THE SCIENCE OF FIBER FUELED

Dear Friends,

I'm excited that you're here! You have to understand, I am a man of science. It is the compass that guides my daily practice as a medical doctor. Don't get me wrong, we don't know everything. But I think there are many areas where we know enough to understand a path to better health. My book, *Fiber Fueled*, is that path…

In writing the book, it was an absolute requirement on my part that the science lead the charge in our quest to deliver optimal gut health. So while I hope you find it an enjoyable read, just know that swirling below the surface are more than 600 references. I reviewed well north of 1000 studies to prepare this book, and at one point had closer to 750 references, before I narrowed it down.

But despite those references, I completely understand how confusing these times are. You can have competing messages being propagated under the claim of "science." You can have doctors saying the opposite thing, and both overwhelming you with information. And then there's the internet, which has become the ultimate source of misinformation in the 21st century.

I want you to be a savvy customer. To have the fundamental tools to understand the basics of clinical research. To know what the hierarchy of research is, and to sniff out the pseudoscience or the quack doctor when they're present. My hope is that you'll end up discovering what you need to hear, even if it's not necessarily what you want to hear. I want you to be able to find the truth through all the noise out there.

And with that in mind, I prepared this guide to **The Science of Fiber Fueled**. I hope you enjoy it, and I hope it helps you in your quest to better health.

Onward together!

THE SCIENCE OF
FIBER FUELED

RESEARCH 101: A BEGINNERS GUIDE TO NAVIGATING INCONSISTENT HEALTH INFORMATION

WHY DO WE NEED SCIENCE?

Because without it, we know NOTHING.

There are laws of nature that exist and our entire world is built around them. They are absolute and reproducible. When we properly understand them, we can manipulate them to our advantage.

They are working right now, literally as you read the words on this page. They are everywhere and all encompassing. Whether we choose to accept them and whether we understand them or not these laws will continue to exist and continue to be the force that drives how our world works. And how our health works.

Science is the process we use to understand these laws of nature. It is our window into fields like mathematics, physics, chemistry, biology and ecology – just to name a few.

Proper science builds understanding and that means we get closer to the truth. It's incredibly powerful and absolutely necessary when your health lies in the balance.

DR. WILL BULSIEWICZ
THE PLANT FED GUT

ON A MOST BASIC LEVEL, HOW DO WE LEARN ABOUT SCIENCE?

Through observation and pattern recognition.

We just discussed that the laws of nature are reproducible. What this means is that because they are reproducible, they will consistently show up to create a pattern. Science is the process we use to identify and study the patterns that define the laws of nature.

Our search for these patterns can be called research. You don't have to be a total nerd like me to do research! Every single one of us is doing research every minute of every day, we just may not realize it.

When you shoot a basketball and the ball falls short of the rim, and you suspect it's due to not using your legs enough, you are conducting research. Next time, you'll use your legs more. When you notice that your temper is short because you didn't sleep well the night before, you are conducting research. Next time, you will try to go to bed earlier. And when you have spaghetti with a heavy dose of tomato sauce, then get heartburn – once again, research.

What most of us think of as research is the formal process of describing these patterns, but it's the same thing we're doing throughout the day. When a person uses their experience, they are invoking the patterns that they've noted and accumulated through the years.

Here's my point: It all comes back to research. Every single choice that we make is the result of our understanding of the laws of nature. Every single one. In order to make the best choices, we should take advantage of the highest quality research evidence available. And there is an agreed upon hierarchy of evidence.

WHAT ARE THE DIFFERENT TYPES OF STUDIES?

When we think about making our health-related choices, the question becomes “What is the evidence?” There’s a hierarchy that exists that allows us to gravitate towards stronger science.

The lowest level is the simple observation. We call this an anecdote, or **case report**. All science starts with these simple observations. The problem with anecdotes is that we’re looking for patterns, and a single observation is only one data point. That’s not a lot of strength for pattern recognition.

But if we start to stack observations on top of each other, now we’re building power in terms of our pattern recognition. Two or more anecdotes would be considered a **case series**. If we collect information about a large group of people, it’s called a **cohort**. The cohort can be collected retrospectively or prospectively. We prefer prospective because this is less prone to bias because the data can be collected in real time whether than trying to be accessed and collected in hindsight. These cohort studies could include thousands and thousands of patients, allowing us to use powerful statistical methods to find patterns and actually have confidence that they are more than just chance.

But if we want to truly know what something does, the best thing to do is a **randomized, controlled trial**. *Randomized* means that people are randomly assigned to one of two different groups. *Controlled* means that one of the groups is going to receive a standard treatment, such as a placebo. It is even better if the investigators and study participants are “blinded”, meaning they don’t know who got what intervention until the study is done. This entire study format is designed to help us avoid bias because, as you’ll see, bias is our biggest threat to quality research.

But there's a problem. How do you study rare events or things that can take years or even decades to occur?

It's impossible to do a randomized, controlled trial for diet and cancer or diet and heart disease. But those are our top two killers. So how can we study them?

The way to do this is to combine different modalities. We start with the large population studies like cohorts, and analyze the data to identify patterns associated with the development of heart disease or cancer. Then, we look at mechanistic studies. These may include **test tube studies**, **animal model studies**, or human studies using a **biomarker** or intermediary endpoint. *When multiple different layers of research all point in the same direction then you have tremendous power. And that's what ultimately leads to scientific consensus.*

All of this is to say that every type of study has its own strengths and limitations. Let me show you:

STUDY TYPE	DESCRIPTION	STRENGTHS	WEAKNESSES
BASIC RESEARCH (Animal models, genetic engineering, cell studies, biochemistry, genetic studies)	Laboratory research aimed at improving our understanding or prediction of natural phenomena.	Allows us to study mechanisms of disease in a controlled environment on a very basic level	These are not studies of real humans under real living conditions and therefore must always be taken with a grain of salt because they often do not translate
CASE REPORTS/CASE SERIES (anecdotes)	Description of a singular or multiple human experience	Can be used to form hypotheses or describe an experience for rare events (such as complications after therapy or treatment of rare conditions)	The weakest form of research, it has virtually no statistical power and therefore is highly subject to chance findings

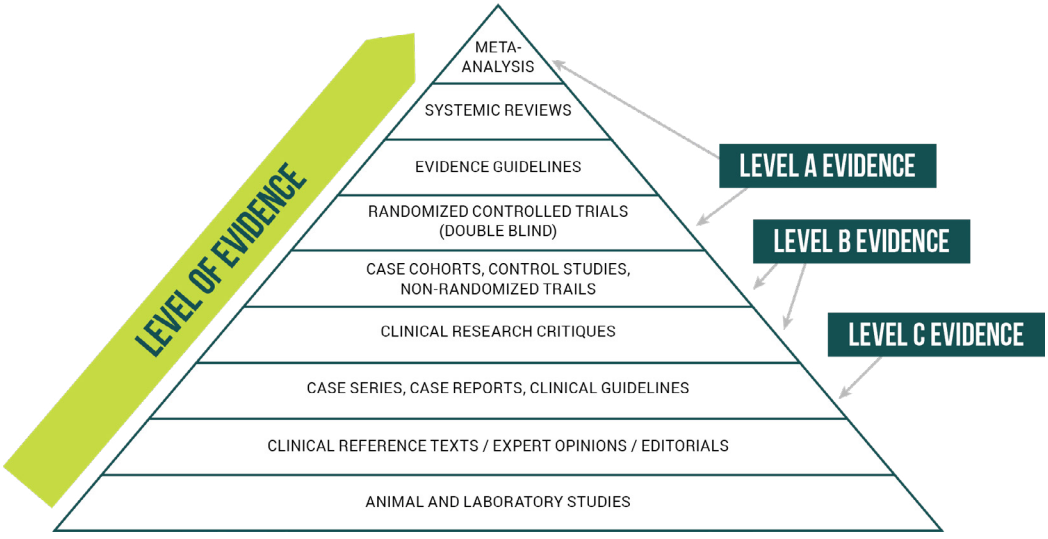
continued previous page

STUDY TYPE	DESCRIPTION	STRENGTHS	WEAKNESSES
EPIDEMIOLOGY STUDIES (Case control, Cross-sectional, Ecological)	These are retrospective methods to identify patterns and factors associated with health and illness states contained in a certain population.	Low cost, can quickly obtain data and information, highly useful for rare or slow forming or new diseases (like the Coronavirus), can identify associations that are followed up in further study	They provide association without being able to prove causation and there is a risk of selection bias and faulty recall
COHORT STUDIES (Prospective or historical)	A large population that is organized and monitored specifically to detect connections between exposure and development of disease	Strong statistical power and actual data monitoring the human experience over time	More expensive, can take years to develop, do not prove causation, may be unable to adequately capture rare or slowly forming events
INTERVENTIONAL CLINICAL STUDIES (Clinical trials involving drugs, devices, supplements or nutrition)	Groups are randomized with one receiving a specific intervention while another is the comparison group (placebo)	When properly done, these are the strongest studies available because they allow us to control and isolate to see the effect of an intervention	Extremely expensive, can take years to develop, may be unable to adequately capture rare or slowly forming events
SECONDARY RESEARCH (Systematic review and meta-analysis)	A systematic review is a methodical and comprehensive review of the research on a topic while a meta-analysis is when the data is compiled into one	When properly conducted they bring forward the best available evidence for a focused clinical question and attempts to reduce bias and pooling samples to increase statistical power and confidence	The details of the individual studies being compiled should be reviewed and understood and there is a risk that these studies are substantially different and not well suited for pooling data

As mentioned before, there is a hierarchy to our research. We're supposed to give priority to the highest quality research. That's not to say that the strongest study automatically wins, but rather we need to weight the evidence

When you're thinking about research, here's the method that I personally follow and used in writing this book:

1. Start with your question. For example, "What is the strongest predictor of a healthy gut microbiome?"
2. Do a thorough review of the published medical literature.
3. Look at the entire body of evidence that you discovered in your review.
    A. Does it all point in the same direction? If all layers of evidence point in the same direction – laboratory, translational, population-based and interventional studies – then you have very strong scientific power. This is how you rapidly form scientific consensus
    B. Are there discrepancies? Does one study say one thing, while another study says the opposite? Then this needs to be rectified. In doing this, you need to look at the details of the study to have a complete understanding of the strengths, weaknesses, and limitations of the studies. Most of the time, we are going to prioritize the findings coming from the studies higher on the hierarchy – systematic reviews and meta-analyses, randomized trials, prospective cohorts. Not always, but most of the time.



In writing *Fiber Fueled*, you will find that I opted for the highest quality evidence wherever available. For example, I was fully aware that there have been numerous books villainizing legumes and whole grains. Most of the arguments that have been made have been selectively sharing with you the animal model and test tube research. But when I looked at the weight of the evidence, I saw quite clearly how healthy these foods are. It was incontrovertible. And so I shared with you the high quality studies – systematic reviews and meta-analyses, randomized trials and large scale population studies – that consistently demonstrate that humans live longer and healthier lives when they consume legumes and whole grains.

Take a step back for a moment and consider what I've just told you. You have been sold fad diets through the years that are cherry picking animal and laboratory studies but ignoring systematic reviews and meta-analyses, randomized trials and population studies. Take a look again at our pyramid of evidence. You are being fed low quality research while the opposing high quality research is being ignored. You now understand that that's a formula for misinformation, not high quality science. So should we be surprised that these fad diets never stick, and that ultimately we discover that they don't really work? Of course not, because the science is WEAK.

CAN YOU PROVE ANYTHING WITH A SINGLE STUDY?

Generally not. Here's the thing… It always starts with a clinical question. For example, "Are whole grains healthy or not?"

In *Fiber Fueled*, I share with you a systematic review by Dr. Dagfinn Aune and a team of epidemiologists at the School of Public Health of the Imperial College London. It was published in the British Medical Journal, one of the top medical journals in the world, in 2016. In it they did a systematic review of 48,380 studies, of which they included information from 45 cohort studies relevant to

whole grain consumption and human health. These were studies from around the world. And in this one systematic review, they yielded a powerful result – increasing your daily whole grain consumption by just two pieces of whole grain bread rewarded the participants with a reduced risk of coronary heart disease, cardiovascular disease, and total cancer as well as lower likelihood of death from all causes, respiratory diseases, infectious diseases, diabetes, and all non-cardiovascular, non-cancer causes.

Sounds convincing, right? And it is in fact a systematic review and meta-analysis, which is at the top of the pyramid. But in order to properly answer the question, we should be doing a complete review of the available evidence, and then consider the weight of the evidence. If the weight of the evidence, including that systematic review and meta-analysis, supports that whole grains are healthy then we need to stand in support of whole grains.

And as I show you in *Fiber Fueled*, this isn't the only evidence to support the healthful properties of whole grains. In Chapter 2 I shared the study by Genoni et al. where a long term paleolithic diet, devoid of whole grains, was associated with changes in the gut microbiota that increased the production of TMAO, a blood marker that's been connected to increased risk of heart disease, stroke, diabetes and chronic kidney disease, among others. Then in Chapter 4 I shared additional prospective cohort studies, systematic reviews and meta-analyses further connecting whole grains to reduced risk of heart disease, stroke, and diabetes, among others.

I spoke before about looking at the entire weight of evidence. When it comes to whole grains, there is consistency among the highest quality evidence – whole grains heal and are anti-inflammatory.

WHAT IS BIAS AND WHY IS IT THE BIGGEST THREAT TO SCIENCE?

Bias is the conscious or unconscious prejudice that one has towards a particular topic. It's a very loaded, complicated matter because bias can be unconscious. If you believe a certain thing to be true, you may not even realize that you tend to favor the studies that confirm what you believe to be true

This is a huge problem when it comes to science. The highest quality science comes from a place where we relieve ourselves of any and all bias, and allow the research to speak to us. As I've already laid out, you use the weight of the entire evidence to determine what the science is saying to you.

This process relies on the absence of bias to be true and honest. If there is bias by the researcher, then it will translate in the results. According to a study published in the British Medical Journal, industry-sponsored research is four times more likely to yield a positive result than unsponsored research. This is a huge problem.

But it's equally problematic in our interpretation of the research. If we have a bias that we seek to fulfill, whether conscious or unconscious, then we are much more likely to interpret what we read through that context.

It's one thing when we have our unconscious bias. But it's a much bigger problem when it's overt and conscious. The more overt our bias, the more aggressive we will be about twisting research to make it what we want it to be.

Sadly, you see this happen online. There are people who seek out the source that tells them what they want to hear. They then elevate that source, while simultaneously discrediting the opposing view.

Another example is the "expert" who has an agenda. Unfortunately, there are

people who make a living off of an idea. Independent of the scientific merit of that idea, if they make a living off of it then they are going to be far more likely to support that idea through their interpretation and dissemination of research. In some cases, this is mild. But in others, it can lead to people who flat out reject the scientific consensus and choose to promote ideas that fall somewhere on a spectrum between bad research to misleading to flat out lies. It's scary because they only drag you further away from the truth.

HOW CAN WE FIND THE TRUTH AMONG ALL THE NOISE?

I have to tell you, I'm quite fearful of people and their conspiracy theories. I've heard so many patients tell me their theory that organized healthcare, including doctors like myself, actually want people to be sick so they can make money off of them. Wow. That's terrifying to imagine. But it's also completely untrue.

No one goes to medical school, devotes their life with long days and nights of work and routinely taking call in the middle of the night, just so they can inflict harm on people for their own self gain. Let me be real – if it was about the money I would've gone into banking.

After college, I earned a medical degree and a master's degree, spent 8 years working 80 hours a week in my residency and fellowship for less than minimum wage, accumulated massive loans that compounded their interest, and at the age of 34 finally emerged on the other side able to start my career. Life would've been a lot easier if I chose a different path, and with the grades that I obtained in order to get myself into medical school I had plenty of options of what direction to go.

But with that said, there are definitely people out there who have an agenda. Just because they tell you what you may want to hear doesn't mean that they

are telling you what you should hear. Just because they are a doctor doesn't mean that they are telling you high quality research or the truth.

We have to be prepared to find the highest quality sources and the truth among the noise. Trust is an important concept. We need to be careful who we are trusting with our health – it's too important. And we have to get away from seeking out the opinion that tells us what we want to hear. We have to be willing to find the person who tells us what we NEED to hear, instead.

When evaluating your experts, I'd encourage you to consider these points:

1. What qualifications do they have to make them an expert in the field?
    - A. Beware the person speaking outside of their expertise. Just because they went to medical school doesn't mean they are qualified to speak on any and all related health topics. I'm board certified as an internal medicine doctor, but I would never claim to be a heart expert or brain expert. There are people who do years of training on those subjects and I am not one of them.
    - B. You should also be careful with the person who "claims to be an expert" but doesn't have the formal training. These people will often make claims that they know more than those who have formal training, which is an attempt to erode confidence in the institutions that train our best and brightest.
2. Is there something they want you to purchase?
    - A. For example, do they claim to have a supplement that will fix the problem that they helped you identify? Beware the person who is pushing you towards a purchase where they actually reap a financial reward.
3. Do they make claims along the lines of, "Everyone else is overlooking or missing this one important point, and I have discovered the solution to all of your problems."
    - A. Beware the "lone wolf" who claims to have the cure all. Or the person who claims that the entire scientific world is missing a key point, and that they have found that point. Almost every single time, they are promoting bad science. Once or twice a generation a scientist will make claims such as these and

subsequently prove to be right – but those are the ones that we give a Nobel Prize too. They're not the ones peddling a fad diet. There are zero authors of a fad diet who have been considered for a Nobel Prize.

B. You should look to see who else supports the assertion of this person. Is there literally anyone from the scientific community willing to step forward and agree with the principles? Or is there universal rejection by the scientific community? Are their only supporters the ones who share the same beliefs? These are all things to consider.

4. Do they overtly promote low grade science (test tube studies, animal studies, anecdotes) but ignore the high quality evidence (systematic review and meta-analysis, RCTs, prospective cohorts) that say otherwise?

A. These are overt signs of an agenda. The only way to get your argument to work is to ignore the research that stands in the way.

B. Be wary of testimonials, which are meant to convince you of something without necessarily having the science to back it up.

5. Do they consistently reach the same conclusion, even when they are presented with research that would suggest otherwise?

A. If they always seem to figure out a way to reach the same conclusion, no matter what research you throw their way, then it seems that they likely have an agenda that they're trying to fulfill.

6. Have they taken a position that is anti-science? Claiming that research is flawed and therefore shouldn't be trusted, or that everything is corrupted and therefore cannot be trusted?

A. These are arguments made with the intent of tearing down or marginalizing research, which once again is an overt sign of an agenda. You tear down or marginalize research that doesn't fit your agenda because it stands in the way of your argument.

B. Be wary of the person who shoots down science by saying, "I'm a unique individual and that's not true for me!" Science is not perfect and we do not

expect it to predict everything, but it is our tool to draw closer to the truth and to degrade it based upon a single individual's experience is effectively the same as prioritizing anecdotes over high quality research studies.

A FEW CLOSING THOUGHTS.

It's a more confusing time than ever, and that's largely due to the internet and the absolute flooding of our mind with information. It seems like everyone out there is hoping to get in our head and alter our thoughts with their ideas. It is our responsibility to act as the gatekeeper. We need to determine which information we choose to accept and let in. If we opt for high quality information, it brings us closer to the truth and we can use that information to enrich our lives. If we allow low quality information, feed our biases, or choose bad experts, then we will end up less healthy and confused. Now more than ever we need to use the concepts that I've laid out in this document to find that higher quality information. And then, we need to help our friends and family find this information by elevating and celebrating high quality information when you find it. If you enjoyed this research guide and found it helpful, tell your friends to check it out. If you loved my book, share it on your social media. If you found a podcast that was useful, do an Instagram story about it.

AND NOW, WITHOUT FURTHER ADO, ALL 600+ REFERENCES FROM FIBER FUELED!:

INTRODUCTION

at least seventy million of you: Anne F. Peery et al., "Burden of Gastrointestinal Disease in the United States: 2012 Update," Gastroenterology 143, no. 5 (November 2012): 1179-1187.e3, https://doi.org/10.1053/j.gastro.2012.08.002.

scientifically proven to actually reverse heart disease: Dean Ornish et al., "Intensive Lifestyle Changes for Reversal of Coronary Heart Disease," JAMA 280, no. 23 (December 16, 1998): 2001–7, https://doi.org/10.1001/jama.280.23.2001.

shown to lengthen telomeres: Dean Ornish et al., "Effect of Comprehensive Lifestyle Changes on Telomerase Activity and Telomere Length in Men with Biopsy-Proven Low-Risk Prostate Cancer: 5-Year Follow-up of a Descriptive Pilot Study," The Lancet. Oncology 14, no. 11 (October 2013): 1112–20, https://doi.org/10.1016/S1470-2045(13)70366-8.

forty third in the world in life expectancy: "The World Factbook — Central Intelligence Agency," accessed July 31, 2019, https://www.cia.gov/library/publications/the-world-factbook/rankorder/2102rank.html.

CHAPTER 1

At that time sixty percent of gut microbes: Ming-Wun Wong et al., "Impact of Vegan Diets on Gut Microbiota: An Update on the Clinical Implications," Tzu-Chi Medical Journal 30, no. 4 (2018): 200–203, https://doi.org/10.4103/tcmj.tcmj_21_18.

Very quickly, we identified 15,000 species: Daniel N. Frank et al., "Molecular-Phylogenetic Characterization of Microbial Community Imbalances in Human

Inflammatory Bowel Diseases," Proceedings of the National Academy of Sciences of the United States of America 104, no. 34 (August 21, 2007): 13780–85, https://doi.org/10.1073/pnas.0706625104.

12,900 papers on the topic: Patrice D. Cani, "Human Gut Microbiome: Hopes, Threats and Promises," Gut 67, no. 9 (September 1, 2018): 1716–25, https://doi.org/10.1136/gutjnl-2018-316723.

It takes an average of seventeen years: Zoë Slote Morris, Steven Wooding, and Jonathan Grant, "The Answer Is 17 Years, What Is the Question: Understanding Time Lags in Translational Research," Journal of the Royal Society of Medicine 104, no. 12 (December 2011): 510–20, https://doi.org/10.1258/jrsm.2011.110180.

sixty million Americans are chronically infected: Monica E. Parise, Peter J. Hotez, and Laurence Slutsker, "Neglected Parasitic Infections in the United States: Needs and Opportunities," The American Journal of Tropical Medicine and Hygiene 90, no. 5 (May 7, 2014): 783–85, https://doi.org/10.4269/ajtmh.13-0727.

In this case, we carry thirty-nine trillion: Ron Sender, Shai Fuchs, and Ron Milo, "Are We Really Vastly Outnumbered? Revisiting the Ratio of Bacterial to Host Cells in Humans," Cell 164, no. 3 (January 28, 2016): 337–40, https://doi.org/10.1016/j.cell.2016.01.013.

That number clearly outpaces: Sender, Fuchs, and Milo.

Diversity of species is critically important: Francisco Guarner and Juan-R. Malagelada, "Gut Flora in Health and Disease," Lancet (London, England) 361, no. 9356 (February 8, 2003): 512–19, https://doi.org/10.1016/S0140-6736(03)12489-0; Cynthia L. Sears, "A Dynamic Partnership: Celebrating Our Gut Flora," Anaerobe 11, no. 5 (October 2005): 247–51, https://doi.org/10.1016/j.anaerobe.2005.05.001.

alter the evolution of 50 generations of microbes: T. D. Luckey, "Introduction to Intestinal Microecology," The American Journal of Clinical Nutrition 25, no. 12 (December 1972): 1292–94, https://doi.org/10.1093/ajcn/25.12.1292.

We call the health promoting compounds: Katerina Tsilingiri and Maria Rescigno, "Postbiotics: What Else?," Beneficial Microbes 4 (December 27, 2012): 69–75, https://doi.org/10.3920/BM2012.0046.

The healthier the gut, the better the chance: Sophie Viaud et al., "The Intestinal Microbiota Modulates the Anticancer Immune Effects of Cyclophosphamide," Science (New York, N.Y.) 342, no. 6161 (November 22, 2013): 971–76, https://doi.org/10.1126/science.1240537.

They work as teams: Liping Zhao et al., "Gut Bacteria Selectively Promoted by Dietary Fibers Alleviate Type 2 Diabetes," Science (New York, N.Y.) 359, no. 6380 (09 2018): 1151–56, https://doi.org/10.1126/science.aao5774.

Bacterial endotoxin is produced by: Steven M. Opal, "Endotoxins and Other Sepsis Triggers," Contributions to Nephrology 167 (2010): 14–24, https://doi.org/10.1159/000315915.

Bacterial endotoxemia has been linked to: A. P. Moran, M. M. Prendergast, and B. J. Appelmelk, "Molecular Mimicry of Host Structures by Bacterial Lipopolysaccharides and Its Contribution to Disease," FEMS Immunology and Medical Microbiology 16, no. 2 (December 1, 1996): 105–15, https://doi.org/10.1111/j.1574-695X.1996.tb00127.x; Emily M. L. Chastain and Stephen D. Miller, "Molecular Mimicry as an Inducing Trigger for CNS Autoimmune Demyelinating Disease," Immunological Reviews 245, no. 1 (January 2012): 227–38, https://doi.org/10.1111/j.1600-065X.2011.01076.x; J. M. Moreno-Navarrete et al., "Circulating Lipopolysaccharide-Binding Protein (LBP) as a Marker of Obesity-Related Insulin Resistance," International Journal of Obesity (2005) 36, no. 11 (November 2012): 1442–49, https://doi.org/10.1038/ijo.2011.256; Philipp M. Lepper et al., "Association of Lipopolysaccharide-

Binding Protein and Coronary Artery Disease in Men," Journal of the American College of Cardiology 50, no. 1 (July 3, 2007): 25–31, https://doi.org/10.1016/j.jacc.2007.02.070; Armando Guerra Ruiz et al., "Lipopolysaccharide-Binding Protein Plasma Levels and Liver TNF-Alpha Gene Expression in Obese Patients: Evidence for the Potential Role of Endotoxin in the Pathogenesis of Non-Alcoholic Steatohepatitis," Obesity Surgery 17, no. 10 (October 2007): 1374–80, https://doi.org/10.1007/s11695-007-9243-7; Patrice D. Cani et al., "Metabolic Endotoxemia Initiates Obesity and Insulin Resistance," Diabetes 56, no. 7 (July 1, 2007): 1761–72, https://doi.org/10.2337/db06-1491; Bambos M. Charalambous et al., "Role of Bacterial Endotoxin in Chronic Heart Failure: The Gut of the Matter," Shock (Augusta, Ga.) 28, no. 1 (July 2007): 15–23, https://doi.org/10.1097/shk.0b013e318033ebc5; Xinhua Zhan, Boryana Stamova, and Frank R. Sharp, "Lipopolysaccharide Associates with Amyloid Plaques, Neurons and Oligodendrocytes in Alzheimer's Disease Brain: A Review," Frontiers in Aging Neuroscience 10 (2018): 42, https://doi.org/10.3389/fnagi.2018.00042; Zeyu Huang and Virginia Byers Kraus, "Does Lipopolysaccharide-Mediated Inflammation Have a Role in OA?," Nature Reviews. Rheumatology 12, no. 2 (February 2016): 123–29, https://doi.org/10.1038/nrrheum.2015.158.

even in those who are healthy: Luis Furuya-Kanamori et al., "Asymptomatic Clostridium Difficile Colonization: Epidemiology and Clinical Implications," BMC Infectious Diseases 15 (November 14, 2015), https://doi.org/10.1186/s12879-015-1258-4.

We also were seeing C. Diff pop up: Ciarán P. Kelly and J. Thomas LaMont, "Clostridium Difficile--More Difficult than Ever," The New England Journal of Medicine 359, no. 18 (October 30, 2008): 1932–40, https://doi.org/10.1056/NEJMra0707500; J. Freeman et al., "The Changing Epidemiology of Clostridium Difficile Infections," Clinical Microbiology Reviews 23, no. 3 (July 2010): 529–49, https://doi.org/10.1128/CMR.00082-09.

Sixty percent of the weight of your stool: A. M. Stephen and J. H.

Cummings, “The Microbial Contribution to Human Faecal Mass,” Journal of Medical Microbiology 13, no. 1 (February 1980): 45–56, https://doi.org/10.1099/00222615-13-1-45.

In 1989 Strachan proposed the “Hygiene Hypothesis”: D. P. Strachan, “Hay Fever, Hygiene, and Household Size.,” British Medical Journal 299, no. 6710 (November 18, 1989): 1259–60, https://doi.org/10.1136/bmj.299.6710.1259.

As I mentioned, a full seventy percent: G. Vighi et al., “Allergy and the Gastrointestinal System,” Clinical and Experimental Immunology 153 Suppl 1 (September 2008): 3–6, https://doi.org/10.1111/j.1365-2249.2008.03713.x.

the microbiota help foster proper development of immune cells: Vanessa K. Ridaura et al., “Cultured Gut Microbiota from Twins Discordant for Obesity Modulate Adiposity and Metabolic Phenotypes in Mice,” Science (New York, N.Y.) 341, no. 6150 (September 6, 2013), https://doi.org/10.1126/science.1241214.

the incidence of asthma increased at least tenfold: R. Beasley et al., “Prevalence and Etiology of Asthma,” The Journal of Allergy and Clinical Immunology 105, no. 2 Pt 2 (February 2000): S466-472, https://doi.org/10.1016/s0091-6749(00)90044-7.

Since the 1950s, the rates of type 1 diabetes: Jean-Francois Bach, “The Effect of Infections on Susceptibility to Autoimmune and Allergic Diseases,” The New England Journal of Medicine 347, no. 12 (September 19, 2002): 911–20, https://doi.org/10.1056/NEJMra020100.

For example, the number of new cases of type 1 diabetes: International Diabetes Federation (2015) IDF Diabetes Atlas, 7th Ed, www.diabetesatlas.org/across-the-globe.html

Croatia, for example, has seen an increase in Crohn’s disease: Payam Behzadi,

Elham Behzadi, and Reza Ranjbar, "The Incidence and Prevalence of Crohn's Disease in Global Scale," SOJ Immunology 3, no. 2 (May 13, 2015), https://doi.org/10.15226/soji/3/2/00125; Siew C. Ng et al., "Worldwide Incidence and Prevalence of Inflammatory Bowel Disease in the 21st Century: A Systematic Review of Population-Based Studies," Lancet (London, England) 390, no. 10114 (23 2018): 2769–78, https://doi.org/10.1016/S0140-6736(17)32448-0.

