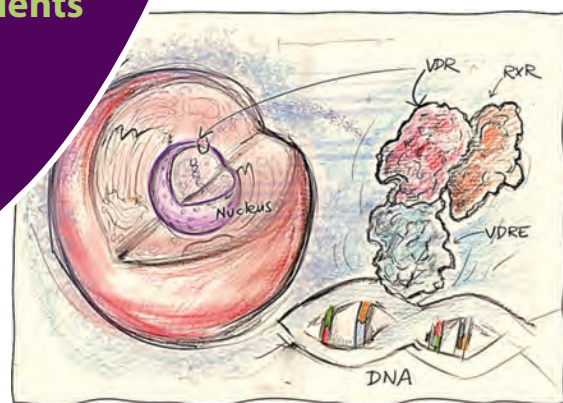


Nutrigenomics: From Epicure to Epigenetics—Engaging Students With Nutrition Through the Human Genome

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ABSTRACT

Is food a unifying concept in biology? With the new subdiscipline of nutrigenomics, it might be. Food is arguably the most focused on aspect of everyday life besides sleep. In fact, even in sleep, humans often dream about food. In prehistoric times and even today for many people, the procurement of food requires skillful efforts, cooperation, and energy. Today, in the modern, industrial world, food is no longer appreciated from this perspective. Biology students, like most people in the modern, industrial world, often experience a disconnect between food, nutrition, and the planet. For biology students that disconnect is exacerbated and further extended to concepts of nutrient procurement, cellular respiration, ecology, evolution, and genomics. Such concepts as nutrient scarcity or abundance and how food shaped human cultural practices and contributed to genetic and phenotypic divergence are part of the evolutionary framework of nutrigenomics. Our current genome and food-related practices have diverged from our primate relatives and continue to impact our genome in the present. From tooth shape to digestive enzymes, human digestive physiologies vary greatly due to geography, cultural practices, genetic variation (SNPs), and epigenetics. There is now, however, a connecting concept, which is a branch of genomics known as nutrigenomics, that has the potential to draw in and refocus student attention on many of the basic biological ideas students struggle with.

Key Words: nutrigenomics, genomics, nutrition, disease, ecology.

○ Introduction

Today, in the industrialized world, food has become both abundant and confusing. The wide array of choices, diets, and processed foods has made eating less intuitive and more confounding. Parallel to this complexity is the rise of chronic diseases such as obesity, diabetes,

inflammatory bowel disease, mental health issues, cancer, and metabolic syndrome. These diseases have grown considerably in the last few decades. Even traditional cultures that have adopted Western dietary patterns experience these health issues.

For millennia, food was locally grown and often used medicinally. Plants, herbs, and spices mirrored the soil composition and the local microbiomes, and they induced epigenetic effects in the humans who cultivated and consumed them. In the genomic era, the biochemistry of plants and their environmental interactions have been shown to influence genetic expression and disease susceptibility.

Enter nutrigenomics, which has come to be known as the study of how nutrition influences gene expression and how genetic variations affect nutrient needs. This definition, however, is primarily focused on therapeutics and identification of those human variants. In our recently developed and taught nutrigenomics course, however, students got an opportunity to see the vast interconnectivity of plants, human genomes, microbes, and diets on disease patterns and on individual health. They learned how soil, microbes, and environment can radically alter food and its biochemical effects on gene expression and molecular pathways. This emerging field, if applied to teaching biology even for a single lesson plan, can bridge complex topics in biology. In this way, biological units become planetary interactions over time, united through food. Nutrigenomics can provide a compelling framework for teaching students how everyday dietary choices impact their own biology, providing them with

real-life and real-time examples of immediate actions between what they eat and their own gene expression. Nutrients can provide the essential elements of DNA repair, they can regulate genes,

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and in some cases, prevent birth defects. Nutrition was once often relegated to a single course within the biology curriculum; however, the emergence of nutrigenomics has expanded its role into the broader field of genomics, allowing it to serve as a framework for exploring diverse biological concepts and generating meaningful critical-thinking questions.

By connecting food, soil, ecology, environmental toxins, and genetics, nutrigenomics offers a powerful and interdisciplinary approach to biology education. It also allows students to take the abstraction of the genome and put it in the context of their own lives and with a subject they can all relate to—food. In real life, nutrigenomics effortlessly demonstrates the direct impact of what we eat on our epigenome and microbiome, altering the phenotypic outcome on a day-to-day basis. It also links people to their land of origin, to their unique biogeographies, and to their specialized adaptations. Nutrigenomics further highlights how chronic diseases can be treated based on individual genomes and the food choices we make and it gives insight into the current surge in metabolic diseases, which most Americans have. It also delves into such problematic environmental concerns as how consuming plastic affects the body, or how “forever chemicals” get into food and what they might do to the genome. From pesticides to farmed fish, to the astonishing chemistry of plants, nutrigenomics has something that every student can relate to. In this paper we will provide background for educators and activities that educators can use to introduce nutrigenomics to their students. We have tried a variety of activities during the course of a semester and provided a select few of them in this paper, which include an authentic STEAM-based activity that has been used in our nutrigenomics course at the University level.

○ What is Nutrigenomics?

Nutrigenomics is a branch of genomic medicine focused on the biochemical relationship between food and the genome. Its underlying principle is that nutrients and bioactive compounds obtained through diet influence fundamental cellular processes, including metabolism, DNA repair, apoptosis, and gene regulation. However, the biological impact of food begins long before nutrients enter the body. The composition of food is shaped by ecological processes, including soil chemistry, microbial interactions, plant metabolism, and nutrient availability within ecosystems.

