SPOTLIGHT ON YAMANASHI

Science at the foot of Mt. Fuji

Japan's Yamanashi prefecture has a lot to say for itself when it comes to cutting-edge R&D.

BY TIM HORNYAK

IT MAY NOT be a familiar name. but if you've ever seen a photo of Mt. Fuji looming over a reflective lake, you've seen Yamanashi. The prefecture is known for much more than stunning mountain vistas, though: it produces everything from grapes and peaches to robots and undersea internet cables.

An inland prefecture to the west of Tokyo, Yamanashi sits near the geographic center of Honshu - the largest of Japan's islands. It's an important link between the hightech factories surrounding Tokyo, the industrial areas around the Sea of Japan, and the industrial heartland around the city of Nagoya.

The yellow robot empire

One of Yamanashi's most famous technology exports are the industrial robots manufactured by

Fanuc. The company is a giant in the global robotics industry, and its trademark vellow machines serve as mechatronic ambassadors for the prefecture. First known for making computer numerical control (CNC) devices for industrial automation, Fanuc was spun out of Fujitsu in 1972 and began making robots five years later, soon outgrowing its base in Hino City, western Tokyo. In 1984, it completed a new head office, R&D laboratory and CNC factory in Oshino, at the foot of Mt. Fuji, and never looked back. It now claims a worldwide installation base of 2.4 million CNC controls and 250,000 robots. Last year, it said it would invest about ¥130 billion (\$1.2 billion) on a new factory and labs in Yamanashi in a bid to improve its robots' speed and reliability. It's currently recruiting for positions in Japan and overseas

in R&D, production technology, sales and service.

"A major merit of our location in Yamanashi is that our engineers can immerse themselves in an area blessed with nature and a cool climate," says Fanuc spokesman Keisuke Fujii.

Science strengths

Robots are just a small part of the R&D landscape of Yamanashi. The prefecture's 2016 basic science plan calls for cultivating local science and technology while dealing with problems such as the aging population, globalization of business, and the migration of manufacturing to overseas. In a 2015 report, Yamanashi's Comprehensive Research Organization for Science and Technology highlighted examples of local research: how different light wavelengths can affect egg laying in hens; development of an anion exchange electrolyte membrane for fuel cells; and how groundwater resources in the northern part of Mt. Fuji can be managed.

A major center for research is the University of Yamanashi in Kofu, about 120 km west of Tokyo. It can trace its roots back to the 18th century Kitenkan Kofu School of Learning, which taught Confucian values as part of the educational policies of the Tokugawa samurai regime of the time. The school survived the downfall of feudalism and went through several reincarnations before becoming a university in 1949. Today it hosts about 5,000 students, and was recently in the news when alumnus Satoshi Omura was awarded the 2015 Nobel Prize in Physiology or Medicine, alongside collaborator William Campbell of Drew University, for work on drugs that led to treatments for river blindness and elephantiasis. They shared the award with Chinese scientist Youyou Tu, who discovered a novel therapy to combat malaria.

"The University of Yamanashi serves as a local base of knowledge to contribute to regional and world development," says Shinji Shimada, president of the University of Yamanashi. "Our research covers fuel cells, clean energy, watershed environmental science, developmental engineering, brain science and medical device development, in addition to viticulture and crystallography."

The university has notched significant results in biology as well. One specialization is the cloning of mice for reproductive biotechnology studies. Building on a tradition of cloning innovations, university researchers recently succeeded in producing mouse clones from cells derived from urine. The noninvasive technique could help with studies of endangered species.





The Tokaido Shinkansen bullet train.

The maglev bullet train

Just in time for the Tokyo Olympics in 1964, Japan launched its groundbreaking Shinkansen bullet train. The first commercial train to operate at over 200 kph when it connected Tokyo and Osaka, as is sped past Mt. Fuji it became a symbol of Japan's postwar growth and innovation. The Tokaido Shinkansen, as the line is called, is the most heavily used high-speed rail line in the world, with daily capacity of 340,000. With not a single fatality due to accidents, it also has an admirable safety record. Operator Central Japan Railway is now building the next-generation bullet train, a magnetic levitation (maglev) line that will connect Tokyo with Nagoya, a distance of 286 km, in 40 minutes.

Yamanashi Prefecture is the site of a test track that will be part of the new maglev line when it opens in 2027. Powered by superconducting magnets, the L0 series train set a world speed record for a manned train of 603 kph in April 2015.