Well, the mice all developed inflamed lungs: Maria Gloria Dominguez-Bello and Martin J. Blaser, "Asthma: Undoing Millions of Years of Coevolution in Early Life?," Science Translational Medicine 7, no. 307 (September 30, 2015): 307fs39-307fs39, https://doi.org/10.1126/scitranslmed.aad2741.

Her body mass index increased: Neha Alang and Colleen R. Kelly, "Weight Gain after Fecal Microbiota Transplantation," Open Forum Infectious Diseases 2, no. 1 (January 2015): ofv004, https://doi.org/10.1093/ofid/ofv004.

Despite the fact that both mice: Gerard Clarke et al., "Minireview: Gut Microbiota: The Neglected Endocrine Organ," Molecular Endocrinology 28, no. 8 (August 1, 2014): 1221–38, https://doi.org/10.1210/me.2014-1108.

As we discussed before, autoimmune type 1 diabetes: Alexandra Paun, Christopher Yau, and Jayne S. Danska, "The Influence of the Microbiome on Type 1 Diabetes," Journal of Immunology (Baltimore, Md.: 1950) 198, no. 2 (15 2017): 590–95, https://doi.org/10.4049/jimmunol.1601519.

Type 2 diabetes has been linked to: Etan Orgel and Steven D. Mittelman, "The Links between Insulin Resistance, Diabetes, and Cancer," Current Diabetes Reports 13, no. 2 (April 2013): 213–22, https://doi.org/10.1007/s11892-012-0356-6.

They were 98% accurate: Hideto Sonoda et al., "Colorectal Cancer Screening with Odour Material by Canine Scent Detection," Gut 60, no. 6 (June 2011): 814–19, https://doi.org/10.1136/gut.2010.218305.

emerging studies are showing that specific bacteria in the colon: Keisuke Kosumi et al., "Dysbiosis of the Gut Microbiota and Colorectal Cancer: The Key Target of Molecular Pathological Epidemiology," Journal of Laboratory and Precision Medicine 3 (September 2018), https://doi.org/10.21037/jlpm.2018.09.05.

with a number of emerging cancers: Amy M. Sheflin, Alyssa K. Whitney, and Tiffany L. Weir, "Cancer-Promoting Effects of Microbial Dysbiosis," Current Oncology Reports 16, no. 10 (October 2014): 406, https://doi.org/10.1007/s11912-014-0406-0; Aadra P. Bhatt, Matthew R. Redinbo, and Scott J. Bultman, "The Role of the Microbiome in Cancer Development and Therapy," CA: A Cancer Journal for Clinicians 67, no. 4 (08 2017): 326–44, https://doi.org/10.3322/caac.21398.

This led to a change in their gut microbiota: Ruud S. Kootte et al., "Improvement of Insulin Sensitivity after Lean Donor Feces in Metabolic Syndrome Is Driven by Baseline Intestinal Microbiota Composition," Cell Metabolism 26, no. 4 (October 3, 2017): 611-619.e6, https://doi.org/10.1016/j.cmet.2017.09.008.

Using solely an individuals gut microbial profile: David Zeevi et al., "Personalized Nutrition by Prediction of Glycemic Responses," Cell 163, no. 5 (November 19, 2015): 1079–94, https://doi.org/10.1016/j.cell.2015.11.001.

It's a loss of diversity in the gut microbiota: Patrice D. Cani et al., "Involvement of Gut Microbiota in the Development of Low-Grade Inflammation and Type 2 Diabetes Associated with Obesity," Gut Microbes 3, no. 4 (August 2012): 279–88, https://doi.org/10.4161/gmic.19625.

improved metabolic health and insulin sensitivity: Justin L. Sonnenburg and Fredrik Bäckhed, "Diet-Microbiota Interactions as Moderators of Human Metabolism," Nature 535, no. 7610 (07 2016): 56–64, https://doi.org/10.1038/nature18846.

Gut microbes secrete the enzyme β-glucuronidase: Claudia S. Plottel and Martin J. Blaser, "Microbiome and Malignancy," Cell Host & Microbe 10, no. 4 (October 20, 2011): 324–35, https://doi.org/10.1016/j.chom.2011.10.003.

No surprise, we find damage to the gut: Matthias W. Laschke and Michael D. Menger, "The Gut Microbiota: A Puppet Master in the Pathogenesis of Endometriosis?," American Journal of Obstetrics and Gynecology 215, no. 1 (2016): 68.e1-4, https://doi.org/10.1016/j.ajog.2016.02.036; James M. Baker, Layla Al-Nakkash, and Melissa M. Herbst-Kralovetz, "Estrogen-Gut Microbiome Axis: Physiological and Clinical Implications," Maturitas 103 (September 2017): 45–53, https://doi.org/10.1016/j.maturitas.2017.06.025; Robert F. Schwabe and Christian Jobin, "The Microbiome and Cancer," Nature Reviews. Cancer 13, no. 11 (November 2013): 800–812, https://doi.org/10.1038/nrc3610; James J. Goedert et al., "Investigation of the Association between the Fecal Microbiota and Breast Cancer in Postmenopausal Women: A Population-Based Case-Control Pilot Study," Journal of the National Cancer Institute 107, no. 8 (August 2015), https://doi.org/10.1093/jnci/djv147; Dana Chase et al., "The Vaginal and Gastrointestinal Microbiomes in Gynecologic Cancers: A Review of Applications in Etiology, Symptoms and Treatment," Gynecologic Oncology 138, no. 1 (July 2015): 190–200, https://doi.org/10.1016/j.ygyno.2015.04.036.

Clostridium scindens is a gut bacteria: Jason M. Ridlon et al., "Clostridium Scindens: A Human Gut Microbe with a High Potential to Convert Glucocorticoids into Androgens," Journal of Lipid Research 54, no. 9 (September 2013): 2437–49, https://doi.org/10.1194/jlr.M038869.

A healthy gut microbiome keeps our estrogens and androgens in balance: Yanjie Guo et al., "Association between Polycystic Ovary Syndrome and Gut Microbiota," PLoS ONE 11, no. 4 (April 19, 2016), https://doi.org/10.1371/journal.pone.0153196; Lisa Lindheim et al., "Alterations in Gut Microbiome Composition and Barrier Function Are Associated with Reproductive and Metabolic Defects in Women with Polycystic Ovary Syndrome (PCOS): A Pilot Study," PLoS ONE 12, no. 1 (January 3, 2017), https://doi.org/10.1371/journal.

pone.0168390.

loss of testosterone and sperm production: Kelton Tremellen, "Gut Endotoxin Leading to a Decline IN Gonadal Function (GELDING) - a Novel Theory for the Development of Late Onset Hypogonadism in Obese Men," Basic and Clinical Andrology 26 (2016): 7, https://doi.org/10.1186/s12610-016-0034-7.

bacteria control the release of guaiacol: Hadar Neuman et al., "Microbial Endocrinology: The Interplay between the Microbiota and the Endocrine System," FEMS Microbiology Reviews 39, no. 4 (July 1, 2015): 509–21, https://doi.org/10.1093/femsre/fuu010.

The healthy microbes produce a fragrance: R. J. Dillon, C. T. Vennard, and A. K. Charnley, "A Note: Gut Bacteria Produce Components of a Locust Cohesion Pheromone," Journal of Applied Microbiology 92, no. 4 (2002): 759–63; Shirley Raveh et al., "Female Partner Preferences Enhance Offspring Ability to Survive an Infection," BMC Evolutionary Biology 14 (January 23, 2014): 14, https://doi.org/10.1186/1471-2148-14-14.

Every time we kiss: Remco Kort et al., "Shaping the Oral Microbiota through Intimate Kissing," Microbiome 2, no. 1 (November 17, 2014): 41, https://doi.org/10.1186/2049-2618-2-41.

there are over five hundred million nerves: Emeran A. Mayer, "Gut Feelings: The Emerging Biology of Gut-Brain Communication," Nature Reviews. Neuroscience 12, no. 8 (July 13, 2011): 453–66, https://doi.org/10.1038/nrn3071.

Gut microbes both produce and respond to: Mark Lyte, "Microbial Endocrinology," Gut Microbes 5, no. 3 (May 1, 2014): 381–89, https://doi.org/10.4161/gmic.28682.

90% of serotonin and 50% of dopamine: Jessica M. Yano et al., "Indigenous

Bacteria from the Gut Microbiota Regulate Host Serotonin Biosynthesis," Cell 161, no. 2 (April 9, 2015): 264–76, https://doi.org/10.1016/j.cell.2015.02.047; Clarke et al., "Minireview."

Precursors of serotonin and dopamine: Mark Lyte, "Microbial Endocrinology in the Microbiome-Gut-Brain Axis: How Bacterial Production and Utilization of Neurochemicals Influence Behavior," PLoS Pathogens 9, no. 11 (November 14, 2013), https://doi.org/10.1371/journal.ppat.1003726; Neuman et al., "Microbial Endocrinology."

Sara Gerhardt and M. Hasan Mohajeri, "Changes of Colonic Bacterial Composition in Parkinson's Disease and Other Neurodegenerative Diseases," Nutrients 10, no. 6 (June 2018): 708, https://doi.org/10.3390/nu10060708; Giulia Umbrello and Susanna Esposito, "Microbiota and Neurologic Diseases: Potential Effects of Probiotics," Journal of Translational Medicine 14 (October 19, 2016), https://doi.org/10.1186/s12967-016-1058-7.

overlap between irritable bowel syndrome (IBS) and depressed mood: Emeran A. Mayer, "Irritable Bowel Syndrome," New England Journal of Medicine 358, no. 16 (April 17, 2008): 1692–99, https://doi.org/10.1056/NEJMcp0801447.

they produce the same amount of gas: Giles Major et al., "Colon Hypersensitivity to Distension, Rather Than Excessive Gas Production, Produces Carbohydrate-Related Symptoms in Individuals With Irritable Bowel Syndrome," Gastroenterology 152, no. 1 (2017): 124-133.e2, https://doi.org/10.1053/j.gastro.2016.09.062.

gut microbes control our cravings: Joe Alcock, Carlo C. Maley, and C. Athena Aktipis, "Is Eating Behavior Manipulated by the Gastrointestinal Microbiota? Evolutionary Pressures and Potential Mechanisms," BioEssays: News and Reviews in Molecular, Cellular and Developmental Biology 36, no. 10 (October 2014): 940–49, https://doi.org/10.1002/bies.201400071.

we've found that "chocolate desiring" people: Serge Rezzi et al., "Human Metabolic Phenotypes Link Directly to Specific Dietary Preferences in Healthy Individuals," Journal of Proteome Research 6, no. 11 (November 2007): 4469–77, https://doi.org/10.1021/pr070431h.

twenty percent of disease is based on genetics: Stephen M. Rappaport, "Genetic Factors Are Not the Major Causes of Chronic Diseases," PloS One 11, no. 4 (2016): e0154387, https://doi.org/10.1371/journal.pone.0154387.

99% of your DNA comes from microbes: Junjie Qin et al., "A Human Gut Microbial Gene Catalogue Established by Metagenomic Sequencing," Nature 464, no. 7285 (March 4, 2010): 59–65, https://doi.org/10.1038/nature08821.

as much as 90% different: Jairam K. P. Vanamala, Rob Knight, and Timothy D. Spector, "Can Your Microbiome Tell You What to Eat?," Cell Metabolism 22, no. 6 (December 1, 2015): 960–61, https://doi.org/10.1016/j.cmet.2015.11.009.

Dr. Elena Verdu from McMaster University: Heather J Galipeau and Elena F Verdu, "Gut Microbes and Adverse Food Reactions: Focus on Gluten Related Disorders," Gut Microbes 5, no. 5 (October 30, 2014): 594–605, https://doi.org/10.4161/19490976.2014.969635.

We are a superorganism: Baoli Zhu, Xin Wang, and Lanjuan Li, "Human Gut Microbiome: The Second Genome of Human Body," Protein & Cell 1, no. 8 (August 2010): 718–25, https://doi.org/10.1007/s13238-010-0093-z.

CHAPTER 2

More than seventy two percent of Americans are overweight: https://www.cdc.gov/nchs/fastats/obesity-overweight.htm

life expectancy just dropped for the third year in a row: https://www.cdc.gov/nchs/data/hus/2017/fig20.pdf , accessed October 26, 2019

And now sixty percent of Americans: Elizabeth D. Kantor et al., "Trends in Prescription Drug Use Among Adults in the United States From 1999-2012," JAMA 314, no. 17 (November 3, 2015): 1818–31, https://doi.org/10.1001/jama.2015.13766.

Consider that in 2014 alone: According to U.S. government data cited by Consumer Reports: https://www.consumerreports.org/prescription-drugs/too-many-meds-americas-love-affair-with-prescription-medication/ , accessed October 26, 2019

In order, they are: heart disease: https://www.cdc.gov/nchs/data/hus/2017/019.pdf , accessed October 26, 2019

Big Pharma runs the studies: https://www.cdc.gov/antibiotic-use/community/programs-measurement/state-local-activities/outpatient-antibiotic-prescriptions-US-2015.html , accessed October 26, 2019; https://clincalc.com/DrugStats/EPC/ProtonPumpInhibitor , accessed October 26, 2019; Charles Argoff, "NSAIDs or Opioids, Damned If You Do, Damned If You Don't?: Evidence-Based Selections to Optimize Therapeutic Goals and Minimize Harms," Pain Medicine 14, no. S1 (2013): S40–42, https://doi.org/10.1111/pme.12289.

In the late nineteenth century the average life expectancy: https://www.cdc.gov/nchs/data/hus/2017/015.pdf , accessed October 26, 2019

Infectious diseases such as smallpox: David S. Jones, Scott H. Podolsky, and Jeremy A. Greene, "The Burden of Disease and the Changing Task of Medicine," The New England Journal of Medicine 366, no. 25 (June 21, 2012): 2333–38, https://doi.org/10.1056/NEJMp1113569.

"close the books on infectious diseases.": "Antibiotics 1928 - 2000," accessed October 26, 2019, http://www.abc.net.au/science/slab/antibiotics/history.htm.

The number of food additives skyrockets: "Why The FDA Has Never Looked

At Some Of The Additives In Our Food," NPR.org, accessed October 26, 2019, https://www.npr.org/sections/thesalt/2015/04/14/399591292/why-the-fda-is-clueless-about-some-of-the-additives-in-our-food.

Today more than eighty percent of all genetically modified crops: Stephen O. Duke Stephen B. Powles, "Glyphosate-Resistant Crops and Weeds: Now and in the Future," January 21, 2010, http://agbioforum.org/v12n34/v12n34a10-duke.htm.

This is a boon for genetically engineered farming: Jane E. Brody, "Are G.M.O. Foods Safe?," The New York Times, April 23, 2018, sec. Well, https://www.nytimes.com/2018/04/23/well/eat/are-gmo-foods-safe.html.

Meanwhile, the use of toxic herbicides: "Glyphosate Is Spreading Like a Cancer Across the U.S.," EWG, accessed October 26, 2019, https://www.ewg.org/agmag/2015/04/glyphosate-spreading-cancer-across-us.

forty one percent increase in non-Hodgkins lymphoma: Luoping Zhang et al., "Exposure to Glyphosate-Based Herbicides and Risk for Non-Hodgkin Lymphoma: A Meta-Analysis and Supporting Evidence," Mutation Research 781 (September 2019): 186–206, https://doi.org/10.1016/j.mrrev.2019.02.001.

organic foods were less likely to develop non-Hodgkin lymphoma: Julia Baudry et al., "Association of Frequency of Organic Food Consumption With Cancer Risk," JAMA Internal Medicine 178, no. 12 (December 2018): 1597–1606, https://doi.org/10.1001/jamainternmed.2018.4357.

type 2 diabetes is actually a protective mechanism: W. P. Newman and R. G. Brodows, "Insulin Action during Acute Starvation: Evidence for Selective Insulin Resistance in Normal Man," Metabolism: Clinical and Experimental 32, no. 6 (June 1983): 590–96, https://doi.org/10.1016/0026-0495(83)90029-x.

Just five days of ciprofloxacin: Les Dethlefsen et al., "The Pervasive Effects of

an Antibiotic on the Human Gut Microbiota, as Revealed by Deep 16S RRNA Sequencing," PLoS Biology 6, no. 11 (November 18, 2008): e280, https://doi.org/10.1371/journal.pbio.0060280.

Most species recover within 4 weeks: Hedvig E. Jakobsson et al., "Short-Term Antibiotic Treatment Has Differing Long-Term Impacts on the Human Throat and Gut Microbiome," PloS One 5, no. 3 (March 24, 2010): e9836, https://doi.org/10.1371/journal.pone.0009836.

And just four days of three broad spectrum antibiotics: Albert Palleja et al., "Recovery of Gut Microbiota of Healthy Adults Following Antibiotic Exposure," Nature Microbiology 3, no. 11 (2018): 1255–65, https://doi.org/10.1038/s41564-018-0257-9.

The result of all these antibiotics is a "new normal": M. P. Francino, "Antibiotics and the Human Gut Microbiome: Dysbioses and Accumulation of Resistances," Frontiers in Microbiology 6 (2015): 1543, https://doi.org/10.3389/fmicb.2015.01543.

twenty three percent of antibiotic prescriptions are flat out inappropriate: "Outpatient Antibiotic Prescriptions — United States, 2015 | Community | Antibiotic Use | CDC," January 16, 2019, https://www.cdc.gov/antibiotic-use/community/programs-measurement/state-local-activities/outpatient-antibiotic-prescriptions-US-2015.html; Kao-Ping Chua, Michael A. Fischer, and Jeffrey A. Linder, "Appropriateness of Outpatient Antibiotic Prescribing among Privately Insured US Patients: ICD-10-CM Based Cross Sectional Study," BMJ 364 (January 16, 2019): k5092, https://doi.org/10.1136/bmj.k5092.

twenty four percent of tested drugs altered gut bacteria: Lisa Maier et al., "Extensive Impact of Non-Antibiotic Drugs on Human Gut Bacteria," Nature 555, no. 7698 (29 2018): 623–28, https://doi.org/10.1038/nature25979.

proton pump inhibitors increase the risk: Lucio Lombardo et al., "Increased

Incidence of Small Intestinal Bacterial Overgrowth during Proton Pump Inhibitor Therapy," Clinical Gastroenterology and Hepatology: The Official Clinical Practice Journal of the American Gastroenterological Association 8, no. 6 (June 2010): 504–8, https://doi.org/10.1016/j.cgh.2009.12.022; Anca Trifan et al., "Proton Pump Inhibitors Therapy and Risk of Clostridium Difficile Infection: Systematic Review and Meta-Analysis," World Journal of Gastroenterology 23, no. 35 (September 21, 2017): 6500–6515, https://doi.org/10.3748/wjg.v23.i35.6500.

Nonsteroidal anti-inflammatory drugs like ibuprofen and naproxen alter the gut microbiota: Ashwin N. Ananthakrishnan et al., "Aspirin, Nonsteroidal Anti-Inflammatory Drug Use, and Risk for Crohn Disease Ulcerative Colitis," Annals of Internal Medicine 156, no. 5 (March 6, 2012): 350–59, https://doi.org/10.1059/0003-4819-156-5-201203060-00007; Koji Otani et al., "Microbiota Plays a Key Role in Non-Steroidal Anti-Inflammatory Drug-Induced Small Intestinal Damage," Digestion 95, no. 1 (2017): 22–28, https://doi.org/10.1159/000452356; Carmelo Scarpignato et al., "Rifaximin Reduces the Number and Severity of Intestinal Lesions Associated With Use of Nonsteroidal Anti-Inflammatory Drugs in Humans," Gastroenterology 152, no. 5 (2017): 980-982.e3, https://doi.org/10.1053/j.gastro.2016.12.007; I. Bjarnason et al., "Side Effects of Nonsteroidal Anti-Inflammatory Drugs on the Small and Large Intestine in Humans," Gastroenterology 104, no. 6 (June 1993): 1832–47, https://doi.org/10.1016/0016-5085(93)90667-2; M. A. M. Rogers and D. M. Aronoff, "The Influence of Non-Steroidal Anti-Inflammatory Drugs on the Gut Microbiome," Clinical Microbiology and Infection 22, no. 2 (February 1, 2016): 178.e1-178.e9, https://doi.org/10.1016/j.cmi.2015.10.003.

Oral contraceptives have been associated with: Ronald Ortizo et al., "Exposure to Oral Contraceptives Increases the Risk for Development of Inflammatory Bowel Disease: A Meta-Analysis of Case-Controlled and Cohort Studies," European Journal of Gastroenterology & Hepatology 29, no. 9 (September 2017): 1064–70, https://doi.org/10.1097/MEG.0000000000000915.

The average American eats: "What Are We Eating? What the Average American Consumes in a Year (Image)," mindbodygreen, August 2, 2010, https://www.mindbodygreen.com/0-1198/What-Are-We-Eating-What-the-Average-American-Consumes-in-a-Year-Image.html.

The U.S. also has the highest meat consumption: "List of Countries by Meat Consumption per Capita," in Wikipedia, October 13, 2019, https://en.wikipedia.org/w/index.php?title=List_of_countries_by_meat_consumption_per_capita&oldid=920997271.

and they live ten years longer: "Column: Loma Linda Residents Live a Really, Really Long Time. It's Not Because of Their Health Insurance," Los Angeles Times, May 30, 2017, https://www.latimes.com/opinion/op-ed/la-oe-goldberg-loma-linda-healthcare-20170530-story.html.

The result is a dramatic loss of gut microbial diversity: Peter J. Turnbaugh et al., "Marked Alterations in the Distal Gut Microbiome Linked to Diet-Induced Obesity," Cell Host & Microbe 3, no. 4 (April 17, 2008): 213–23, https://doi.org/10.1016/j.chom.2008.02.015.

The average American consumes: "What Are We Eating?"

We only need a few ounces: Nicola Wilck et al., "Salt-Responsive Gut Commensal Modulates TH17 Axis and Disease," Nature 551, no. 7682 (30 2017): 585–89, https://doi.org/10.1038/nature24628.

Numerous food additives have: Marit K. Zinöcker and Inge A. Lindseth, "The Western Diet–Microbiome-Host Interaction and Its Role in Metabolic Disease," Nutrients 10, no. 3 (March 17, 2018), https://doi.org/10.3390/nu10030365.

For example, two commonly used emulsifiers: Benoit Chassaing et al., "Dietary Emulsifiers Impact the Mouse Gut Microbiota Promoting Colitis and Metabolic Syndrome," Nature 519, no. 7541 (05 2015): 92–96, https://doi.org/10.1038/

nature14232.

Titanium dioxide (TiO) nanoparticles: Gabriela Pinget et al., "Impact of the Food Additive Titanium Dioxide (E171) on Gut Microbiota-Host Interaction," Frontiers in Nutrition 6 (2019), https://doi.org/10.3389/fnut.2019.00057; Pedro A. Ruiz et al., "Titanium Dioxide Nanoparticles Exacerbate DSS-Induced Colitis: Role of the NLRP3 Inflammasome," Gut 66, no. 7 (July 1, 2017): 1216–24, https://doi.org/10.1136/gutjnl-2015-310297.

they induce changes in the microbiome that promote inflammation: Jotham Suez et al., "Artificial Sweeteners Induce Glucose Intolerance by Altering the Gut Microbiota," Nature 514, no. 7521 (October 9, 2014): 181–86, https://doi.org/10.1038/nature13793; Jotham Suez et al., "Non-Caloric Artificial Sweeteners and the Microbiome: Findings and Challenges," Gut Microbes 6, no. 2 (2015): 149–55, https://doi.org/10.1080/19490976.2015.1017700 ; Stephanie Olivier-Van Stichelen, Kristina I. Rother, and John A. Hanover, "Maternal Exposure to Non-Nutritive Sweeteners Impacts Progeny's Metabolism and Microbiome," Frontiers in Microbiology 10 (2019): 1360, https://doi.org/10.3389/fmicb.2019.01360; Iryna Liauchonak et al., "Non-Nutritive Sweeteners and Their Implications on the Development of Metabolic Syndrome," Nutrients 11, no. 3 (March 16, 2019), https://doi.org/10.3390/nu11030644; Nadia Haq et al., "Aspartame and Sucralose-Induced Fatty Changes in Rat Liver," Journal of the College of Physicians and Surgeons--Pakistan: JCPSP 29, no. 9 (September 2019): 848–51, https://doi.org/10.29271/jcpsp.2019.09.848; M. Yanina Pepino et al., "Sucralose Affects Glycemic and Hormonal Responses to an Oral Glucose Load," Diabetes Care 36, no. 9 (September 2013): 2530–35, https://doi.org/10.2337/dc12-2221.

Just ten years later we're seeing 500,000 infections per year: Freeman et al., "The Changing Epidemiology of Clostridium Difficile Infections"; Fernanda C. Lessa et al., "Burden of Clostridium Difficile Infection in the United States," The New England Journal of Medicine 372, no. 9 (February 26, 2015): 825–34, https://doi.org/10.1056/NEJMoa1408913.

But a 2018 publication in Nature showed that: J. Collins et al., "Dietary Trehalose Enhances Virulence of Epidemic Clostridium Difficile," Nature 553, no. 7688 (January 18, 2018): 291–94, https://doi.org/10.1038/nature25178.

every ten percent increase in consumption of ultra-processed: Thibault Fiolet et al., "Consumption of Ultra-Processed Foods and Cancer Risk: Results from NutriNet-Santé Prospective Cohort," BMJ (Clinical Research Ed.) 360 (14 2018): k322, https://doi.org/10.1136/bmj.k322; Laure Schnabel et al., "Association Between Ultraprocessed Food Consumption and Risk of Mortality Among Middle-Aged Adults in France," JAMA Internal Medicine 179, no. 4 (April 1, 2019): 490–98, https://doi.org/10.1001/jamainternmed.2018.7289.

a high fat diet causes an unhealthy balance in the microbiota: Rebecca Pedersen et al., "The Effect of High-Fat Diet on the Composition of the Gut Microbiota in Cloned and Non-Cloned Pigs of Lean and Obese Phenotype," Gut Microbes 4, no. 5 (October 2013): 371–81, https://doi.org/10.4161/gmic.26108; "High-Fat Maternal Diet during Pregnancy Persistently Alters the Offspring Microbiome in a Primate Model | Nature Communications," accessed August 6, 2019, https://www.nature.com/articles/ncomms4889; Edmond Huang et al., "Composition of Dietary Fat Source Shapes Gut Microbiota Architecture and Alters Host Inflammatory Mediators in Mouse Adipose Tissue," JPEN. Journal of Parenteral and Enteral Nutrition 37, no. 6 (2013), https://doi.org/10.1177/0148607113486931; Chenhong Zhang et al., "Interactions between Gut Microbiota, Host Genetics and Diet Relevant to Development of Metabolic Syndromes in Mice," The ISME Journal 4, no. 2 (February 2010): 232–41, https://doi.org/10.1038/ismej.2009.112; Claire Barbier de La Serre et al., "Propensity to High-Fat Diet-Induced Obesity in Rats Is Associated with Changes in the Gut Microbiota and Gut Inflammation," American Journal of Physiology - Gastrointestinal and Liver Physiology 299, no. 2 (August 2010): G440–48, https://doi.org/10.1152/ajpgi.00098.2010; Kyung-Ah Kim et al., "High Fat Diet-Induced Gut Microbiota Exacerbates Inflammation and Obesity in Mice via the TLR4 Signaling Pathway," PLoS ONE 7, no. 10 (October 16, 2012), https://doi.org/10.1371/journal.pone.0047713;

B. M. Carvalho et al., "Modulation of Gut Microbiota by Antibiotics Improves Insulin Signalling in High-Fat Fed Mice," Diabetologia 55, no. 10 (2012): 2823–34, https://doi.org/10.1007/s00125-012-2648-4; Tiphaine Le Roy et al., "Intestinal Microbiota Determines Development of Non-Alcoholic Fatty Liver Disease in Mice," Gut 62, no. 12 (December 1, 2013): 1787–94, https://doi.org/10.1136/gutjnl-2012-303816; Ridaura et al., "Cultured Gut Microbiota from Twins Discordant for Obesity Modulate Adiposity and Metabolic Phenotypes in Mice."

A recent study in humans held dietary fiber constant: Yi Wan et al., "Effects of Dietary Fat on Gut Microbiota and Faecal Metabolites, and Their Relationship with Cardiometabolic Risk Factors: A 6-Month Randomised Controlled-Feeding Trial," Gut 68, no. 8 (August 1, 2019): 1417–29, https://doi.org/10.1136/gutjnl-2018-317609.

We see this validated in microbiome studies: Jorge R. Mujico et al., "Changes in Gut Microbiota Due to Supplemented Fatty Acids in Diet-Induced Obese Mice," British Journal of Nutrition 110, no. 4 (August 2013): 711–20, https://doi.org/10.1017/S0007114512005612; M. Hidalgo et al., "Effect of Virgin and Refined Olive Oil Consumption on Gut Microbiota. Comparison to Butter," Food Research International 64 (October 1, 2014): 553–59, https://doi.org/10.1016/j.foodres.2014.07.030; Ian A. Myles et al., "Effects of Parental Omega-3 Fatty Acid Intake on Offspring Microbiome and Immunity," PLoS ONE 9, no. 1 (January 29, 2014), https://doi.org/10.1371/journal.pone.0087181; Sanjoy Ghosh et al., "Fish Oil Attenuates Omega-6 Polyunsaturated Fatty Acid-Induced Dysbiosis and Infectious Colitis but Impairs LPS Dephosphorylation Activity Causing Sepsis," PLoS ONE 8, no. 2 (February 6, 2013), https://doi.org/10.1371/journal.pone.0055468; Sanjoy Ghosh et al., "Diets Rich in N-6 PUFA Induce Intestinal Microbial Dysbiosis in Aged Mice," The British Journal of Nutrition 110, no. 3 (August 28, 2013): 515–23, https://doi.org/10.1017/S0007114512005326; Venkatesh Mani, James H Hollis, and Nicholas K Gabler, "Dietary Oil Composition Differentially Modulates Intestinal Endotoxin Transport and Postprandial Endotoxemia," Nutrition & Metabolism 10 (January

10, 2013): 6, https://doi.org/10.1186/1743-7075-10-6; Elaine Patterson et al., "Impact of Dietary Fatty Acids on Metabolic Activity and Host Intestinal Microbiota Composition in C57BL/6J Mice," The British Journal of Nutrition 111 (February 20, 2014): 1–13, https://doi.org/10.1017/S0007114514000117.

