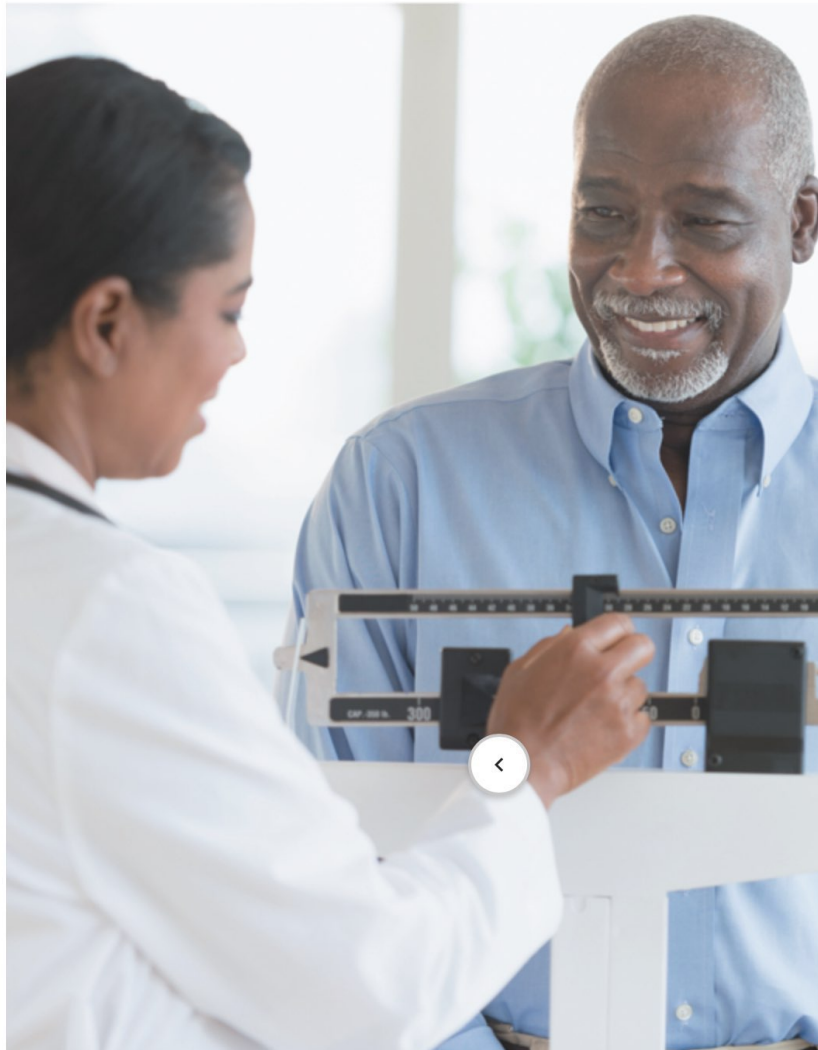


In Depth 1.5

New Frontiers in Nutrition and Health



Learning Outcomes

After studying this In Depth, you should be able to:

- 1.1 Discuss the potential benefits and challenges of nutrigenomics.
- 1.2 Explain how research into the human microbiome is influencing our understanding of nutrition and health.
- 1.3 Identify several health benefits of phytochemicals.



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Imagine a patient visiting his physician for his annual exam. He is 20 pounds overweight and his blood pressure is elevated. The physician takes a blood sample for genetic testing, then sends the patient to a technician to extract a sample of the microbes living in his colon. At the close of the visit, she hands her patient a prescription: *2 servings of fresh fruits, 2 servings of fresh vegetables, a bowl of oatmeal, a cup of soy milk, and 2 cups of yogurt daily.* The patient accepts the prescription gratefully, assuring his physician as he says goodbye, “I’ll stop at the market on my way home!”

Sound unreal? As researchers uncover more evidence of a link between our genes, microbes, phytochemicals, and health, it’s possible that scenarios like this could become familiar. Here, we explore these new frontiers **In Depth**. Who knows? When you finish reading, you might find yourself writing up your own health-promoting grocery list!

