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Agriculture Makes a Difference Contributions to the region and the world through agricultural studies

Tokai University School of Agriculture — Kumamoto's Only School of Agriculture: Our Pride and Responsibility

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QOL Close Up: Aiming to contain increasing bovine leukemia Search for infectionand onset-resistance factors and development of simple diagnostic methods Kumamoto Prefecture is one of the nation's leading producers of foodstuffs such as beef cattle and vegetables, yet no other university in the prefecture has a School of agriculture. As the only such school in Kumamoto, the Tokai University School of Agriculture works together with local farmers and municipalities to conduct a wide range of research work related to farming, from regional agricultural promotion to partnerships with Asian countries.

In March 2018, Tokai University announced that to improve its educational environment, some of the functions of the School of Agriculture and Graduate Course of Agriculture Sciences would be moved from their current Kumamoto Campus to the area adjacent to the Kumamoto Airport where the Space Information Center is now located. In this issue, Professor Kohei Cho, Executive Director of the Research Promotion Division, discusses the School of Agriculture's initiatives and the enthusiasm over the new campus with Professor Tomohiro Araki, Provost of the Kyushu Campuses.

History of Tokai University School of Agriculture — Contributing to communities in Kumamoto, a farming prefecture

Araki: The predecessor of the Tokai University School of Agriculture was the Agriculture Department at Kyushu Tokai University. Kyushu Tokai University was founded in 1973, and in 1980, the School of Agriculture was established at a facility in Aso. The current Tokai University School of Agriculture was established in 2008 when Kyushu Tokai University and Hokkaido Tokai University were merged into Tokai University. Dr. Shigeyoshi Matsumae, the founder of Tokai University, said that the School of Agriculture was created "to be a department where members of the community, particularly farmers, could come with their shoes on."

Cho: Dr. Matsumae was from Kumamoto, so from the start he wanted to create a department that would contribute to communities in Kumamoto, which is a major farming prefecture.

Araki: That's right. The current School of Agriculture

has inherited this original spirit in that we actively work with local farmers. Representative of this is our "Monitor-Farmer System" which began soon after the School of Agriculture was founded. In this program, the university researchers and leading farmers in the prefecture conduct research together to promote agriculture. Farmers test cutting-edge technology developed by the university researchers, and the university researchers address the issues faced by the farmers. Nationwide, this is an incredibly unique program and it has received high praise in external evaluations. Recently, to encourage farmers to share more of their skills and resources with students, some of them have been invited to teach mock classes as guest lecturers. Kumamoto is a farming prefecture. As the only school of agriculture in Kumamoto, we believe we have a responsibility to contribute to the farming community in Kumamoto.

Distinctive research focusing on health and the environment

Cho: Could you explain the research themes which your group is focusing on at this moment?



Tomohiro Araki

Provost, Kyushu Campuses, Tokai University Professor, Department of Bioscience, School of Agriculture

Araki is a specialist in protein chemistry. His research involves isolating the proteins that operate inside organisms and investigating the relationships between their structure and function. Recently, he began attempting to use advancements in proteomes and proteomic methods to rapidly analyze tiny protein samples.



Kohei Cho

Executive Director, Research Promotion Division, Tokai University

School of Information Science and Technology Executive Director, Tokai University Research and Information Center (TRIC)

As head of the Research Promotion Division, Cho provides support to researchers at the university and promotes partnerships within the university, with scientists at other schools, and between industry, academia, and government. Cho is a satellite remote sensing specialist and has used satellite data in a wide range of research, including real-time monitoring, analyses of sea ice distribution variations, and environmental and disaster monitoring. Araki: First, there is the research on grass-fed cattle. Japan's wagyu beef is famous all over the world, but this marbled meat is created by raising Japanese Black cattle in barns and feeding them high-calorie imported feed. The School of Agriculture's grass-fed cattle are totally different. They graze on wild grass on the plains of Aso. Higo Japanese Brown cattle are very suited to being raised this way. In addition to being highly disease resistant, Japanese Brown cattle are gentle and easy to control even when grazing. They produce lean meat with little marbling, which is extremely healthy. When aged, it makes for incredibly juicy and flavorful meat. I specialize in protein chemistry and have investigated how umami levels increase as meat ages. I found that when meat is put into a vacuum pack and aged for 40 days at a low temperature of around 0 to 2 degrees Celsius, the increase in amino acid levels accelerates due to the action of an enzyme called protease in the cells.

Cho: I listened to Junior Associate Professor Atsushi Kashimura (School of Agriculture, Department of Animal Science) present his research on raising Japanese Brown cattle at the 3rd "Agriculture, Food, Health" QOL Seminar, which was held recently alongside an opening ceremony of the Aso practical training field. After the presentation, we had grilled steaks made from the meat of Japanese Brown cattle. The meat was mild and delicious.

