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Keio University
Bio2Q Human Biology Microbiome Quantum Research Center

Keio University Human Biology-Microbiome-Quantum Research Center (Bio2Q)

Why Do People Respond Differently to Medicine?

— Surprising Connections Between Your Gut Bacteria and the Medicine You Take

Bio2Q Researchers

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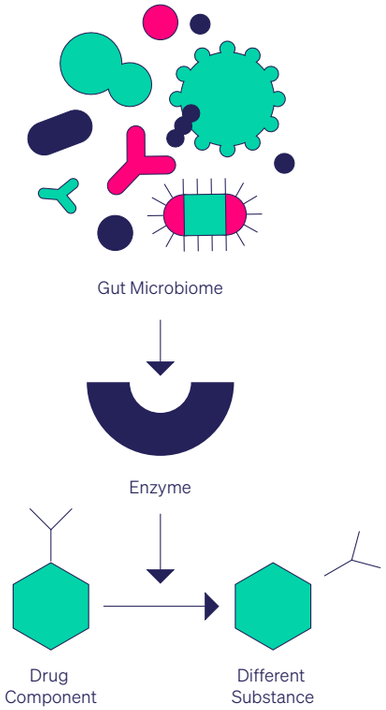
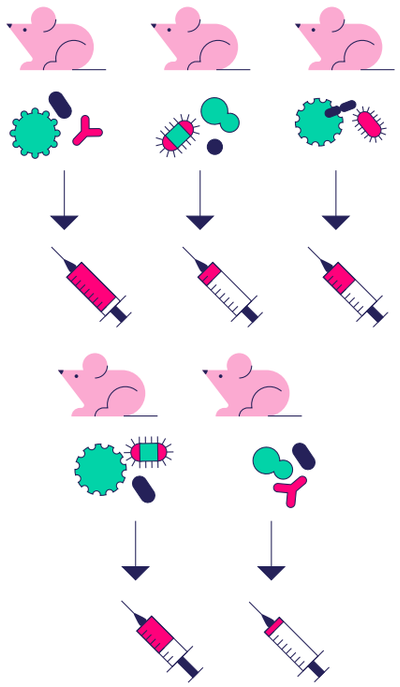


Enzymes produced by gut bacteria can break down drug components into other substances, potentially altering how the drug works.



When five genetically identical germ-free mice were given different gut bacteria, the amount of the drug in their blood varied.

Could you tell us about your research?

I am studying how gut bacteria may influence how well the medications we take work.

Our gut contains an enormous number of bacteria—greater than 1,000 species that live alongside us. Because these bacteria have evolved along with us, they play a crucial role in maintaining our health. However, the number and types of gut bacteria can vary greatly from person to person.

In some people, gut bacteria may metabolize drugs to make it less effective or cause side effects. My research looks at how these gut bacteria interact with the various medications we take.

Could you give us a specific example?

My current research focuses on Parkinson's disease, which is most commonly treated with a drug called levodopa. Levodopa works upon being converted into dopamine after entering the brain. If the drug is metabolized before reaching the brain, the drug becomes less effective. Levodopa can be metabolized by both our body and by certain gut bacteria, but the enzymatic pathway differs slightly between the two. For example, Parkinson's disease patients are often given another drug to prevent our body from converting levodopa into dopamine too early, but the same drug cannot stop the metabolism by gut bacteria.

Before I began my research, it was already known that one type of gut bacterium could convert levodopa into dopamine, but we found that this bacterium was rare amongst our Parkinson's disease patients. So I hypothesized that other bacteria may also contribute to the difference in drug effectiveness between patients. I collected various bacterial strains from patients and tested how much each strain could metabolize levodopa. Ultimately, I discovered that many types of bacteria were indeed capable of doing so.

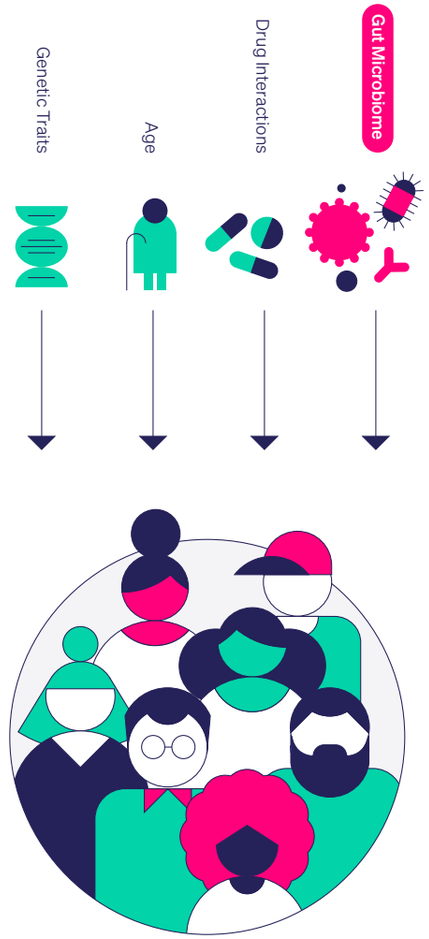
How do you go about investigating this in concrete terms?

