommunity

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