# Innovation in Japan

## Results from Reforms

Japanese academic reforms over the last decade have encouraged entrepreneurship and technology transfer from universities to industry. These reforms are now yielding results. Science and business leaders hope these changes push Japan into the next phase of innovation development, with increased flexibility and transparency, a more global focus, and more national and international collaboration. Japanese scientists are ready. After delays caused by the March 2011 triple disaster of earthquake, tsunami, and nuclear power plant failure, the lights are on again in Japanese research laboratories. Although recovery and reconstruction are priorities, the long-term goals of developing sustainable energy sources and solving the health challenges of an aging population continue to be major focus areas. **By Chris Tachibana**

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The Japanese government wants practical, globally useful applications from its science programs, and the sooner the better. "We intend to have societal or economic impact more clearly and more quickly—that is our aim," says Michiharu Nakamura, president of the **Japan Science and Technology Agency** (**JST**), an independent organization within the **Ministry of Education, Culture, Sports, Science and Technology** (**MEXT**). "We're trying to find new capabilities from basic research as soon as possible, and transfer technology sooner."

Using science and technology to address societal challenges is the theme of the Fourth Basic Plan for Science and Technology, a roadmap for Japanese science in 2011–2015 from Japan's Council on Science and Technology Policy. The plan was passed by the Japanese cabinet in August 2011 after revisions to include reconstruction and recovery strategies for the March 2011 earthquake and its consequences. However, a core focus on addressing the need for sustainable energy and the medical issues of an aging population remains unchanged. The sense that science and technology could drive a return to global economic competitiveness is clear.

"Japan is moving toward exploiting innovations more efficiently, and the earthquake is not going to stop that," says Richard B. Dasher. He is director of the **Stanford University US-Asia Technology Management Center** and knows both Japan and earthquakes. He was the first non-Japanese person in senior university governance, at Tohoku University, and remembers the decade of rebuilding at Stanford after the 1989 Loma Prieta earthquake. Dasher says true innovation means bringing an idea into real-world practice, but turning a research breakthrough into a global application requires the combined efforts of industry and university research, typically funded by the government. However, after World War II, Japanese universities and industry had an aloof relationship. Industry researchers maintained personal contacts with their former university mentors, but professors were civil employees, which limited their entrepreneurial possibilities and hindered technology transfer. Until recently, funding for academics and industry was siloed in separate government agencies, MEXT and the Ministry of Economy, Trade and Industry (METI). However, a 1998 law created technology-licensing organizations—essentially technology transfer departments—to move basic research results into applications. In 2004, a change in intellectual property law freed professors to start companies. Educational and research institutions, industry, and government are still adjusting, but Dasher believes Japan is on the brink of a more mature phase in innovation development, saying, "It feels like a glacier about to calve: you can see the cracks and splits and see it is just about to go."

### THE NEW INNOVATION MODELS

Satoshi Kawata is a professor at **Osaka University** and director of the Photonics Advanced Research Center, and a chief scientist at **RIKEN,** a MEXT research institute. He took advantage of the new laws to found **Nanophoton,** with 13 full-time employees, including eight Ph.D.s. Nanophoton produces laser Raman microscopes, which generate images based on energy shifts that occur in laser photons when they interact with molecular bonds. The technique identifies molecules based on distinct laser-scattering patterns and creates images of biological continued>



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samples that show both structure and molecular composition. Nanophoton's microscopes are used in pharmaceutical research to study small molecules and in materials science to analyze polymers and semiconductors.

A recent collaboration with Mikiko Sodeoka, chief scientist and director of the Synthetic Organic Chemistry Laboratory, RIKEN Advanced Science Institute, and director of the JST ERATO Live Cell Chemistry Project shows the technique's potential. In a 2011 *Journal of the American Chemical Society* article, the group showed that an alkyne—just two carbon atoms in a triple bond—acted as a Raman tag. The alkyne could replace bulky fluorescent tags or proteins currently used for imaging, whose large size can change the properties, localization, and function of smaller biomolecules. "We looked for a method using a tiny tag that does not affect the biological profile of the small molecule," says Sodeoka. "We had the idea that we could detect the alkyne directly by Raman microscopy." Putting an alkyne on a nucleotide analog allowed visualization of chromosomes in unfixed, unstained living cells without interference from untagged endogenous proteins and other biomolecules. Sodeoka says the ultimate goal is real-time continuous imaging, for example for detecting transient interactions between receptors and ligands.

