THE JAPAN PRIZE FOUNDATION

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2022 Japan Prize Laureates Announced



Prof. Katalin Karikó Senior Vice President, BioNTech SE Adjunct Professor, Perelman School of Medicine, University of Pennsylvania Professor, University of Szeged Hungary/ USA



Prof. Drew Weissman Professor of Medicine, University of Pennsylvania School of Medicine Director Penn Institute for RNA Innovation USA

Fields Eligible for the Award: Materials and Production

For pioneering research contributing to the development of mRNA vaccines

COVID-19 vaccinations began in the United States and United Kingdom ahead of the rest of the world in December 2020, and people in Japan also became eligible to receive the vaccines in February 2021. It was initially thought that it would take years to develop the vaccines, but mass production became possible in only around one year, thus saving many lives and stemming economic losses across the globe. The vaccines are now serving as a powerful tool in bringing the global pandemic to a close. These mRNA (or messenger-RNA) vaccines differ from conventional vaccines.

Like DNA, mRNA is a type of nucleic acid, and it serves as the blueprint for protein synthesis in the body. Research into medical applications for mRNA was conducted alongside research into DNA in the 1990s, but it was abandoned due to obstacles caused by undesired immune response.

However, in 2005, Professors Katalin Karikó and Drew Weissman discovered that by replacing the uridine in mRNA with a modified nucleic acid called pseudouridine, they could suppress that undesired immune response. Furthermore, in 2008, they announced that using pseudouridine allowed them to achieve their goal of increased protein production. These discoveries opened the doors to using mRNA in medical applications and made it possible for COVID-19 vaccines to be developed quickly.



Prof. Christopher Field Director, Woods Institute for the Environment, Stanford University Professor for Interdisciplinary Environmental Studies

USA

Fields Eligible for the Award: Biological Production, Ecology/Environment

For outstanding contributions to estimation of global biospheric productivity and climate change science using advanced formulas based on observation

Estimates based on the dynamics of the global biosphere are essential for accurate prediction of future climate change. Particularly important is to clarify what effect plants, which serve as sinks for carbon dioxide (CO₂), have on climate change. Without an understanding of that, it is impossible to know how much the reduction of artificial CO₂ emissions will help in stopping the progress of global warming.

Professor Christopher Field has spent much of his career accumulating data on living leaves through in-field observation, and he used that data to make it possible to express how the photosynthetic rate of leaves is dependent on the environment in which they grow. Moreover, he developed the equations that enable a plant ecosystem to be considered a single virtual leaf: the "Big-leaf Model." He then integrated this with climate models, satellite observations, and oceanographic research to clarify the global distribution of CO₂ absorption across both land and sea, and to identify the factors that affect CO₂ concentration in the atmosphere.

Field's research has become the scientific basis for the climate change measures being implemented today through such initiatives as the Paris Agreement, an international framework for combatting global warming, and the Intergovernmental Panel on Climate Change (IPCC).

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The establishment of the Japan Prize was motivated by the Japanese government's desire to create an internationally recognized award that would contribute to scientific and technological development around the world. With the support of numerous donations, the Japan Prize Foundation received endorsement from the Cabinet Office in 1983.

The Japan Prize is awarded to scientists and engineers from around the world who have made creative and dramatic achievements that help progress their fields and contribute significantly to realizing peace and prosperity for all humanity. Researchers in all fields of science and technology are eligible for the award, with two fields selected each year in consideration of current trends in scientific and technological development. In principle, one individual in each field is recognized with the award, and receives a certificate, a medal, and a monetary prize. Each Award Ceremony is attended by the current Emperor and Empress, heads of the three branches of government and other related officials, and representatives from various other elements of society.

Field of Materials and Production

Achievement : For pioneering research contributing to the development of mRNA vaccines

Prof. Katalin Karikó (Hungary/ USA)

Born: January 17, 1955 (Age: 67) Senior Vice President, BioNTech SE Adjunct Professor, Perelman School of Medicine, University of Pennsylvania Professor, University of Szeged

Prof. Drew Weissman (USA) Born: September 7, 1959 (Age: 62) Professor of Medicine, University of Pennsylvania School of Medicine Director Penn Institute for RNA Innovation

The role of mRNA in protein synthesis

Vaccines are medicines that remind the immune system to attack proteins particular to specific pathogens in order to gain immunity (i.e., resistance) to external pathogens such as viruses and bacteria.

