



## Review

## Nutrigenomics in cancer: Revisiting the effects of natural compounds



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## ARTICLE INFO

## Keywords:

Nutrigenomics

Natural compounds

Cancer

## ABSTRACT

Nutrigenomics effects have an important role in the manipulation of dietary components for human benefit, particularly in cancer prevention or treatment. The impact of dietary components, including phytochemicals, is largely studied by nutrigenomics, looking at the gene expression and molecular mechanisms interacting with bioactive compounds and nutrients, based on new ‘omics’ technologies. The high number of preclinical studies proves the relevant role of nutrigenomics in cancer management. By deciphering the network of nutrient-gene connections associated with cancer, relevant data will be transposed as therapeutic interventions for this devastating pathology and for fulfilling the concept of personalized nutrition. All these are presented under the nutrigenomics canopy for a better comprehension of the relation between ingested phytochemicals and chemoprevention or chemotherapy. The profits from the nutrigenomics progress, with a particular focus on the coding and noncoding genes related to the exposure of natural compounds need to be validated. A precise attention receives the evaluation of the role of natural compounds in tandem with conventional therapy using genomic approaches, with emphasis on the capacity to inhibit drug resistance mechanisms. All these relevant nutrigenomics aspects are summarized in the present review paper. It is concluded that further nutrigenomics studies are required to improve our understanding related to the complex mechanisms of action of the natural compounds and for their appropriate application as gears in cancer therapy.

## 1. Introduction

Hippocrates, the father of modern medicine, asserted, “*Let the food be thy medicine and the medicine be thy food*”. The classical validating examples are those related to the Asian diet (rich in soy, fish and green tea) associated with reduced incidence of breast cancer [1], the Mediterranean diet [2,3] or red wine consumption related to decreased levels of cardiovascular diseases, a phenomenon known as the “French

paradox” [4,5]. A large number of epidemiological studies stipulate that a healthy diet, rich in fruit and vegetables protects our body against cancer and other chronic diseases such as cardiovascular pathology, diabetes and aging. All these findings are attributed to the huge amount of *plant secondary metabolites* responsible for flavor, taste and color. A giant class of natural compounds is retrieved in literature as *phytochemicals* and has been proven to have a wide assortment of beneficial effects in human health [6–9]. There are several options to

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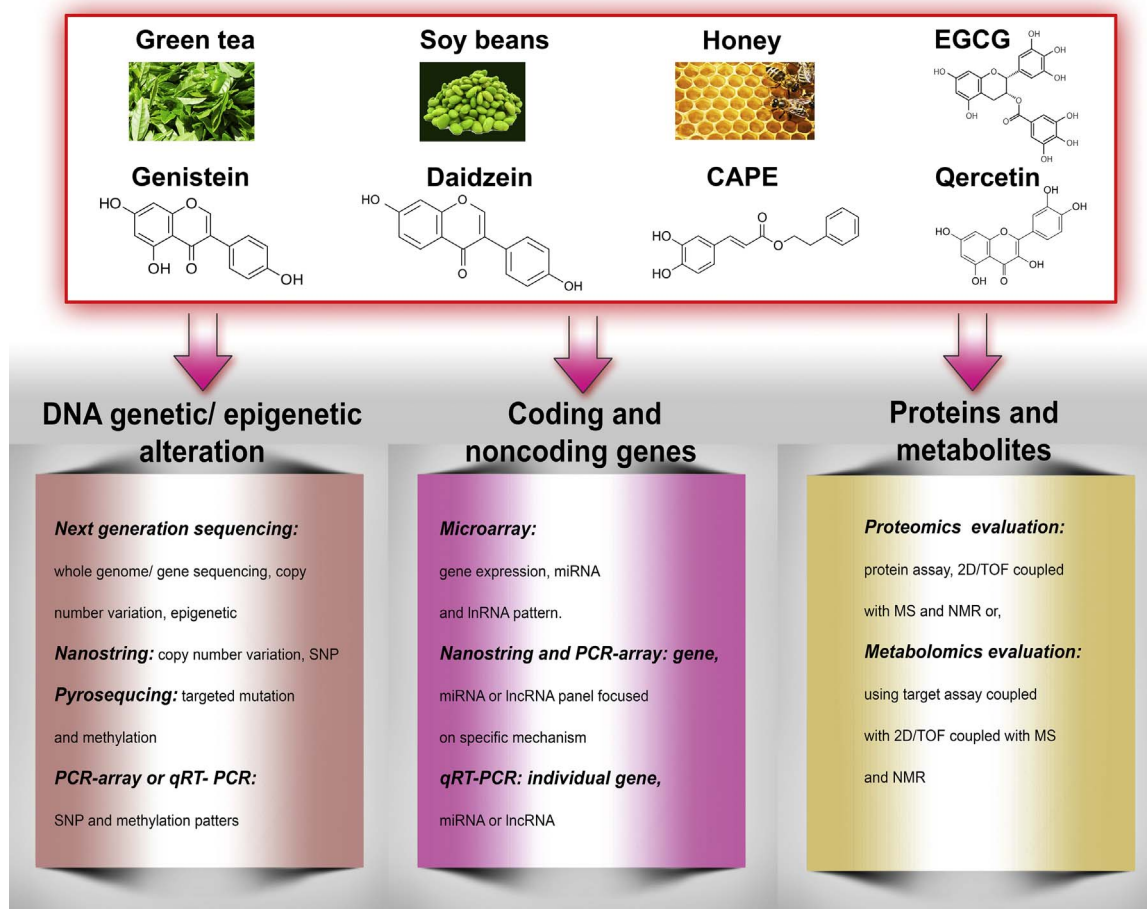