"The Advanced Biotechnology Center is equipped with 17 micromanipulator sets – one of the largest collections in the world," says director Teruhiko Wakayama, a mouse cloning pioneer who coauthored the study.

"We are making use of this equipment for efforts such as creating genetically modified mice, preserving germ cells through freeze-drying, commercialization of somatic cell cloning technology, revival of endangered or extinct species through cloning, and even using reproductive technology on the International Space Station. We're developing technology that humanity will need in the near future," he says.

The university's Clean Energy Research Center was set up in 2001, focusing on the development of practical fuel cells for vehicles, households, portable devices and thermal power plants. An affiliated Fuel Cell Nanomaterials Center was established in 2008. Another division develops new materials for solar energy conversion.

"Each of our divisions collaborates with entities such as the New Energy and Industrial Technology Development Organization (NEDO) to implement large-scale national research projects," says center director Hiroyuki Uchida. That kind of collaboration has produced results such as the FCM-3D-Oxy, a device developed by Junji Inukai and marketed as the world's first system that allows for real-time observation of the concentration of oxygen in fuel cells through microprobes inserted perpendicular to a membrane-electrode assembly, giving researchers a valuable tool to diagnose the efficiency of a cell.

The Fuel Cell Nanomaterials Center is one of several research groups at the University of Yamanashi that is recruiting researchers, says spokesperson Izumi Mochizuki. Under its tenure-track promotion system, the university has hired young researchers from Japan and abroad for assistant professor positions.

Building the internet's backbone

A UFO-styled building in the city of Otsuki in eastern Yamanashi plays a key role in the growth and stability of the infrastructure underpinning the global internet. This factory, run by electronics giant NEC, produces optical submarine repeaters: long, missile-shaped devices that boost data signals as they travel through cables on the bottom of the ocean. About 99 percent of internet traffic courses through undersea cable networks, which stretch as far as 39,000 km – about the length of the equator – and NEC is one of the largest cable system manufacturers in the world. The repeaters weigh up to 700 kg and are set on the ocean floor every 40 to 100 km to verify and boost signal integrity. Otsuki was the hometown of Koji Kobayashi, one of the founders of NEC, and today the 80 staff at the NEC plant produce 40 repeaters every month.

Last week, the company announced – alongside six international partners – the opening of a new trans-Pacific cable with capacity for 10 terabytes per second per fiber pair; a hundredfold improvement in the speed of previous cables. The line will link the west coast of the US with major cities in Japan and elsewhere in Asia. The cable itself, consisting of six fiber pairs, is capable of transmitting 60 terabytes, the equivalent of 600,000 digital copies of this magazine, every second.

"The construction of high speed, high capacity optical networks is essential for meeting the IT era's increasing need for rapid access to heavy volumes of information," says Shuji Yamashita, vice president at NEC Yamanashi, which is currently hiring technicians for development of optical equipment production technology.

"Even though Yamanashi does not share Japan's expansive coastline, repeaters produced at NEC Yamanashi enable submarine cables to function effectively in harsh ocean conditions at depths of approximately 8,000 meters, for an expected duration of 25 years."

"NEC has maintained one of the world's top shares in submarine cable construction since founding nearly 30 years ago," Yamashita says. "Going forward, NEC aims to continue capitalizing on its Yamanashi facilities to reinforce the company's contributions to social infrastructure throughout the world."

Within easy reach of Tokyo, Yamanashi offers a wealth of science and engineering opportunities for researchers in search of something different. Ever-present on the horizon, Mt. Fuji has inspired Japanese poets and artists here for generations. Perhaps it has started to inspire researchers, too.

This content was commissioned and edited by the Naturejobs editor



Prizing originality and innovation

Renowned for its strength in nanotechnology and medical sciences and as the alma mater of Satoshi Ōmura, co-awardee of the 2015 Nobel Prize in Physiology or Medicine, the University of Yamanashi has a wealth of research achievements. Moreover, the recently rebuilt University of Yamanashi Hospital is gaining international recognition for providing top-level medical care.

tanding on the helipad atop the university hospital, Shinji Shimada, president of the University of Yamanashi, notes: "From here, you can see some of the best views of Mount Fuji to the south, the Yatsugatake Mountains to the north and the Southern Alps to the west."

"At the foot of these mountains, there is very clean water," he continues. "That's why Yamanashi is famous not only for its water, but also for many kinds of fruits such as grapes, peaches and cherries, and, of course, its vineyards."