Stoichiogenomics provides a framework for understanding how the availability and balance of elements within an environment influence biological systems and evolutionary processes. By examining elemental composition, such as nitrogen availability, stoichiogenomics helps explain how environmental constraints shape the production of proteins, nucleic acids, and other cellular components. Nitrogen, for example, is often a limiting nutrient that influences growth, metabolism, and natural selection. Changes in nutrient availability can create selective pressures that favor adaptations in the biochemical composition and regulation of proteins, RNAs, and metabolic pathways.

Integrating stoichiogenomics with nutrigenomics creates a broader evolutionary perspective in which nutrients are not simply consumed molecules but represent the outcome of complex interactions among geology, ecology, evolution, and genetics. The nutrients available within an ecosystem influence the foods organisms acquire, the biochemical pathways they rely on, and ultimately

the genomic responses that contribute to adaptation and biological diversity.

So, micronutrients may ultimately effect the composition of proteins and the amount of them in food, such as plants, fungi, and meat. A 2006 paper examined the availability of resources such as nitrogen and phosphorus in the environment and how it reflected in the composition of proteins in living organisms (Elser et al., 2006). Investigations such as this reveal information that relates directly to the field of nutrigenomics. Students can utilize papers similar to this one to explore the relationship of soil composition and food in greater detail. Nutrigenomics considers how individual genetic profiles can impact unique nutritional needs of people. Nutrigenomics also focuses on how specific foods can prevent or even treat diseases, including cancer by up regulating or down regulating cancer-related genes. Understanding nutrigenomics requires examining food origins, agricultural practices, environmental impacts, and plant biochemistry along with human genetic variations.

A holistic nutrigenomics course might begin with soil science where students can explore rhizospheres, root exudates, and nitrogen-fixing bacteria, which are all critical components of plant nutrition. Photosynthesis, too, can become part of the nutrigenomic lesson plan and it can serve as the ultimate starting point for talking about food. It can demonstrate to students a more tangible and concrete example of how sunlight moves through plants and generates the great diversity of that kingdom and the plant adaptations such as sugary fruits, which attract animals to eat them and disperse seeds. In another example of nutrigenomic curriculum diversity, the vitamin D receptor (VDR) provides an engaging link between sunlight, nutrition, and gene regulation. It is even hypothesized to be the critical receptor in the evolution of skin color (Yuen & Jablonski, 2010). Even if educators don't dedicate a full unit to nutrigenomics, incorporating a few of these concepts can bridge biology units and reinforce concepts such as gene regulation, metabolism, evolution, and ecological principles.

○ Nutrigenomics & Evolution

Much of biology in cells involves securing energy sources. Many genetic pathways are critical to converting food into energy. For plants, that energy comes from the sun (photosynthesis), for animals, that energy comes from consuming other organisms. Plants don't simply need sunlight, they need micronutrients to run their photosynthetic processes and this is important for students to see, as some nutrients are similar to animals, others like magnesium are required in greater quantity and also provided by rocks, soil, and water. From complex biomes to nutrient availability, nutrient procurement shapes and is shaped by biogeochemical cycles and evolutionary dynamics. Variation is distributed based on availabilities, on climate, on variation in protein isoforms, and in the alleles themselves. Beyond soil and nutrition, nutrigenomics emphasizes individuality and speaks to this evolutionary variation in the genome. A familiar example is lactose persistence, which is an evolutionary adaptation to dairy consumption and a trait, not a disease. There are such variations in human populations for number of macronutrients as well. In such cultures as the Inuit, their once stable diet of meat and fat from marine animals has enabled Inuit people to live successfully

in a cold climate for thousands of years without chronic illnesses such as heart disease, but after switching to a Western diet and lifestyle, that population is now battling the same patterns of disease as many Americans (Sharma et al., 2015). The Inuit population has unique genetic adaptations that allow them to metabolize high-fat diets rich in marine mammals and fish who have acquired essential fatty acids up the food chain. Most students would think that the Inuit people would be at a high risk for cardiovascular disease with a high-fat diet, but they were not. Many students would initially assume that Inuit populations would be at a high risk for cardiovascular disease because of their historically high-fat diet. This assumption reflects a common misconception that all dietary fats have the same biological effects. However, fats represent a diverse group of molecules with different structures, functions, and physiological impacts. A key discovery highlighting the interaction between diet and genetics involves variants within the FADS (fatty acid desaturase) gene cluster, particularly FADS1 and FADS2, which influence how polyunsaturated fatty acids (PUFAs) are processed. These variants provide an example of how human populations can adapt to long-term dietary patterns by modifying biochemical pathways involved in fatty acid metabolism. This example challenges the simplistic view that “fat” is inherently harmful and demonstrates how the effects of nutrients depend on their chemical properties, ecological context, and interactions with the genome. This may be the mechanism by which Inuit people are protected against inflammation and cardiovascular disease (Fumagalli et al., 2015). The adoption of Western diets that are high in processed carbohydrates and synthetic fats can make once adaptive variations maladaptive. Inuits have rising rates of obesity, type 2 diabetes, acne, autoimmune diseases, and heart disease (Mahmud, 2020) attributed to a Western diet. This highlights the mismatch between evolved genetic traits and modern food, one that is seen consistently across non-Western or traditional cultures where an epidemic of disease has resulted from adopting the Western diet (Kopp, 2019).

