JTB PHOTO/UIG VIA GETTY

Kanagawa hosts a concentration of heavy industry.

A smart place to work

Cheap housing, close proximity to Tokyo and a burgeoning research ecosystem are thrusting the ancient prefecture of Kanagawa into the modern world.

BY BRETT DAVIS

Given its ready access to the economic juggernaut of Tokyo, it would be easy to imagine next-door Kanagawa and its metropolitan area of Yokohama–Kawasaki to be little more than a satellite 'bed town'. But the region is very much a destination in its own right — a rich ecosystem built on a pairing of the industry and research and development (R&D) for which Japan is renowned.

Kanagawa is the second most populous of Japan's 47 prefectures, and home to the nation's second largest city, Yokohama. The region stretches along the coast of the country, from the south of Tokyo to the foot of Mount Fuji (see 'Centre of an island'). The bayside area forms what is known as the Keihin region — Japan's largest concentration of heavy-industry and manufacturing organizations. The region was the industrial powerhouse of Japan's rapid recovery after the Second World War, but it has now evolved a new character, driven by the promotion of an innovative R&D culture and attractive incentives for international investment.

"Kanagawa has the largest pool of researchers in Japan," says Tōru Hashimoto, executive director of development cooperation for Yokohama City Government. "We have so many research labs and institutes, and a real environment of innovation." Hashimoto points to the technology giant Apple as a beneficiary of that environment. In 2016, the world's most valuable company established one of its first R&D centres outside the United States in the prefecture. "I think this shows how attractive this area has become for global R&D," Hasimoto says.

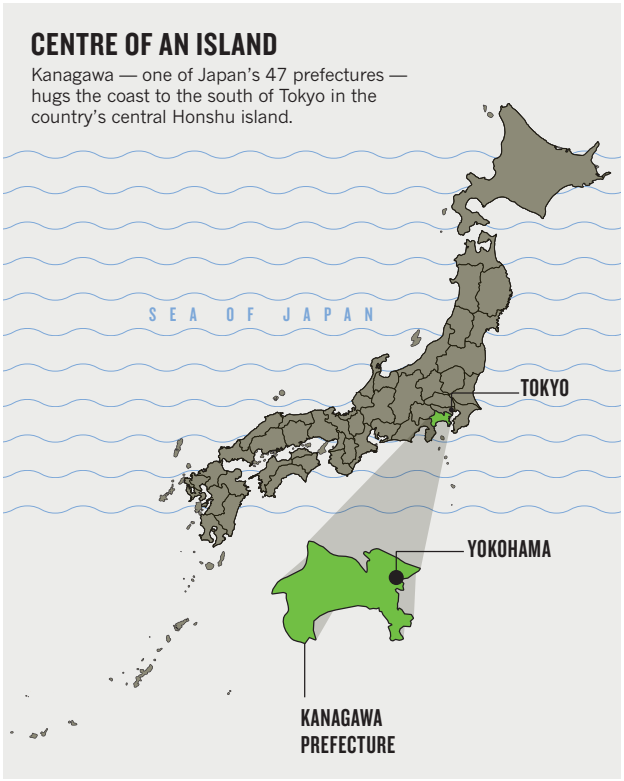
Kanagawa claims more than 60,000 research staff, a full 50% more than in Tokyo. They work in more than 1,000 research facilities, and many are in the prefecture's 40 universities. They include some of Japan's foremost institutes: the RIKEN Yokohama Campus, the Yokohama Institute for Earth Sciences, the New Energy and Industrial Technology Development Organization, the Tokyo Institute of Technology and Keio University.

INNOVATION BY DESIGN

Kanagawa receives the obvious rewards that come from hosting so many research institutions. It is part of the Yokohama–Tokyo ▶

region, the world's most prolific innovation centre. More than 94,000 patents were filed from the region in 2011–15, double the number from runner-up Shenzhen–Hong Kong and three times more than from third-placed Silicon Valley.

This culture is fed by the leading industrial firms that call the region home — including engineering giants Nissan and Bosch, computer manufacturers Fujitsu and Toshiba and chemical companies Shiseido and Takeda Pharmaceutical. These and hundreds of other engineering and technology firms are spurring a new culture for research labs and creating a healthy environment of collaboration between research and engineering. "In recent years, we have made a deliberate and very careful conversion from a manufacturing-dependent economy to one that is very much focused on research and innovation," says Hashimoto. "This has resulted in a remarkable change in the composition of our workforce to be more research-oriented, and we see that trend continuing."



A HISTORIC MELTING POT

Kanagawa was once the ultimate seat of power in Japan. For almost four centuries, the southern city of Kamakura was a major seat of power in Shōgun-era Japan, and it is thought to have been the fourth largest city in the world during the thirteenth century, after Hangzhou, Cairo and Fez. When Kamakura was destroyed by the Tokugawa Shogunate, the nation's capital was relocated to what is now Tokyo. The resulting 200 years of isolationist policy in Kamakura was eventually brought to an abrupt end in 1858 when the United States and Japan — in the shadow of American gunboats — negotiated the opening of Yokohama and other Kanagawa ports for international trade. Yokohama quickly became a portal for everything Western, a true melting pot where foreign ideas, influences and technology were blended with Japanese sense and tradition before being scattered across the country.

"Through that period, the port of Yokohama was very important," says Hashimoto. "It was the first place in Japan to get street lighting, water treatment, a lighthouse, iron bridges, street design and even railways — all Western technologies that were introduced to Japan through Yokohama."

By the end of the nineteenth century, Yokohama was a vibrant city with a population of half a million, and bursting with technological innovations, entrepreneurship and foreigners. Yet this would all be brought to an abrupt end with the Great Kanto Earthquake of 1923, which levelled almost every building in the area. Rebuilding began in earnest, only for the city to be ruined again by air raids in the Second World War. Yet it was from these embers that Japan found the means for its economic and industrial resurgence, which was driven in no small part by the rapid restoration and rise of the Keihin Industrial Zone with its concentration of heavy industry, including steel mills, oil refineries, petrochemical complexes and shipyards.

