Do you have a message for the young people reading this?

I encourage you to first ask questions and then try to answer them in your own way. Traditional education often focuses on answering others' questions, which is necessary, but I urge you to value the questions that arise from your own thinking. Experiencing the joy of solving your own questions is crucial. By repeating this process, you'll discover what truly interests you and what you want to pursue.

Curiosity is vital, but a solid foundation in basic academic knowledge is also essential. Without a strong liberal arts education, you may struggle to be taken seriously overseas and might only grasp superficial aspects of what's happening around you. A lack of understanding in fundamental areas could lead to being dismissed in more advanced discussions. To achieve your dreams and goals, you need to become intelligent enough to answer the questions you might face in the future.

Create your own questions and come up with answers in your own way. That is how you can create a unique academic discipline.

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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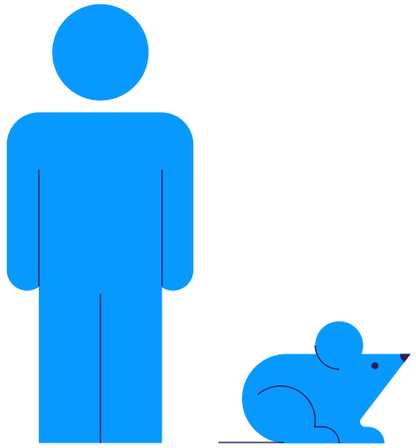
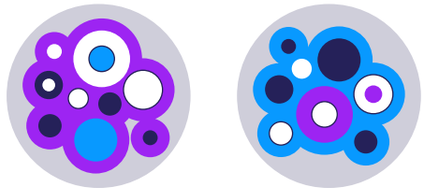
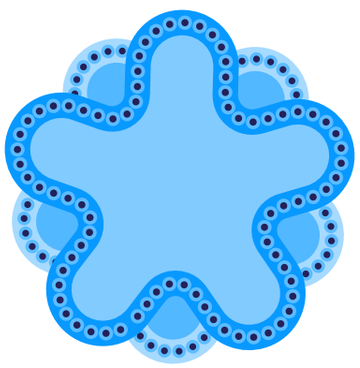


Human / Model Organism



Pluripotent Stem Cell

Tissue Stem Cells



Organoid

Please tell us about your research.

Each researcher has unique goals. I began as a gastroenterologist, so I want to understand the causes of gastrointestinal diseases. Diseases can often be described by abnormalities in shape, as seen during gastroendoscopy, or by functional disorders. For example, when consuming cola, the body detects sugar intake, secretes hormones to manage blood sugar levels, and signals the brain to stop drinking once enough sugar is absorbed. When these functions fail, it results in disease.

The human body operates through complex feedback mechanisms, where distant organs communicate via nerves, hormones, or blood vessels. However, the full complexity of this system remains largely unexplored because no models exist to study it comprehensively.

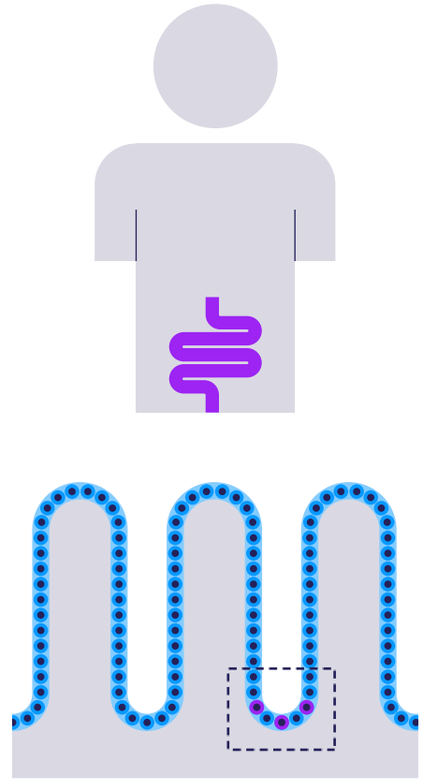
Traditional research has focused on breaking down complex systems into understandable components, but this approach has limitations. Consequently, researchers shifted their approach to reproducing organs and cells rather than disassembling them, leading to the development of organoid technology. While creating a complete organ from scratch is currently impossible, the goal is to reproduce tissue structures from a single cell into minimal functional units that control specific functions. These “organoids” allow us to understand the abnormalities in shape and function that underlie diseases, offering a new way to explore the human body's complexity.