They even enhance microbial diversity: Cristina Menni et al., "Omega-3 Fatty Acids Correlate with Gut Microbiome Diversity and Production of N-Carbamylglutamate in Middle Aged and Elderly Women," Scientific Reports 7 (December 1, 2017), https://doi.org/10.1038/s41598-017-10382-2. Robert Caesar et al., "Crosstalk between Gut Microbiota and Dietary Lipids Aggravates WAT Inflammation through TLR Signaling," Cell Metabolism 22, no. 4 (October 6, 2015): 658–68, https://doi.org/10.1016/j.cmet.2015.07.026; Suzanne Devkota et al., "Dietary Fat-Induced Taurocholic Acid Production Promotes Pathobiont and Colitis in IL-10−/− Mice," Nature 487, no. 7405 (July 5, 2012): 104–8, https://doi.org/10.1038/nature11225; Wan Shen, H. Rex Gaskins, and Michael K. McIntosh, "Influence of Dietary Fat on Intestinal Microbes, Inflammation, Barrier Function and Metabolic Outcomes," The Journal of Nutritional Biochemistry 25, no. 3 (March 1, 2014): 270–80, https://doi.org/10.1016/j.jnutbio.2013.09.009; Mani, Hollis, and Gabler, "Dietary Oil Composition Differentially Modulates Intestinal Endotoxin Transport and Postprandial Endotoxemia."

It even disrupts our normal biological rhythm: Vanessa Leone et al., "Effects of Diurnal Variation of Gut Microbes and High-Fat Feeding on Host Circadian Clock Function and Metabolism," Cell Host & Microbe 17, no. 5 (May 13, 2015): 681–89, https://doi.org/10.1016/j.chom.2015.03.006.

For example, plant protein increases the growth of: Świątecka Dominika et al., "The Study on the Impact of Glycated Pea Proteins on Human Intestinal Bacteria," International Journal of Food Microbiology 145, no. 1 (January 31, 2011): 267–72, https://doi.org/10.1016/j.ijfoodmicro.2011.01.002.

These bacteria produce toxins like: Isabel J. Skypala et al., "Sensitivity to Food

Additives, Vaso-Active Amines and Salicylates: A Review of the Evidence," Clinical and Translational Allergy 5 (October 13, 2015), https://doi.org/10.1186/s13601-015-0078-3; Wei Zheng and Sang-Ah Lee, "Well-Done Meat Intake, Heterocyclic Amine Exposure, and Cancer Risk," Nutrition and Cancer 61, no. 4 (2009): 437–46, https://doi.org/10.1080/01635580802710741.

Hydrogen sulfide has been associated with: Suzanne Devkota and Eugene B. Chang, "Interactions between Diet, Bile Acid Metabolism, Gut Microbiota, and Inflammatory Bowel Diseases," Digestive Diseases (Basel, Switzerland) 33, no. 3 (2015): 351–56, https://doi.org/10.1159/000371687.

Secondary bile salts have been associated with: Hana Ajouz, Deborah Mukherji, and Ali Shamseddine, "Secondary Bile Acids: An Underrecognized Cause of Colon Cancer," World Journal of Surgical Oncology 12 (May 24, 2014): 164, https://doi.org/10.1186/1477-7819-12-164.

No surprise, this results in: Lawrence A. David et al., "Diet Rapidly and Reproducibly Alters the Human Gut Microbiome," Nature 505, no. 7484 (January 23, 2014): 559–63, https://doi.org/10.1038/nature12820; Prévost Jantchou et al., "Animal Protein Intake and Risk of Inflammatory Bowel Disease: The E3N Prospective Study," American Journal of Gastroenterology 105, no. 10 (October 2010): 2195–2201, https://doi.org/10.1038/ajg.2010.192.

Increased TMAO means increased risk of: Gard F. T. Svingen et al., "Increased Plasma Trimethylamine-N-Oxide Is Associated with Incident Atrial Fibrillation," International Journal of Cardiology 267 (September 15, 2018): 100–106, https://doi.org/10.1016/j.ijcard.2018.04.128; W. H. Wilson Tang, Daniel Y. Li, and Stanley L. Hazen, "Dietary Metabolism, the Gut Microbiome, and Heart Failure," Nature Reviews Cardiology 16, no. 3 (March 2019): 137–54, https://doi.org/10.1038/s41569-018-0108-7; Robert A. Koeth et al., "Intestinal Microbiota Metabolism of L-Carnitine, a Nutrient in Red Meat, Promotes Atherosclerosis," Nature Medicine 19, no. 5 (May 2013): 576–85, https://doi.org/10.1038/nm.3145; Manuel H. Janeiro et al., "Implication of Trimethylamine N-Oxide

(TMAO) in Disease: Potential Biomarker or New Therapeutic Target," Nutrients 10, no. 10 (October 2018): 1398, https://doi.org/10.3390/nu10101398.

gut microbiota that just doesn't know how to make TMAO: Koeth et al., "Intestinal Microbiota Metabolism of L-Carnitine, a Nutrient in Red Meat, Promotes Atherosclerosis."

about four weeks after giving up red meat: Zeneng Wang et al., "Impact of Chronic Dietary Red Meat, White Meat, or Non-Meat Protein on Trimethylamine N-Oxide Metabolism and Renal Excretion in Healthy Men and Women," European Heart Journal 40, no. 7 (February 14, 2019): 583–94, https://doi.org/10.1093/eurheartj/ehy799.

Meanwhile the control group got worse: D. Ornish et al., "Can Lifestyle Changes Reverse Coronary Heart Disease? The Lifestyle Heart Trial," Lancet (London, England) 336, no. 8708 (July 21, 1990): 129–33, https://doi.org/10.1016/0140-6736(90)91656-u.

animal protein can produce weight loss in the short term, but causes a shift in the microbiome: Wendy R. Russell et al., "High-Protein, Reduced-Carbohydrate Weight-Loss Diets Promote Metabolite Profiles Likely to Be Detrimental to Colonic Health," The American Journal of Clinical Nutrition 93, no. 5 (May 1, 2011): 1062–72, https://doi.org/10.3945/ajcn.110.002188.

In a recent study, consumption of a long-term Paleolithic diet: Angela Genoni et al., "Long-Term Paleolithic Diet Is Associated with Lower Resistant Starch Intake, Different Gut Microbiota Composition and Increased Serum TMAO Concentrations," European Journal of Nutrition, July 5, 2019, https://doi.org/10.1007/s00394-019-02036-y.

The animal based diet saw the disturbing: David et al., "Diet Rapidly and Reproducibly Alters the Human Gut Microbiome."

It's just 47 years: Gwartney Daniel et al., "Mp47-17 Rates of Mortality Are Higher among Professional Male Bodybuilders," Journal of Urology 195, no. 4S (April 1, 2016): e633–e633, https://doi.org/10.1016/j.juro.2016.02.336.

CHAPTER 3

ninety-seven percent of us consume an excess of protein: Victor L. Fulgoni, "Current Protein Intake in America: Analysis of the National Health and Nutrition Examination Survey, 2003-2004," The American Journal of Clinical Nutrition 87, no. 5 (May 2008): 1554S-1557S, https://doi.org/10.1093/ajcn/87.5.1554S.

Less than three percent of Americans: Moshfegh, Alanna; Goldman, Joseph; and Cleveland, Linda. 2005. What We Eat in America. NHANES 2001-2002. Usual Nutrient Intakes from Food Compared to Dietary Reference Intakes. U.S. Department of Agriculture. Agricultural Research Service. https://www.ars.usda.gov/ARSUserFiles/80400530/pdf/0102/usualintaketables2001-02.pdf , accessed October 26, 2019

vicious cycle of food addiction, weight gain, and constant hunger: Belinda S. Lennerz et al., "Effects of Dietary Glycemic Index on Brain Regions Related to Reward and Craving in Men," The American Journal of Clinical Nutrition 98, no. 3 (September 2013): 641–47, https://doi.org/10.3945/ajcn.113.064113.

complex carbs actually lower blood sugar: Dagfinn Aune et al., "Whole Grain and Refined Grain Consumption and the Risk of Type 2 Diabetes: A Systematic Review and Dose-Response Meta-Analysis of Cohort Studies," European Journal of Epidemiology 28, no. 11 (November 2013): 845–58, https://doi.org/10.1007/s10654-013-9852-5; Janine A. Higgins, "Whole Grains, Legumes, and the Subsequent Meal Effect: Implications for Blood Glucose Control and the Role of Fermentation," Journal of Nutrition and Metabolism 2012 (2012), https://doi.org/10.1155/2012/829238; Ashkan Afshin et al., "Consumption of Nuts and Legumes and Risk of Incident Ischemic Heart Disease, Stroke, and Diabetes: A Systematic Review and Meta-Analysis," The American Journal

of Clinical Nutrition 100, no. 1 (July 2014): 278–88, https://doi.org/10.3945/ajcn.113.076901; Maria Conceição de Oliveira, Rosely Sichieri, and Anibal Sanchez Moura, "Weight Loss Associated with a Daily Intake of Three Apples or Three Pears among Overweight Women," Nutrition (Burbank, Los Angeles County, Calif.) 19, no. 3 (March 2003): 253–56; Jaimie N. Davis, Valerie A. Hodges, and M. Beth Gillham, "Normal-Weight Adults Consume More Fiber and Fruit than Their Age- and Height-Matched Overweight/Obese Counterparts," Journal of the American Dietetic Association 106, no. 6 (June 1, 2006): 833–40, https://doi.org/10.1016/j.jada.2006.03.013; Luc Dauchet et al., "Fruit and Vegetable Consumption and Risk of Coronary Heart Disease: A Meta-Analysis of Cohort Studies," The Journal of Nutrition 136, no. 10 (October 1, 2006): 2588–93, https://doi.org/10.1093/jn/136.10.2588; Davis, Hodges, and Gillham, "Normal-Weight Adults Consume More Fiber and Fruit than Their Age- and Height-Matched Overweight/Obese Counterparts"; Earl S. Ford and Ali H. Mokdad, "Fruit and Vegetable Consumption and Diabetes Mellitus Incidence among U.S. Adults," Preventive Medicine 32, no. 1 (January 1, 2001): 33–39, https://doi.org/10.1006/pmed.2000.0772; Erica M. Holt et al., "Fruit and Vegetable Consumption and Its Relation to Markers of Inflammation and Oxidative Stress in Adolescents," Journal of the American Dietetic Association 109, no. 3 (March 2009): 414–21, https://doi.org/10.1016/j.jada.2008.11.036; Satya P. Sharma et al., "Paradoxical Effects of Fruit on Obesity," Nutrients 8, no. 10 (October 14, 2016), https://doi.org/10.3390/nu8100633.

there are 400,000 plants on our planet, 300,000 of them being edible: Carl Lachat et al., "Dietary Species Richness as a Measure of Food Biodiversity and Nutritional Quality of Diets," Proceedings of the National Academy of Sciences of the United States of America 115, no. 1 (January 2, 2018): 127–32, https://doi.org/10.1073/pnas.1709194115.

60,000 of these helpful enzymes: Abdessamad El Kaoutari et al., "The Abundance and Variety of Carbohydrate-Active Enzymes in the Human Gut Microbiota," Nature Reviews. Microbiology 11, no. 7 (2013): 497–504, https://doi.org/10.1038/nrmicro3050.

Every single plant, every single type of fiber: Zhao et al., "Gut Bacteria Selectively Promoted by Dietary Fibers Alleviate Type 2 Diabetes"; Seth Rakoff-Nahoum, Kevin R. Foster, and Laurie E. Comstock, "The Evolution of Cooperation within the Gut Microbiota," Nature 533, no. 7602 (12 2016): 255–59, https://doi.org/10.1038/nature17626.

Each type of fiber we consume produces: Asa M. Henningsson, Inger M. E. Björck, and E. Margareta G. L. Nyman, "Combinations of Indigestible Carbohydrates Affect Short-Chain Fatty Acid Formation in the Hindgut of Rats," The Journal of Nutrition 132, no. 10 (October 2002): 3098–3104, https://doi.org/10.1093/jn/131.10.3098; J. Phillips et al., "Effect of Resistant Starch on Fecal Bulk and Fermentation-Dependent Events in Humans," The American Journal of Clinical Nutrition 62, no. 1 (July 1995): 121–30, https://doi.org/10.1093/ajcn/62.1.121.

"a substrate that is selectively utilized: Glenn R. Gibson et al., "Expert Consensus Document: The International Scientific Association for Probiotics and Prebiotics (ISAPP) Consensus Statement on the Definition and Scope of Prebiotics," Nature Reviews Gastroenterology & Hepatology 14, no. 8 (August 2017): 491–502, https://doi.org/10.1038/nrgastro.2017.75.

Ninety to ninety five percent of polyphenols: M. N. Clifford, "Diet-Derived Phenols in Plasma and Tissues and Their Implications for Health," Planta Medica 70, no. 12 (December 2004): 1103–14, https://doi.org/10.1055/s-2004-835835.

Similarly, omega 3 polyunsaturated fatty acids: Lauri O. Byerley et al., "Changes in the Gut Microbial Communities Following Addition of Walnuts to the Diet," The Journal of Nutritional Biochemistry 48 (October 1, 2017): 94–102, https://doi.org/10.1016/j.jnutbio.2017.07.001; Lara Costantini et al., "Impact of Omega-3 Fatty Acids on the Gut Microbiota," International Journal of Molecular Sciences 18, no. 12 (December 7, 2017): 3, https://doi.org/10.3390/ijms18122645.

Eating fiber also increases the diversity of species: Tien S. Dong and Arpana Gupta, "Influence of Early Life, Diet, and the Environment on the Microbiome," Clinical Gastroenterology and Hepatology 17, no. 2 (January 1, 2019): 231–42, https://doi.org/10.1016/j.cgh.2018.08.067; Jun Miyoshi et al., "Peripartum Antibiotics Promote Gut Dysbiosis, Loss of Immune Tolerance, and Inflammatory Bowel Disease in Genetically Prone Offspring," Cell Reports 20, no. 2 (11 2017): 491–504, https://doi.org/10.1016/j.celrep.2017.06.060; Caesar et al., "Crosstalk between Gut Microbiota and Dietary Lipids Aggravates WAT Inflammation through TLR Signaling."

This change prevents the growth of: Sylvia H. Duncan et al., "The Role of PH in Determining the Species Composition of the Human Colonic Microbiota," Environmental Microbiology 11, no. 8 (August 2009): 2112–22, https://doi.org/10.1111/j.1462-2920.2009.01931.x.

suppress dangerous strains like E. coli and Salmonella: C. A. Cherrington et al., "Short-Chain Organic Acids at Ph 5.0 Kill Escherichia Coli and Salmonella Spp. without Causing Membrane Perturbation," The Journal of Applied Bacteriology 70, no. 2 (February 1991): 161–65, https://doi.org/10.1111/j.1365-2672.1991.tb04442.x; L. Prohászka et al., "The Role of Intestinal Volatile Fatty Acids in the Salmonella Shedding of Pigs," Zentralblatt Fur Veterinarmedizin. Reihe B. Journal of Veterinary Medicine. Series B 37, no. 8 (October 1990): 570–74, https://doi.org/10.1111/j.1439-0450.1990.tb01098.x.

literally eat away at the intestinal lining: Mahesh S. Desai et al., "A Dietary Fiber-Deprived Gut Microbiota Degrades the Colonic Mucus Barrier and Enhances Pathogen Susceptibility," Cell 167, no. 5 (17 2016): 1339-1353.e21, https://doi.org/10.1016/j.cell.2016.10.043.

ten percent of our daily caloric requirements: E. N. Bergman, "Energy Contributions of Volatile Fatty Acids from the Gastrointestinal Tract in Various Species," Physiological Reviews 70, no. 2 (April 1990): 567–90, https://doi.org/10.1152/physrev.1990.70.2.567.

the main source of energy for our colonocytes: W. E. Roediger, "Utilization of Nutrients by Isolated Epithelial Cells of the Rat Colon," Gastroenterology 83, no. 2 (August 1982): 424–29.

This blood-gut barrier is meant for protection: Ashkan Farhadi, Jeremy-Z. Fields, and Ali Keshavarzian, "Mucosal Mast Cells Are Pivotal Elements in Inflammatory Bowel Disease That Connect the Dots: Stress, Intestinal Hyperpermeability and Inflammation," World Journal of Gastroenterology 13, no. 22 (June 14, 2007): 3027–30, https://doi.org/10.3748/wjg.v13.i22.3027.

SCFA butyrate actually REPAIRS "leaky gut": Hong-Bo Wang et al., "Butyrate Enhances Intestinal Epithelial Barrier Function via Up-Regulation of Tight Junction Protein Claudin-1 Transcription," Digestive Diseases and Sciences 57, no. 12 (December 2012): 3126–35, https://doi.org/10.1007/s10620-012-2259-4; Bin Liu et al., "Butyrate Protects Rat Liver against Total Hepatic Ischemia Reperfusion Injury with Bowel Congestion," PloS One 9, no. 8 (2014): e106184, https://doi.org/10.1371/journal.pone.0106184.

affects the function of the intestinal lining: Thomas T. Macdonald and Giovanni Monteleone, "Immunity, Inflammation, and Allergy in the Gut," Science (New York, N.Y.) 307, no. 5717 (March 25, 2005): 1920–25, https://doi.org/10.1126/science.1106442.

sensitization and altered motility that persists: S. Srinivasan and J. W. Wiley, "New Insights into Neural Injury, Repair, and Adaptation in Visceral Afferents and the Enteric Nervous System," Current Opinion in Gastroenterology 16, no. 1 (January 2000): 78–82; QiQi Zhou et al., "MicroRNA-29a Regulates Intestinal Membrane Permeability in Patients with Irritable Bowel Syndrome," Gut 59, no. 6 (June 2010): 775–84, https://doi.org/10.1136/gut.2009.181834; QiQi Zhou et al., "Decreased MiR-199 Augments Visceral Pain in Patients with IBS through Translational Upregulation of TRPV1," Gut 65, no. 5 (May 2016): 797–805, https://doi.org/10.1136/gutjnl-2013-306464.

increase colonic motility and decrease visceral hypersensitivity: Rodolphe Soret et al., "Short-Chain Fatty Acids Regulate the Enteric Neurons and Control Gastrointestinal Motility in Rats," Gastroenterology 138, no. 5 (May 2010): 1772–82, https://doi.org/10.1053/j.gastro.2010.01.053; S. a. L. W. Vanhoutvin et al., "The Effects of Butyrate Enemas on Visceral Perception in Healthy Volunteers," Neurogastroenterology and Motility: The Official Journal of the European Gastrointestinal Motility Society 21, no. 9 (September 2009): 952-e76, https://doi.org/10.1111/j.1365-2982.2009.01324.x.

SCFAs have been shown to inhibit three: H. Lührs et al., "Butyrate Inhibits NF-KappaB Activation in Lamina Propria Macrophages of Patients with Ulcerative Colitis," Scandinavian Journal of Gastroenterology 37, no. 4 (April 2002): 458–66, https://doi.org/10.1080/003655202317316105; Lidija Klampfer et al., "Inhibition of Interferon Gamma Signaling by the Short Chain Fatty Acid Butyrate," Molecular Cancer Research: MCR 1, no. 11 (September 2003): 855–62; C S Byrne et al., "The Role of Short Chain Fatty Acids in Appetite Regulation and Energy Homeostasis," International Journal of Obesity (2005) 39, no. 9 (September 2015): 1331–38, https://doi.org/10.1038/ijo.2015.84; Marco A. R. Vinolo et al., "Suppressive Effect of Short-Chain Fatty Acids on Production of Proinflammatory Mediators by Neutrophils," The Journal of Nutritional Biochemistry 22, no. 9 (September 2011): 849–55, https://doi.org/10.1016/j.jnutbio.2010.07.009.

SCFAs make immune cells more tolerant: Pamela V. Chang et al., "The Microbial Metabolite Butyrate Regulates Intestinal Macrophage Function via Histone Deacetylase Inhibition," Proceedings of the National Academy of Sciences of the United States of America 111, no. 6 (February 11, 2014): 2247–52, https://doi.org/10.1073/pnas.1322269111.

helping to prevent food allergy and sensitivity: Jian Tan et al., "Dietary Fiber and Bacterial SCFA Enhance Oral Tolerance and Protect against Food Allergy through Diverse Cellular Pathways," Cell Reports 15, no. 12 (21 2016): 2809–24, https://doi.org/10.1016/j.celrep.2016.05.047.

SCFAs can even communicate directly: Nicholas Arpaia et al., "Metabolites Produced by Commensal Bacteria Promote Peripheral Regulatory T-Cell Generation," Nature 504, no. 7480 (December 19, 2013): 451–55, https://doi.org/10.1038/nature12726; Yukihiro Furusawa et al., "Commensal Microbe-Derived Butyrate Induces the Differentiation of Colonic Regulatory T Cells," Nature 504, no. 7480 (December 19, 2013): 446–50, https://doi.org/10.1038/nature12721.

Suffice it to say that Crohn's: Michael D. Kappelman et al., "Recent Trends in the Prevalence of Crohn's Disease and Ulcerative Colitis in a Commercially Insured US Population," Digestive Diseases and Sciences 58, no. 2 (February 2013): 519–25, https://doi.org/10.1007/s10620-012-2371-5.

In people with Crohn's, we see: Daniel N. Frank et al., "Disease Phenotype and Genotype Are Associated with Shifts in Intestinal-Associated Microbiota in Inflammatory Bowel Diseases," Inflammatory Bowel Diseases 17, no. 1 (January 2011): 179–84, https://doi.org/10.1002/ibd.21339; Wei Wang et al., "Increased Proportions of Bifidobacterium and the Lactobacillus Group and Loss of Butyrate-Producing Bacteria in Inflammatory Bowel Disease," Journal of Clinical Microbiology 52, no. 2 (February 2014): 398–406, https://doi.org/10.1128/JCM.01500-13; Ray Boyapati, Jack Satsangi, and Gwo-Tzer Ho, "Pathogenesis of Crohn's Disease," F1000prime Reports 7 (2015): 44, https://doi.org/10.12703/P7-44; Carolina Palmela et al., "Adherent-Invasive Escherichia Coli in Inflammatory Bowel Disease," Gut 67, no. 3 (2018): 574–87, https://doi.org/10.1136/gutjnl-2017-314903.

further enhancing dysbiosis and the rise of more E. coli: Marjorie De la Fuente et al., "Escherichia Coli Isolates from Inflammatory Bowel Diseases Patients Survive in Macrophages and Activate NLRP3 Inflammasome," International Journal of Medical Microbiology: IJMM 304, no. 3–4 (May 2014): 384–92, https://doi.org/10.1016/j.ijmm.2014.01.002; Marie-Agnès Bringer et al., "Replication of Crohn's Disease-Associated AIEC within Macrophages Is Dependent on TNF-α Secretion," Laboratory Investigation; a Journal of

Technical Methods and Pathology 92, no. 3 (March 2012): 411–19, https://doi.org/10.1038/labinvest.2011.156.

This loss of balance in the gut, decrease in good bacteria: Maiko Sasaki et al., "Invasive Escherichia Coli Are a Feature of Crohn's Disease," Laboratory Investigation; a Journal of Technical Methods and Pathology 87, no. 10 (October 2007): 1042–54, https://doi.org/10.1038/labinvest.3700661; Eytan Wine et al., "Adherent-Invasive Escherichia Coli, Strain LF82 Disrupts Apical Junctional Complexes in Polarized Epithelia," BMC Microbiology 9 (August 26, 2009): 180, https://doi.org/10.1186/1471-2180-9-180.

depletion of F. prausnitzii and the immune system: Harry Sokol et al., "Faecalibacterium Prausnitzii Is an Anti-Inflammatory Commensal Bacterium Identified by Gut Microbiota Analysis of Crohn Disease Patients," Proceedings of the National Academy of Sciences of the United States of America 105, no. 43 (October 28, 2008): 16731–36, https://doi.org/10.1073/pnas.0804812105.

semi-vegetarian diet maintained a ninety two percent remission rate: Mitsuro Chiba et al., "Lifestyle-Related Disease in Crohn's Disease: Relapse Prevention by a Semi-Vegetarian Diet," World Journal of Gastroenterology 16, no. 20 (May 28, 2010): 2484–95, https://doi.org/10.3748/wjg.v16.i20.2484.

beneficial for disease remission in rheumatoid arthritis: J. Kjeldsen-Kragh et al., "Vegetarian Diet for Patients with Rheumatoid Arthritis--Status: Two Years after Introduction of the Diet," Clinical Rheumatology 13, no. 3 (September 1994): 475–82, https://doi.org/10.1007/bf02242946; I. Hafström et al., "A Vegan Diet Free of Gluten Improves the Signs and Symptoms of Rheumatoid Arthritis: The Effects on Arthritis Correlate with a Reduction in Antibodies to Food Antigens," Rheumatology (Oxford, England) 40, no. 10 (October 2001): 1175–79, https://doi.org/10.1093/rheumatology/40.10.1175; John McDougall et al., "Effects of a Very Low-Fat, Vegan Diet in Subjects with Rheumatoid Arthritis," Journal of Alternative and Complementary Medicine (New York, N.Y.) 8, no. 1 (February 2002): 71–75, https://doi.org/10.1089/107555302753507195;

Ann-Charlotte Elkan et al., "Gluten-Free Vegan Diet Induces Decreased LDL and Oxidized LDL Levels and Raised Atheroprotective Natural Antibodies against Phosphorylcholine in Patients with Rheumatoid Arthritis: A Randomized Study," Arthritis Research & Therapy 10, no. 2 (2008): R34, https://doi.org/10.1186/ar2388.

randomized controlled trial forty-one percent of patients on a vegan diet: Hafström et al., "A Vegan Diet Free of Gluten Improves the Signs and Symptoms of Rheumatoid Arthritis."

dysbiosis has been associated several types of cancer: Sheflin, Whitney, and Weir, "Cancer-Promoting Effects of Microbial Dysbiosis."

butyrate inhibits HDACs: L. B. Bindels et al., "Gut Microbiota-Derived Propionate Reduces Cancer Cell Proliferation in the Liver," British Journal of Cancer 107, no. 8 (October 9, 2012): 1337–44, https://doi.org/10.1038/bjc.2012.409; S. Siavoshian et al., "Butyrate and Trichostatin A Effects on the Proliferation/Differentiation of Human Intestinal Epithelial Cells: Induction of Cyclin D3 and P21 Expression," Gut 46, no. 4 (April 2000): 507–14, https://doi.org/10.1136/gut.46.4.507; S. Khan and G. B. Jena, "Protective Role of Sodium Butyrate, a HDAC Inhibitor on Beta-Cell Proliferation, Function and Glucose Homeostasis through Modulation of P38/ERK MAPK and Apoptotic Pathways: Study in Juvenile Diabetic Rat," Chemico-Biological Interactions 213 (April 25, 2014): 1–12, https://doi.org/10.1016/j.cbi.2014.02.001; M. A. Glozak and E. Seto, "Histone Deacetylases and Cancer," Oncogene 26, no. 37 (August 13, 2007): 5420–32, https://doi.org/10.1038/sj.onc.1210610.

Every day between fifty and seventy billion cells: J. C. Reed, "Dysregulation of Apoptosis in Cancer," Journal of Clinical Oncology: Official Journal of the American Society of Clinical Oncology 17, no. 9 (September 1999): 2941–53, https://doi.org/10.1200/JCO.1999.17.9.2941.

SCFAs help us in the fight against cancer: P. A. Gill et al., "Review Article: Short

Chain Fatty Acids as Potential Therapeutic Agents in Human Gastrointestinal and Inflammatory Disorders," Alimentary Pharmacology & Therapeutics 48, no. 1 (2018): 15–34, https://doi.org/10.1111/apt.14689; Michiko Aoyama, Joji Kotani, and Makoto Usami, "Butyrate and Propionate Induced Activated or Non-Activated Neutrophil Apoptosis via HDAC Inhibitor Activity but without Activating GPR-41/GPR-43 Pathways," Nutrition (Burbank, Los Angeles County, Calif.) 26, no. 6 (June 2010): 653–61, https://doi.org/10.1016/j.nut.2009.07.006; Tain-Hsiung Chen et al., "Sodium Butyrate Activates ERK to Regulate Differentiation of Mesenchymal Stem Cells," Biochemical and Biophysical Research Communications 355, no. 4 (April 20, 2007): 913–18, https://doi.org/10.1016/j.bbrc.2007.02.057; Kim Y. C. Fung et al., "Butyrate-Induced Apoptosis in HCT116 Colorectal Cancer Cells Includes Induction of a Cell Stress Response," Journal of Proteome Research 10, no. 4 (April 1, 2011): 116, https://doi.org/10.1021/pr1011125.

protection against colorectal and breast cancer: Andrew Reynolds et al., "Carbohydrate Quality and Human Health: A Series of Systematic Reviews and Meta-Analyses," The Lancet 393, no. 10170 (February 2, 2019): 434–45, https://doi.org/10.1016/S0140-6736(18)31809-9.

repeatedly shown to protect us from colon cancer: Bindels et al., "Gut Microbiota-Derived Propionate Reduces Cancer Cell Proliferation in the Liver"; Daryl C. Drummond et al., "Clinical Development of Histone Deacetylase Inhibitors as Anticancer Agents," Annual Review of Pharmacology and Toxicology 45 (2005): 495–528, https://doi.org/10.1146/annurev.pharmtox.45.120403.095825; Fung et al., "Butyrate-Induced Apoptosis in HCT116 Colorectal Cancer Cells Includes Induction of a Cell Stress Response," 11; V. Medina et al., "Induction of Caspase-3 Protease Activity and Apoptosis by Butyrate and Trichostatin A (Inhibitors of Histone Deacetylase): Dependence on Protein Synthesis and Synergy with a Mitochondrial/Cytochrome c-Dependent Pathway," Cancer Research 57, no. 17 (September 1, 1997): 3697–3707; Jian Tan et al., "The Role of Short-Chain Fatty Acids in Health and Disease," Advances in Immunology 121 (2014): 91–119, https://doi.

org/10.1016/B978-0-12-800100-4.00003-9; Trond Ulven, "Short-Chain Free Fatty Acid Receptors FFA2/GPR43 and FFA3/GPR41 as New Potential Therapeutic Targets," Frontiers in Endocrinology 3 (2012): 2, https://doi.org/10.3389/fendo.2012.00111.

