THE JAPAN PRIZE FOUNDATION
Akasaka Twin Tower East, 13th Floor, 2-17-22
Akasaka, Minato-ku, Tokyo, 107-0052, JAPAN
Tel : +81-3-5545-0551 Fax : +81-3-5545-0554
www.japanprize.jp

Japan Prize News
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JAPAN PRIZE

2012 Japan Prize Laureates Announced

Dr. Janet Rowley, Dr. Brian Druker, and Dr. Nicholas Lydon for developing a new therapeutic drug targeting cancer-specific molecules
Dr. Masato Sagawa for developing the world's highest performing permanent magnet and contributing to energy conservation

"Healthcare and Medical Technology" field

Dr. Janet D. Rowley
Blum-Riese Distinguished Service Professor of Medicine, Molecular Genetics & Cell Biology and Human Genetics The University of Chicago
USA

Dr. Brian J. Druker
Professor
Director, OHSU Knight Cancer Institute
Oregon Health & Science University
USA

Dr. Nicholas B. Lydon
Founder and Director
Blueprint Medicines
USA

"Environment, Energy and Infrastructure" field

Dr. Masato Sagawa
President
Intermetallics Co., Ltd.
Japan

The Japan Prize Foundation has decided to award the 2012 Japan Prizes to Dr. Janet Rowley, Blum-Riese Distinguished Service Professor of Medicine, Molecular Genetics & Cell Biology and Human Genetics, The University of Chicago; Dr. Brian Druker, Professor and Director, OHSU Knight Cancer Institute, Oregon Health & Science University; Dr. Nicholas Lydon, Founder and Director, Blueprint Medicines; and Dr. Masato Sagawa, President, Intermetallics Co., Ltd.

Dr. Rowley, Dr. Druker and Dr. Lydon will be awarded in the field of "Healthcare and Medical Technology" for the development of a new therapeutic drug targeting cancer-specific molecules.

In the field of "Environment, Energy and Infrastructure" Dr. Sagawa will be awarded for the development of the world's highest performing Nd-Fe-B type permanent magnet, and thereby contributing to energy conservation.

The Laureates will be formally honored at the Presentation Ceremony to be held in Tokyo on April 25, 2012.

JAPAN PRIZE

The Japan Prize is awarded to scientists throughout the world who have been credited with original and outstanding achievements and have made major contributions to the advancement of science and technology, thereby manifestly furthering the cause of peace and the prosperity of mankind.

While the prize encompasses all categories of science and technology, two fields of study are designated for the prize each year in consideration of developments in science and technology.
Each Japan Prize laureate receives a certificate of merit and a commemorative medal. A cash prize of 50 million yen is also awarded to each prize field.

"Healthcare and Medical Technology" field

Achievement : Development of a new therapeutic drug targeting cancer-specific molecules

Dr. Janet D. Rowley
Born : April 5, 1925 (Age 86)
Blum-Riese Distinguished Service Professor of Medicine, Molecular Genetics & Cell Biology and Human Genetics, The University of Chicago

Dr. Brian J. Druker
Born : April 30, 1955 (Age 56)
Professor and Director of OHSU Knight Cancer Institute, Oregon Health & Science University

Dr. Nicholas B. Lydon
Born : February 27, 1957 (Age 54)
Founder and Director, Blueprint Medicines

Summary

Chronic myelogenous leukemia (CML) is a disease which is caused when a hematopoietic stem cell in the bone marrow turns cancerous. In 2001, with the introduction of the molecularly targeted drug imatinib, treatment results dramatically improved. The origin of imatinib began in 1973 when Dr. Janet Rowley discovered that chromosomes 9 and 22 were recombined in the white blood cells of patients with CML. Dr. Brian Druker and Dr. Nicholas Lydon succeeded in developing a drug which suppressed the activity of the BCR-ABL protein which occurs as a result of the chromosomal recombination. At present, molecularly targeted drugs are indispensable to the treatment of cancer and autoimmune diseases, and the results obtained from the studies of Dr. Rowley, Dr. Druker and Dr. Lydon underscored the importance of developing molecularly targeted drugs, providing a guiding post for future research.