Located in the heart of the fertile Kofu Basin in central Japan, the University of Yamanashi's proximity to the nation's oldest wine-making region has cultivated strong ties between academia and industry. The university is home to the Institute of Enology and Viticulture — the only one of its kind in Japan — where researchers are developing new wine-making technologies and training the next generation of wine specialists.

"We value original research," says Shimada, "And we also prize international collaborations. Through wine technologies, for example, we have deepened partnerships with institutes in France, the US and Australia. In water-management studies, we have collaborated most recently with Nepal."

"Our university is well known for its world-class fuel-cell technologies and medical sciences. And in April 2016, we strengthened our interdisciplinary research capabilities by creating the Integrated Graduate School of Medicine, Engineering and Agricultural Sciences."

Promoting such close interactions between the physical and life science

departments is rare among Japanese universities. Shimada explains that multidisciplinary approaches are essential for future breakthroughs and healthcare innovations.

The roots of the university extend back to the Edo Period, with the founding of Kitenkan, the Kofu branch of the Shoheizaka school under the control of the Shogun's government in 1795. The university has since undergone several transformations; notably, the former Yamanashi University was integrated with the medical school in 2002, and the University of Yamanashi became a national university corporation in 2004.

With just under 5,000 students, University of Yamanashi is much smaller than the big-city universities of Tokyo, Kyoto and Osaka. But Shimada notes that this may allow for greater communication between students and faculty. By launching an initiative called Office Hour, whereby any member of the university can visit his office informally, Shimada himself is promoting an open-door approach to increase opportunities for dialogue.

A Nobel legacy

The university has garnered much attention in the past year due to Satoshi \bar{O} mura being awarded the 2015 Nobel Prize in Physiology or Medicine. He graduated from the University of Yamanashi in 1958 and was a research associate at the then Faculty of Engineering from 1963 to 1965.

"This is an outstanding achievement," says Shimada. "We conferred the honorary title of Special Distinguished Doctor on Ōmura in a ceremony in 2015."

Only the third Japanese scientist to receive the Nobel Prize in Physiology or Medicine, Ōmura shared it with William Campbell, for their discoveries leading to novel therapies against infections caused by nematode parasites, and with Tu Youyou for her work against malaria.

"The work of Ōmura is exceptional; his contributions led to the discovery of avermectin and the development of ivermectin, which have saved the lives of many people around the world," Shimada notes.

Developed in collaboration with Merck, ivermectin has transformed the lives of millions afflicted by onchocerciasis (river blindness) and lymphatic filariasis (an infection caused by nematodes). Ivermectin is reported to be effective against malaria, tuberculosis, dengue fever and other neglected tropical diseases.

"Ivermectin is also significant in the fight against scabies — an enormous skin problem around the world, so this really is



Kyodo News



a very special drug," says Shimada, who is president of the Japanese Dermatological Association. In addition, Ōmura's research led to the discovery of staurosporine, the world's first protein kinase inhibitor of microbial origin. This compound led to the development of imatinib, a key drug now used for the treatment of leukaemia.

Ōmura impresses on his students the importance of nurturing *ichi-go ichi-e*, ('once-in-a-lifetime encounters') and living by the concept of *shisei sokudatsu* (showing 'sincerity and empathy towards others').

As a celebration of Ōmura's achievements, the University of Yamanashi has started awarding scholarships to outstanding students in various fields. There are also plans to build a commemorative complex that may include a new hall named after Ōmura, a renovated wine research institute, a facility to showcase the original gate of Kitenkan and a crystal science institute, relating to the region's history as Japan's largest producer of crystal jewellery. Shimada says: "We warmly welcome all donations from individuals as well as institutes to support the development of these facilities."

Human-to-human connections

As he walks down the corridors of the university hospital, Shimada engages in lively conversation with hospital staff. "We have over 600 beds in our hospital," he explains. "And we're particularly proud of our state-of-the-art operating theatres."

In addition to robotic surgery using the da Vinci Surgical System, the hospital is equipped with an Elekta linear accelerator, which enables precise imaging of tumours and Tomo Therapy technology for advanced radiation therapy.

NATUREJOBS SPOTLIGHT ON YAMANASHI



The hospital has two hybrid operating theatres, one with an Artis zeego system and the other with a 3-tesla magnetic resonance imaging system. These cutting-edge devices permit intra-operative image-guided surgery and minimally invasive surgery.