COVID-19 infects human cells by attaching to them using spike proteins (the red, club-shaped elements seen in Figure 1.) Previous coronavirus research has shown that fragments of those spike proteins can act as antigens and activate the immune system to produce antibodies.

The problem with using spike proteins in vaccines is how to get them into the body. It is possible to administer them directly, as is done with conventional vaccines, but mRNA vaccines harness mRNA, which serves as a blueprint for cells to synthesize spike proteins, and which can be synthesized artificially before being administered.

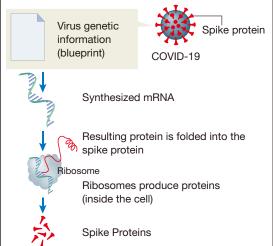
Our bodies know which proteins to make by using our genetic blueprint or DNA. The information on DNA needed for protein synthesis is copied over to the mRNA, whereupon the ribosomes in the cells read that information and begin synthesizing protein. This biological function is used to effectively produce spike proteins within the body.

How the COVID-19 vaccine works

What mechanisms do COVID-19 vaccines harness to prevent viral infection and reduce symptom severity?

First, vaccination allows the spike protein-coded mRNA to enter the body. That mRNA uses the body's protein synthesis ability to produce spike proteins. Since these proteins are recognized as coming from outside of the body, also known as "non-self" proteins, the immune system is activated

Figure 1: The role of mRNA in protein synthesis



to produce antibodies (left image in Fig. 2). Once the immune system has made a record of spike proteins, if COVID-19 virions enter the body, a rapid immune response is induced (right image in Fig. 2).

Vaccines were conventionally made using attenuated versions of a virus or even the viral pathogens themselves, so it took time to guarantee a vaccine's safety, i.e., to guarantee that the vaccine would not cause illness, and to confirm its effectiveness in granting immunity to the disease being targeted. On the other hand, the induced production of spike proteins in the body involves no use of an actual virus, so there is no risk of infection, and the antigenic efficiency of spike proteins can be easily shown, so such vaccines can be made highly effective.

This is the basic mechanism through which the mRNA COVID-19 vaccine works.

Paving the way to mRNA drugs with pseudouridine

The reason why mRNA had not been used in pharmaceutical products was because it degrades quickly in vivo and, particularly when administered from outside the body, it is recognized as abnormal by the body thereby triggering an inflammatory immune response. As a result, cells administered with mRNA were dying before they could produce the amount of protein needed to acquire immunity, and vaccines were causing fevers and other issues in recipients.

Professors Katalin Karikó and Drew Weissman began collaborating in 1998 when they were both at the Perelman School of Medicine at the University of Pennsylvania in the hopes of conducting research into the potential of harnessing mRNA in drug creation. In 2005, they discovered that they could look at mRNA as a single substance, and that they could replace its constituent uridine with a modified version called pseudouridine, thereby suppressing any undesired immune response (see Fig. 3).

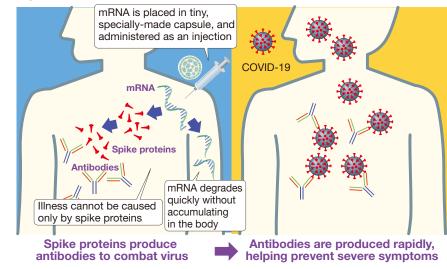
At the time, it was known that immune response can be caused when mRNA introduced from outside the body binds to Toll-like receptors on the cell membrane, but it was not yet known that this binding occurs by way of uridine. After repeated experimentation, Karikó and Weissman learned that mRNA with pseudouridine does not bind to those receptors.

After years of mRNA research and related technological development, a vaccine is born

The mRNA vaccine may seem to have appeared all of a sudden, but in reality, mRNA first began to be considered for use in medical applications more than 30 years ago. Research has continued since then, even though it did not lead to development of any drugs. It wasn't until 2020 and the urgent need presented by the COVID-19 pandemic arrived that a practical mRNA vaccine was successfully made.

Bolstering the seemingly short-term development of the mRNA vaccine was the accumulated wisdom of the entire body of molecular biology





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research. Particularly important was Karikó and Weissman's 2005 discovery that pseudouridine could replace uridine, which made it possible to administer mRNA from external sources. Moreover, they showed in 2008 that pseudouridine-mRNA efficiently produces proteins in vivo, and in 2012, they successfully achieved highly-efficient protein production within mice. These fundamentally important findings were the result of the collaboration between the two researchers.

