

4. Survey results in “Life science”

4.1. Trends in noteworthy domains

4.1.1. Progress in cancer research

Since 1981 cancer has been Japan’s biggest killer, and the importance of this disease is reflected in the results of this survey, with six of the top 20 topics in degree of importance cancer-related. We can put this down to the fact that interest in cancer is not limited to researchers who are cancer experts, but is also found in researchers from a cell biology and molecular biology background. Improvements in the treatment of cancer using surgery, radiotherapy and chemotherapy have been achieved for individual cases, and the five-year survival rate is steadily rising, albeit very slowly. But unfortunately, despite the tremendous efforts of researchers and the massive injection of funds, we are still waiting for a breakthrough in the development of a cancer drug that can promise a dramatic improvement in the survival rate.

Over the past ten years, Japan has promoted research that sought to elucidate the essence of cancer, based on the comprehensive anti-cancer strategy formulated at a special cancer-related cabinet meeting in 1983. This work has led to an understanding that cancer is cell mutation caused by the progress of genetic mutation at multiple levels due to a range of factors, including oncogenes and unexpressed oncogenes, and different cancer treatments can be used according to individual cancer characteristics. Of late, wide-ranging attention has been drawn to cancer characteristics, genetic instability, and the relationship between gene polymorphism and carcinogenic susceptibility. On the other hand, unfortunately we have not seen the desired progress in the important areas of cancers caused by the environment, development of new chemotherapeutic agents, and cancer immunotherapy. A reason for this is a lack of basic research data in the more complex aspects, such as avoiding side-effects and tumor heterogeneity, and because of this research had come to a standstill. It is also a fact, though, that experts have begun searching in a new direction, namely gene therapy, based on bioscience technology and basic cell biology research results. For example, the fact that analysis of carcinogenesis centering on oncogenes and the signal transmission system in cancer cell growth, and research into cancer cell growth, infiltration and metastasis control mechanisms through extracellular substrate molecules and various growth factors is being promoted vigorously has signaled a new phase in the biological approach to cancer treatment. The identification of a gene causing breast cancer (BRCA1) through genetic analysis of families with a history of breast cancer, centering on genome research, will contribute significantly to the establishment of gene therapy for the prevention of cancer. A great deal of effort is also going into the development of gene therapy techniques that aim at selectively destroying cancer cells through the framework of apoptosis.

Surgery can be an extremely effective means of treating some cancers if they are detected and treated early enough, excluding cancers located in areas that cannot be operated on, such as brain tumors. Cancers are indeed diverse, and it is this very diversity that has made the treatment of cancer so difficult. It is, however, pleasing to see that research based on current gene analysis is slowly shedding light on the complex biological phenomenon that is the cancer cell, and this should increase our understanding about cancer diversity. The advance of modern civilization is taking a heavy toll on the global environment, so it is crucial for our future that we search for and identify external environment or other lifestyle factors that can turn a healthy cell cancerous, and clarify the connection between those external factors and carcinogenesis. Though it will be possible to use genetic screening to identify and treat groups at risk of cancer, the fact that not all people with potential cancer-causing genes develop the disease in any of its forms means that researchers have to proceed very carefully along this line of research, ensuring it does not lead to any possibility of discrimination against the human rights of affected individuals whatsoever.

In this survey we selected important themes in the four domains of 1) basic biological elucidation of cancer, 2) widespread use of methods for the early diagnosis of cancer, 3) development and widespread use of effective cancer treatments, and 4) epidemiological surveys of cancer risk factors (cancer characteristics). The forecasted realization time for topic “01: Identification of most genes related to cancer, and elucidation of the relationships between those genes and carcinogenesis” is 2014; “02: Development of anti-cancer agents which

target the manifestation functions of cancer genes” is 2010; “28: Widespread use of treatment methods for dysdifferentiating carcinogenic cells” is 2020; “48: Development of drugs capable of preventing the occurrence of certain types of cancer” is 2010; “49: Practical use of effective means to prevent metastasis of cancer” is 2013; and “72: Elucidation of the factors within daily life which influence the process of carcinogenesis” is 2012.

It is hoped that in addition to the extensive research into the suppression of cancer carried out thus far and the tremendous effort of researchers, the results of this Delphi survey will not only be of use in future cancer research, but also help to further improve the level of individual basic research, facilitate the prevention, diagnosis and treatment of cancers whose progress is not readily discernible due to a range of complex factors, and expand the basic cytobiological knowledge of cancer.

(Moriaki Kusakabe)

4.1.2. High-speed genome analysis technology and application of genome information

All living organisms produce proteins based on their inherent genetic information. The process by which genetic information is translated into “form” and “function” such as protein, in short the manifestation process, is represented by the flow DNA \rightarrow RNA \rightarrow protein. This information flow is referred to as “central dogma,” and occurs continually in humans and most other living organisms. This is a fundamental action that is at the core of life.

The genome structure is described by the sequence of bases (A (adenine), T (thymine), C (cytosine), and G (guanine)) of a chromosome DNA, and the whole base sequence over the full length of the genome amounts to about five million in a coliform bacillus, and a massive three billion or so in humans. Genes are read by messenger RNA made up of on average 2,000 base pairs (from several hundred up to almost 20,000). These are for coding proteins, and within the whole genome of humans and mice, there are about 100,000 genes, accounting for about 5% of the whole genome. Elucidating the genome of an organism and the whole genetic structure will provide information about the structure of proteins coded by genes, and will contribute significantly to the life science field.

In the previous survey, respondents forecasted that determining the entire DNA base sequences in human chromosomes would be realized in 2010, but in this survey, respondents revised their forecast to about 2003. The main reasons for this reassessment to an earlier year are the advancements in genome technology and the rapid development of new technologies, discussed later, that have taken place over the past few years.

The effects that the genome project will bring are:

- i) Capability of analyzing the sequence information that encodes all proteins (nucleotides over the entire length of mRNA), which is the genetic product, and the entire primary structure of a genome; and
- ii) Development of new generation genome technologies that can determine this.

In life science in the 21st century, the process of linking genes and their functions is expected to be accelerated by base sequence information and high-speed DNA analysis technology. This information and technology will become a decisive intellectual resource not only in medical science and biology, but in environment issues, improvement of agricultural species and livestock breeds, and biological manufacturing technology as well.

In the medical science and biology fields, analysis has shifted from hereditary diseases caused by single genes to multiple-factor hereditary diseases. The mutant genes causing the ten major hereditary diseases in humans (e.g. muscular dystrophy) have already been isolated, but even though adult diseases (e.g. diabetes, hypertension, and arteriosclerosis), mental diseases and cancer, which affect all humankind, are all hereditary disease, few attempts have been made to elucidate the causes because of the large numbers of genes involved in each of the diseases (topic 74). Research into these human diseases require pure-breed and crossbreed experiments, and this reinforces the value of genome analysis of mice and other laboratory animals for the following reasons.

1. High homology between human and mouse genes;
2. Commonality of many human and mouse diseases;
3. Genes can be obtained from the mice in all stages of their life cycle, but this is not the case for humans;
and
4. Crossbreed experiments are possible, and results can be obtain quickly.

In this sense, topic “21: Practical use of technology to analyze whole genome sequence in livestock breeding, and fisheries, agriculture and forestry” is important.

The gene identification approach will probably shift from the positional cloning method to the positional candidate method once the position of each cDNA (cDNA is DNA created from the removal and copying of mRNA, which carries DNA messages in the process of protein synthesis; this corresponds to the information on the protein blueprint extracted from the genome) on the chromosome is clarified through cDNA and genome base sequence information built up from the genome project. And through the clarification of the whole gene sequence, a new approach to drug preparation is possible. Coupled with advancement in research in new molecular biology fields (aging, cell death, differentiation, morphogenesis, etc.), these cDNA will also form the basis of gene therapy.

Information about the whole gene will provide valuable data for analysis of the higher-order structures of proteins and the basic cell motive. In this sense, topic “25: Establishment of technologies enabling prediction of the functions of proteins from their higher-order structures” is important. This will also be a source of basic information for next generation brain sciences and issues such as aging.

Analysis of human genome will teach us much about the process of human development, because locked within the genome is the history of human evolution. This analysis should also provide us with knowledge about human differences and genealogy.

If we can build up our knowledge base about not just human genome, but that of various other organisms as well, we will have a better understanding of the relationships between organisms, and also of the ecosystem in which we all live.

It is pleasing to see that Japan has developed its own techniques for several new methods (PCR-SSCP, RLGS (RLCS), molecular indexing, full-length cDNA synthesizing) in a field where there is a constant pursuit for the development of new techniques for genome technology. On the other hand, while techniques such as DNA chip technology are expected to speed up DNA analysis (DNA diagnosis) dramatically in the future, Japan is lagging well behind in R&D, so urgent action in this field is essential. In the previous survey, the development of methods for collecting and storing data on and identification of higher-order animals, as reflected by the “completion of a comprehensive human protein data library,” is forecasted to be realized in 2014.

What is most important from now on is the development of high-speed and low-cost technologies for determining base sequences. We want to be able to extract data in volumes of three billion base pairs for higher organisms at a rate 10-100 times faster than current levels. From the mid 1990s, advances have been made in bringing together analysis resources involving numerous fluorescent sequencers and the work of many people as a large-scale system for determining bases sequences, and this is now functioning as a genome center.

Centers that can determine base sequences of 20–80Mbp a year have been established in Europe and the U.S., and these are the first moves toward a shift to “big science” in medicine and biology. However, new techniques have been appearing in quick succession in the development of basic methods and cost cutting, and DNA analysis centers that use small but high-performance systems are expected to appear in the very near future. Most technologies in this field have been developed in Europe or the U.S., so acquiring the intellectual property rights to these technologies is a crucial task for Japan. In fact it is not an exaggeration to say that the future of Japan’s DNA analysis industry (gene analysis, diagnosis, treatment and drug development) in the 21st century rests on the outcome of this intellectual property rights issue.

Regarding the intellectual property rights covering genome analysis data, in response to an application by

research institutions in the U.S. and U.K. for patents for base sequence data on genome fragments, the courts ruled that patents cannot be approved unless the data are connected with functions in the genome structure. Therefore considerably more effort will be made in linking genes and their functions using dictionaries produced from genome analysis.

Thus in promoting genome technology, it is extremely important for us to strike a balance between development and organization aimed at making it more systematic on the one hand, and international competition and cooperation on the other.

The following are some of the issues facing this technology in the future.

First, with expectations that the human genome will be completely mapped out around 2003, we have to fully discuss Japan's contribution to this and Japan's national interest (cost versus effect), and formulate policies that set the foundations for life science into the 21st century. Determination of the entire primary structure of genome and the full cDNA chain is the principal goal of genome technology, but following this we must move quickly to establish a new life science base with our sights on how we can utilize a single dictionary (generally, the beginning of the second phase of genome science; this is referred to as the post-genome era, but I do not believe this is an appropriate term).

Next, rapid progress is expected in the connection of each gene with its manifestation character (identification of the genes causing mutation), elucidation of the cascade among all genes that takes into account the entire genome (topic 23), analysis of genome and full cDNA chain in new drug development technology and all organisms, and elucidation of the mutual operation between genetic products. Progress will also be seen in the analysis of gene functions other than those fragments transcribed from the genome structure, and also in the description of the diversity of the human genome.

As was often pointed out, in the case where topic "03: Utilization of information about the gene structure of each individual patient in diagnosis and treatment" is realized, we must ensure that elucidation of an individual's genetic information does not disadvantage that individual. And this will probably require considerable debate.

Clearly, genome research is about to enter a new phase. It is also clear that the effective use of the mass of information assembled from genome research will greatly expedite life science research. We will need to develop the next-generation computer science that will enable us to process and analyze this rapidly expanding information base. It is important to examine and establish without delay a research structure and human resources development system that respond to the new era in medical science, biology and other natural sciences through the emergence of new research styles using the volumes of base sequence information.

(Yoshihide Hayashizaki)

4.1.3. Molecular mechanisms of development, differentiation and morphogenesis

Life on our planet started 3.8 billion years ago, and we humans, currently the most advanced life-form, have much in common with other eukaryotes; the life process from a single fertilized egg, through development, differentiation, and morphogenesis to the adult form in humans is in principle no different from that in all other animals. That so, it is entirely natural that being so curious about our own existence, humans have for ages craved an answer to the simple scientific question of to what extent are we similar to and different from other animals, and how is that process predetermined and how is it differentiated. To what extent can our current level of life science answer this question, when will we have a complete answer, and how do researchers with an interest in this field feel about this are all questions that raise considerable interest. It is also natural that there is considerable interest in the mechanism by which genetic defects trigger disease, and the aging mechanism that brings on change in the living body with the passage of time, and also whether it is possible to prevent or treat this.

At the time of the previous survey in 1991, the best techniques for analyzing development, differentiation and the molecular mechanism of morphogenesis were gene cloning using the gene recombination and polymerase chain reaction (PCR) methods, base sequence determination, and functional analysis based on

these results and homology at the protein level. These are still important techniques, but these days the techniques of specification of the gene manifestation segment through in situ hybridization, gene knock-out, preparation of transgenic individuals, and effect analysis of artificial manipulation at the development stages of the individual, which can be referred to as developmental engineering are more widely used. These techniques reveal the genes connected with development, differentiation and formation of tissue and the individual, and analyze the links between these genes and hereditary diseases. Furthermore, in relation to aging, advances have been seen in the elucidation of the mechanism and actual state of aging at the molecular level, as typified by telomerase.