Understanding the molecular mechanism that triggers chronic myelogenous leukemia

Decoding of the human genome in 2003 and rapid improvements in technologies for genetic analyses have led to high expectations for the medical applications of these technologies. In cancer research, many of the genetic abnormalities that cause cancer have been discovered and many drugs targeting these molecular abnormalities are being introduced.

The forerunner of molecularly targeted drugs is imatinib for CML. The research leading to the development of imatinib goes back to the 1960's and 70's when gene analysis technologies as we know them today, had not been introduced. The first breakthrough was the detection of an abnormal chromosome, the Philadelphia chromosome, in the white blood cells of patients with CML.

Around that time, Dr. Janet Rowley had received a doctorate from the University of Chicago School of Medicine and was leading a fruitful life as a doctor, medical researcher and a mother. In 1962, she studied in the U.K. for 1 year as a researcher dispatched from the NIH (U.S. National Institutes of Health) where she learned methods to distinguish healthy chromosomes from abnormal ones.

After returning home, Dr. Rowley continued her research in the Department of Hematology at her alma mater. One of the subjects she worked on was the Philadelphia chromosome. By using quinacrine fluorescence and Giemsa staining of chromosomes, the leading-edge research methods of the time, Dr. Rowley clarified the chromosomal mechanisms that created the Philadelphia chromosome. A human cell nucleus has 22 sets of autosomal chromosomes and 1 set of sex chromosomes, but in patients with CML, chromosomes 9 and 22 recombine (reciprocal translocation), causing the Philadelphia chromosome to be formed.

Dr. Rowley's research had an enormous impact on the understanding of the chromosome abnormalities that cause cancer. Dr. Rowley also made the connection between acute myelogenous leukemia and the reciprocal translocation of human chromosomes 8 and 21.

Aiming to develop side effect-free anticancer drugs that target specific genes

Dr. Rowley's studies, carried out in the 1970's, opened the way for the development of an effective therapy for CML. Discoveries from several international research groups led to the recognition that the reciprocal translocation between chromosomes 9 and 22 caused the *ABL* gene found on chromosome 9 to be combined with the *BCR* gene on chromosome 22. This abnormal fusion gene, *BCR-ABL*, produces a protein with elevated tyrosine kinase activity that causes CML.

Tyrosine kinases are essential enzymes that regulate various cellular functions, including cell differentiation, proliferation and immune reactions. Thus, in the early 1980's, many oncologists began to think that "tyrosine kinases which had gone out of control could cause cells to turn cancerous." Dr. Brian Druker who was beginning his career as an oncologist at the Dana-Farber Cancer Institute in Boston, U.S., was one of them.

Dr. Druker who focused his research on CML, embarked on finding a drug to inhibit the action of the BCR-ABL protein, and established a collaboration with Dr. Nicholas Lydon of Ciba-Geigy. At the time, most anticancer drugs killed the tumor, but also damaged normal cells. Both Dr. Druker and Dr. Lydon agreed that by inhibiting the action of the BCR-ABL protein, which only CML patients have, they could develop an effective drug with minimal side effects. It heralded a new drug development technique in which a drug specifically targets a causative molecular abnormality in cancer.

However, there were many issues. In the human body, there are more than 90 tyrosine kinases. If several tyrosine kinases were inhibited, there was a possibility that serious side effects would be seen. In 1986, Dr. Lydon working at the pharmaceutical company Ciba-Geigy (now Novartis Pharma) established a program to identify compounds that could inhibit the enzymatic activity of tyrosine kinases using a reagent provided by Dr. Druker from his research on tyrosine kinases. Dr. Lydon's group made good progress and in 1993, after Dr. Druker had established his own laboratory, they began a collaboration aimed at determining the clinical application of compounds discovered by Dr. Lydon and his research team. In 1996, Dr. Druker and Dr. Lydon published an article about a new compound, imatinib that killed cultured cells containing the *BCR-ABL* gene without affecting normal cells.

