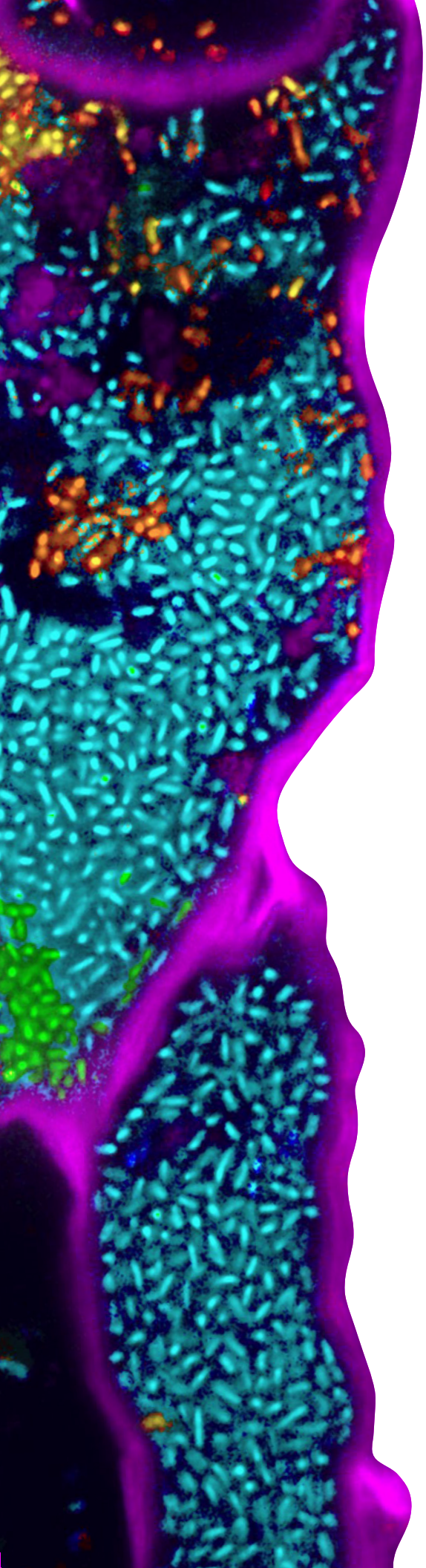

Stanford | MEDICINE

The Microbiome — The Next Frontier of Precision Medicine

If the old adage is true—we are what we eat—then what we are eating is making us sick. Poor diet contributes to nearly 700,000 deaths in the United States every year, making it one of the leading causes of mortality in our country.

The past few decades have brought an unprecedented rise in the global rates of cardiovascular disease, diabetes, obesity, cancer, and numerous autoimmune diseases. Chronic disease is occurring earlier in life, and poor metabolic health and unhealthy food choices are driving this epidemic.

Advancements in science have shifted our thinking about food and health. New discoveries show that the gut is a control center for multiple aspects of our biology, including our immune status, metabolism, and neurobiology. The typical Western diet, which is high in addictive, ultra-processed, hyper-palatable convenience foods, is having a disturbingly deleterious effect on our microbiome—the trillions of bacteria that reside in and on our bodies—and on our health.

Stanford brings a unique capability to researching the diet-microbiome-immune system connection. World-renowned innovators—Christopher Gardner, PhD; Justin Sonnenburg, PhD; Erica Sonnenburg, PhD; and Mark Davis, PhD—are working together to create a global hub for human microbiome research. Their expertise in dietary intervention, microbiome science, and immune-system profiling makes Stanford a leader in this emerging field.

Through this multidimensional approach, we can see how certain foods affect a person's microbiome and immune system in real time and in turn employ dietary changes to prevent and treat disease. Our efforts will establish diet as a powerful, controllable tool for disease prevention and optimized cognitive, emotional, and physical performance and health.

◂ *Commensal gut bacterial species living within plant cell wall material in a mouse colon.*

Capitalizing on the plasticity of immune and microbiome health

Research is accelerating our understanding of the microbiome, most notably its properties, its effect on the immune system and gut-brain axis, and diet-microbiome-host interactions. It's been found that the gut microbiome and immune system communicate and mutually regulate one another—imbalances in the gut microbiome can lead to the development of chronic inflammatory disruptions. But research has also discovered that the gut is impressively resilient and malleable: The same plasticity that makes the microbiome susceptible to deterioration presents a huge opportunity to recover a healthy microbiome and positively modulate human health.

Stanford has a rare combination of cutting-edge capabilities to conduct safe and ethical experiments in humans while monitoring the biology underlying health changes in real time. These include:

Microbiome profiling | The microbiome has emerged as a central actor in dictating chronic inflammation and causing or exacerbating disease. Primary research at The Sonnenburg Lab focuses on developing innovative strategies to prevent and treat disease in humans via the gut microbiota.

