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Nutrition and Toxicogenomics: A short Review

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Abstract

Food science and Technology deals with dietary components and works towards preserving their nutritional values and sometime converting these to some value added products keeping in mind the sensory qualities as desired by the customers. However, time has come to attach significance to the toxicological effect of these dietary components too. In pharmacology, such studies have been already taken note of and development of personalized drugs is being talked about. On the same lines, development of personalized food is being studied (though with lot of skepticism). This review deals with such a development (which is still at its infancy), using nutrigenomics database and tools from toxicogenomics.

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Introduction

It has been observed that many dietary components are easily assimilable by certain individuals, whereas to others it proves to be toxic in varying degree. Toxicogenomics are a set of tools which helps scientists to comprehend the health effects after exposure to different substances in the environment – collectively termed as toxicants. Such toxicological studies, using this potent set of tools has advanced in drug designing in pharmacological science. It has made some head way in the practice of clinical medicine.

In modern day's food science, more emphasis is given to methods of preservation of nutritional values of different food material along with its sensory qualities and digestive qualities over an extended period of normal shelf life. Secondly, it also focuses on value-addition to different food materials (by improving some of the sensory qualities along with nutritional qualities) so that the processors are able to get higher profit margins. Such studies involve understanding the physics and chemistry of the food components to make the right judgment regarding the type of process that needs to be adopted. However, the fact that all the food items are not suited by the digestive and physiological system of many individuals is often ignored.

The human genome project has provided tools for understanding such toxicological phenomena at molecular level which has helped the food scientists and nutritionist to design special food or diets for intolerant individuals. Toxicogenomics is one such set of tools which is very handy to study these toxicological effects.

Nutrigenomics

In the field of food science and nutrition science such pioneering integration has evolved in two directions: nutrigenomics and nutrigenetics. Nutrigenomics not only involves the study of dietary components on the expression and regulation of genes, but also of proteins and metabolites (Ordovas and Mooser, 2004; Mutch., *et al.* 2005; Rawson, 2008). In other words, a nutrigenomics approach is a holistic one that examines the effect of nutrients at all levels, from gene expression to metabolic pathways (Neeha and Kinth, 2013).

Disorders that scientists previously thought to be heritable, can be identified as genetic disorders with set pathological effects (Aglave., *et al*. 2009). This means that nutrigenomics is research focusing on identifying and understanding molecular-level interaction between nutrients and other dietary bio actives with the genome (Braicu., *et al*. 2017). Existing information from genetic research directs emerging research in nutrigenomics. Individuals within the same population or even the same family have genetic variability (Bull and Fenech, 2008). For example, Prader-Willi syndrome, a disease whose most distinguishing factor is insatiable appetite, has been specifically linked to an epigenetic pattern in which the paternal copy in the chromosomal region is deleted, and the maternal loci is inactivated by excess methylation (Grant and Xia, 2013). Thus nutrigenomics looks at specific biomarkers within each individual (Ardekani and Jabbari, 2009) and can be used to design certain nutrients, or a 'nutriome which would ensure proper physiological activities (Bull and Fenech, 2008). Genome damage caused by micronutrient deficiency may be just as severe as damage owed to exposure to certain environmental carcinogens (Bull and Fenech, 2008). If these micronutrients can be identified, with concrete evidence, the risk for cancer in some individuals could be significantly reduced. One such micronutrient may be folate. In one experiment, folate was given to cells in different concentrations and those with less folate exhibited as much damage to their chromosomes as they would have exhibited with a heavy amount of radiation (Bull and Fenech, 2008).

Nutrigenomics and cancer therapy

Nutrigenomics has the potential to develop alternative treatments for cancer where the cells have altered metabolism as compared to normal cells (Simopoulos and Ordovás, 2004). The alternative way of energy production in cancer cell metabolism, For example the Warburg effect, in which glycolysis and lactic acid fermentation are the key metabolic routes for energy production instead of oxidative reduction, can be inhibited easily by certain Polyunsaturated fatty acids (PUFA).Similarly certain altered metabolism of cancer cells requiring certain cofactors can be inhibited by providing these cofactors in excess by the dietary route (Simopoulos and Ordovás, 2004). This means that the Nutrigenomics approach to arrest the growth and spread of neoplasm is often preferred over other means, as these do not show many of the harsh side-effects of the routine therapeutics.

Nutrigenetics

Nutrigenetics, on the other hand deals with the individual's genetic background and the interaction between diet and the genome (Ordovas and Mooser, 2004). The realization of the fact that dietary components is able to interact and affect molecular mechanisms involving an organism's physiology, has made researchers develop a deeper insight in the field of nutrition. One of the important genetic data that has helped pharmacists to design drugs suitable for an individual is the single nucleotide polymorphism (SNP). Many scientists have discovered that such polymorphism plays a vital role in absorption, transportation, metabolism and storage of certain nutrients in the body of an individual (Daniel and Klein, 2013). It has been observed that certain disorders may be linked to certain SNP or other localized patterns, variation within a population may yield many more polymorphisms (Bisen., *et al*. 2010). Each may have a negligible effect by itself, yet the cumulative effects may be significant.