With the addition of the helipad in 2015, the University of Yamanashi Hospital is gaining accolades for its fast-response capabilities and top-level intensive care units.

The university is also exploring innovative disaster-prevention strategies. U-shaped dampers and rubber bearings strengthen the hospital building to minimize damage caused by earthquakes. Benches that can be transformed into hotplates and seats that fold out into emergency toilets have been installed outdoors.

"After the 2011 Tohoku earthquake, we sent 22 teams of doctors and nurses to Minamisanriku, a 9-hour drive from here," says Shimada. "I joined 124 people there to do everything we could to help."

As of April 2016, in response to the ongoing earthquakes in Kumamoto, "the University of Yamanashi was one of the quickest to provide aid," says Shimada. "Perhaps those human connections are ultimately what matter most."



Contact Website: www.yamanashi.ac.jp/en/

Excelling in fuel-cell research

Home to two world-leading, government-backed centres dedicated to green energy — the Fuel Cell Nanomaterials Center and the Clean Energy Research Center — the University of Yamanashi is spearheading the development of highperformance, low-cost fuel cells.

n the last decade, Japan's leading role in fuel-cell development has been strengthened by strategic government support for clean energy. For example, Japan's Fourth Strategic Energy Plan (2014) set out objectives for realizing large-scale market penetration of fuel cells. These ambitious undertakings, combined with Japan's strength in the automotive sector, have raised the bar for researchers developing next-generation fuelcell technologies.

Unique comprehensive approach

While many institutes around the world are racing to realize breakthroughs in fuel cells, none are quite like the Fuel Cell Nanomaterials Center at the University of Yamanashi.

"Our comprehensive approach sets us apart," says centre director, Akihiro liyama. "We are the largest institution in Japan to research and develop fuel-cell materials, including catalysts and electrolytes. Specifically, we are seeking to determine the mechanisms that control fuel cell performance and durability. To help us achieve that, we use industry-level performance evaluation technologies. While other institutes conduct research on catalysts or electrolytes, not many do both, and even fewer have such an array of evaluation facilities."

liyama observes that the centre's comprehensive approach has yet to be fully adopted in the USA, Europe or China.

"Covering materials research right through to evaluation — that's our great strength," he explains. "Based on this approach, our High-Performance Fuel Cell (HiPer-FC) Project has realized several successful outcomes." Launched in April 2008, the HiPer-FC Project was the impetus behind the establishment of the Fuel Cell Nanomaterials Center, and it led to advances in platinum-alloy catalysts and highly durable hydrocarbon electrolyte membranes.

"The successor to the HiPer-FC project is our new five-year Superlative, Stable and Scalable Performance Fuel Cells (SPer-FC) project, which began in May 2015 and is also funded by NEDO," says liyama.

The SPer-FC project's goals include developing 'SPer-materials' for catalysts (anode and cathode) and membranes and designing membrane-electrode assemblies — the basic unit of fuel cell operation — with improved durability and reliability, which will be critical for the successful commercialization of fuel cells.

In partnership with industry

Unlike fuel-cell development in the USA, that in Japan is predominantly industry driven, says liyama. "For example, Panasonic and Toshiba are the two major suppliers of the residential fuel-cell system called ENE-FARM. In the automotive



industry, Honda and Toyota are part of the Fuel Cell Commercialization Conference of Japan, which is promoting the development of fuel cells for industry."

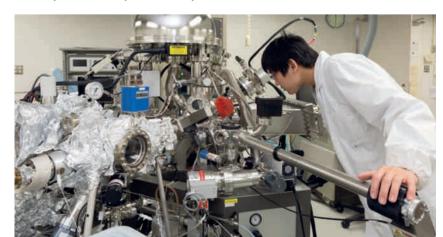
These efforts are steering towards Japan's goals of realizing a 'hydrogen society'. Iiyama says: "Electricity and heat are the two major secondary energy sources in Japan. Hydrogen, as a supplementary fuel, will become more significant. The cost of hydrogen is currently the biggest obstacle."

liyama believes that industry–academia collaborations are vital for enabling industry "to disclose technology road maps, supply information about actual usage conditions and propose appropriate evaluation tests." He comments: "We are happy to collaborate, particularly in the materials evaluation and analysis area, to better understand the mechanisms underlying fuel-cell phenomena."

Postdoctoral researchers interested in working at the centres are encouraged to explore this path. "We offer an excellent environment with the most advanced facilities," says liyama. "There are plenty of opportunities to gain research experience from basic science to applications at the industrial level."