Many students now enjoy sushi as a normal part of an American diet, many, however, do not know what sushi is, or where it comes from. When the topic was introduced in class,

most students enjoyed talking about their favorite type of sushi, which led to an interesting teaching point. With just one slide of a sushi roll or an image of brown algae at the beach we started a discussion on seaweed, and the different selection of microbes in their gut of Japanese people who can better digest and extract nutrients from seaweed. This ability is linked not to their own human genes, but to genes found in the microbes of their gut. Researchers have discovered that certain strains of gut bacteria in Japanese individuals have acquired genes from marine bacteria through a process called horizontal gene transfer (Hehemann et al., 2010). These marine bacteria, commonly found on raw seaweed such as *nori*, possess enzymes called porphyranases. Porphyranases can break down complex carbohydrates in seaweed cell walls and allow more nutrients to come from seaweed when eaten and digested. Students might try and classify seaweed. I asked students what seaweed is related to—is it plants, animals, protists? Because traditional Japanese diets have included raw seaweed for centuries, these microbial genes have become established in the gut flora of many Japanese individuals. The gut microbiota of Westerners is considerably different, as their gut microbiome lacks those seaweed-digesting enzymes (Hehemann et al., 2010). When we examine various ethnic groups around the world, we see plants and animals local to those communities, coevolving thousands of years through diet, and producing the epigenetic changes specific to that group and that ecology. We can even explore compounds such as turmeric and its anti-cancer properties and its ability to mitigate the inflammatory response, or shitake mushrooms, a traditional staple in Japanese cooking with anticancer properties. Many of the small molecules in plants act in an epigenetic manner and they provide a dynamic narrative of environmental and genetic relationships often emphasizing the constant epigenetic influences throughout the genome of cells. By examining genomic diversity and traditional cultural food practices, educators can present nutrition as an evolutionary narrative as well as an anthropological one. This approach not only personalizes biology but also contextualizes it within human history and adaptation. We have provided a table of examples and sample questions to pose to students to start a discussion (see Table 1).

Table 1. Some phytonutrients, their food source, and their activity.

Phytonutrient	Primary Food Sources	Epigenetic/Genomic Mechanism
Resveratrol	Red grapes, red wine, berries, peanuts	Activates SIRT1, influences DNA methylation patterns, modulates genes involved in inflammation and lifespan
Allicin	Garlic	Inhibits histone deacetylases (HDACs); upregulates phase II detoxification enzymes and modulates apoptotic genes
Flavonoids (e.g., quercetin, EGCG)	Green tea, apples, onions, citrus fruits, berries	Can inhibit DNA methyltransferases (DNMTs) and HDACs, Can restore silenced tumor suppressor gene expression
Ellagic Acid	Pomegranates, strawberries, raspberries, walnuts	Alters DNA methylation of key genes in estrogen receptor and Wnt pathways; anti- carcinogenic properties
Glucosinolates (→ sulforaphane)	Broccoli, Brussels sprouts, kale, cabbage	Inhibit HDACs; modulate gene expression related to apoptosis, detoxification, and inflammation

○ The Multifaceted Fate of the VDR Receptor

Vitamin D's roles in the body are still being uncovered and most students might think that vitamin D comes largely from milk products when most of it is synthesized via the sun. Central to the function of vitamin D in the body is its complementary receptor—the VDR. This is a nuclear receptor that binds the active form of vitamin D, calcitriol (1,25-dihydroxyvitamin D₃). Once activated, VDR functions as a transcription factor, influencing the expression of hundreds of genes. VDR interacts directly with DNA, and it acts as a key regulator of the genome (Carlberg, 2022). While it has its classical role in calcium and phosphate homeostasis in bones, it is also critical for mineral absorption in the intestine. The VDR has also been implicated in a broad array of non-skeletal processes and disease risks attributable to low levels of sunlight and to polymorphisms in the human genome. A variety of papers discuss the risk of Alzheimer's disease, increasing infertility, and lung cancer risk associated with both VDR and vitamin D (Plantone et al., 2024).

VDR is expressed in nearly every tissue type, including immune cells, skin, pancreas, brain, and muscle, highlighting its pleiotropic nature. This is an opportunity to discuss an often poorly understood idea in genetics, pleiotropic effects. In the immune system, VDR activation modulates both innate and adaptive responses, enhancing antimicrobial peptide expression while dampening overactive T cell responses, suggesting therapeutic potential in autoimmune diseases and infection (Chun et al., 2014). In cancer biology, VDR is involved in cell cycle regulation, apoptosis, and differentiation, with some studies showing that VDR signaling may inhibit tumor progression (Feldman et al., 2014). The role of sunlight in immune response and in cancer prevention is becoming more and more apparent. Students might speculate if sunlight is part of nutrigenomics, and, if in fact, it can be classified as a “nutrient.”

From an evolutionary perspective, the VDR may have originally evolved as a UV sensor, linking the availability of sunlight to genetic regulation. This concept bridges the ancient relationship between sunlight; photosynthesis, which produces vitamin D precursors in plants and fungi; and human physiology (Carlberg, 2022). As such, studying the VDR receptor provides an integrative teaching point that connects evolution, solar exposure, endocrine function, and epigenetic gene regulation. It gives students an opportunity to visualize receptors on the nucleus, which most students in biology do not encounter. In Figure 1 we have illustrated a nuclear receptor so students can consider the VDR receptor as a hormonal “direct link” to gene networks. This elegant design allows for rapid transmission of external environmental cues to the genome of a cell (see Figure 1).

○ Micronutrients: From Periodic Table to Plate

The periodic table, a staple in biology and chemistry classrooms, often fades from view in advanced molecular biology discussions. Yet many trace elements such as zinc (Zn), selenium (Se), sulfur (S), manganese (Mn), iodine (I), magnesium (Mg), and iron (Fe) are indispensable micronutrients that serve as cofactors, redox agents, and structural components in enzymes and cellular pathways. These elements are not synthesized by the body; they originate from rocks and soil, enter food chains through plants and microbes, and ultimately reach us via diet.