As is the case in science, in some aspects developments at times exceed expectations. The formation of an individual based on information in the nucleus originating from tissue cells of the adult form, which had been thought to be exclusive to plants, was done with a sheep, which essentially differs little from humans. The paper* announced to the world that a cloned individual had been born. In this survey, the forecasted realization time of topic “15: Development of technology to regenerate organs or individuals from separated animal cells” is 2023, and of topic “78: Practical use of technology for producing cloned individuals from the cells of livestock” is 2015; but these two topics suddenly became reality shortly after the round two questionnaire. Of course, if the premise “using cells grown *in vitro*” is attached, realization will be quite some time in the future, if at all.

Topic “24: Development of technology to analyze the genes manifested in a single cell in higher animals with an accuracy in the order of 1 mRNA molecule” will be a powerful tool in tracing the progress leading to the elucidation of the molecular mechanisms from development to formation of the individual, but it is unlikely to be realized before 2014, while the forecasted realization time for topic “23: Elucidation of the mechanism by which differentiation and functions from fertilized egg to individual are manifest in mice etc.” is 2023, and for topic “84: Complete elucidation of the molecular mechanisms of development and differentiation” it is 2022. The knowledge derived from this process will probably be used in the realization of other topics, and most researchers believe topic “29: Widespread use of methods of multiplying stem cells in test tubes and using them for treatment purposes” will be realized in 2015, and topic “28: Widespread use of treatment methods for dysdifferentiating carcinogenic cells” in 2020. Organ donation and the use of artificial organs in organ transplants is currently the subject of much debate in Japan, and in this regard, topic “47: Elucidation and artificial control of the molecular mechanisms of the morphogenesis of human organs” is expected to be realized in 2022, but it is interesting to note that the realization times for topics “15: Development of technology to regenerate organs or individuals from separated animal cells” and “54: Clinical application of technology enabling organs to regenerate through the multiplication of their own cells” are 2023 and 2021, respectively.

Naturally, elucidation of the molecular mechanisms of development, differentiation and morphogenesis, in itself, generates high expectations of “expansion of intellectual resources,” but when it is linked with topics dealing with actual diseases and their treatment, and such issues as artificial organ formation, expectations tend to be higher regarding “response to people’s needs.” These themes contain various difficult ethical questions and their progress will have to be subject to public acceptance, and how these are dealt with will have a significant influence on realization times.

(Kazuo Nagai)

4.1.4. Brain functions

The 21st century is said to be the “century of the brain,” and expectations about brain research are currently extremely high. First, it appears possible that we will find answers about human mental functions, and based on this, new concepts about what it is to be human are expected to be established in the next century. Second, hopes are high regarding research into the causes of mental and nervous diseases, such as dementia, and the development of treatments for those diseases. Third, with the elucidation of brain functions, there will also be

* The paper announcing the world’s first successful creation of a cloned sheep by a team headed by Dr. Ian Wilmut at the Roslin Institute near Edinburgh, Scotland, was published in the journal *Nature* (27 February 1997).

high expectations for the application of that knowledge in engineering fields such as artificial intelligence and more advanced computers, an especially important theme for countries like Japan that need to build industries that can generate high added value.

Rapid advances are being made in molecular-level research into the mechanisms being applied when neurons encode information as electric signals, and transmit those signals to adjacent neurons — ion channels, neurotransmitter receptors, and their modification — through the introduction of molecular biological methods and advances in physiological methods. Against this backdrop, the mechanism of learning and memory, one of the higher functions of the brain, is being actively researched at the synapse level. Typical examples are “long-term potentiation” and “long-term depression” of synaptic transmission discovered in the hippocampus, regarded as an essential structure in certain memory functions, and molecular mechanisms here are gradually being elucidated. We can perhaps look forward to its overall elucidation and development of drugs that will improve memory and learning functions in the relatively near future. But we do not know how changes in synaptic plasticity are actually linked to memory, and this perhaps illustrates that while tremendous progress is being achieved in the elemental aspects of brain research, research into the functions of the brain as an integrated organ is falling further behind. What has the potential to cut away this disparity is the technology to produce mice lacking in unique genes (knock-out mice) using homologous recombination, and with this technology, when a certain gene is lacking (coded protein) we can examine abnormalities shown by the mouse from the molecule and cell level to the behavior level. The function of genes (protein) lacking from the start of development are readily compensated by other genes (protein), so in some aspects it is difficult to interpret the results. Nonetheless, scientists are in the process of developing techniques to limit the manifestation or non-manifestation of certain genes to specific cell groups, or change the genes at will after development of the individual, and if these techniques prove successful, they will do much to lessen the disparity mentioned above.

At present, research into the cerebral cortex, the foundation of high-level brain functions, is most advanced in the vision area, and what this research has revealed is that subjectively unified visual experiences are processed in parallel by way of information processing in the cerebral cortex; for example, when we see a red apple fall from a tree, we experience this as a uniform consciousness, but in the brain the information — form (apple), color (red) and action (falling) — is processed separately in different spheres. How these parallel and dispersed processes are combined in the brain to form a uniform conscious experience is one of the great mysteries of the brain that we have yet to unravel, and the fact that in the past few years brain scientists have begun to look seriously at issues such as this is a sign that “consciousness,” which to date has been the realm of philosophers, is now being approached from a scientific angle. Research into brain functions that form the foundations of language and thought is methodologically difficult because these skills are regarded as peculiar to humans, and it is far from easy to devise a specific strategy for this. To date mainstream research into brain functions has focused on recording the activity of single neurons using microelectrodes, but microelectrodes alone have their limitations in measuring mental functions formed by the cooperation among and functioning of massive numbers of neurons. What is needed is a method that can record the activity of large numbers of neurons simultaneously over an extended period and analyze the data obtained effectively. We can also look forward to advances in recent non-invasive research methods, such as positron emission tomography (PET) and functional MRI. To date researchers have been examining functional maps of associated areas in the human brain drawn up psychologically using patients with brain damage, but new non-invasive methods are already making a major contribution to the preparation of functional maps of healthy brains. And we can look forward to these methods making similar contributions to research into speech and thought. But these methods do not observe nerve activity directly, rather they observe changes in blood flow or glucose metabolism resulting from nerve activity, so there are some limitations. It is hoped that PET will be able to show how and in what area of the brain functional molecules change following brain activity by labeling functional molecules such as neurotransmitters or their messengers within the cells, and similar substances and injecting them into the human subject.

It is crucial that research into brain functions does not focus entirely on the “hardware,” such as neurons, synapse, on the linkage between neurons, and intuitive understanding and hypotheses based on this, but proceeds parallel to and in cooperation with theoretical research using mathematical models. For this,

interdisciplinary research that includes engineers is essential, and I have no doubts that such research will bear fruit also when knowledge of brain functions is applied in the field of engineering.

(Masaki Sakurai)

4.1.5. Elucidation of plant functions and its use

Research aimed at elucidating plant functions has advanced remarkably over the last ten years, and one of the main reasons for this is that researchers across the world have focused on the shepherd's purse as a model plant. Various genetic maps are steadily being completed thanks to the smooth progress of the genome project using the shepherd's purse coupled with the accumulation and analysis of numerous mutants, and this is indeed a milestone in plant research to date. On the other hand, plants are a vital source of food for humanity, and like the shepherd's purse project, genome projects with rice, maize, tomatoes and other important agricultural products are also proceeding smoothly, and it should be noted that with various genetic maps being prepared using numerous mutants accumulated over many years of research, scientists are beginning to isolate the myriad of genes that control the agriculturally important properties.

Efficient gene introduction methods were developed earlier for plants than for animals, and from the early 1990s, many practical recombinant plants, such as pest- and herbicide-resistant farm products, have been raised. In 1996, food from recombinant farm products was first consumed on a wide scale not just in the U.S. and Canada, but in Europe and Japan as well, and this is an extremely important development for the future of humankind. In the previous survey, the topic "Widespread use of new plants produced using gene manipulation technology for food" was forecasted to be realized in 2003, but it was actually realized seven years earlier, illustrating the rapid pace of research in this field. Behind this is an understanding among researchers throughout the world that solving the food shortage that is likely to accompany the population explosion predicted in the first half of the next century is absolutely crucial for the survival of humankind.

The biggest issues directly confronting humankind on a global scale are food, environmental degradation and energy problems, and in this survey we set many topics connected with the elucidation and use of various plant functions thought to be vital to the resolution of these problems, but excluding topics "35: Widespread use of bioplastic production so it accounts for 10% of total worldwide plastic production" and "91: Development of technologies which dramatically improve photosynthetic ability in order to increase food production," the perceived degree of importance to Japan is generally lower than that of medical topics, and especially those dealing with cancer. Certainly, aging and its related medical care are important issues that cannot be ignored in any developed nation, but if we think at the global level, surely feeding the world's expanding population is more important than medical care in the long-term survival of the human race, and without food, medical care has little significance. We in Japan depend on imports for most of our food, and in our daily lives there is no hint of any food crisis. We are living in an era of plenty as far as food is concerned, yet in other parts of the world people are still dying of starvation in huge numbers. A future world food crisis will impact on Japan just as much as it will on many other countries, so we need to do much more to try to resolve the food problem before it becomes critical.

The most important measures we can take to put and end to food shortages and environmental destruction that some have said will reach crisis proportions in the early part of the next century will be to elucidate the various plant functions, improve plant species, and utilize those plant functions at a high level. If we look at the survey topics from this perspective, there is a concern that the forecasted realization times may be on the late side; for example, the forecasted realization time of topic "92: Practical application of breeding techniques for plants resistant to dry and saline conditions aimed at desertification prevention" was 2009 in the previous survey but 2014 in this survey, and that of topic "91: Development of technologies which dramatically improve photosynthetic ability in order to increase food production" was 2011 before but 2017 this time. Elucidation of plant functions and research into the utilization of those functions are the foundations upon which humankind will survive, so it is crucial that research into this moves ahead so that topics such as these can be realized earlier than forecasted.

(Hiroshi Kamada)

4.1.6. Structural biology

Research aimed at trying to understand life phenomena based on the three-dimensional structure of biopolymer is said to have started with the elucidation of the three-dimensional structure of protein using X-ray crystal analysis in the 1960s. Because of advances over the past five years in protein engineering technology that allows us to produce recombinant protein or new protein efficiently, mass supply of protein that previously had been difficult or impossible to produce naturally is now possible, and with this, elucidation of the three-dimensional structure of protein progressed rapidly, and a new academic field of “structural biology” was born. Structural biology seeks to elucidate biofunction mechanisms based on the three-dimensional structures of biopolymers such as proteins and nucleic acid and their changes, and through this, to understand life phenomena, and it is expected to generate new basic concepts and research guidelines not just for the basic sciences, such as biophysics and molecular biology, but also for life science and biotechnology over a broad range of applied fields, including medicine, pharmacy, and engineering.

As of October 15, 1996 the Protein Data Bank (PDB) contained 4,873 registered structures, 1,051 more than in October 1995. This highlights the tremendous advances made in three-dimension structure analysis technology during these twelve months. Researchers can now analyze hundreds of thousands of protein structures that they could not before, and papers detailing analyses of conjugated proteins that interact with nucleic acids such as DNA binding protein were published one after the other. Large-scale production of recombinant protein using genetic engineering techniques and advances in new analysis technologies such as synchrotron radiation are expected to generate a further rapid increase in the number of registered structures.

The structural biology topic “04: Development of methods for surmising new functions of proteins from human genome information” is forecasted to be realized in 2011. Advances in gene analysis technology and its growing use and the progress of the genome analysis project are pushing up dramatically the number of genes whose base sequences are being determined. There is thought to be considerable demand for methods of predicting the kind of functions genes and gene products perform within an organism, including prediction of three-dimensional structures. The realization of this is linked to the realization of topic “25: Establishment of technologies enabling prediction of the functions of proteins from their higher-order structures,” which is forecasted to take place in 2014, but work in the development of methods of predicting higher-order structures from primary order structures of proteins is expected to become more dynamic as the number of three-dimensional structures of proteins registered in the PDB soars. Topic “17: Practical use of continuous, industrial-scale production of protein by means of a non-cellular protein synthesizing technique” is an encouraging theme for examining the structures and functions of proteins coded by new genes, and though industrial-scale production is not expected before 2015, the technique does show promise for manufacturing gene products from unknown genes, and analyzing their structures and functions. As for improving the catalytic functions of enzymes through structural biology, topic “13: Development of biomimetic elements with better functional characteristics than enzymes” is expected to be realized in 2014. Scientists are looking to the development of new catalysts that compensate for the weaknesses in enzymes through the elucidation of the 3-D structure of the active part of enzymes and the molecular design and synthesis of biomimetic elements based on this. Along with this, topic “16: Practical use of technology to design/synthesize thermostable protein” is forecasted to be realized in 2009, and in the future the elucidation of the 3-D structures of thermostable enzymes from thermophilic bacteria and super-thermophilic bacteria will make the molecular design of thermostable enzymes possible, and catalytic reactions using thermostable enzymes on an industrial scale will be put to practical use.

In conclusion, we expect progress in the analysis of biopolymer at the molecular level, and while the forecasted realization time of topic “19: Elucidation of the molecular mechanism of life creation” is well into the future, we can look forward to interesting results from research that steadily moves toward the origin of life through advances in structural biology.

