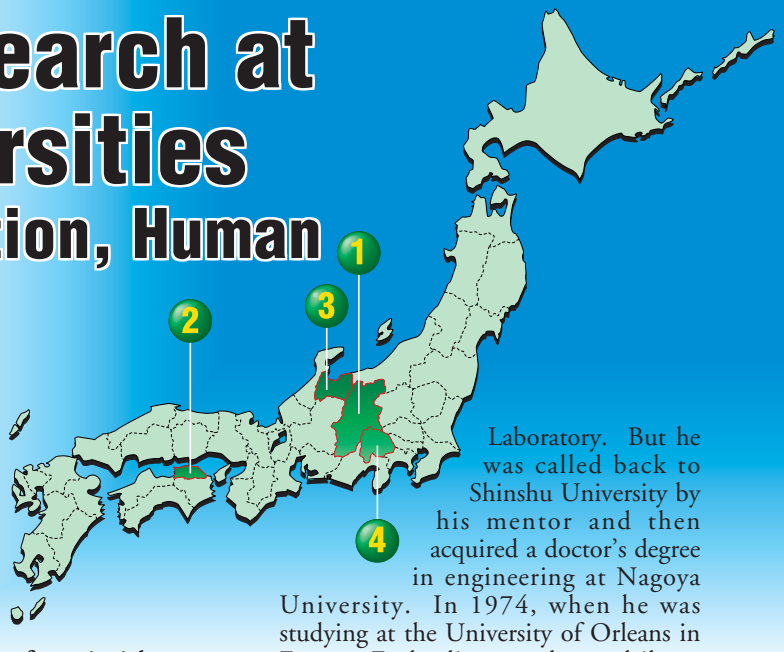
World-class Research at Provincial Universities

Contributing to Innovation, Human Resource Development

By Satoru MATSUDA



WHILE the fast progress of economic globalization is reducing the barriers of national boundaries, gaps between Tokyo and provincial areas are narrowing in Japan thanks to an improvement in the transportation network and rapid development of information technology (IT). Universities are competing for intellectual accumulation, and prominent researchers tend to gather at prestigious and big-name schools in major urban areas. On the other hand, there are some researchers who make it their mission to meet the needs of provincial areas or seek to carry on research that can only be done in those areas.

The Ministry of Education, Culture, Sports, Science and Technology (MEXT) launched a "Knowledge Cluster" creation project in fiscal 2002 as part of its efforts to help innovation in provincial areas. The project involves local governments, provincial universities and local business corporations. MEXT launched another project in fiscal 2006 to support local strongholds designed to develop human resources and help revitalize provincial areas. From among the MEXT-backed projects, this article will introduce unique researchers at provincial universities who have achieved world-class research results.

From Silk Culture to Electronics, Nanotechnology

1 The most successful in the Knowledge Cluster project is Nagano Prefecture which is full of clean air and water at the foot of the Japan Alps. In the central Japan prefecture, researchers are making efforts to promote R&D and industrialize carbon nanotubes and carbon nanofiber, which is thicker than nanotubes. Both are regarded as leading nanotechnological materials that are expected to provide the next generation of industrial infrastructure on a global scale. The key player is Morinobu Endo, 61, a professor at Shinshu University, who has developed technology to mass-produce carbon nanofiber, called the "Endo Fiber." *(Photo 1)*

The Endo Fiber is widely used for lithium-ion cells for mobile phone handsets and laptop computers. Work is currently under way to use the fiber, which is light in weight, strong and heat-resistant, for capacitors that would replace lead batteries and also for advanced composite materials on a commercial basis.

Endo was born and raised in the city of Suzaka, Nagano Prefecture, whose mainstay industry rapidly changed from silk culture and yarn making to electronic equipment after World War II. "Factories where silkworm cocoons used to be boiled to make yarn collapsed and, instead, clean, glassed-in plants were built one after another where ladies in white worked," Endo says. "Also came highly educated engineers. Nice houses replaced mulberry fields in a very short term. Shocked at the change in my childhood, I decided to become an engineer."