THAT REALLY LAID THE FOUNDATION FOR STATE-OF-THE-ART LIFE-SCIENCES RESEARCH AND THE CONCENTRATION OF INDUSTRIES.

By the 1980s, Keihin had become so successful that the Yokohama region risked being entirely consumed by heavy industry. Recognizing a need for diversification, local government decided to convert shipyards and warehouses into mixed-use business, industry, research and residential zones and create centres of employment, collaboration and innovation. Since then, successive governments have actively nurtured this environment. The most prominent of these districts, Minato Mirai 21, now forms the vibrant central business centre of Yokohama.

CLUSTERS SPEED UP RESEARCH

A region with so many R&D institutions is bound to form research clusters with a specific scientific focus, and Kanagawa boasts many. Two of the largest are Yokosuka Research Park, with its concentration of leading wireless and mobile-communications companies, and Kanagawa Science Park, which spans a wide a range of sectors.

R&D enterprises in the region benefit from a multitude of economic incentives and support, including various incubation and innovation platforms. For example, the Keihin area has been designated a Life Innovation Comprehensive Special Zone by the national government. That brings with it a variety of incentives, including tax relief, relaxed regulations and business subsidies specifically. Further inland is the Sagami Robotics Industry Special Zone, where many of Japan's leading and most innovative robotics companies are rapidly expanding the technology into practical applications, such as of life-support robots.

"We have had a particular focus on well-being and health care, starting roughly 20 years ago when we attracted RIKEN to establish a new life-sciences research institute in Yokohama," says Kousuke Adachi, director of the life-innovation promotion division of the City of Yokohama. "Then, in 2003, we established the Leading Venture Plaza near the RIKEN Yokohama Campus as a low-cost incubation facility for biotech start-ups. That really laid the foundation for state-of-the-art life-sciences research and the concentration of industries in this field."

The city also set up a life-innovation platform (LIP) in Yokohama to act as a network for cooperation between industry, academia and government in biotechnology and life sciences.

"Through the LIP, leading Japanese pharmaceutical companies and manufacturers of medical equipment, as well as leading academic institutes such as RIKEN and financial institutions, support the work of small enterprises and ventures," says Adachi. "In all, we now have some 90 organizations participating in the LIP as a bridge between academia and the private sector to create and implement innovative projects, stimulating Yokohama's economy and connecting the results of projects with advances in health care and

well-being for our citizens."

Kanagawa offers researchers a range of opportunities, from academic positions with organizations such as RIKEN and the Japan Agency for Marine–Earth Science and Technology (JAMSTEC), to industrial R&D with global technology giants. Finding the right position from abroad can be tricky — Japanese recruitment systems are often archaic and heavy on detailed documentation — but foreigners are generally afforded a warm welcome and respect as a source of international expertise, and most English-speaking foreign researchers can get by quite well without needing to know the local language, says Kyaw Moe, who moved to Kanagawa from Tokyo to work at the Yokohama Institute for Earth Sciences in 2001 (see 'A researcher's life in Kanagawa').

That welcome does have its limits. One of the more common pathways for securing a research position in Japan is a fellowship position through the Japan Society for the Promotion of Science, but they generally last for only a couple of years and are researchers can only ever get one. Those who hope to stay longer will need to find a position with an employer who is willing to sponsor a visa application.

People fortunate enough to find a longerterm position at a university can find the strict hierarchy stifling and difficult to climb. However, the government has tried to tackle that through its Top Global University Project, which offers better employment conditions and opportunities to attract international researchers.

Kanagawa has much to offer as an alternative to Tokyo for a place to live. It is on the fringe of the limelight, yet close enough to feel part of the global circuit. Its cheaper rents and house prices and more relaxed lifestyle make Kanagawa attractive to expats and locals alike. And it may well offer researchers new opportunities in the innovation capital of Japan. ■

Brett Davis *is a freelance writer based in Melbourne, Australia.*

Q&A: KYAW MOE

A researcher's life in Kanagawa

Kyaw Moe is a principal research scientist with the Research and Development Center for Ocean Drilling Science at the Yokohama Institute for Earth Sciences (YES), part of the Japan Agency for MarineEarth Science and Technology. Originally from Burma, Moe spent almost ten years at the University of Tokyo as a doctoral and postdoctoral researcher, before joining YES in June 2001.

What is your area of research?
I'm a marine geologist. My work with YES focuses on ultra-deep ocean drilling, at depths of greater than 2,000 metres. I now research high-resolution geochemical profiling to support resource exploration. I can spend two months or more at sea each year aboard YES's drill ship; the remainder of my time is spent in the lab in Yokohama. I've also been involved in earthquake research and marine seismic surveys.

What's special about YES in your field?
YES has so many facilities for our research: we have a very capable ultra-deep drill ship and port, our own supercomputer and of course many talented researchers. It is a very attractive institute for anyone in this field, and it is really the only institute of its kind in the world. We are proud of what we do here.

Are there many foreign researchers at YES?
There is a large community of foreign researchers at YES. Some are here for the long term, but we also get many on one-, two-, three-year and longer visits. Often they stay longer than planned. We also collaborate with researchers around the world, so I very much feel part of the global research community.

What's special about research in Kanagawa?
I think this region has a very high level of research and innovation, particularly around some of the advanced high-tech industries. The Tokyo Bay coastline has been an industrial zone for a long time with many big names like Nissan, Toshiba and Shiseido, and now we are seeing a lot of collaboration with the many world-class research institutes located nearby. I think the smart-city movement and the push for renewable energy has been a particularly big draw for many tech companies.

How does life in Kanagawa compare with in Tokyo?
The lifestyle is completely different. Tokyo is crowded and getting around is difficult. Here we are not far from Tokyo, but we have a beautiful port, and you drive for 20 minutes and you're in stunning countryside — beaches and Kamakura to the south, and Mount Hakone and Mount Fuji to the west. Apartments are also bigger and cheaper, and there is so much to do outdoors. It is a very nice place to live. K.M.