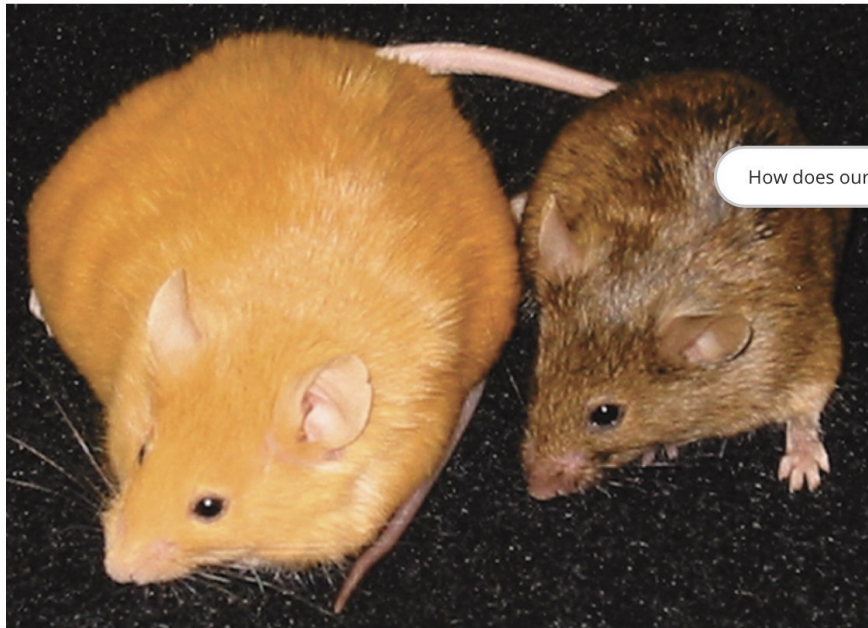
How does our diet affect our genes?

LO 1 Discuss the potential benefits and challenges of nutrigenomics.

Agouti mice are specifically bred for scientific studies. These mice are normally yellow in color, obese, and prone to cancer and diabetes, and they typically have a short life span. When agouti mice breed, these traits are passed on to their offspring. Look at the picture of the agouti mice in **Figure 1**; do you see a difference? The mouse on the right is obviously brown and of normal weight; but what you can't see is that it did not inherit its parents' susceptibility to disease and therefore will live a longer, healthier life. What caused this dramatic difference between parent and offspring? The answer is diet!

Figure 1

Prompted only by a change in her diet before she conceived, an inbred agouti mouse (*left*) gave birth to a young mouse (*right*) that differed not only in appearance but also in its susceptibility to disease.



How does our diet affect our microbiome? >

The Foods We Eat Can Influence Gene Expression

In 2003, researchers at Duke University reported that, when they changed the mother's diet just before conception, they could "turn off" the agouti gene, and any offspring born to that mother

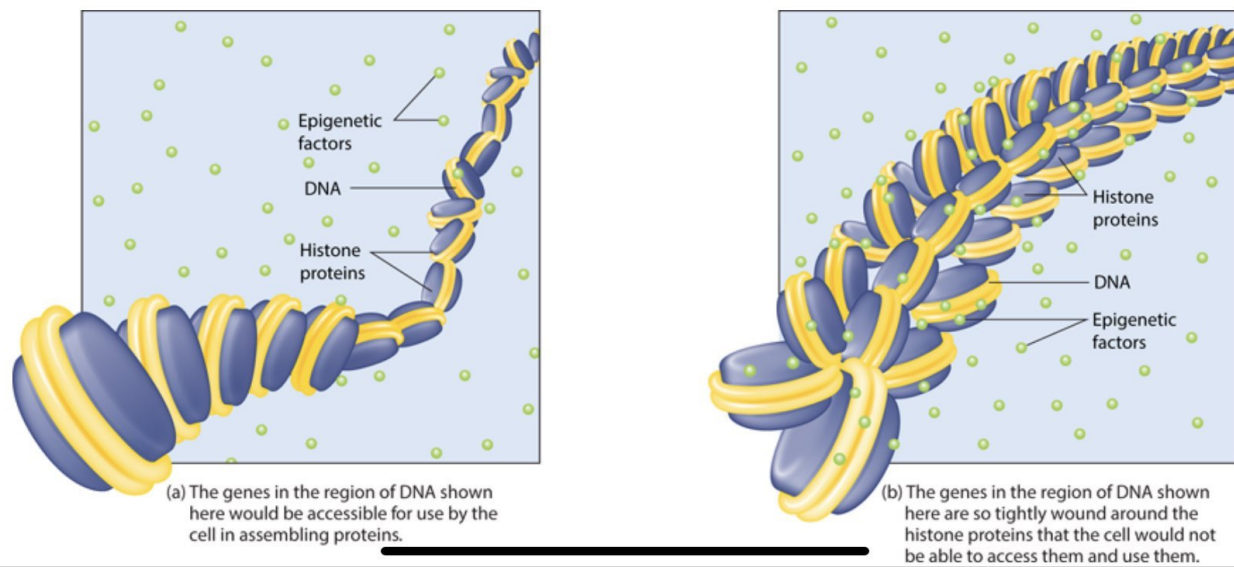
The Foods We Eat Can Influence Gene Expression

