HEME, HEALTH, AND THE PLANT-BASED DIET

By Pat Brown, CEO and Founder, Impossible Foods

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MEAT IS DESTROYING THE ENVIRONMENT AND OUR HEALTH.

Today, an astonishing 45% of the land surface of Earth is used as land for grazing and raising livestock, or growing crops to feed them. Animal agriculture puts more greenhouse gases into the atmosphere than all cars, trucks, trains, buses, ships, airplanes, and rockets combined. It pollutes and consumes more freshwater than any other industry. The clearing of forests to raise animals and the crops that feed them is the major driver of habitat loss and extinction of wild species.

Furthermore, cattle, pigs and chickens are major sources of food-borne illnesses and major incubators for dangerous viruses, including potentially lethal strains of influenza and even Ebola. The overuse of antibiotics in animal agriculture has created a public health crisis by rendering a growing number of bacterial infections in humans resistant to available antibiotics.

A growing body of epidemiological data suggests that eating a lot of “red meat” — the colloquial term for mammalian muscle — may be bad for your health and that replacing animal-derived protein in the diet with plant-derived protein could significantly reduce overall mortality rates. For example, in 2015, the International Agency for Research on Cancer (IARC) of the World Health Organization, evaluated the carcinogenicity of the consumption of red meat and processed meat. The report classified the consumption of meat from mammals as “probably carcinogenic,” associated mainly with colorectal cancer, pancreatic cancer and prostate cancer. It classified processed meat (sausages, bacon and cured meats, etc.) as “carcinogenic to humans.”

MAKING A BETTER BURGER

A core part of our mission is to make delicious meat sustainably — bypassing animals and making it directly from plants. We've spent more than six years studying animal meat at the molecular level to discover how it "works"--how it handles and cooks, and especially how it produces the flavors and textures people love.

Our first product, the Impossible Burger, uses 75% less water, generates 87% less greenhouse gases, requires 95% less land and 100% fewer cows. It delivers the same protein and iron as a burger made from a cow — but its protein comes mostly from plants, and it's produced without the use of hormones or antibiotics, does not create a reservoir for dangerous pathogens, and contains no cholesterol or slaughterhouse contaminants. If everyone who eats beef burgers today chose Impossible Burgers instead, the positive impact on our planet and global health would be profound.

But some people have asked us if the Impossible Burger is *too* similar to a burger from cows. They wonder whether people who regularly eat our burger might experience the same long-term health risks associated with a diet rich in red meat from mammals.

We are confident the answer is no. And here's why.

OUR PLANT-BASED MEAT IS MADE FROM SAFE INGREDIENTS

The Impossible Burger is made from simple plant ingredients that people have been cooking with and eating safely for thousands of years: protein from potatoes, wheat and soy, and fat from coconuts. It also contains nutrients — vitamins, amino acids, simple sugars, minerals and iron — that are found in other healthy food we eat.

In our effort to understand what makes meat so delicious, we discovered that one molecule — heme — is primarily responsible for generating the unmistakable, craveable flavor and aroma of cooked meat.

For more than a billion years, heme has been one of the most ubiquitous and important molecules in nature. Heme is an important part of every cell in every animal and plant. Heme, in a protein called hemoglobin, gives your blood the ability to carry oxygen throughout your body. In fact, your own bloodstream right now contains about as much heme as 300 pounds of Impossible burgers.

Heme also plays a critical role in the process by which your cells burn calories to create the energy they need to live. It is so essential for our survival that poisons like cyanide and carbon monoxide are deadly precisely because they bind and inactivate heme. Heme is a molecule worth understanding if only for its vital role in keeping us alive.

But there's more.

The exceptionally high quantities of heme that animal tissues require to meet their energy demands are also responsible for the unique flavors and aromas that make meat taste like meat. The heme in mammalian muscle gives raw meat its "bloody" flavor. And the release of heme during cooking catalyzes the explosion of flavors and aromas that makes burgers — or any kind of meat — taste so "meaty."