Transforming healthcare based on ME-BYO

The Kanagawa prefectural government is accelerating advances in healthcare through academia–industry–government collaborations rooted in THE ME-BYO CONCEPT — a unique response to Japan's aging society.


Yuji Kuroiwa, prefectural governor

By 2050, Japan is projected to have the highest proportion of centenarians in the world. Kanagawa, southwest of Tokyo and home to 9.1 million people, is one of the fastest aging prefectures in the country. To lead the way in tackling challenges posed by this unprecedented demographic change, the Kanagawa prefectural government is unveiling new strategies of the Healthcare New Frontier (HCNF) policy package.

"Medical technologies alone will not be enough to address the issue of our super-aging population," says prefectural governor, Yuji Kuroiwa. "So it's imperative to drive advances in healthcare at the societal level, to help people of all ages become more aware of ways to improve our health on a day-to-day basis."

To propel this change, Kanagawa prefecture has been promoting numerous projects based on the 'ME-BYO' concept. Derived from the Japanese word *mibyo* (literally meaning 'pre-disease'), which has its roots in 2,000-year-old traditional Chinese medicine, ME-BYO refers to the continuum between health and sickness.

THE TOTAL NUMBER OF RESEARCHERS IN KANAGAWA ACTUALLY EXCEEDS THAT OF TOKYO

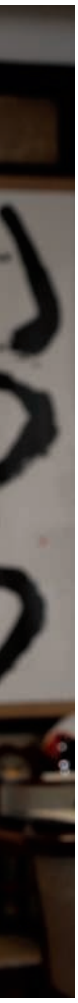
"Everybody is somewhere on the ME-BYO gradation scale," explains Kuroiwa. "Our approach is a paradigm shift away from the dualistic healthy-or-sick mode of thought, as experience shows there are no such clear-cut distinctions." The term was patented in 2015 and ME-BYO was officially included in Japanese national healthcare policy in February 2017.

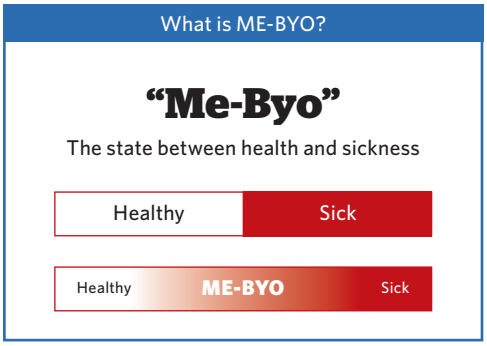
By encouraging people to monitor their ME-BYO status, the wider goal is to develop technologies and practices (relating, for example, to diet) that may help prevent or delay the onset of illnesses and extend healthy longevity.

A WORLD-CLASS BIOMEDICAL HUB

As part of the HCNF policy, Kanagawa is invigorating research and development of life science-related businesses through its activities in three special zones: the Life Innovation in Keihin Coastal Areas Comprehensive Special Zone for International Comprehensive Competitiveness Development, (where leading companies such as Johnson & Johnson already have bases near Haneda International Airport); the Sagami Robotic Industry Special Zone (where life-supporting robots are being developed and trained); and Kanagawa itself, which is part of the National Strategic Special Zone for the Tokyo area.

In Tonomachi, Kawasaki City, located within the Life Innovation Special Zone, the prefectural government established the Life Innovation






ME-BYO Summit 2017 held in Hakone, Kanagawa prefecture


Life Innovation Center (LIC)


CYBERDYNE Inc., Robot Suit "HAL®"


Sailing venue for the 2020 Summer Olympics

Center (LIC) in 2016 through a public and private partnership. Dedicated to advancing the industrialization of regenerative and cellular medicine, the LIC houses industries from startups to major companies that conduct various research and development. It provides an advanced research environment, where researchers have access to shared equipment for cell analysis and other regenerative activities.

Kuroiwa says many incentives exist for companies to establish bases in Kanagawa, including subsidies, tax breaks and low-interest financing totalling up to JP¥1 billion, plus free startup offices and ground-level support.

INSPIRING THE NEXT GENERATION OF HEALTH PROFESSIONALS

Set to open in 2019, the Health Innovation School is a graduate school that will become part of the Kanagawa University of Human Services.

Through a planned two-year Master of Public Health programme, the Health Innovation School will enable graduates to acquire skills in areas including data science, regenerative medicine, health technology and social systems. An English curriculum will be available for international students.

"As aging is a global issue, people who come to Kanagawa will find that what they learn here will be relevant to the future of their home countries," says Kuroiwa. "We welcome all those interested in facing this challenge together."

Put simply, he continues, Kanagawa is a microcosm of Japan. Not only does it contain historical sites of interest such as Kamakura and the popular urban areas of Yokohama and Kawasaki, but it also has mountains, hot springs and beaches — the famous Shonan area will be the sailing venue for the 2020 Summer Olympics.

"Moreover, in terms of the research environment, we are second to none," he says. "The total number of researchers in Kanagawa actually exceeds that of Tokyo."

A GLOBAL OUTLOOK

Looking ahead, Kuroiwa envisions that the next technological breakthrough will be the rise of the Internet of Human Health. Equipping homes with sensors designed to monitor health and well-being could in future provide valuable data, which may be integrated into personalized ME-BYO clinical records.

International collaboration, he says, is vital for developing evidence-based approaches and promoting understanding of the ME-BYO model. To this end, the first ME-BYO summit was held in 2015. A total of 310 delegates attended the summit, including representatives from the World Health Organization, the US National Institutes of Health and the Harvard School of Public Health. An official declaration of intent was signed at this summit. The second summit was held in Hakone on 20–21 October 2017, centred on the theme of 'calibrating ME-BYO'.

Kuroiwa also has plans further afield. He is building relationships with organizations including Johns Hopkins University, Stanford University and the UK's Cell and Gene Therapy Catapult, as well as governmental and municipal bodies in Asia and Europe.