(Izumi Kumagai)

4.1.7. Substance and energy conversion

Humankind has created industries that produce substances necessary for survival and general life through the skillful use of the capability to convert substances and energy inherent in living creatures. Good examples of this include the fermentation and microorganism industries, which utilize the substance and energy conversion capabilities of microorganisms, and the oil and fat manufacturing industry and agriculture, which utilize the substance and energy conversion capabilities of plants.

In recent years attempts to use these substance and energy conversion capabilities of organisms to resolve various global environmental problems have attracted world attention. These attempts include biomass fuel using recyclable biomass resources, production of bioplastics, fixing biological CO₂ using microscopic algae, and application of bioprocesses to the chemical industry, which is imposing an increasingly serious burden on the global environment because of its numerous production processes that use various kinds of organic solvents. Biomimetic research aimed at copying the substance and energy conversion capabilities of organisms, such as carbon or nitrogen fixing, and research aimed at developing artificial systems that exceed organic functions are expanding on a world scale in the research area of supermolecular chemistry.

In this survey, we prepared 11 topics connected with substance and energy conversion, of which six deal with global environmental problems — “35: Widespread use of bioplastic production so it accounts for 10% of total worldwide plastic production,” “36: Widespread use of fuel oil production technology using microorganisms etc. so it accounts for 10% of total worldwide fuel oil production,” “37: Widespread use in chemical industry processes of biological catalysts which are resistant to organic solvents, heat, etc.,” “38: Establishment of a system for biologically reducing and fixing CO₂ using energy other than light,” “39: Practical use of technology for the biological fixation of highly concentrated carbon dioxide at thermal power plants” and “81: Practical use of plants accumulating high amounts of hydro-carbon as fuel sources” — and five deal with the construction of biomimetic artificial systems — “17: Practical use of continuous, industrial-scale production of protein by means of a non-cellular protein synthesizing technique,” “18: Development of light energy elements patterned after photosynthetic response,” “31: Development of engineering technologies that apply biological energy conversion mechanisms,” “32: Development of technology for synthesizing artificial cells that replace such functions as cell membrane transport and substance conversion” and “33: Development of artificial membranes with functions similar to biological membranes.”

The six topics dealing with the global environment have an average degree of importance of 71.2, just over five higher than the overall average of the life science field (66.1). Topic “35: Widespread use of bioplastic production so it accounts for 10% of total worldwide plastic production” is the highest with 87, and ranks fifth among all life science topics. This result reflects the belief that the widespread use of biodegradable bioplastics produced from recycled material can alleviate the problem of waste plastic disposal, which is a major burden on the global environment, and resolve the various problems that arise from the fact that the majority of fossil fuels, which are not recyclable, are consumed in plastic production. Most of the six topics also exceeded 90% in the expected effect “resolution of global problems,” and are ranked high among the top topics with this expected effect. Topic 37 was slightly higher in “contribution to socioeconomic development” with 82%.

As for the five topics dealing with construction of biomimetic artificial systems, topic “18: Development of light energy elements patterned after photosynthetic response” is rated the highest in degree of importance with an index of 77, but with degree of importance indices between 58 and 63, the other four topics are below the overall life science average. All five topics have “contribution to socioeconomic development” as the main expected effect, ranging from 65% to 77%, and all are ranked high among the top topics with this expected effect.

The forecast realization times of all 11 topics connected with substance and energy conversion range between 2013 and 2021, slightly earlier than the overall average forecasted realization time for life science. The earliest is topic “35: Widespread use of bioplastic production so it accounts for 10% of total worldwide plastic production” at 2013, but in the past few years, a joint team comprising members from three universities including the University of Durham in the U.K. and the Mon Santo company successfully extracted bioplastic

from matured seeds and leaves of rape plants into which they had implanted genes from microorganisms that produce copolymerized polyester. This lowered production costs substantially, which in turn has given impetus to its practical use, so the realization time of this topic could actually be realized several years earlier than forecasted.

For four of the six topics dealing with the global environment, the response rate for Japan as the leading country is a high 50-70% (excluding topics 38 and 81), and this is roughly the same as that for U.S.A. Considering the overall life science rates are 82% for the U.S.A. and 36% for Japan, we can say that the level of research in Japan into technology to apply substance and energy conversion capabilities of organisms to the global environment is on a par with that in the United States, and that this is one area where much is expected from the contribution Japan can make. Of the measures the government should adopt to help realize these topics, “promote exchanges among industrial, academic and government sectors and different fields” and “increase government research funding” are rated quite high, showing an awareness among respondents that more effort has to be made to promote such exchanges through NEDO and RITE projects etc., and that more money has to be allocated for research.

(Teruyuki Nagamune)

4.1.8. Immune system

(1) Trends in immunology research over the past five years

i) Background and major research trends to date

In the latter half of the 19th century various pathogenic bacteria were identified as a part of programs to prevent infectious diseases, and research proved that immunity can be built up against an infectious microorganisms by introducing a weakened version of that microorganism into the body, and with this the concept of vaccination was put forward. Later it was shown that the immune response is classified into humoral immunity, which utilizes circulating antibodies, and cellular immunity, which utilizes lymphocytes, and that each kind of immunity requires the interaction of lymphocytes. Both old and new research themes in immunology are (1) how are antigen-specific lymphocytes chosen, and growth and differentiation induced; (2) how is the diversity and multiformity of the immune response formed; (3) what are the mechanisms by which immune tolerance appears; and (4) what is the substance of immune memory. In the 1970s it was discovered that the reconstitution of antibody genes, which are B-cell antigen receptors, is evoked following the B-cell differentiation stage, and the antigen specificity of antibodies and molecular mechanisms of diversity manifestation were elucidated. In the 1980s, the structure of T-cell antigen receptors (TCR) and major histocompatibility complex (MHC) genes were isolated, and it was found that T-cells recognize antigen peptides and self MHC molecules by means of TCR complex on the cell surface and are then activated. It was also shown that T-cells that respond actively to their own antigens are eliminated at the maturation/differentiation stage within the thymus. The latter half of the 1980s was marked by the search for cytokines and their receptor genes, which are essential for the activation, growth and differentiation of immune response cells. Numerous immunologically functional molecules and binding molecules were newly identified, and their importance in immunoregulation was established. There is no doubt that the explosive progress of research in this field can be put down to technological innovation and progress in gene manipulation and cell engineering, and the active introduction of transgenic mouse production techniques.

Major research themes have been (1) antigen analysis of foreign pathogenic microorganisms that activate the immune system, and classification of the host responses to these microorganisms; (2) identification of molecules responsible for the immune response (humoral and cellular) to pathogenic microorganisms, and the groups of cells that are involved in this response (T and B lymphocytes and macrophages); (3) isolation of TCR and elucidation of antigen peptides recognized by TCR complex and self MHC; (4) isolation and functional analysis of the immunologically functional molecules (cytokines, binding molecules, secondary stimulant molecules, etc.); and (5) elucidation of the cellular characteristic and molecular mechanisms of immune tolerance, i.e. the elimination of self-reactive cells during the maturation process. Thus the main interest during this period was focused on when the immunological “self” and “not-self” recognition mechanism would be elucidated, and at that time the forecasted realization time was about 2006.

ii) Major research projects over the past five years

- 1) Fas and FasL genes were isolated and their structures determined. Functional analysis of recombinant Fas/FasL and analysis using Fas antibodies revealed that the Fas/FasL system causes apoptosis, and as a result of gene mutation, the Fas/FasL system struggles to eliminate self-reactive cells, leading to autoimmune disease. This analysis also revealed that apoptosis, including the Fas/FasL system, has a significant part in the elimination of self-reactive cells, and clarified the molecular mechanisms behind this. Research regarding general cell death also advanced in great strides. These days, the elucidation of the molecular mechanism of cell apoptosis is one of the hottest research domains in biology.
- 2) Research into whether a humoral or cellular immune response is triggered by an antigen stimulus (immunodominance) moved forward in leaps and bounds. It showed that newly discovered cytokine IL-12 triggers a cellular immune response, while IL-4 is closely linked to a humoral immune

response.

- 3) Progress was made in elucidating the molecular mechanisms of cell signaling through immunologically functional molecules (antigen receptor complex, cytokine receptors, binding molecules, CD40, etc.). A new tyrosine kinase (JAK, Tec, etc.) family gene was isolated, and it was revealed that the gene's activation is important for signal transmission through immunologically functional genes. Furthermore, a new transcription activating molecule (STAT family) gene was isolated, and its role in signal transmission is being clarified.
- 4) Gene homologous recombination technology was widely incorporated into immunological research, producing gene knock-out mice lacking specific immunologically functional molecules. To date, knock-out mice lacking more than 50 kinds of immune-related molecules have been produced. This has helped to clarify the role of antigen receptors, transcription factors and tyrosine kinase in the early development of lymphocytes within the body, the function of cytokines and receptors connected with growth and differentiation and the molecular mechanisms of cytokine signal transmission, the role of molecules connected with lymphocyte cell death, the role of binding molecules and various enzymes connected with the effector phase of immunity, and the role of previously unknown molecules in the control of the immune response.
- 5) The causative genes of X-linked immunodeficiency syndrome were determined, and analysis of the form of the disease progressed. From this it was clarified that X-linked serious complex immunodeficiency (XSCID) is caused by growth abnormality in T and B lymphocytes due to mutation of IL-2 receptor γ chain, that in X-linked hyperIgM syndrome the isotype conversion of immunoglobulin is not possible because of mutation of CD40 RIGANDO, and that X-linked agammaglobulin syndrome (XLA) is an abnormal differentiation of B cells caused by mutation of BURUTON tyrosine kinase (Btk).

(2) Current topics in immunity

Genetic isolation of the functioning molecules involved in immunoregulation and determination of their overall structure, the structure of T and B lymphocyte antigen receptors and the molecular mechanism of diversity manifestation, and the molecular mechanism of lymphocyte activation, growth and differentiation have been clarified. However, there still remains much to uncover, including the molecular mechanism of immune tolerance and its failure; the mechanism by which self-reactive cells are eliminated (apoptosis); the mechanism by which a dominant immune response (humoral or cellular, Th1 or Th2) to an antigen is determined; the cellular nature and molecular mechanism of an immune response through the mucosa; the mechanism of intractable inflammation, which can be seen in autoimmune disease and allergic disorders, and its control; immunoregulation for viral infections; molecular mechanisms of immune diseases and repair of the immune system. Examples of this include: 1) elucidation of the mechanism by which differentiation from multifunctional stem cells to lymph stem cells is predetermined, and the micro-environment under which this occurs; 2) analysis of the detailed mechanism by which T (thymus-derived) cells that have a strong recognition of self peptide and self histocompatibility molecules are eliminated in the thymus, and its failure; 3) molecular mechanism by which foreign protein antigens are resolved to as far as peptides within antigen cells and join with MHC; 4) the molecular mechanism of lymphocyte activation, non-response, tolerance and cell death; 5) cell signaling mechanism from immunologically functional molecules on the cell membrane; 6) analysis of infectious parasites and the host's immune response; 7) elucidation and repair of the mechanism of intractable inflammation and its control; 8) the induction mechanism of mucosa immunity and of immune tolerance by means of oral antigens; and 9) molecular mechanism by which immune memory is maintained.

(3) Importance and future prospects

As more cell groups, molecules and genes connected with the immune system are identified, and the secrets behind the molecular mechanism of immune cell growth and differentiation and the induction mechanism of immune tolerance are steadily revealed, researchers are beginning to question how the immune system at the individual level is regulated by these molecules and cells. And an urgent task researchers have is to elucidate the molecular mechanism of diseases caused by an immune response (autoimmune disease, allergies, transplant rejection, and intractable inflammation) and develop methods of repairing the immune system. In this survey we prepared four topics (05, 06, 07 and 70), and the importance index is quite high in all four (average 74.6), indicating a high level of interest in this domain among the respondents. However, forecasted realization times are all after 2010, which is slightly later than the times forecasted by the experts, and this made us realize the difficulty faced in resolving the topics and the need for more effort by researchers. Considering the importance of the topics and the high level of public interest, it is vital that everyone concerned gives even more support to the research effort.

Virtually nothing is known about how the immune system as a high-level function regulatory system functions while interfering with the nervous and endocrine systems. The results for the topic dealing with this (topic 71) in this survey showed that there is considerable interest in this theme (importance index of 78), but its realization is expected to be quite some time away (2017). Considering the importance of and high level of interest in this theme, I firmly believe much more support has to be given to the research effort. It is interesting to note that the importance index of topic “27: Elucidation of the immune mechanisms which distinguish between ‘self’ and ‘not self’” is, at 70, lower than we expected, and the forecasted realization time is later than that of the previous survey. The importance index of topic 08, which deals with apoptosis, at 65 is also lower than expected. The fact that this is a relatively new theme (it suddenly attracted world attention from the 1990s with a succession of discoveries) probably had some bearing on its survey results.

As mentioned above, research in immunity is indeed multi-faceted and diverse. The importance and future prospects of research themes in immunology as biology, and applied science in clinical medicine, and as a high-level function regulatory system are extremely high, and the results of this survey support this. The research contribution and expectations of Japan in the immunology domain are high, also as reflected in the survey results. The future of research in this domain promises to be exciting.