Araki: Next, we are working on a "cyclical brewing project" that aims to make shochu liquor with zero waste production. Shochu is a distilled liquor, so liquefied lees remain after distillation. In the past, it was dumped into the sea, but this was banned after the London Convention was ratified. Now it is usually incinerated as industrial waste. In the cyclical brewing project, we try to find ways to reuse shochu lees. Shochu is made from the murasakimasari potato, which contains anthocyanins.

Cho: Do you mean purple sweet potato?

Araki: That's right. When you make shochu with this sweet potato, anthocyanins appear in the lees, which gives it a color like red wine. This can be turned into a food material to make functional food products. So far, we have used it to make moromi vinegar and dessert sauces. After making the food products, the remaining lees become feed for livestock, which generate excrement that can be returned to the fields to grow more sweet potatoes. Once this cycle starts, there is nothing to throw away. We conduct this kind of functional research and development through partnerships between industry, academia, and the government. More recently, research led by Professor Shin Yasuda (School of Agriculture, Department of Bioscience) on evidence-based functional analyses of highly functional anti-aging foods, research by Professor Kazuhiko Imakawa (Research Institute of Agriculture) on bovine leukosis (see "QOL Close Up" in this issue), and anti-aging research by Professor Ryoji Nagai (Department of Bioscience) have also attracted attention.

Cho: The Research Promotion Division is in

charge of coordinating industry-academiagovernment partnerships for the entire University. Various companies have made inquiries about Professor Nagai's research, which is likely to be useful in areas such as diagnosing lifestyle-related diseases. We also have high expectations for a medicalagricultural partnership with Professor Masato Sato of the School of Medicine (Surgical science, School of Medicine), who is studying cartilage regenerative medicine.

The School of Agriculture in a comprehensive university: Collaborating with other faculties and international exchanges

Cho: Tokai University has 19 faculties, which allows various forms of cooperation and collaboration between different faculties. In addition to the medical-agricultural partnership I mentioned earlier, recently there have been discussions at the School of Agriculture about using robots in farming, which will make the relationship with the School of Engineering more important. The connection with the School of Health Studies may also be important from the viewpoint of health and food. These examples show how faculties can freely collaborate with each other, which I think is one of the strengths of Tokai University as a comprehensive university.

Araki: In terms of international initiatives, we have a series of Asian Agricultural Symposia. The first symposium was held in Kumamoto in 1982, and since then, several meetings have been held in Asian countries such as the Philippines, Thailand, and Singapore. Each symposium has a theme, and in the beginning, they often dealt with remote sensing, which happens to be your specialty.

Cho: Remote sensing is a technology to monitor the Earth's environment from sensors onboard satellites and airplanes. When the United States launched the Landsat satellite in 1972, its first goal was to observe the Earth's surface to obtain information on agricultural and forestry resources, geography, cartography etc. Because there are no borders for satellite observations from space, it is an area where international cooperation is natural and necessary.

Araki: These symposia have also addressed the environment, food production, and in 2018, the focus was the impact of the 2016 Kumamoto earthquake on agriculture. Most of the participants at the symposia have been graduate students and researchers from universities and research institutes. As a new initiative, we have recently been inviting students from nearby high schools to give poster presentations in English, to give young people the chance to experience an international conference. Explaining a poster and answering questions in English is a very valuable experience for these students.

Automated farming, a new campus: New developments in agricultural research

Cho: Agriculture is an aging industry that less



people are working in. I think now is the time for young people to work on developing new methods, such as using IT in farming.

Araki: The reason it is an aging industry is that no one is willing to take over farms. These days, even people who are farming say they do not want their children to take over the work from them because they do not want them to struggle. The reality is that farming is a lot of work for not much pay. If we want more successors or new entrants, we need to turn agriculture into an industry that can be profitable.

Cho: It is like switching from the practice of personally checking on one's fields to using remote sensing. While satellites have limited resolution, recently it has become easier to use drones to take photographs from low altitudes. I think it is time for the researchers of agriculture, information science and engineering to work together to use these technologies to create new forms of agricultural management. The relocation of the School of Agriculture on the same campus with the Space Information Center would be a good opportunity for starting this research collaboration.

Araki: And the campus is right next to Kumamoto Airport. I have never heard of a campus where you can walk to the airport. I heard there are plans to add more international flights at Kumamoto Airport. In the future, the campus could become a base for transmitting the richness of Kumamoto's agriculture from Tokai University to the rest of Asia.

Cho: The automation of agriculture does not mean that information from the field is no longer needed. Information from remote sensing can only obtain overviews of wide areas. These images become valuable only when they are combined with what people see on the ground and the actual work of farming.