Important though is the blend of traditional and new thinking. "Japan is already at the forefront of high-quality medical research and access to medical services," he says. "By docking cutting-edge technologies with the ME-BYO concept, we aim to confront the biggest challenges of today and tomorrow." ■

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Practicing medicine with compassion

St. Marianna University School of Medicine prides itself on highly advanced medical care and outcomes-based education, underpinned by RESPECT FOR THE DIGNITY OF LIFE.


Shoichi Ozaki, president of SMU

St. Marianna University School of Medicine (SMU) was founded in 1971 by Professor Kamon Akashi, a devout Catholic. The occasion was marked by the gift of a chalice and paten from Pope Paul VI. "SMU is the only school of medicine in Japan with a Christian background, and the spirit of Christianity is reflected in its philosophy," says President Shoichi Ozaki.

LEARNING MEDICINE WITH HEAD AND HEART

SMU aims to nurture individuals with a desire to serve society with compassion and to train physicians to conduct clinically relevant research that contributes to human welfare.

With a new curriculum launched in 2016, SMU provides various opportunities for students to practice and reflect on their own learning. This 'outcomes-based' style of education aims to foster independent thinking by focusing on the skills students acquire, rather than the facts they are taught.

For example, in the 'Early Exposure to the Life Cycle' programme, first-year students receive training in a maternity clinic, kindergarten, hospital and aged care facility. By interacting with patients, students gain clinical experience across the phases of life, helping them to grasp the purpose of studying medicine and the ethical issues faced by healthcare practitioners. This experience reinforces the qualities students need to serve their patients well.

The new curriculum aligns with global standards set by the World Federation for Medical Education. While this ensures a quality education, it also means that graduates will be eligible for Educational Commission for Foreign Medical Graduates certification from 2023.

With access to four closely linked hospitals and one clinic, students can learn the latest medical technologies. They may also study abroad in South Korea, China, and other Asian countries — honouring the school founder's pledge to support regions without doctors and his desire to nurture practitioners in Southeast Asia. SMU has plans to expand this programme as it builds relationships in Europe and North America.

SMU AIMS TO NURTURE INDIVIDUALS WHO DESIRE TO SERVE SOCIETY WITH COMPASSION

TACKLING URGENT NICHE NEEDS

SMU is committed to providing outstanding care for patients with rare diseases as well as more common illnesses. The university's physicians, non-physician scientists, clinical trials personnel and pharmacists work as a single team to further develop patient-centred care.

One example is SMU's work on the rare intractable disease, human T-cell leukaemia virus type 1 (HTLV-1)-associated myelopathy (known as HAM), which is characterized by symptoms including dysuria and leg paralysis.

"SMU is spearheading world-class research on HAM, on carbon monoxide (CO) poisoning, and on infertility, especially in patients with primary ovarian insufficiency," says Ozaki.

A team led by Yoshihisa Yamano in SMU's Department of Rare Diseases Research is investigating HAM. He opened a HAM-specific outpatient clinic a decade ago, which has


Chalice and paten honouring SMU's founding


The SMU chapel/special education facility


Yoshihisa Yamano


Taku Tanaka


Nao Suzuki


Kazuo Yudo

improved understanding of this rare disease and conducts clinical trials.

"We want to bring hope to patients with rare diseases," Yamano says.

"These patients face numerous challenges over their clinical course — from diagnosis and throughout treatment. Only through working together can we improve patient outcomes, and SMU is proud to continue such efforts."

NON-INVASIVE THERAPY FOR CO POISONING

SMU researchers are also exploring patient-friendly therapies for CO poisoning. CO — a highly toxic, tasteless and odourless gas produced by cars and some heaters — accounts for more than 60% of poisoning deaths in Japan. Current treatments have limited effects and fail to lower the morbidity and mortality rates.

CO is toxic because it decreases oxygen delivery to vital organs and tissues: inhaling CO leads to the formation of a carboxyhaemoglobin, COHb, which is over 200-fold more stable than the blood's usual oxygen carrier, oxyhaemoglobin (O2Hb). One approach to treatment is to use light irradiation, which can dissociate CO from COHb.

Taku Tanaka and colleagues at Kawasaki Municipal Tama Hospital, one of SMU's linked hospitals, used in vitro human blood samples to determine the most effective light radiation level for COHb dissociation. They showed that light intensity of 500,000 lux — as a comparison, 100,000 lux is direct sunlight — yields an effective dose of radiation.

Researchers elsewhere are testing a light radiation probe inserted through the oesophagus in mice. Tanaka's team is exploring a less invasive approach. They plan to develop a device, a jacket for example, that emits light radiation on the pulmonary surface and could be used onsite or during patient transport to the hospital. They are also considering a more direct method, such as a light-emitting intravascular catheter, that would be used only in a medical facility.

FERTILITY PRESERVATION

"Infertility is an urgent issue in Japan's rapidly aging society, and SMU is working with patients experiencing infertility due to age or illness," says Nao Suzuki, chairman of the Department of Obstetrics and Gynecology.

SMU stands at the forefront of research in Asia on infertility treatment and fertility preservation for young cancer patients. Two treatment methods — ovarian tissue cryopreservation by vitrification and in vitro activation followed by conventional freezing of ovarian tissue — extend options for women who, because of age or illness, are facing fertility issues. Both were developed at SMU and have gained worldwide attention.

SMU currently houses the world's largest single ovarian tissue transplantation facility. Three healthy babies attest to the treatments' success.

BRINGING THE FRUITS OF RESEARCH TO SOCIETY

SMU's mission of caring is buoyed by its business acumen. SMU has been active in securing patents and technologies through its Center for the Promotion of Intellectual Enterprise. "The Center, through industry collaboration, has developed the ovarian tissue freezing kit Ova Cryo Kit Type M, Alzheimer's and dementia identification software STM-COMET Ver. II, and parenteral nutrition bags, for which SMU owns the patent, copyright and design rights, respectively," says Center chief, Kazuo Yudo.