This elemental thread links geology, soil science, local and global agriculture to cellular physiology and gene regulation. For example, zinc stabilizes the structure of transcription factors such as zinc-finger proteins and is essential for the function of receptors such as the VDR, which regulates the transcription of hundreds of genes (Haase & Rink, 2014). Selenium, another trace element,

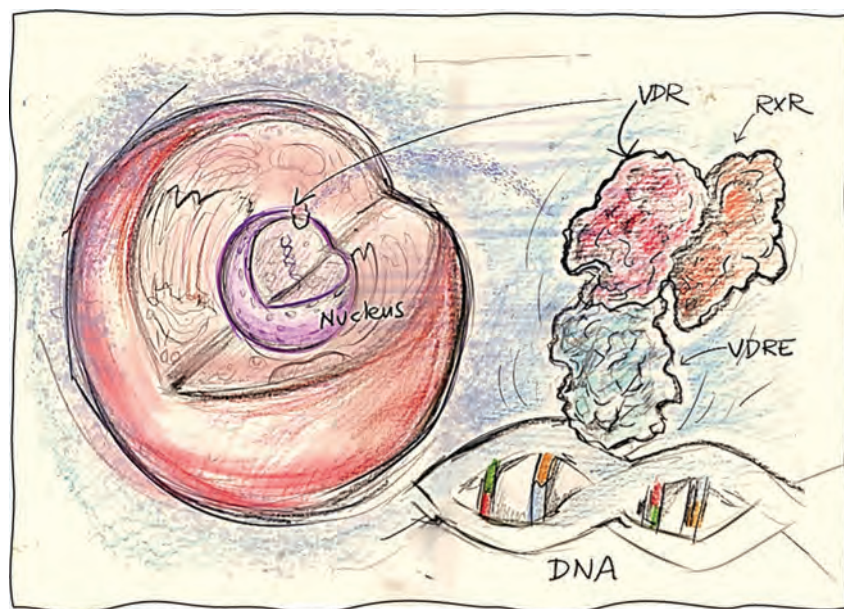


Figure 1. In this image we see the VDR functioning with VDRE (vitamin D response element) is a specialized sequence of DNA found at the promotor region. VDR and VDRE complex with RXN (retinoid X receptor). This complex can lead to the activation or repression of gene transcription.

is a key component of antioxidant enzymes such as glutathione peroxidase, protecting cells from oxidative damage and influencing immune function (Rayman, 2012).

The emerging field of nutrigenomics explores how genetic variation influences individual responses to micronutrient intake. Polymorphisms in genes coding for nutrient transporters, metabolizing enzymes, or receptors (such as VDR or MTHFR) can alter how individuals absorb, utilize, or respond to dietary minerals and vitamins (Ferguson, 2009). MTHFR is another critical gene affecting DNA synthesis. MTHFR stands for methylenetetrahydrofolate reductase. This is a gene that encodes an enzyme that is involved in the metabolism of folate, a B vitamin. And so, placing these elements in a culinary context, repositions the periodic table not only as a chemical tool but also as a map of biological potential and a diagram encoded in DNA, shaped by environment, and nourished through food.

By linking the elements of the periodic table to metabolic pathways, transcriptional control, and health outcomes, students can also visualize how planetary chemistry becomes human biology. This reconnection also emphasizes the biological consequences of soil degradation, industrial agriculture, and micronutrient loss in modern food systems. These are just a few of the factors increasingly recognized as public health concerns and of interest to students. We tried several activities that integrated the above ideas:

1. Using the periodic table, we had students trace the element (e.g., zinc) to the molecule's function in both plants and animals (which varies) and then to a possible deficiency.
2. In the "Soil-Plant-Human Axis" we had students trace a micronutrient from the soil (e.g., selenium) from soil composition through plant uptake to its role in enzymatic function in the human body. We then had groups of students research any existing genes that participated in this micronutrient's pathway.
3. For the "Nutrigenomics Prenatal Case Studies" topic students are introduced to SNPs (e.g., in the VDR or MTHFR genes) to show how elemental needs vary with genotype. Of particular interest is the MTHFR gene. The MTHFR gene produces an enzyme essential for processing folate into its active form, which is needed for DNA synthesis and methylation which is a key epigenetic process that turns genes on or off. Certain variants of the MTHFR gene, such as C677T, reduce enzyme efficiency, leading to lower methylation capacity. This can interfere with proper neural tube development in embryos. Folic acid (a synthetic form of folate) is crucial during early pregnancy because it supports these methylation reactions, helping to prevent neural tube defects such as spina bifida. Supplementing with folic acid ensures enough active folate is available, even when MTHFR function is reduced (Crider et al., 2011).
4. One overlap between a wet lab and nutrigenomics is the "Cross-disciplinary Nutrient Lab." Here students would grow plants in varied mineral soils and analyze the mineral content of their tissues or observe phenotypic changes. This could be an ongoing lab where terrariums maintain various plant species. Students can use regular plant food on one group (experimental) versus no plant food on another group (control) and then speculate about how those nutrients get assimilated

into food. We do not have a lab in our nutrigenomics course; however, this is not difficult to implement where a lab is available.

○ Nutrigenomics & the Epigenetic Power of Phytonutrients

Nutrigenomics is the study of how nutrients and bioactive food compounds interact with the genome to influence gene expression, metabolic pathways, and overall health outcomes, but it can be much more when different perspectives are employed. A core focus within nutrigenomics is the epigenetic modulation of gene activity through dietary compounds. Students will be introduced to genetic variation in populations as well and will see the acronym SNPs or single nucleotide polymorphisms, which are the most frequent type of genetic variation among people where a single building block (A, T, G, C) is changed. Epigenetics refers to heritable changes in gene function that occur without alterations to the DNA sequence itself, commonly through mechanisms such as DNA methylation, histone modification, and noncoding RNA regulation. Emerging evidence suggests that plant-derived phytonutrients can act as epigenetic modulators, helping to prevent or delay chronic diseases by altering the expression of genes involved in inflammation, oxidative stress, detoxification, and tumor suppression. Some students ask questions such as why vegetables are important if cellulose can't be used as an energy source. When we examine the astonishing number and interactions of plant compounds with the genome, that question becomes easily answered. The students in Temple's nutrigenomic course pursued a number of investigative activities to showcase the genomic influence of phytonutrients in foods that students easily recognized. In recent years, one compound, resveratrol, a polyphenol found in red grapes and berries, was implicated in reversing aging through the SIRT1 gene. It is a well-studied compound with potent epigenetic activity and it has been shown to activate the SIRT1 gene, a NAD⁺-dependent deacetylase involved in aging and metabolic regulation. It has also been shown to influence DNA methylation patterns in cancer-related genes (Baur & Sinclair, 2006). Most students are familiar with garlic but not with allicin, the bioactive sulfur compound in garlic. This substance was shown to exhibit histone deacetylase (HDAC) inhibition as it can also modulate the expression of phase II detoxification enzymes, enhancing cellular defense mechanisms against oxidative stress (Zhang et al., 2024). It is through such everyday substances, such as garlic on a student's slice of pizza, that biology becomes relatable and gains more meaning.