The most important characteristic of mRNA is that it can be artificially designed to make cells produce the specific protein desired. Harnessing this feature not only allows for the creation of vaccines to use against other infectious diseases, but it can also be used to create cancer treatments that produce antibody proteins effective in treating cancer, and can be used in regenerative medicine to treat heart failure and other ailments. Clinical trials are already underway for applications like these.

The development/manufacture of new drugs that use mRNA is accelerating and expanding, leaving us poised on the edge of a revolution in the field of medicine.

It is all thanks to the research of Professor Katalin Karikó and Professor Drew Weissman.

Figure 3 : Paving the way to mRNA drugs with pseudouridine

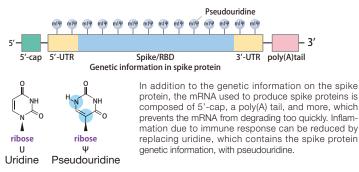


Figure 4 : The development of mRNA vaccines

Year		Details
1960s	1961	Discover of mRNA (F. Jacob, J. Monod)
19005	1969	Laboratory synthesis of protein using mRNA isolated from living creature
1970s	1971	Drug transport using liposomes achieved
1000	1984	mRNA synthesized
1980s	1989	mRNA in cationic liposomes administered to human cells and frog embryos
1990s	1990	mRNA injected into mouse muscle and proteins synthesized (Wolff et al)
	1992	Trial of mRNA as therapeutic drug for hereditary disease (in rats)
	1995	Trial of mRNA in cancer treatment (in mice)
	1998	Professors Karikó and Weissman begin research collaboration
2000s	2004	Inflammatory response from mRNA administration is discovered to be due to TLRs
	2005	Modified mRNA found to suppress unwanted TLR immune response *1
	2008	Modified mRNA found to increase protein expression efficiency *2
2010s	2011	Development of mRNA purification method (Karikó et al)
	2012	In vivo protein production using modified mRNA achieved (mice)*3
	2012	Self-amplified mRNA vaccine created
	2017	Beginning of clinical trials of Zika virus vaccine using modified mRNA (in mice and primates). Development of HIV-1 vaccine using modified mRNA (in mice)
2020s	2020	Creation of COVID-19 vaccines using modified mRNA (BioNTech/Pfizer, Moderna)

Blue text: Accomplishments of Profs. Karikó and Weissman

①Research into the medical applications of mRNA was conducted in the 1990s,

but it was deemed too difficult due to mRNA instability and inflammatory response. ②Basic lipid nanoparticle model for mRNA transport developed

③Revival of mRNA vaccine research

- Refs: Molecular Therapy, 27(4) (2019) (Special Issue) ; E. Dolgen, Nature , 597,318(2021)
- *1 Karikó, Katalin; Buckstein, Michael; Ni, Houping; Weissman, Drew; "Suppression of RNA recognition by Toll-like receptors: the impact of nucleoside modification and the evolutionary origin of RNA". *Immunity.* 23(2), 165-175 (2005).
 *2 Karikó, Katalin; Muramatsu, Hirom; Welsh, Frank A.; Ludwig, János; Kato, Hiroki; Akira,
- *2 Kariko, Katalin; Muramatsu, Hiromi; Welsh, Frank A.; Ludwig, János; Kato, Hiroki; Akira, Shizuo; Weissman, Drew (November 2008). "Incorporation of pseudouridine into mRNA yields superior nonimmunogenic vector with increased translational capacity and biological stability". *Molecular Therapy*, **16** (11): 1833-1840.
- versus suberior informitmicipante vector with increased transational capacity and biological cal stability". *Molecular Therapy*, **16** (11): 1833-1840.
 *3 Kartiko, Katalin, Muramatsu, Hiromi, Keller, Jason M.; Weissman, Drew; "Increased Erythropoiesis in Mice Injected With Submicrogram Quantities of Pseudouridine-containing mRNA Encoding Erythropoietin", *Molecular Therapy*, **20**(5), 948-953(2012)

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Field of Biological Production, Ecology/Environment

Achievement : For outstanding contributions to estimation of global biospheric productivity and climate change science using advanced formulas based on observation

Prof. Christopher Field (USA)

Born: March 12, 1953 (Age: 68) Director, Woods Institute for the Environment, Stanford University Professor for Interdisciplinary Environmental Studies

Measuring photosynthetic and transpiration rates of living leaves

Plants absorb CO₂ in the atmosphere through photosynthesis and convert it into organic matter. However, a great variety of plants can be found on Earth, and the photosynthetic rate of each plant depends on the climate, the soil, its altitude, and other factors particular to the environment in which it grows.