Contact

Fuel Cell Nanomaterials Center Website: fc-nano.yamanashi.ac.jp/ english/ Clean Energy Research Center Website: www.clean.yamanashi. ac.jp/en/



Mastering the science of wine

The one-of-a-kind Institute of Enology and Viticulture at the University of Yamanashi is Japan's premier facility for wine research and education. By building on links with international wine organizations and working closely with local grape growers and wineries, the institute is advancing wine studies and wine-making technologies.

ounded in 1947, the Institute of Enology and Viticulture was originally a research centre for fermentation technologies. It was here that Nobel laureate Satoshi Ōmura first conducted his research on microorganisms in the early 1960s. Today, the institute specializes in wine research through projects on wine microbiology, genetic engineering and biochemical processes.

Researching wine making

"We have three laboratories and an experimental winery facility," explains Tohru Okuda, director of the institute.

"Researchers at the Laboratory of Wine Microbiology and Biotechnology collect wild yeasts and lactic bacteria for wine making," says Okuda. "The Laboratory of Fruit Genetic Engineering focuses on developing disease-resistant grapes without using chemicals. It is also developing new trellis systems for grapes, such as the Hayashi Smart System, which are designed to enhance productivity and increase labour efficiency. Finally, the Laboratory of Biofunctional Science, which is where I work, focuses on analysing wine components to discover how to enhance wine quality and taste. We use biochemical





methods to better understand the roles of tannin, anthocyanin and various enzymes."

Unusually, the institute is licensed by the government to produce alcoholic beverages for research purposes. Each year, the institute can produce up to 1,800 litres of fruit wine, 900 litres of fortified wine and 900 litres of brandy. Okuda says: "Although legal restrictions prevent us from selling the wines we produce ourselves, we collaborate with local wineries, such as Sapporo Wine's Katsunuma Winery and Chateau Mercian, to produce University of Yamanashi-branded wines."

Leading the way with education

Okuda explains that the institute also serves as an educational centre for students and those working in the industry: "This is why we recently decided to build an extension to our existing facilities, which will enable us to offer in-depth training programmes for wine specialists."

The institute runs the Wine Frontier Leader Training Program, which includes lectures by guest speakers from the Japan Sommelier Association, the Yamanashi Winery Union, Yamanashi Prefectural Government, design companies, the University of Bordeaux, the Australian Wine Research Institute and the University of California, Davis. About 70 alumni work as wine scientists, mostly in Japan.

Vital connections

Since 1984, the institute has served as the Japan Chapter of the American Society of Enology and Viticulture (ASEV). As chairperson of ASEV Japan, Okuda comments: "Our links with ASEV are very important. The relationship between the University of Yamanashi and University of California, Davis, is particularly strong. Also, learn-

ing from the success of wineries in California's Napa Valley has been highly valuable."

"In March 2016, we signed an agreement with Oenoviti International,

a large consortium managed by the University of Bordeaux in France," says Okuda. "It's important for us to continue widening our network and to be open to collaboration."

Okuda is also participating in a new project to help revive Fukushima. "We are trying to make a new wine-producing area in Fukushima. I planted some grape seedlings" he says. "We hope to make this new wine in time for the 2020 Tokyo Olympics."

Contact

The Institute of Enology and Viticulture Website: www.wine.yamanashi.ac.jp/ iev/E-IEV.html

Probing brain connectivity

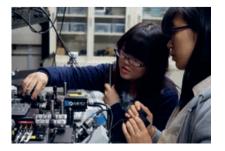
Collaborative projects led by the University of Yamanashi's Frontier Brain Science Project Team are breaking down the traditional barriers between pharmacology, biochemistry, physiology, medicine and engineering. As a result, the university is advancing both basic and clinical brain science.

growing body of evidence suggests that glial cells — the most common type of cell in the central nervous system — play a much more significant role in brain functions than previously thought. Rather than merely supporting neurons, glial cells are now credited for controlling key communication pathways. And as glial cell dysfunction has been linked with brain disorders such as Alzheimer's and Parkinson's diseases, more and more scientists are investigating the basis of glial cell activation as a way to develop new therapeutics.

Interdisciplinary studies of glial cells

Schuichi Koizumi, professor at the Department of Neuropharmacology, part of the Interdisciplinary Graduate School of Medicine and Engineering at the University of Yamanashi, says: "Our department was quick to recognize the potential of glial cells, which greatly outnumber neurons and may hold the key to uncovering brain connectivity. That's why our research focuses on glial cells."