Once our scientists discovered the essential role of heme in giving meat its unique and delicious flavors, we searched the plant world for a heme protein that would match the fundamental properties of the heme in animal meat. Every plant contains many different heme proteins with diverse, important functions. We tested many heme proteins from many plants. One of them was leghemoglobin, found in the roots of legumes, where it helps them extract nitrogen from the air to enrich the soil. When we mixed leghemoglobin with plant proteins, fats and other simple nutrients, it transformed what would otherwise have been a dull tasting veggie burger into...*meat!* And the meat cooked, smelled and tasted like meat from a cow.

Before we were willing to use it in our products, we needed to be certain of the safety of soy leghemoglobin. We analyzed it to determine if soy leghemoglobin shared any meaningful similarity to known allergens; it does not. We performed additional allergenicity studies (including tests on protein digestion, heat sensitivity and acid sensitivity) to make sure it was safe. And we conducted a comprehensive toxicology study *(scroll down for details)* in which rats were fed amounts of leghemoglobin that, relative to their size and weight, vastly exceeded anything a human could consume in the Impossible Burger, with absolutely no ill effects.

All of these studies convinced us that this plant-derived heme protein, like every other heme protein in our diet, is safe to eat. But to fully understand why we believe in the safety and nutritional value of leghemoglobin, and why it matters, it's important to understand what we know — and don't know — about the long term health impacts of eating beef.

WHY IS BEEF BAD FOR YOUR HEALTH?

The best evidence that eating red meat might be unhealthy comes from large epidemiological studies, most of which find that people who self-report a high level of red meat consumption have higher rates of certain types of cancer, especially colorectal cancer. Taken at face value, the epidemiological data suggest that consumption of red meat increases the lifetime risk of developing colorectal cancer by about 10 percent. In other words, the typical American meat eater has a lifetime colorectal cancer risk of about 4.4 percent, compared to about 4 percent for someone who consumes essentially no red meat.

If red meat consumption is harmful to health, what might be responsible for the effect? Mammalian tissue is complex and contains many things that are not found in comparable quantities — or not found at all — in other foods. Most of these red-meat-specific components turn out to be unimportant for making a great burger, but one or more of them may be unhealthy for humans: Numerous hypotheses have been proposed, including carcinogenic viruses that infect cows and can be transmitted to humans, a pro-inflammatory sugar that's abundant in red meat and found exclusively in non-human mammals, and environmental contaminants that accumulate in livestock, among others. Because mammalian tissues contain an abundance of heme, it's been carefully evaluated as a hypothetical factor.

Because heme occurs naturally in every animal and plant, it's been part of the daily diet of every human being since the dawn of humanity. As the most readily absorbed form of iron in nature, heme has been a vital source of iron in the diets of humans and other omnivores for millions of years. The abundance of heme in animal tissues is what makes meat a particularly good source of iron. A relative lack of dietary heme in many parts of the world is a major driver of iron deficiency, which is by far the most common nutritional deficiency in the world, affecting 1.6 billion people, including almost half of the pre-school children and 40% of pregnant women globally. Because of the value of heme as a source of iron in the human diet, medical experts commonly recommend increasing heme consumption during pregnancy, when women are at risk of iron-deficiency anemia.

Because heme is abundant in mammalian meat, some people question whether there's a link between heme consumption and cancer. In fact, a 2017 study by the American Institute for Cancer Research reviewed all of the available evidence and concluded that there is no statistically significant epidemiological evidence linking heme iron and colorectal, colon or rectal cancer.

Heme is probably the red meat-associated compound whose health effects have been most thoroughly scrutinized. In many studies, rodents were fed doses of heme (adjusted for body weight) that vastly exceed what any human would or could possibly consume — the equivalent of between 30 and 300 pounds of burgers per day. Even at these ludicrously large doses, heme had no observable effect, in any of these studies, on the overall health of the rodents and *none* of the heme-fed mice or rats developed cancer.

Across all these studies, feeding massive doses of heme to cancer-prone rats and mice resulted in no overall ill health effects, no cancers, and no reproducible effects that might be related to cancer — an extraordinary record of safety.

