Nutritional genomics

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1 Introduction

Here is a story: Carl suffers from digestion problems and wants to know why. He decides to pay a company to sequence selected parts of his genome and discover afterward that he possesses some alleles associated with lactase nonpersistence. In other words, Marc is intolerent to lactose because of its genes, and decide to stop its consumption.

This example of ultra-personalized diet could soon become fairly spread among the population. Indeed, it is a rapidly growing field as shown by 23andMe, a leader of the personal genomics market who has already 2 millions customers genotyped.

2 What is Nutritional genomics?

Nutritional genomics is the study of genes and nutrients interactions, using high-throughput genomic tools.

It can be divided into two disciplines[1] :

Nutrigenetics : Aims to identify how genetic variation affects response to nutrients. This information can be applied to optimize health and prevent or treat diseases.

Nutrigenomics : Examines the effect of nutrients on genome, proteome, metabolome and the resulting changes in physiology. This information can be used to find nutrients which have a positive influence on our genome.

3 How can it be useful?

There is high hopes that it will allow evidence-based personalized diets, help to prevents diseases and raise awareness of consumers and food producers.

4 What techniques are used?

The techniques used in this field are the genomics ones.

The general principle is to compare the DNA of participants with and without a particular trait or disease (case and control group), and from that to deduce the specific genes associated with those features.

Thousands of associations between genetic variants and diseases or traits have already been identified, and maps of these variants have been created.

The current price of genome sequencing is around $1000, however most of us will be identical for over 99% of the genome. [2]

Micro-arrays techniques are one of the most widely used tools. It allows to quantify mRNA expression from all genes in a single measurement.

SNP genotyping array generally queries 0.1% of the genome looking at specific bases (called Single Nucleotide Polymorphisms) that have been statistically associated with a number of phenotypes. The cost of this

[1] There is still a lot of confusion and nutrigenetics is often referred as nutrigenomics...

[2] Nucleotide diversity is the average proportion of nucleotides that differ between two individuals. The human nucleotide diversity is estimated to be 0.1% to 0.4% of base pairs.

technique is ten times lower than a complete sequencing of DNA.

Yet, Genome-Wide Association Studies, which sequences the whole genome, remain very useful to discover news SNPs associated with a specific phenotype.

Typically a saliva sample suffices to do the analysis.

5 Applications

5.1 Nutrigenomics

Cancer

5.1.1 Carcino what?

A carcinogen is a substance or agent that causes cancer.

A large part of the cancers are caused by abnormalities in the genetic material of the cells. The damage to DNA can be done directly (genotoxic agent[3]), or by inducing a mutation (non-genotoxic[4]).

In our eating habits, some of the most famous carcinogen nutrients are processed meats, red meats[1][5] and alcohol.[2]

5.1.2 The broccoli, an example of anti-carcinogen

For several years it has been known that broccoli may help prevent cancer thanks to its high content in sulforaphane[6] but it is only recently that we discovered how.[3]

"Researchers from Oregon State University (OSU) found that sulforaphane reduced the expression of long noncoding RNAs (lncRNAs) in prostate cancer cells, which disrupted the cells' ability to form colonies - a hallmark of metastatic cancer.

Previously believed to be "junk DNA" with no significant function, lncRNAs have increasingly emerged as key players in the development of numerous cancers, including prostate, breast, stomach, and lung cancers.

Studies have suggested that lncRNAs can regulate gene expression - the process by which genes are switched on or off in order to do their jobs. When lncRNAs become dysregulated, it is believed that they can fuel disease development."

To reach their findings, the researchers conducted whole-genome sequencing on normal human prostate cells and prostate cancer cells.

They found that the prostate cancer cells showed high expression of lncRNAs, particularly one called LINC01116.However after administration of sulforaphane to the prostate cancer cells, LINC01116 levels were significantly reduced.

5.2 Nutrigenetics

In particular, SNPs may influence the way individuals absorb, transport, store or metabolize nutrients.

Lactose

Lactase persistence is the ability to continue to produce the lactase enzyme during adulthood, which allows a good digestion of the lactose of the milk.