What I initially wanted to understand was how gut bacteria may affect a drug's bioavailability.* We used genetically identical mice, some with gut bacteria and others germ-free, and gave them levodopa to see how much reached the bloodstream. The germ-free mice had higher levels of the drug in their blood, suggesting that gut bacteria has an effect on the drug's bioavailability.

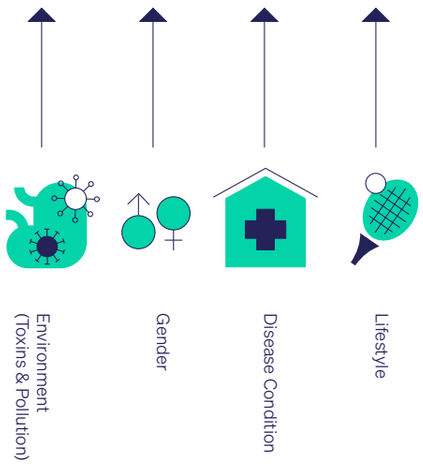
Next, we introduced stool samples from five Parkinson's patients into five separate groups of germ-free mice. Since the mice were genetically identical, the only variable was the gut bacteria they received. When we gave them levodopa, the amount of the drug in their blood varied depending on which patient's bacteria they carried. In other words, a drug's effectiveness may depend on the specific gut bacteria a person has.

We are currently collecting bacterial strains from patient stool samples and exposing them to levodopa to see whether the drug levels decrease. If they do, it means the bacteria are altering the drug, so the next step is to determine what it is being converted into. Based on sequencing data, we can identify the bacterial species to determine which ones are capable of metabolizing the drug.

*Bioavailability: A measure of how much of a drug, once administered, reaches the bloodstream and becomes available to target sites of the body.



Individual Differences in Drug Response



The effectiveness of a drug can vary from person to person, and gut bacteria may be one reason for that.

Recent studies by other researchers have led to a wave of discoveries that has sparked growing interest in the idea that gut bacteria may metabolize not only drugs for Parkinson's disease, but many others as well. Interestingly, there are even cases where a drug only works after being processed by gut bacteria. The collection of gut bacteria have far more genes than humans and therefore can process a wide range of substances. We are starting to see many new possibilities, and it feels like an exciting time in this field of research.

It's surprising to learn about the various roles gut bacteria play in our bodies. What kinds of practical uses might this research have?

There are often several different drugs available to treat the same disease, and it is not always clear at first which one will work best for a given patient. Doctors usually try out different options to find the one that works most effectively with the fewest side effects. But if we knew, for example, that a patient with a specific gut bacterium might respond better to a certain drug, we could test their gut bacteria in advance and start with the drug that's more likely to be effective. That kind of approach could be very helpful in clinical practice.

Another possibility is that if a certain bacterium—not typically found in most people—turns out to improve how a drug works, we may be able to administer that bacterium alongside the drug to enhance its effectiveness. By adjusting the gut microbiota to either promote or prevent drug metabolism, we could improve how well the drug works.

Even amongst the most widely prescribed drugs, less than half of patients may respond well to them, which is less than what you might expect. Researchers initially looked at human genetics to explain this variation, but more recently, attention has shifted toward gut bacteria. This is a relatively new direction in the field.

Gut bacteria have far more genes than humans and process a wide range of substances.

Do you collaborate with other researchers at Bio2Q?

I have been working on several projects with Dr. Kenya Honda's lab—he is a leading expert on gut bacteria. Dr. Honda has shown a strong interest in this research and has been incredibly supportive. I help mentor his students, and we have a close working relationship.

Another colleague at Bio2Q is Professor Morinobu Seki, an expert in Parkinson's disease. He has a wealth of experience and frequently shares insights that aren't easily found in academic papers. For instance, he once pointed out which types of patients tend to respond poorly to levodopa. This insight led me into thinking how gut bacteria may be involved, leading to a new aspect of my research.

Bio2Q is a stimulating environment where ideas and information constantly flow. I was not studying gut bacteria at all before joining Bio2Q, but with the support of many people, I have been able to get this far. Research does not have to be done alone— I have been learning by talking with others about how they approach their work and what kinds of research they are doing.

Do you have a message for our younger readers?

I think if you want to pursue scientific research, it is important to be comfortable with English. After all, it is the common language of science.

Personally, I believe speaking and listening are even more important than reading and writing. You can always ask someone to help correct your writing, but exchanging ideas means being able to talk and listen directly. Even when speaking with professors, there can be grammar mistakes, but what really matters is being able to communicate effectively. Instead of worrying too much about grammar, I think it's better to focus on whether your ideas are coming across.

> **In science, English is the shared language. What matters most isn't perfect grammar—it's being able to share ideas.**

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What is Bio2Q?

Bio2Q is a world-class research center at Keio University. It aims to use quantum computing and AI to analyze the interaction between Human Biology and Microbiome, revealing uncharted territories of the human body and developing new treatments for intractable diseases.

It is the first private university to be selected for the World Premier International Research Center Initiative (WPI) program promoted by the Ministry of Education, Culture, Sports, Science and Technology (MEXT).

Bio2Q

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