After completing studies at Shinshu University's graduate school of engineering, he joined Hitachi Ltd., which he had long admired. He was scheduled to launch development of semiconductor technology at Hitachi's Central Research Laboratory. But he was called back to Shinshu University by his mentor and then acquired a doctor's degree in engineering at Nagoya University. In 1974, when he was studying at the University of Orleans in France, Endo discovered a multilayer and tubular carbon molecule, which was later named carbon nanotube by Sumio Iijima, a senior research fellow at NEC Corp. and also a professor at Meijo University. After returning to Japan in 1976, he began to produce the Endo Fiber. But at the time it cost ¥500,000 to produce 1 kilogram of the fiber, which was too high compared with ¥10,000 for ordinary carbon fiber.

"I took the fiber to the National Aeronautics and Space Administration (NASA) and Bell Laboratories," says Endo. "They gave high marks to the fiber but turned me away, saying its cost was too high. It was interesting scientifically but not technologically." Following 10 years of hardship, he developed a new production process in the middle of the 1980s and reduced the production cost

Photo 1 Photo: Satoru Matsuda

Prof. Morinobu Endo, the developer of technology to mass-produce carbon nanofiber, sits with a prototype engine starter that has replaced the conventional lead battery with a carbon nanofiber capacitor.

to tens of hundreds of yen per kilogram. Showa Denko K.K. mass-produced the fiber on a commercial basis.

An Attraction Is Nagano People's Creative Mentality

"There are four peaks for technological development," Endo says. "The first one is the peak of science. This means whether results of an experiment can be repeated or not. The second one is the peak of technology. It is how to industrialize. The third one is the peak of the economy. This questions the social value of a product – how to use the product and how much users would pay to purchase. And the fourth one that has appeared recently is the peak of society. Any product needs to avoid risks to the environment and the human body and to win social recognition."

After being successful in cutting production costs, Endo was invited to assume a professorship at a prestigious state-run university that is one of Japan's seven former imperial universities. But he declined the offer, recalling his mentor at Nagoya University who had urged him to contribute to Nagano Prefecture. A number of factories producing precision instruments and electronic products such as watches and cameras are concentrated in Nagano Prefecture. "What is most attractive of Nagano people is that they have creative mentality. They also love to argue," Endo says. "In a debate, they would certainly say, 'Yes, but…,' and would not easily accept the other's argument. This is their fundamental phrase of creativity."

From Sugar for Japanese Sweets to Rare Sugar

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Kagawa Prefecture is located along the Inland Sea on Japan's smallest main island Shikoku. Its farmers have grown sugarcane since the days of the Edo period (1603-1867) when the territory was ruled by the Takamatsu clan. A variety of sugar called *Wasanbon,* mainly used for Japanese sweets, was Kagawa's specialty product. Led by Ken Izumori, 64, a professor and head of the Kagawa University Rare Sugar Research Center, Kagawa Prefecture's Knowledge Cluster project continued for five years through fiscal 2006 for R&D and industrialization of monosaccharide, or rare sugar, that is rarely found in nature.

The structure of monosaccharide is simple compared with that of polysaccharides such as starch. There are about 50 species of rare sugar. No research had been done on rare sugar for a long time. But rare sugar has drawn attention since a kind of sugar alcohol, called xylitol, was developed in Finland. Hydrogen was added to xylose, a kind of monosaccharide, to make xylitol, which tastes as sweet as sugar but decreases the risk of dental decay. It has come to be used as a sweetener for chewing gum and toothpaste. Rare sugar is currently believed to be potentially useful for medicine, food, cosmetics and agrichemicals.