For every five grams of increased fiber consumption,: Mingyang Song et al., "Fiber Intake and Survival After Colorectal Cancer Diagnosis," JAMA Oncology 4, no. 1 (January 1, 2018): 71–79, https://doi.org/10.1001/jamaoncol.2017.3684.

fiber fueled diet lowers your risk of developing cancer: Monica Dinu et al., "Vegetarian, Vegan Diets and Multiple Health Outcomes: A Systematic Review with Meta-Analysis of Observational Studies," Critical Reviews in Food Science and Nutrition 57, no. 17 (November 22, 2017): 3640–49, https://doi.org/10.1080/10408398.2016.1138447; Timothy J. Key et al., "Cancer in British Vegetarians: Updated Analyses of 4998 Incident Cancers in a Cohort of 32,491 Meat Eaters, 8612 Fish Eaters, 18,298 Vegetarians, and 2246 Vegans," The American Journal of Clinical Nutrition 100 Suppl 1 (July 2014): 378S-85S, https://doi.org/10.3945/ajcn.113.071266; Lap Tai Le and Joan Sabaté, "Beyond Meatless, the Health Effects of Vegan Diets: Findings from the Adventist Cohorts," Nutrients 6, no. 6 (May 27, 2014): 2131–47, https://doi.org/10.3390/nu6062131.

di**etary fiber published in The Lancet, Dr. Reynolds:** Reynolds et al., "Carbohydrate Quality and Human Health."

They help protect against glucose intolerance: Douglas J. Morrison and Tom Preston, "Formation of Short Chain Fatty Acids by the Gut Microbiota and Their Impact on Human Metabolism," Gut Microbes 7, no. 3 (03 2016): 189–200, https://doi.org/10.1080/19490976.2015.1134082; Filipe De Vadder et al., "Microbiota-Generated Metabolites Promote Metabolic Benefits via Gut-Brain Neural Circuits," Cell 156, no. 1–2 (January 16, 2014): 84–96, https://doi.org/10.1016/j.cell.2013.12.016.

soluble fiber is protective against type 2 diabetes: A. I. Vinik and D. J. Jenkins,

"Dietary Fiber in Management of Diabetes," Diabetes Care 11, no. 2 (February 1988): 160–73, https://doi.org/10.2337/diacare.11.2.160.

SCFA-producing microbes that improve blood sugar regulation: Zhao et al., "Gut Bacteria Selectively Promoted by Dietary Fibers Alleviate Type 2 Diabetes."

Same meal at dinner, but different effects: T. M. Wolever et al., "Second-Meal Effect: Low-Glycemic-Index Foods Eaten at Dinner Improve Subsequent Breakfast Glycemic Response," The American Journal of Clinical Nutrition 48, no. 4 (October 1988): 1041–47, https://doi.org/10.1093/ajcn/48.4.1041; D. J. Jenkins et al., "Exceptionally Low Blood Glucose Response to Dried Beans: Comparison with Other Carbohydrate Foods," British Medical Journal 281, no. 6240 (August 30, 1980): 578–80, https://doi.org/10.1136/bmj.281.6240.578; Rebecca C. Mollard et al., "First and Second Meal Effects of Pulses on Blood Glucose, Appetite, and Food Intake at a Later Meal," Applied Physiology, Nutrition, and Metabolism = Physiologie Appliquee, Nutrition Et Metabolisme 36, no. 5 (October 2011): 634–42, https://doi.org/10.1139/h11-071.

We now understand that this happens because the bacteria that we empowered at lunch: Furio Brighenti et al., "Colonic Fermentation of Indigestible Carbohydrates Contributes to the Second-Meal Effect," The American Journal of Clinical Nutrition 83, no. 4 (April 2006): 817–22, https://doi.org/10.1093/ajcn/83.4.817.

SCFAs also lower cholesterol by: Morrison and Preston, "Formation of Short Chain Fatty Acids by the Gut Microbiota and Their Impact on Human Metabolism."

Further, SCFAs directly activate a receptor in fat cells: Ikuo Kimura et al., "The Gut Microbiota Suppresses Insulin-Mediated Fat Accumulation via the Short-Chain Fatty Acid Receptor GPR43," Nature Communications 4 (2013): 43, https://doi.org/10.1038/ncomms2852.

Additionally, SCFAs promote the release of satiety hormones: Gill et al., "Review Article."

increased satiety hormones after eating a plant based burger: Marta Klementova et al., "A Plant-Based Meal Increases Gastrointestinal Hormones and Satiety More Than an Energy- and Macronutrient-Matched Processed-Meat Meal in T2D, Obese, and Healthy Men: A Three-Group Randomized Crossover Study," Nutrients 11, no. 1 (January 2019): 157, https://doi.org/10.3390/nu11010157.

Finally, patients with symptomatic coronary artery disease: Fredrik H. Karlsson et al., "Symptomatic Atherosclerosis Is Associated with an Altered Gut Metagenome," Nature Communications 3 (2012): 1245, https://doi.org/10.1038/ncomms2266.

protect against congestive heart failure and hight blood pressure: Francine Z. Marques et al., "High-Fiber Diet and Acetate Supplementation Change the Gut Microbiota and Prevent the Development of Hypertension and Heart Failure in Hypertensive Mice," Circulation 135, no. 10 (March 7, 2017): 964–77, https://doi.org/10.1161/CIRCULATIONAHA.116.024545.

prevent atherosclerosis by maintaining gut barrier function and limiting bacterial endotoxin release: Kazuyuki Kasahara et al., "Interactions between Roseburia Intestinalis and Diet Modulate Atherogenesis in a Murine Model," Nature Microbiology 3, no. 12 (2018): 1461–71, https://doi.org/10.1038/s41564-018-0272-x.

less butyrate and more TMAO: Xiao Cui et al., "Metagenomic and Metabolomic Analyses Unveil Dysbiosis of Gut Microbiota in Chronic Heart Failure Patients," Scientific Reports 8 (December 1, 2018), https://doi.org/10.1038/s41598-017-18756-2.

SCFAs work similar magic on the blood brain barrier: Viorica Braniste et al.,

"The Gut Microbiota Influences Blood-Brain Barrier Permeability in Mice," Science Translational Medicine 6, no. 263 (November 19, 2014): 263ra158, https://doi.org/10.1126/scitranslmed.3009759.

This has been demonstrated in models of Alzheimer's: Megan W. Bourassa et al., "Butyrate, Neuroepigenetics and the Gut Microbiome: Can a High Fiber Diet Improve Brain Health?," Neuroscience Letters 625 (20 2016): 56–63, https://doi.org/10.1016/j.neulet.2016.02.009.

SCFAs interfere with the formation of this exact same amyloid: Lap Ho et al., "Protective Roles of Intestinal Microbiota Derived Short Chain Fatty Acids in Alzheimer's Disease-Type Beta-Amyloid Neuropathological Mechanisms," Expert Review of Neurotherapeutics 18, no. 1 (January 2018): 83–90, https://doi.org/10.1080/14737175.2018.1400909.

butyrate protects the brain in models of Parkinson's: Sorabh Sharma, Rajeev Taliyan, and Sumel Singh, "Beneficial Effects of Sodium Butyrate in 6-OHDA Induced Neurotoxicity and Behavioral Abnormalities: Modulation of Histone Deacetylase Activity," Behavioural Brain Research 291 (September 15, 2015): 306–14, https://doi.org/10.1016/j.bbr.2015.05.052; Sarah K. Kidd and Jay S. Schneider, "Protection of Dopaminergic Cells from MPP+-Mediated Toxicity by Histone Deacetylase Inhibition," Brain Research 1354 (October 1, 2010): 172–78, https://doi.org/10.1016/j.brainres.2010.07.041; R. St Laurent, L. M. O'Brien, and S. T. Ahmad, "Sodium Butyrate Improves Locomotor Impairment and Early Mortality in a Rotenone-Induced Drosophila Model of Parkinson's Disease," Neuroscience 246 (August 29, 2013): 382–90, https://doi.org/10.1016/j.neuroscience.2013.04.037; Jiaming Liu et al., "Sodium Butyrate Exerts Protective Effect against Parkinson's Disease in Mice via Stimulation of Glucagon like Peptide-1," Journal of the Neurological Sciences 381 (October 15, 2017): 176–81, https://doi.org/10.1016/j.jns.2017.08.3235; Bourassa et al., "Butyrate, Neuroepigenetics and the Gut Microbiome."

Parkinson's disease have lower levels of the bacteria: Ali Keshavarzian et al.,

"Colonic Bacterial Composition in Parkinson's Disease," Movement Disorders 30, no. 10 (2015): 1351–60, https://doi.org/10.1002/mds.26307; Marcus M. Unger et al., "Short Chain Fatty Acids and Gut Microbiota Differ between Patients with Parkinson's Disease and Age-Matched Controls," Parkinsonism & Related Disorders 32 (November 1, 2016): 66–72, https://doi.org/10.1016/j.parkreldis.2016.08.019.

high fiber diet demonstrate better cognitive control: Naiman A. Khan et al., "Dietary Fiber Is Positively Associated with Cognitive Control among Prepubertal Children," The Journal of Nutrition 145, no. 1 (January 2015): 143–49, https://doi.org/10.3945/jn.114.198457.

Westernization has led to a loss of gut microbial diversity: Samuel A. Smits et al., "Seasonal Cycling in the Gut Microbiome of the Hadza Hunter-Gatherers of Tanzania," Science (New York, N.Y.) 357, no. 6353 (25 2017): 802–6, https://doi.org/10.1126/science.aan4834.

African Americans have sixty five times more colon cancer: Stephen J. D. O'Keefe et al., "Fat, Fibre and Cancer Risk in African Americans and Rural Africans," Nature Communications 6 (April 28, 2015): 6342, https://doi.org/10.1038/ncomms7342; S. J. O'Keefe et al., "Rarity of Colon Cancer in Africans Is Associated with Low Animal Product Consumption, Not Fiber," The American Journal of Gastroenterology 94, no. 5 (May 1999): 1373–80, https://doi.org/10.1111/j.1572-0241.1999.01089.x.

One interesting study involved switching the diets: O'Keefe et al., "Fat, Fibre and Cancer Risk in African Americans and Rural Africans."

microbial diversity that could be compounded over a series of generations: Erica D. Sonnenburg et al., "Diet-Induced Extinctions in the Gut Microbiota Compound over Generations," Nature 529, no. 7585 (January 14, 2016): 212–15, https://doi.org/10.1038/nature16504.

CHAPTER 4

A diet that maximizes a variety of dietary fibers and resistant starches: El Kaoutari et al., "The Abundance and Variety of Carbohydrate-Active Enzymes in the Human Gut Microbiota"; J. H. Cummings and G. T. Macfarlane, "The Control and Consequences of Bacterial Fermentation in the Human Colon," The Journal of Applied Bacteriology 70, no. 6 (June 1991): 443–59, https://doi.org/10.1111/j.1365-2672.1991.tb02739.x.

a 2014 study compared the overall nutritional value of multiple different diets: Peter Clarys et al., "Comparison of Nutritional Quality of the Vegan, Vegetarian, Semi-Vegetarian, Pesco-Vegetarian and Omnivorous Diet," Nutrients 6, no. 3 (March 24, 2014): 1318–32, https://doi.org/10.3390/nu6031318.

Barley has a PREbiotic fiber called beta-glucan: Mattia P. Arena et al., "Barley β-Glucans-Containing Food Enhances Probiotic Performances of Beneficial Bacteria," International Journal of Molecular Sciences 15, no. 2 (February 20, 2014): 3025–39, https://doi.org/10.3390/ijms15023025; Evdokia K. Mitsou et al., "Prebiotic Potential of Barley Derived β-Glucan at Low Intake Levels: A Randomised, Double-Blinded, Placebo-Controlled Clinical Study," Food Research International 43, no. 4 (May 1, 2010): 1086–92, https://doi.org/10.1016/j.foodres.2010.01.020; Kay M. Behall, Daniel J. Scholfield, and Judith Hallfrisch, "Diets Containing Barley Significantly Reduce Lipids in Mildly Hypercholesterolemic Men and Women," The American Journal of Clinical Nutrition 80, no. 5 (November 2004): 1185–93, https://doi.org/10.1093/ajcn/80.5.1185; Kay M. Behall, Daniel J. Scholfield, and Judith Hallfrisch, "Comparison of Hormone and Glucose Responses of Overweight Women to Barley and Oats," Journal of the American College of Nutrition 24, no. 3 (June 2005): 182–88, https://doi.org/10.1080/07315724.2005.10719464.

selenium, which is important for thyroid health: Elias E. Mazokopakis et al., "Effects of 12 Months Treatment with L-Selenomethionine on Serum Anti-TPO Levels in Patients with Hashimoto's Thyroiditis," Thyroid: Official Journal of the American Thyroid Association 17, no. 7 (July 2007): 609–12, https://doi.

org/10.1089/thy.2007.0040.

oats have phenolic acids that offer: Chung-Yen Chen et al., "Avenanthramides and Phenolic Acids from Oats Are Bioavailable and Act Synergistically with Vitamin C to Enhance Hamster and Human LDL Resistance to Oxidation," The Journal of Nutrition 134, no. 6 (June 2004): 1459–66, https://doi.org/10.1093/jn/134.6.1459; Liping Liu et al., "The Antiatherogenic Potential of Oat Phenolic Compounds," Atherosclerosis 175, no. 1 (July 2004): 39–49, https://doi.org/10.1016/j.atherosclerosis.2004.01.044.

kick your gut microbes into high gear: Priyanka Kajla, Alka Sharma, and Dev Raj Sood, "Flaxseed-a Potential Functional Food Source," Journal of Food Science and Technology 52, no. 4 (April 2015): 1857–71, https://doi.org/10.1007/s13197-014-1293-y; Mette Kristensen et al., "Flaxseed Dietary Fibers Lower Cholesterol and Increase Fecal Fat Excretion, but Magnitude of Effect Depend on Food Type," Nutrition & Metabolism 9 (February 3, 2012): 8, https://doi.org/10.1186/1743-7075-9-8.

arabinoxylan oligosaccharides shown to boost healthy gut microbes: Isabelle E. J. A. François et al., "Effects of Wheat Bran Extract Containing Arabinoxylan Oligosaccharides on Gastrointestinal Parameters in Healthy Preadolescent Children," Journal of Pediatric Gastroenterology and Nutrition 58, no. 5 (May 2014): 647–53, https://doi.org/10.1097/MPG.0000000000000285; Kevin C. Maki et al., "Digestive and Physiologic Effects of a Wheat Bran Extract, Arabino-Xylan-Oligosaccharide, in Breakfast Cereal," Nutrition (Burbank, Los Angeles County, Calif.) 28, no. 11–12 (December 2012): 1115–21, https://doi.org/10.1016/j.nut.2012.02.010; Bram Damen et al., "Consumption of Breads Containing in Situ-Produced Arabinoxylan Oligosaccharides Alters Gastrointestinal Effects in Healthy Volunteers," The Journal of Nutrition 142, no. 3 (March 2012): 470–77, https://doi.org/10.3945/jn.111.146464; Gemma E. Walton et al., "A Randomised, Double-Blind, Placebo Controlled Cross-over Study to Determine the Gastrointestinal Effects of Consumption of Arabinoxylan-Oligosaccharides Enriched Bread in Healthy Volunteers,"

Nutrition Journal 11 (June 1, 2012): 36, https://doi.org/10.1186/1475-2891-11-36; Isabelle E. J. A. François et al., "Effects of a Wheat Bran Extract Containing Arabinoxylan Oligosaccharides on Gastrointestinal Health Parameters in Healthy Adult Human Volunteers: A Double-Blind, Randomised, Placebo-Controlled, Cross-over Trial," The British Journal of Nutrition 108, no. 12 (December 28, 2012): 2229–42, https://doi.org/10.1017/S0007114512000372.

increased SCFA levels more than inulin: Nielson T. Baxter et al., "Dynamics of Human Gut Microbiota and Short-Chain Fatty Acids in Response to Dietary Interventions with Three Fermentable Fibers," MBio 10, no. 1 (29 2019), https://doi.org/10.1128/mBio.02566-18.

If you heat and cool repeatedly: J. G. Muir and K. O'Dea, "Measurement of Resistant Starch: Factors Affecting the Amount of Starch Escaping Digestion in Vitro," The American Journal of Clinical Nutrition 56, no. 1 (July 1992): 123–27, https://doi.org/10.1093/ajcn/56.1.123.

Seaweed rocks fiber content that is: M. Lahaye, "Marine algae as sources of fibres: Determination of soluble and insoluble dietary fibre contents in some 'sea vegetables,'" Journal of the Science of Food and Agriculture 54, no. 4 (1991): 587–94, https://doi.org/10.1002/jsfa.2740540410; Laurie O'Sullivan et al., "Prebiotics from Marine Macroalgae for Human and Animal Health Applications," Marine Drugs 8, no. 7 (July 1, 2010): 2038–64, https://doi.org/10.3390/md8072038.

there are at least 8,000 of them: Rui Hai Liu, "Health Benefits of Fruit and Vegetables Are from Additive and Synergistic Combinations of Phytochemicals," The American Journal of Clinical Nutrition 78, no. 3 (September 1, 2003): 517S-520S, https://doi.org/10.1093/ajcn/78.3.517S.

"Apple Fiber Constipation Relief," LIVESTRONG.COM, accessed August 14, 2019, https://www.livestrong.com/article/355320-apple-fiber-constipation-relief/.

Quercetin-3-galactoside, quercetin-3-glucoside,: Jeanelle Boyer and Rui Hai Liu, "Apple Phytochemicals and Their Health Benefits," Nutrition Journal 3 (May 12, 2004): 5, https://doi.org/10.1186/1475-2891-3-5.

apples have been found to reduce the risk of developing cancer: Boyer and Liu.

that was additive and synergistic: Liu, "Health Benefits of Fruit and Vegetables Are from Additive and Synergistic Combinations of Phytochemicals."

Heme iron comes from animal products: Wei Bao et al., "Dietary Iron Intake, Body Iron Stores, and the Risk of Type 2 Diabetes: A Systematic Review and Meta-Analysis," BMC Medicine 10 (October 10, 2012): 119, https://doi.org/10.1186/1741-7015-10-119; Ana Fonseca-Nunes, Paula Jakszyn, and Antonio Agudo, "Iron and Cancer Risk--a Systematic Review and Meta-Analysis of the Epidemiological Evidence," Cancer Epidemiology, Biomarkers & Prevention: A Publication of the American Association for Cancer Research, Cosponsored by the American Society of Preventive Oncology 23, no. 1 (January 2014): 12–31, https://doi.org/10.1158/1055-9965.EPI-13-0733; Wei Yang et al., "Is Heme Iron Intake Associated with Risk of Coronary Heart Disease? A Meta-Analysis of Prospective Studies," European Journal of Nutrition 53, no. 2 (2014): 395–400, https://doi.org/10.1007/s00394-013-0535-5.

The vitamin C from a lemon cranks up: L. Hallberg, M. Brune, and L. Rossander, "The Role of Vitamin C in Iron Absorption," International Journal for Vitamin and Nutrition Research. Supplement = Internationale Zeitschrift Fur Vitamin- Und Ernahrungsforschung. Supplement 30 (1989): 103–8.

increase the bioavailability of curcumin by 2000%: G. Shoba et al., "Influence of Piperine on the Pharmacokinetics of Curcumin in Animals and Human Volunteers," Planta Medica 64, no. 4 (May 1998): 353–56, https://doi.org/10.1055/s-2006-957450.

just two pieces of whole grain bread rewarded the participants: Dagfinn Aune et al., "Whole Grain Consumption and Risk of Cardiovascular Disease, Cancer, and All Cause and Cause Specific Mortality: Systematic Review and Dose-Response Meta-Analysis of Prospective Studies," BMJ (Clinical Research Ed.) 353 (June 14, 2016): i2716, https://doi.org/10.1136/bmj.i2716.

whole grains reduces your risk of death by five percent: Hongyu Wu et al., "Association between Dietary Whole Grain Intake and Risk of Mortality: Two Large Prospective Studies in US Men and Women," JAMA Internal Medicine 175, no. 3 (March 2015): 373–84, https://doi.org/10.1001/jamainternmed.2014.6283.

eating the most whole grains had a fourteen percent lower risk of stroke: Liqun Fang et al., "Association between Whole Grain Intake and Stroke Risk: Evidence from a Meta-Analysis," International Journal of Clinical and Experimental Medicine 8, no. 9 (2015): 16978–83.

twenty percent reduction in the risk of colorectal cancer for every three servings of whole grains: Dagfinn Aune et al., "Dietary Fibre, Whole Grains, and Risk of Colorectal Cancer: Systematic Review and Dose-Response Meta-Analysis of Prospective Studies," BMJ (Clinical Research Ed.) 343 (November 10, 2011): d6617, https://doi.org/10.1136/bmj.d6617.

whole grains daily was linked to lower body mass index and less belly fat: Janice I. Harland and Lynne E. Garton, "Whole-Grain Intake as a Marker of Healthy Body Weight and Adiposity," Public Health Nutrition 11, no. 6 (June 2008): 554–63, https://doi.org/10.1017/S1368980007001279.

found to be protective on sub-analysis: Aune et al., "Whole Grain and Refined Grain Consumption and the Risk of Type 2 Diabetes."

whole grains were good for the gut: Sally M. Vanegas et al., "Substituting Whole Grains for Refined Grains in a 6-Wk Randomized Trial Has a Modest

Effect on Gut Microbiota and Immune and Inflammatory Markers of Healthy Adults," The American Journal of Clinical Nutrition 105, no. 3 (March 1, 2017): 635–50, https://doi.org/10.3945/ajcn.116.146928.

Paleolithic diet made the gut microbiota less healthy: Genoni et al., "Long-Term Paleolithic Diet Is Associated with Lower Resistant Starch Intake, Different Gut Microbiota Composition and Increased Serum TMAO Concentrations."

healthy subjects without celiac spent a month on a gluten free diet: Giada De Palma et al., "Effects of a Gluten-Free Diet on Gut Microbiota and Immune Function in Healthy Adult Human Subjects," The British Journal of Nutrition 102, no. 8 (October 2009): 1154–60, https://doi.org/10.1017/S0007114509371767.

there was a difference in immune reactivity in a test tube: Lea B. S. Hansen et al., "A Low-Gluten Diet Induces Changes in the Intestinal Microbiome of Healthy Danish Adults," Nature Communications 9 (December 1, 2018), https://doi.org/10.1038/s41467-018-07019-x.

IMPROVED intestinal integrity and reduced intestinal permeability: E. G. Christensen et al., "Bifidogenic Effect of Whole-Grain Wheat during a 12-Week Energy-Restricted Dietary Intervention in Postmenopausal Women," European Journal of Clinical Nutrition 67, no. 12 (December 2013): 1316–21, https://doi.org/10.1038/ejcn.2013.207.

A "low gluten" diet causes loss of the genes: B. S. Hansen et al., "A Low-Gluten Diet Induces Changes in the Intestinal Microbiome of Healthy Danish Adults."

people consumed more gluten their risk of ischemic heart disease decreased: Benjamin Lebwohl et al., "Long Term Gluten Consumption in Adults without Celiac Disease and Risk of Coronary Heart Disease: Prospective Cohort Study," BMJ (Clinical Research Ed.) 357 (May 2, 2017): j1892, https://doi.org/10.1136/bmj.j1892.

It's worth noting that this is the complete opposite of: Jonas F. Ludvigsson et al., "Nationwide Cohort Study of Risk of Ischemic Heart Disease in Patients with Celiac Disease," Circulation 123, no. 5 (February 8, 2011): 483–90, https://doi.org/10.1161/CIRCULATIONAHA.110.965624.

down by twenty percent compared to fifty years ago: "FAOSTAT," accessed October 26, 2019, http://www.fao.org/faostat/en/#data/CC.

Your waist gets smaller: Yanni Papanikolaou and Victor L. Fulgoni, "Bean Consumption Is Associated with Greater Nutrient Intake, Reduced Systolic Blood Pressure, Lower Body Weight, and a Smaller Waist Circumference in Adults: Results from the National Health and Nutrition Examination Survey 1999-2002," Journal of the American College of Nutrition 27, no. 5 (October 2008): 569–76, https://doi.org/10.1080/07315724.2008.10719740.

Your blood pressure and cholesterol drops: Helen Hermana M. Hermsdorff et al., "A Legume-Based Hypocaloric Diet Reduces Proinflammatory Status and Improves Metabolic Features in Overweight/Obese Subjects," European Journal of Nutrition 50, no. 1 (February 2011): 61–69, https://doi.org/10.1007/s00394-010-0115-x; Saman Abeysekara et al., "A Pulse-Based Diet Is Effective for Reducing Total and LDL-Cholesterol in Older Adults," The British Journal of Nutrition 108 Suppl 1 (August 2012): S103-110, https://doi.org/10.1017/S0007114512000748.

Your blood sugar balances: Nerea Becerra-Tomás et al., "Legume Consumption Is Inversely Associated with Type 2 Diabetes Incidence in Adults: A Prospective Assessment from the PREDIMED Study," Clinical Nutrition (Edinburgh, Scotland) 37, no. 3 (2018): 906–13, https://doi.org/10.1016/j.clnu.2017.03.015.

heart attack or developing colon cancer just got chopped in half: Edmond K. Kabagambe et al., "Decreased Consumption of Dried Mature Beans Is Positively Associated with Urbanization and Nonfatal Acute Myocardial Infarction," The Journal of Nutrition 135, no. 7 (July 2005): 1770–75, https://doi.

org/10.1093/jn/135.7.1770; P. N. Singh and G. E. Fraser, “Dietary Risk Factors for Colon Cancer in a Low-Risk Population,” American Journal of Epidemiology 148, no. 8 (October 15, 1998): 761–74, https://doi.org/10.1093/oxfordjournals.aje.a009697.

lost more weight even though they ate the same number of calories: Hermsdorff et al., “A Legume-Based Hypocaloric Diet Reduces Proinflammatory Status and Improves Metabolic Features in Overweight/Obese Subjects.”

They have a number of health benefits, including: Gianluca Rizzo and Luciana Baroni, “Soy, Soy Foods and Their Role in Vegetarian Diets,” Nutrients 10, no. 1 (January 2018): 43, https://doi.org/10.3390/nu10010043; J. W. Anderson, B. M. Johnstone, and M. E. Cook-Newell, “Meta-Analysis of the Effects of Soy Protein Intake on Serum Lipids,” The New England Journal of Medicine 333, no. 5 (August 3, 1995): 276–82, https://doi.org/10.1056/NEJM199508033330502; T. Hertrampf et al., “The Bone-Protective Effect of the Phytoestrogen Genistein Is Mediated via ER Alpha-Dependent Mechanisms and Strongly Enhanced by Physical Activity,” Bone 40, no. 6 (June 2007): 1529–35, https://doi.org/10.1016/j.bone.2007.02.006.

Equol can be produced by 50-60% of Asian people: Rizzo and Baroni, “Soy, Soy Foods and Their Role in Vegetarian Diets.”

diets high in carbohydrates (really meaning fiber) and low in saturated fat: I. R. Rowland et al., “Interindividual Variation in Metabolism of Soy Isoflavones and Lignans: Influence of Habitual Diet on Equol Production by the Gut Microflora,” Nutrition and Cancer 36, no. 1 (2000): 27–32, https://doi.org/10.1207/S15327914NC3601_5; Eva Lydeking-Olsen et al., “Soymilk or Progesterone for Prevention of Bone Loss--a 2 Year Randomized, Placebo-Controlled Trial,” European Journal of Nutrition 43, no. 4 (August 2004): 246–57, https://doi.org/10.1007/s00394-004-0497-8; Charlotte Atkinson et al., “In Vitro Incubation of Human Feces with Daidzein and Antibiotics Suggests Interindividual

Differences in the Bacteria Responsible for Equol Production," The Journal of Nutrition 134, no. 3 (March 2004): 596–99, https://doi.org/10.1093/jn/134.3.596.

both navy beans and black beans increased numbers of beneficial SCFA-producing bacteria: Jennifer M. Monk et al., "Navy and Black Bean Supplementation Primes the Colonic Mucosal Microenvironment to Improve Gut Health," The Journal of Nutritional Biochemistry 49 (2017): 89–100, https://doi.org/10.1016/j.jnutbio.2017.08.002.

In a randomized crossover study, chickpea consumption: W. M. U. Fernando et al., "Diets Supplemented with Chickpea or Its Main Oligosaccharide Component Raffinose Modify Faecal Microbial Composition in Healthy Adults," Beneficial Microbes 1, no. 2 (June 2010): 197–207, https://doi.org/10.3920/BM2009.0027.

may beneficially impact the intestinal environment: Dominika et al., "The Study on the Impact of Glycated Pea Proteins on Human Intestinal Bacteria."

one – and only one – food shown to make people live longer: Irene Darmadi-Blackberry et al., "Legumes: The Most Important Dietary Predictor of Survival in Older People of Different Ethnicities," Asia Pacific Journal of Clinical Nutrition 13, no. 2 (2004): 217–20.