SMU is a leader in the education, development and provision of highly advanced medicine supported by state-of-the-art facilities and technologies. With Christian philosophy as a deep-running thread, SMU holds a unique and strong position in Japan and the world. ■

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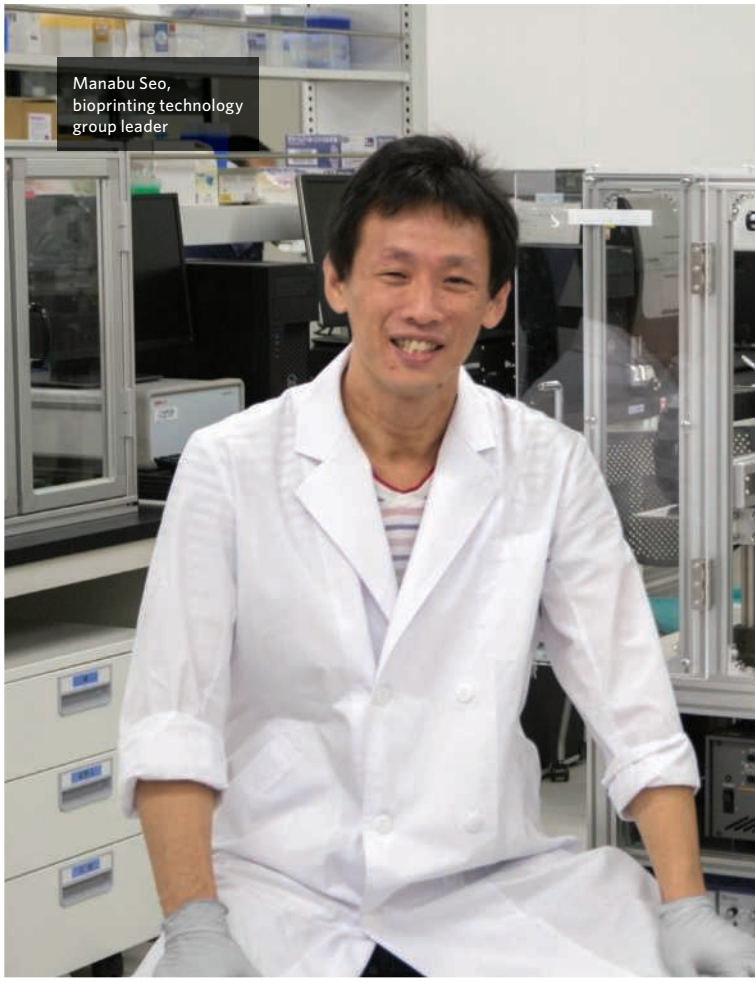
3D printing human parts

RICOH scientists are pushing the boundaries of their printing technologies to create INNOVATION IN HEALTHCARE.


Manabu Seo, bioprinting technology group leader

Imagine repairing a patient's injury with fresh human tissue or replacing a damaged heart with a perfect replica — one that was printed using technology similar to an office inkjet printer. It may sound like science fiction, but Japanese imaging and electronics company RICOH is working toward just that.

With over 80 years of experience in innovation, RICOH is applying their printing technology to healthcare. Known as bioprinting, the company's scientists are swapping primary colour cartridges for ink chambers containing cells and hydrogels.

By arranging cells as 3D tissues, the company's vision is to print living materials — such as tissues and organs — and realize the potential to revolutionize regenerative medicine and to push printing technology to even further outcomes for patients.

INVESTMENT WITH VISION

Visionary science is fuelled by inspiration. In 2013, RICOH scientist Daisuke Takagi attended a lecture on tissue engineering at a printing technology conference. There he glimpsed an opportunity to create a new application for the company's state-of-the-art instruments: printing the building blocks of life.

After returning to RICOH, Takagi established a small research team to develop inkjet-based bioprinting and create inkjet heads that are suitable for printing inks containing biological materials.

Just as the company was reinforcing its strategy to invest in new businesses, the team began a bioprinting collaboration with Osaka University through a national research project.

In 2016, RICOH expanded its capacity for biomedical research by establishing new laboratories in the Kanagawa Life Innovation Center.

THE FINE PRINT

The ability to print living cells has big potential, but faces several technical challenges.

Cells are much larger than the pigments in common printer inks, which means they sink to the bottom of any chamber, if kept stationary, and can quickly clog up a printer nozzle.

Living cells also require environmental conditions similar to those found inside the human body to stay alive and form functional tissue, so "the materials that can be used for cell ink are very limited," explains RICOH printing technologies specialist, Manabu Seo.

Leading a team of engineers, Seo developed a new printing head specifically designed to print living cell suspensions.

PRINTING CELLS IS A PROMISING IDEA WHOSE TIME HAS COME

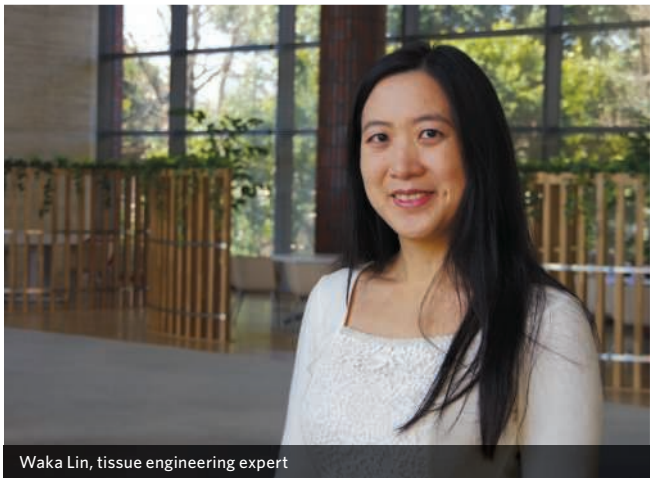
Replacing the nozzle of the common inkjet printer, the new inkjet head ejects, or 'prints', droplets of cell ink through a moving membrane on to a surface. Meanwhile, the inkjet head vibrates between ejections to prevent cells from settling to the bottom of the ink chamber.