(Kiyoshi Takatsu)

4.1.9. Medical engineering

(1) Technological change

This is a domain in which various technologies are applied, and areas that have achieved remarkable progress over the past several years have all been backed by advances in basic technology. Contributing the most has been the progress in biotechnology in recent years, but advances in micromachine technology, virtual reality technology and superconductivity technology (generation of strong magnetic fields, and micro-magnetic field measuring technology), and the development of medical polymers and multimedia technology in home medical care have also played a key role. Many of the topics realized over past surveys are based on biotechnology, and in medical engineering, the mainstream seems to be shifting from a situation where only artificial products are used, to one now where cells and tissues are altered using biotechnology, and this is used in conjunction with artificial products. The same can be said about micromachine technology. Although there are still many hurdles that have to be surmounted before realization, the production of artificial micro-organs and tissues using micromachine technology is beginning to show signs of possibility, and this is an important force driving research in this domain. The same applies to the following technologies as well.

(2) Current topics

i) Artificial organs

Trial production and research is aimed at fully implantable artificial hearts and various other artificial organs. Although there are still many problems that have to be resolved, even with today's technology the development of compact, high-performance systems or batteries for energy transmission into the body, development of material that does not cause thrombus formation, development of microsensors that can be used within the body (within blood vessels), and the development of control algorithms are possible.

The forecasted realization time of topic "52: Development of an entirely implantable artificial kidney" is 2013. Work on the development of hybrid artificial organs (especially metabolic artificial organs) using cultured cells of organisms has been progressing, and an artificial liver of this kind has reached the clinical trial stage in the treatment of severe hepatitis (in Europe and the U.S.). And while the results are still not perfect, the number of papers presented at international academic societies and the like has been increasing rapidly, and there seems no doubt that research in this area will become a growing trend in the future (however, there is still much to be resolved regarding cultured cell reconstruction technology and the improvement and reduction in size of systems that can be used over the long term). The forecasted realization time of topic "51: Practical use of artificial organs incorporating human cells and tissues" is 2015. One direction this kind of artificial organ research is heading is the regeneration of organs using biotechnology. This is still very much at the embryonic stage, and research is at the point where various kinds of growth factors are extracted from the organism for examination, and although a degree of liver cell regeneration has been realized, the multiplication and regeneration of any organs to the desired size is still a long way off. Reflecting the current state of research, the forecasted realization time of topic "54: Clinical application of technology enabling organs to regenerate through the multiplication of their own cells" is 2021, the latest time of any topic covered thus far. But from a non-expert's point of view, considering the progress in biotechnology over the past few years, the realization of this theme could well be earlier than expected.

Another theme in this field relates to micromachines and virtual reality, and research here is aimed at producing micro-interface arrays that enable direct multi-channel input and output through the body's nervous system, and through this system, create artificial sense, such as vision. Artificial inner ears are already available, and artificial retinas have reached the stage where some animal experimentation is being conducted, but as yet the number of channels is limited, and many technical breakthroughs and considerable time will be required before this technology can be put to practical use. The forecasted realization of topics related to this — "53: Development of an artificial retina, allowing the visually impaired to regain their sight" and "56: Establishment of interface technology between neural information

and artificial organism structures” — are quite close at, respectively, 2019 and 2020.

Problems that have to be overcome when leaving an artificial object in the body for an extended period are the biocompatibility, resistance to thrombus formation and the selective permeability (parts that come into direct contact with blood) of the material used, and although not spectacular, steady progress is being made.

ii) Medical micromachines

Medicine is said to be the most promising domain for the application of micromachine technology, and hopes have been high since development of this technology first began. Although there is some question as to exactly what constitutes a micromachine, the generally accepted perception is a microscopic device that can be inserted into the body (in blood vessels, the spinal column, and the bronchiole) and has some form of treatment or diagnostic function within the body. In the early stages of micromachine technology, the general public had the idea that these machines were just around the corner, but even though it may be possible to produce extremely tiny devices (running gears), numerous technologies essential for the development of fully functional micromachines, such as energy transmission, microsensors that correspond to vision and other senses, and the transmission of such sensory information, biocompatible material, material that does not cause thrombus formation, and the means to direct the micromachine into the target location, are as yet out of our reach. Thus the reality is that considerable time and massive development effort will be needed before an overall system is developed and functioning. In this survey the forecasted realization time of topic “62: Development of diagnostic and medical treatment micromachines capable of traveling on their own inside organisms” is relatively early at 2015, but in the experts eyes, this is too early, so it would be interesting to know upon what the general respondents based their forecasts. Research is currently focused on minimum invasive surgery, in which surgery is performed in the stomach cavity and chest cavity using tiny precision endoscope systems and micromanipulators operated from outside the body through the TORAKAARU (narrow tube through which the instrument is passed), and is expected to lead to even smaller instruments with combined functions (endoscope and manipulator) that can be applied to surgery in blood vessels, the spinal column, and the bronchiole.

iii) Medical application of virtual reality

Considerable research is being directed to the medical application of virtual reality. The remote surgical system is one in which a surgeon performs surgery on a patient at a different location using a slave manipulator (surgical instrument), but through VR technology the surgeon has the sensation that he or she is actually operating directly on the patient. Research in this area has been quite extensive in Europe and the U.S. (especially in the U.S.), particularly in view of the potential military application of this technology. The same can be said about the application of VR to microsurgery. It creates the virtual space of a much expanded surgical area. But how real does this artificial sense of reality have to be? Perfect VR requires the development of microsensors and systems that can give feedback on the detected sensation to the body (an interface that exchanges information directly with the nervous system), and a system that cuts down the time lag in information transmission to acceptable levels. This could be possible to a degree even with current technologies, provided sufficient money, effort and time is spent on the research. The forecasted realization times of topics “75: Widespread use of remote surgery systems utilizing virtual reality technology” and “76: Widespread use of vicarious experience devices which allow bed-ridden patients to take vacations, etc.” are also quite early (this of course depends on the level of the virtual reality) at, respectively, 2011 and 2008.

As mentioned above, work is being done on the development of interface systems that facilitate direct multi-channel input and output through the body’s nervous system, and also research into the control of artificial prostheses using information from the nervous system and, in the other direction, the generation of artificial sensations through stimulation of the nervous system.

iv) High-speed biofunction measuring devices

The development of computerized tomography (CT) and the subsequent development of MRI have made it possible to obtain clear structural images of internal organs using non-invasive techniques, and this has contributed enormously to disease diagnosis. The focus of research is now on using similar methods to obtain tomographic images that show bodily functions, such as metabolism, and not just organ structures, and on maximizing image speed to determine local time-series change of metabolism etc. At this stage, functional MRI is being put to practical use in estimating the active parts of the brain using the magnetic difference between oxyhemoglobin and deoxyhemoglobin, and the high-speed measurement of MRI connected with P or S, which is currently only applied to spectroscopy, will be realized in the near future.

As for non-invasive methods, magnetic maps of the brain and heart obtained by micro-magnetic measurement are already being used widely, and similarly, functional measurement methods using light (optical CT, etc.) are also now used extensively. Both methods still have problems in identifying the local parts of dipoles and space resolution, but further developments are expected in the future.

(3) Future prospects

I discussed the future prospects of individual items in the preceding sections, so here I will touch on general problem areas.

Need is naturally the main driving force of developments in medical engineering, but it is impossible to discuss future prospects in terms of the extent of need in isolation. One reason for this is that since medical engineering is an applied science, its progress largely depends on the progress of basic technology; a breakthrough in basic technology will bring about progress in medical engineering where that breakthrough can be applied, and quite often this can come from completely unexpected directions. Research in this field generally requires expensive equipment and facilities, so when the money goes, so too does the research, so research funding has an enormous influence on the progress of the research (there are many examples in the U.S. where projects (laboratories) simply vanished because of cuts to research grants from NIH and other organizations). Because of this, it is not always easy to judge how topics that have currently attracted attention will progress in the future. But the fact that a topic is attracting attention in itself shows that some kind of breakthrough in basic technology has taken place and progress is expected, or that the country is trying to appropriate a research budget on a priority basis because of a need. Progress in the topics mentioned above will therefore be commensurate with the amount of funds invested in research. Regarding my area of expertise, the forecasted realization times in this survey are somewhat more optimistic than what I forecast (perhaps because the survey results include the hopes of people outside this field). From a specialist's viewpoint, many technological breakthroughs will be necessary before these topics can be realized, and my feeling is that this will be difficult to achieve by the forecasted realization times. To realize these topics earlier, effective management of budgetary measures (especially the massive research budget that at present seems to be scattered around at random), and a stronger cooperative structure among researchers in related fields (especially the basic fields of chemistry and applied physics) are essential.

(Kunihiko Masubuchi)

4.1.10. Sensors and computers

The sensor and computer field is a combination of life science, electronics, optics and micromachines, and technological advances in areas that become the basis of individual devices are largely reflected in the advancement of this field.

The field itself can be looked at in terms of progress of materials based on biosubstances and electronic devices, and in terms of the receipt and processing of information through the application in electronics of new knowledge obtained from advances in life science.

Recent achievements in this field have been the creation of biomaterial useful in sensors and

biocomputers through genetic engineering and protein alteration technologies. Research is being conducted into sensors that utilize the functions of various protein molecules, such as enzymes and antibodies, but some have not been suitable for practical use as the molecules themselves were unstable, or deactivation into elements was too great because of fixation. However, efforts are being made to resolve these problems by altering protein molecules or modification through genetic engineering. The practical use of technology to design/synthesize thermostable protein is expected to be realized in 2009, and this will facilitate the use of many biosensors. And it is forecasted that through the use of thermostable proteins, biodevices that can be used in electronics will be developed in 2015.

On the other hand, transducers, typified by terminals made up of sensors, are also undergoing major changes. On the surface, this does not seem to be connected with life science technology itself, but currently one of the important directions of research in this field is miniaturization, and besides terminals, new conceptual sensors, such as SAW and optometric methods are being developed. Application of microdevices is not limited to the monitoring of individual organisms or tissues, which has already been tried in clinical tests; the monitoring of individual cells will become possible. And research is already heading in this direction.

As a future technology, nano-devices will become possible through advances in electronics. These devices will allow real-time measurement of cell functions, and this in turn will expand our knowledge in life science. They can also be applied in systems without suitable probe pigment, and the *in vivo* monitoring of various organisms will reveal previously unknown phenomena within cells.

It is forecasted that the design/synthesis of thermostable protein (2009) and development of biomimetic elements with better functional characteristics than enzymes (2014) will lead to the development of biodevices that can be used in electronics (2015) and the development of basic concepts of biocomputers based on this (2016). At present, biocomputers and neural-computers are viewed as different concepts, but there is a possibility that they may be merged over time.

This is because the following forecasts were made about neural-computers. It is forecast that experimental techniques for recording and analyzing the activities of a large numbers of neurons simultaneously and over a long period of time will be developed in 2011, and this will dramatically expand our knowledge about information processing in the nervous system, and advance our analysis of brain functions. It is also forecasted that the relationship between learning/memory and synaptic plasticity will be elucidated in 2017. This will build up the knowledge necessary for computer development, leading to the development of neural-computers with new logic structures modeled on brain functions in 2018. It is also forecasted that electric circuits with similar self-organization and self-restoration functions as neural networks will be developed in 2018, and at this stage, biocomputers and neural-computers will probably begin to merge. This neural-computer will be a first-generation device, and the elucidation of the neurobiological basis for emotion in 2021 and the elucidation of brain mechanisms for logical reasoning in 2023 will probably lead to the development of second- and third-generation neural-computers.

In 2025 interfaces that enable a direct linkage between computer and brain will be developed, and this will probably mark the beginning of a new century for the brain and computer. Brains could be helped by computers, and conversely, computers may seek the opinion of brains. Forecasting this far ahead has a touch of science fiction about it, but by that time, there will probably be a need for clear ethical standards in relation to this.

(Izumi Kubo)

4.2. Forecast topic framework

In the course of compiling forecast topics, a framework representing the organization of technologies in tabulated matrix form was drawn up for each field, with objectives and technological domains defining the rows and columns of the table, respectively. The framework is designed to present an overall picture of technological development in each field in terms of future prospects, importance, etc. as seen from the present perspective, and is also used as a working framework for future reviews of forecast topics.

Table 4.2-1 Forecast Topic Framework for Life Science Field

Domain \ Objective	Molecules	Cells	Tissues and organs	Individuals	Groups
Medical care	01 02 03 04 05 06 07 08	27 28 29	47 48 49 50 51 52 53 54 55 56	67 68 69 70 71 72 73 74 75 76	
Information	09 10		57 58		
Food	11	30		77 78	91 92
Industry	12 13 14 15 16 17 18	31 32 33 34 35 36 37	59 60 61 62		
Environment and energy		38 39 40		79 80 81	
Elucidation of biological phenomena that form the basis of various technologies	19 20 21 22 23 24 25 26	41 42 43 44 45 46	63 64 65 66	82 83 84 85 86	93
Other				87 88 89 90	94

* Figures appearing in the table represent topic numbers.

4.3. Topics with high degree of importance

Degree of importance index scores (Note 1) averaged at 66.1 for topics in the life science field as a whole. Topics considered of particular importance to Japan (top 20 topics in terms of degree of importance index score) are listed in the table below. The importance attached to cancer-related topics stood out, with up to six of them featuring in the top 20. Environment-related topics also ranked high, with six included in the top 20.

