Profile of Kazuo Shinozaki

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Plant molecular biologist Kazuo Shinozaki found the spark of scientific inspiration in a Nobel Prize in physics. Shinozaki's interest in science was triggered by Sin-Itiro Tomonaga winning the Nobel Prize in Physics in 1965, along with Richard Feynman and Julian Schwinger. "I was especially interested in quantum physics as a way to understand the universe, and Professor Tomonaga became kind of a hero for me, so I decided to become a scientist during my senior high school," says Shinozaki.

As Shinozaki explored physics, he chanced upon physicist Erwin Schrodinger's book, What is Life? and became enthralled by molecular biology. "I was very interested in understanding life at the molecular level, and I became interested in protein function as a way to understand what life is," he says.

So, Shinozaki decided to join Osaka University's Institute of Protein Research for undergraduate studies in biology. To learn molecular biology, he seized an opportunity to work in renowned molecular biologist Reiji Okazaki's laboratory during his graduate studies in Nagoya University. "He was known for discovering the small Okazaki fragment in DNA elongation," says Shinozaki. "I realized that DNA is much, much more interesting," he says.

Shinozaki continued to work on plant DNA throughout his career, deciphering gene regulation in plants and discovering important genes and factors involved in plant responses to environmental stresses, such as drought and cold. He often harnessed cutting-edge technology, which led to significant achievements, including the first whole-genome sequence of the tobacco chloroplast and a large-scale functional genomics project using Arabidopsis. In his Inaugural Article, Shinozaki describes some of his recent efforts to elucidate the unfolded protein response in plant stress responses and root growth (1). Shinozaki now directs a gene discovery research group at the RIKEN Center for Sustainable Resource Science and was elected to the National Academy of Sciences as an International Member in 2020.

**Delving into Recombinant DNA**

After his doctorate, Shinozaki joined the National Institute of Genetics at Mishima as a research associate under the aegis of Masahiro Sugiura. "He had just started to use recombinant DNA technology to analyze chloroplast DNA," says Shinozaki. "It’s a major organelle for photosynthesis, and I and Masahiro Sugiura tried to isolate many genes from the tobacco chloroplast genome," he says. This research effort culminated in their deciphering the whole chloroplast genome in 1986 (2).

Shinozaki's time in Sugiura's laboratory led to his meeting Kazuko Yamaguchi, who would become his wife and a frequent collaborator throughout the rest of his career.

Kazuo Shinozaki. Image credit: Kazuo Shinozaki (Gene Discovery Research Group, RIKEN Center for Sustainable Resource Science, Tsukuba, Japan).

"We were both very interested in molecular biology," he says. In Mishima, Shinozaki first learned to use recombinant DNA technology, eventually using it to understand complex eukaryotic gene expression and regulation. "I was very impressed with gene regulation, especially transcriptional regulation, and with Jacob and Monod's work on operon theory, which is quite a beautiful regulatory system of how genes work," he says.

After his work on the tobacco chloroplast genome, Shinozaki began a postdoctoral fellowship at Nam-Hai Chua's laboratory at The Rockefeller University in 1987. "He was really a frontrunner on transgenic research and transcriptional regulation in plant genes to analyze the plant regulatory network," says Shinozaki. "Fortunately, my wife Kazuko [and I] could work as postdoctoral fellows in his laboratory for 2 years to learn transgenic technology in plants and learn international standards of research and development in the [United States]," he says. It is also where Shinozaki learned to work with the model plant Arabidopsis thaliana, which would form the basis of much of his future research.

**Productive Period at RIKEN**

Shinozaki returned to Japan in 1989 and started his own laboratory at RIKEN, where he focused on discovering the genes involved in plant stress responses. "The plant response to severe environmental stress is mainly regulated at the transcriptional level, so we decided to collect various types of genes based on genomic technology,"

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Translating Basic Research to Crop Plants

When RIKEN started a Plant Science Center in 2005, Shinozaki was appointed as its director. Around this time, he started using metabolomics to discover and understand metabolites in plants and also worked on deciphering the functions of plant hormones, such as abscisic acid. “We have various tools to analyze the plant, such as transcriptome analysis, RNA sequence, or metabolome analysis, and so we can analyze them and we can discover new metabolites or new genes for plant responses,” he says.