More commonly appreciated molecules such as carotenoids (seen in the chromatogram made in photosynthesis lab) as well as flavonoids, such as quercetin and epigallocatechin gallate (EGCG), have been widely studied for their ability to influence epigenetic mechanisms. They can inhibit DNA methyltransferases (DNMTs) and HDACs, apparently restoring the expression of silenced tumor suppressor genes (Fang et al., 2007). And this is another great teaching point. Students can keep little gardens or convert their school campuses to organic vegetable gardens to observe how food is grown and gain tangible experience with it. Simply showing brightly colored foods or even bringing them into class, like oranges or red peppers can start a discussion. In the nutrigenomics class at Temple, students would see a red pepper and we asked, "Can this change your epigenome?" Teachers can design their own activities surrounding food and connect those foods with specific

phytonutrients and then to an epigenetic activity. Students are surprised to know that such common place vegetables contain such potent biochemistry. Ellagic acid, found in berries and pomegranates, is yet another compelling epigenetic agent. It has been reported to influence methylation profiles in estrogen receptor and Wnt signaling pathways, which are crucial in hormone-sensitive cancers (Zhou et al., 2008). Glucosinolates, abundant in cruciferous vegetables such as broccoli are hydrolyzed to isothiocyanates such as sulforaphane, which can inhibit HDACs and modulate gene expression often supporting apoptosis and detoxification of cancer cells (Myzak et al., 2007).

Collectively, these phytonutrients demonstrate their convincing potential to modulate gene activity via epigenetic pathways and demonstrate to students the direct impact of dietary choices on the genome, disease, and phenotype. One such highly visible example is the pigment astaxanthin found in red algae. This compound when consumed up the food chain can be seen in the pinkish color of wild shrimp and wild salmon. It is also why pink flamingos are pink and when they don't consume their normal diet, their feathers are gray. Astaxanthin is a naturally occurring red pigment belonging to the carotenoid family. Astaxanthin is red-orange, and it has been shown to exert powerful antioxidants and anti-inflammatory effects, some of which are mediated through epigenetic mechanisms. Studies indicate that astaxanthin can modulate the expression of genes involved in oxidative stress and inflammation exerting an effect on DNA methylation patterns and altering histones. This carotenoid may also affect microRNA expression, thereby regulating cellular pathways linked to aging, cancer, and metabolic diseases (Fassett & Coombes, 2011).

This visual example really makes the progression of nutrient effects highly visible, and it requires only showing a few images or even the carapace of shrimp or lobsters alongside red algae. Phytonutrients bridge botany, physiology, and genomics and their inclusion in the diet represents a powerful, non-invasive strategy for disease prevention and personalized health therapeutics. Many phytonutrients exert direct influence on the genome as well as the mitochondria and the Krebs cycle. Students can revisit those challenging topics and pathways through exploring the role of a single mineral or phytonutrient. Future nutrigenomic research will further illuminate how diet can “reprogram” our genome toward health, especially when tailored to an individual's genetic makeup, and this is a topic that students seemed most fascinated by. See Table 1 for a summary of some of the phytonutrients discussed here.

Another topic, one that has become a social ritual for college students, is drinking coffee. This topic captivated students' attention and had them thinking about their daily habit of consuming lattes. Once a beverage of adults only, coffee, in its many modern manifestations reveals yet another impact of a plant on the human genome. The CYP1A2 gene on chromosome 15 encodes an enzyme in the cytochrome P450 family, primarily responsible for about 95% of caffeine metabolism in the liver. A common SNP in this gene known as the rs76255 can result in two main variants. This means coffee confers different effects to different genomes and people. Humans with the CYP1A2 *1F (AA genotype) are the “fast metabolizers” of the caffeine, while CYP1A2 *1A (AC or CC genotypes) are the “slow metabolizers.” People with the AA genotype (homozygous for the A allele) tend to metabolize caffeine more quickly, meaning the stimulating effects of caffeine wear off faster, and adverse cardiovascular effects are generally lower. Conversely, those with AC or CC genotypes metabolize

caffeine more slowly, so caffeine remains in their system longer, potentially increasing the risk for hypertension, myocardial infarction, or impaired glucose metabolism, especially if caffeine intake is high. Sensitivity to caffeine—and therefore to coffee-related beverages—is directly experienced through effects such as temporarily raised heart rate, offering another concrete example of SNPs and genetic variation (Palatini et al., 2009). A key finding of caffeine research is the study by Cornelis et al. (2006) that found that slow metabolizers (C allele carriers) who consumed more than 2 cups of coffee per day had a significantly increased risk of nonfatal heart attacks, while fast metabolizers (AA) had no such increased risk. As with all apparent phenotypes, there is never just one gene involved. Students should be reminded of this frequently so that they recognize that to produce a phenotype, there is often a mélange of genes acting in networks. There are new emerging genes that are potentially part of the “coffee response.” One of these is the ADORA2A (rs5751876) gene which codes for the adenosine A2A receptor, this is believed to be targeted by caffeine to create the feeling of being “awake.” Variants (e.g., TT genotype) have been shown to be associated with some of the effects of coffee that are not so pleasant, such as agitation and anxiety after consuming caffeinated beverages. While not coffee, some people have died from consuming “charged” beverages, perhaps not realizing that they are sensitive and may be adversely affected by excessive caffeine. Another outcome of this research is that in some people coffee is cardio protective and may increase the health of the heart. One drink or food doesn't fit all, the overarching message of nutrigenomics.