Araki: Moving the School of Agriculture near the airport does not mean we are leaving the field or stopping our partnerships with local people. The Aso facility has been an integrated campus that has both places to study and places for practical training. Grass-fed cattle, which need large pastures, and our natural farms of rice paddy, which we have had since the School of Agriculture was founded, are not easily moved, so they will stay in Aso. We plan to acquire fields near the new airport campus to make it an integrated campus as well.

Achieving a healthy life through eating: Future goals and expectations

Araki: Modern agriculture is not only about production, but comprises the entire chain of events that takes produce from processing to people's tables. All aspects of our lives fall under the purview of the School of Agriculture. This includes plants, which are also part of our environment; all animals related to human life, not just livestock; and functional foods in the field of biotechnology.

Cho: I heard that the goal of modern agriculture is what is called "presymptomatic disease, preventing and caring for diseases in their presymptomatic stage"

Araki: That is correct. Although medical advancements have certainly extended the human life span, the improvement in quality of life that Tokai University aims to achieve does not mean to prolong the time spent in the hospital. I think the School of Agriculture can play a role in keeping people healthy longer through diet and lifestyle.

Cho: I have heard that female enrollment is increasing at other agriculture departments. What can you tell us about that?

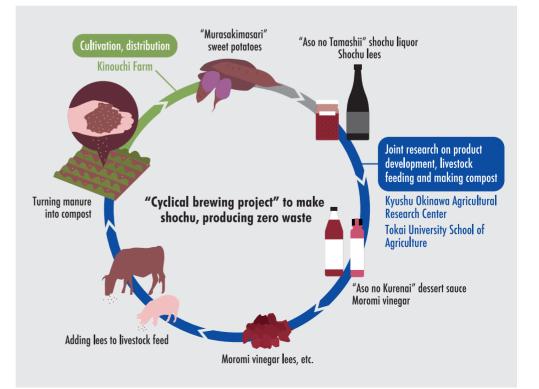
Araki: More than half the students in animalrelated departments are women. Many students enter these departments out of a fondness for wild animals or pets; and as they care for livestock, they come to love these animals as well.

Cho: I realized how important it was to disseminate information when I heard some students saying that they had read about research related to the keyword "animal" and thus, got interested in the department.

Araki: Actually, "Agriculture" is the keyword for the entire Kyushu Campus. This is true not only for the School of Agriculture. The School of Business Administration also has programs related to agricultural management and agribusiness. The School of Engineering is developing technology for IT agriculture, as well as for plant factories. A major feature of the Kyushu Campus is this collaboration between Kumamoto Prefecture's only agriculture department and multiple other departments over the keyword "agriculture."

Cho: As we discussed earlier, the proximity of the airport to the new campus makes travel so convenient, that we hope to have many visitors from other countries. Thus, the new campus may play the role of a hub in Asia, particularly focused on agricultural research. World university rankings are important indicators for universities. Research and internationalization are given particular weight in these assessments. The School of Agriculture makes contributions in both these fields through cutting-edge research, dissemination of information across Asia, and holding agricultural symposia. We have high hopes for the future of the School of Agriculture.

Araki: Thank you. I think Kumamoto Prefecture also has high hopes for us, particularly in serving as a hub. Centered around the axis of farming, Kumamoto Prefecture could become the core of Asia in the field of agricultural studies. The best way forward is for the university to continue to work together with local governments.



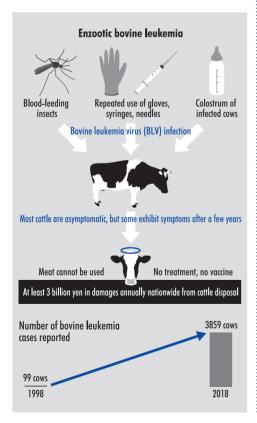


Aiming to contain increasing bovine leukemia Search for infection- and onset-resistance factors and development of simple

diagnostic methods

A research group that counts among its members Professor Kazuhiko Imakawa of the Tokai University Research Institute of Agriculture and Junior Associate Professor Toshiaki Inenaga of the School of Agriculture's Department of Animal Science, is working to find markers that will help identify cattle with infection- and onset-resistance to enzootic bovine leukemia (EBL), an infectious disease associated with a high mortality rate once onset occurs.

EBL is an infectious disease caused by bovine leukemia virus (BLV). The number of reported cases in Japan has risen from 99 in 1998 to 3,859 in 2018. Many animals remain asymptomatic even after being infected with BLV; however, several years after infection, a small percentage of animals develop symptoms such as swollen lymph nodes, loss of energy, extreme emaciation, diarrhea, and constipation. Additionally, even in asymptomatic animals, the virus resides in the body, which can become a source of infection to other animals. There are no vaccines available that can prevent this infection, and effective treatment measures after the onset are also not available. Most affected animals are found at meat processing centers and must be completely disposed of, which causes major losses for livestock farmers. "The growth in the number of animals with EBL onset has increased from 99 to 3,859 only over the last 20 years. Isn't that strange? We believe that if the School of Agriculture does not solve this, who else will?" Professor Imakawa said.