Immune-system profiling | Stanford's Human Immune Monitoring Center conducts robust immune-profiling assays and has amassed large quantities of data on a variety of participants to inform our studies. By taking blood draws over the course of food and microbiome interventions, researchers receive longitudinal immune-response data of approximately 350 unique parameters to help identify which foods increase or decrease inflammation and chronic disease markers in humans.

Data analysis | Given the highly individualized nature of the microbiome, multi-omic data sets across study participants allow individualized, precise patterns to be discerned. Powerful data-science tools allow us to integrate huge microbiome and immune-status data sets and relate these to dietary interventions and subsequent health outcomes, leading to algorithms clinicians can implement to help patients improve their health.

Diet studies | For more than 25 years, Dr. Gardner has studied what to consume and what to avoid for optimal health, and how best to motivate individuals to achieve healthy dietary behaviors. His team is composed of world leaders in measuring and achieving dietary change in humans for extended lengths of time, using cutting-edge behavioral theory strategies, wearables, and nutrition interventions.

Data-driven diet research

Stanford researchers want to change the way we think about food, preventive medicine, and the traditional prescription pad—to recognize the power of nutrition to heal, optimize our health, and achieve balanced, long-term wellness.

Drug discovery and FDA approval is a lengthy, costly, and failure-prone process. Food, alternatively, is generally recognized as safe by the FDA, which has allowed us to conduct dietary trials directly in humans, rather than in mice first, exponentially accelerating our progress. Assessing health status in real time through in-depth tracking of the microbiome and immune health will allow for rapid feedback on effective personalized and foundational diets. By understanding how diet interacts with human microbiota, and molecularly characterizing the body's response to specific food inputs using high-dimensional profiling, this research gets to the underlying root causes of disease and seeks to treat patients with the food in their refrigerator and pantry, rather than the drugs in their medicine cabinets.

The role of diet in improving health is gaining acceptance across the medical community. The NIH has focused its attention on the untapped potential of the diet-host-microbiome relationship—confirming what Drs. Gardner and Sonnenburg discovered years ago—that "food as medicine" is essential for optimal health and to reduce the burden of disease. Yet research funding remains limited, restricting progress in this transformative area.

A recent trial conducted at Stanford by this research team, which was published in *Cell* in 2021, demonstrated the power of fermented foods, such as yogurt and kombucha, to increase gut microbiome diversity and decrease more than two dozen inflammatory markers in healthy adults. Now is the time to determine which diets have the power to reverse inflammation-driven autoimmune and other chronic diseases.

Stanford has laid out a bold vision to accelerate progress and take advantage of scientific advancements to develop individualized, actionable dietary recommendations in a clinical setting—to create a precise, personalized, diet-by-biology encyclopedia to achieve positive health outcomes. Just as clinicians request blood pressure, glucose, and lipid panels, we imagine a future where they can also order an inflammatory panel and microbiome score. From there, physicians could monitor a patient's microbiome, inflammatory pathways, and immune function over the course of a lifetime and in response to dietary interventions.

Mark M. Davis, PhD

Dr. Davis is the Burt and Marion Avery Family Professor, professor of microbiology and immunology, and director of the Stanford Institute for Immunity, Transplantation and Infection. He is interested in the unique challenges of, and solutions to, studying the human immune system, particularly in the context of infectious diseases and vaccination strategies. Dr. Davis' lab is working to develop metrics for immunological health.

Christopher Gardner, PhD

Dr. Gardner is the Rehnborg Farquhar Professor at the Stanford Prevention Research Center. For the past 20 years, he has investigated the potential health benefits of various dietary components or food patterns, exploring these interventions in randomized controlled trials in free-living adult populations.

Justin Sonnenburg, PhD

Dr. Sonnenburg is a professor of microbiology and immunology at Stanford, and recipient of the NIH Director's New Innovator Award and Pioneer Award. Dr. Sonnenburg and his wife, **Erica Sonnenburg, PhD**, senior research scientist, are the authors of the book *The Good Gut: Taking Control of Your Weight, Your Mood, and Your Long-Term Health*. Their laboratory develops and employs diverse technologies to understand mechanisms that govern interactions within the intestinal microbiota and between the microbiota and the host. Their work has been published in top journals including *Nature*, *Science*, and *Cell*.

Tackling chronic disease with diet

Diet-based interventions have great potential for preventing inflammation-based disease before they take hold. They are also being used to holistically treat conditions fueled by chronic inflammation, at early stages, and in conjunction with standard-of-care treatment. We have forged connections with faculty throughout Stanford University School of Medicine who are invested in taking a nutrition-science approach with their patient populations as an adjunct to traditional therapies.