Table 4.3-1 Top 20 Topics in Terms of Degree of Importance Index

Topic	Degree of importance index	Forecasted realization time (year)
49 <u>Practical use</u> of effective means to prevent metastasis of cancer.	91	2013
74 <u>Identification</u> and classification by the molecular etiology of the genes related to diabetes, hypertension, and arteriosclerosis, typical geriatric diseases which exhibit multiple-factor hereditary traits.	88	2012
48 <u>Development</u> of drugs capable of preventing the occurrence of certain types of cancer.	87	2010
02 <u>Development</u> of anti-cancer agents which target the manifestation functions of cancer genes.	87	2010
35 <u>Widespread</u> production of bioplastics using microorganisms and plants, accounting for 10% of the total volume of worldwide plastic production.	87	2013
01 Identification of <u>multiple</u> genes related to cancer, and <u>elucidation</u> of the relationships between those genes and carcinogenesis.	86	2014
67 <u>Become possible</u> to cure senile dementia of Alzheimer type.	86	2016
91 <u>Development</u> of technologies which dramatically improve photosynthetic ability in order to increase food production.	86	2017

Topic	Degree of importance index	Forecasted realization time (year)
72 Scientific <u>elucidation</u> of the factors within daily life (eating habits, air quality, etc.) which influence the process of carcinogenesis.	83	2012
52 <u>Development</u> of an entirely implantable artificial kidney.	83	2013
28 Control of signal transduction in the carcinogenesis of cells, and <u>widespread use</u> of treatment methods for dysdifferentiating carcinogenic cells.	82	2020
07 Elucidation of the environmental factors and control mechanisms of the immune response which triggers allergies such as hay fever and atopy, <u>facilitating the complete control</u> over immediate type hyper-sensitivity.	82	2014
36 <u>Widespread</u> production of alcohol and other fuel oils utilizing microorganisms, seaweed, etc., accounting for 10% of total worldwide fuel oil production.	81	2015
29 Complete understanding of the factors contributing to stem cell multiplication, and <u>widespread use</u> of the practice of multiplying stem cells, as necessary, in test tubes and using them for treatment purposes.	81	2015
54 Establishment and <u>clinical application</u> of technology <u>enabling</u> organs to regenerate through the multiplication of their own cells.	80	2021
71 <u>Elucidation</u> of the mutual regulatory mechanisms of the immune system, nervous system, and endocrine system, and utilization of such knowledge in the treatment of disease and promotion of health.	78	2017
51 <u>Practical use</u> of artificial organs (pancreases, kidneys, livers, etc.) incorporating human cells and tissues.	78	2015
39 <u>Practical use</u> of technology for biological fixation of highly-concentrated carbon dioxide emitted from steam power plants.	78	2017
80 <u>Production</u> of genetically engineered plants with high CO ₂ fixing ability, as a means of preserving the environment.	77	2012
18 <u>Development</u> of light energy elements patterned after photosynthetic response.	77	2017

Note 1: Degree of importance index = (number of “high” responses × 100 + number of “medium” responses × 50 + number of “low” responses × 25 + number of “unnecessary” responses × 0) ÷ total number of degree of importance responses

4.4. Forecasted realization times

Forecasted realization times were distributed as shown in the diagram below.

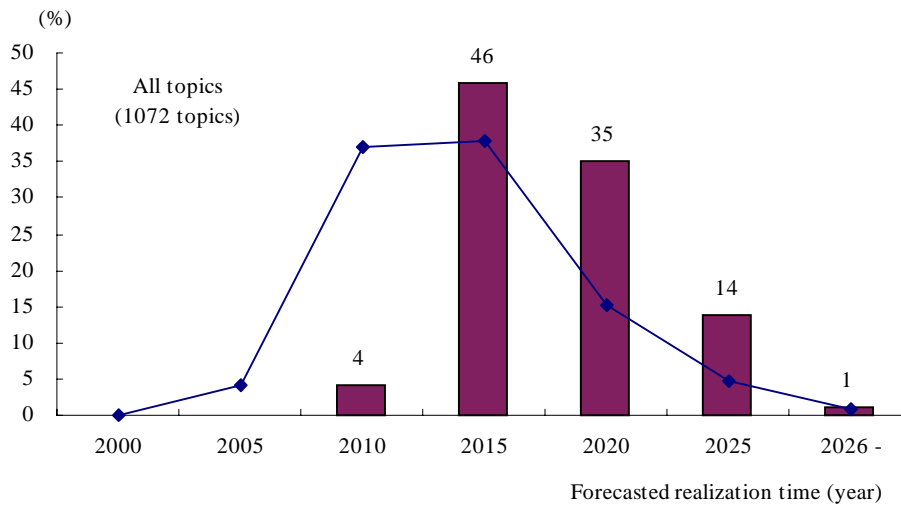


Fig. 4.4-1 Trends in Forecasted Realization Times

Nearly half of the forecasted realization times in the life science field fell between 2011 and 2015. Compared to the general trend covering all topics, forecasted realization times were somewhat on the remote side. This seems to be due to the fact that, because of the nature of this field, many forecast topics were related to basic research, which tends to involve numerous difficulties and uncertainties that must be overcome in the process of their realization.

4.5. Current leading countries etc.

Responses to the question concerning current leading countries etc. were as shown in the diagram below. Named by an overwhelming number of respondents, the U.S. ranked No. 1, with Japan and the EU trailing with similar scores.

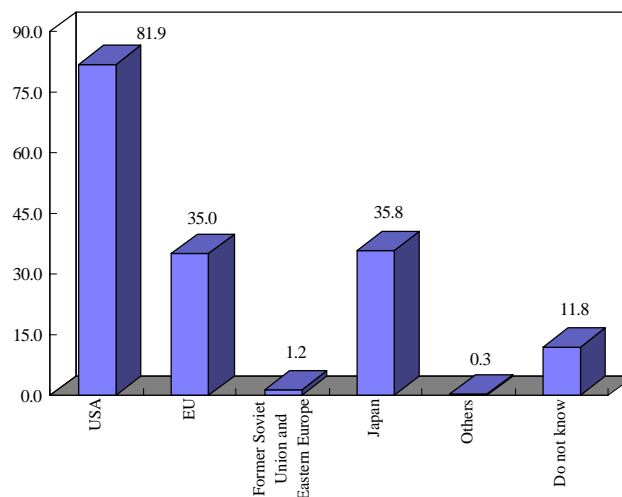


Fig. 4.5-1 Current Leading Countries etc. (%)

4.6. Comparison with the 5th Survey (previous survey)

Of the 94 topics included in the latest survey, 23 (24%) were identical to the previous survey, 18 (19%) were modified, and 53 (56%) were newly introduced. For identical topics, the results of the latest survey were compared with those of the previous survey in terms of degree of importance index scores and forecasted realization times, as shown in the table below.

Degree of importance index scores rose for 3 topics, with “09: Development of biodevices that can be used in electronics” experiencing the greatest jump. Scores remained the same for 1 topic and fell for 19 topics. The following topics saw the greatest drop: “25 : Establishment of technologies enabling prediction of the functions of proteins from their higher-order structures”, “41: Elucidation of relationships between higher-order structures and functions of the nuclei in eukaryotic cells”, and “92: Practical application of breeding techniques for plants resistant to dry and saline conditions aimed at desertification prevention”, down 23, 25 and 31 points, respectively.

From the 4th to the 5th Survey, forecasted realization times for all topics were pushed back. Likewise, from the 5th to the 6th Survey, no topic was brought forward.

Table 4.6-1 Comparison with 5th Survey for Identical Topics

Topic	Degree of importance index / forecasted realization time	
	6th survey	5th survey
09 <u>Development</u> of biodevices (protein transistors, for example) that can be used in electronics.	64/2015	59/2010
10 <u>Systematization</u> of the basic concepts of bio-computer architecture.	64/2016	68/2008
25 <u>Establishment</u> of technologies enabling <u>prediction of the functions</u> of proteins from their higher-order structures.	66/2014	89/2006
27 <u>Elucidation</u> of the immune mechanisms which distinguish between “self” and “not self”.	70/2013	86/2004
31 <u>Development</u> of technologies, such as biomotors, using the biological energy conversion mechanisms.	59/2016	64/2011
32 <u>Development</u> of technology for synthesizing artificial cells that replace cellular functions such as cell membrane transport, substance conversion, energy conversion, etc.	58/2021	63/2019
41 <u>Elucidation</u> of relationships between higher-order structures and functions of the nuclei in eukaryotic cells.	54/2015	79/2008
49 <u>Practical use</u> of effective means to prevent metastasis of cancer.	91/2013	97/2007
51 <u>Practical use</u> of artificial organs (pancreases, kidneys, livers, etc.) incorporating human cells and tissues.	78/2015	81/2009
57 <u>Development</u> of neural-computers with new logic structures modeled on brain functions.	74/2018	81/2010
58 <u>Development</u> of interfaces enabling direct linkage between the computer and the brain.	65/2025	63/2020
59 <u>Development</u> of devices with self-assembling, self-organizing, and self-recovering capabilities.	61/2022	64/2018
61 <u>Development</u> of materials similar to organisms, which have self-recognizing and judging functions.	55/2019	59/2016
65 <u>Elucidation</u> of brain mechanisms for logical reasoning.	67/2023	81/2020
67 <u>Become possible</u> to cure senile dementia of Alzheimer type.	86/2016	93/2015
68 <u>Elucidation</u> of the cause of manic-depressive psychosis at the molecular level.	74/2016	81/2009
69 <u>Elucidation</u> of the cause of schizophrenia at the molecular level.	74/2016	82/2010
73 <u>Development</u> of a complete in vitro embryo cultivation technique based on artificial placentas for small mammals.	54/2017	58/2009
81 <u>Practical use</u> of plants accumulating high amount of <u>hydro-carbon</u> as fuel sources.	68/2015	69/2012

Topic	Degree of importance index / forecasted realization time	
	6th survey	5th survey
86 <u>Elucidation</u> of the neurobiological basis for emotion.	57/2021	58/2017
87 Elucidation of physiological effects of <u>gravity-free state</u> and <u>development</u> of measures for preventing deterioration in biological functions caused by the weightless state.	45/2016	43/2012
88 <u>Development</u> of technologies for breeding and cultivating organisms in (cosmo) space.	43/2015	43/2007
92 <u>Practical application</u> of breeding techniques for plants resistant to dry and saline conditions aimed at desertification prevention.	61/2014	92/2009

Note: Up until the 5th Survey, realization meant realization in Japan unless otherwise specified. However, this was changed to mean realization somewhere in the world in the 6th Survey. Therefore, care should be taken when comparing forecasted realization times from the two surveys.