The engineers also modified their system to print different cell and hydrogel layers on top of one another, allowing them to build 3D tissues in a single print run.

Tests revealed success. The new inkjet technology ejects a consistent number of cells as it prints, over 90% of cells survive the printing process, and the system can print viable cell layers as stacks of over 10 layers.

Tissue engineering expert Waka Lin and her team of biologists analyse the printed cells and tissues and develop them for new applications.


Yoshinori Yamashita, president and CEO


Waka Lin, tissue engineering expert

So far, the scientists have successfully printed fibroblasts, and are working with iPS-derived cardiac cells, skin keratinocytes, vascular endothelial cells and neuronal cells.

As one of the first biologists recruited at RICOH, Lin is inspired by the fast progress of the technology. "My role was first to help set up a cell culture laboratory and educate our staff in bioanalytical studies," she recalls. "Now I am developing future biomedical applications using printed tissues."

OPEN FOR INNOVATION

As laboratories around the world are working to create bioprinting technologies, RICOH's advantage is the company's ability to efficiently collaborate between expert teams, including engineers, material scientists, information technologists, and now, cellular biologists.

"The engineers in charge are professionals who can analyse any issue at its core to present unique solutions," says Lin. "So we aim to develop a high-precision system expected to be a cut above more common types of printers."

RICOH's bioprinting engineers are now developing optical monitoring devices to improve their cell dispensing precision and are optimizing the components in their cell ink.

The company's ultimate goal is the 'printing of life': regenerating full organs for human transplantation. While aspirational, the idea may not be a pipe dream.

"In 100 years, if some breakthrough was made to replace cells with biomimetic materials, then some kind of life-saving printer could be by the bedside in every hospital," says Lin.

Meanwhile, RICOH's bioprinting team are looking for collaborators in the biomedical and bioengineering fields, including scientists, engineers and clinicians, to help their cell printing technology reach its full potential.

"RICOH enables knowledge creation through digitalizing and connecting workplaces in the office and on the frontlines," says company CEO Yoshinori Yamashita. "We are applying our inkjet technology to healthcare using open innovation."

The scientists are also looking to explore directions they may have not even yet conceived. "The concept of bioprinting at first seemed extremely challenging," says Lin. "But seeing the fast progress of 3D printing in general, printing cells is a promising idea whose time has come." ■

Embracing new collaboration to accelerate product development

Takeda aims to create a vibrant, 'open innovation' ecosystem in Japan. Shonan will become the place where diverse researchers and projects translate Japan-born, CUTTING-EDGE SCIENCE INTO INNOVATIVE HEALTH SOLUTIONS, for the benefit of patients locally and across the globe.

In a 400-metre-long building, about an hour south of Tokyo, a revolution is taking place that may not only improve and save people's lives; it has the potential to alter the very fabric of Japanese corporate culture.

The revolution centres on what is now known as Shonan Health Innovation Park in Fujisawa City. Here, the owner Takeda Pharmaceuticals is opening its state-of-the-art facility to external researchers. This move is intended to fast-track scientific discovery by nurturing an entrepreneurial culture and supporting startup and venture capital companies.

Toshio Fujimoto, the general manager of Shonan Health Innovation Park, says the decision is a response to the rapid pace of scientific discovery. "Science is progressing in some areas almost exponentially," Fujimoto points out. "And the reality is that in-house research is no longer keeping up with progress in areas such as stem cell therapy, bioinformatics and gene therapy."

He cites examples from the United States and Europe, where increasingly venture and startup companies commercialize research that they then pass on to pharmaceutical companies.

"We have to adapt to this external reality," Fujimoto says. "In the past the pharmaceutical industry emphasized in-house research with a great amount of secrecy — but times have changed. Today, we're embracing an externalization strategy that puts emphasis on partnerships with the best in the field."

It is a bold step with no guarantees, as Fujimoto admits: "But we believe this is the right path and we're deeply committed."

Just how 'different' Takeda's approach is within Japanese culture cannot be overstated. Seigo Izumo, head of Scientific Affairs Japan, global head of Takeda's Regenerative Medicine Unit, and a former Harvard academic who spent many years working in the United States, points to the American approach as a comparison.

"The culture in the United States is that if you create a startup and you fail, it isn't a problem. The fact you try and fail has value," Izumo says. "In Japan, once you fail you have a strong sense of shame as an individual and that is attached to you as well by society. That leads to risk-averse behaviour. This tendency for risk aversion is also prevalent even among venture fund managers in Japan."

This cultural difference, Izumo believes, underpins the large gap in the numbers of startup companies between Japan and the United States.

CREATING AN ENTREPRENEURIAL CULTURE REQUIRES A CHANGE IN MINDSET TO PUSH BOUNDARIES

Creating a culture where risk is embraced requires a change in mindset to push boundaries. Takeda is working with staff to help them embrace this transformation through training and leadership workshops, as well as mentoring them during the process of creating their own companies.

"It is very exciting, and at times it can be hard for those who are averse to change, but I think it is a model that really enriches people's lives through being exposed to different environments and people," he says. "These are real opportunities for staff to get out of their comfort zone and push their boundaries."

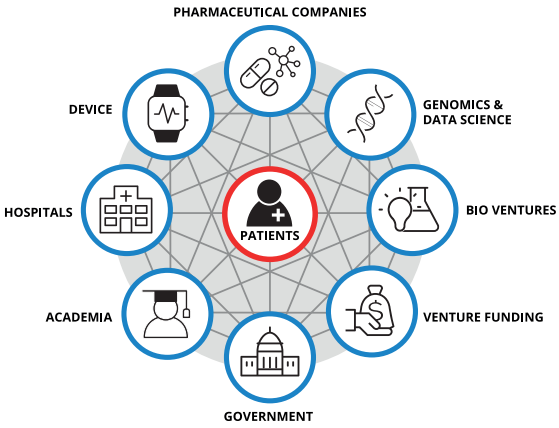
The new approach has grown organically since Takeda's partnership with 2012 Nobel laureate Shinya Yamanaka.