Metabolic disease | Obesity, metabolic syndrome, and diabetes are linked to dietary habits, the gut microbiome, and chronic inflammation, making them especially susceptible to amelioration through dietary intervention. One of our collaborators, Michael Snyder, PhD, is a world leader in conducting multi-omics analysis of the prediabetic population. We have also collaborated with Sun Kim, MD, a world-renowned endocrinologist, to conduct supplement-based (prebiotic) microbiome-targeted interventions.

Chronic immune conditions | Several chronic immune disorders are caused and exacerbated by excess immune activation, including asthma and allergy. With Kari Nadeau, MD, PhD, a leader in pediatric and adult asthma and allergy research and treatment, we are interested in mitigating these recurrent inflammatory responses with modulation of the microbiome through dietary interventions, such as fermented foods.

Aging | Conditions such as decreased vaccine response, diabetes, arthritis, Alzheimer's disease, and heart disease are perpetuated by age-associated chronic inflammation, or "inflamm-aging." Bali Pulendran, PhD, and Dr. Davis have worked extensively with cohorts of older individuals whose immune systems have been extensively profiled, providing a window into this inflamm-aging phenotype. Crashes in microbial diversity in older populations have also been noted, with evidence that microbiome deterioration precedes (and may be contributing to) age-associated declines in health. Microbiome-targeted interventions offer a unique opportunity to prevent, delay, or reverse inflamm-aging.

Early psychosis | Emerging evidence demonstrates that schizophrenia and psychosis may be exacerbated by inflammatory status as well as gut microbial composition. Researchers at Stanford working with patients with early schizophrenia have been exploring immune triggers for psychosis and are interested in exploring diet as a lever to help temper psychotic symptoms as they develop.

This work is critical

Despite the widespread recognition of the potential of diet to impact human health, there is a severe mismatch with available funding to support these efforts. The reality is simple: Food is not a lucrative pharmaceutical endeavor, and food-based research is not as well-financed as drug or supplement studies.

Early results from our pipeline of projects show tremendous promise, but the current pace to acquire funding is not compatible with achieving impactful change. To keep the momentum going, investments are vital for success.

There is an urgent need for progress in this realm of human health. Stanford has the faculty to make this paradigm shift a reality and the technology to reveal the wiring underlying the diet-host-microbiome connection. But to move this novel framework into the real world, we need to build up our human studies research base with more samples, more participants, and more data. We need to expand and diversify our host variables, including genetics, microbial abundance, and chemical parameters. Funding is needed to accelerate this important work and enable the microbiome revolution to be fully realized to help people achieve better health.

Create impact

Imagine a world where we can significantly reduce lifestyle diseases with just the foods we eat. You can be an essential part of the team that transforms the way we think about food, health, and disease prevention. With Drs. Sonnenburg, Gardner, and Davis' research roadmap and your philanthropic support, this vision can be a reality.

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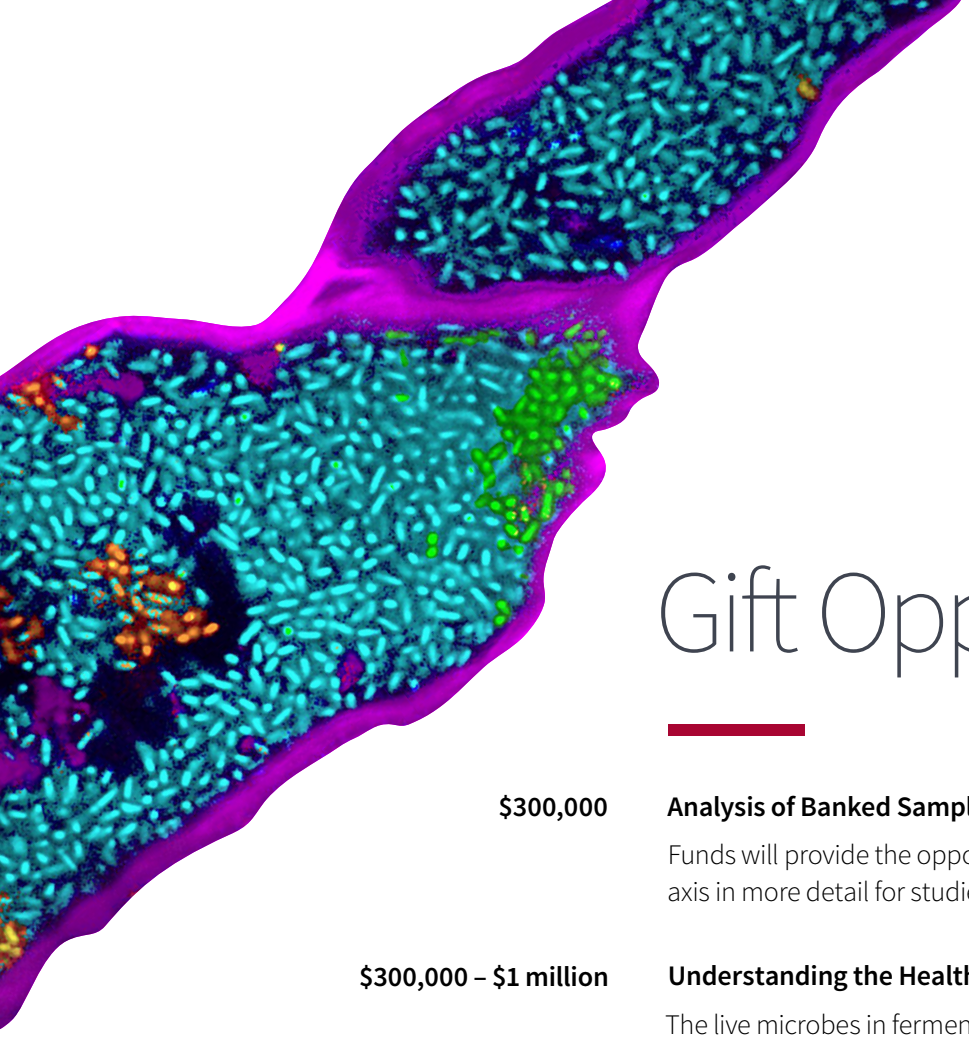