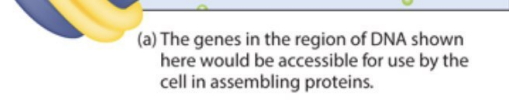
In 2003, researchers at Duke University reported that, when they changed the mother's diet just before conception, they could "turn off" the agouti gene, and any offspring born to that mother would appear normal.¹ As you might know, a *gene* is a segment of DNA, the substance responsible for inheritance, or the passing on of traits from parents to offspring. An organism's *genome* is its complete set of DNA, which is found in the nucleus of its cells. Genes are regions of DNA that encode instructions for assembling specific proteins. In other words, genes are *expressed* in proteins; for instance, one way that the agouti gene is expressed is in the pigment proteins that produce yellow fur.

The Duke University researchers interfered with normal gene expression in their agouti mice by manipulating the mice's diet. Specifically, they fed the mother mice a diet that was high in methyl donors, compounds that can donate a methyl group (CH₃) to another molecule. Such compounds are called *epigenetic factors*. The prefix *epi-* means above or near, so epigenetic factors work close to genes without changing the DNA itself. They do this by binding to regions on the proteins (called histones) around which DNA spools (Figure 2). This affects how tightly or loosely the DNA and its histones are wound: The genes in loosely wound DNA are accessible to the cell for use in protein synthesis, whereas the genes in tightly bound regions cannot be read.

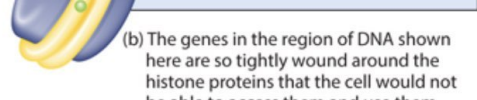
Figure 2

The binding of epigenetic factors to histone proteins causes physical and functional changes. (a) When DNA is loosely wrapped around its histones, its genes are more accessible for use in protein synthesis. (b) When DNA is tightly wound around its histones, its genes are inaccessible; thus, these genes are not expressed as proteins.





(a) The genes in the region of DNA shown here would be accessible for use by the cell in assembling proteins.



(b) The genes in the region of DNA shown here are so tightly wound around the histone proteins that the cell would not be able to access them and use them.

In the agouti mice, the methyl donors in the mothers' diet made the agouti gene unreadable. In essence, they turned it off. When the mothers conceived, their offspring still carried the agouti gene on their DNA, but their cells no longer used the gene to make proteins. Thus, the traits, such as obesity, that were linked to the agouti gene did not appear in the offspring. These Duke University studies were some of the first to directly link a dietary intervention to a genetic modification and contributed significantly to the emerging science of *nutrigenomics* (*nutritional genomics*).

Nutrigenomics Studies Food-Gene Interactions

Nutrigenomics^① is a scientific discipline studying the interactions among genes, the environment, and nutrition. Until the late 20th century, scientists believed that the genes a person is born with determined his or her traits rigidly, but we now know that genetic expression is influenced by diet, body weight, substance use, and many other factors. This helps explain why the appearance and health of identical twins—who have the same DNA—commonly change as the twins age.