ONE MORE STUDY: OUR OWN

We agonized over whether to conduct any study using animals as subjects. But our mission depends on competing against animal-derived meats anywhere they might be sold. And, unfortunately, animal-feeding studies are an industry standard practice — essential to our ability to compete against animal-derived meats in large retailers or restaurant chains in the United States and overseas.

In our study, rats consumed at least 100 times more soy leghemoglobin than an extreme consumer of our burgers would ever be exposed to, every day, for 28 days — a benchmark for safety and toxicity evaluations. The experiments were reviewed by top experts in toxicology and rodent histopathology.

As expected from the numerous previous studies of heme itself and other heme proteins, **our studies found no evidence of any deleterious effects at all** — no adverse impact on overall health, growth and well-being, no inflammation, injury or any other abnormalities in any tissue or organ, and specifically no evidence of cancer or any putative precursors to cancer — from consumption of heme (in our case, soy leghemoglobin), at doses vastly exceeding what any human could consume from our products.

Separate "genotoxicity" tests in cultured cells to assess whether leghemoglobin might be capable of causing chromosome damage, mutagenicity or missegregation of chromosomes found no evidence of genotoxicity. In other words, the studies found none of the mechanisms associated with cancer.

Thus, based on our own extensive studies as well as a comprehensive review of previous published studies, we concluded that heme, and specifically soy leghemoglobin, is completely and unequivocally safe for human consumption.

Our rigorous safety testing comes amidst overwhelming evidence that moving toward a plant-based diet yields both huge benefits for the health of our planet and huge public health benefits, including a reduction in cancer risk (e.g., Springmann, Tilman, World Resources Institute). Made from plants, the Impossible Burger contains beneficial phytonutrients, minerals and vitamins. It contains no animal proteins and is produced using no hormones or antibiotics — an important public health advantage, given the growing threat of antibiotic-resistant pathogens emerging from livestock facilities that render life-saving antibiotics ineffective.

WE ARE COMMITTED TO SCIENTIFIC TESTING, SAFETY AND TRANSPARENCY

Impossible Foods' top priorities are the health and safety of our customers. But we don't expect you to take *our* word for it.

People want and deserve deep insight into the foods they eat. That's why we voluntarily submitted all the results of our rat-feeding study, as well as many other safety tests, to the US Food and Drug Administration, which opens up companies' data to public scrutiny by publishing it on the FDA's website.

In addition, we voluntarily submitted our extensive tests, analyses and interpretation to two respected academic journals: International Journal of Toxicology and Molecular Nutrition and Food Research. The journals subjected the articles and accompanying data to their independent, anonymous peer review process. We had no role in choosing the academic peer-reviewers; we don't even know who they are. Based solely on the strength of the data, without any input from Impossible Foods or the FDA, and on the recommendation of anonymous expert peer-reviewers, both journals' editors accepted our articles and findings for publication.

Our goal is to be the most transparent company in the food industry. Whether you are a curious consumer, a scientist or a journalist, a fan or a skeptic, a vegan or an omnivore, we want to answer all of your questions and concerns. We will never take your confidence in our company and products for granted; we want to earn it. **And we will.**

Check out locations serving the Impossible Burger *and* our FAQs *for more info. More questions? Contact us at* hello@impossiblefoods.com*.*

Dr. Patrick O. Brown is the CEO and Founder of Impossible Foods, and a former pediatrician, Professor Emeritus at the Stanford University School of Medicine, and Co-founder of the Public Library of Science (PLOS). Brown was elected to the United States National Academy of Sciences and the National Academy of Medicine, and is a Fellow of the American Association for the Advancement of Science. He received the American Cancer Society's 2006 Medal of Honor for Basic Research, acknowledging "his revolutionary development of low-cost, accessible automated microarrays, and his life-saving contributions to the field of functional genomics...which in turn has produced insights into critical genetic information for diseases such as leukemia, lymphoma, prostate cancer, and early stage breast cancer."

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