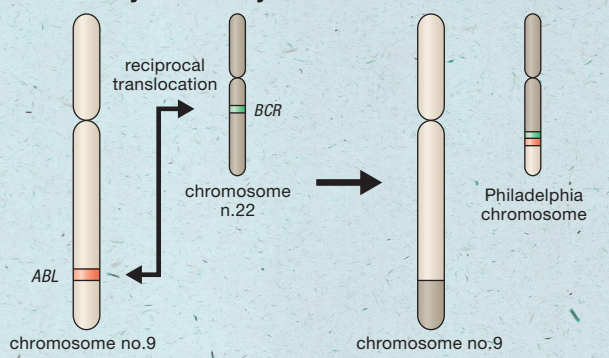
Progress in molecularly targeted drugs opens the way for the treatment of intractable diseases

The article published by Dr. Druker and Dr. Lydon immediately attracted the attention of oncologists. In 1998, Novartis Pharma began clinical trials with imatinib with Dr. Druker serving as the principal investigator. The trials verified that imatinib inhibits the action of the BCR-ABL protein and by doing so led to dramatic improvements in the survival of patients with CML. The remarkable effectiveness and safety of the drug for patients with CML led to regulatory approval of imatinib (trade name Glivec) in the US and Japan in May 2001 and November 2001, respectively.

The molecular mechanism of action of imatinib has also been made clear. Tyrosine kinases are activated when they receive an external stimulus. This leads to binding of ATP (adenosine 3 phosphate), which allows the activated tyrosine kinase to send a proliferation signal to the cell nucleus. In contrast, the BCR-ABL protein is constantly activated, binding ATP, causing the cells to proliferate in a deregulated way (resulting in cancer). By binding to the ATP binding site of the BCR-ABL protein, imatinib prevents ATP from being bound to and activating the BCR-ABL protein. As a result, a cell proliferation signal is not transmitted, enabling the proliferation of CML cells to be inhibited.

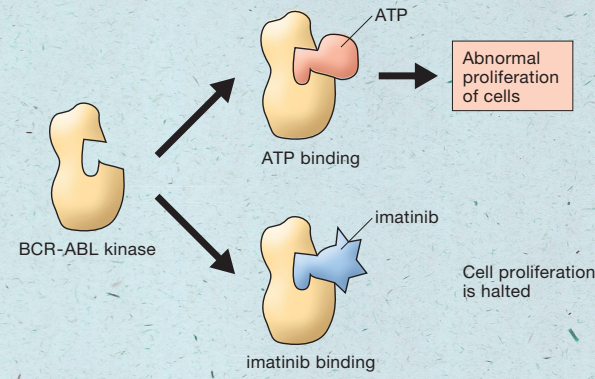
CML is a disease which occurs in 40,000 people worldwide per year. Historically, if the disease reached the blastic phase, there was no effective treatment. Owing to the introduction of imatinib, resulting from the studies of Dr. Rowley, Dr. Druker and Dr. Lydon, the blastic phase can largely be avoided and CML has been converted to a manageable condition. Their work has allowed molecularly targeted drugs including low-molecular weight compounds such as imatinib and antibodies to become the focus of drug development for intractable diseases such as cancer and autoimmune disorders.

Diagram 1 : Recombination of chromosomes discovered by Dr. Rowley



In many CML patients, a recombination of chromosome no. 9 and no. 22 can be seen. As a result, the *ABL* gene and the *BCR* gene are fused, forming BCR-ABL kinase.

Diagram 2 : Imatinib mechanism



BCR-ABL kinase binds itself to ATP without any signal transmission substance and causes unlimited proliferation. By attaching itself to the ATP binding site, imatinib inhibits this process.

"Environment, Energy and Infrastructure"field

Achievement : Developing the world's highest performing Nd-Fe-B type permanent magnet and contributing to energy conservation

Dr. Masato Sagawa
Born : August 3, 1943 (Age 68)
President, Intermetallics Co., Ltd.

