WPI Research Center
Keio University

Bio2Q Human Biology Microbiome Quantum Research Center

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

Gut bacteria may one day play a role in treating brain tumors

Bio2Q Researchers

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FIG. 1

Glioblastoma cells move individually through the brain along blood vessels and nerve fibers, multiplying once they settle in new areas of the brain. It is difficult to remove them all through surgery.

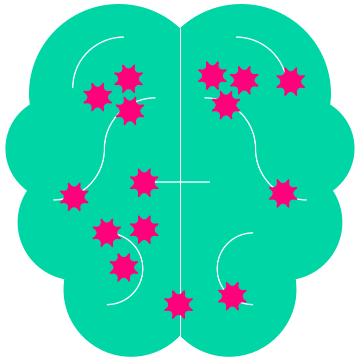
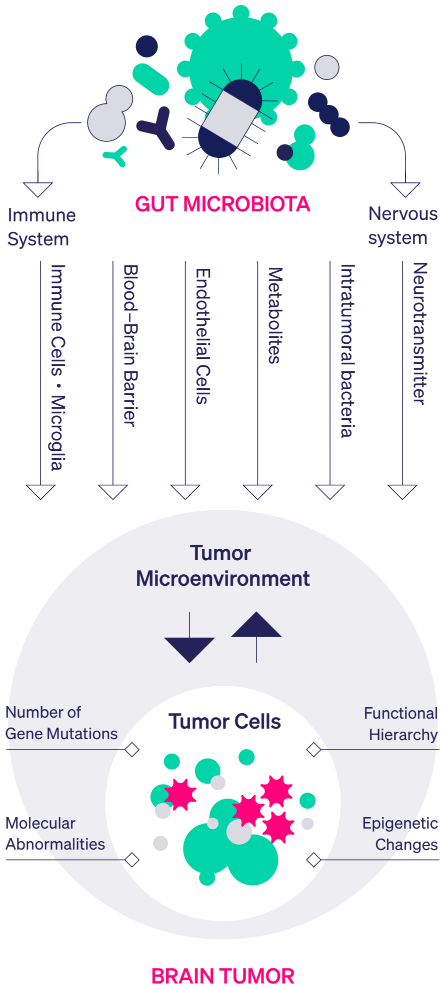


FIG. 2

Brain tumor cells and their surrounding environment influence each other in complex ways. Many of the factors in the tumor's environment appear to be influenced by gut bacteria.



Could you tell us about your research?

You might be surprised to learn that brain tumors are connected to the gut, an organ far from the brain. My research focuses on the link between malignant brain tumors—in particular, a highly treatment-resistant type called glioblastoma—and gut bacteria.

Glioblastoma is a type of brain tumor that develops when brain cells called glial cells multiply abnormally. It is one of the most aggressive forms of brain cancer, with an average life expectancy of around two years after diagnosis. While many cancers can spread rapidly, glioblastoma progresses even faster than others.

For cancers in other organs, removing the tumor through surgery is often common practice. But in malignant brain tumors like glioblastoma, cancer cells have often already spread throughout the brain by the time they are diagnosed, making surgery alone ineffective. (See Fig. 1) Chemotherapy and radiation, on the other hand, also damage surrounding healthy brain cells, making it difficult to treat with the intensity needed to eliminate the cancer completely. In short, malignant brain tumors are difficult to cure with either surgery or standard therapies like chemotherapy and radiation.

It's clearly a very tough disease to treat.

That's right. Glioblastoma is a strange kind of cancer. It doesn't spread to other organs like many others do. Each cancer cell moves through the brain, searching for an environment it can thrive in, and grows once it finds a suitable location. That's why I thought it might be more effective to disrupt the environment that allows cancer to survive rather than target the cancer cells themselves, which led me to begin researching the energy metabolism of cancer cells.