Division	Topic serial No.	Topic	Questionnaire round	Number of respondents	Degree of expertise (%)			Importance (index, %)				Expected effect (%)			Forecasted realization time					Leading countries (%)					Measures the government should adopt (%)					Potential problems (%)								
					High	Medium	Low	Index	High	Medium	Low	Unnecessary	Socioeconomic development	Resolution of global problems	People's needs	Expansion of intellectual resources						USA	EU	Former Soviet Union and Eastern Europe	Japan	Other countries	Do not know	Foster human resources	Promote exchanges among industrial, academic and government sectors and different fields	Upgrade advanced facilities and equipment	Develop a research base	Increase government research funding	Adjust regulations (relax/toughen)	Others	Adverse effect on the natural environment	Adverse effect on safety	Adverse effect on morals, culture or society	Other adverse effects
					2001	2006	2011	2016	2021	2026	Will not be realized (%)	Do not know (%)	USA	EU	Former Soviet Union and Eastern Europe	Japan	Other countries	Do not know	Foster human resources	Promote exchanges among industrial, academic and government sectors and different fields	Upgrade advanced facilities and equipment	Develop a research base	Increase government research funding	Adjust regulations (relax/toughen)	Others	Adverse effect on the natural environment	Adverse effect on safety	Adverse effect on morals, culture or society	Other adverse effects									
Molecules	1	Identification of <u>multiple</u> genes related to cancer, and <u>elucidation</u> of the relationships between those genes and carcinogenesis.	1	290	22	37	41	82	65	31	4	0	19	2	87	51		8	7	96	41	0	38	0	2	66	24	28	55	53	3	0	1	27	37	1		
			2	233	23	35	42	86	73	26	1	0	15	1	93	45		2	3	98	42	0	39	0	1	75	18	21	62	57	3	0	0	25	49	0		
			X	53	100	0	0	94	89	9	2	0	15	0	89	66		0	0	100	53	0	49	0	0	87	32	17	58	55	0	2	0	23	47	0		
	2	Development of anti-cancer agents which target the manifestation functions of cancer genes.	1	283	16	39	45	82	67	28	4	1	37	1	93	18		3	6	93	34	0	28	0	5	55	52	28	31	47	10	0	4	12	27	3		
			2	228	16	37	47	87	75	22	3	0	35	0	96	13		2	4	95	33	0	32	0	2	64	58	19	25	48	7	0	2	16	33	2		
			X	37	100	0	0	91	86	8	3	3	38	0	92	19		0	0	97	49	0	46	0	0	76	73	16	27	54	5	0	5	16	27	3		
	3	Utilization of information about the gene structure of each individual patient in diagnosis and treatment.	1	289	17	37	45	65	40	42	15	3	19	1	90	27		13	7	88	39	1	24	0	6	42	25	17	66	33	18	1	1	67	70	0		
			2	231	15	36	49	67	39	54	7	1	15	0	97	19		9	3	94	44	0	25	0	3	47	21	13	77	34	17	0	0	57	75	1		
			X	34	100	0	0	81	62	38	0	0	21	0	100	26		3	0	100	56	0	24	3	0	44	21	9	74	38	26	0	0	56	88	0		
	4	Development of methods for surmising new functions of proteins from human genome information.	1	281	22	42	36	71	47	45	8	0	34	5	59	63		2	6	90	44	1	28	0	6	60	32	27	57	45	3	0	1	17	26	1		
2			230	19	43	38	71	45	50	4	0	31	3	62	64		2	2	95	48	1	28	0	2	69	20	19	66	50	2	0	0	12	30	1			
X			44	100	0	0	87	75	23	2	0	45	2	66	77		2	0	100	61	2	34	0	0	70	23	20	73	59	2	0	0	11	18	0			
5	Elucidation of the molecular structure of the manifestation and adhesion control of binding molecules, and <u>control</u> over cancer, autoimmune disease, and chronic inflammation by controlling these binding molecules.	1	244	19	41	40	68	42	47	11	0	23	1	90	34		10	10	88	35	1	47	0	5	64	39	21	16	55	3	0	2	9	16	3			
		2	202	15	39	47	68	39	55	7	0	17	0	94	26		4	7	93	31	0	51	0	4	72	41	15	9	62	2	0	0	8	18	1			
		X	30	100	0	0	87	76	21	3	0	20	0	97	40		0	7	100	50	0	73	0	0	83	60	13	7	70	0	0	0	3	17	0			
6	Elucidation of various immunologically functional molecules responsible for organ transplant rejection, thereby <u>making it possible</u> to completely control organ transplants.	1	249	15	34	51	72	48	42	8	1	23	0	94	29		10	10	94	39	0	28	0	2	63	39	21	15	50	19	1	2	17	49	2			
		2	201	10	33	56	73	48	48	4	1	17	0	96	17		9	7	95	39	0	26	0	1	73	35	15	10	58	17	0	0	13	55	2			
		X	21	100	0	0	90	80	20	0	0	29	0	95	19		10	0	100	67	0	33	0	0	71	52	14	10	71	33	0	0	0	52	5			
7	Elucidation of the environmental factors and control mechanisms of the immune response which triggers allergies such as hay fever and atopy, <u>facilitating the complete control</u> over immediate type hyper-sensitivity.	1	263	15	27	58	77	59	34	7	1	21	4	95	20		6	8	82	34	0	45	0	10	64	42	22	15	54	2	0	5	11	11	4			
		2	212	14	24	62	82	65	31	3	0	17	3	97	16		4	5	90	32	0	48	0	6	75	43	17	6	62	0	0	4	9	13	2			
		X	29	100	0	0	87	75	21	4	0	28	3	97	14		3	7	100	34	0	66	0	0	86	66	7	7	79	0	0	0	7	7	0			
8	Elucidation of the molecular structure of apoptosis, <u>making it possible to create and remove</u> cells at will.	1	265	23	32	45	64	38	44	17	1	15	3	72	57		11	12	88	35	0	40	1	6	66	32	22	17	56	3	0	6	9	30	2			
		2	209	22	32	46	65	35	52	12	0	10	2	78	56		9	8	91	37	0	47	0	5	75	30	14	10	63	3	0	4	7	33	1			
		X	46	100	0	0	78	57	41	2	0	17	4	80	65		9	4	100	52	0	67	0	0	89	35	17	11	74	4	0	4	4	26	0			
9	Development of biodevices (protein transistors, for example) that can be used in electronics.	1	172	13	22	65	62	36	43	19	2	74	17	23	31		8	9	72	25	0	37	1	16	52	52	22	5	44	1	1	9	6	12	4			
		2	132	11	22	67	64	35	50	14	1	80	11	27	26		6	4	86	22	1	46	0	8	62	61	14	2	55	0	2	5	5	14	2			
		X	14	100	0	0	75	50	50	0	0	64	29	21	43		14	0	79	7	0	50	0	0	57	79	7	0	43	0	7	7	0	14	0			
10	Systematization of the basic concepts of bio-computer architecture.	1	148	11	27	62	65	41	42	12	4	71	11	17	53		7	9	77	22	1	28	0	14	57	55	24	7	41	1	1	4	4	14	2			
		2	124	10	20	70	64	36	51	11	2	78	6	15	44		5	6	85	23	2	29	0	11	64	62	20	3	48	1	2	2	4	20	1			
		X	12	100	0	0	67	42	50	0	8	75	8	0	58		0	0	92	0	0	33	0	0	67	58	25	0	42	0	8	0	0	0	0			

(Note) See page 7 for the interpretation of the graphs.

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					High	Medium	Low	Index	High	Medium	Low	Unnecessary	Socioeconomic development	Resolution of global problems	People's needs	Expansion of intellectual resources																				
Molecules	11	Establishment of a nitrogen fixation mechanism mimicking the biological processes.	1	182	10	34	56	64	37	46	15	2	39	91	6	17		4	12	60	38	3	20	1	26	54	38	24	11	52	3	1	51	1	4	2
			2	145	10	32	59	65	36	52	10	1	42	91	5	12		5	6	68	37	3	19	0	25	66	40	21	6	58	2	2	57	1	3	1
			X	14	100	0	0	71	50	36	14	0	36	100	14	0		7	0	86	36	7	14	0	7	64	29	29	7	64	0	0	64	0	0	0
	12	Practical use of technology to alter the functions of biological molecules and cells by means of molecular evolutionary engineering techniques.	1	226	22	37	41	63	33	52	15	0	59	47	38	37		5	7	77	31	0	37	0	15	57	38	24	23	49	9	0	30	8	21	1
			2	187	21	33	46	61	29	59	12	0	66	42	35	30		3	3	88	34	0	43	0	7	70	35	18	18	54	6	1	36	7	20	1
			X	39	100	0	0	74	49	49	3	0	74	36	38	36		0	0	97	44	0	56	0	3	79	44	18	18	62	8	0	26	5	13	3
	13	Development of biomimetic elements (stable molecules which have the same functions as those of biological molecules and which are made up of components other than peptides) with better functional characteristics than enzymes.	1	186	15	35	50	64	38	44	17	2	69	42	25	27		8	8	68	27	1	37	0	22	59	48	25	11	45	2	1	18	7	7	2
			2	154	14	29	57	62	33	52	14	1	78	33	21	19		6	3	79	24	1	40	0	16	66	49	20	7	47	1	2	23	8	5	1
			X	21	100	0	0	67	38	52	10	0	71	29	33	38		10	5	95	43	5	57	0	0	67	48	14	5	57	5	0	14	5	5	0
	14	Development of biomimetic elements which duplicate themselves according to information.	1	146	8	34	59	54	24	48	22	5	58	25	21	43		14	12	63	16	1	20	0	26	55	45	20	10	38	3	0	18	5	14	1
			2	119	8	27	65	51	17	54	26	3	65	18	17	37		13	10	70	13	1	18	0	24	64	42	18	8	40	3	0	20	5	15	0
			X	10	100	0	0	78	60	30	10	0	60	30	20	80		10	0	100	30	10	50	0	0	60	30	30	10	70	0	0	20	0	10	0
	15	Development of technology to regenerate organs or individuals from separated animal cells.	1	247	14	30	56	65	39	44	14	3	32	13	79	41		17	16	70	35	1	21	0	20	60	28	26	11	51	10	0	11	11	55	1
			2	201	12	26	62	67	40	48	11	1	31	9	84	31		18	9	80	32	0	19	0	15	73	23	22	5	58	8	0	8	9	63	0
			X	24	100	0	0	79	58	42	0	0	42	13	88	38		4	0	100	58	0	50	0	0	75	38	29	4	71	13	0	8	21	50	0
	16	Practical use of technology to design/synthesize thermostable protein.	1	240	22	35	43	62	33	51	16	0	71	43	24	23		0	4	77	31	1	60	0	13	58	46	20	21	40	2	0	19	3	5	3
			2	187	22	34	44	62	30	60	10	0	80	33	19	12		1	2	84	26	1	74	0	5	67	55	17	13	46	1	1	25	2	5	1
			X	41	100	0	0	71	46	46	7	0	80	37	15	22		2	0	88	29	0	80	0	2	63	56	15	17	49	2	0	15	0	7	0
	17	Practical use of continuous, industrial-scale production of protein by means of non-cellular protein synthesizing techniques.	1	203	11	42	47	61	34	46	19	2	67	49	29	19		3	8	60	21	11	33	0	26	51	49	19	10	44	2	0	17	6	7	2
			2	166	10	36	54	60	29	56	14	2	77	42	19	9		2	6	67	17	8	39	0	21	56	60	14	4	48	2	0	20	4	5	1
X			17	100	0	0	81	71	18	6	6	76	53	6	24		6	0	88	24	41	53	0	0	53	71	6	6	59	0	0	12	0	0	0	
18	Development of light energy elements patterned after photosynthetic response.	1	170	11	34	55	72	51	38	10	1	60	79	6	26		4	11	71	38	1	31	0	18	57	48	30	8	49	1	1	22	4	4	2	
		2	136	10	30	60	77	57	35	7	1	68	76	5	17		1	4	79	38	0	31	0	14	64	51	25	1	58	0	0	27	3	1	2	
		X	14	100	0	0	86	71	29	0	0	71	79	0	7		0	0	86	50	0	50	0	7	64	36	21	0	43	0	0	21	0	0	0	
19	Elucidation of the molecular mechanism of life creation.	1	234	9	31	60	52	27	35	29	8	7	11	16	89		21	18	71	36	6	21	0	19	59	14	21	14	49	3	1	7	4	35	2	
		2	194	7	27	66	50	21	42	32	5	4	4	9	93		21	17	80	40	6	19	0	14	70	9	19	7	56	3	1	2	3	45	1	
		X	13	100	0	0	65	46	31	15	8	8	8	23	100		23	0	85	54	23	31	0	0	69	15	23	8	46	8	8	8	0	46	0	
20	Complete elucidation of the molecular mechanism explaining the cell cycle in higher order mammals (humans, mice).	1	248	18	39	44	62	35	44	20	2	13	6	53	76		4	6	93	54	1	42	0	5	73	19	23	21	63	1	0	4	4	17	2	
		2	205	16	34	50	61	31	52	16	1	8	3	49	83		4	6	95	57	0	46	0	2	80	10	22	14	67	0	0	2	2	19	0	
		X	33	100	0	0	88	75	25	0	0	6	9	61	88		0	0	100	73	0	58	0	0	88	6	42	9	82	0	0	0	6	18	0	