Summary

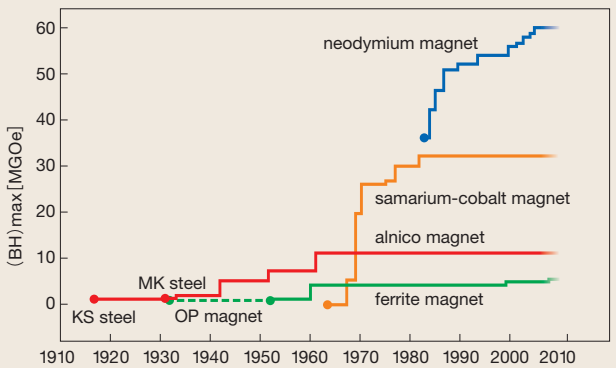
One of the fundamental materials which support our highly industrialized society is a permanent magnet. In order to respond to the expectations for a stronger magnet, the Sm-Co(samarium-cobalt) magnet was developed in the 1960's. However, because cobalt was a rare resource, the scope of its application was limited. Amid such a climate, Dr. Masato Sagawa embarked on the challenge of achieving a permanent magnet using iron, an abundant resource. Dr. Sagawa engaged in research and development of magnetic materials from a completely different perspective to the conventional. In 1982, he discovered the Nd-Fe-B(neodymium-iron-boron) magnet that has the world's largest energy product which breaks the Sm-Co magnet's record in the maximum energy product, and achieved the industrialization of this magnet. Motors which use neodymium magnets are compact, lightweight and highly efficient. Thus, they have greatly contributed to the solution of global environmental issues through power-saving industrial and household electronic products as well as through the high efficiency of new energy sources such as wind power generators.

The progress of permanent magnets using rare earth elements has created modern industry

A permanent magnet refers to an object which continues to supply magnetic flux without the supply of external magnetic fields or electric currents. The ancient Greek philosopher Plato, in his writing "Ion," refers to "magnesia stone" which attracts iron, indicating that the existence of permanent magnets was known from ancient times.

Man created permanent magnets by his own hand in the 18th Century. At that time, only weak magnets could be made which were used for compass indicators. However, in the 20th Century when the use of electric power gained momentum, expectations were raised toward permanent magnets to create a stable magnetic field. Thereafter, many permanent magnets were developed. For example, in 1917 Kotaro Honda of Japan invented the KS steel, and in 1931 Tokushichi Mishima invented the MK steel, and later the Alnico magnet. In 1937 Yogoro Kato and Takeshi Takei invented the OP magnet and later the ferrite magnet. By means of the appearance of highly efficient generators and motors, mankind was able to attain the age of high-tech industry.

Diagram 3 : History of permanent magnet development



Rare earth magnets have significantly higher maximum magnetic energy product in comparison to conventional permanent magnets. Among them, neodymium magnets exceed 50MGOe and have been mass produced.

The development race of permanent magnets reached a turning point in the 1960's with progress in the research of rare earth magnets. Rare earth magnets are magnets which have as their primary components metal compounds consisting of rare earth elements and cobalt. The samarium-cobalt magnet which was developed first was refined in the 1970's, and the value of the "maximum energy product" (MGOe: megagauss-oersted), indicating magnetic performance, was dramatically boosted (Diagram 3).

However, the samarium-cobalt magnet had disadvantages. Both cobalt and samarium were scarce and costly resources, and they were not magnetic materials which could meet large demand. Thus, in the 1970's, there was a growing demand for an inexpensive, strong magnet.

The creation of neodymium magnet was inspired by a symposium lecture

The desire to invent with one's own hands a rare earth magnet without the use of cobalt...such was the big dream of Dr. Masato Sagawa who joined a domestic electronic company after completing a doctorate course at the graduate school of Tohoku University. Dr. Sagawa received an important inspiration when he attended a symposium. At the symposium, Dr. Masaaki Hamano, who was the leading researcher for rare earth permanent magnets who now serves as a fellow of the Society of Non-Traditional Technology, gave a speech about the difficulty of replacing cobalt with iron in the rare earth magnets.

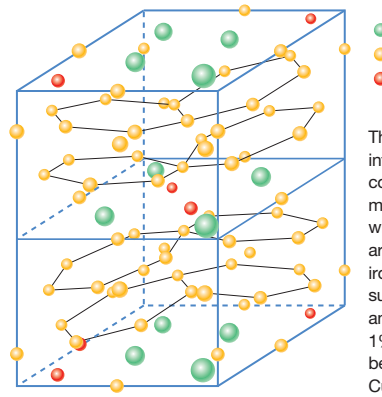
One of the challenges in rare earth magnets using iron was the low Curie temperature which is known as the temperature above which the magnetic ordering disappears. In the crystal structure composed of rare earth and iron, the interatomic distance of the iron was too close, which causes the low Curie temperature. This was the explanation of Dr. Hamano.

While listening to the lecture, an idea came to Dr. Sagawa's head. The idea was, "if elements with small atomic diameter such as carbon or boron were placed between the rare earth and iron atoms, the distance between iron and iron would be extended and the Curie temperature could be raised." Also, "as rare earth elements, neodymium which is a more abundant resource and with greater magnetic moment, should be used in place of samarium."