Policy changes that encouraged professors to commercialize innovations are the reason his company exists, says Kawata, adding that he wants Nanophoton "to be an example of success." Nanophoton, which rents space on campus, gives students hands-on entrepreneurial experience. "Students are happy to earn money here doing development, English translation, and product assembly rather than working at McDonald's, because they learn things about running a company," says Kawata.

In contrast to Nanophoton's nano-sized innovation model is a collaboration between electronics and communications giant **Fujitsu** and the **University of Tokyo's Research Center for Advanced Science and Technology** (**RCAST**). Their drug discovery project shows how the resources of a large industry partner can be applied to basic research. Drug discovery begins with a target protein that might be regulated through small molecule binding. For example, statin drugs bind and inhibit an enzyme in cholesterol production to lower blood cholesterol. Traditionally, small molecule drugs are found by wet-lab screening of chemical libraries for compounds that bind and regulate the target. This can be a hit-or-miss process that takes years. Sophisticated computer simulations can design molecules that interact with the target, accelerating this process and expanding candidate possibilities. However, they require tremendous computer power. In 2004, Fujitsu began efforts in information technology (IT)-based drug development, based on 20 years of creating computational chemistry software. In 2010, a supercomputer for IT-based drug discovery was built at RCAST.

The project is funded by Fujitsu, and its goals, says Shunji Matsumoto of the Fujitsu Bio-IT Business Development Unit, are "building the platform, training our team, and getting highly available compounds as drug candidates." Fujitsu will have the intellectual property license for potential drug candidates. Matsumoto says that IT-based drug design requires supercomputer power because even highly specific compound-target interactions can be transient, dissociating in nanoseconds, and are complicated by the water-based physiological environment. The Fujitsu-RCAST supercomputer overcomes these challenges by rapidly modeling thousands of compounds in various bound and unbound states to find the most promising candidates. The first targets of the project are in diabetes and cancer.

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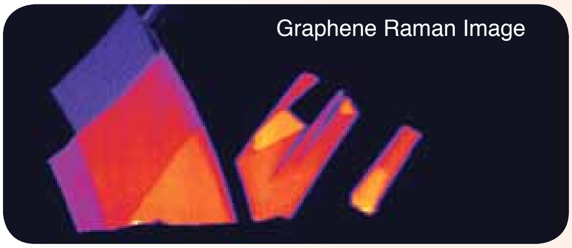


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Academic-industry relationships are not new in Japan, although the old-school style is a professor handing off a basic research idea to a company. The new model, encouraged by JST and other funding agencies, is much more collaborative. An example is the AK project between **Astellas Pharma** and **Kyoto University,** started in 2007 and funded by MEXT and Astellas. The budget was 600 million yen ($7.8 million) in the first three years, with 4 of 10 initial projects selected to continue with 1,400 million yen in support annually. Although Kyoto University's most famous discovery might be the 2006 publication of induced pluripotent stem (iPS) cells, immunology and antibody therapy have long been a research focus in Japan, particularly at Kyoto University. The AK project builds on this tradition. After just three years, the project had discovered 14 potential drug targets in B cell development, immune tolerance, and atopic dermatitis, and filed 18 patent applications.

Shuh Narumiya, professor of pharmacology and director of the Medical Innovation Center and the AK Project, Kyoto University Graduate School of Medicine, says that in addition to seeking scientific innovations, the project employs a novel research strategy for Japan, giving young investigators autonomy to try a variety of approaches. From the company side, the level of integration with the university is unusually extensive, says Toichi Takenaka, professor, Graduate School of Pharmaceutical Sciences, Chemical Biology, University of Tokyo, and Astellas Pharma president and board chair until his retirement in 2011. "The AK project has its own research laboratories on the medical school campus, with basic research scientists from the university and drug discovery scientists from Astellas working with clinical research scientists from clinical departments," says Takenaka. He says advantages of the collaboration are fast decision-making, a focus on the most important projects, an uninterrupted pipeline from target discovery to drug development, and productive management of intellectual property.

## FIGHTING CHERRY PICKING AND THE GALAPAGOS EFFECT

A problem with exclusive company-university partnerships such as the AK project or the Fujitsu-RCAST collaboration is that potential innovations are controlled by a single continued>