> Reconstruction of complex tissue structures from a single cell had been considered difficult in mammals.

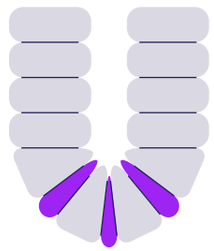
Is it different from iPS technology?

iPS technology reprograms cells to a near-embryonic pluripotent stem cell state. In contrast, organoid technology creates tissue from disparate cells by leveraging their natural ability to organize into structures. For example, intestinal cells form specific shapes due to spatial relationships and communication among cell types, such as epithelium, fibroblasts, and nerves, using proteins called “niche factors.” By identifying and applying these factors in vitro, disparate cells can be induced to form tissue.

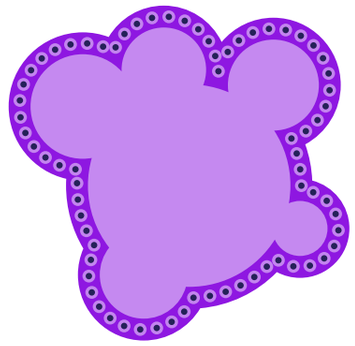
Around 2000, stem cell research focused on growing cells from skin, nerves, and blood through transplantation and culture. Researchers then expanded their focus to investigate what organ structures stem cells could create and began replicating cell and tissue functions. While reconstructing complex tissue structures from a single cell was possible in lower animals, it was considered difficult in mammals. The development of organoid technology around 2010 overcame these challenges, allowing for more advanced tissue and organ reproduction in mammals, marking a significant advance in regenerative medicine.



Intestinal Epithelial Cells



Stem Cell



Intestinal Organoid

You say you happened to succeed, but did you have any essential intuitions?

The word "serendipity" (lucky coincidence) is crucial in research. When researchers worldwide compete, they often pursue similar predictions and projects. However, unexpected discoveries or ideas from discussions with peers can lead to different goals. These accidental findings are unintentional, making it important to engage with colleagues and conduct various experiments repeatedly. Intelligence, luck, and physical stamina are all important factors in this process.

If you don’t find something interesting, it’s easy to give up. Curiosity drives ingenuity and persistence. Discovering something intriguing motivates further exploration because of curiosity. Without nurturing a positive environment and the excitement of discovery, not only science but many aspects of life would become dull. Discoveries are made one by one, eventually leading to summaries and presentations, which then spark new questions. This cycle continues, with each step potentially leading to a larger question in your thought process. Although more difficult challenges require longer periods of trial and error, stopping an attempt because it is difficult is not advisable. This is the credo of our lab.

How are you involved in Bio2Q?

The Bio2Q project aims to solve problems that were previously unsolvable by organically linking researchers from different fields. When you zoom in on the intestine, you can see the villus (carpet-like) structure. Our research focuses on the epithelium, the outermost part of the intestine. We artificially reproduce this epithelial structure in a dish by extracting stem cells, which generate all the necessary codes. We've managed to replicate the intestine's shape to some extent, and the next goal is to replicate its functions, specifically digestion and absorption. For example, when nutrients enter the body, the brain and pancreas regulate their absorption using hormones and neural circuits. To mimic this process, we need sensor cells, but we haven't yet fully understood how these sensors work.

Moreover, bacteria in the intestines require the expertise of microbiologists, along with mass spectrometry to identify the metabolites they produce. Neuroscientists are also needed to understand how the brain detects these compounds and how the nervous system connects. Additionally, computational knowledge is crucial because these circuits are computationally complex. We have unique technology to create organs and their functional units, known as organoids. While we’ve developed the technology to create structures, the actual absorption of nutrients and the transmission of information through sensors are yet to be realized. To achieve this, we may need to combine two or three types of organoids and/or cells, such as by co-culturing with neurons, immune cells, and intestinal bacteria. This is what some people call an “assembloid,” representing the next generation in organoid technology. It is likely the most challenging aspect, but we are eager to tackle it in the Bio2Q project, pushing the boundaries of what organoid technology can achieve.