There are 2 steps in inventing a magnet. The first step is to find an intermetallic compound that has great makings for a high performance magnet. The second step is "making a permanent magnet" in order to develop the optimum alloy microstructure based on the new intermetallic compound. Following the symposium, Dr. Sagawa immediately began working on the experiment of magnetic materials combining these elements, and after a few months discovered the Nd-Fe-B intermetallic compound. He had a succession of new ideas for making a permanent magnet based on the new intermetallic compound, but because the company he was affiliated with was engaged in a different project, he was not able to engage in full-scale development of a new permanent magnet.

Amid such a background, it was Sumitomo Special Metals Company (now Hitachi Metals Limited, NEOMAX Company) that took notice of the potential of Nd-Fe-B magnet and welcomed Dr. Sagawa to join them. Dr. Sagawa, along with the Sumitomo Special Metals development team, embarked on the effort for making a permanent magnet, and within a few months after Dr. Sagawa joined this company and 5 years from his initial inspiration, a new permanent magnet base on the Nd-Fe-B intermetallic compound was borne; it has a Curie temperature as high as 310℃ and the maximum magnetic energy product of 35MGOe. Around the same time, certain companies overseas also took notice of the Nd-Fe-B magnet, but Dr. Sagawa and his associates continued to pioneer new approaches in the research for the commercialization of the new magnet. For example, in producing the magnet, a sintering method which had high volume efficiency and a wide range of application had been selected by Dr. Sagawa. To industrialize this process, it was necessary to develop a sophisticated technology to form a microstructure suited for a high performance permanent magnet by handling ferromagnetic particles broken down into micron order.

Diagram 4 : Revealed structure of Nd-Fe-B magnets



The crystal structure of the intermetallic compound which constitutes the Nd-Fe-B magnet. The structure in which the neodymium atoms are between the layers that iron atoms form produces superior magnetic properties, and boron which is a mere 1% of the weight is thought to be effective in raising the Curie temperature.

In addition, they were still in the process of development and had various issues to overcome before commercialization, such as further improvements in heat resistance and corrosion resistance. However, by replacing a part of the neodymium with dysprosium, heat resistance was improved and with the newly developed coating technique, the heat corrosion problem was also overcome.

The progress of neodymium magnets has achieved energy conservation and is contributing greatly to the preservation of the global environment

Neodymium magnet, the world's strongest magnet was created from the inspiration gained at the symposium in 1978. In the 1980's and 1990's, research and development was carried out, and presently, neodymium magnets which have the dream-like performance of 50MGOe are being mass produced.

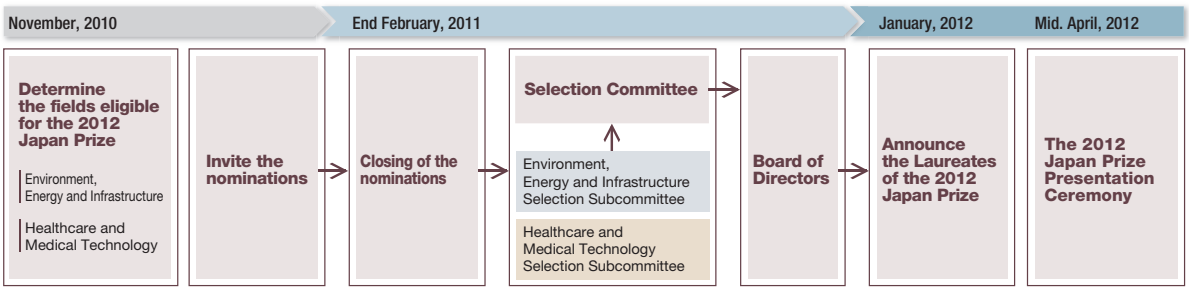
Additionally, the impact that neodymium magnets have had on society has also proved extremely great. Not only they have made possible higher performance electronic products including HDDs, which serve as external storage for computers, but they have also contributed towards the development of environmental technology such as energy conservation and new energy sources.