In the early 1980s, Field developed a device that could measure both photosynthetic and transpiration rates of leaves (see photos below). It allowed for the control of temperature, humidity, and CO₂ concentration to measure photosynthetic and transpiration rates of leaves under various conditions.

The most advantageous aspect of this device was its portability. Without that, plants would have to be gathered and brought to a laboratory, which affected the environment and biological activity, and therefore resulted in inaccurate data.

This device enabled researchers to analyze plants in-situ using the "living leaves" of plants rooted in the soil. They could then gather real data that reflected the growing environment, as there was no longer any need to collect or move the plants.

Field brought the device to various areas to gather a vast amount of data during his field surveys and experiments.

Equipment used to measure photosynthetic rate and transpiration of living leaves.



The equipment can all be stored

Analyzing a living plant leaf in soil.

Leaf photosynthesis and stomatic function

Stomata are tiny pores found on the surface of plant leaves, and stomatal resistance is used to describe how easily CO_2 and water vapor pass through

the stomata of a leaf. By incorporating Field's formulas for photosynthesis, it became possible to estimate the flow of CO₂ and water vapor between plants and the atmosphere.

Field continued to engage in theoretical research based in the data he gathered in his field surveys and experiments. He made it possible to describe complex plant phenomena in a quantitative way by expressing photosynthetic rate in leaves through a function that depends on temperature, light, atmospheric CO₂ concentration, leaf nitrogen level, and other factors.

Nitrogen has a significant influence on photosynthesis rate. Field revealed how photosynthesis rate depends on leaf nitrogen content and irradiance levels (see Fig. 1). This research has also contributed to agricultural efforts to improve the efficiency of nitrogen fertilizers.

Field's formulas were introduced into the climate models essential to understanding and predicting climate change caused by global warming.

CO₂ is extracted from the atmosphere through the opening and closing of the stomata, and water vapor drawn up from the roots is also released (see Fig. 2).

Field's equations were introduced into climate models, and with the addition of living plants, the carbon cycle – i.e. the interchange and flow of CO₂ between plants and the atmosphere and oceans – became a new part of the climate models.

This made it possible to answer questions such as how the rise in atmospheric CO_2 concentration and temperature affects plant growth and photosynthesis rates, and what sort of feedbacks are produced. That understanding led to the ability to predict future climate change through understanding the CO_2 cycle.

CO2 absorption in the global biosphere

Field's formulas are based upon observational data, and were developed to treat plant ecosystems as a single, virtual leaf. Gaining a qualitative understanding of the environmental response of complex vegetation through these formulas was significant because it broadened the applicability of the analytical model to cover both terrestrial vegetation and marine biospheres.

In collaboration with Earth observation researchers at NASA and other organizations, Field used data gathered by observational satellites to estimate how much CO_2 is being absorbed by which vegetation – i.e. plant photosynthetic productivity – around the planet.

In addition, by collaborating with marine researchers and integrating their data from marine biospheres, he was able to create the first global CO₂ absorption and emission distribution map that included both terrestrial and marine ecosystems (see Fig.3 map).

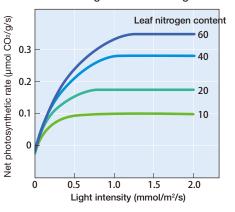
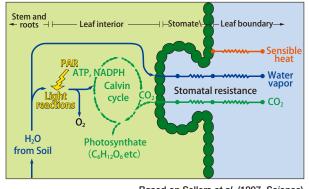


Figure 1: Relationship between photosynthetic rate, leaf nitrogen content and light intensity Figure 2: Leaf photosynthesis and stomatic function



Stomatal resistance measures how easily CO² and water vapor pass through the stomata of a leaf. By incorporating Field's formulas for photosynthesis, it became possible to estimate the flow of CO² and water vapor between plants and the atmosphere.

Based on Sellers et al. (1997, Science)

Based on Field (1983, Oecologia)

in a carrying case. Field et al. (1982, Plant, Cell & Environment)

Artificial CO₂ emissions and CO₂ absorption in the environment

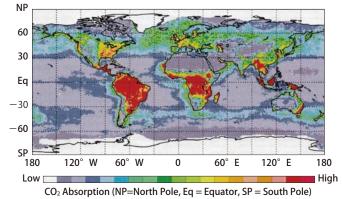
Field was also able to estimate how much artificially produced CO₂ would be absorbed by land and marine ecosystems, and how much would remain in the atmosphere (see chart in Fig. 4).