In addition, as we saw with the agouti mice, epigenetic factors can affect gene expression not only in our own body but also in our offspring. In the Duke University study, switching off the agouti gene caused beneficial changes in the offspring mice. But sometimes flipping the switch can be harmful, as when paternal obesity causes epigenetic changes in sperm cells that increase the risk for certain types of cancer in the offspring.²

Several commonly observed phenomena are now thought to be due at least in part to epigenetics. For example, it has long been noted that some people will lose weight on a specific diet and exercise program, whereas others following the same program will not. Some people who smoke develop cardiovascular disease or cancer, whereas others do not. And in some people, moderate alcohol consumption appears to reduce the risk of cardiovascular disease, whereas in other people, it does not. These varying results are now thought to depend to a certain extent on how these factors affect genetic expression.^{3,4}

Nutrigenomics Could Lead to Personalized Nutrition

Recently, a working group of the American Society for Nutrition published a list of urgent research needs, one of which was for research into nutrigenomics.⁵ One goal of this research would be to increase our understanding of how specific foods or nutrients interact with specific genes. This could help reduce the prevalence of diet-related diseases and possibly even treat existing conditions through diet alone.⁶

Nutrigenomics research could also lead to personalized nutrition. Today, dietary advice is based primarily on observations of large populations. But advice that is generally appropriate for a population might not be appropriate for every individual within that population. Advances in nutrigenomics could eliminate this concern by making it possible to provide each individual with a personalized diet. In this future world, analysis of your DNA would guide an RD in creating a diet tailored to your genetic makeup. By identifying both foods to eat and foods to avoid, this personalized diet would help you turn on beneficial genes and turn off genes that could be harmful.

If the promises of nutrigenomics strike you as pie in the sky, you're not alone. Many researchers caution, for example, that dietary "prescriptions" to prevent or treat chronic diseases would be extremely challenging, because multiple genes may be involved, as well as countless nutritional and environmental factors. In addition, genetics researchers currently believe that there are about 21,000 to 25,000 genes in human DNA, but that these genes represent only a fraction of the DNA in body cells.⁷ The remaining regions of DNA are considered noncoding but are thought to have other functions, many of which may influence nutrition and health. Moreover, the pathways for genetic expression are extremely complex, and turning on a gene may have a beneficial effect on one body function but a harmful effect on another. To complicate the matter further, other factors such as age, gender, and lifestyle will also affect how different foods interact with these different genetic pathways. In short, the number of variables that would have to be considered in order to develop a "personalized diet" is staggering.

We might first encounter nutrigenomics in diagnostic testing. In this process, a blood or tissue sample of DNA would be genetically analyzed to predict how foods and dietary supplements might interact with that individual's genes and how a change in diet might affect those interactions. Genetic counseling would be required to help consumers understand the meaning and recommendations suggested by their genetic profile.

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We might also begin to see more specialized foods promoted for specific conditions. For example, consumers currently have an array of foods to choose from if they want to lower their cholesterol or enhance their bone health. More such foods will likely be developed, and food packages of the future might even be coded for certain genetic profiles.

We may be decades away from a "personalized diet," but one thing is clear right now. Research into nutrigenomics is changing not only the way we look at food but also the science of nutrition itself.

How does our diet affect our microbiome?

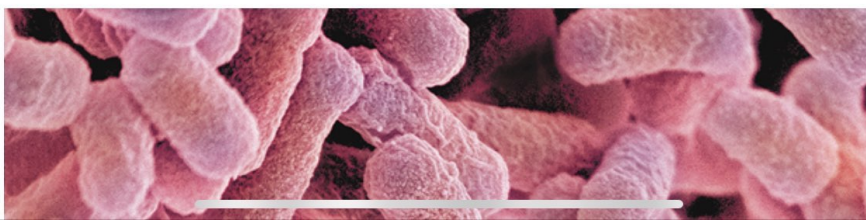
LO 2 Explain how research into the human microbiome is influencing our understanding of nutrition and health.