Gift Opportunities

$300,000

Analysis of Banked Samples from Recently Completed Studies

Funds will provide the opportunity to explore the microbiome-immune axis in more detail for studies that have already been conducted.

$300,000 – $1 million

Understanding the Health-Promoting Impact of Fermented Foods

The live microbes in fermented foods have been found to have a profound impact on our microbiome and our health. Funds will enable laboratory investigation into bioactive compounds and health-promoting microbes present in fermented foods to better understand how microbially transformed foods decrease inflammation and regulate metabolism.

$100,000 – $1 million

Creating an Expanded Patient Portfolio

This opportunity can build in increments of $100,000 (10 participants per $100,000) or scale to a full study of one or multiple new population groups for $500,000 to $1 million.

Funding would support the expansion of our human studies research with a broader range of ethnically diverse participants, additional disease states, and distinct age ranges to more accurately reflect the real world. Focusing on inflammatory diseases, these studies could include specific patient populations such as those with inflammatory bowel disease, aging adults, children with food allergies, and people with autoimmune diseases and diabetes.

$500,000 – $1 million

The Microbiome and Mental Health

The gut microbiome is connected, directly or indirectly, to most facets of human biology, including the brain and central nervous system. Funding would enable pilot studies that look at the role of microbiome-targeted diets in addressing mental health issues and improving cognitive function throughout life.

$3 million

Expanded Ketogenic vs. Mediterranean Diet Study

Funds will enable a full-scale definitive study expanding on the exciting preliminary results of a study comparing the ketogenic and Mediterranean diets and their impact on blood glucose control while simultaneously addressing additional impacts on the microbiome, inflammation, and other health factors. This new, larger study will provide precision-nutrition insight and will require a five-fold increase in participants (200) and a longer study duration of six months.

$1 – $4 million

Microbiome Recovery Foundational Study

Funds will enable a foundational study to develop an orally administered microbial community (bacterial species depleted in the industrialized microbiome) for treating and preventing a range of diseases. This microbial "cocktail" would be delivered orally and serve as a refined step beyond fecal transplants, which have been used to replenish microbiome diversity in specific diseases. The multi-year study would require a phased approach, starting in the lab before moving to human trials.

- Phase I (cocktail formulation and lab testing) | $1 million over three years
- Phase II (human study) | $3 million over three years

$2 million (endowed) or **$125,000** per year (expendable)

Postdoctoral Training Fellowships

Postdoctoral fellows play a vital role in the execution of research. Being able to offer them fellowships helps Stanford attract the most talented trainees with a diversity of interests and expertise. Endowed named fellowships provide a stable source of funding for advanced training of the next generation of scientists in the field of microbiome research. Expendable funds give them the freedom to pursue high-risk, high-reward research not typically supported by traditional funders.

$6 million

Endowed Professorship

A named professorship would ensure continued excellence and leadership by providing financial stability to the university and the School of Medicine. The endowed chair provides income that guarantees the holder's salary, a structure that not only helps acknowledge the accomplishments of a deserving faculty member, but also perpetually frees up funds for other purposes, such as attracting top young trainees and faculty, and conducting research.

Gifts of any size

Microbiome Expendable Research Funds

These funds are designed to jumpstart the most creative research ideas, allowing investigators to pursue promising avenues of inquiry and ultimately develop effective new diagnostic techniques and therapies. These gifts will fuel innovative early-stage research projects that require the generation of preliminary data to receive federal grants in today's conservative funding environment. Much of the innovative microbiome research at Stanford has been enabled soley through this type of funding.