Artificial CO₂ emissions are rising every year, and the amount of CO₂ absorbed by oceans is rising accordingly, but Field discovered that CO₂ absorbed by terrestrial vegetation fluctuates wildly from year to year. It was thought that CO₂ was absorbed by land vegetation in a stable way, but that turned out not to be the case. His estimation showed that any CO₂ not absorbed on land remains in the atmosphere, and is thereby responsible for the rise of atmospheric CO₂ concentration.

Through his research, Field has been able to show how much CO₂ is absorbed by marine and terrestrial ecosystems as global warming continues unabated, and to show how many years it will take to reduce atmospheric CO₂ concentration if humanity is able to reduce its CO₂ emissions and limit deforestation and other related changes in land use and land cover.

Field's research began with the observation of a single leaf and developed into a way to study global biospheric productivity using CO₂ emissions, contributing immensely to the study of climate change, and laying the scientific foundation for international discussions to implement the measures needed to combat global warming.

Figure 3: Distribution of CO2 absorption in the global biosphere



Field et al. (1998, Science)

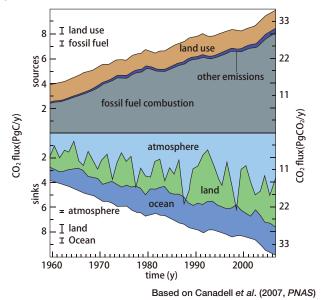


Figure 4: Artificial CO₂ emissions and environmental CO₂ absorption

Nomination and Selection Process

- Every November, the Field Selection Committee of The Japan Prize Foundation designates and announces two fields in which the Japan Prize will be awarded two years hence. At the same time, the Foundation calls for over 15,000 nominators, strictly comprised of prominent scientists and researchers from around the world invited by the Foundation, to nominate the candidates through the Web System. The deadline for nominations is the end of January of the following year.
- For each field, a Selection Subcommittee conducts a rigorous evaluation of the candidates' academic achievements. The conclusions are then forwarded to the Selection Committee, which conducts evaluations of candidates' achievements from a wider perspective, including contributions to the progress of science and technology, and significant advancement towards the cause of world peace and prosperity, and finally the selected candidates are recommended for the Prize.
- The recommendations are then sent to the Foundation's Board of Directors, which makes the final decision on the winners.
- The nomination and selection process takes almost two years from the time that the fields are decided. Every January, the winners of that year's Japan Prize are announced. The Presentation Ceremony is held in April in Tokyo.

2	020		2021	2022	
	July - October	November	January	November January	April
	1	→ 2 3	→ 4	5 → 6 7	8
1	Consider the eligible fie (Board of Directors) Materials and Production Biological Production, E	n	Prize	5 Japan Prize (Selection Committee) Materials and Production (Selection Subcommittee) Biological Production, Ecology/Environment (Sele	ection Subcommittee)
2	Determine the eligible f (Board of Directors)	fields for the 2022 Japan	ı Prize	6 Selecting the Laureates of the 2022 Japan Prize (Board of Directors)	
3	Invite the nominations			7 Announce the Laureates of the 2022 Japan Prize	
4	Closing of the nomination	ions		8 The 2022 Japan Prize Presentation Ceremony	

Members of the 2022 Japan Prize Selection Committee

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 Makoto Asashima Deputy Director General of Advanced Comprehensive Research Organization, Research Professor, Teikyo University Academic Advisor, Japan Society for the Promotion of Science Professor Emeritus, The University of Tokyo Deputy Chairman Yoichiro Matsumoto Professor Emeritus The University of Tokyo Selection Subcommittee for the "M 	 Mariko Hasegawa President President President The Graduate University for Advanced Studies, SOKENDAI Hiroto Ishida Director The Japan Prize Foundation Kazunori Kataoka Vice Chairperson, Kawasaki Institute of Industrial Promotion Director General, Innovation Center of NanoMedicine (iCONM) Professor Emeritus, The University of Tokyo Masayuki Matsushita Director The Japan Prize Foundation 	 Kyosuke Nagata President University of Tsukuba Hideyuki Okano Professor Keio University School of Medicine Tatsuya Okubo Executive Vice President, Professor School of Engineering, The University of Tokyo Hiroto Yasuura Director General, Fukuoka Asian Urban Research Center Professor Emeritus, Kyushu University
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Selection Subcommittee for the "Bi	Professor Graduate School of Engineering, The University of Tokyo • Koji Ishibashi Chief Scientist Cluster for Pioneering Research, RIKEN • Ological Production, Ecology/Environ	Specially Appointed Professor Graduate School of Engineering Science, Osaka University Hideyuki Yasuda Professor Graduate School of Engineering, Kyoto University mment" field
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- Toru Shimada Professor Faculty of Science, Gakushuin University
- Hirokazu Toju Associate Professor