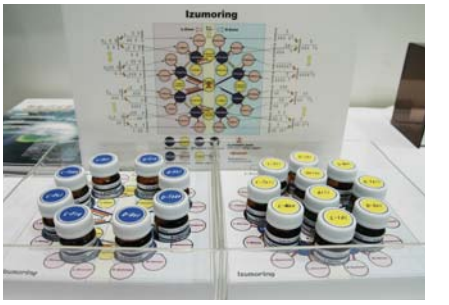
It is Izumori who has continued to study rare sugar since the 1970s. He is known as a world-class authority in that field. Kagawa University has the sole rare sugar research center in the world that is also the headquarters of the International Society of Rare Sugars.

New Enzyme Found from Hill behind Campus

Izumori seized the chance of pushing ahead his studies around 1991 when a microorganism was found from a clump of soil that a student of the Faculty of Agriculture collected from a hill behind a cafeteria on the university campus. Discovery of a new enzyme, called D-tagatose 3-epimerase (DTE), which is produced by the microorganism, has made it possible to process fructose into rare sugar such as D-psicose. Izumori has built up a conceptual tree called an *Izumoring,* which systematically illustrates ring-form structures of a variety of rare sugar species, their monocular mechanisms and synthetic enzymes. Fushimi Pharmaceutical Co., which is headquartered in the city of Marugame, Kagawa Prefecture, has begun selling test reagents made from each species of rare sugar, based on the results of those studies. *(Photo 2)*

Kagawa University, which merged with Kagawa Medical University in 2003, has achieved progress in the field of analytical studies of physiologic functions of rare sugar. Animal experiments

Photo 2 Photo: Satoru Matsuda



Reagents of rare sugar based on "Izumoring," made and sold by Fushimi Pharmaceutical Co.

have showed that a kind of rare sugar, called D-allose, functions to protect cells in the event of blood shortage in the brain, heart and liver. It also has been found to have anti-cancer functions. D-psicose has been found to have functions to promote insulin secretion by the pancreas and to prevent arterial sclerosis. Drug makers have come to purchase test reagents made of each species of rare sugar. Mass production is expected if they are successful in commercialization.

After graduating from the Faculty of Agriculture of Kagawa University, Izumori completed a master's course at Osaka Prefectural University's graduate school of agriculture. He was called back by his mentor to Kagawa University. He is currently conducting joint research with George W. Fleet, a professor at Oxford University in Britain, on a new *Izumoring* that would systematize a bigger number of rare sugar species. He says he has felt none of the handicap that often harasses researchers at a provincial university. In fact, he says, "There are areas of research that can only be done in provincial areas or that cannot be done if there is too much research funding."

Izumori goes on to say, "When you go on a pilgrimage to the 88 holy sites in Shikoku, you will take taxis and stay at comfortable hotels if you have sufficient money. But if you have no money to do so, you need to walk to visit the holy places, you will be impressed with nature, and you may make many friends at inexpensive lodgings. This means there still remain matters in the field of natural science that have to be discovered with research done at a walking pace."

Izumori has been keen to help promote science education in high schools. With the help of the local board of education, he renovated a closed school-

Photo 3 Photo: Satoru Matsuda

Prof. Ken Izumori, keen to help promote science education in high schools, teaches students at a practical workshop on rare sugar.

house in the town of Miki, Kagawa Prefecture, into a learning center on rare sugar research that opened in October 2007. In December that year, he invited some 30 students and teachers from high schools to three days and two nights of a practical workshop on rare sugar and advanced biotechnology. *(Photo 3)* The participants' schools, designated as "super science high schools" by MEXT, are promoting advanced science education.

Jena, the Birthplace of Carl Zeiss, Is the Model

3

Professors Endo and Izumori have played key roles in directly promoting innovation in provincial areas. There is another example of excellent management capabilities that have changed an area through the cooperation of medical science and engineering technology. It is Dr. Yasuo Nannichi, now 74, a professor emeritus at the University of Tsukuba, who advises the Toyama New Industry Organization (TONIO) of Toyama Prefecture. Toyama, which faces the Sea of Japan, is known for its agriculture and fishery as well as industrial activities. It is called one of the most livable areas in Japan, mainly because of comparably spacious housing conditions. Toyama's per capita floor space is the largest among Japan's 47 prefectures. Meanwhile, Toyama has been famous as a pharmaceutical center for three centuries, dating back to the Edo period. Today, there are about 300 business offices related to drugs in Toyama. However, Toyama's drug sales have gone downhill over the last century.