They're actually ubiquitous in nature: Jeremy M. Berg, John L. Tymoczko, and Lubert Stryer, "Lectins Are Specific Carbohydrate-Binding Proteins," Biochemistry. 5th Edition, 2002, https://www.ncbi.nlm.nih.gov/books/NBK22545/.

based on test tube and animal model studies: "Dietary Lectins as Disease Causing Toxicants," Science Alert, accessed October 26, 2019, https://doi.org/10.3923/pjn.2009.293.303.

have all been implicated as protective against cancer: L. Yu et al., "Reversible Inhibition of Proliferation of Epithelial Cell Lines by Agaricus Bisporus (Edible Mushroom) Lectin," Cancer Research 53, no. 19 (October 1, 1993): 4627–32; Maria E. Carrizo et al., "The Antineoplastic Lectin of the Common Edible Mushroom (Agaricus Bisporus) Has Two Binding Sites, Each Specific for a Different Configuration at a Single Epimeric Hydroxyl," The Journal of Biological Chemistry 280, no. 11 (March 18, 2005): 10614–23, https://doi.org/10.1074/jbc.M411989200; M. Jordinson et al., "Vicia Faba Agglutinin, the Lectin Present in Broad Beans, Stimulates Differentiation of Undifferentiated Colon Cancer Cells," Gut 44, no. 5 (May 1999): 709–14, https://doi.org/10.1136/gut.44.5.709; Prashanta Kumar Panda et al., "Antitumor Effect of Soybean Lectin Mediated through Reactive Oxygen Species-Dependent Pathway," Life Sciences 111, no. 1–2 (August 28, 2014): 27–35, https://doi.org/10.1016/j.lfs.2014.07.004; Senjam Sunil Singh, Sanjenbam Kunjeshwori Devi, and Tzi Bun Ng, "Banana Lectin: A Brief Review," Molecules (Basel, Switzerland) 19, no. 11 (November 17, 2014): 18817–27, https://doi.org/10.3390/molecules191118817; C. Z. Bai et al., "Stimulation of Dendritic Cell Maturation and Induction of Apoptosis in Lymphoma Cells by a Stable Lectin from Buckwheat Seeds," Genetics and Molecular Research: GMR 14, no. 1 (March 27, 2015): 2162–75, https://doi.org/10.4238/2015.March.27.3; Lu-Gang Yu et al., "Protein Phosphatase 2A, a Negative Regulator of the ERK Signaling Pathway, Is Activated by Tyrosine Phosphorylation of Putative HLA Class II-Associated Protein I (PHAPI)/Pp32 in Response to the Antiproliferative Lectin, Jacalin," The Journal of Biological Chemistry 279, no. 40 (October 1, 2004): 41377–83, https://doi.org/10.1074/jbc.M400017200; Constanze Ebert et al., "Inhibitory Effect of the Lectin Wheat Germ Agglutinin (WGA) on the Proliferation of AR42J Cells," Acta Histochemica 111, no. 4 (2009): 335–42, https://doi.org/10.1016/j.acthis.2008.11.017.

Costa Rica outperforms the United States in life expectancy: Luis Rosero-Bixby and William H. Dow, "Exploring Why Costa Rica Outperforms the United States in Life Expectancy: A Tale of Two Inequality Gradients," Proceedings of the National Academy of Sciences of the United States of America 113, no. 5

(February 2, 2016): 1130–37, https://doi.org/10.1073/pnas.1521917112.

CHAPTER 5

Statistically that's fifteen to twenty percent of people: M. C. E. Lomer, "Review Article: The Aetiology, Diagnosis, Mechanisms and Clinical Evidence for Food Intolerance," Alimentary Pharmacology & Therapeutics 41, no. 3 (February 2015): 262–75, https://doi.org/10.1111/apt.13041.

Fifty to eighty percent of people: Paula A. Hayes, Marianne H. Fraher, and Eamonn M. M. Quigley, "Irritable Bowel Syndrome: The Role of Food in Pathogenesis and Management," Gastroenterology & Hepatology 10, no. 3 (March 2014): 164–74; Lena Böhn et al., "Self-Reported Food-Related Gastrointestinal Symptoms in IBS Are Common and Associated with More Severe Symptoms and Reduced Quality of Life," The American Journal of Gastroenterology 108, no. 5 (May 2013): 634–41, https://doi.org/10.1038/ajg.2013.105.

you are 99.9% genetically the same: 1000 Genomes Project Consortium et al., "A Global Reference for Human Genetic Variation," Nature 526, no. 7571 (October 1, 2015): 68–74, https://doi.org/10.1038/nature15393.

If you had an identical twin, you'd most closely resemble your twin: Peter J. Turnbaugh et al., "A Core Gut Microbiome in Obese and Lean Twins," Nature 457, no. 7228 (January 22, 2009): 480–84, https://doi.org/10.1038/nature07540.

get one hundred grams of fiber or more per day: Smits et al., "Seasonal Cycling in the Gut Microbiome of the Hadza Hunter-Gatherers of Tanzania."

seventy five percent of the world's population are deficient: Yuval Itan et al., "A Worldwide Correlation of Lactase Persistence Phenotype and Genotypes," BMC Evolutionary Biology 10 (February 9, 2010): 36, https://doi.org/10.1186/1471-2148-10-36.

regular consumption of lactose over the course of ten days led to adaptation: S. R. Hertzler and D. A. Savaiano, "Colonic Adaptation to Daily Lactose Feeding in Lactose Maldigesters Reduces Lactose Intolerance," The American Journal of Clinical Nutrition 64, no. 2 (August 1996): 232–36, https://doi.org/10.1093/ajcn/64.2.232.

improved efficiency of lactose digestion and reduced gas production by three fold: S. R. Hertzler, D. A. Savaiano, and M. D. Levitt, "Fecal Hydrogen Production and Consumption Measurements. Response to Daily Lactose Ingestion by Lactose Maldigesters," Digestive Diseases and Sciences 42, no. 2 (February 1997): 348–53, https://doi.org/10.1023/a:1018822103911.

associated with prostate cancer and Parkinson's disease: Dagfinn Aune et al., "Dairy Products, Calcium, and Prostate Cancer Risk: A Systematic Review and Meta-Analysis of Cohort Studies," The American Journal of Clinical Nutrition 101, no. 1 (January 2015): 87–117, https://doi.org/10.3945/ajcn.113.067157; Yan Song et al., "Whole Milk Intake Is Associated with Prostate Cancer-Specific Mortality among U.S. Male Physicians," The Journal of Nutrition 143, no. 2 (February 2013): 189–96, https://doi.org/10.3945/jn.112.168484; Katherine C. Hughes et al., "Intake of Dairy Foods and Risk of Parkinson Disease," Neurology 89, no. 1 (July 4, 2017): 46–52, https://doi.org/10.1212/WNL.0000000000004057; Elsa H. Spencer, Hope R. Ferdowsian, and Neal D. Barnard, "Diet and Acne: A Review of the Evidence," International Journal of Dermatology 48, no. 4 (April 2009): 339–47, https://doi.org/10.1111/j.1365-4632.2009.04002.x.

increased risk of hip fracture: Diane Feskanich et al., "Milk Consumption during Teenage Years and Risk of Hip Fractures in Older Adults," JAMA Pediatrics 168, no. 1 (January 2014): 54–60, https://doi.org/10.1001/jamapediatrics.2013.3821.

high milk intake was associated with increased risk of: Karl Michaëlsson et al., "Milk Intake and Risk of Mortality and Fractures in Women and Men: Cohort

Studies," BMJ (Clinical Research Ed.) 349 (October 28, 2014): g6015, https://doi.org/10.1136/bmj.g6015.

lactose is actually a prebiotic: Andrew Szilagyi, "Redefining Lactose as a Conditional Prebiotic," Canadian Journal of Gastroenterology = Journal Canadien De Gastroenterologie 18, no. 3 (March 2004): 163–67, https://doi.org/10.1155/2004/350732.

When we damage the gut and reduce diversity: Brent L. Williams et al., "Impaired Carbohydrate Digestion and Transport and Mucosal Dysbiosis in the Intestines of Children with Autism and Gastrointestinal Disturbances," PLoS ONE 6, no. 9 (September 16, 2011), https://doi.org/10.1371/journal.pone.0024585; "Mechanisms by Which Gut Microorganisms Influence Food Sensitivities | Nature Reviews Gastroenterology & Hepatology," accessed August 27, 2019, https://www.nature.com/articles/s41575-018-0064-z.

methane gas slows gut motility: Mark Pimentel et al., "Methane, a Gas Produced by Enteric Bacteria, Slows Intestinal Transit and Augments Small Intestinal Contractile Activity," American Journal of Physiology. Gastrointestinal and Liver Physiology 290, no. 6 (June 2006): G1089-1095, https://doi.org/10.1152/ajpgi.00574.2004.

constipation increases the amount of gas: Ashok Attaluri et al., "Methanogenic Flora Is Associated with Altered Colonic Transit but Not Stool Characteristics in Constipation without IBS," The American Journal of Gastroenterology 105, no. 6 (June 2010): 1407–11, https://doi.org/10.1038/ajg.2009.655.

About 1% of Americans have celiac disease: Naiyana Gujral, Hugh J. Freeman, and Alan B. R. Thomson, "Celiac Disease: Prevalence, Diagnosis, Pathogenesis and Treatment," World Journal of Gastroenterology 18, no. 42 (November 14, 2012): 6036–59, https://doi.org/10.3748/wjg.v18.i42.6036.

In other words, it's impossible to have celiac disease: Katri Kaukinen et al.,

"HLA-DQ Typing in the Diagnosis of Celiac Disease," The American Journal of Gastroenterology 97, no. 3 (March 2002): 695–99, https://doi.org/10.1111/j.1572-0241.2002.05471.x.

A pathologist uses special criteria: M. N. Marsh, "Gluten, Major Histocompatibility Complex, and the Small Intestine. A Molecular and Immunobiologic Approach to the Spectrum of Gluten Sensitivity ('celiac Sprue')," Gastroenterology 102, no. 1 (January 1992): 330–54; G. Oberhuber, G. Granditsch, and H. Vogelsang, "The Histopathology of Coeliac Disease: Time for a Standardized Report Scheme for Pathologists," European Journal of Gastroenterology & Hepatology 11, no. 10 (October 1999): 1185–94, https://doi.org/10.1097/00042737-199910000-00019.

studies showing that Grade I and II are celiac too: Jonas F. Ludvigsson et al., "The Oslo Definitions for Coeliac Disease and Related Terms," Gut 62, no. 1 (January 2013): 43–52, https://doi.org/10.1136/gutjnl-2011-301346; Barbara Zanini et al., "Celiac Disease With Mild Enteropathy Is Not Mild Disease," Clinical Gastroenterology and Hepatology 11, no. 3 (March 1, 2013): 253–58, https://doi.org/10.1016/j.cgh.2012.09.027.

blood tests for celiac disease are usually positive for Grade III or IV: K. Rostami et al., "Sensitivity of Antiendomysium and Antigliadin Antibodies in Untreated Celiac Disease: Disappointing in Clinical Practice," The American Journal of Gastroenterology 94, no. 4 (April 1999): 888–94, https://doi.org/10.1111/j.1572-0241.1999.983_f.x.

Wheat allergy almost always develops in childhood: Ruchi S. Gupta et al., "The Prevalence, Severity, and Distribution of Childhood Food Allergy in the United States," Pediatrics 128, no. 1 (July 2011): e9-17, https://doi.org/10.1542/peds.2011-0204.

extremely rare to develop wheat allergy as an adult: Corinne A. Keet et al., "The Natural History of Wheat Allergy," Annals of Allergy, Asthma & Immunology:

Official Publication of the American College of Allergy, Asthma, & Immunology 102, no. 5 (May 2009): 410–15, https://doi.org/10.1016/S1081-1206(10)60513-3.

85 percent of adults with dermatitis herpetiformis: P. Collin et al., "High Incidence and Prevalence of Adult Coeliac Disease. Augmented Diagnostic Approach," Scandinavian Journal of Gastroenterology 32, no. 11 (November 1997): 1129–33, https://doi.org/10.3109/00365529709002992.

85% of people with gluten-related neurologic conditions: Marios Hadjivassiliou et al., "Autoantibodies in Gluten Ataxia Recognize a Novel Neuronal Transglutaminase," Annals of Neurology 64, no. 3 (September 2008): 332–43, https://doi.org/10.1002/ana.21450; Panagiotis Zis et al., "Transglutaminase 6 Antibodies in Gluten Neuropathy," Digestive and Liver Disease: Official Journal of the Italian Society of Gastroenterology and the Italian Association for the Study of the Liver 49, no. 11 (November 2017): 1196–1200, https://doi.org/10.1016/j.dld.2017.08.019; Luis Rodrigo et al., "Gluten Ataxia Is Better Classified as Non-Celiac Gluten Sensitivity than as Celiac Disease: A Comparative Clinical Study," Immunologic Research 64, no. 2 (April 2016): 558–64, https://doi.org/10.1007/s12026-015-8750-1.

researchers gave people with "gluten sensitivity" an oatmeal bar: Gry I. Skodje et al., "Fructan, Rather Than Gluten, Induces Symptoms in Patients With Self-Reported Non-Celiac Gluten Sensitivity," Gastroenterology 154, no. 3 (2018): 529-539.e2, https://doi.org/10.1053/j.gastro.2017.10.040.

And for some patients with irritable bowel syndrome: Emma Altobelli et al., "Low-FODMAP Diet Improves Irritable Bowel Syndrome Symptoms: A Meta-Analysis," Nutrients 9, no. 9 (August 26, 2017), https://doi.org/10.3390/nu9090940; Derrick K. Ong et al., "Manipulation of Dietary Short Chain Carbohydrates Alters the Pattern of Gas Production and Genesis of Symptoms in Irritable Bowel Syndrome," Journal of Gastroenterology and Hepatology 25, no. 8 (August 2010): 1366–73, https://doi.org/10.1111/j.1440-1746.2010.06370.x.

low FODMAP diet, may lead to harm of the beneficial bacteria: Heidi M. Staudacher et al., "Fermentable Carbohydrate Restriction Reduces Luminal Bifidobacteria and Gastrointestinal Symptoms in Patients with Irritable Bowel Syndrome," The Journal of Nutrition 142, no. 8 (August 2012): 1510–18, https://doi.org/10.3945/jn.112.159285; Emma P. Halmos et al., "Diets That Differ in Their FODMAP Content Alter the Colonic Luminal Microenvironment," Gut 64, no. 1 (January 2015): 93–100, https://doi.org/10.1136/gutjnl-2014-307264; Tim J. Sloan et al., "A Low FODMAP Diet Is Associated with Changes in the Microbiota and Reduction in Breath Hydrogen but Not Colonic Volume in Healthy Subjects," PloS One 13, no. 7 (2018): e0201410, https://doi.org/10.1371/journal.pone.0201410.

low FODMAP diet led to significant declines in several important micronutrients: Farida J, Shah E, Ball S, et al Micronutrient intake changes with the low FODMAP and mNICE Diets. In: World Congress of Gastroenterology; 2017.

CHAPTER 6

cooperative fashion to clean the ocean: Ping Hu et al., "Simulation of Deepwater Horizon Oil Plume Reveals Substrate Specialization within a Complex Community of Hydrocarbon Degraders," Proceedings of the National Academy of Sciences of the United States of America 114, no. 28 (11 2017): 7432–37, https://doi.org/10.1073/pnas.1703424114.

Fourteen thousand year old bread: Amaia Arranz-Otaegui et al., "Archaeobotanical Evidence Reveals the Origins of Bread 14,400 Years Ago in Northeastern Jordan," Proceedings of the National Academy of Sciences of the United States of America 115, no. 31 (31 2018): 7925–30, https://doi.org/10.1073/pnas.1801071115.

wheat/barley-based beer mixture dating back 13,000 years: Li Liu et al., "Fermented Beverage and Food Storage in 13,000 y-Old Stone Mortars at Raqefet Cave, Israel: Investigating Natufian Ritual Feasting," Journal of

Archaeological Science: Reports 21 (October 1, 2018): 783–93, https://doi.org/10.1016/j.jasrep.2018.08.008.

In Sweden there are 9,200 year old pits: Adam Boethius, "Something Rotten in Scandinavia: The World's Earliest Evidence of Fermentation," Journal of Archaeological Science 66 (February 1, 2016): 169–80, https://doi.org/10.1016/j.jas.2016.01.008.

In China, researchers found a 9,000-year-old: Patrick E. McGovern et al., "Fermented Beverages of Pre- and Proto-Historic China," Proceedings of the National Academy of Sciences of the United States of America 101, no. 51 (December 21, 2004): 17593–98, https://doi.org/10.1073/pnas.0407921102.

But most of our food today is on a whole new level: "Focusing on Preservatives: How They Keep Food Fresh," EurekAlert!, accessed October 26, 2019, http://www.eurekalert.org/pub_releases/2002-11/acs-fop111202.php.

In one study, sulfites damaged: Sally V. Irwin et al., "Sulfites Inhibit the Growth of Four Species of Beneficial Gut Bacteria at Concentrations Regarded as Safe for Food," PloS One 12, no. 10 (2017): e0186629, https://doi.org/10.1371/journal.pone.0186629.

lactic acid has been shown to: Carolina Iraporda et al., "Lactate and Short Chain Fatty Acids Produced by Microbial Fermentation Downregulate Proinflammatory Responses in Intestinal Epithelial Cells and Myeloid Cells," Immunobiology 220, no. 10 (October 2015): 1161–69, https://doi.org/10.1016/j.imbio.2015.06.004; Stefan Kahlert et al., "Physiological Concentration of Exogenous Lactate Reduces Antimycin A Triggered Oxidative Stress in Intestinal Epithelial Cell Line IPEC-1 and IPEC-J2 In Vitro," PloS One 11, no. 4 (2016): e0153135, https://doi.org/10.1371/journal.pone.0153135.

Studies have shown that vinegar: F. Brighenti et al., "Effect of Neutralized and Native Vinegar on Blood Glucose and Acetate Responses to a Mixed

Meal in Healthy Subjects," European Journal of Clinical Nutrition 49, no. 4 (April 1995): 242–47; Carol S. Johnston and Amanda J. Buller, "Vinegar and Peanut Products as Complementary Foods to Reduce Postprandial Glycemia," Journal of the American Dietetic Association 105, no. 12 (December 2005): 1939–42, https://doi.org/10.1016/j.jada.2005.07.012; Carol S. Johnston, Cindy M. Kim, and Amanda J. Buller, "Vinegar Improves Insulin Sensitivity to a High-Carbohydrate Meal in Subjects With Insulin Resistance or Type 2 Diabetes," Diabetes Care 27, no. 1 (January 1, 2004): 281–82, https://doi.org/10.2337/diacare.27.1.281; Tomoo Kondo et al., "Vinegar Intake Reduces Body Weight, Body Fat Mass, and Serum Triglyceride Levels in Obese Japanese Subjects," Bioscience, Biotechnology, and Biochemistry 73, no. 8 (August 2009): 1837–43; S. Kondo et al., "Antihypertensive Effects of Acetic Acid and Vinegar on Spontaneously Hypertensive Rats," Bioscience, Biotechnology, and Biochemistry 65, no. 12 (December 2001): 2690–94, https://doi.org/10.1271/bbb.65.2690; Lixin Na et al., "Vinegar Decreases Blood Pressure by Down-Regulating AT1R Expression via the AMPK/PGC-1α/PPARγ Pathway in Spontaneously Hypertensive Rats," European Journal of Nutrition 55, no. 3 (April 2016): 1245–53, https://doi.org/10.1007/s00394-015-0937-7; E. Ostman et al., "Vinegar Supplementation Lowers Glucose and Insulin Responses and Increases Satiety after a Bread Meal in Healthy Subjects," European Journal of Clinical Nutrition 59, no. 9 (September 2005): 983–88, https://doi.org/10.1038/sj.ejcn.1602197; Takashi Fushimi et al., "Dietary Acetic Acid Reduces Serum Cholesterol and Triacylglycerols in Rats Fed a Cholesterol-Rich Diet," The British Journal of Nutrition 95, no. 5 (May 2006): 916–24, https://doi.org/10.1079/bjn20061740.

microbes in the diet by up to 10,000 fold: Jenna M. Lang, Jonathan A. Eisen, and Angela M. Zivkovic, "The Microbes We Eat: Abundance and Taxonomy of Microbes Consumed in a Day's Worth of Meals for Three Diet Types," PeerJ 2 (2014): e659, https://doi.org/10.7717/peerj.659; Muriel Derrien and Johan E. T. van Hylckama Vlieg, "Fate, Activity, and Impact of Ingested Bacteria within the Human Gut Microbiota," Trends in Microbiology 23, no. 6 (June 2015): 354–66, https://doi.org/10.1016/j.tim.2015.03.002.

In the study comparing 5 days on a plant-based versus animal-based diet: David et al., "Diet Rapidly and Reproducibly Alters the Human Gut Microbiome."

enhance conversion of health-promoting flavonoids in cherries: Pasquale Filannino et al., "Metabolism of Phenolic Compounds by Lactobacillus Spp. during Fermentation of Cherry Juice and Broccoli Puree," Food Microbiology 46 (April 2015): 272–79, https://doi.org/10.1016/j.fm.2014.08.018.

These are the same Lactobacillus species: Verbeke K. (2014). Prebiotics and synbiotics: how do they affect health? in Clinical Insights: Probiotics, Prebiotics and Gut Health, eds Floch M. H., Kim A., editors. (London: Future Medicine Ltd.), 47–61.

Recent research has found that nattokinase: Hongjie Chen et al., "Nattokinase: A Promising Alternative in Prevention and Treatment of Cardiovascular Diseases," Biomarker Insights 13 (2018): 1177271918785130, https://doi.org/10.1177/1177271918785130.

able to synthesize vitamin K and B vitamins: Bhawani Chamlagain et al., "Ultra-High Performance Liquid Chromatographic and Mass Spectrometric Analysis of Active Vitamin B12 in Cells of Propionibacterium and Fermented Cereal Matrices," Food Chemistry 166 (January 1, 2015): 630–38, https://doi.org/10.1016/j.foodchem.2014.06.068; Pasquale Russo et al., "Riboflavin-Overproducing Strains of Lactobacillus Fermentum for Riboflavin-Enriched Bread," Applied Microbiology and Biotechnology 98, no. 8 (April 2014): 3691–3700, https://doi.org/10.1007/s00253-013-5484-7.

Melatonin and GABA are both: M. A. Martín-Cabrejas et al., "Chapter 6 - Melatonin Synthesis in Fermented Foods," in Fermented Foods in Health and Disease Prevention, ed. Juana Frias, Cristina Martinez-Villaluenga, and Elena Peñas (Boston: Academic Press, 2017), 105–29, https://doi.org/10.1016/B978-0-12-802309-9.00006-6; J. Quílez and M. Diana, "Chapter 5 - Gamma-

Aminobutyric Acid-Enriched Fermented Foods," in Fermented Foods in Health and Disease Prevention, ed. Juana Frias, Cristina Martinez-Villaluenga, and Elena Peñas (Boston: Academic Press, 2017), 85–103, https://doi.org/10.1016/B978-0-12-802309-9.00005-4.

They've been shown to inhibit unhealthy microbes: Maria L. Marco et al., "Health Benefits of Fermented Foods: Microbiota and Beyond," Current Opinion in Biotechnology 44 (2017): 94–102, https://doi.org/10.1016/j.copbio.2016.11.010.

PREbiotic exopolysaccharides produced during fermentation: Nuria Salazar et al., "Exopolysaccharides Produced by Lactic Acid Bacteria and Bifidobacteria as Fermentable Substrates by the Intestinal Microbiota," Critical Reviews in Food Science and Nutrition 56, no. 9 (July 3, 2016): 1440–53, https://doi.org/10.1080/10408398.2013.770728.

Fermentation of red ginseng increases: Mi-Ra Oh et al., "Postprandial Glucose-Lowering Effects of Fermented Red Ginseng in Subjects with Impaired Fasting Glucose or Type 2 Diabetes: A Randomized, Double-Blind, Placebo-Controlled Clinical Trial," BMC Complementary and Alternative Medicine 14 (July 11, 2014): 237, https://doi.org/10.1186/1472-6882-14-237.

Twenty-five different antioxidant peptides: C. Martinez-Villaluenga, E. Peñas, and J. Frias, "Chapter 2 - Bioactive Peptides in Fermented Foods: Production and Evidence for Health Effects," in Fermented Foods in Health and Disease Prevention, ed. Juana Frias, Cristina Martinez-Villaluenga, and Elena Peñas (Boston: Academic Press, 2017), 23–47, https://doi.org/10.1016/B978-0-12-802309-9.00002-9.

Fermentation of soy milk with Lactobacillus paracasei: Shen-Shih Chiang, Jiunn-Wang Liao, and Tzu-Ming Pan, "Effect of Bioactive Compounds in Lactobacilli-Fermented Soy Skim Milk on Femoral Bone Microstructure of Aging Mice," Journal of the Science of Food and Agriculture 92, no. 2 (2012):

328–35, https://doi.org/10.1002/jsfa.4579.

Fermentation removes ninety five percent of them: N. R. Reddy and M. D. Pierson, “Reduction in Antinutritional and Toxic Components in Plant Foods by FermentationaaThe Term ‘Plant Foods’ Is Used in the Context of Food Derived from Plant Sources.,” Food Research International 27, no. 3 (January 1, 1994): 281–90, https://doi.org/10.1016/0963-9969(94)90096-5.

help us biodegrade and reduce pesticide residues: Jorge Regueiro et al., “A Review on the Fermentation of Foods and the Residues of Pesticides-Biotransformation of Pesticides and Effects on Fermentation and Food Quality,” Critical Reviews in Food Science and Nutrition 55, no. 6 (2015): 839–63, https://doi.org/10.1080/10408398.2012.677872.

There is not a great way to dispose of the feces: Dagne D. Hill, William E. Owens, and Paul B. Tchoounwou, “Impact of Animal Waste Application on Runoff Water Quality in Field Experimental Plots,” International Journal of Environmental Research and Public Health 2, no. 2 (August 2005): 314–21.

processed meat or fish has been associated with colorectal: “Preservation and Processing,” World Cancer Research Fund, April 24, 2018, https://www.wcrf.org/dietandcancer/exposures/preservation-processing.

association between stomach cancer and pickled vegetable consumption: Jian-Song Ren et al., “Pickled Food and Risk of Gastric Cancer--a Systematic Review and Meta-Analysis of English and Chinese Literature,” Cancer Epidemiology, Biomarkers & Prevention: A Publication of the American Association for Cancer Research, Cosponsored by the American Society of Preventive Oncology 21, no. 6 (June 2012): 905–15, https://doi.org/10.1158/1055-9965.EPI-12-0202.

Stomach cancer is a huge problem: Yeerae Kim et al., “Stomach Cancer Incidence Rates among Americans, Asian Americans and Native Asians from

1988 to 2011," Epidemiology and Health 37 (2015): e2015006, https://doi.org/10.4178/epih/e2015006.

Most cases are the result of H. pylori: Hyun Ja Kim et al., "Fresh and Pickled Vegetable Consumption and Gastric Cancer in Japanese and Korean Populations: A Meta-Analysis of Observational Studies," Cancer Science 101, no. 2 (February 2010): 508–16, https://doi.org/10.1111/j.1349-7006.2009.01374.x.

salt and its byproducts actually accelerate the inflammation: Hui Liu et al., "Diet Synergistically Affects Helicobacter Pylori-Induced Gastric Carcinogenesis in Nonhuman Primates," Gastroenterology 137, no. 4 (October 2009): 1367-1379.e1-6, https://doi.org/10.1053/j.gastro.2009.07.041; Paula Jakszyn et al., "Endogenous versus Exogenous Exposure to N-Nitroso Compounds and Gastric Cancer Risk in the European Prospective Investigation into Cancer and Nutrition (EPIC-EURGAST) Study," Carcinogenesis 27, no. 7 (July 2006): 1497–1501, https://doi.org/10.1093/carcin/bgl019.

fermenting cabbage produces the enzymes: Marja Tolonen et al., "Plant-Derived Biomolecules in Fermented Cabbage," Journal of Agricultural and Food Chemistry 50, no. 23 (November 6, 2002): 6798–6803, https://doi.org/10.1021/jf0109017.

the average Korean eats forty-eight pounds: "Koreans Kimchi Consumption per Year," accessed October 26, 2019, https://infograph.venngage.com/p/127037/koreans-kimchi-consumption-per-year.

Gives rise to multiple probiotic strains: Heejae Lee et al., "Functional Properties of Lactobacillus Strains Isolated from Kimchi," International Journal of Food Microbiology 145, no. 1 (January 31, 2011): 155–61, https://doi.org/10.1016/j.ijfoodmicro.2010.12.003.

Lowers cholesterol: In Hwa Choi et al., "Kimchi, a Fermented Vegetable,

Improves Serum Lipid Profiles in Healthy Young Adults: Randomized Clinical Trial," Journal of Medicinal Food 16, no. 3 (March 2013): 223–29, https://doi.org/10.1089/jmf.2012.2563.

Promotes weight loss: Eun Kyoung Kim et al., "Fermented Kimchi Reduces Body Weight and Improves Metabolic Parameters in Overweight and Obese Patients," Nutrition Research (New York, N.Y.) 31, no. 6 (June 2011): 436–43, https://doi.org/10.1016/j.nutres.2011.05.011.

Includes anti-inflammatory: Bohkyung Kim et al., "Anti-Aging Effects and Mechanisms of Kimchi during Fermentation under Stress-Induced Premature Senescence Cellular System," Food Science and Biotechnology 20, no. 3 (June 1, 2011): 643–49, https://doi.org/10.1007/s10068-011-0091-9.

Improves insulin sensitivity: So-Yeon An et al., "Beneficial Effects of Fresh and Fermented Kimchi in Prediabetic Individuals," Annals of Nutrition & Metabolism 63, no. 1–2 (2013): 111–19, https://doi.org/10.1159/000353583.

it may protect us from cancer: Myung-Sunny Kim et al., "Effects of Kimchi on Human Health," Medicine 97, no. 13 (March 30, 2018), https://doi.org/10.1097/MD.0000000000010163; Chang-Suk Kong et al., "Antiproliferative Effect of Chitosan-Added Kimchi in HT-29 Human Colon Carcinoma Cells," Journal of Medicinal Food 13, no. 1 (February 2010): 6–12, https://doi.org/10.1089/jmf.2009.1213; Kun-Young Park et al., "Kimchi and an Active Component, Beta-Sitosterol, Reduce Oncogenic H-Ras(V12)-Induced DNA Synthesis," Journal of Medicinal Food 6, no. 3 (2003): 151–56, https://doi.org/10.1089/10966200360716544.