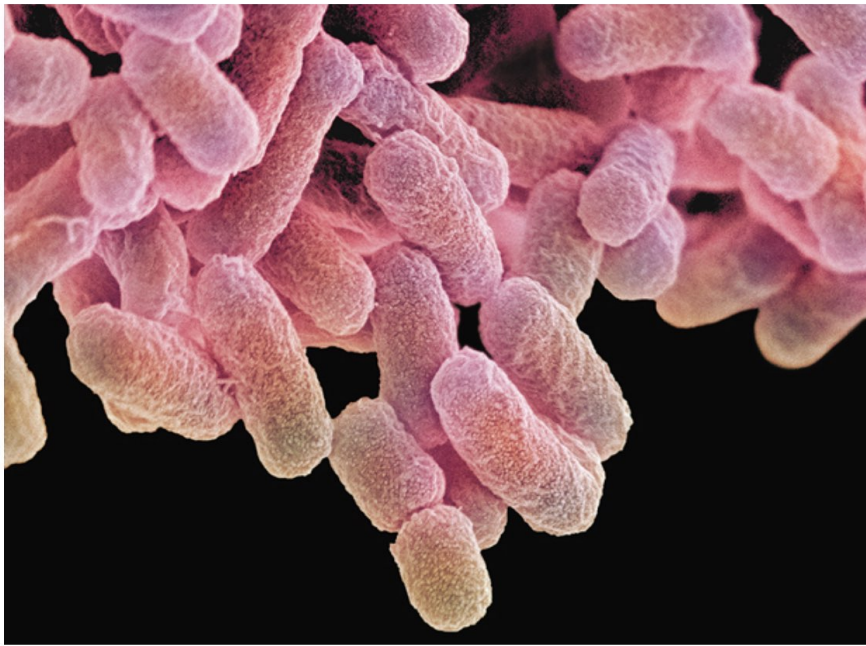
We like to think of ourselves as discrete, individual organisms, but it's not true. The human body is a lush microbial ecosystem containing about 40 trillion *microorganisms* (microscopic organisms such as bacteria)—that's more than the number of our human body cells!⁸ These microorganisms and their genes, both of which are referred to as the human microbiome⁹, interact with our human cells and genes in a dizzying number of ways that affect our health.

A Healthy Microbiome Promotes a Healthy Body

Research suggests that a healthy microbiome fulfills many functions in the body that promote human health. For example, our microbiome enables us to digest foods and absorb nutrients that otherwise would be unavailable to us. This may be in part because genes in our microbiome may complement the functions of human genes required for digestion—genes that may be missing or incompletely encoded in the human genome.⁹ Moreover, the microbiome is thought to:^{9,10,11,12,13,14}

- Supply compounds used to replace worn-out tissues of the intestine
- Produce certain essential vitamins
- Protect against intestinal infections
- Provide some protection against the development of obesity and type 2 diabetes
- Degrade potential carcinogens (cancer-causing agents) in foods
- Produce anti-inflammatory chemicals, thereby providing some protection against eczema, asthma, and allergies, as well as certain inflammatory disorders of the esophagus, stomach, and small and large intestine.





The human body is a microbial ecosystem containing about 40 trillion microorganisms, such as this gut bacteria.

Taking a broad-spectrum antibiotic prescribed to fight an infection not only kills the invading bacteria but also depletes the healthful bacteria in our microbiome. In fact, overuse of antibiotics is increasingly linked to intestinal disorders, asthma, and many other health problems. Given this research, you're probably wondering how you can build and maintain a robust microbiome. That's where probiotics and prebiotics come in.

Probiotics and Prebiotics Nourish the Microbiome

Probiotics and prebiotics are two groups of **functional foods**; that is, foods with biologically active ingredients that provide health benefits beyond basic nutrition. They qualify as functional foods because, in addition to the nutrients they provide, they help grow your microbiome.

Probiotics are foods or supplements that contain live microorganisms that benefit human health. Interest in probiotic foods was sparked in the early 1900s with the work of Elie Metchnikoff, a Nobel Prize-winning scientist. Dr. Metchnikoff linked the long, healthy lives of Bulgarian peasants with their consumption of fermented milk products, such as yogurt and a creamy beverage called kefir. Subsequent research identified the bacteria in fermented milk products—typically *Lactobacillus* and *Bifidobacterium*—as the factor that promoted health.



Beneficial bacteria, such as those found in yogurt or kefir, are a part of probiotic foods.