Associate Professor Center for Ecological Research, Kyoto University

(alphabetical order, titles as of November, 2021)

Eligible Fields for the 2023 Japan Prize

Areas of Physics, Chemistry, Informatics, and Engineering

Electronics, Information, and Communication

Background and Rationale:

The widespread adoption of IoT is producing vast amounts of data which fuel AI, such as deep learning, with substantial advances. As a result, innovative systems have been created in a variety of fields, and the revitalization of economic activities and the evolution of academic studies have been brought about.

Further societal, economic and academic advancements are envisaged through the development of fundamental technologies, such as optical and wireless networks, information security, semiconductor devices, robotics, and quantum computers, and the innovative systems capable of integrating these fundamental technologies.

Such technologies could solve many societal challenges that human society faces, including climate change, food problems, energy issues, health issues, educational problems, and more. These technologies are highly expected to contribute to attaining safer, more secure, and more sustainable societies.

Eligible Achievements:

The 2023 Japan prize in the field of Electronics, Information, and Communication will reward significant breakthroughs in fundamental technologies and systems which have contributed to creating safer and sustainable society, increased resilience to natural disasters/infectious diseases, and creation of new industries. Novel fundamental technologies that will contribute to the future development of society will also be eligible.

Areas of Life Science, Agriculture, and Medicine

Life Sciences

Background and Rationale:-

The life sciences seek to better comprehend the complex and subtle mechanisms underlying the activity of all living organisms. Since the mid-20th century, researchers in this field have made great strides by analyzing the function of genes and cells. Through high-speed analysis of genetic information and targeted genetic engineering in a variety of organisms and individual humans, and through improved imaging technologies to visualize the microstructure of cells and tissues, the life sciences are pioneering new approaches to improving our lives and maintaining our health. Playing a key role in controlling the global COVID-19 pandemic crisis, basic life-science knowledge built up over decades contributed to the astonishing speed at which novel vaccines were developed. The life sciences seek an ever deeper understanding of life through ever more advanced technologies, such as single-cell analysis and new lines of enquiry into how epigenetics controls gene expression.

With due regard for bioethics, the search for a deeper understanding of biological phenomena will, we hope, generate new methods of medical treatment, inform sound judgment needed to ensure humanity's sustainable development, and contribute to people's well-being.

Eligible Achievements : -

The 2023 Japan Prize in the field of Life Sciences will reward significant contributions to society through discoveries of new biological phenomena and elucidation of biological regulatory mechanisms as well as major advances in scientific technology that make possible deeper understanding of biological functions.

Fields Selection Committee for the 2023 Japan Prize

Chairman	Members	Members			
Michiharu Nakamura Counselor to the President Japan Science and Technology Agency Director, The Japan Prize Foundation	Yozo Fujino President, Josai University Professor Emeritus, The University of Tokyo Professor Emeritus, Yokohama National University	Tomoko M. Nakanishi President, Hoshi University Professor Emeritus / Project Professor, The University of Tok Commissioner, Japan Atomic Energy Commission			
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Schedule (2023-2025)

The eligible fields for the Japan Prize (2023 to 2025) have been decided for the two research areas, respectively. These fields rotate every year in a three year cycle.

Every year the Fields Selection Committee announces the eligible field for the next three years.

eas of Physic	es, Chemistry, Informatics, and Engineering	Areas of Life Science, Agriculture, and Medicine		
Year	Eligible Fields	Year	Eligible Fields	
2023	Electronics, Information, and Communication	2023	Life Science	
2024	Resources, Energy, Environment, and Social Infrastructure	2024	Medical Science and Medicinal Science	
2025	Materials and Production	2025	Biological Production, Ecology/ Environment	