○ Why Dirt Matters

In our course we did not start off with nutrition but rather with soil. We wanted students to follow the flow of nutrients from rocks and organic matter to water and soil and that's why having a garden on campus is quite essential for connecting concepts in biology together. Regardless of the food, the soil it is grown in and how it is produced play significant roles in its nutrient density. Starting with the soil allows the topic of nutrigenomics to take on an ecological as well as microbiological dimension. It helps students recall nutrient cycling such as the nitrogen cycle; it allows them to think cyclically about the planet. The “where things come from question,” is essential for students to see relationships. Through soil, students can recognize that nutrient deficiency in the soil can translate into nutrient deficiency in the food and that a soil's fertility and the diversity of the microbiome is essential. In one activity we have students trace a mineral, such as selenium from the soil to the food to a number of genetic networks in the body. It is up to the student to report on one genomic mechanism. In our course students also had to consider alterations to food, how modern chemicals such as plastic and “forever chemicals,” factor into nutrition, epigenetics, and the microbiome. The connection between the soil, nutrition, and disease, particularly deficiencies, shows students that there is a continuum of life processes and an interdependency of them. The disease Pica presents as an interesting point of discussion.

Pica is a psychological disorder characterized by the persistent craving and consumption of non-nutritive substances such as dirt, clay, chalk, ice, or paper (Abu et al., 2025). Pica is often associated with nutritional deficiencies—particularly iron and zinc deficits—and can also co-occur with developmental

conditions such as autism spectrum disorder and intellectual disabilities. Pica does not appear to be associated with a single gene; rather, its development likely involves a combination of genetic, biological, environmental, and cultural influences. Although genetics may contribute to susceptibility, the disorder also highlights the relationship between craving behaviors and physiological needs, particularly attempts to compensate for nutrient deficiencies. Some studies have identified familial patterns and genetic overlaps with other compulsive or neurodevelopmental disorders, suggesting a possible polygenic influence. However, environmental, nutritional, and cultural factors remain major contributors to the expression of this behavior. Pica presents an interesting discussion question for students to consider (Abu et al., 2025).

○ Appendix, Evolutionary Remnant, or Reprisal?

In biology, the appendix is often labeled as vestigial, and the appendix falls under the umbrella of nutrigenomics. It also opens up a fascinating question for students and researchers alike. Why do our closest relatives have a fully functional appendix, but we do not? Is the appendix the result of genes down regulated in humans because of diet, fire, a life indoors? When did this transition happen? Did Neanderthals have a functioning appendix? What about early hominids? Do people today, somewhere in the world, have a functioning or partially functioning appendix? This narrative is evolving like all biological systems and raises open, speculative questions for students. For nutrigenomics, the appendix provides a compelling teaching moment. Students can explore its potential role in cellulose digestion, its similarity to functioning primate appendices, and its hypothesized role as a microbiome reservoir, perhaps an organ where microbes could remain dormant. The human appendix and the chimpanzee appendix differ quite a bit in both function and structure. Asking students to reflect on these evolutionary changes in diet and digestion can make for an interesting discussion. In chimpanzees and other herbivorous primates, the appendix is part of a larger cecum, which plays a critical role in fermenting and digesting cellulose-rich plant material through symbiotic gut microbes. These microbes produce enzymes such as cellulases that break down cellulose, a major component of plant cell walls. Humans have an appendix that is much smaller and does not appear to function. This might reflect a dietary shift along the path of our evolution, but what about vegans and vegetarians of today? This brings our nutrigenomics discussion back to diet and its effects. While humans possess gut microbes, our microbiota lacks the diversity and abundance of cellulose-degrading bacteria. Genomic studies suggest that the loss of certain cellulase-producing microbial species and perhaps the loss of regulatory elements in the exome may have occurred during human evolution. While humans do not possess endogenous (human-encoded) cellulase genes, some epigenetic changes may have influenced the expression of host genes that affect gut environment, immune response, or microbial colonization, indirectly reducing our capacity to digest cellulose. However, more research is needed to fully understand the epigenetic regulation involved. The shift in diet and anatomy is also supported by comparative genomics, which shows differences in gut-associated immune gene regulation between humans and other primates (McKenna et al., 2008).

○ Teeth, Jaws, Evolution, & the Modern Diet

The jaws and teeth are one of the fastest changing traits in modern humans. They have undergone rapid evolutionary modifications over the past 10,000 years, especially since the advent of agriculture. Compared with our ancestors and with other primates, modern humans have significantly smaller jaws and faces. Interestingly modern humans still retain the same number of teeth (Nowzari & Jorgensen, 2022). This inspires an evolutionary perspective regarding diet. It demonstrates that food doesn't just shape metabolisms but also facial and body structure. We might ask students why modern humans have the same number of teeth with smaller jaws? Why would they retain that trait? Modern, industrialized communities have moved beyond cooking and are even more removed from their ancestors because of processed foods and sugary drinks that have been developed to require almost no chewing at all. Masticatory muscles or mechanical digestion has been radically reduced in the Western diet. Discuss what that means for the future of the human jaw. Which genes might have reduced expression? What would the phenotype progressively become if we primarily consumed cold, sugary coffee beverages? This makes a great storyboarding activity to add to the nutrigenomics discussion. Genomic studies suggest that certain genes involved in craniofacial development, such as *RUNX2*, *PAX9*, and *MSX1*, may be involved in the rapid changes occurring in the modern jaw and chewing muscles. Some of these genes are under relaxed selection pressure due to reduced environmental demands on the jaw. Moreover, regulatory regions in the genome, including enhancers and non-coding RNAs that have been shown to control these developmental genes, may have evolved rapidly in humans. Rapid teeth and jaw evolution also suggests epigenetic factors at work such as methylation changes and histone modifications that may further influence jaw morphology in response to environmental cues (Lacruz et al., 2019; Lieberman, 2011). This complex interplay between genes, development, and culture illustrates how rapid evolutionary change can be driven not just by DNA sequence, but by microbiomes and epigenetics—and, therefore, by the food, cooking, and products we consume.