Furthermore, motors using neodymium magnets are more compact and have higher efficiency in comparison to the conventional dielectric motors. Thus, they are used extensively from household electronic appliances such as air conditioners, refrigerators and vacuum machines to elevators, transport machinery, machine tools and heavy construction machinery, thereby contributing greatly to energy conservation. Motors account for a high percentage in the global power demand, and in Japan, for instance, it occupied 57% of the domestic power demand in 2005. By replacing traditional induction motors with high efficiency motors using neodymium magnets, a considerable amount of electricity can be saved. Additionally, not only are they used as effective measures against global warming and application for wind-generated electricity which is rapidly spreading as a new source of energy, but they are also used for all hybrid and electric cars. Thus, their contribution toward energy conservation and the reduction of carbon dioxide emissions is steadily increasing.

In 1988, Dr. Sagawa founded Intermetallics, a research and development company. In cooperation with university researchers, he has pioneered new potential for neodymium magnets. For example, in order to improve the temperature properties, a large quantity of dysprosium is used in neodymium magnets. However, similar to cobalt, dysprosium is a very rare resource. Intermetallics has developed a new manufacturing process where dysprosium use can be reduced to a half or eventually to one-tenth in order to achieve the same conventional magnetic force. It is anticipated that this can lead to increasing popularity of environmentally friendly electric cars and effective use of natural resources.

Nominations and Selection Process

- Every November the Fields 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 13,000 nominators, strictly comprised of prominent scientists and researchers from around the world invited by the Foundation, to nominate the candidates through the web by JPNS (Japan Prize Nomination System). The deadline for nominations is the end of February of following year.
- For each field, a Selection Subcommittee conducts a rigorous evaluation of the candidates' academic achievements. The conclusions are then forwarded to 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 one year 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 mid-April in Tokyo.



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(alphabetical order, titles as of December, 2011)

Fields Eligible for the 2013 Japan Prize Selected

Areas of Physics, Chemistry and Engineering

Materials and Production

Background and rationale:

Discoveries and inventions of new materials with unprecedented functions as well as advanced production technologies have brought about numerous technological innovations, thereby contributing greatly to the advancement of society.
Development of materials with new functions such as semiconductors, natural products, nano-materials and new catalysts, and also new production technologies such as computer-aided design and manufacturing and measuring techniques have all contributed in creating highly developed and innovative industries of today.
In order to make effective use of finite resources, protect the environment and maintain the continuous prosperity of our society, further development of materials with new functions and epoch-making production technologies have come to be indispensable.

Achievement eligible:

The 2013 Japan Prize in the fields of "Materials and Production" is awarded to individuals who have made significant contributions to society by achieving momentous scientific and technological breakthroughs that improve the quality and safety of people's lives by designing and developing materials with new functions, or advanced production technologies that will create new products and industries.

Areas of Life Science, Agriculture and Medicine

Biological Production and Biological Environment

Background and rationale:

The existence of human being on Earth is completely dependent on the continuous and diverse use of biological resources. In recent years, however, the biological environment of our planet which fosters indispensable biological resources is deteriorating rapidly.
Despite the advent of many technological innovations that have dramatically increased our food production capacity, the human race is set to outgrow that capacity at an even greater pace.
In order to protect the precious biological environment in our global society, there is an ever growing need for development of environmental technologies for conservation of biodiversity and creation of sustainable and environmentally-conscious biological production technologies.

Achievement eligible:

The 2013 Japan Prize in the fields of "Biological Production and Biological Environment" is awarded to individuals who have made significant contributions to the welfare of society by achieving momentous scientific and technological breakthroughs in development of technologies that will measure, evaluate and respond to the effects of human activity on the environment, thereby helping to protect and conserve biodiversity and biological environment, or eradicate hunger and poverty by improving biological productivity of food and other useful materials.

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(alphabetical order, titles as of December, 2011)

Schedule (2013-2015)

The fields eligible for the Japan Prize (2013 to 2015) have been decided for the two research areas, respectively.
These fields rotate every three years, basically.
Every year the Fields Selection Committee announces the eligible fields for the next three years.

Areas of Physics, Chemistry and Engineering

Year	Eligible Fields
2013	Materials, Production
2014	Electronics, Information, Communication
2015	Resources, Energy, Social Infrastructure

Areas of Life Science, Agriculture and Medicine

Year	Eligible Fields
2013	Biological Production, Biological Environment
2014	Life Science
2015	Medical Science, Medicinal Science