Kazuhiko Imakawa

Professor, Research Institute of Agriculture

Imakawa researches the retroviral DNA that remains in mammalian genomes, focusing on how these viruses impacted the evolution of mammals. His goal is to help create a robust farming industry that can withstand environmental and outside pressures by solving problems at livestock production and by providing farmers with new technologies.

BLV is a type of retrovirus that infects bovine lymphocytes through blood-feeding insects such as mosquitoes and horseflies; repeated use of gloves, needles, and other implements in caring for livestock; or is passed from mother cows to their calves. Retrovirus is a general term used for RNA viruses possessing reverse transcriptase, which use the host's cellular mechanisms to proliferate. These viruses utilize reverse transcriptase to synthesize DNA using their own RNA as a template and incorporate their own genetic information into host cell's DNA.

According to Professor Imakawa, previous studies by other teams aimed at preventing infection focused solely on the virus itself or cattle immunity, and most of these studies intended to identify receptors involved in viral infection of lymphocytes or elucidate the mechanism underlying viral proliferation. However, only about 11% of infection- or onsetresistant cases can be attributed to viruses or specific genes, while the remaining 89% cases remain unexplained. Prof. Imakawa said, "We believe that there is a mechanism to control infection and onset of the disease which exists in the cattle, not the virus. One reason why we began this research is because of a person who retired as the Director of Shonan Livestock Health Center in Kanagawa Prefecture. This person realized that some of the stud bulls might have a higher resistance to BLV, and entered a doctoral program to prove it"

Prior to the beginning of this study, Prof. Imakawa et al. used the individual identification number of cattle to track the difference in BLV infection rates and post-infection onset rates among different stud bull bloodlines over 10 years. There was no difference in the infection rate among the stud bulls; however, they found major differences in onset rates. For some stud bulls, no cases of disease onset were observed among their calves or the next progeny. This suggests that some bulls have developed resistance to bovine leukemia and this resistance is inherited genetically.

Currently, we are analyzing the genetic expression and SNPs in the genome of cattle that are resistant to infection and onset. (An SNP is a DNA mutation involving a change to only one base. For example, SNP occurs at a rate of one in approximately 1000 bases positions in humans. It is thought to be the cause of individual differences, such as resistance to diseases and effectiveness of drugs. Based on the amount of provirus (virus) in the body as detected by BLV antibody test and PCR method, the cattle reported within the jurisdiction of Shonan Livestock Health Service in Kanagawa Prefecture were divided into five groups: infected cattle, cattle that have not yet reached onset, but the number of viruses has increased, cattle that have maintained a low level of virus, cattle that are kept in the same ranch as the infected cattle but are not infected, and uninfected cattle kept in a clean ranch. Blood sampling was performed followed by gene expression and SNP analysis in these groups.



Although the analysis is still ongoing, it has already been confirmed that there are gene clusters and SNPs on multiple chromosomes related to BLV infection or cattle leukemia. In addition, genetic markers have been found to distinguish uninfected cattle in infected farms, infected cattle with low viral load, and infected cattle with enhanced viral load. If only stud bulls from bloodlines that are resistant to BLV infection or onset can be selected and used as breeding bulls, it can result in improved BLV resistance in all offspring. In addition, if cattle with increased virus in the body and higher chances of onset can be detected early and easily, it is believed that the extent of damage to livestock farmers due to the disposal of infected animals can be greatly reduced.

Moreover, Prof. Imakawa studied the improvement of the intra-uterine environment by examining the events happening in the uterus at the time of implantation of fertilized eggs to improve the pregnancy rate of cattle that has declined in recent years. He is also involved in the research on the placenta formation and origin of mammals through the relationship between retroviral DNA (endogenous retrovirus) remaining in mammalian genes and the placenta.

Regarding his research, Prof. Imakawa said, "My theme seems to be scattered at first glance but bovine leukemia is caused by a retrovirus, and it is possible that mammals have different placenta depending on the species due to endogenous retroviruses. The maternal and fetal genes are different, but the fetus can be implanted without being eliminated by maternal immunity, thanks to the endogenous retroviruses regulating the immunity. That is how everything is connected."

Retrovirus-derived genes comprise more than 10% of the bovine genome and about 8% of the human genome. It can be said that the mammalian genome co-exists with the virus. Prof. Imakawa thinks that a virus that cannot co-exist with the host organism may cause a disease. "Perhaps, viruses want to co-exist with mammals and cause diseases in those where co-existence is not possible. I would like to prove that they will eventually completely co-exist with the host." he said.