## FEATURED PARTICIPANTS

**Astellas Pharma**
www.astellas.us

**Fujitsu**
www.fujitsu.com/global

**Japan External Trade Organization (JETRO)**
www.jetro.org

**Japan Science and Technology Agency**
www.jst.go.jp/EN/index.html

**Japan Society for the Promotion of Science**
www.jsps.go.jp/english/index.html

**Kyoto University**
www.kyoto-u.ac.jp/en

**Ministry of Education, Culture, Sports, Science and Technology (MEXT)**
www.mext.go.jp/english

**Nanophoton**
www.nanophoton.jp/eng/index.html

**Osaka University**
www.osaka-u.ac.jp/en

**RCAST, University of Tokyo**
www.rcast.u-tokyo.ac.jp/en

**RIKEN**
www.riken.jp/engn/index.html

**Sharp Solar**
www.sharpusa.com/SolarElectricity.aspx

**Smart Solar International**
www.smart-solar-inc.com

**Stanford US-Asia Technology Management Center**
www.asia.stanford.edu

company, which might develop only a few, rather than the range of applications possible from basic research, says Robert Kneller of RCAST, who has written extensively on this issue. Although Narumiya says the AK project allows outside licensing of intellectual property that Astellas is not interested in developing, Kneller says that exclusive partnerships tend to cut projects that don't show tangible results early, hindering blue-sky research that takes longer to develop. The arrangement results in cherry picking of a few ideas by industry. "Big companies might develop one aspect of a discovery, but not the full panoply of applications, and discoveries can get lost," says Kneller. Another issue in Japanese innovation is the Galapagos effect: discoveries are often adapted only for the island nation of 127 million people. Those that are successful globally—for example in electronics—are useful to other countries incidentally rather than by design.

Technology analysts think that both the limitations of exclusive partnerships and the Galapagos effect can be overcome if Japanese research and development embraces openness and flexibility. Changing the old attitudes and infrastructure might increase the productivity and efficiency of innovation development. Examples include encouraging job market mobility, foreign exchange programs, expanded interdisciplinary and international collaborations, and education in global entrepreneurial thinking.

A global technology field with a natural opening for Japan is photovoltaic cells, the units of solar panels that convert light energy into electricity. Renewable energy is needed worldwide and Japan has strengths in materials science and a commitment to green technology, with government support for sustainable energy development since the 1970s. More recently, the **Japan Society for the Promotion of Science,** an independent organization under MEXT that promotes scientific programs, gave $40 million through its $1.5 billion Funding Program for World-Leading Innovative R&D on Science and Technology (FIRST) program to Hiroshi Segawa of RCAST for a project on photovoltaics that use organic molecules and polymers as light-absorbing components. These have a high capacity to absorb light, although they are currently less stable and less efficient than inorganic materials such as silicon.

Organic photovolatics may or may not be the future, but solar energy remains a high priority in Japan, says Toshiro Matsuyama, who was the manager, Corporate Advanced Technology Planning Corporate Research and Development Group at **Sharp.** "We have many good engineers working on photovoltaics. And people are even more concerned about energy after the Fukushima nuclear power plant disaster." Matsuyama is currently technical advisor at **Smart Solar,** a three-year-old spin-off company from the University of Tokyo that is developing concentrated photovoltaic systems that convert optically concentrated solar light to electricity. Current solar energy systems tend to be made for huge spaces like U.S. deserts, or on a small scale, for Japanese rooftops. However, solar panels are a scalable technology, so Japanese advances can be applied to big systems. Japan could also lead in developing sophisticated, application-specific systems to optimize solar power use, says Matsuyama, because "extending the power from a rooftop to a household, or from a desert to a city is different. This is the direction solar is going, partly in developing materials, partly in how you use the power." Matsuyama says he hopes the next innovations come from Japan. The country has large corporations with a history of spending for decades, if necessary, to develop new technology, he says, citing Sharp's 30-year development of liquid-crystal display (LCD) television, starting with applying the technology to small-screen electronics.

### TRANSFORMATIONS LEADING TO THE NEXT INNOVATION PHASE

The push to redefine industry-academic partnerships and increase technology transfer comes as the labor market is transforming. Unlike previous generations, young people no longer expect lifetime employment at a single institution. As Japan's population ages, the number of immigrant students and workers is expected to rise, which could add diversity and new ideas to research and corporate teams. This feels unsettling, but is ultimately beneficial, says Stanford's Dasher, who thinks research and development in Japan "has been a little too stable. We should see changes over the next 10 to 20 years as pressure for these changes is applied."

For those seeking calm after the 2011 disasters though, Kenichi Kawamoto, executive director of the **Japanese External Trade Organization** (**JETRO**) New York has a reassuring message. "The earthquake was a tragic event," he says, "but I'm proud of the Japanese people for recovering quickly. It shows that they should be confident that they can make a contribution to the global market and society." The earthquake itself might have created the path for these contributions. Says JST's Nakamura, "We received very warm sympathy and support from other countries. We will never forget that support."

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