○ Activities With a Nutrigenomic Lesson Plan

What's for Breakfast?

Students can trace the origins of their breakfast foods too. Where did each item come from? What species or compounds are involved? What genes or variants might exist for the digestion and assimilation of this food? Are they macronutrients, phytonutrients, or minerals? For example, students would list the food they had for breakfast, such as vanilla yogurt. The vanilla bean comes from a plant that comes from an orchid plant *Vanilla planifolia*, which is native to Mexico and parts of Central America. Students may list the bioactive compounds of vanilla, which have medicinal properties. Then they can explore yogurt, what's yogurt? Who can't eat yogurt? What trait is associated with milk products? Ask students questions that relate to the topic you most want to discuss.

Still-Life Phytonutrient Investigation

Students analyze a classical painting of food, identify depicted items, research their phytonutrients, create a print of that painting and label the nutrient contents of the food (see Figure 2).

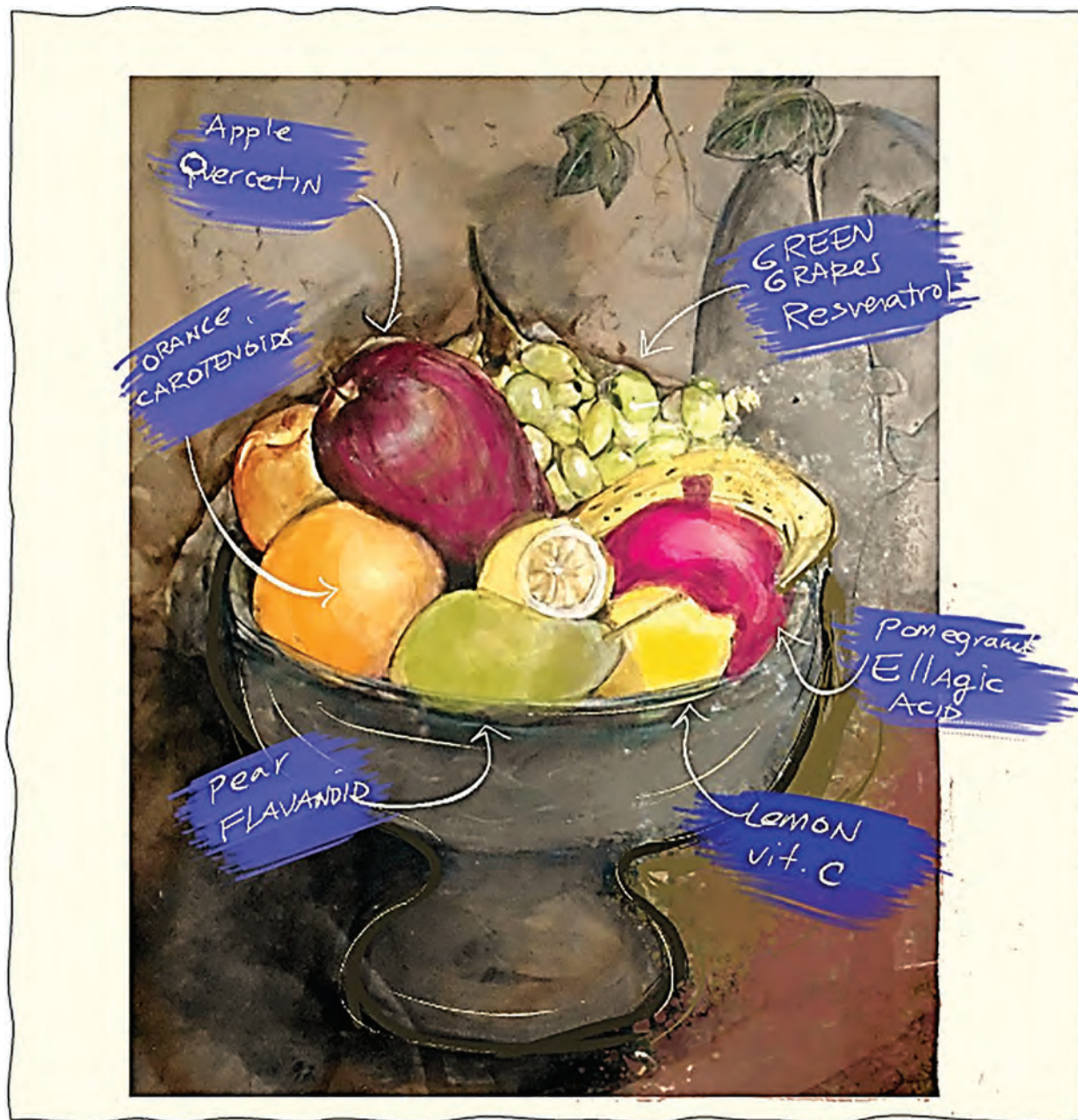


Figure 2. A fun activity for students using a painting of fruit (classical art works great) where students label the food and then name one phytonutrient. This can expand to naming an epigenetic mechanism as well.