When a person consumes probiotics, the bacteria survive in the large intestine for a few days. There, they're thought to exert many beneficial actions. For example, studies support a reduction in "transit time" of wastes through the large intestine in people who regularly consume yogurt, reducing their risk for constipation.¹⁵ The probiotics in yogurt may also reduce the risk for diabetes.¹⁶ And some laboratory studies have shown that probiotics can help reduce infection and inflammation, an effect that may reduce college students' susceptibility to colds! In a recent randomized, double-blind, placebo-controlled study, nearly 600 college students were given either a probiotic supplement or a placebo. Those who consumed the probiotic supplement experienced significantly fewer cold/flu symptoms and significantly more healthy days than students who received the placebo.¹⁷

Again, probiotic bacteria live only for a short time. This means that probiotic foods and supplements should be consumed on a daily basis to be most effective. They must also be properly stored and consumed within a relatively brief period of time to confer maximal benefit. In general, refrigerated foods containing probiotics have a shelf life of 3 to 6 weeks, whereas refrigerated supplements keep about 12 months. However, because the probiotic content of foods is much more stable than that of supplements, yogurt and other probiotic foods may be a better health bet.

Now that you know a little more about probiotics, you may be wondering how they're related to prebiotics. We've said that probiotic foods and supplements contain living and helpful bacteria. In contrast, **prebiotics** are nondigestible food ingredients (typically carbohydrates) that support the growth and/or activity of probiotic bacteria. In other words, prebiotics don't feed you, but they do feed your microbiome. An example is inulin, a carbohydrate found in a few fruits, onions, certain green vegetables, and some grains. Many **processed foods**—that is, foods manipulated in some way before being sold—also ~~claim to be probiotic. For example, inulin~~ is added to certain brands of



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How do phytochemicals enhance our health?

LO 3 Identify several health benefits of phytochemicals.

As you'll discover throughout this text, plant foods are loaded with nutrients, including carbohydrates, vitamins, minerals, and water. Many also contain healthful fats and protein. They're also a great source of dietary fiber, a nondigestible carbohydrate that promotes body functioning. But another advantage of plants is their phytochemicals. *Phyto* means "plant," so **phytochemicals** are literally plant chemicals. While plants are growing, these naturally occurring compounds are believed to protect them from pests, the UV radiation they capture, and the oxygen they produce. What makes them important to nutrition scientists is that phytochemicals are believed to have health-promoting properties for humans who consume them.

Thousands of different phytochemicals have been identified.¹⁸ They're present in **whole foods**—foods such as fruits and vegetables sold in their natural state—as well as in many processed foods such as soy products, chocolate, coffee, tea, wine, and beer. Any one food can contain hundreds.

Figure 3 identifies a few of the most common phytochemical groups.

Web Links >

Figure 3

Health claims and food sources of phytochemicals.

Phytochemical	Health Claims	Food Source
Carotenoids: alpha-carotene, beta-carotene, lutein, lycopene, zeaxanthin, etc.	Diets with foods rich in these phytochemicals may reduce the risk for cardiovascular disease, certain cancers (e.g., prostate), and age-related eye diseases (cataracts, macular degeneration).	Red, orange, and deep-green vegetables and fruits, such as carrots, cantaloupe, sweet potatoes, apricots, kale, spinach, pumpkin, and tomatoes
Flavonoids: ¹ flavones, flavonols (e.g., quercetin), catechins (e.g., epigallocatechin gallate or EGCG), anthocyanidins, isoflavonoids, etc.	Diets with foods rich in these phytochemicals are associated with lower risk for cardiovascular disease and cancer, possibly because of reduced inflammation, blood clotting, and blood pressure and increased detoxification of carcinogens or reduction in replication of cancerous cells.	Berries, black and green tea, chocolate, purple grapes and juice, citrus fruits, olives, soybeans and soy products (soy milk, tofu, soy flour, textured vegetable protein), flaxseed, whole wheat
Phenolic acids: ¹ ellagic acid, ferulic acid, caffeic acid, etc.	Similar benefits as flavonoids.	Coffee beans, fruits (apples, pears, berries, grapes, oranges, prunes, strawberries)

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ellagic acid,
ferulic acid,
caffeic acid,
curcumin, etc.

Similar benefits as flavonoids.

Coffee beans, fruits
(apples, pears,
berries, grapes,
oranges, prunes,
strawberries),
potatoes, mustard,
oats, soy



Phytoestrogens:²
genistein,
diadzein,
lignans

Foods rich in these
phytochemicals may provide
benefits to bones and reduce
the risk for cardiovascular
disease and cancers of
reproductive tissues (e.g.,
breast, prostate).