Fig. 1.

achieve a diet rich in beneficial phytochemicals. The simplest approach is to select phytochemicals-enriched nutrients or other beneficial related nourishments, encompassing one or more health-promoting products [3,7], retrieved under the name “functional food” fortified in essential nutrients that was proved to provide health benefits [10,11]. Another option is to use products enriched in bioactive agents, commonly known as nutraceuticals [9,12]. These healthy promoting products derived from natural sources can be used in a concentrated formula as enriched extracts or as capsules, termed dietary supplement. The development of functional supplements is sustained by *nutrigenomics*, allowing the identification of those bioactive natural compounds that sustain a healthy genome and are properly customized for each individual genotype and genome status. The phenomenon of crossing point concerning *Nutrients – Genes – Cancer* is multifaceted and needs to be deciphered, but recent advances in nutrigenetics as individual genetic “make-up” and nutrigenomics as the whole genes picture sustain it.

Cancer is a multifactorial and comprehensive disease, characterized by multiple genetic mutations and alterations of more solfeggios of pathways and mechanisms. It is mainly a heterogeneous manifestation of similar hallmarks with uncontrolled evolution, limited treatment potential and some degree of cure. The natural compounds are able to target several of the altered pathways, interfering during early tumorigenesis, but also during late carcinogenic steps, invasion, the proangiogenic and the metastatic phase (luteolin treatment). Dietary natural compounds can influence cancer risk and tumour behavior. Around 30–40% of cancers are known to be influenced by diet, being related to cancer histological type, molecular subtype, tumor markers and prediction markers for response to therapy [13].

The vital role of nutrigenomics in cancer management is already

ascertained. By clarifying the network of nutrient-gene-cancer connections associated with tumor pathology, relevant data can be integrated in therapeutic strategies and interventions for this deadly “game”. A major aim is data integration into translational research. Nutrigenomics’ main focus is to improve molecular understanding of the nutrition role in genomic communication and exchanges, including the individual genotype. The concentration stands at genomic, proteomic and metabolomics levels.

Despite many unknown mechanisms and a lack of clear understanding of the relationship between consumption and effects, these diets can be considered a synergism or even an additive effect as consequence of all the phytonutrients ingested, which makes them much more difficult to investigate. The topic remains highly debatable. This is mainly due to the wide diversity of study designs, the selection of the most relevant cell line or animal model, and the measured endpoint. Therefore, there is an urgent need for assessing the complex interconnections between diet and health status by investigating the protective role of natural compounds on human wellbeing. The obtained data should be connected with the complex environmental exposure. Consequently, simply consuming such healthy phytochemicals is not sufficient. Food supplies with native forms of these compounds can achieve the maximal antitumor effect. The problem is related to the high concentration of phytochemicals required for reaching the biological effect, impossible to be retrieved from natural sources. Furthermore, some studies show that the role of some natural compounds is still questionable [14]. Other works point that biological effects of health-promoting foods can be better explained by looking not at single constituents but at the complex, often synergistic, effects displayed by the mixtures of bioactive compounds present in the respective food products [15]. In the survey presented herein we discuss

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