Student's Personal Dietary Portrait

For this activity, students made lists of the food they most often consumed in a week. The list was not limited; however, most students listed 20 different foods or less. From this list they constructed a “dietary portrait,” which was called “You are what you eat.” In this visualization of their own food consumption, they also had to list major nutrients and chemicals in the food they ate, whether that food was processed, and where it came from (see Figure 4). There was no special format for creating the portrait and students were encouraged to decide how they wanted to visualize this. For a classical example, we used the Italian painter **Giuseppe Arcimboldo** (1526–1593) whose painting is on our course space to inspire the portraits (see Figure 3). While Arcimboldo was a traditional painter in the Renaissance, he did make entertaining art to amuse wealthy court officials.

Some faces were made of food, books, and fruit. They were curiosities and investigations and for our nutrigenomics class they worked well (Rybova). Have students visit the work of Arcimboldo to inspire their portraits and reflect on their food choices. Please remind students that their dietary choices are not a negative or positive reflection of them personally, but rather an inventory of what they have consumed. This is a reflective experience and one that helps students observe their preferences and patterns.

You may also want to start your lesson plan off with a film about soil or show it sometime in between a discussion on food. This most fundamental topic is almost never discussed in biology and yet it is the matrix of plant composition and ultimately the food we consume. This is possibly the best way to link several biological ideas together in one film. It also provides an easily accessible material



Figure 3. Archimboldo's most famous work in his "Four Seasons" series titled "Vertumnus," a portrait of Holy Roman Emperor Rudolf II as the Roman god of vegetation

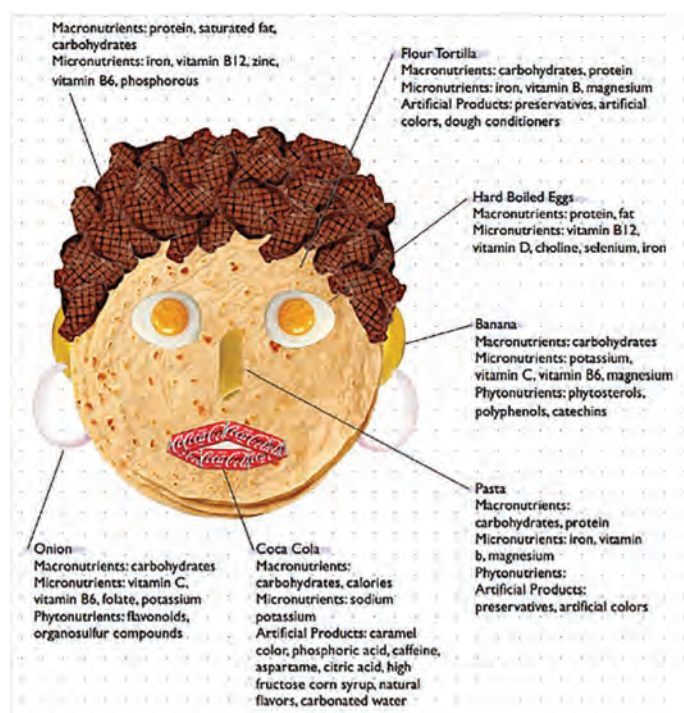


Figure 4. A student's portrait from the nutrigenomics course

(dirt) for students to reflect on as the topic of nutrigenomics unfolds. We explored this topic with the film "DIRT," which is available on YouTube. A 2009 documentary about how soil affects food and health. Here is a link to the movie, which can be watched for free: <https://www.youtube.com/watch?v=pbl7UIOvdJA>.

Lastly, students and teachers are encouraged to build their own small garden to grow plants and vegetables on campus, uniting biology, nutrigenomics, and gardening together for a well-rounded and concrete learning experience. Here are resources for teachers to consider:

- Making terrariums in the classroom: <https://www.youtube.com/watch?v=9B7aULFjrc>
- Making "edible forest" in class https://www.youtube.com/watch?v=1ttXg_6Dvyk&t=145s
- Creating "living walls" for inside or outside buildings for urban schools: <https://www.youtube.com/shorts/wJdBtOoBDUU> and <https://www.youtube.com/watch?v=WuoLZqDN-kk>
- Growing indoor herbs (with all those interesting phytonutrients): <https://www.youtube.com/watch?v=uHLChW4R5vw>
- Creating community and school gardens: <https://www.youtube.com/watch?v=MzywSGZYTws>
- Creating a "food scape" garden and planting: <https://www.youtube.com/watch?v=tcmzSLXbNaY>
- Visiting an old "food forest" garden in Pennsylvania: <https://www.islands.com/1977953/pennsylvania-unique-historic-food-forest-miracle-garden-edon-flourishing-philly/>

○ Conclusion

Food and nutrition can be a unifying concept in biology. The topic is both practical and attractive to students. Nutrigenomics combines the metabolic, genomic, and environmental worlds together to draw students into discussions in fundamental biological topics. It also provides a reflective perspective on how food shapes the genome. Through the emerging field of nutrigenomics, students can explore diet, health, disease, and revisit such topics as the Tricarboxylic acid cycle, the periodic table of elements, epigenetics, evolution, ecology, and macro and micronutrients. Nutrigenomics also brings the complex and fascinating chemistry of plant compounds to light, bridging botany, ethnobotany, and photosynthesis to molecular, genomic, and cellular processes. Lastly, nutrigenomics allows students to reflect on their own choices, providing opportunities to explore the growing intersection of food, mental health, the modern Western diet, ecology, and the current industrial practices of growing food. Nutrigenomics can go beyond the classroom into the lab, and into the campus of high schools and colleges, where students can gain practical and important knowledge about soil, the soil microbiome, where food comes from, and relate that back to the soil and their unique genome of the individual.

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