Nannichi worked on R&D of semiconductor lasers at NEC. After moving to the University of Tsukuba, he initiated a campaign to invite Leona Esaki, a Nobel laureate and the inventor of the Esaki Diode, as the university's president. He believes Ezaki's appointment served as a starting point to revitalize Japanese academia.

On his retirement from the university, Nannichi was asked to be a senior advisor to the Toyama Technology Foundation, a predecessor to TONIO. He was also appointed as the director of the Toyama Industrial Technology Center (TITC). Then, the TITC had no section on semiconductor processing. The Ministry of International Trade and Industries (currently the Ministry of Economy, Trade and Industry, or METI) provided financial support to the TITC to set up the section. The question was whether the setup would be effectively utilized or not. With researchers having no specialized backgrounds in semiconductors but having courage to start a new project, an able group was organized.

Ideas were sought after for the TITC's application for MEXT's big Knowledge Cluster project. As a core of the application, it was decided to deal with the handling of single cells for biomedical treatment, which was proposed by Atsushi Muraguchi, a professor of immunology at the University of Toyama, and Eiichi Tamiya, a professor of biosensor technology at the Japan Advanced Institute of Science and Technology (currently professor at the University of Osaka).

Though lacking any specific data, the proposal was, fortunately, accepted as a temporary mini-project. As a first step, Nannichi decided to conduct R&D on biochips that are capable of sorting out lymphocytic cells that will react to specific viruses and microorganisms. With dedicated work by TITC members, necessary data were accumulated quickly. The research on the basic biochip, a silicon chip with a quarter of a million holes of about 10 microns in diameter, was successful. In the following season, the Toyama cluster project was formally and fully accepted.

Medical people ask constantly for the modification of chips. Usually, new chips have been supplied by the next

Photo 4 Photo: Satoru Matsuda

Yasuo Nannichi, professor emeritus at the University of Tsukuba, stands with a cell-picking machine trade-named "Cellporter" he has helped develop.

morning. Furthermore, R&D efforts for the cluster project led to the creation of new industries in Toyama. Sugino Machine Ltd. of Uozu city has developed a cell-picking machine, trade-named Cellporter. And Richell Corp. of Toyama city has produced plastics microchips. This was a rare story of success of very close cooperation between physiological science and semiconductor-processing technology.

Nannichi patterned the provincial development model after Jena in the former East Germany, the birthplace of Carl Zeiss, the world's leading optical equipment supplier. He utilized support both by MEXT and METI. But he most appreciates the courage of TITC members, who plunged into deep water when they started R&D in a new technology area they had been unfamiliar with. "Without their decision (and a bit of luck), there is no cluster project of today," he says. *(Photo 4)*

Raising World-class 'Bachelors of Wine Science'

4

There is a unique researcher who is developing human resources. He is Michikatsu Sato, 59, a specially appointed professor at the University of Yamanashi in charge of the university's Institute of Enology and Viticulture, an organization under the university's Graduate School of Medicine and Engineering. The institute has a "Base for Lifelong Development of Human Resources for Wine" established in 2006 as part of MEXT's project aimed at backing local strongholds that will develop human resources and help jump-start provincial

areas. Sato formerly headed the Wines and Spirits Institute of Mercian Corp.

Yamanashi Prefecture, which is close to Tokyo and to the north of Mt. Fuji, is the birthplace of Japanese wine and ranks at the top in Japan in terms of grape and wine production. But grape growers are graying and face difficulties in finding successors. On the other hand, winemakers face tough competition from imports.

The base for raising wine-related personnel opens a comprehensive wine education course for about 10 graduate students and young wine-brewing experts every year that is comparable to those of the University of Bordeaux and the University of Bourgogne, both in France, and the University of California, Davis, in the United States. It plans to award a "bachelor's degree in the science of wine" to those who have passed end-of-course exams.