Miso may help prevent breast: Seiichiro Yamamoto et al., "Soy, Isoflavones, and Breast Cancer Risk in Japan," Journal of the National Cancer Institute 95, no. 12 (June 18, 2003): 906–13, https://doi.org/10.1093/jnci/95.12.906; Gerald B. Sharp et al., "Relationship of Hepatocellular Carcinoma to Soya Food Consumption: A Cohort-Based, Case-Control Study in Japan," International

Journal of Cancer 115, no. 2 (June 10, 2005): 290–95, https://doi.org/10.1002/ijc.20897; Gong Yang et al., "Prospective Cohort Study of Soy Food Intake and Colorectal Cancer Risk in Women," The American Journal of Clinical Nutrition 89, no. 2 (February 2009): 577–83, https://doi.org/10.3945/ajcn.2008.26742.

miso does not raise blood pressure: Hiromitsu Watanabe et al., "A Miso (Japanese Soybean Paste) Diet Conferred Greater Protection against Hypertension than a Sodium Chloride Diet in Dahl Salt-Sensitive Rats," Hypertension Research: Official Journal of the Japanese Society of Hypertension 29, no. 9 (September 2006): 731–38, https://doi.org/10.1291/hypres.29.731.

Calcium, vitamin K and isoflavones: Megumi Kubota and Hirotoshi Shimizu, "[Nutrition and bone health. Soybean and soy foods, and bone health]," Clinical Calcium 19, no. 10 (October 2009): 1514–19, https://doi.org/CliCa091015141519.

suggesting that kefir, yogurt, and other fermented dairy products: "Changes in Diet and Lifestyle and Long-Term Weight Gain in Women and Men. - PubMed - NCBI," accessed October 26, 2019, https://www.ncbi.nlm.nih.gov/pubmed/?term=N+Engl+J+Med+2011%3B+364%3A2392-2404; Mu Chen et al., "Dairy Consumption and Risk of Type 2 Diabetes: 3 Cohorts of US Adults and an Updated Meta-Analysis," BMC Medicine 12 (November 25, 2014): 215, https://doi.org/10.1186/s12916-014-0215-1; Simone J. P. M. Eussen et al., "Consumption of Dairy Foods in Relation to Impaired Glucose Metabolism and Type 2 Diabetes Mellitus: The Maastricht Study," The British Journal of Nutrition 115, no. 8 (2016): 1453–61, https://doi.org/10.1017/S0007114516000313; Sabita S. Soedamah-Muthu et al., "Consumption of Dairy Products and Associations with Incident Diabetes, CHD and Mortality in the Whitehall II Study," The British Journal of Nutrition 109, no. 4 (February 28, 2013): 718–26, https://doi.org/10.1017/S0007114512001845.

phytic acid is reduced by sixty two percent: H. W. Lopez et al., "Prolonged Fermentation of Whole Wheat Sourdough Reduces Phytate Level and

Increases Soluble Magnesium," Journal of Agricultural and Food Chemistry 49, no. 5 (May 2001): 2657–62, https://doi.org/10.1021/jf001255z.

sourdough also has less gluten: Carlo Giuseppe Rizzello et al., "Use of Selected Sourdough Lactic Acid Bacteria to Hydrolyze Wheat and Rye Proteins Responsible for Cereal Allergy," European Food Research and Technology 223, no. 3 (July 1, 2006): 405–11, https://doi.org/10.1007/s00217-005-0220-x.

sourdough has a lower glycemic index: S. Bo et al., "The Acute Impact of the Intake of Four Types of Bread on Satiety and Blood Concentrations of Glucose, Insulin, Free Fatty Acids, Triglyceride and Acylated Ghrelin. A Randomized Controlled Cross-over Trial," Food Research International (Ottawa, Ont.) 92 (2017): 40–47, https://doi.org/10.1016/j.foodres.2016.12.019.

CHAPTER 7

Growth of SCFA producing gut microbes: Evelyne M. Dewulf et al., "Insight into the Prebiotic Concept: Lessons from an Exploratory, Double Blind Intervention Study with Inulin-Type Fructans in Obese Women," Gut 62, no. 8 (August 2013): 1112–21, https://doi.org/10.1136/gutjnl-2012-303304; Jelena Vulevic et al., "A Mixture of Trans-Galactooligosaccharides Reduces Markers of Metabolic Syndrome and Modulates the Fecal Microbiota and Immune Function of Overweight Adults," The Journal of Nutrition 143, no. 3 (March 2013): 324–31, https://doi.org/10.3945/jn.112.166132; D. B. A. Silk et al., "Clinical Trial: The Effects of a Trans-Galactooligosaccharide Prebiotic on Faecal Microbiota and Symptoms in Irritable Bowel Syndrome," Alimentary Pharmacology & Therapeutics 29, no. 5 (March 1, 2009): 508–18, https://doi.org/10.1111/j.1365-2036.2008.03911.x.

Reduced counts of unhealthy microbes: Dewulf et al., "Insight into the Prebiotic Concept"; Vulevic et al., "A Mixture of Trans-Galactooligosaccharides Reduces Markers of Metabolic Syndrome and Modulates the Fecal Microbiota and Immune Function of Overweight Adults."

Reduced bacterial endotoxin levels: Dewulf et al., "Insight into the Prebiotic Concept"; Ricardo Fernandes et al., "Effects of Inulin-Type Fructans, Galacto-Oligosaccharides and Related Synbiotics on Inflammatory Markers in Adult Patients with Overweight or Obesity: A Systematic Review," Clinical Nutrition 36, no. 5 (October 1, 2017): 1197–1206, https://doi.org/10.1016/j.clnu.2016.10.003.

Reduced inflammatory markers like C-reactive protein: Fernandes et al., "Effects of Inulin-Type Fructans, Galacto-Oligosaccharides and Related Synbiotics on Inflammatory Markers in Adult Patients with Overweight or Obesity"; Vulevic et al., "A Mixture of Trans-Galactooligosaccharides Reduces Markers of Metabolic Syndrome and Modulates the Fecal Microbiota and Immune Function of Overweight Adults."

Improvement in parameters of diabetes: Vulevic et al., "A Mixture of Trans-Galactooligosaccharides Reduces Markers of Metabolic Syndrome and Modulates the Fecal Microbiota and Immune Function of Overweight Adults"; Nicole J. Kellow, Melinda T. Coughlan, and Christopher M. Reid, "Metabolic Benefits of Dietary Prebiotics in Human Subjects: A Systematic Review of Randomised Controlled Trials," The British Journal of Nutrition 111, no. 7 (April 14, 2014): 1147–61, https://doi.org/10.1017/S0007114513003607; Elena Barengolts, "GUT MICROBIOTA, PREBIOTICS, PROBIOTICS, AND SYNBIOTICS IN MANAGEMENT OF OBESITY AND PREDIABETES: REVIEW OF RANDOMIZED CONTROLLED TRIALS," Endocrine Practice: Official Journal of the American College of Endocrinology and the American Association of Clinical Endocrinologists 22, no. 10 (October 2016): 1224–34, https://doi.org/10.4158/EP151157.RA.

Lower total cholesterol: Bruna T. S. Beserra et al., "A Systematic Review and Meta-Analysis of the Prebiotics and Synbiotics Effects on Glycaemia, Insulin Concentrations and Lipid Parameters in Adult Patients with Overweight or Obesity," Clinical Nutrition (Edinburgh, Scotland) 34, no. 5 (October 2015): 845–58, https://doi.org/10.1016/j.clnu.2014.10.004; Vulevic et al., "A Mixture of

Trans-Galactooligosaccharides Reduces Markers of Metabolic Syndrome and Modulates the Fecal Microbiota and Immune Function of Overweight Adults."

Lower triglycerides: Beserra et al., "A Systematic Review and Meta-Analysis of the Prebiotics and Synbiotics Effects on Glycaemia, Insulin Concentrations and Lipid Parameters in Adult Patients with Overweight or Obesity"; Vulevic et al., "A Mixture of Trans-Galactooligosaccharides Reduces Markers of Metabolic Syndrome and Modulates the Fecal Microbiota and Immune Function of Overweight Adults."

Increased HDL cholesterol: Beserra et al., "A Systematic Review and Meta-Analysis of the Prebiotics and Synbiotics Effects on Glycaemia, Insulin Concentrations and Lipid Parameters in Adult Patients with Overweight or Obesity"; Vulevic et al., "A Mixture of Trans-Galactooligosaccharides Reduces Markers of Metabolic Syndrome and Modulates the Fecal Microbiota and Immune Function of Overweight Adults."

Reduced fat mass: Fernandes et al., "Effects of Inulin-Type Fructans, Galacto-Oligosaccharides and Related Synbiotics on Inflammatory Markers in Adult Patients with Overweight or Obesity."

Improved satiety with an increase in: Nathalie M. Delzenne et al., "Impact of Inulin and Oligofructose on Gastrointestinal Peptides," The British Journal of Nutrition 93 Suppl 1 (April 2005): S157-161, https://doi.org/10.1079/bjn20041342; Patrice D. Cani et al., "Gut Microbiota Fermentation of Prebiotics Increases Satietogenic and Incretin Gut Peptide Production with Consequences for Appetite Sensation and Glucose Response after a Meal," The American Journal of Clinical Nutrition 90, no. 5 (November 2009): 1236–43, https://doi.org/10.3945/ajcn.2009.28095; Kellow, Coughlan, and Reid, "Metabolic Benefits of Dietary Prebiotics in Human Subjects"; Steven A. Abrams et al., "A Combination of Prebiotic Short- and Long-Chain Inulin-Type Fructans Enhances Calcium Absorption and Bone Mineralization in Young Adolescents," The American Journal of Clinical Nutrition 82, no. 2 (August 1,

2005): 471–76, https://doi.org/10.1093/ajcn/82.2.471.

Improved absorption of calcium and magnesium: Abrams et al., "A Combination of Prebiotic Short- and Long-Chain Inulin-Type Fructans Enhances Calcium Absorption and Bone Mineralization in Young Adolescents"; Leah Holloway et al., "Effects of Oligofructose-Enriched Inulin on Intestinal Absorption of Calcium and Magnesium and Bone Turnover Markers in Postmenopausal Women," The British Journal of Nutrition 97, no. 2 (February 2007): 365–72, https://doi.org/10.1017/S000711450733674X.

In a randomized, placebo-controlled trial of patients with IBS: Silk et al., "Clinical Trial."

you'll also find IMOs in miso, soy sauce: Dorothee Goffin et al., "Will Isomalto-Oligosaccharides, a Well-Established Functional Food in Asia, Break through the European and American Market? The Status of Knowledge on These Prebiotics," Critical Reviews in Food Science and Nutrition 51, no. 5 (May 2011): 394–409, https://doi.org/10.1080/10408391003628955.

Each of these supplements is a natural prebiotic: Johnson W. McRorie, "Evidence-Based Approach to Fiber Supplements and Clinically Meaningful Health Benefits, Part 1: What to Look for and How to Recommend an Effective Fiber Therapy," Nutrition Today 50, no. 2 (March 2015): 82–89, https://doi.org/10.1097/NT.0000000000000082.

"confer a health benefit on the host.": Colin Hill et al., "Expert Consensus Document: The International Scientific Association for Probiotics and Prebiotics Consensus Statement on the Scope and Appropriate Use of the Term Probiotic," Nature Reviews Gastroenterology & Hepatology 11, no. 8 (August 2014): 506–14, https://doi.org/10.1038/nrgastro.2014.66.

just like our healthy gut microbes these probiotics should: Eamonn M.M. Quigley, "Prebiotics and Probiotics in Digestive Health," Clinical

Gastroenterology and Hepatology 17, no. 2 (January 2019): 333–44, https://doi.org/10.1016/j.cgh.2018.09.028.

they generally don't colonize your gut permanently: Anatoly Bezkorovainy, "Probiotics: Determinants of Survival and Growth in the Gut," The American Journal of Clinical Nutrition 73, no. 2 (February 1, 2001): 399s–405s, https://doi.org/10.1093/ajcn/73.2.399s; Niv Zmora et al., "Personalized Gut Mucosal Colonization Resistance to Empiric Probiotics Is Associated with Unique Host and Microbiome Features," Cell 174, no. 6 (06 2018): 1388-1405.e21, https://doi.org/10.1016/j.cell.2018.08.041.

within two to five days it'll be like you never: Christina L. Ohland and Wallace K. Macnaughton, "Probiotic Bacteria and Intestinal Epithelial Barrier Function," American Journal of Physiology. Gastrointestinal and Liver Physiology 298, no. 6 (June 2010): G807-819, https://doi.org/10.1152/ajpgi.00243.2009.

helping to unleash SCFAs from our prebiotics: Ravinder Nagpal et al., "Human-Origin Probiotic Cocktail Increases Short-Chain Fatty Acid Production via Modulation of Mice and Human Gut Microbiome," Scientific Reports 8, no. 1 (August 23, 2018): 1–15, https://doi.org/10.1038/s41598-018-30114-4; Christine M. Carey et al., "The Effect of Probiotics and Organic Acids on Shiga-Toxin 2 Gene Expression in Enterohemorrhagic Escherichia Coli O157:H7," Journal of Microbiological Methods 73, no. 2 (May 2008): 125–32, https://doi.org/10.1016/j.mimet.2008.01.014.

Probiotics often help with digestive symptoms: S. Guglielmetti et al., "Randomised Clinical Trial: Bifidobacterium Bifidum MIMBb75 Significantly Alleviates Irritable Bowel Syndrome and Improves Quality of Life--a Double-Blind, Placebo-Controlled Study," Alimentary Pharmacology & Therapeutics 33, no. 10 (May 2011): 1123–32, https://doi.org/10.1111/j.1365-2036.2011.04633.x; Philippe Ducrotté, Prabha Sawant, and Venkataraman Jayanthi, "Clinical Trial: Lactobacillus Plantarum 299v (DSM 9843) Improves Symptoms of Irritable Bowel Syndrome," World Journal of Gastroenterology 18, no. 30 (August 14,

2012): 4012–18, https://doi.org/10.3748/wjg.v18.i30.4012; Alexander C. Ford et al., "Efficacy of Prebiotics, Probiotics, and Synbiotics in Irritable Bowel Syndrome and Chronic Idiopathic Constipation: Systematic Review and Meta-Analysis," The American Journal of Gastroenterology 109, no. 10 (October 2014): 1547–61; quiz 1546, 1562, https://doi.org/10.1038/ajg.2014.202; G. Sisson et al., "Randomised Clinical Trial: A Liquid Multi-Strain Probiotic vs. Placebo in the Irritable Bowel Syndrome--a 12 Week Double-Blind Study," Alimentary Pharmacology & Therapeutics 40, no. 1 (July 2014): 51–62, https://doi.org/10.1111/apt.12787; Mehran Rogha, Mozhdehalsadat Zahiri Esfahani, and Amir Houshang Zargarzadeh, "The Efficacy of a Synbiotic Containing Bacillus Coagulans in Treatment of Irritable Bowel Syndrome: A Randomized Placebo-Controlled Trial," Gastroenterology and Hepatology from Bed to Bench 7, no. 3 (2014): 156–63; Elham Jafari et al., "Therapeutic Effects, Tolerability and Safety of a Multi-Strain Probiotic in Iranian Adults with Irritable Bowel Syndrome and Bloating," Archives of Iranian Medicine 17, no. 7 (July 2014): 466–70, https://doi.org/0141707/AIM.003; Chang Hwan Choi et al., "A Randomized, Double-Blind, Placebo-Controlled Multicenter Trial of Saccharomyces Boulardii in Irritable Bowel Syndrome: Effect on Quality of Life," Journal of Clinical Gastroenterology 45, no. 8 (September 2011): 679–83, https://doi.org/10.1097/MCG.0b013e318204593e; Peter J. Whorwell et al., "Efficacy of an Encapsulated Probiotic Bifidobacterium Infantis 35624 in Women with Irritable Bowel Syndrome," The American Journal of Gastroenterology 101, no. 7 (July 2006): 1581–90, https://doi.org/10.1111/j.1572-0241.2006.00734.x; P. Moayyedi et al., "The Efficacy of Probiotics in the Treatment of Irritable Bowel Syndrome: A Systematic Review," Gut 59, no. 3 (March 2010): 325–32, https://doi.org/10.1136/gut.2008.167270; D. Guyonnet et al., "Effect of a Fermented Milk Containing Bifidobacterium Animalis DN-173 010 on the Health-Related Quality of Life and Symptoms in Irritable Bowel Syndrome in Adults in Primary Care: A Multicentre, Randomized, Double-Blind, Controlled Trial," Alimentary Pharmacology & Therapeutics 26, no. 3 (August 1, 2007): 475–86, https://doi.org/10.1111/j.1365-2036.2007.03362.x; A. Agrawal et al., "Clinical Trial: The Effects of a Fermented Milk Product Containing Bifidobacterium Lactis DN-173 010 on Abdominal Distension

and Gastrointestinal Transit in Irritable Bowel Syndrome with Constipation," Alimentary Pharmacology & Therapeutics 29, no. 1 (January 2009): 104–14, https://doi.org/10.1111/j.1365-2036.2008.03853.x; Dong Hyun Sinn et al., "Therapeutic Effect of Lactobacillus Acidophilus-SDC 2012, 2013 in Patients with Irritable Bowel Syndrome," Digestive Diseases and Sciences 53, no. 10 (October 2008): 2714–18, https://doi.org/10.1007/s10620-007-0196-4; K. Kajander et al., "Clinical Trial: Multispecies Probiotic Supplementation Alleviates the Symptoms of Irritable Bowel Syndrome and Stabilizes Intestinal Microbiota," Alimentary Pharmacology & Therapeutics 27, no. 1 (January 1, 2008): 48–57, https://doi.org/10.1111/j.1365-2036.2007.03542.x; Damien Paineau et al., "The Effects of Regular Consumption of Short-Chain Fructo-Oligosaccharides on Digestive Comfort of Subjects with Minor Functional Bowel Disorders," The British Journal of Nutrition 99, no. 2 (February 2008): 311–18, https://doi.org/10.1017/S000711450779894X; Silk et al., "Clinical Trial"; B. J. Dolin, "Effects of a Proprietary Bacillus Coagulans Preparation on Symptoms of Diarrhea-Predominant Irritable Bowel Syndrome," Methods and Findings in Experimental and Clinical Pharmacology 31, no. 10 (December 2009): 655–59, https://doi.org/10.1358/mf.2009.31.10.1441078; Vicente Lorenzo-Zúñiga et al., "I.31, a New Combination of Probiotics, Improves Irritable Bowel Syndrome-Related Quality of Life," World Journal of Gastroenterology 20, no. 26 (July 14, 2014): 8709–16, https://doi.org/10.3748/wjg.v20.i26.8709; Youngran Yeun and Jaejin Lee, "Effect of a Double-Coated Probiotic Formulation on Functional Constipation in the Elderly: A Randomized, Double Blind, Controlled Study," Archives of Pharmacal Research 38, no. 7 (July 2015): 1345–50, https://doi.org/10.1007/s12272-014-0522-2; Veronica Ojetti et al., "The Effect of Lactobacillus Reuteri Supplementation in Adults with Chronic Functional Constipation: A Randomized, Double-Blind, Placebo-Controlled Trial," Journal of Gastrointestinal and Liver Diseases: JGLD 23, no. 4 (December 2014): 387–91, https://doi.org/10.15403/jgld.2014.1121.234.elr; Christian Schumann, "Medical, Nutritional and Technological Properties of Lactulose. An Update," European Journal of Nutrition 41 Suppl 1 (November 2002): I17-25, https://doi.org/10.1007/s00394-002-1103-6; M. Nyman, "Fermentation and Bulking Capacity of Indigestible Carbohydrates: The Case

of Inulin and Oligofructose," The British Journal of Nutrition 87 Suppl 2 (May 2002): S163-168, https://doi.org/10.1079/BJNBJN/2002533; Dan L. Waitzberg et al., "Effect of Synbiotic in Constipated Adult Women - a Randomized, Double-Blind, Placebo-Controlled Study of Clinical Response," Clinical Nutrition (Edinburgh, Scotland) 32, no. 1 (February 2013): 27–33, https://doi.org/10.1016/j.clnu.2012.08.010.

In inflammatory bowel disease, probiotics have: Paolo Gionchetti et al., "High-Dose Probiotics for the Treatment of Active Pouchitis," Diseases of the Colon and Rectum 50, no. 12 (December 2007): 2075–82; discussion 2082-2084, https://doi.org/10.1007/s10350-007-9068-4; Siddharth Singh et al., "Treatment and Prevention of Pouchitis after Ileal Pouch-Anal Anastomosis for Chronic Ulcerative Colitis," The Cochrane Database of Systematic Reviews, no. 11 (November 23, 2015): CD001176, https://doi.org/10.1002/14651858.CD001176.pub3; Rodrigo Bibiloni et al., "VSL#3 Probiotic-Mixture Induces Remission in Patients with Active Ulcerative Colitis," The American Journal of Gastroenterology 100, no. 7 (July 2005): 1539–46, https://doi.org/10.1111/j.1572-0241.2005.41794.x; W. Kruis et al., "Maintaining Remission of Ulcerative Colitis with the Probiotic Escherichia Coli Nissle 1917 Is as Effective as with Standard Mesalazine," Gut 53, no. 11 (November 2004): 1617–23, https://doi.org/10.1136/gut.2003.037747; B. J. Rembacken et al., "Non-Pathogenic Escherichia Coli versus Mesalazine for the Treatment of Ulcerative Colitis: A Randomised Trial," Lancet (London, England) 354, no. 9179 (August 21, 1999): 635–39, https://doi.org/10.1016/s0140-6736(98)06343-0.

known to treat antibiotic associated diarrhea: Susanne Hempel et al., "Probiotics for the Prevention and Treatment of Antibiotic-Associated Diarrhea: A Systematic Review and Meta-Analysis," JAMA 307, no. 18 (May 9, 2012): 1959–69, https://doi.org/10.1001/jama.2012.3507; H. Szajewska and M. Kołodziej, "Systematic Review with Meta-Analysis: Saccharomyces Boulardii in the Prevention of Antibiotic-Associated Diarrhoea," Alimentary Pharmacology & Therapeutics 42, no. 7 (October 2015): 793–801, https://doi.org/10.1111/apt.13344; Lisa Cimperman et al., "A Randomized, Double-Blind,

Placebo-Controlled Pilot Study of Lactobacillus Reuteri ATCC 55730 for the Prevention of Antibiotic-Associated Diarrhea in Hospitalized Adults," Journal of Clinical Gastroenterology 45, no. 9 (October 2011): 785–89, https://doi.org/10.1097/MCG.0b013e3182166a42; Arthur C. Ouwehand et al., "Probiotics Reduce Symptoms of Antibiotic Use in a Hospital Setting: A Randomized Dose Response Study," Vaccine 32, no. 4 (January 16, 2014): 458–63, https://doi.org/10.1016/j.vaccine.2013.11.053; Catherina J. M. Koning et al., "The Effect of a Multispecies Probiotic on the Intestinal Microbiota and Bowel Movements in Healthy Volunteers Taking the Antibiotic Amoxycillin," The American Journal of Gastroenterology 103, no. 1 (January 2008): 178–89, https://doi.org/10.1111/j.1572-0241.2007.01547.x.

protect against developing Clostridiodes dificile: Christine Sm Lau and Ronald S. Chamberlain, "Probiotics Are Effective at Preventing Clostridium Difficile-Associated Diarrhea: A Systematic Review and Meta-Analysis," International Journal of General Medicine 9 (2016): 27–37, https://doi.org/10.2147/IJGM.S98280.

probiotics actually impair the microbiota's ability to stabilize: Jotham Suez et al., "Post-Antibiotic Gut Mucosal Microbiome Reconstitution Is Impaired by Probiotics and Improved by Autologous FMT," Cell 174, no. 6 (06 2018): 1406-1423.e16, https://doi.org/10.1016/j.cell.2018.08.047.

probiotics can also improve our ability to process lactose: "Scientific Opinion on the Substantiation of Health Claims Related to Live Yoghurt Cultures and Improved Lactose Digestion (ID 1143, 2976) Pursuant to Article 13(1) of Regulation (EC) No 1924/2006," EFSA Journal 8, no. 10 (2010): 1763, https://doi.org/10.2903/j.efsa.2010.1763.

Some specific strains that have been shown to be beneficial: S. Nobaek et al., "Alteration of Intestinal Microflora Is Associated with Reduction in Abdominal Bloating and Pain in Patients with Irritable Bowel Syndrome," The American Journal of Gastroenterology 95, no. 5 (May 2000): 1231–38,

https://doi.org/10.1111/j.1572-0241.2000.02015.x; Liam O'Mahony et al., "Lactobacillus and Bifidobacterium in Irritable Bowel Syndrome: Symptom Responses and Relationship to Cytokine Profiles," Gastroenterology 128, no. 3 (March 2005): 541–51, https://doi.org/10.1053/j.gastro.2004.11.050; Tamar Ringel-Kulka et al., "Probiotic Bacteria Lactobacillus Acidophilus NCFM and Bifidobacterium Lactis Bi-07 versus Placebo for the Symptoms of Bloating in Patients with Functional Bowel Disorders: A Double-Blind Study," Journal of Clinical Gastroenterology 45, no. 6 (July 2011): 518–25, https://doi.org/10.1097/MCG.0b013e31820ca4d6.

Even a group of healthy people reported: Takafumi Sakai et al., "Fermented Milk Containing Lactobacillus Casei Strain Shirota Reduces Incidence of Hard or Lumpy Stools in Healthy Population," International Journal of Food Sciences and Nutrition 62, no. 4 (June 2011): 423–30, https://doi.org/10.3109/09637486.2010.542408.

probiotic colonization can be personalized: Zmora et al., "Personalized Gut Mucosal Colonization Resistance to Empiric Probiotics Is Associated with Unique Host and Microbiome Features."

they help regulate blood sugar after meals: Kellow, Coughlan, and Reid, "Metabolic Benefits of Dietary Prebiotics in Human Subjects."

There was minimal effect on metabolic parameters: Saman Khalesi et al., "A Review of Probiotic Supplementation in Healthy Adults: Helpful or Hype?," European Journal of Clinical Nutrition 73, no. 1 (2019): 24–37, https://doi.org/10.1038/s41430-018-0135-9.

safety record has been excellent: Quigley, "Prebiotics and Probiotics in Digestive Health."

There are case reports of: Quigley; Marc Gh Besselink et al., "Probiotic Prophylaxis in Predicted Severe Acute Pancreatitis: A Randomised, Double-

Blind, Placebo-Controlled Trial," Lancet (London, England) 371, no. 9613 (23 2008): 651–59, https://doi.org/10.1016/S0140-6736(08)60207-X; Satish Rao et al., "Brain Fogginess, Gas and Bloating: A Link between SIBO, Probiotics and Metabolic Acidosis," Clinical and Translational Gastroenterology 9, no. 6 (June 2018), https://doi.org/10.1038/s41424-018-0030-7.

that's what worked for constipation in a placebo-controlled trial: Philip A. Waller et al., "Dose-Response Effect of Bifidobacterium Lactis HN019 on Whole Gut Transit Time and Functional Gastrointestinal Symptoms in Adults," Scandinavian Journal of Gastroenterology 46, no. 9 (September 2011): 1057–64, https://doi.org/10.3109/00365521.2011.584895.

bacteria work in "guilds": Chenhong Zhang et al., "Dietary Modulation of Gut Microbiota Contributes to Alleviation of Both Genetic and Simple Obesity in Children," EBioMedicine 2, no. 8 (August 2015): 968–84, https://doi.org/10.1016/j.ebiom.2015.07.007.

multistrain probiotics tend to outperform single strain: H. M. Timmerman et al., "Monostrain, Multistrain and Multispecies Probiotics--A Comparison of Functionality and Efficacy," International Journal of Food Microbiology 96, no. 3 (November 15, 2004): 219–33, https://doi.org/10.1016/j.ijfoodmicro.2004.05.012; C. M. C. Chapman, G. R. Gibson, and I. Rowland, "Health Benefits of Probiotics: Are Mixtures More Effective than Single Strains?," European Journal of Nutrition 50, no. 1 (February 2011): 1–17, https://doi.org/10.1007/s00394-010-0166-z.

Without a special delayed release capsule: Bezkorovainy, "Probiotics."

CHAPTER 8

whole fruit does not cause "weight gain.": Monica L. Bertoia et al., "Changes in Intake of Fruits and Vegetables and Weight Change in United States Men and Women Followed for Up to 24 Years: Analysis from Three Prospective Cohort Studies," PLoS Medicine 12, no. 9 (September 2015): e1001878, https://

doi.org/10.1371/journal.pmed.1001878; Kerstin E. E. Schroder, "Effects of Fruit Consumption on Body Mass Index and Weight Loss in a Sample of Overweight and Obese Dieters Enrolled in a Weight-Loss Intervention Trial," Nutrition (Burbank, Los Angeles County, Calif.) 26, no. 7–8 (August 2010): 727–34, https://doi.org/10.1016/j.nut.2009.08.009.

they actually lower blood sugar and insulin: Riitta Törrönen et al., "Berries Modify the Postprandial Plasma Glucose Response to Sucrose in Healthy Subjects," The British Journal of Nutrition 103, no. 8 (April 2010): 1094–97, https://doi.org/10.1017/S0007114509992868; Riitta Törrönen et al., "Postprandial Glucose, Insulin and Glucagon-like Peptide 1 Responses to Sucrose Ingested with Berries in Healthy Subjects," The British Journal of Nutrition 107, no. 10 (May 2012): 1445–51, https://doi.org/10.1017/S0007114511004557; Riitta Törrönen et al., "Berries Reduce Postprandial Insulin Responses to Wheat and Rye Breads in Healthy Women," The Journal of Nutrition 143, no. 4 (April 2013): 430–36, https://doi.org/10.3945/jn.112.169771.