Referring to the uniquely close links between the university's life sciences and engineering departments, Koizumi explains that joint projects are vital for achieving new discoveries.



"Interdisciplinary understanding is very important," he says. "All of our projects involve close interdepartmental cooperation. Working with project partners, including Toshihisa Ohtsuka of the Department of Biochemistry who focuses on active zone proteins and Kazuo Kitamura of the Department of Physiology who works on *in vivo* brain imaging, we can clarify each of the many layers of brain science, ranging from the molecular level to the whole-body level."

"Based on the central concept of seamless, cross-hierarchical and interdisciplinary research, our goal is to encourage *souhatsusei*, a Japanese word I love and that means developments based on synergistic effects," Koizumi explains. "In

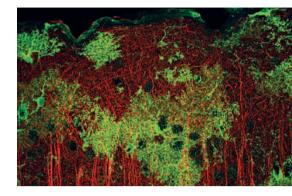
this way, our research can lead to unexpected achievements."

"Through collaborating with our colleagues in the Engineering Department, including Kiyoshi Kobayashi and Hirokazu Hori, we have obtained vastly improved images of the brain based on the newest advances in scanning probe microscopy," says Koizumi. In playful homage to super-resolved fluorescence microscopy, whose developers were awarded the 2014 Nobel Prize in Chemistry, Koizumi's team has tentatively named their new technique surprisingly resolved fluorescence microscopy.

Exploring glial cells' role in chronic pain

Most recently, Koizumi has collaborated with researchers in Japan (Junichi Nabekura of National Institute of Physiological Sciences), South Korea and Australia to investigate the root causes of





chronic pain. In experiments with mice, the researchers showed that astrocytes star-shaped glial cells — located in the sensory part of the brain are directly involved in the production of neuropathic pain.

They found that activating astrocytes in the primary somatosensory cortex led proteins called thrombospondins being released, which in turn gave rise to chronic pain. The study may provide valuable new clues for treating chronic pain.

"The significance of this finding is that glial cells — not neurons — are responsible for triggering chronic pain," explains Koizumi.

Koizumi encourages students interested in pursuing careers in neuroscience to consider the University of Yamanashi. "Our leading research on glial cells is expected to lead to the next breakthroughs in brain science and medicine," he says.

"This year, we also launched a new educational programme called the Frontier Brain Sciences Program, which officially begins in September 2016. Graduate students in this programme can attend international meetings and learn a lot of techniques from many different laboratories around the world."

Contact

Frontier of Brain Science Project Team E-mail: skoizumi@yamanashi.ac.jp Website: www.med.yamanashi.ac.jp/ clinical_basic/pharmaco/0-English/Ehome.html

A biotech centre with big ambitions

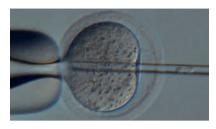
Cloning technologies have the potential to revolutionize our lives by advancing agricultural innovation and regenerative medicine and by boosting our understanding of long-extinct species. Those are some of the research areas being pursued at the University of Yamanashi's Advanced Biotechnology Center.

rom creating the world's first cloned mice to exploring the possibility of 'unlimited' cloning (that is, producing successive generations of clones from one donor), the ultimate goal of experiments devised by mouse-cloning expert Teruhiko Wakayama, a professor at the Advanced Biotechnology Center, is to do what nobody else has succeeded in doing before.

Freeze-dried sperm

Speaking at the laboratory he helped start at the University of Yamanashi, Wakayama reflects: "Technique is very important. One advantage of working at a relatively small university is that we can hone our techniques and focus on these niche fields. For example, nobody thought it would be possible to generate mice from freezedried sperm. Nobody had ever tried this before. We gave it a go and succeeded."

Wakayama and his team's work on freeze-dried sperm showed for the first time that it was possible to generate mice from freeze-dried sperm preserved at room temperature. "Compared with existing cryogenic technologies, the freezedried method is revolutionary, as there's



no need to use liquid nitrogen," explains Wakayama. "So the cost can be reduced and it's safer. But so far, we can preserve at room temperature for only a few months."

A real-life Jurassic Park?

Another breakthrough reported by Wakayama's team in 2008 was 'resurrecting' dead mice that had been frozen for 16 years to produce healthy cloned mice. This led to speculation that resurrecting the woolly mammoth and creating a real-life Jurassic Park might not be far off. "Although this is not possible now, it might become possible in the future," says Wakayama.