Shinozaki also embraced his role as director and guided colleagues as they pursued new research directions. “There are many important plant hormone functions that were determined in [the] RIKEN Plant Science Center, and my colleagues also worked very efficiently to find important new factors and genes in the plant stress response,” he says. “RIKEN Plant Science Center became very famous in the plant science field, which was a proud moment for us,” says Shinozaki.

In 2013, Shinozaki became the director of RIKEN’s newly launched Center for Sustainable Resource Science, aimed at conducting interdisciplinary research. “It was important for us to integrate research among biologists, chemists, and chemical biologists to use basic research to contribute to a sustainable society,” he says. The center marked the continuation of a lifelong effort by Shinozaki to find real-world applications of his research, especially in collaboration with his wife.

From the time in the late 1980s that both Shinozaki and Yamaguchi-Shinozaki started working on plant responses to environmental stress, they were interested in translating their basic research to crops. A few years after they returned to Japan, Yamaguchi-Shinozaki became a faculty member at the Japan International Research Center for Agricultural Research, which was part of Japan’s agriculture ministry. “Fortunately, we could collaborate to work on Arabidopsis, and she expanded our work to apply it to crops, such as rice, wheat, and soybean,” says Shinozaki. “It’s quite important for us to apply our basic knowledge to real crop breeding,” he says.

The duo also worked on international collaborations with crop scientists from CGIAR (formerly the Consultative Group for International Agricultural Research). “So, we could collaborate with many good researchers, and we could apply what we learnt about Arabidopsis genes to crops, such as rice, wheat, soybean, and so on, based on international cooperation,” says Shinozaki. The collaboration included using the genes Shinozaki identified to breed-enhanced versions of crop plants. “Some genes are quite useful for the breeding of drought tolerance and in increasing yield under dry conditions, so these are important genes for crop production in the future,” he says.

More recently, Shinozaki has also delved into how plants detect stress, including in his Inaugural Article (1).

Plant Stress Signaling

As Shinozaki studied plant stress responses, he became interested in the unfolded protein response, which applies stress to eukaryotic cells. Three transcription factors—bZIP17, bZIP28, and bZIP60—play an important role in the unfolded protein response in plant cells. When Shinozaki’s colleague, June-Sik Kim, isolated double mutants of the bZIP17 and bZIP28 genes, he found that the double-mutant bZIP17/28 showed a short root phenotype. “So, we became interested in the role of the unfolded protein response in root growth,” says Shinozaki.

Kim isolated a suppressor mutant of the bZIP17/28 double mutant and found that it had longer roots. He localized the underlying mutation to the transcription cofactor TBP-ASSOCIATED FACTOR 12b (TAF12b). “We think that TAF12b is a key transcription factor acting between plant stress response and plant growth, especially root growth,” says Shinozaki. “It’s quite a new discovery, so we selected this paper as my Inaugural Article for PNAS,” he says. The researchers also isolated several other suppressor mutants and are continuing to elucidate the unfolded protein response in plant growth and environmental responses.

Shinozaki also recently discovered another molecule involved in plant stress signaling: the short peptide CLE25 (6, 7). “It functions as a long-distance signal molecule from root to leaves,” says Shinozaki. “The roots sense dry conditions, and CLE25 is induced and transported from roots to leaves through vasculature and induces both the closing of the stomata and abscisic acid-inducible gene expression,” he says. Shinozaki hopes to explore the potential of CLE25 and similar signaling molecules in breeding drought-resistant crops.

Harnessing Technological Progress

Shinozaki stepped down as director of the RIKEN Center for Sustainable Resource Science in 2020 and has since...
taken on an advisory role. “I encourage my colleagues to pursue new subjects, especially plant phenotyping,” he says. “We are very interested in phenotyping to understand the whole plant responses to drought or cold stress, and phenotyping is quite important for crop performance,” says Shinozaki.

Researchers at RIKEN have developed a quantitative phenotyping system to analyze continuous plant growth under controlled environmental conditions (7). “So, we can get a lot of images with different types of cameras, and we can use different types of mutants or cultivars or ecotypes to analyze phenotype, and I’m very interested in a genome-to-phenome approach for data science in plants,” says Shinozaki.

The fact that Shinozaki continues to embrace new techniques to study plants is no surprise. “I was very lucky to work during a period of great progress in life science and biology,” says Shinozaki. “Every 10 years or so new technology came up, such as recombinant DNA technology, transgenic technology, molecular genetics in model systems, genomics, and functional genomics,” he says. “These days genome editing and artificial intelligence are the new frontiers, and I encourage my colleagues to always [embrace] new areas of science.”

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