For example, one small orange: https://nutritiondata.self.com/facts/fruits-and-fruit-juices/1966/2 , accessed October 26 2019

One cup of OJ packs in: https://nutritiondata.self.com/facts/beverages/7568/2 , accessed October 26, 2019

apples are an excellent source of: Boyer and Liu, "Apple Phytochemicals and Their Health Benefits"; P. Knekt et al., "Quercetin Intake and the Incidence of Cerebrovascular Disease," European Journal of Clinical Nutrition 54, no. 5 (May 2000): 415–17.

Oranges have vitamin C and antioxidant flavonoids: Paolo Rapisarda et al., "Effect of Cold Storage on Vitamin C, Phenolics and Antioxidant Activity of Five Orange Genotypes [Citrus Sinensis (L.) Osbeck]," Postharvest Biology and Technology 49, no. 3 (September 1, 2008): 348–54, https://doi.

org/10.1016/j.postharvbio.2008.02.002; Hang Xiao et al., “Monodemethylated Polymethoxyflavones from Sweet Orange (Citrus Sinensis) Peel Inhibit Growth of Human Lung Cancer Cells by Apoptosis,” Molecular Nutrition & Food Research 53, no. 3 (March 2009): 398–406, https://doi.org/10.1002/mnfr.200800057; Peter A. Roussos, “Phytochemicals and Antioxidant Capacity of Orange (Citrus Sinensis (l.) Osbeck Cv. Salustiana) Juice Produced under Organic and Integrated Farming System in Greece,” Scientia Horticulturae 129, no. 2 (June 10, 2011): 253–58, https://doi.org/10.1016/j.scienta.2011.03.040; Christine Morand et al., “Hesperidin Contributes to the Vascular Protective Effects of Orange Juice: A Randomized Crossover Study in Healthy Volunteers,” The American Journal of Clinical Nutrition 93, no. 1 (January 2011): 73–80, https://doi.org/10.3945/ajcn.110.004945; Elisabeth Wisker, Martina Daniel, and Walter Feldheim, “Effects of a Fiber Concentrate from Citrus Fruits in Humans,” Nutrition Research 14, no. 3 (March 1, 1994): 361–72, https://doi.org/10.1016/S0271-5317(05)80175-7; C. L. Wabner and C. Y. Pak, “Effect of Orange Juice Consumption on Urinary Stone Risk Factors,” The Journal of Urology 149, no. 6 (June 1993): 1405–8, https://doi.org/10.1016/s0022-5347(17)36401-7.

postponed cognitive decline and made their brain behave like it was thirty months younger: Elizabeth E. Devore et al., “Dietary Intakes of Berries and Flavonoids in Relation to Cognitive Decline,” Annals of Neurology 72, no. 1 (July 2012): 135–43, https://doi.org/10.1002/ana.23594.

twenty three percent less chance of developing Parkinson’s: X. Gao et al., “Habitual Intake of Dietary Flavonoids and Risk of Parkinson Disease,” Neurology 78, no. 15 (April 10, 2012): 1138–45, https://doi.org/10.1212/WNL.0b013e31824f7fc4.

improvements in cognitive performance: Adrian R. Whyte, Graham Schafer, and Claire M. Williams, “Cognitive Effects Following Acute Wild Blueberry Supplementation in 7- to 10-Year-Old Children,” European Journal of Nutrition 55, no. 6 (September 2016): 2151–62, https://doi.org/10.1007/s00394-015-1029-4.

In a one-cup serving of strawberries: https://nutritiondata.self.com/facts/fruits-and-fruit-juices/ , accessed October 26, 2019

whole grains such as reduced risk of coronary heart disease: Aune et al., "Whole Grain Consumption and Risk of Cardiovascular Disease, Cancer, and All Cause and Cause Specific Mortality."

required by the eyes to prevent macular degeneration: Bronwyn Eisenhauer et al., "Lutein and Zeaxanthin—Food Sources, Bioavailability and Dietary Variety in Age-Related Macular Degeneration Protection," Nutrients 9, no. 2 (February 2017): 120, https://doi.org/10.3390/nu9020120.

reduces the risk of getting cataracts: L. Chasan-Taber et al., "A Prospective Study of Carotenoid and Vitamin A Intakes and Risk of Cataract Extraction in US Women," The American Journal of Clinical Nutrition 70, no. 4 (October 1999): 509–16, https://doi.org/10.1093/ajcn/70.4.509.

eliminates carcinogenic secondary bile acids: "Steam Cooking Significantly Improves in Vitro Bile Acid Binding of Collard Greens, Kale, Mustard Greens, Broccoli, Green Bell Pepper, and Cabbage," Nutrition Research 28, no. 6 (June 1, 2008): 351–57, https://doi.org/10.1016/j.nutres.2008.03.007.

improve bile salt binding activity: "Steam Cooking Significantly Improves in Vitro Bile Acid Binding of Collard Greens, Kale, Mustard Greens, Broccoli, Green Bell Pepper, and Cabbage."

four grams of fiber: https://nutritiondata.self.com/facts/vegetables-and-vegetable-products/2627/2 , accessed October 26, 2019

thiocyanates, sulforaphane, and indoles that may help: Olga Azarenko, Mary Ann Jordan, and Leslie Wilson, "Erucin, the Major Isothiocyanate in Arugula (Eruca Sativa), Inhibits Proliferation of MCF7 Tumor Cells by Suppressing Microtubule Dynamics," PloS One 9, no. 6 (2014): e100599, https://doi.

org/10.1371/journal.pone.0100599.

Bok choy is great for your bones: P. Weber, "Vitamin K and Bone Health," Nutrition (Burbank, Los Angeles County, Calif.) 17, no. 10 (October 2001): 880–87, https://doi.org/10.1016/s0899-9007(01)00709-2; R. P. Heaney et al., "Absorbability of Calcium from Brassica Vegetables: Broccoli, Bok Choy, and Kale," Journal of Food Science 58, no. 6 (1993): 1378–80, https://doi.org/10.1111/j.1365-2621.1993.tb06187.x.

glowing, radiant skin with improved elasticity: Ruta Ganceviciene et al., "Skin Anti-Aging Strategies," Dermato-Endocrinology 4, no. 3 (July 1, 2012): 308–19, https://doi.org/10.4161/derm.22804.

Traditional cultures are thought to have evolved: A. P. Simopoulos, "Evolutionary Aspects of Diet, the Omega-6/Omega-3 Ratio and Genetic Variation: Nutritional Implications for Chronic Diseases," Biomedicine & Pharmacotherapy = Biomedecine & Pharmacotherapie 60, no. 9 (November 2006): 6, https://doi.org/10.1016/j.biopha.2006.07.080; A. P. Simopoulos, "The Importance of the Ratio of Omega-6/Omega-3 Essential Fatty Acids," Biomedicine & Pharmacotherapy = Biomedecine & Pharmacotherapie 56, no. 8 (October 2002): 6, https://doi.org/10.1016/s0753-3322(02)00253-6.

It's a ratio that when skewed can promote disease: Simopoulos, "The Importance of the Ratio of Omega-6/Omega-3 Essential Fatty Acids."

Flax seeds are an excellent source of omega-3: "Chia vs. Hemp vs. Flax," Quick and Dirty Tips, accessed October 27, 2019, https://www.quickanddirtytips.com/health-fitness/healthy-eating/chia-vs-hemp-vs-flax.

Flax is also particularly rich in lignans: Julie K. Mason and Lilian U. Thompson, "Flaxseed and Its Lignan and Oil Components: Can They Play a Role in Reducing the Risk of and Improving the Treatment of Breast Cancer?," Applied Physiology, Nutrition, and Metabolism = Physiologie Appliquee, Nutrition

Et Metabolisme 39, no. 6 (June 2014): 663–78, https://doi.org/10.1139/apnm-2013-0420; Elizabeth C. Lowcock, Michelle Cotterchio, and Beatrice A. Boucher, "Consumption of Flaxseed, a Rich Source of Lignans, Is Associated with Reduced Breast Cancer Risk," Cancer Causes & Control: CCC 24, no. 4 (April 2013): 813–16, https://doi.org/10.1007/s10552-013-0155-7; Wendy Demark-Wahnefried et al., "Pilot Study to Explore Effects of Low-Fat, Flaxseed-Supplemented Diet on Proliferation of Benign Prostatic Epithelium and Prostate-Specific Antigen," Urology 63, no. 5 (May 2004): 900–904, https://doi.org/10.1016/j.urology.2003.12.010.

Basil alone has numerous phytochemicals: Manjeshwar Shrinath Baliga et al., "Ocimum Sanctum L (Holy Basil or Tulsi) and Its Phytochemicals in the Prevention and Treatment of Cancer," Nutrition and Cancer 65 Suppl 1 (2013): 26–35, https://doi.org/10.1080/01635581.2013.785010.

The allicin appears to target: S. Ankri and D. Mirelman, "Antimicrobial Properties of Allicin from Garlic," Microbes and Infection 1, no. 2 (February 1999): 125–29.

And it promotes the growth of Bifidobacteria: Ning Zhang et al., "Study on Prebiotic Effectiveness of Neutral Garlic Fructan in Vitro," Food Science and Human Wellness 2, no. 3 (September 1, 2013): 119–23, https://doi.org/10.1016/j.fshw.2013.07.001.

alliums are also an excellent source of PREbiotic fiber: V. Prasanna Kumar, K. V. Harish Prashanth, and Y. P. Venkatesh, "Structural Analyses and Immunomodulatory Properties of Fructo-Oligosaccharides from Onion (Allium Cepa)," Carbohydrate Polymers 117 (March 6, 2015): 115–22, https://doi.org/10.1016/j.carbpol.2014.09.039; Jane G. Muir et al., "Fructan and Free Fructose Content of Common Australian Vegetables and Fruit," Journal of Agricultural and Food Chemistry 55, no. 16 (August 8, 2007): 6619–27, https://doi.org/10.1021/jf070623x.

There's a placebo controlled trial: P. Josling, "Preventing the Common Cold with a Garlic Supplement: A Double-Blind, Placebo-Controlled Survey," Advances in Therapy 18, no. 4 (August 2001): 189–93.

organosulfur compounds like allicin detoxify carcinogens: Anna A. Powolny and Shivendra V. Singh, "Multitargeted Prevention and Therapy of Cancer by Diallyl Trisulfide and Related Allium Vegetable-Derived Organosulfur Compounds," Cancer Letters 269, no. 2 (October 8, 2008): 305–14, https://doi.org/10.1016/j.canlet.2008.05.027.

allium veggies contain at least twenty four: Rune Slimestad, Torgils Fossen, and Ingunn Molund Vågen, "Onions: A Source of Unique Dietary Flavonoids," Journal of Agricultural and Food Chemistry 55, no. 25 (December 12, 2007): 10067–80, https://doi.org/10.1021/jf0712503.

added benefit of anthocyanidins: Slimestad, Fossen, and Vågen.

The flavonoids have anti-inflammatory effects: Paula Ravasco et al., "Colorectal Cancer: Can Nutrients Modulate NF-KappaB and Apoptosis?," Clinical Nutrition (Edinburgh, Scotland) 29, no. 1 (February 2010): 42–46, https://doi.org/10.1016/j.clnu.2009.06.006.

These antioxidant compounds also appear to: Carmia Borek, "Garlic Reduces Dementia and Heart-Disease Risk," The Journal of Nutrition 136, no. 3 Suppl (2006): 810S-812S, https://doi.org/10.1093/jn/136.3.810S.

Cancer is cured, inflammation is squashed: D. T. Verhoeven et al., "Epidemiological Studies on Brassica Vegetables and Cancer Risk," Cancer Epidemiology, Biomarkers & Prevention: A Publication of the American Association for Cancer Research, Cosponsored by the American Society of Preventive Oncology 5, no. 9 (September 1996): 733–48; Yu Jiang et al., "Cruciferous Vegetable Intake Is Inversely Correlated with Circulating Levels of Proinflammatory Markers in Women," Journal of the Academy of Nutrition

and Dietetics 114, no. 5 (May 2014): 700-708.e2, https://doi.org/10.1016/j.jand.2013.12.019; Xianglan Zhang et al., "Cruciferous Vegetable Consumption Is Associated with a Reduced Risk of Total and Cardiovascular Disease Mortality," The American Journal of Clinical Nutrition 94, no. 1 (July 2011): 240–46, https://doi.org/10.3945/ajcn.110.009340; Carrie Waterman et al., "Isothiocyanate-Rich Moringa Oleifera Extract Reduces Weight Gain, Insulin Resistance, and Hepatic Gluconeogenesis in Mice," Molecular Nutrition & Food Research 59, no. 6 (June 2015): 1013–24, https://doi.org/10.1002/mnfr.201400679; C. J. Henry and B. Emery, "Effect of Spiced Food on Metabolic Rate," Human Nutrition. Clinical Nutrition 40, no. 2 (March 1986): 165–68; Karen J. Auborn et al., "Indole-3-Carbinol Is a Negative Regulator of Estrogen," The Journal of Nutrition 133, no. 7 Suppl (July 2003): 2470S-2475S.

the cancer protective effects of sulforaphane: Y. Zhang et al., "A Major Inducer of Anticarcinogenic Protective Enzymes from Broccoli: Isolation and Elucidation of Structure," Proceedings of the National Academy of Sciences of the United States of America 89, no. 6 (March 15, 1992): 2399–2403, https://doi.org/10.1073/pnas.89.6.2399.

Protects us from cancer by seven mechanisms: Y. Zhang and P. Talalay, "Anticarcinogenic Activities of Organic Isothiocyanates: Chemistry and Mechanisms," Cancer Research 54, no. 7 Suppl (April 1, 1994): 1976s–81; Zhang et al., "A Major Inducer of Anticarcinogenic Protective Enzymes from Broccoli"; Praveen Rajendran et al., "Nrf2 Status Affects Tumor Growth, HDAC3 Gene Promoter Associations, and the Response to Sulforaphane in the Colon," Clinical Epigenetics 7 (2015): 102, https://doi.org/10.1186/s13148-015-0132-y; Gaurav Kumar et al., "Isothiocyanates: A Class of Bioactive Metabolites with Chemopreventive Potential," Tumour Biology: The Journal of the International Society for Oncodevelopmental Biology and Medicine 36, no. 6 (June 2015): 4005–16, https://doi.org/10.1007/s13277-015-3391-5; Stephanie M. Tortorella et al., "Dietary Sulforaphane in Cancer Chemoprevention: The Role of Epigenetic Regulation and HDAC Inhibition," Antioxidants & Redox Signaling 22, no. 16 (June 1, 2015): 1382–1424, https://doi.org/10.1089/ars.2014.6097; Liping Wang

et al., “Sulforaphane Inhibits Thyroid Cancer Cell Growth and Invasiveness through the Reactive Oxygen Species-Dependent Pathway,” Oncotarget 6, no. 28 (September 22, 2015): 25917–31, https://doi.org/10.18632/oncotarget.4542; Minhee Kim et al., “Benzyl Isothiocyanate Suppresses High-Fat Diet-Stimulated Mammary Tumor Progression via the Alteration of Tumor Microenvironments in Obesity-Resistant BALB/c Mice,” Molecular Carcinogenesis 54, no. 1 (January 2015): 72–82, https://doi.org/10.1002/mc.22159; Parul Gupta et al., “Metastasis of Breast Tumor Cells to Brain Is Suppressed by Phenethyl Isothiocyanate in a Novel In Vivo Metastasis Model,” PloS One 8, no. 6 (2013): e67278, https://doi.org/10.1371/journal.pone.0067278; Breeze E. Cavell et al., “Anti-Angiogenic Effects of Dietary Isothiocyanates: Mechanisms of Action and Implications for Human Health,” Biochemical Pharmacology 81, no. 3 (February 1, 2011): 327–36, https://doi.org/10.1016/j.bcp.2010.10.005.

Undermines lung, colon, breast, prostate: Julie E. Bauman et al., “Prevention of Carcinogen-Induced Oral Cancer by Sulforaphane,” Cancer Prevention Research (Philadelphia, Pa.) 9, no. 7 (July 2016): 547–57, https://doi.org/10.1158/1940-6207.CAPR-15-0290; C. Clifford Conaway et al., “Phenethyl Isothiocyanate and Sulforaphane and Their N-Acetylcysteine Conjugates Inhibit Malignant Progression of Lung Adenomas Induced by Tobacco Carcinogens in A/J Mice,” Cancer Research 65, no. 18 (September 15, 2005): 8548–57, https://doi.org/10.1158/0008-5472.CAN-05-0237; Praveen Rajendran et al., “HDAC Turnover, CtIP Acetylation and Dysregulated DNA Damage Signaling in Colon Cancer Cells Treated with Sulforaphane and Related Dietary Isothiocyanates,” Epigenetics 8, no. 6 (June 1, 2013): 612–23, https://doi.org/10.4161/epi.24710; Young-Sam Keum et al., “Pharmacokinetics and Pharmacodynamics of Broccoli Sprouts on the Suppression of Prostate Cancer in Transgenic Adenocarcinoma of Mouse Prostate (TRAMP) Mice: Implication of Induction of Nrf2, HO-1 and Apoptosis and the Suppression of Akt-Dependent Kinase Pathway,” Pharmaceutical Research 26, no. 10 (October 2009): 2324–31, https://doi.org/10.1007/s11095-009-9948-5; Yanyan Li et al., “Sulforaphane, a Dietary Component of Broccoli/Broccoli Sprouts, Inhibits Breast Cancer Stem Cells,” Clinical Cancer Research: An Official Journal of the

American Association for Cancer Research 16, no. 9 (May 1, 2010): 2580–90, https://doi.org/10.1158/1078-0432.CCR-09-2937; Rex Munday et al., "Inhibition of Urinary Bladder Carcinogenesis by Broccoli Sprouts," Cancer Research 68, no. 5 (March 1, 2008): 1593–1600, https://doi.org/10.1158/0008-5472.CAN-07-5009; Albena T. Dinkova-Kostova et al., "Protection against UV-Light-Induced Skin Carcinogenesis in SKH-1 High-Risk Mice by Sulforaphane-Containing Broccoli Sprout Extracts," Cancer Letters 240, no. 2 (August 28, 2006): 243–52, https://doi.org/10.1016/j.canlet.2005.09.012; Yanyan Li et al., "Sulforaphane Inhibits Pancreatic Cancer through Disrupting Hsp90-P50(Cdc37) Complex and Direct Interactions with Amino Acids Residues of Hsp90," The Journal of Nutritional Biochemistry 23, no. 12 (December 2012): 3, https://doi.org/10.1016/j.jnutbio.2011.11.004; John D. Clarke, Roderick H. Dashwood, and Emily Ho, "Multi-Targeted Prevention of Cancer by Sulforaphane," Cancer Letters 269, no. 2 (October 8, 2008): 291–304, https://doi.org/10.1016/j.canlet.2008.04.018.

Shuts down the pro-inflammatory pathways: Zhaojun Dong et al., "Sulforaphane Protects Pancreatic Acinar Cell Injury by Modulating Nrf2-Mediated Oxidative Stress and NLRP3 Inflammatory Pathway," Oxidative Medicine and Cellular Longevity 2016 (2016): 2, https://doi.org/10.1155/2016/7864150; Dong et al., 2.

Works as a powerful antioxidant: Dong et al., "Sulforaphane Protects Pancreatic Acinar Cell Injury by Modulating Nrf2-Mediated Oxidative Stress and NLRP3 Inflammatory Pathway"; Carlos Enrique Guerrero-Beltrán et al., "Protective Effect of Sulforaphane against Oxidative Stress: Recent Advances," Experimental and Toxicologic Pathology: Official Journal of the Gesellschaft Fur Toxikologische Pathologie 64, no. 5 (July 2012): 503–8, https://doi.org/10.1016/j.etp.2010.11.005; Zhihong Zhao et al., "Sulforaphane Attenuates Contrast-Induced Nephropathy in Rats via Nrf2/HO-1 Pathway," Oxidative Medicine and Cellular Longevity 2016 (2016): 9825623, https://doi.org/10.1155/2016/9825623; Yonggang Wang et al., "Sulforaphane Attenuation of Type 2 Diabetes-Induced Aortic Damage Was Associated with

the Upregulation of Nrf2 Expression and Function," Oxidative Medicine and Cellular Longevity 2014 (2014): 123963, https://doi.org/10.1155/2014/123963; Xinjin Chi et al., "Sulforaphane Reduces Apoptosis and Oncosis along with Protecting Liver Injury-Induced Ischemic Reperfusion by Activating the Nrf2/ARE Pathway," Hepatology International 9, no. 2 (April 2015): 321–29, https://doi.org/10.1007/s12072-014-9604-y.

May benefit Parkinson's, and recovery from stroke: Fabiana Morroni et al., "Neuroprotective Effect of Sulforaphane in 6-Hydroxydopamine-Lesioned Mouse Model of Parkinson's Disease," Neurotoxicology 36 (May 2013): 63–71, https://doi.org/10.1016/j.neuro.2013.03.004; Rui Zhang et al., "Neuroprotective Effects of Sulforaphane on Cholinergic Neurons in Mice with Alzheimer's Disease-like Lesions," International Journal of Molecular Sciences 15, no. 8 (August 18, 2014): 14396–410, https://doi.org/10.3390/ijms150814396; Alessio Alfieri et al., "Sulforaphane Preconditioning of the Nrf2/HO-1 Defense Pathway Protects the Cerebral Vasculature against Blood-Brain Barrier Disruption and Neurological Deficits in Stroke," Free Radical Biology & Medicine 65 (December 2013): 1012–22, https://doi.org/10.1016/j.freeradbiomed.2013.08.190; Pramod K. Dash et al., "Sulforaphane Improves Cognitive Function Administered Following Traumatic Brain Injury," Neuroscience Letters 460, no. 2 (August 28, 2009): 103–7, https://doi.org/10.1016/j.neulet.2009.04.028; Qian Zhou et al., "Sulforaphane Protects against Rotenone-Induced Neurotoxicity in Vivo: Involvement of the MTOR, Nrf2, and Autophagy Pathways," Scientific Reports 6 (24 2016): 32206, https://doi.org/10.1038/srep32206; Morroni et al., "Neuroprotective Effect of Sulforaphane in 6-Hydroxydopamine-Lesioned Mouse Model of Parkinson's Disease"; David Vauzour et al., "Sulforaphane Protects Cortical Neurons against 5-S-Cysteinyl-Dopamine-Induced Toxicity through the Activation of ERK1/2, Nrf-2 and the Upregulation of Detoxification Enzymes," Molecular Nutrition & Food Research 54, no. 4 (April 2010): 532–42, https://doi.org/10.1002/mnfr.200900197; Ji Man Han et al., "Protective Effect of Sulforaphane against Dopaminergic Cell Death," The Journal of Pharmacology and Experimental Therapeutics 321, no. 1 (April 2007): 249–56, https://doi.org/10.1124/jpet.106.110866.

Reduces amyloid beta plaques: Zhang et al., "Neuroprotective Effects of Sulforaphane on Cholinergic Neurons in Mice with Alzheimer's Disease-like Lesions"; Rui Zhang et al., "Sulforaphane Ameliorates Neurobehavioral Deficits and Protects the Brain from Amyloid β Deposits and Peroxidation in Mice with Alzheimer-like Lesions," American Journal of Alzheimer's Disease and Other Dementias 30, no. 2 (March 2015): 183–91, https://doi.org/10.1177/1533317514542645; Hyunjin Vincent Kim et al., "Amelioration of Alzheimer's Disease by Neuroprotective Effect of Sulforaphane in Animal Model," Amyloid: The International Journal of Experimental and Clinical Investigation: The Official Journal of the International Society of Amyloidosis 20, no. 1 (March 2013): 7–12, https://doi.org/10.3109/13506129.2012.751367.

Improves mood, as well as anxiety: Ji-Chun Zhang et al., "Prophylactic Effects of Sulforaphane on Depression-like Behavior and Dendritic Changes in Mice after Inflammation," The Journal of Nutritional Biochemistry 39 (2017): 134–44, https://doi.org/10.1016/j.jnutbio.2016.10.004; María Dolores Martín-de-Saavedra et al., "Nrf2 Participates in Depressive Disorders through an Anti-Inflammatory Mechanism," Psychoneuroendocrinology 38, no. 10 (October 2013): 2010–22, https://doi.org/10.1016/j.psyneuen.2013.03.020.

Boosts brain function, improving memory: Yumi Shirai et al., "Dietary Intake of Sulforaphane-Rich Broccoli Sprout Extracts during Juvenile and Adolescence Can Prevent Phencyclidine-Induced Cognitive Deficits at Adulthood," PloS One 10, no. 6 (2015): e0127244, https://doi.org/10.1371/journal.pone.0127244; Siyoung Lee et al., "Sulforaphane Alleviates Scopolamine-Induced Memory Impairment in Mice," Pharmacological Research 85 (July 1, 2014): 23–32, https://doi.org/10.1016/j.phrs.2014.05.003.

Regulates the immune system, ameliorating autoimmune: Bin Li et al., "Sulforaphane Ameliorates the Development of Experimental Autoimmune Encephalomyelitis by Antagonizing Oxidative Stress and Th17-Related Inflammation in Mice," Experimental Neurology 250 (December 2013): 239–49, https://doi.org/10.1016/j.expneurol.2013.10.002; Katja Schmitz et al., "'Disease

Modifying Nutricals' for Multiple Sclerosis," Pharmacology & Therapeutics 148 (April 2015): 85–113, https://doi.org/10.1016/j.pharmthera.2014.11.015; Jin-Sun Kong et al., "Inhibition of Synovial Hyperplasia, Rheumatoid T Cell Activation, and Experimental Arthritis in Mice by Sulforaphane, a Naturally Occurring Isothiocyanate," Arthritis and Rheumatism 62, no. 1 (January 2010): 159–70, https://doi.org/10.1002/art.25017.

Flips the body into fat-burning mode to promote weight loss: Kyeong-Mi Choi et al., "Sulforaphane Attenuates Obesity by Inhibiting Adipogenesis and Activating the AMPK Pathway in Obese Mice," The Journal of Nutritional Biochemistry 25, no. 2 (February 1, 2014): 201–7, https://doi.org/10.1016/j.jnutbio.2013.10.007; Naoto Nagata et al., "Glucoraphanin Ameliorates Obesity and Insulin Resistance Through Adipose Tissue Browning and Reduction of Metabolic Endotoxemia in Mice," Diabetes 66, no. 5 (2017): 1222–36, https://doi.org/10.2337/db16-0662.

twenty three out of twenty eight pathogenic bacterial: Noelle L. Johansson, Charles S. Pavia, and Jen Wei Chiao, "Growth Inhibition of a Spectrum of Bacterial and Fungal Pathogens by Sulforaphane, an Isothiocyanate Product Found in Broccoli and Other Cruciferous Vegetables," Planta Medica 74, no. 7 (June 2008): 747–50, https://doi.org/10.1055/s-2008-1074520.

Protects the heart by improving lipids, lowering blood pressure: Paul C. Evans, "The Influence of Sulforaphane on Vascular Health and Its Relevance to Nutritional Approaches to Prevent Cardiovascular Disease," The EPMA Journal 2, no. 1 (March 2011): 9–14, https://doi.org/10.1007/s13167-011-0064-3; Yang Bai et al., "Sulforaphane Protects against Cardiovascular Disease via Nrf2 Activation," Oxidative Medicine and Cellular Longevity 2015 (2015): 407580, https://doi.org/10.1155/2015/407580; Mustafa Zakkar et al., "Activation of Nrf2 in Endothelial Cells Protects Arteries from Exhibiting a Proinflammatory State," Arteriosclerosis, Thrombosis, and Vascular Biology 29, no. 11 (November 2009): 1851–57, https://doi.org/10.1161/ATVBAHA.109.193375; Gamarallage V. K. Senanayake et al., "The Dietary Phase 2 Protein Inducer Sulforaphane Can

Normalize the Kidney Epigenome and Improve Blood Pressure in Hypertensive Rats," American Journal of Hypertension 25, no. 2 (February 2012): 229–35, https://doi.org/10.1038/ajh.2011.200; George S. G. Shehatou and Ghada M. Suddek, "Sulforaphane Attenuates the Development of Atherosclerosis and Improves Endothelial Dysfunction in Hypercholesterolemic Rabbits," Experimental Biology and Medicine (Maywood, N.J.) 241, no. 4 (February 2016): 426–36, https://doi.org/10.1177/1535370215609695; Charlotte N. Armah et al., "Diet Rich in High Glucoraphanin Broccoli Reduces Plasma LDL Cholesterol: Evidence from Randomised Controlled Trials," Molecular Nutrition & Food Research 59, no. 5 (May 2015): 918–26, https://doi.org/10.1002/mnfr.201400863.

Improves insulin sensitivity: Carolina Guerini de Souza et al., "Metabolic Effects of Sulforaphane Oral Treatment in Streptozotocin-Diabetic Rats," Journal of Medicinal Food 15, no. 9 (September 2012): 795–801, https://doi.org/10.1089/jmf.2012.0016; Annika S. Axelsson et al., "Sulforaphane Reduces Hepatic Glucose Production and Improves Glucose Control in Patients with Type 2 Diabetes," Science Translational Medicine 9, no. 394 (14 2017), https://doi.org/10.1126/scitranslmed.aah4477.

correcting diabetic heart and kidney damage: Yang Bai et al., "Prevention by Sulforaphane of Diabetic Cardiomyopathy Is Associated with Up-Regulation of Nrf2 Expression and Transcription Activation," Journal of Molecular and Cellular Cardiology 57 (April 2013): 82–95, https://doi.org/10.1016/j.yjmcc.2013.01.008; Wenpeng Cui et al., "Prevention of Diabetic Nephropathy by Sulforaphane: Possible Role of Nrf2 Upregulation and Activation," Oxidative Medicine and Cellular Longevity 2012 (2012): 821936, https://doi.org/10.1155/2012/821936.