Yamanaka's discovery in 2007 that mature human cells could be reprogrammed into immature cells, with the ability to develop into all types of cells in the body, has led to new research into induced pluripotent stem (iPS) cells.

"Professor Yamanaka wanted to see the fruits of his research come to clinical fruition," Izumo recalls. In December 2015, Takeda and Kyoto University's Center for iPS Cell Research and Application (CiRA), led by Yamanaka, launched a 10-year collaboration, known as T-CiRA.

With 10 projects and over 100 staff, T-CiRA aims to develop innovative therapies for use in areas such as cancer, heart failure, type 1 diabetes mellitus, neurodegenerative disorders, gastrointestinal

The park offers access to state-of-the-art research facilities.



Industry, government, and academia will come together to incubate and accelerate the translation of cutting-edge science into impactful health solutions for patients in Japan and around the world.

Abundant shared spaces provide greater opportunities to network, foster collaboration, and support work-life balance.

diseases and intractable muscle diseases.

Izumo says a hallmark of the programme is that academic researchers from Kyoto and Yokohama City universities and RIKEN research institute spend part of their time working at Shonan Health Innovation Park, alongside Takeda researchers.

All participants — the universities, academic researchers and Takeda — have seen the benefits of the co-location.

"Because everything is here — the infrastructure and committed staff — progress is faster," Izumo says. "In a university laboratory there are a lot of ideas, but academics also have other missions and their research facility isn't set up for product development."

The success of T-CiRA was the confidence boost Takeda management needed to broaden their approach. Takeda has now created a number of companies within Shonan Health Innovation Park, including Axcelead Drug Discovery Partners, SCOHIA PHARMA, Cardurion, SEEDSUPPLY, ChromaJean, and Chordia Therapeutics.

Noile-Immune Biotech, a spin-off from Yamaguchi University and the National Cancer Center, has committed to moving its research to the Park. And K-Pharma, an offshoot of Keio University focusing on central nervous system disease, also plans to locate its laboratory in the Park. As well, Izumo is negotiating potential links between the Park and foreign research institutions.

"I would like to see the innovation park become a very unique research ecosystem that is Japan-based, but has an international outlook that's recognized and appreciated by the global research community."

For Fujimoto and Izumo, global recognition and an influx of new tenants will validate the innovation park concept. This will be an indicator that Takeda has taken the right step. But, as a surgeon and a physician, respectively, their main criteria for success will be "how we can bring innovative treatments to patients faster, and ultimately whether these treatments will help patients." ■

Takeda

www.takeda.com

Adding bacteria to the mix to improve community health

Kirin is harnessing MORE THAN 60 YEARS OF EXPERIENCE in fermentation and pharmaceutical technologies to serve the health and well-being of consumers.

Demand for functional foods — those that offer benefits beyond basic nutrition — is tipped to keep increasing, with rapid growth in the industry due to the aging population and boom in the health and wellness trend. Japan, where functional beverages fill vending machines and convenience store shelves, has experienced dramatic and sustained growth and its consumption rates are now one of the highest in the world. The experience and technological expertise of Kirin, a leading Japanese beer and beverage company, shows it to be a major player in this industry.

LEVERAGING EXPERT IN FERMENTATION

Kirin, since taking over the Japan Brewery in 1907, has developed a reputation as a company that produces beer and soft drinks. Diversifying during the 1970s and 1980s, Kirin now holds major subsidiaries in the food and pharmaceuticals markets. By 2000, the increasing demand for health products led Kirin to turn its experience and knowledge in fermentation and biotechnology to begin research and development of functional foods. In the current competitive market, contributing to the "health and well-being" of the community has become a key philosophy of the Kirin brand.

In 2008, Kirin launched an intra-company collaboration called the Kirin Health Project to leverage the strengths of its subsidiaries in the healthcare field with the goal of improving the health of society. The company has since released various functional products. Their most recent range consists of beverages, yoghurts and supplements containing a proprietary lactic acid bacteria (LAB) strain proven to protect from the influenza virus.

ANTI-VIRAL BACTERIA

Fermented milks have been known for their health effects since prehistoric times. More than a century ago, Nobel laureate Ilya Mechnikov suggested that LAB, which was used to prevent milk from spoiling, could also be used to manipulate gut bacteria to promote health. LAB are widely found in natural foods and manufactured in dairy products: they have become one of the most extensively studied food substances for their health benefits.

In 2012, Kirin researchers collaborated with their subsidiaries and external research institutes to perform a screen to identify a unique LAB strain that stimulates plasmacytoid dendritic cells (pDCs). Not only do pDCs produce an immune-stimulating signal with anti-viral actions, but they also present viral antigens to immune cells that recognize and remember pathogens for adaptive immunity. Daisuke Fujiwara, senior manager and lead scientist of the project at Kirin, explains that pDCs "are the commander-in-chief of anti-viral immunity." Through this screening process, Kirin researchers identified the strain they called *Lactococcus lactis* strain Plasma (JCM 5805) after pDCs. "This strain is the only LAB that activates pDCs directly," says Fujiwara. Direct activation of pDCs means that "we can expect much more activity against virus infections from Lactococcus Plasma than from conventional LABs," he adds.

STUDIES SUGGEST THAT LACTOCOCCUS PLASMA MAY DELIVER MORE ACTIVITY AGAINST VIRUSES THAN CONVENTIONAL LACTIC ACID BACTERIA

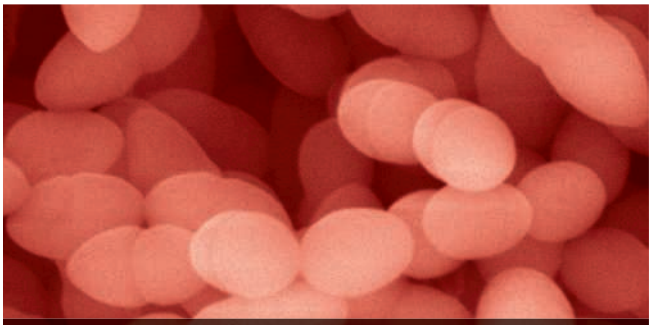
Kirin has tested Lactococcus Plasma as a probiotic in daily doses of yoghurt-based beverages and capsules in six human clinical trials in healthy subjects, and an epidemiological study in children. Consumers of the yoghurt had lower incidence of the flu, and reduced symptoms, compared to the rest of the population.