"Next, we will generate clones from taxidermied animals. We have already collected a nucleus from long-preserved fur. If the fur is in good condition, it may be possible to bring back extinct species."

Wakayama's ambitions do not end there. Through his 'space pup' experiment conducted in collaboration with the Japan Aerospace Exploration Agency, he is investigating the effects of space radiation and zero gravity on mouse germ cells. The first mice generated from space-preserved sperm were born in 2014.





And as of April 2016, Wakayama reached the 34th generation of mouse clones with no signs of genetic damage in his serial recloning experiments based on somatic cell nuclear transfer (SCNT).

Designer experimental facilities

Designing his own laboratory meant that Wakayama could minimize the distance between the mouse facilities and the micromanipulation room — a key consideration in SCNT experiments, as inefficiencies are rife. "Mouse embryos are tiny and very sensitive," says Wakayama. "So carrying them down a

long corridor can drastically reduce the survival rate. Here, the rooms are adjacent, which allows us to reduce the stress on the embryos."

"We have 17 micromanipulators designed in collaboration with Olympus. They're highly specialized and configured for mammalian embryo manipulation, which will enable experiments that have never been tried or even dreamt of."

Speaking about his long-term plans, Wakayama says: "My goal is to increase the success rate and to increase cloning efficiency. This is a very difficult challenge. I also plan to keep working on preservation experiments at room temperature."

"If you want to do these kinds of experiments and if you want to learn micromanipulation techniques, this is the best place in the world," he notes.

Contact

Advanced Biotechnology Center Website: www.ccn.yamanashi.ac.jp/ ~twakayama/LSHP/



Rich bounty around sacred Mount Fuji

Tourism, crafts and culture thrive alongside research and robotics at the foot and on the slopes of Mount Fuji

nown in Japan as the 'kingdom of fruits', Yamanashi is internationally recognized as an entry point to the spectacular Mount Fuji World Heritage Site. The 4,465-square-kilometre inland prefecture, a 90-minute train ride from Tokyo, is a nature lovers' delight.

Its biggest attraction — both in terms of size and number of visitors — is 3,776-metre-high Fuji-san, an active volcano and Japan's highest mountain, which has long been a place of worship and inspiration. In addition, Yamanashi boasts three national parks and one quasi-national park, as well as hot springs, lakes and vast swathes of forest, including Asia's largest white birch forest.

While many visitors are attracted by its traditional temples, culture and crafts, Yamanashi is also a robotics hub and home to the headquarters of FANUC Corporation, one of the world's leading electronics and mechatronics companies. Fuji-san — a world heritage attraction

Artists and poets have been celebrating the stark beauty of Mount Fuji for centuries. The declaration of Mount Fuji as a cultural World Heritage Site by UNESCO in 2013 has boosted tourism, according to Tatsushi Arai, head assistant director of the Department of Tourism. He says, "The number of foreign tourists lodging overnight in Yamanashi increased from around 387,000 in 2012 to 1,313,000 in 2015. These days, local trains to Mount Fuji (Fuji-Q Railway trains) are always packed with tourists from all over the world."

Arai says tourists are attracted by "the look of Mount Fuji in each season," including vistas of it with cherry blossoms around Fuji five lakes and the image of its peak blanketed by thick snow in winter.

"Roughly 200,000 to 300,000 climbers ascend the mountain during the summer climbing season." Many more tourists visit areas such as Fuji Five Lakes, Sengen shrines, the Sea of Trees, limestone caves, hot springs, museums and theme parks.

In the World Heritage list, the mountain is described as "Fuji-san — sacred place and source of inspiration". The volcano,



which last erupted in 1707, has inspired Japanese people's views of nature and has been reflected in art, poetry and religious belief. The tranquil scenes captured on cameras and smart phones today echo those in nineteenth-century prints by renowned artists such as Katsushika Hokusai and Utagawa Hiroshige. The iconic volcano has also been celebrated in classical works, notably the eighth-century Man'yoshu, as well as in haiku and prose.

Arai explains that until the end of the Edo period (1603–1867), very many whiterobed pilgrims ascended the sacred Mount Fuji in an act of worship called *Fujikou*. "Even today, many Japanese people worship Mount Fuji as a sacred mountain. They climb to the summit to watch the sun rise far away and cry 'Banzai!' in chorus." While there is a shrine on top of the peak, Arai considers Mount Fuji itself to be the most gigantic shrine in Japan.