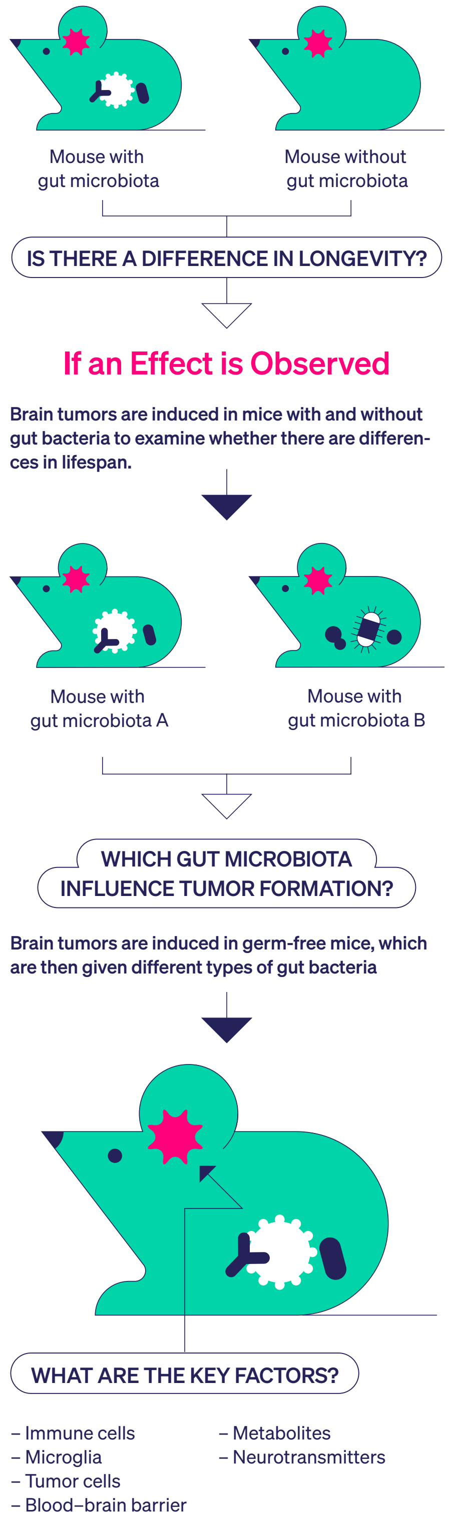
At first, I thought that cutting off their energy supply would stop the cancer cells from growing, moving, or even surviving. But I found that some cells in aggressive brain tumors, such as glioblastoma, are incredibly good at adapting to their environment. They can flexibly switch between using oxygen and using sugar to produce energy, depending on the situation. For example, when there's little oxygen, they quickly stop using it and switch to sugar, pulling energy from sugar and producing lactic acid. Then, when the sugar runs out, they can use the lactic acid as a nutrient. That's why it's so hard to stop their growth by targeting just one energy source.

So I started listing all the factors related to cancer cells, wondering if there was a bigger common thread. As I mapped out the many factors tied to both brain tumors and their surrounding environment (see Fig. 2), one thing kept showing up across the board: gut bacteria. If gut bacteria are indeed linked to brain tumors, then altering that link might lead to new treatments. Gut bacteria, the tiny companions living inside of all of us, could hold the key to treating brain tumors.

For example, when tumor cells begin to form, immune cells (shown on the left side of the figure) attack them. Gut bacteria also play a role in immune responses. They help train immune cells and regulate how they function. The brain also contains cells called microglia, which attack and clear out foreign substances. Studies in mice have shown that the number and activity of microglia vary depending on whether gut bacteria are present. Another possibility is that metabolites produced by gut bacteria affect tumors via the bloodstream. Since gut bacteria seem to be linked to brain tumors in many ways, we're now investigating which of those links has the greatest impact.

FIG. 3

Studying the effects of gut bacteria on brain tumors



Prof. Sampetrean's research is helping find the specific factors within the gut bacteria that influence brain tumors.

How do you actually go about investigating this?

First, we want to find out whether gut bacteria influence whether brain tumors grow or shrink. (See Fig. 3) To do this, we induce brain tumors in mice with and without gut bacteria, then observe whether it affects their lifespan, and if so, whether it makes it shorter or longer.

If gut bacteria do have an effect, the next step is to figure out which specific ones, or which combinations, are responsible. To do this, we use germ-free mice born without bacteria, introduce various types of gut bacteria, and compare how the tumors develop. Once we have identified which gut bacteria or combinations are affecting brain tumors, the next step will be to investigate which features of those bacteria are responsible.

Could this kind of research lead to new treatments for brain tumors?

If metabolites produced by gut bacteria were found to suppress brain tumors, for instance, one approach could be to deliver those metabolites directly. Conversely, if certain metabolites were found to be used only by cancer cells, and not by normal cells, it might be possible to weaken the cancer by controlling those metabolites. Because such treatments would target only cancer cells, they could minimize harm to healthy brain cells.

Gut bacteria, the tiny companions living inside us, could hold the key to treating brain tumors.

What originally led you to start researching brain tumors?

I originally worked as a neurosurgeon, performing operations on patients. But malignant brain tumors like glioblastoma are extremely difficult to cure, whether through surgery, drugs, or radiation. I've witnessed that reality firsthand, again and again. That's what drove me to begin basic research — the quest to understand the fundamental 'why' and "how" behind the disease. I wanted to find some kind of treatment, no matter what.

There was a time when I thought I might return to surgery once a new treatment was found. But 'the breakthrough we need has not happened yet. I still see outpatients, but no new drugs have been approved, and treatment for malignant brain tumors hasn't changed since I first started my research. Patients still face an incredibly challenging prognosis. My goal is to extend the time these patients have, even if only by a little at first, but the ultimate mission is to find a treatment that changes everything.

Do you have a message for our younger readers?

I don't think there's any single "right" way to get into research. People come into research for all sorts of reasons—because they love science, they're fascinated by, for instance, insects, or they want to help cure disease. That kind of diversity is what makes the research world so rich, and it often leads to unexpected discoveries.

Learning about different kinds of researchers can be a great source of inspiration. Reading books or watching interviews with well-known researchers is a great way to start. Finding a role model—someone you admire, or a field of research you're passionate about—and carving out your own unique path is one of the true joys of doing research.

There's no right way to get into research. Discovering different kinds of researchers and finding a role model who resonates with you is one of the real joys of the journey.

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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.

Keio University 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).

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