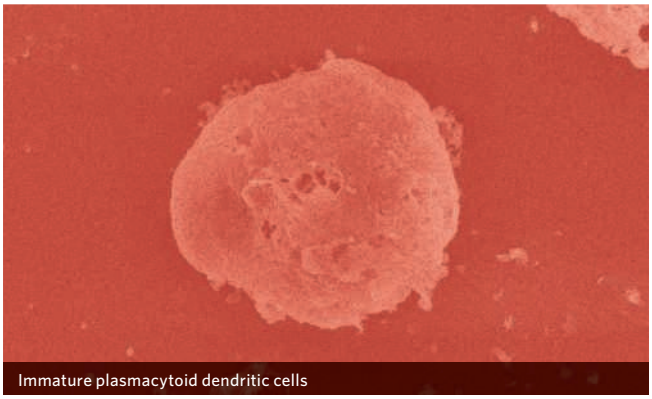
Another benefit of Lactococcus Plasma is that it doesn't have to be alive to induce anti-viral effects. In fact, a heat-killed 'dead' form of the bacteria is just as effective as the live version. This expands the uses of Lactococcus Plasma in products other than yoghurt.

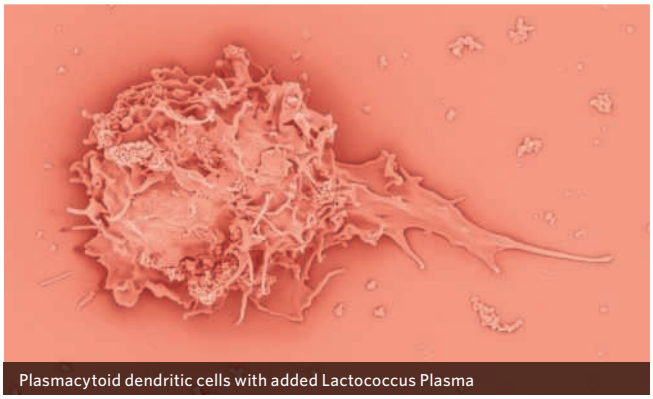
Research into how Lactococcus Plasma works shows that activated pDCs in the intestines can increase


Daisuke Fujiwara, Ph.D.


Kirin's Research Laboratories for Health Science & Food Technologies in Kanagawa prefecture


Lactococcus lactis strain Plasma (JCM 5805)


Immature plasmacytoid dendritic cells


Plasmacytoid dendritic cells with added Lactococcus Plasma

the expression of anti-viral genes in the lungs to impede flu symptoms. While Kirin researchers are still studying the precise mechanisms linking the intestines and peripheral tissues, they think that activated pDCs or the anti-inflammatory signals they produce may be delivered to other organs, such as the lungs, through the bloodstream.

A NEW VENTURE IN A NEW ERA

Kirin set up a collaboration between three Kirin companies in 2012 to market Lactococcus Plasma. The range includes yoghurt from Koiwai Dairy Products, soft drinks from Kirin Beverage, and supplements from Kyowa Hakko Bio.

Kirin is also researching the use of LAB beyond this range of products. They are seeking partners who understand the value of science and share the brand's philosophy with whom they can develop a wider variety of foods not previously considered to benefit from LAB, such as snack foods.

Lactococcus Plasma is not Kirin's first functional ingredient. In early 2012, Kirin released a beverage containing indigestible dextrin, a dietary fibre shown to reduce absorption but increase excretion of fat. The company also sells beverages and foods containing ornithine, an amino acid that enhances liver function to counter the effects of excessive drinking and suppresses the secretion of stress hormones to aid sleep.

As the company takes steps towards a new business venture that utilizes core technologies to bridge the food and medicines markets, Fujiwara says the aim is to provide "a novel food-based approach" to address diversifying health concerns. This is a major step in the company's goal to improve societal health. ■

KIRIN

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Algae reach for the skies

A humble species of algae underpins some big ideas. It can provide HIGHLY NUTRITIOUS FOOD for humans and livestock, capture carbon dioxide from wastewater and the atmosphere, and even generate biofuel for aircraft.

The miracle alga, *Euglena gracilis*, is now in mass production thanks to novel cultivation methods developed by the Japanese company euglena Co. The company is keen to foster new innovative collaborations with the international research community to help them achieve their goals.

Research on *E. gracilis* has a long history in Japan, and euglena Co.'s founder, Mitsuru Izumo, started the company more than a decade ago to harness *E. gracilis*' potential as a healthy, nutritious food supplement. Their *E. gracilis*-based cookies are already aiding the fight against malnutrition in Bangladesh.

Euglena Co. seek to expand their research and development into other applications for *E. gracilis*: one goal is to harness the alga's potential to produce a safe, efficient form of biofuel for aviation.

"Paramylon, a unique carbohydrate extracted from *E. gracilis* cells, is an important ingredient for biofuel production," explains euglena Co.'s Kengo Suzuki. "During anaerobic fermentation, *E. gracilis* produces lipids by converting paramylon. We are currently working on a mutant form of *E. gracilis* with enhanced lipid metabolism that would provide even better yields for biofuel."

To achieve this, euglena Co. seeks collaborators, explains Suzuki. "We welcome new insights and techniques from scientists working in similar fields around the world."

This presents a unique opportunity to help unleash the enormous potential of these tiny algal organisms; perhaps one day the power of *Euglena* really will take to the skies. ■

KENGO SUZUKI, Ph.D.
Director, Head of R&D, euglena Co.

"Paramylon, a unique carbohydrate extracted from *E. gracilis* cells, is an important ingredient for biofuel production"

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