Predicting future eruptions

There is a more sinister aspect to this volcano. Recently, volcanologists have warned of a build-up of magma pressure under the volcano. Climbers are advised to don helmets and goggles in case the volcano spews rocks.

Toshitsugu Fujii, director of the Mount Fuji Research Institute, says the volcano erupted more than 100 times in the past 3,000 years, suggesting an average eruption interval of about 30 years. "But we have not experienced any eruptions in the past 300 years. Such a long interval is ten times Mount Fuji's average dormancy, indicating the next eruption could occur at any time."

The institute acts as a base for research and field studies on the environment and volcanology of Mount Fuji. Research by the institute's 19 full-time scientists and visiting overseas researchers includes studies of the volcano's geology and geochemistry to clarify its precise eruption history. The researchers monitor groundwater levels, since changes are sometimes a precursor to volcanic eruption. The institute plays a key role in providing knowledge about the risks of future eruption to residents and disaster officials.

A professor emeritus at the University of Tokyo and chair of the Coordinating Committee for Prediction of Volcanic Eruptions, Fujii says it is difficult to predict when the next eruption will occur. The danger to people will depend on the mode and extent of the eruption. If there is a largescale explosive eruption, cities to the east of the mountain will be affected by ash fallout. "Even in Tokyo, located 100 kilometres from the mountain, we anticipate over a few centimetres of ash to accumulate."

Fujii expects that the institute's research results will help preserve Mount Fuji as a World Heritage Site. For example, its scientists have found over 24 invasive plant species, "which may wreak havoc on the ecological system in the Mount Fuji area." The researchers want to eliminate these aliens and restore the natural environment. **Our location:**

Located within two hours of the Tokyo metropolitan area, Yamanashi is easy to get to. During summer, trekkers and mountain climbers head to its nature trails and mountain slopes. As the weather cools, autumn sweeps across the prefecture, creating a stunning display of colours, which attract people from all over Japan. The autumn leaves are just one of Yamanashi's more resplendent seasonal attractions; each season brings its own unique landscapes, which enchant the eyes and heart.

From robots to lacquered leather

There is a very different focus at FANUC Corporation's headquarters and research laboratories in Oshino-mura at the foot of Mount Fuji. Here, production lines of lemon-coloured intelligent robots manufacture products such as carbon dioxide laser oscillators and servo motors. Among FANUC's latest products is a long-armed robot machine with the world's largest payload capacity. It can easily lift and manoeuvre heavy objects, such as car bodies, which previously could have been picked up only by cranes. The company has more than 200 offices in 46 countries. About 64,000 people are engaged in producing industrial robots and about 14% of the prefectural income is earned by this industry.

Some of Yamanashi's most distinctive products are based on traditional crafts. For example, production of distinctive Koshu fabrics dates back to 1633. The development of wrinkled, Siwa paper used to make everything from slippers to bags — arose out of a millennium-old tradition of hand-made *washi* paper.

Kofu city in Yamanashi is an internationally known centre of gem-stone cutting and jewellery production, and produces more than a quarter of Japan's jewellery exports. Another product unique to Yamanashi is *inden*, which involves printing intricate lacquer designs on deerskin leather used to produce bags, belts and purses.

Bounty of fruit and wine

Other important industries in Yamanashi include forestry, agriculture, and food

and wine production. The prefecture is Japan's leading producer of peaches, plums, grapes and other fruits. Arai says: "The quality, size and appearance of those fruits are so outstanding that they attract people from all over the world, and they sell at traditional and luxurious fruit shops, like Ginza Sembikiya, which was founded in 1894, in Tokyo."

With more than 80 wineries, Yamanashi produces 30% of Japan's wines, many from native koshu grapes. In 2014, the Cuvée Misawa Akeno Koshu from Grace Winery won the gold medal in the 2014 Decanter World Wine Awards.

Thus, Yamanashi prefecture truly lives up to its reputation as a kingdom of fruit, bearing both literal and metaphorical fruit.



Contacts

Yamanashi Prefecture E-mail:kokusai@pref.yamanashi.lg.jp Tel: +81 55 223 1620 Website:

www.pref.yamanashi.jp/english

Mount Fuji Research Institute Yamanashi Prefectural Government E-mail:kouryu@mfri.pref.yamanashi.jp Tel: +81 555 72 6206 Website:www.mfri.pref.yamanashi.jp