Sato: Developer of Big Hits

Sato is known as Japan's top researcher on wine polyphenol. He is a review board member of the *Journal of Agricultural and Food Chemistry* published by the American Chemical Society. He has achieved a wide range of R&D results.

While serving at Mercian, Sato developed an antibiotic agent, josamycin, which is effective against colds in their early stages. He then devised a technique to confine volatile aromatic components in a cyclic oligosaccharide, cyclodextrin. Pungent components contained in spices such as *wasabi,* mustard and ginger are volatile. An addition of the cyclodextrin element to these spices confines these pungent components in the center of a donut-shaped molecule. This substance has helped tubes of *wasabi* to be widely used at home.

In the field of alcoholic beverages, he was also successful in making canned cocktails a big hit. He was swift to launch studies on functions of polyphenol in the early 1990s after US media reported that an epidemiologic survey showed that red wine is effective to prevent heart diseases. He paid particular attention to a polyphenol substance called resveratrol and used it to develop a supplement as well as a brand of red wine containing twice as much polyphenol as ordinary red wine, which sold very well and ran out of stock at one time.

Meanwhile, engineers from Mercian, Suntory Ltd. and Kikkoman Corp. (the maker of Manns Wine brands), and researchers from Kyoto University and the University of Bordeaux serve as lecturers at the base, rasing wine-related personnel. Sato's large circle of acquaintances helped the institute collect its teaching staff. "There is a large gap between major and minor wineries," Sato says. "Major producers can send their engineers for studies abroad. But smaller ones cannot. This institute needs to provide an international level of education and raise the level of Yamanashi wines."

Boosting Yamanashi Brands to Global Stage

The Institute of Enology and Viticulture has three laboratories – fruit genetic engineering, wine microbiology, and grape/wine biofunctional science. The institute serves as the secretariat of the Japan chapter of the American Society for Enology and Viticulture (ASEV), and has played a leading role in the R&D field.

The head of the institute is Tsutomu Takayanagi, a professor at the University of Yamanashi. Before assuming the professorship, Takayanagi was involved in medical R&D at Meiji Dairies Corp. Then, he brought in biotechnology on a full scale to grape/wine studies at the university.

Grapes usually emit a distinctive aroma when they are getting ripe, sending a message to growers to tell them when to pick them. But some species of grapes emit only a weak aroma. Takayanagi is currently working on means of finding an aroma precursor to correctly forecast the right picking season.

He is also conducting research on DNA and RNA analyses of molds and viruses that may damage grapevines, and on natural microorganisms that may be effective to weaken harmful bacteria and thus replace agrochemicals.

The institute has also produced a range of results. Among them is one achieved by a team led by Fujitoshi Yanagida, an associate professor who used "marine yeast" collected from the ocean to make wine. Sapporo Breweries Ltd. has used this technology to develop a new Sapporo Wine brand on a commercial basis.

"I'd like to establish Yamanashi's brands both at home and abroad using the prefectural products, including the Koshu-brand white wine," Takayanagi says. *(Photo 5)*

Photo 5 Photo: Satoru Matsuda

Specially appointed professor Michikatsu Sato at the University of Yamanashi stands with a bottle of "Yamanashi Koshu 2006" wine made from marine yeast. In the background is a selection of university-brand wines.

"Create Star Researchers from Provincial Areas"

Under the Knowledge Cluster creation project, MEXT will give 18 designated areas subsidies of about ¥500 million per area annually for five years in the first stage. In the second phase starting in fiscal 2007, MEXT will provide six designated areas with ¥500 million–¥1 billion per area for five years. Referring to what provincial universities should look like, MEXT science and academic affairs official Koji Saeki, who is in charge of the project, says: "There still are academic supremacists who assess researchers only with their articles. But we need to appreciate researchers' contributions to regional communities and society as a whole and to help establish star researchers." JS

Satoru Matsuda is a reporter for the Science Section, Jiji Press.