Protects the liver and kidneys: Carlos Enrique Guerrero-Beltrán et al., "Sulforaphane, a Natural Constituent of Broccoli, Prevents Cell Death and Inflammation in Nephropathy," The Journal of Nutritional Biochemistry 23, no. 5 (May 1, 2012): 494–500, https://doi.org/10.1016/j.jnutbio.2011.02.004;

Leobardo Gaona-Gaona et al., "Protective Effect of Sulforaphane Pretreatment against Cisplatin-Induced Liver and Mitochondrial Oxidant Damage in Rats," Toxicology 286, no. 1–3 (August 15, 2011): 20–27, https://doi.org/10.1016/j.tox.2011.04.014.

reducing levels of pathogenic bacteria and bacterial endotoxin release: Nagata et al., "Glucoraphanin Ameliorates Obesity and Insulin Resistance Through Adipose Tissue Browning and Reduction of Metabolic Endotoxemia in Mice"; Johansson, Pavia, and Chiao, "Growth Inhibition of a Spectrum of Bacterial and Fungal Pathogens by Sulforaphane, an Isothiocyanate Product Found in Broccoli and Other Cruciferous Vegetables."

In another study, sulforaphane corrected gut dysbiosis: Canxia He et al., "Sulforaphane Normalizes Intestinal Flora and Enhances Gut Barrier in Mice with BBN-Induced Bladder Cancer," Molecular Nutrition & Food Research 62, no. 24 (2018): e1800427, https://doi.org/10.1002/mnfr.201800427.

10-100 times more sulforaphane: J. W. Fahey, Y. Zhang, and P. Talalay, "Broccoli Sprouts: An Exceptionally Rich Source of Inducers of Enzymes That Protect against Chemical Carcinogens," Proceedings of the National Academy of Sciences of the United States of America 94, no. 19 (September 16, 1997): 10367–72, https://doi.org/10.1073/pnas.94.19.10367.

comparing broccoli sprouts to a supplement: John D. Clarke et al., "Comparison of Isothiocyanate Metabolite Levels and Histone Deacetylase Activity in Human Subjects Consuming Broccoli Sprouts or Broccoli Supplement," Journal of Agricultural and Food Chemistry 59, no. 20 (October 26, 2011): 10955–63, https://doi.org/10.1021/jf202887c.

They contain PREbiotic beta-glucan: Luca Vannucci et al., "Immunostimulatory Properties and Antitumor Activities of Glucans (Review)," International Journal of Oncology 43, no. 2 (August 2013): 357–64, https://doi.org/10.3892/ijo.2013.1974; Dalia Akramiene et al., "Effects of Beta-Glucans on the Immune

System," Medicina (Kaunas, Lithuania) 43, no. 8 (2007): 597–606; Sang Chul Jeong, Sundar Rao Koyyalamudi, and Gerald Pang, "Dietary Intake of Agaricus Bisporus White Button Mushroom Accelerates Salivary Immunoglobulin A Secretion in Healthy Volunteers," Nutrition (Burbank, Los Angeles County, Calif.) 28, no. 5 (May 2012): 527–31, https://doi.org/10.1016/j.nut.2011.08.005; Min Zhang et al., "Dietary Intakes of Mushrooms and Green Tea Combine to Reduce the Risk of Breast Cancer in Chinese Women," International Journal of Cancer 124, no. 6 (March 15, 2009): 1404–8, https://doi.org/10.1002/ijc.24047.

unique protection against breast cancer: B. J. Grube et al., "White Button Mushroom Phytochemicals Inhibit Aromatase Activity and Breast Cancer Cell Proliferation," The Journal of Nutrition 131, no. 12 (December 2001): 3288–93, https://doi.org/10.1093/jn/131.12.3288.

a sixty four percent reduction in breast cancer risk: Zhang et al., "Dietary Intakes of Mushrooms and Green Tea Combine to Reduce the Risk of Breast Cancer in Chinese Women."

Several types contain a substance called agaritine: B. Toth and J. Erickson, "Cancer Induction in Mice by Feeding of the Uncooked Cultivated Mushroom of Commerce Agaricus Bisporus," Cancer Research 46, no. 8 (August 1986): 4007–11; V. Schulzová et al., "Influence of Storage and Household Processing on the Agaritine Content of the Cultivated Agaricus Mushroom," Food Additives and Contaminants 19, no. 9 (September 2002): 853–62, https://doi.org/10.1080/02652030210156340.

Naturally, these are PREbiotic fibers: Priya Ramnani et al., "In Vitro Fermentation and Prebiotic Potential of Novel Low Molecular Weight Polysaccharides Derived from Agar and Alginate Seaweeds," Anaerobe 18, no. 1 (February 1, 2012): 1–6, https://doi.org/10.1016/j.anaerobe.2011.08.003.

fucoxanthin that helps reduce the accumulation of fats: Hayato Maeda et al., "Fucoxanthin from Edible Seaweed, Undaria Pinnatifida, Shows

Antiobesity Effect through UCP1 Expression in White Adipose Tissues," Biochemical and Biophysical Research Communications 332, no. 2 (July 1, 2005): 392–97, https://doi.org/10.1016/j.bbrc.2005.05.002; Kh Muradian et al., "Fucoxanthin and Lipid Metabolism: A Minireview," Nutrition, Metabolism, and Cardiovascular Diseases: NMCD 25, no. 10 (October 2015): 891–97, https://doi.org/10.1016/j.numecd.2015.05.010; Maria Alessandra Gammone and Nicolantonio D'Orazio, "Anti-Obesity Activity of the Marine Carotenoid Fucoxanthin," Marine Drugs 13, no. 4 (April 13, 2015): 2196–2214, https://doi.org/10.3390/md13042196; Hayato Maeda, "Nutraceutical Effects of Fucoxanthin for Obesity and Diabetes Therapy: A Review," Journal of Oleo Science 64, no. 2 (2015): 125–32, https://doi.org/10.5650/jos.ess14226.

organic food had a lower overall risk of cancer: Julia Baudry et al., "Association of Frequency of Organic Food Consumption With Cancer Risk: Findings From the NutriNet-Santé Prospective Cohort Study," JAMA Internal Medicine 178, no. 12 (01 2018): 1597–1606, https://doi.org/10.1001/jamainternmed.2018.4357.

CHAPTER 9

New research indicates that the same plant: Rachel N. Carmody et al., "Cooking Shapes the Structure and Function of the Gut Microbiome," Nature Microbiology, September 30, 2019, 1–12, https://doi.org/10.1038/s41564-019-0569-4.

Coffee contains polyphenols: Fernando Cardona et al., "Benefits of Polyphenols on Gut Microbiota and Implications in Human Health," The Journal of Nutritional Biochemistry 24, no. 8 (August 1, 2013): 1415–22, https://doi.org/10.1016/j.jnutbio.2013.05.001.

It's also the biggest source of antioxidants: Arne Svilaas et al., "Intakes of Antioxidants in Coffee, Wine, and Vegetables Are Correlated with Plasma Carotenoids in Humans," The Journal of Nutrition 134, no. 3 (March 2004): 562–67, https://doi.org/10.1093/jn/134.3.562.

There's actually a gene: Hans-Peter Landolt, "'No Thanks, Coffee Keeps Me Awake': Individual Caffeine Sensitivity Depends on ADORA2A Genotype," Sleep 35, no. 7 (July 1, 2012): 899–900, https://doi.org/10.5665/sleep.1942.

literally 100 times more PREbiotic polyphenol EGCG: David J. Weiss and Christopher R. Anderton, "Determination of Catechins in Matcha Green Tea by Micellar Electrokinetic Chromatography," Journal of Chromatography. A 1011, no. 1–2 (September 5, 2003): 173–80, https://doi.org/10.1016/s0021-9673(03)01133-6.

vitamin C dramatically improves their absorption: Rodney J. Green et al., "Common Tea Formulations Modulate in Vitro Digestive Recovery of Green Tea Catechins," Molecular Nutrition & Food Research 51, no. 9 (September 2007): 1152–62, https://doi.org/10.1002/mnfr.200700086.

binge alcohol consumption causes damage to the gut microbiota: Ece A. Mutlu et al., "Colonic Microbiome Is Altered in Alcoholism," American Journal of Physiology. Gastrointestinal and Liver Physiology 302, no. 9 (May 1, 2012): G966-978, https://doi.org/10.1152/ajpgi.00380.2011.

this is how alcohol causes cirrhosis: G. Vassallo et al., "Review Article: Alcohol and Gut Microbiota - the Possible Role of Gut Microbiota Modulation in the Treatment of Alcoholic Liver Disease," Alimentary Pharmacology & Therapeutics 41, no. 10 (May 2015): 917–27, https://doi.org/10.1111/apt.13164.

Just a single crazy Friday night: Shashi Bala et al., "Acute Binge Drinking Increases Serum Endotoxin and Bacterial DNA Levels in Healthy Individuals," PloS One 9, no. 5 (2014): e96864, https://doi.org/10.1371/journal.pone.0096864.

Just one drink per day: Iona Y. Millwood et al., "Conventional and Genetic Evidence on Alcohol and Vascular Disease Aetiology: A Prospective Study of 500 000 Men and Women in China," The Lancet 393, no. 10183 (May 4, 2019):

000, https://doi.org/10.1016/S0140-6736(18)31772-0.

Just a half drink per day: Wendy Y. Chen et al., "Moderate Alcohol Consumption during Adult Life, Drinking Patterns, and Breast Cancer Risk," JAMA 306, no. 17 (November 2, 2011): 1884–90, https://doi.org/10.1001/jama.2011.1590.

There is strong consensus among the scientific community: IARC Working Group on the Evaluation of Carcinogenic Risks to Humans, "Alcohol Consumption and Ethyl Carbamate," IARC Monographs on the Evaluation of Carcinogenic Risks to Humans 96 (2010): 3–1383; IARC Working Group on the Evaluation of Carcinogenic Risks to Humans, "Personal Habits and Indoor Combustions. Volume 100 E. A Review of Human Carcinogens," IARC Monographs on the Evaluation of Carcinogenic Risks to Humans 100, no. Pt E (2012): 1–538; V. Bagnardi et al., "Light Alcohol Drinking and Cancer: A Meta-Analysis," Annals of Oncology: Official Journal of the European Society for Medical Oncology 24, no. 2 (February 2013): 301–8, https://doi.org/10.1093/annonc/mds337; V. Bagnardi et al., "Alcohol Consumption and Site-Specific Cancer Risk: A Comprehensive Dose-Response Meta-Analysis," British Journal of Cancer 112, no. 3 (February 3, 2015): 580–93, https://doi.org/10.1038/bjc.2014.579; Yin Cao et al., "Light to Moderate Intake of Alcohol, Drinking Patterns, and Risk of Cancer: Results from Two Prospective US Cohort Studies," BMJ (Clinical Research Ed.) 351 (August 18, 2015): h4238, https://doi.org/10.1136/bmj.h4238; Chen et al., "Moderate Alcohol Consumption during Adult Life, Drinking Patterns, and Breast Cancer Risk"; Alexandra J. White et al., "Lifetime Alcohol Intake, Binge Drinking Behaviors, and Breast Cancer Risk," American Journal of Epidemiology 186, no. 5 (September 1, 2017): 541–49, https://doi.org/10.1093/aje/kwx118.

polyphenols in red wine are PREbiotic: Caroline I. Le Roy et al., "Red Wine Consumption Associated With Increased Gut Microbiota α-Diversity in 3 Independent Cohorts," Gastroenterology 0, no. 0 (August 28, 2019), https://doi.org/10.1053/j.gastro.2019.08.024.

resveratrol in red wine has been linked with heart health: T. S. Mohamed Saleem and S. Darbar Basha, "Red Wine: A Drink to Your Heart," Journal of Cardiovascular Disease Research 1, no. 4 (October 2010): 171–76, https://doi.org/10.4103/0975-3583.74259.

Resveratrol in red wine decreases TMAO levels: Ming-liang Chen et al., "Resveratrol Attenuates Trimethylamine-N-Oxide (TMAO)-Induced Atherosclerosis by Regulating TMAO Synthesis and Bile Acid Metabolism via Remodeling of the Gut Microbiota," MBio 7, no. 2 (April 5, 2016): e02210-02215, https://doi.org/10.1128/mBio.02210-15.

SCFAs that trigger the release of satiety hormones: Byrne et al., "The Role of Short Chain Fatty Acids in Appetite Regulation and Energy Homeostasis."

our species consumed whole plant foods: S. Boyd Eaton, "The Ancestral Human Diet: What Was It and Should It Be a Paradigm for Contemporary Nutrition?," The Proceedings of the Nutrition Society 65, no. 1 (February 2006): 1–6.

This is an endogenous, entrainable oscillation: Rachel S. Edgar et al., "Peroxiredoxins Are Conserved Markers of Circadian Rhythms," Nature 485, no. 7399 (May 16, 2012): 459–64, https://doi.org/10.1038/nature11088.

jet lag actually induces dysbiosis: Christoph A. Thaiss et al., "Transkingdom Control of Microbiota Diurnal Oscillations Promotes Metabolic Homeostasis," Cell 159, no. 3 (October 23, 2014): 514–29, https://doi.org/10.1016/j.cell.2014.09.048.

Shift workers are at increased risk for: Maria Carlota Borba Brum et al., "Shift Work and Its Association with Metabolic Disorders," Diabetology & Metabolic Syndrome 7 (2015): 45, https://doi.org/10.1186/s13098-015-0041-4.

We are most insulin sensitive: Ruth E. Patterson and Dorothy D. Sears,

"Metabolic Effects of Intermittent Fasting," Annual Review of Nutrition 37 (21 2017): 371–93, https://doi.org/10.1146/annurev-nutr-071816-064634; Karen L. Gamble et al., "Circadian Clock Control of Endocrine Factors," Nature Reviews. Endocrinology 10, no. 8 (August 2014): 466–75, https://doi.org/10.1038/nrendo.2014.78.

When we deprive ourselves of sleep,: Christian Benedict et al., "Gut Microbiota and Glucometabolic Alterations in Response to Recurrent Partial Sleep Deprivation in Normal-Weight Young Individuals," Molecular Metabolism 5, no. 12 (2016): 1175–86, https://doi.org/10.1016/j.molmet.2016.10.003; Robin M. Voigt et al., "Circadian Disorganization Alters Intestinal Microbiota," PloS One 9, no. 5 (2014): e97500, https://doi.org/10.1371/journal.pone.0097500.

Insufficient sleep is associated with: Rachel R. Markwald et al., "Impact of Insufficient Sleep on Total Daily Energy Expenditure, Food Intake, and Weight Gain," Proceedings of the National Academy of Sciences of the United States of America 110, no. 14 (April 2, 2013): 5695–5700, https://doi.org/10.1073/pnas.1216951110; Jeffrey M. Ellenbogen, "Cognitive Benefits of Sleep and Their Loss Due to Sleep Deprivation," Neurology 64, no. 7 (April 12, 2005): E25-27, https://doi.org/10.1212/01.wnl.0000164850.68115.81; Suzanne E. Goldman et al., "Poor Sleep Is Associated with Poorer Physical Performance and Greater Functional Limitations in Older Women," Sleep 30, no. 10 (October 2007): 1317–24, https://doi.org/10.1093/sleep/30.10.1317; Francesco P. Cappuccio et al., "Sleep Duration Predicts Cardiovascular Outcomes: A Systematic Review and Meta-Analysis of Prospective Studies," European Heart Journal 32, no. 12 (June 2011): 1484–92, https://doi.org/10.1093/eurheartj/ehr007; K. Spiegel, R. Leproult, and E. Van Cauter, "Impact of Sleep Debt on Metabolic and Endocrine Function," Lancet (London, England) 354, no. 9188 (October 23, 1999): 1435–39, https://doi.org/10.1016/S0140-6736(99)01376-8; M. Irwin et al., "Partial Night Sleep Deprivation Reduces Natural Killer and Cellular Immune Responses in Humans," FASEB Journal: Official Publication of the Federation of American Societies for Experimental Biology 10, no. 5 (April 1996): 643–53, https://doi.org/10.1096/fasebj.10.5.8621064; Amie C. Hayley et al., "The

Relationships between Insomnia, Sleep Apnoea and Depression: Findings from the American National Health and Nutrition Examination Survey, 2005-2008," The Australian and New Zealand Journal of Psychiatry 49, no. 2 (February 2015): 156–70, https://doi.org/10.1177/0004867414546700.

It's important not only that we get enough sleep: Andrew E. Rosselot, Christian I. Hong, and Sean R. Moore, "Rhythm and Bugs: Circadian Clocks, Gut Microbiota, and Enteric Infections," Current Opinion in Gastroenterology 32, no. 1 (January 2016): 7–11, https://doi.org/10.1097/MOG.0000000000000227.

bright light impairs melatonin release: Maria Angeles Bonmati-Carrion et al., "Protecting the Melatonin Rhythm through Circadian Healthy Light Exposure," International Journal of Molecular Sciences 15, no. 12 (December 17, 2014): 23448–500, https://doi.org/10.3390/ijms151223448.

our manmade structures are a microbial badlands: Sean M. Gibbons, "The Built Environment Is a Microbial Wasteland," MSystems 1, no. 2 (April 26, 2016): e00033-16, https://doi.org/10.1128/mSystems.00033-16.

moving from a rural environment to the city: Kathryn Winglee et al., "Recent Urbanization in China Is Correlated with a Westernized Microbiome Encoding Increased Virulence and Antibiotic Resistance Genes," Microbiome 5, no. 1 (September 15, 2017): 121, https://doi.org/10.1186/s40168-017-0338-7.

Exposure to the outdoors early in life: Torsten Olszak et al., "Microbial Exposure during Early Life Has Persistent Effects on Natural Killer T Cell Function," Science (New York, N.Y.) 336, no. 6080 (April 27, 2012): 489–93, https://doi.org/10.1126/science.1219328.

Adults who exercise outdoors: Daniel McDonald et al., "American Gut: An Open Platform for Citizen Science Microbiome Research," MSystems 3, no. 3 (June 2018), https://doi.org/10.1128/mSystems.00031-18.

Gardening improves mood, lowers stress: Masashi Soga, Kevin J. Gaston, and Yuichi Yamaura, "Gardening Is Beneficial for Health: A Meta-Analysis," Preventive Medicine Reports 5 (March 2017): 92–99, https://doi.org/10.1016/j.pmedr.2016.11.007.

growing your own veggies has been shown to: "Gardening as a Child May Lead College Students to Eat More Veggies," ScienceDaily, accessed October 27, 2019, https://www.sciencedaily.com/releases/2016/09/160919110301.htm.

We've even found that barefoot contact: James L. Oschman, Gaétan Chevalier, and Richard Brown, "The Effects of Grounding (Earthing) on Inflammation, the Immune Response, Wound Healing, and Prevention and Treatment of Chronic Inflammatory and Autoimmune Diseases," Journal of Inflammation Research 8 (2015): 83–96, https://doi.org/10.2147/JIR.S69656.

And since we will continue to live indoors: Gabriele Berg, Alexander Mahnert, and Christine Moissl-Eichinger, "Beneficial Effects of Plant-Associated Microbes on Indoor Microbiomes and Human Health?," Frontiers in Microbiology 5 (January 29, 2014), https://doi.org/10.3389/fmicb.2014.00015.

forty percent increase in healthy microbes with exercise: Sara C. Campbell et al., "The Effect of Diet and Exercise on Intestinal Integrity and Microbial Diversity in Mice," PloS One 11, no. 3 (2016): e0150502, https://doi.org/10.1371/journal.pone.0150502.

Similarly, in adult humans we see: Jacob M. Allen et al., "Exercise Alters Gut Microbiota Composition and Function in Lean and Obese Humans," Medicine and Science in Sports and Exercise 50, no. 4 (2018): 747–57, https://doi.org/10.1249/MSS.0000000000001495; Wiley Barton et al., "The Microbiome of Professional Athletes Differs from That of More Sedentary Subjects in Composition and Particularly at the Functional Metabolic Level," Gut 67, no. 4 (April 1, 2018): 625–33, https://doi.org/10.1136/gutjnl-2016-313627.

Research shows us that it helps mobilize and empty your stomach: Andreas Franke et al., "Postprandial Walking but Not Consumption of Alcoholic Digestifs or Espresso Accelerates Gastric Emptying in Healthy Volunteers," Journal of Gastrointestinal and Liver Diseases: JGLD 17, no. 1 (March 2008): 27–31.

A short walk stabilizes blood sugar: Henry Zheng et al., "Quantifying the Dose-Response of Walking in Reducing Coronary Heart Disease Risk: Meta-Analysis," European Journal of Epidemiology 24, no. 4 (2009): 181–92, https://doi.org/10.1007/s10654-009-9328-9; Kyoko Kashiwabara et al., "Different Patterns of Walking and Postprandial Triglycerides in Older Women," Medicine & Science in Sports & Exercise 50, no. 1 (January 2018): 79, https://doi.org/10.1249/MSS.0000000000001413; Sheri R. Colberg et al., "Postprandial Walking Is Better for Lowering the Glycemic Effect of Dinner than Pre-Dinner Exercise in Type 2 Diabetic Individuals," Journal of the American Medical Directors Association 10, no. 6 (July 2009): 394–97, https://doi.org/10.1016/j.jamda.2009.03.015.

Fat is burned and weight is lost: T. Kajioka, H. Shimokata, and Y. Sato, "The Effect of Daily Walking on Body Fat Distribution," Environmental Health and Preventive Medicine 5, no. 3 (October 2000): 85–89, https://doi.org/10.1265/ehpm.2000.85.

Your immune system gets stronger: David C. Nieman et al., "Upper Respiratory Tract Infection Is Reduced in Physically Fit and Active Adults," British Journal of Sports Medicine 45, no. 12 (September 1, 2011): 987–92, https://doi.org/10.1136/bjsm.2010.077875.

Your energy levels and mood: Ashish Sharma, Vishal Madaan, and Frederick D. Petty, "Exercise for Mental Health," Primary Care Companion to The Journal of Clinical Psychiatry 8, no. 2 (2006): 106; Derek D. Randolph and Patrick J. O'Connor, "Stair Walking Is More Energizing than Low Dose Caffeine in Sleep Deprived Young Women," Physiology & Behavior 174 (May 15, 2017): 128–35,

https://doi.org/10.1016/j.physbeh.2017.03.013.

A walk outside even unlocks: Marily Oppezzo and Daniel L. Schwartz, "Give Your Ideas Some Legs: The Positive Effect of Walking on Creative Thinking," Journal of Experimental Psychology: Learning, Memory, and Cognition 40, no. 4 (2014): 1142–52, https://doi.org/10.1037/a0036577.

Social media is not only anti-social: Melissa G. Hunt et al., "No More FOMO: Limiting Social Media Decreases Loneliness and Depression," Journal of Social and Clinical Psychology 37, no. 10 (November 8, 2018): 751–68, https://doi.org/10.1521/jscp.2018.37.10.751; Ethan Kross et al., "Facebook Use Predicts Declines in Subjective Well-Being in Young Adults," PLOS ONE 8, no. 8 (August 14, 2013): e69841, https://doi.org/10.1371/journal.pone.0069841.

each one of us has a unique "bacterial cloud": James F. Meadow et al., "Humans Differ in Their Personal Microbial Cloud," PeerJ 3 (2015): e1258, https://doi.org/10.7717/peerj.1258.

We're each emitting about a million: S. Bhangar et al., "Chamber Bioaerosol Study: Human Emissions of Size-Resolved Fluorescent Biological Aerosol Particles," Indoor Air 26, no. 2 (April 2016): 193–206, https://doi.org/10.1111/ina.12195.

Studies show that you're likely to share microbiome: Elizabeth A Archie and Jenny Tung, "Social Behavior and the Microbiome," Current Opinion in Behavioral Sciences, The integrative study of animal behavior, 6 (December 1, 2015): 28–34, https://doi.org/10.1016/j.cobeha.2015.07.008.

These relationships have even been shown to: Simon Lax et al., "Longitudinal Analysis of Microbial Interaction between Humans and the Indoor Environment," Science 345, no. 6200 (August 29, 2014): 1048–52, https://doi.org/10.1126/science.1254529.

Even having our furry friends: Hein M. Tun et al., "Exposure to Household Furry Pets Influences the Gut Microbiota of Infants at 3–4 Months Following Various Birth Scenarios," Microbiome 5, no. 1 (April 6, 2017): 40, https://doi.org/10.1186/s40168-017-0254-x.

In fact, stress alone can create alterations: M. J. Tetel et al., "Steroids, Stress and the Gut Microbiome-Brain Axis," Journal of Neuroendocrinology 30, no. 2 (2018), https://doi.org/10.1111/jne.12548; Jane A. Foster, Linda Rinaman, and John F. Cryan, "Stress & the Gut-Brain Axis: Regulation by the Microbiome," Neurobiology of Stress 7 (December 2017): 124–36, https://doi.org/10.1016/j.ynstr.2017.03.001; Mélanie G. Gareau, Manuel A. Silva, and Mary H. Perdue, "Pathophysiological Mechanisms of Stress-Induced Intestinal Damage," Current Molecular Medicine 8, no. 4 (June 2008): 274–81, https://doi.org/10.2174/156652408784533760; Michael Maes and Jean-Claude Leunis, "Normalization of Leaky Gut in Chronic Fatigue Syndrome (CFS) Is Accompanied by a Clinical Improvement: Effects of Age, Duration of Illness and the Translocation of LPS from Gram-Negative Bacteria," Neuro Endocrinology Letters 29, no. 6 (December 2008): 902–10; A. Ait-Belgnaoui et al., "Probiotic Gut Effect Prevents the Chronic Psychological Stress-Induced Brain Activity Abnormality in Mice," Neurogastroenterology and Motility: The Official Journal of the European Gastrointestinal Motility Society 26, no. 4 (April 2014): 510–20, https://doi.org/10.1111/nmo.12295.

Take away the stress and suddenly: Dong and Gupta, "Influence of Early Life, Diet, and the Environment on the Microbiome."

CHAPTER 10

We're up against habits, cravings, and even addiction: N. P. Shah, "Effects of Milk-Derived Bioactives: An Overview," The British Journal of Nutrition 84 Suppl 1 (November 2000): S3-10, https://doi.org/10.1017/s000711450000218x; M. R. Yeomans et al., "Effects of Nalmefene on Feeding in Humans. Dissociation of Hunger and Palatability," Psychopharmacology

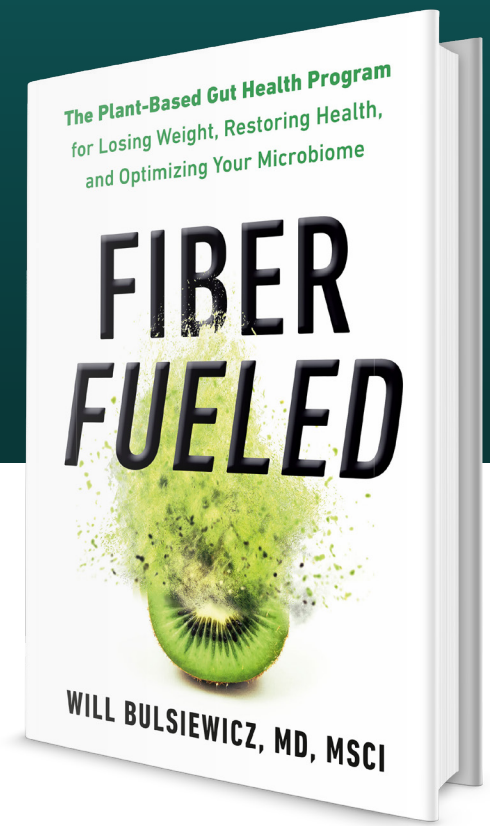
100, no. 3 (1990): 426–32, https://doi.org/10.1007/bf02244618; T. Sakurai et al., "Degradation of Food-Derived Opioid Peptides by Bifidobacteria," Beneficial Microbes 9, no. 4 (June 15, 2018): 675–82, https://doi.org/10.3920/BM2017.0165; Nicole M. Avena, Pedro Rada, and Bartley G. Hoebel, "Evidence for Sugar Addiction: Behavioral and Neurochemical Effects of Intermittent, Excessive Sugar Intake," Neuroscience and Biobehavioral Reviews 32, no. 1 (2008): 20–39, https://doi.org/10.1016/j.neubiorev.2007.04.019; Nicole M. Avena, Pedro Rada, and Bartley G. Hoebel, "Sugar and Fat Bingeing Have Notable Differences in Addictive-like Behavior," The Journal of Nutrition 139, no. 3 (March 2009): 623–28, https://doi.org/10.3945/jn.108.097584.

Quitting these foods can literally: C. H. Wideman, G. R. Nadzam, and H. M. Murphy, "Implications of an Animal Model of Sugar Addiction, Withdrawal and Relapse for Human Health," Nutritional Neuroscience 8, no. 5–6 (December 2005): 269–76, https://doi.org/10.1080/10284150500485221; M. A. Galic and M. A. Persinger, "Voluminous Sucrose Consumption in Female Rats: Increased 'Nippiness' during Periods of Sucrose Removal and Possible Oestrus Periodicity," Psychological Reports 90, no. 1 (February 2002): 58–60, https://doi.org/10.2466/pr0.2002.90.1.58.

The major changes occur within twenty eight days: Zhao et al., "Gut Bacteria Selectively Promoted by Dietary Fibers Alleviate Type 2 Diabetes."

We also know that after antibiotics: Dethlefsen et al., "The Pervasive Effects of an Antibiotic on the Human Gut Microbiota, as Revealed by Deep 16S RRNA Sequencing."

And in their study of TMAO,: Zhu Weifei et al., "Gut Microbe-Generated Trimethylamine N-Oxide From Dietary Choline Is Prothrombotic in Subjects," Circulation 135, no. 17 (April 25, 2017): 1671–73, https://doi.org/10.1161/CIRCULATIONAHA.116.025338; Wang et al., "Impact of Chronic Dietary Red Meat, White Meat, or Non-Meat Protein on Trimethylamine N-Oxide Metabolism and Renal Excretion in Healthy Men and Women."



DISCOVER *FIBER FUELED*

Fiber Fueled is so much more than a health book. It's a step-by-step methodology to stop the misinformation madness caused by the diet industry, and show you the simple, science-backed process for a lifestyle that is effortless, sustainable, and above all else it transforms your health by optimizing your gut microbiome.

With a 28-day program that has menus and more than 65 recipes, along with essential advice on food sensitivities, Fiber Fueled offers the blueprint to start turbocharging your gut for lifelong health today.

SOCIAL

Facebook.com/TheGutHealthMD

Instagram.com/TheGutHealthMD

ThePlantFedGut.com

DR. WILL BULSIEWICZ
THE PLANT FED GUT