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					2001	2006	2011	2016	2021	2026	Will not be realized (%)	Do not know (%)	USA	EU	Former Soviet Union and Eastern Europe	Japan	Other countries	Do not know	Foster human resources	Promote exchanges among industrial, academic and government sectors and different fields	Upgrade advanced facilities and equipment	Develop a research base	Increase government research funding	Adjust regulations (relax/toughen)	Others	Adverse effect on the natural environment	Adverse effect on safety	Adverse effect on morals, culture or society	Other adverse effects									
Molecules	21	Application of human genome analysis methods to other animals and plants, and <u>practical use</u> of technology to analyse whole genome sequence in livestock breeding, and fisheries, agriculture and forestry.	1	281	22	40	38	55	26	47	22	4	19	23	33	74		9	12	86	52	1	39	0	7	53	15	20	67	48	3	0	7	18	35	1		
			2	219	22	36	42	60	29	56	14	1	25	23	31	75		5	4	95	56	0	47	0	4	63	11	15	73	55	2	0	5	16	45	0		
			X	49	100	0	0	73	51	43	4	2	31	22	27	76		6	0	98	53	0	59	0	0	78	12	10	67	59	2	0	4	8	51	0		
	22	Establishment of technology enabling to decipher human DNA modification (methylation) information for all genomes.	1	217	20	33	47	56	24	53	22	1	11	3	52	69		1	11	84	45	0	29	0	10	64	18	22	48	52	2	0	3	16	25	1		
			2	173	20	34	47	54	19	62	19	1	9	2	47	77		1	5	95	52	0	29	0	5	75	9	16	55	54	2	0	3	13	32	0		
			X	34	100	0	0	65	35	56	6	3	9	3	44	74		3	3	100	59	0	26	0	0	76	12	12	47	50	3	0	0	15	35	0		
	23	Elucidation of the transcription cascade for all genes, from fertilized egg to individual, in a single higher animal species, e.g. mice, and the mechanism by which differentiation and functions are manifest.	1	236	20	31	49	65	39	45	15	1	11	3	57	78		11	11	89	51	0	31	0	7	72	15	27	42	60	3	0	3	18	39	1		
			2	193	17	33	50	63	31	61	8	0	6	4	47	89		8	7	93	59	1	33	0	4	81	8	20	40	65	3	0	1	11	44	0		
			X	32	100	0	0	79	58	42	0	0	6	0	50	100		6	0	100	72	0	41	0	0	91	9	22	22	72	0	0	0	16	34	0		
	24	Development of technology to clarify the genes manifested in a single cell in higher animals with an accuracy in the order of 1 mRNA molecule.	1	240	22	34	44	56	25	52	21	2	17	5	41	72		3	13	79	39	0	28	0	14	63	23	25	30	50	3	0	3	8	17	3		
			2	195	16	38	46	55	18	67	15	1	10	2	35	85		2	5	88	36	0	27	0	8	73	15	21	26	54	2	0	1	7	24	1		
			X	31	100	0	0	72	45	52	3	0	10	0	39	90		0	0	97	42	0	35	0	3	84	32	35	19	55	6	0	0	3	19	0		
	25	Establishment of technologies enabling prediction of the functions of proteins from their higher-order structures.	1	269	20	36	43	68	41	48	10	0	52	16	41	70		3	6	88	52	1	35	0	6	58	28	32	41	49	1	0	4	6	7	3		
			2	218	17	36	47	66	35	58	7	0	55	7	31	78		5	3	91	51	1	34	0	1	67	20	27	43	55	1	0	3	6	9	1		
			X	38	100	0	0	81	63	34	3	0	61	11	24	76		11	0	89	53	3	34	0	3	68	26	32	39	61	0	0	3	3	8	0		
26	Practical use of methods for directly determining DNA sequences by physical means such as X-rays.	1	189	14	35	51	55	24	49	25	2	28	6	32	64		9	16	69	35	1	25	0	21	57	29	37	19	45	0	1	5	5	11	2			
		2	157	11	36	53	53	19	56	24	2	22	1	23	78		8	12	76	29	0	24	0	15	61	23	34	15	54	0	1	4	5	17	1			
		X	18	100	0	0	54	29	35	29	6	17	0	0	72		22	0	72	44	0	11	0	11	50	22	39	11	56	0	0	0	0	11	0			
Cells	27	Elucidation of the immune mechanisms which distinguish between "self" and "not self".	1	228	14	34	52	70	45	45	9	0	14	3	80	58		2	4	91	53	0	46	0	4	72	24	26	17	61	1	0	2	11	18	3		
			2	198	11	32	57	70	42	54	5	0	8	2	83	61		1	2	96	55	0	46	0	2	79	14	23	10	67	1	1	2	8	22	1		
			X	22	100	0	0	86	73	27	0	0	23	0	82	82		0	0	100	64	0	68	0	0	95	32	9	9	82	5	0	5	0	14	5		
	28	Control of signal transduction in the carcinogenesis of cells, and <u>widespread use</u> of treatment methods for dysdifferentiating carcinogenic cells.	1	255	16	36	49	79	61	33	6	0	25	2	93	32		11	11	85	44	0	45	1	7	68	32	25	16	59	5	0	2	13	23	2		
			2	205	16	33	51	82	67	29	4	0	16	0	96	22		6	9	93	50	0	49	0	4	77	26	21	8	69	3	0	0	10	25	0		
			X	32	100	0	0	92	84	16	0	0	16	0	100	28		13	0	97	72	0	66	0	0	75	31	22	16	81	6	0	0	19	31	0		
	29	Complete understanding of the factors contributing to stem cell multiplication, and <u>widespread use</u> of the practice of multiplying stem cells, as necessary, in test tubes and using them for treatment purposes.	1	223	17	39	44	79	61	34	5	0	27	4	91	34		2	8	88	45	0	42	0	5	64	35	28	14	57	8	0	2	14	28	0		
			2	181	13	40	47	81	64	32	4	0	16	2	93	29		1	4	92	44	0	44	1	3	75	35	24	7	60	4	0	2	12	35	0		
			X	23	100	0	0	91	83	17	0	0	17	4	96	30		0	0	96	52	0	70	0	0	83	39	17	9	70	9	0	0	17	35	0		
30	Widespread use of foodstuffs which consist of microorganisms, seaweed, and single-cell organisms as the raw materials.	1	216	22	33	44	61	34	44	18	3	41	87	19	7		9	14	49	32	14	48	2	22	41	52	14	7	41	16	2	27	11	19	4			
		2	173	24	27	49	62	34	49	14	3	40	85	13	5		10	8	59	33	10	58	3	17	46	61	9	2	43	14	1	35	12	18	2			
		X	41	100	0	0	70	51	32	12	5	41	83	15	10		10	2	63	61	27	73	10	0	56	56	5	0	51	20	0	24	15	15	5			

(Note) See page 7 for the interpretation of the graphs.

Division	Topic serial No.	Topic	Questionnaire round	Degree of expertise (%)			Importance (index, %)			Expected effect (%)				Forecasted realization time					Leading countries (%)					Measures the government should adopt (%)					Potential problems (%)												
				Number of respondents	High	Medium	Low	Index	High	Medium	Low	Unnecessary	Socioeconomic development	Resolution of global problems	People's needs	Expansion of intellectual resources	2001	2006	2011	2016	2021	2026	Will not be realized (%)	Do not know (%)	USA	EU	Former Soviet Union and Eastern Europe	Japan	Other countries	Do not know	Foster human resources	Promote exchanges among industrial, academic and government sectors and different fields	Upgrade advanced facilities and equipment	Develop a research base	Increase government research funding	Adjust regulations (relax/toughen)	Others	Adverse effect on the natural environment	Adverse effect on safety	Adverse effect on morals, culture or society	Other adverse effects
Cells	31	Development of technologies, such as biomotors, using the biological energy conversion mechanisms.	1	165	12	32	56	60	31	48	21	1	68	41	25	28		5	11	75	27	1	50	0	13	54	49	28	1	51	2	2	11	5	6	3					
			2	137	10	31	58	59	27	56	15	1	76	31	23	25		3	5	80	23	1	52	0	9	64	53	23	1	54	1	2	12	6	5	2					
			X	14	100	0	0	79	57	43	0	0	86	29	21	36		0	0	79	21	0	57	0	14	50	43	36	7	64	0	7	21	14	7	0					
	32	Development of technology for synthesizing artificial cells that replace cellular functions such as cell membrane transport, substance conversion, energy conversion, etc.	1	189	11	32	57	62	33	49	17	1	53	40	41	38		5	16	63	28	1	28	0	28	59	43	28	4	51	1	1	13	5	11	4					
			2	155	10	28	62	58	22	65	12	1	65	37	36	28		9	9	73	27	0	23	0	23	67	47	24	1	56	2	1	17	4	13	3					
			X	15	100	0	0	72	47	47	7	0	73	47	40	47		0	7	93	53	0	53	0	7	67	53	20	0	67	0	0	20	13	0	0					
	33	Development of artificial membranes with similar functions (active transport, energy conversion, information transmission) as biological membranes.	1	199	13	33	54	65	35	54	10	1	57	35	44	30		2	11	72	29	1	38	0	19	60	51	27	3	54	2	1	10	5	8	3					
			2	163	12	30	58	63	29	65	7	0	69	26	45	23		1	6	82	28	1	38	0	13	68	56	21	1	59	1	1	17	4	9	2					
			X	19	100	0	0	84	68	32	0	0	79	37	42	16		0	5	89	32	0	58	0	11	58	58	16	0	68	0	0	16	11	0	0					
	34	Development of experimental techniques for recording and analyzing the activities of a large numbers of neurons simultaneously and over a long period of time.	1	145	15	30	55	68	41	48	11	0	22	2	56	68		2	10	79	34	0	40	1	11	72	37	35	1	62	0	1	1	3	15	1					
			2	118	14	29	58	65	34	56	9	0	21	1	56	76		2	7	84	30	0	39	0	11	79	33	30	0	64	0	1	0	3	20	0					
			X	16	100	0	0	81	63	38	0	0	31	0	50	75		0	0	100	50	0	63	0	0	81	44	50	0	56	0	6	0	0	25	0					
35	Widespread production of bioplastics using microorganisms and plants, accounting for 10% of the total volume of worldwide plastic production.	1	182	21	26	53	78	60	34	6	1	71	88	18	7		3	8	62	42	1	58	0	16	42	66	21	4	51	15	1	42	4	3	3						
		2	153	17	27	56	87	75	23	3	0	70	90	14	4		3	6	76	48	1	67	1	10	41	73	16	1	59	13	1	49	3	1	1						
		X	26	100	0	0	86	73	23	4	0	73	92	12	4		0	0	85	58	0	81	0	0	23	62	19	0	50	27	0	46	0	0	0						
36	Widespread production of alcohol and other fuel oils utilizing microorganisms, seaweed, etc., accounting for 10% of total worldwide fuel oil production.	1	174	22	30	48	76	56	36	6	2	57	88	7	5		7	13	53	34	6	40	5	25	43	57	19	5	49	15	1	39	5	3	3						
		2	145	21	26	53	81	65	30	4	1	58	90	5	1		7	9	68	39	4	53	1	16	47	63	10	2	59	13	1	44	3	1	1						
		X	31	100	0	0	82	67	27	7	0	65	84	3	3		10	3	74	48	13	68	0	6	52	48	13	3	65	19	0	42	3	3	0						
37	Widespread use in chemical industry processes of biological catalysts which are resistant to organic solvent, heat, and highly-concentrated products.	1	143	31	26	43	71	46	46	7	0	78	70	10	9		2	6	69	36	1	67	0	12	46	60	22	4	45	6	1	23	6	3	3						
		2	126	27	25	48	72	46	52	2	1	82	71	5	2		3	2	75	29	1	71	0	10	49	63	15	2	51	6	2	30	3	1	2						
		X	34	100	0	0	81	65	32	0	3	82	82	0	3		3	0	71	26	0	65	0	3	62	56	12	9	71	3	3	26	0	3	3						
38	Establishment of a system for biologically reducing and fixation CO2 using energy other than light.	1	140	11	29	60	66	43	38	16	3	37	88	5	16		10	17	52	29	4	27	0	28	51	28	27	4	51	3	1	31	6	2	3						
		2	116	7	28	66	65	41	43	13	3	33	91	3	4		8	11	62	25	2	26	1	24	66	25	21	1	57	3	1	37	4	0	2						
		X	8	100	0	0	75	63	13	25	0	25	100	0	0		25	0	88	38	0	63	0	0	75	13	13	0	50	0	0	13	0	0	0						
39	Practical use of technology for biologically fixation of highly-concentrated carbon dioxide emitted from steam power plants.	1	154	16	25	58	73	53	35	11	1	40	89	11	8		12	8	49	29	2	42	2	21	47	50	25	3	50	8	0	32	6	3	3						
		2	128	14	25	61	78	62	28	8	2	35	90	5	2		13	5	60	26	1	55	2	19	54	59	15	1	58	6	0	36	4	1	2						
		X	18	100	0	0	88	78	17	6	0	39	94	0	0		11	6	72	33	6	78	6	0	67	44	17	0	61	0	0	22	0	0	0						
40	Widespread use of worldwide environmental remediation using genetically-engineered microorganisms released into the environment.	1	193	21	35	44	68	42	46	9	3	34	91	19	10		9	14	73	38	2	32	2	13	50	43	19	11	44	30	1	67	9	15	1						
		2	152	20	38	42	70	45	49	5	1	32	93	13	3		6	4	84	41	1	35	1	8	62	48	13	7	52	26	1	72	8	12	0						
		X	30	100	0	0	83	67	30	3	0	43	97	3	7		7	3	97	57	0	40	0	3	77	30	10	3	57	47	3	80	7	7	0						