A well known phenomenon, which is more than often a consequence of SNP, is the development of obesity that is individuals with high BMI than normal. Obesity has been linked to FTO and APO B genes. In case of SNP in FTO gene, the AA genotype had a higher BMI as compared to TT genotype when the individuals were on high fat and low carbohydrate diet (Doo and Kim, 2015; Sonestedt., *et al*. 2009). On the other hand, the APO B rs12535 variation, is a well-studied SNP involving MC4R, SH2B1, MTCH2, SEC16B etc. genes. It was observed that individuals with high fat containing diet (> 35%) and having A/G heterozygous genotype were highly obese as compared to G/G homozygous individuals (Doo and Kim, 2015; Philips., *et al.* 2011). These sorts of variations due to SNPs are some time unique

to certain ethnic races (Doo and Kim, 2015). For example, the ability to digest lactose in adults is better in cattle-raising populations (Gerbault., *et al.* 2011).

The absence of genetic knowledge might have misled many nutritional recommendations and therefore, it became imperative to study the relationship between genes and diet.

Toxicogenomics

If one looks at the nutrigenomics then one would see that it deals primarily with database management and mining. However, to generate new data it is essential that certain analysis be carried out with different diet components and sees how it influences the gene expression. In order to do so one needs to carry out certain experimentation using certain tools which are only found in transcript genomics or transcriptomics and toxicogenomics. Briefly it can be said that transcriptomics analysis will deal with the manner in which the transcription of gene is altered (by seeing the altered mRNA) so that the proteins now will have different structure and accordingly change the metabolic routes in physiology of that individual. It cannot conclude whether such changes will benefit the individual or not. This can be done using tools of toxicogenomics only. These tools were soon found to be supplemented with certain other set of tools to get an accurate insight of the effects.

Toxicogenomics is defined as a combination of conventional toxicology with high-throughput technology.The term toxicogenomics was popularized in the literature in the late 1990s (Nuwaysir., *et al.* 1999), when microarray technology emerged to display the capability of simultaneously monitoring the expression of thousands of genes. Toxicogenomics extended its scope and finally, it is also referred as "transcriptomics" (Liu and Gio,2012). Presently it includes related metabonomics and proteomics, when efficient detection methods for proteins and metabolites arose through high-throughput techniques.

Modern toxicogenomics classifies toxicity based on comparison of gene transcriptional responses in presence of a particular compound (with unknown toxicity) with those for which the transcriptional profiles have been characterized as toxicological endpoints (Newmann and Galvez, 2002). Gene expression microarrays are essential tools of toxicogenomics, needed for defining mechanism of action of toxicants at a particular given time. This is unlike toxicology, where the toxic effects are a continuum effects governed by temporal and spatial faciors strictly dependent upon the exposure conditions to the toxicant (Newmann and Galvez, 2002). It shows the changes, brought about by dietary components at genomic and proteomics level, much earlier and at very low level of detection, than that could be detected by any other means using microarray techniques (Irwin., *et al*. 2004) so that the food scientist or food technologist can design (personalize) food which can prevent such harmful effect.

Toxicogenomics focuses on assessing the safety of compounds using gene expression profiles. Gene expression signatures from large toxicogenomics databases are expected to perform better than small databases in identifying biomarkers for the prediction and evaluation of safety of diet components, based on a compound's toxicological mechanisms in animal target organs (Igarashi., *et al*. 2015). Over the past 10 years, the Japanese Toxicogenomics Project consortium (TGP) has been developing a large-scale toxicogenomics database consisting of data from 170 compounds (mostly drugs) with the aim of improving and enhancing safety assessment. Most of the data generated by the project (e.g. gene expression, pathology, lot number) are freely available to the public via Open TG-GATEs (Toxicogenomics Project-Genomics Assisted Toxicity Evaluation System).

Conclusions

The pharmaceutical industry has begun to reap the harvest from a range of new technologies like proteomics, pharmacogenomics, metabolomics and molecular toxicology like toxicogenomics and the related analysis tools that are becoming increasingly integrated in the area of drug discovery and development (Ganter., *et al*. 2008) with sole objective of personalization of medicines.

In the field of food science and technology, the creation of Nutrigenomics and Toxicogenomics supplemented with the tools of toxicogenomics, would provide the most critical approaches to understand the interactions between nutritional molecules, genetic polymorphisms, and the biological system as a whole with the objective of personalization of diet.

However, the nutritionist and the food technologists are not in favour of using such methods in designing of personalized diets as they fear that such applications would produce large quantity of biological data in a single study which will sometime submerge the original query.

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