Small changes in the lactase gene of some population sustain this enzyme expression into adulthood. This adaptation helped them to consume lots of milk and survive in environments with otherwise sparse food supplies.[4]

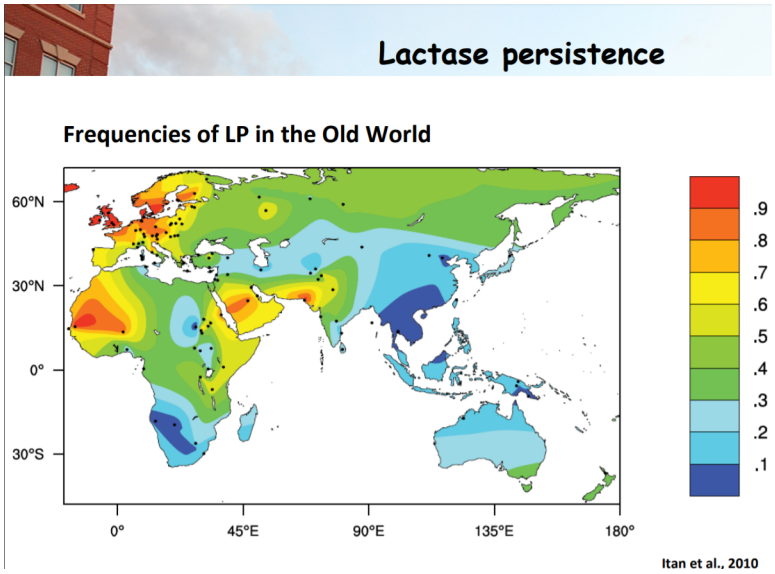
For instance the ability to digest lactose, the principal sugar of milk, also in adulthood spread in cattle-rising populations.

[3] cause direct and irreversible genetic damage or mutations by binding to the DNA

[4] Do not cause direct changes in DNA, but also makes the cancer harder to predict...

[5] recent researches tend to show that the associated chemicals (e.g nitrites) may play for a large part

[6] component found in numerous cruciferous vegetables: Brussels sprout, cabbage, cauliflower, bok choy, kale, collards,radish,etc



Obesity

A major goal for nutrigenetic researchers is to identify genes that make certain individuals more susceptible to obesity and obesity-related diseases.

Genetic variation may affect appetite, calorie intake, and macronutrient preference, as well as insulin signaling, inflammation, adipogenesis (the formation of fat cells), and lipid metabolism.

Multiple studies have found association between SNPs and obesity, and a serie of gene have been found to be linked with obesity.[7]

Of course even if genes play a role, we can't underestimate the potential impact of a person's lifestyle and environment.

6 Conclusion

In recent years, the mapping of the human genome an increased information on SNPs. We can hope that the map of SNPs in the human genome will provide powerful molecular tools to understand the role of nutrition in human health and disease and help defining optimal diets by tailoring food to individual genotypes.

The development of the SNPs mapping may also provoke the apparition of various genetic risk scores, associated the genome of an individual with a degree of risk for a given disease or for a sensibility to a food.

Finally, we should remind ourselves that factors in personalizing nutrition recommendations includes not just genotype but also the phenotype and the microbiome.In particular,the field of microbiome research[5, 6] is still young but seems promising to better understand what it now called "the Second Brain".

[7]Some of the most famous are FTO,APO B, SNPs MC4R, SH2B1, MTCH2, SEC16B genes

References

[1] *OMS information on meat and cancer*. URL: http://www.who.int/features/qa/cancer-red-meat/fr/.

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[4] *Nutrigenetics overview*. URL: https://www.uncnri.org/wp-content/uploads/2016/07/NRI_NGx_Overview_Kohlmeier_05222016.pdf.

[5] *Human genetics shape the gut microbiome*. URL: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4255478/f.

[6] *Genetics or lifestyle: What is it that shapes our microbiome?* URL: https://www.sciencedaily.com/releases/2018/02/180228131043.htm.

7 Annexe

7.1 Some carcinogens and anti-carcinogens with their cancer association

Dietary component	Polymorphic gene	Cancer site
Carcinogens		
Heterocyclic amines (red & processed meat)	*NAT-2, NAT-1, CYP1A2*	Colorectal, breast, other sites
Polycyclic hydrocarbons (red & processed meat)	*CYP1A1, GSTM1*	Gastrointestinal tract
Nitrosamines (fried potatoes)	*CYP2E1*	Nasopharyngeal, stomach
Alcohol	*GSTM1, ADH (ALDH)*	Colorectal
Aflatoxins (polluted grains)	*CYP2E1*	Liver
Anticarcinogens		
Cruciferous vegetables	*CYP1A2, GST*	Colorectal, other sites
Fruits & vegetables	*CYP1A2, GST*	Many sites
Calcium/vitamin D	*Vitamin D receptor*	Colorectal, prostate
Retinoids	*Retinoic acid receptor*	Variant acute promylocytic Leukemia, skin, others
Folate, methionine	*MTHFR*	Colorectal, cervix