Soybeans and soy
products (soy milk,
tofu, soy flour, textured
vegetable protein),
flaxseed, whole grains



Organosulfur
compounds:
allylic sulfur
compounds,
indoles,
isothiocyanates, etc.

Foods rich in these
phytochemicals may protect
against a wide variety of cancers.

Garlic, leeks, onions,
chives, cruciferous
vegetables (broccoli,
cabbage, cauliflower),
horseradish, mustard
greens



¹ Flavonoids, phenolic acids, and stilbenes are three groups of phytochemicals called phenolics. The phytochemical Resveratrol is a stilbene. Flavonoids and phenolic acids are the most abundant phenolics in our diet.

² Phytoestrogens include phytochemicals that have mild or anti-estrogenic action in our body. They are grouped together based on this similarity in biological function, but they also can be classified into other phytochemical groups, such as isoflavonoids.

Nutri-case

HANNAH



HANNAH



“On my way home from school today, I was really hungry, and when I passed a convenience store about halfway home, I just had to go in. I looked around for something healthy, like a banana or an apple, but they didn’t have anything fresh. So I bought some pretzels. I know pretzels aren’t exactly a health food, but at least they’re low fat, right?”

Hannah and her mother live in an urban neighborhood that has 11 different fast-food outlets and four convenience stores but lacks a grocery store. There is no local farmer’s market or community garden. In order to buy fresh produce, they have to travel to a more affluent neighborhood several miles away. Given the importance of phytochemicals to a healthful diet, can you think of at least two strategies Hannah and her mother could use to increase their access to affordable produce?

Like probiotics and prebiotics, phytochemicals are not classified as nutrients—that is, substances necessary for sustaining life. Yet eating an abundance of phytochemical-rich foods has been shown to protect against a number of diseases. Here are just a few examples of the proposed benefits of phytochemicals:^{19,20,21,22,23,24}

Like probiotics and prebiotics, phytochemicals are not classified as nutrients—that is, substances necessary for sustaining life. Yet eating an abundance of phytochemical-rich foods has been shown to protect against a number of diseases. Here are just a few examples of the proposed benefits of phytochemicals:^{19,20,21,22,23,24}

- Reduce inflammation linked to the development of cardiovascular disease, cancer, and Alzheimer's disease, allergies, and arthritis.
- Protect against unhealthful blood cholesterol levels associated with cardiovascular disease.
- Impede the initiation and progression of cancer by helping to detoxify carcinogens, slow tumor growth, inhibit communication among cancer cells, and provoke cancer cells to self-destruct.
- Combat infections by enhancing our immune function and acting as antibacterial and antiviral agents.

Although you might assume that the more phytochemicals you consume the better, that's somewhat simplistic. They appear to be beneficial in the low doses commonly provided by foods, but they may be ineffective or even harmful when consumed as supplements. This may be due to their mode of action: instead of *protecting* our cells, phytochemicals might benefit our health by *stressing* our cells, causing them to rev up their internal defense systems. Cells are very well equipped to deal with minor stresses, but not with excessive stress, which may explain why clinical trials with phytochemical supplements may not show the same benefits as high intakes of plant foods, and can even be harmful. For example, a classic study found that supplementing with 20 to 30 mg/day of a phytochemical called beta-carotene for 4 to 6 years *increased* lung cancer risk by 16% to 28% in smokers.^{25,26} In short, whereas there is ample evidence to support the health benefits of a plant-based diet, phytochemical supplements should be avoided.





Avoid phytochemical supplements in favor of whole foods.

So what's the take-home message from all this new research? Eat sensibly—for your genes, your microbiome, and your health. To increase your prebiotic and phytochemical intake, build a rainbow of colors on your plate; for instance, black beans, onions, peppers, and tomatoes over brown rice, a green salad sprinkled with nuts or seeds—and why not fruit salad for dessert! Oats and wheat are also rich in prebiotics and phytochemicals, as are tofu and soy milk, and many dark green vegetables. Probiotics, too, should be part of your daily diet. Try Greek yogurt drizzled with honey, or pour yourself a glass of kefir, which tastes like a yogurt smoothie. In short, a probiotic-rich plant-based diet may be just the prescription you need for better health.