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					High	Medium	Low	Index	High	Medium	Low	Unnecessary	Socioeconomic development	Resolution of global problems	People's needs	Expansion of intellectual resources	2001 2006 2011 2016 2021 2026						USA	EU	Former Soviet Union and Eastern Europe	Japan	Other countries	Do not know	Foster human resources	Promote exchanges among industrial, academic and government sectors and different fields	Upgrade advanced facilities and equipment	Develop a research base	Increase government research funding	Adjust regulations (relax/toughen)	Others	Adverse effect on the natural environment	Adverse effect on safety	Adverse effect on morals, culture or society	Other adverse effects
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Cells	41	Elucidation of relationships between higher-order structures and functions of the nuclei in eukaryotic cells.	1	229	17	36	48	57	26	51	22	2	5	7	30	87		2	12	84	48	1	31	0	11	75	21	27	14	61	0	0	3	4	10	3			
			2	180	15	34	51	54	19	61	19	1	3	3	25	93		2	7	91	52	0	31	0	7	82	13	21	8	66	1	0	3	3	13	2			
			X	27	100	0	0	72	46	50	4	0	0	0	15	100		0	4	100	70	0	33	0	0	85	11	26	19	63	4	0	4	4	19	0			
	42	Development of technology that artificially alters organella genes and causes the altered organella genes to function within cells.	1	192	16	40	44	52	20	52	27	2	17	32	36	58		2	10	78	39	0	29	0	15	67	24	22	18	55	1	0	11	5	15	2			
			2	158	14	38	48	53	17	62	21	1	14	25	33	72		3	6	85	39	0	27	0	10	77	20	14	9	59	1	0	12	3	17	1			
			X	22	100	0	0	65	33	62	5	0	18	27	23	77		5	9	95	59	0	41	0	0	82	14	18	0	64	0	0	9	5	23	0			
	43	Development of technology capable of synthesizing living cells by using only artificially produced chemical compounds.	1	198	5	34	61	42	13	41	35	11	29	22	23	66		44	17	40	16	2	13	0	38	47	26	19	7	36	4	1	18	5	25	2			
			2	154	5	27	69	44	11	49	33	7	26	13	18	80		48	14	45	12	1	9	0	42	60	18	14	4	41	3	2	18	3	33	1			
			X	7	100	0	0	39	14	43	14	29	29	29	14	86		71	0	86	14	14	29	0	0	71	14	29	14	43	0	0	29	0	43	0			
	44	Elucidation of the entire molecular mechanisms of signal transduction in plants, from the perception of external signal such as low temperature, to the phenotypic expression such as cold resistance.	1	171	16	35	49	62	31	56	11	2	29	82	6	50		1	9	74	44	1	39	1	17	67	27	25	22	57	1	0	29	2	4	2			
			2	134	15	30	55	63	27	70	3	0	25	85	1	47		1	5	81	49	0	46	1	10	78	25	22	14	64	1	0	32	1	2	1			
			X	20	100	0	0	78	55	45	0	0	20	90	0	65		0	5	85	65	0	55	5	0	75	15	45	10	70	0	0	45	0	0	0			
	45	Elucidation of the entire molecular mechanisms of the construction of cytoskeleton in plants.	1	147	9	34	57	50	18	49	29	4	15	44	4	69		1	12	71	44	0	29	0	15	66	15	23	13	50	1	0	10	1	3	2			
			2	114	10	27	63	49	13	57	29	1	11	46	0	79		1	6	82	45	0	28	0	15	79	11	18	7	58	0	0	17	0	1	0			
			X	11	100	0	0	64	27	73	0	0	18	45	0	82		0	0	82	64	0	55	0	0	82	0	27	9	64	0	0	9	0	0	0			
	46	Practical use of elementary particle beam technology in genetic engineering.	1	109	6	34	61	52	21	46	30	3	45	23	23	37		0	12	68	21	1	30	0	19	47	41	33	6	39	0	0	4	7	6	2			
			2	85	7	27	66	53	19	57	23	1	65	19	14	36		1	7	85	18	0	35	0	12	61	44	34	1	47	1	0	2	6	5	0			
			X	6	100	0	0	50	17	50	33	0	67	17	0	50		0	0	100	0	0	50	0	0	83	50	17	17	33	0	0	0	0	0	0			
Tissues and organs	47	Elucidation and artificial control of the molecular mechanisms of the morphogenesis of human organs.	1	201	12	29	59	65	39	44	16	1	21	2	83	46		6	15	76	37	1	29	0	15	67	30	27	10	56	5	0	3	10	37	2			
			2	163	11	26	63	66	37	54	9	1	15	2	87	43		6	10	86	29	0	26	0	10	74	27	23	5	64	4	0	2	10	44	0			
			X	18	100	0	0	79	59	41	0	0	6	6	89	67		6	6	94	44	0	39	0	6	78	28	17	6	67	22	0	0	17	44	0			
	48	Development of drugs capable of preventing the occurrence of certain types of cancer.	1	259	16	33	51	83	68	27	4	1	37	3	97	18		3	7	84	42	1	48	0	12	58	49	22	11	53	7	1	3	11	19	3			
			2	212	15	32	53	87	75	23	2	0	33	1	96	9		2	5	91	44	0	54	0	6	66	53	17	6	59	6	1	2	8	22	1			
			X	32	100	0	0	95	91	9	0	0	38	6	97	13		3	0	100	50	0	78	3	0	66	59	19	6	75	19	0	13	16	19	0			
	49	Practical use of effective means to prevent metastasis of cancer.	1	246	18	34	48	87	76	22	2	0	24	1	95	18		4	7	84	46	0	46	0	8	60	45	26	15	58	4	0	2	11	16	2			
			2	203	15	31	54	91	82	16	2	0	22	0	97	11		3	2	91	48	0	49	0	6	70	51	19	9	67	2	0	1	10	19	1			
			X	31	100	0	0	97	94	6	0	0	29	3	97	23		6	0	97	58	0	65	0	3	68	45	23	10	74	10	0	3	16	19	0			
	50	Widespread use of technologies for long-term (semi-permanent) culturing and preservation of organs.	1	202	9	34	57	71	48	41	11	1	30	3	94	16		4	12	81	37	1	29	0	11	55	46	23	6	49	16	0	3	17	49	2			
			2	167	10	29	62	72	48	46	6	0	28	2	95	7		5	7	88	34	1	26	0	10	65	48	15	4	57	16	1	1	16	62	0			
			X	16	100	0	0	84	69	31	0	0	44	13	81	6		6	0	88	44	0	56	0	6	69	69	13	0	50	6	0	0	31	63	0			

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					2001	2006	2011	2016	2021	2026	Will not be realized (%)	Do not know (%)	USA	EU	Former Soviet Union and Eastern Europe	Japan	Other countries	Do not know	Foster human resources	Promote exchanges among industrial, academic and government sectors and different fields	Upgrade advanced facilities and equipment	Develop a research base	Increase government research funding	Adjust regulations (relax/toughen)	Others	Adverse effect on the natural environment	Adverse effect on safety	Adverse effect on morals, culture or society	Other adverse effects									
Tissues and organs	51	Practical use of artificial organs (pancreases, kidneys, livers, etc.) incorporating human cells and tissues.	1	177	9	32	59	75	53	43	4	1	37	0	98	9		2	8	80	33	2	37	0	11	56	58	25	3	54	16	0	1	17	42	2		
			2	147	10	29	62	78	58	40	3	0	35	1	98	4		1	4	87	28	1	38	0	7	61	63	20	2	62	15	0	1	16	47	0		
			X	14	100	0	0	88	77	23	0	0	50	0	93	7		7	7	100	43	7	71	0	0	50	71	14	0	57	21	0	0	14	36	0		
	52	Development of an entirely implantable artificial kidney.	1	144	10	27	63	79	60	34	5	1	26	0	95	8		3	8	70	30	1	37	0	17	53	65	26	2	49	9	1	0	13	26	3		
			2	119	8	22	70	83	67	30	3	0	20	1	98	5		4	4	84	28	0	38	0	10	61	72	21	0	57	3	2	0	14	29	1		
			X	10	100	0	0	90	80	20	0	0	30	0	100	0		10	0	90	30	0	60	0	0	40	100	30	0	60	0	0	0	0	20	0		
	53	Development of an artificial cornea, allowing the visually impaired to regain their sight.	1	112	5	21	73	68	45	42	12	2	22	0	96	9		19	12	56	19	1	13	0	27	54	46	24	1	45	4	0	0	11	21	3		
			2	95	4	22	74	74	52	41	6	1	22	0	100	3		16	7	69	15	1	18	0	26	67	53	21	0	58	2	1	0	15	23	1		
			X	4	100	0	0	56	25	50	25	0	25	0	100	0		0	0	100	25	0	50	0	0	75	25	25	0	50	0	0	0	0	0	0		
	54	Establishment and clinical application of technology enabling organs to regenerate through the multiplication of their own cells.	1	179	9	28	62	74	51	43	6	1	25	2	95	17		9	15	66	31	1	28	1	23	58	43	23	6	51	11	1	1	15	37	1		
			2	150	8	29	63	80	60	40	1	0	22	1	99	11		7	6	78	23	0	28	1	18	69	47	20	3	63	8	1	0	13	42	0		
			X	12	100	0	0	96	92	8	0	0	50	0	100	17		8	0	100	50	0	50	0	0	67	58	25	8	50	0	0	0	0	25	0		
	55	Development of artificial muscle elements.	1	94	10	24	66	58	28	50	20	2	23	0	86	14		5	14	52	24	2	26	0	31	56	46	24	2	41	1	0	0	12	18	3		
			2	80	6	19	75	57	23	61	16	0	25	0	95	8		6	6	64	18	1	30	0	26	64	50	24	0	49	1	0	0	13	19	0		
			X	5	100	0	0	75	60	20	20	0	80	0	100	20		0	0	80	40	0	80	0	0	60	60	60	0	60	0	0	0	20	20	0		
	56	Establishment of interface technology between neural information and artificial organism structures.	1	101	10	26	64	65	39	46	11	3	49	1	77	29		7	10	70	23	0	31	0	18	55	53	30	2	48	2	1	0	12	23	1		
			2	91	9	18	74	61	30	58	10	2	47	1	78	23		5	5	84	20	0	37	0	12	64	51	24	1	54	1	0	0	11	26	1		
			X	8	100	0	0	81	63	38	0	0	75	0	88	50		0	0	100	50	0	88	0	0	63	63	38	0	75	0	0	0	0	0	0		
	57	Development of neural-computers with new logic structures modeled on brain functions.	1	118	6	25	69	73	50	44	4	2	74	2	38	53		4	8	86	30	1	42	0	6	65	55	31	2	52	1	0	2	8	27	1		
			2	104	3	19	78	74	50	46	3	1	85	0	33	49		3	6	90	26	1	42	0	2	69	57	24	0	55	0	0	1	8	31	1		
			X	3	100	0	0	100	100	0	0	0	67	0	100	53		33	0	100	33	0	100	0	0	100	100	33	0	33	0	0	0	0	33	0		
	58	Development of interfaces enabling direct linkage between the computer and the brain.	1	102	8	26	66	68	43	44	9	3	58	1	57	38		22	10	70	24	0	30	0	13	54	49	32	0	41	2	0	2	15	36	1		
			2	93	6	19	74	65	37	52	10	2	69	0	57	34		17	6	81	22	0	28	1	13	61	48	26	0	47	2	0	1	13	41	0		
			X	6	100	0	0	83	67	33	0	0	50	0	50	67		17	0	100	50	0	83	0	0	83	67	33	0	50	0	0	0	0	33	0		
59	Development of devices with self-assembling, self-organizing, and self-recovering capabilities.	1	93	10	27	63	62	34	49	11	6	65	3	41	34		11	18	67	22	0	26	0	26	55	52	34	2	43	1	0	2	4	15	2			
		2	80	6	24	70	61	27	66	6	1	75	0	38	30		10	10	75	18	0	25	0	21	61	56	29	1	44	0	0	1	5	20	0			
		X	5	100	0	0	80	60	40	0	0	60	0	20	40		0	20	100	20	0	80	0	0	40	100	40	0	40	0	0	0	0	0	0	0		
60	Development of electric circuits with similar self-organization and self-restoration functions as neural networks.	1	83	7	27	66	66	41	42	15	1	69	0	37	36		8	11	71	19	2	35	0	17	55	55	34	1	37	2	0	1	6	14	1			
		2	75	4	28	68	63	31	58	11	0	81	0	35	32		5	8	79	17	3	35	0	15	65	55	24	0	39	1	0	1	5	19	0			
		X	3	100	0	0	83	67	33	0	0	67	0	100	36		0	33	100	33	0	100	0	0	100	100	0	0	67	0	0	0	0	0	0			

(Note) See page 7 for the interpretation of the graphs.

Division	Topic serial No.	Topic	Questionnaire round	Number of respondents	Degree of expertise (%)			Importance (index, %)				Expected effect (%)			Forecasted realization time						Leading countries (%)					Measures the government should adopt (%)					Potential problems (%)								
					High	Medium	Low	Index	High	Medium	Low	Unnecessary	Socioeconomic development	Resolution of global problems	People's needs	Expansion of intellectual resources	2001 2006 2011 2016 2021 2026						USA	EU	Former Soviet Union and Eastern Europe	Japan	Other countries	Do not know	Foster human resources	Promote exchanges among industrial, academic and government sectors and different fields	Upgrade advanced facilities and equipment	Develop a research base	Increase government research funding	Adjust regulations (relax/toughen)	Others	Adverse effect on the natural environment	Adverse effect on safety	Adverse effect on morals, culture or society	Other adverse effects
					Will not be realized (%)	Do not know (%)	USA	EU	Former Soviet Union and Eastern Europe	Japan	Other countries	Do not know	Foster human resources	Promote exchanges among industrial, academic and government sectors and different fields	Upgrade advanced facilities and equipment	Develop a research base	Increase government research funding	Adjust regulations (relax/toughen)	Others	Adverse effect on the natural environment	Adverse effect on safety	Adverse effect on morals, culture or society	Other adverse effects																
Tissues and organs	61	Development of materials similar to organisms, which have self-recognizing and judging functions.	1	104	5	21	74	60	31	47	20	2	61	5	55	27		10	11	62	23	1	30	0	23	54	51	26	2	46	1	0	6	6	19	2			
			2	80	3	23	75	55	19	65	15	1	70	1	65	18		11	8	69	19	1	25	0	25	60	53	15	0	46	1	0	4	4	23	1			
			X	2	100	0	0	50	0	100	0	0	100	0	100	0		0	0	100	0	0	100	0	0	100	50	0	0	100	0	0	0	0	0	0	0		
	62	Development of diagnostic and medical treatment micromachines capable of traveling on their own inside organisms (body cavity organs).	1	114	8	22	70	71	46	47	5	1	54	0	90	17		6	11	66	24	1	54	0	21	54	65	29	2	47	2	1	3	17	14	4			
			2	91	5	23	71	69	40	55	4	0	47	0	96	9		3	3	77	19	0	51	0	18	66	75	19	0	51	2	2	1	20	14	0			
			X	5	100	0	0	90	80	20	0	0	60	0	100	20		0	0	100	40	0	100	0	0	60	80	60	0	60	0	20	0	0	0	0			
	63	Elucidation of the molecular mechanisms for formation of neuronal networks at the molecular level.	1	159	11	31	58	66	37	53	8	1	16	0	62	74		3	6	86	45	0	39	0	9	72	25	35	10	62	1	0	1	6	13	2			
			2	130	7	28	65	64	30	65	5	0	9	0	62	82		0	5	92	45	0	36	0	3	78	17	28	5	64	0	0	1	6	15	0			
			X	9	100	0	0	94	89	11	0	0	33	0	44	89		0	0	89	56	0	44	0	0	78	0	33	0	56	0	0	0	0	11	0			
	64	Elucidation of relationship between learning/memory and synaptic plasticity.	1	153	10	31	58	68	41	50	9	1	16	0	58	75		2	6	86	42	1	42	0	8	73	27	37	7	61	1	0	0	8	20	2			
			2	126	8	29	63	68	39	56	5	0	10	0	58	81		0	2	92	41	1	39	0	2	79	18	31	2	64	0	0	0	5	21	1			
			X	10	100	0	0	95	90	10	0	0	30	0	50	90		0	0	90	40	0	50	0	0	80	10	60	0	70	0	0	0	10	10	0			
	65	Elucidation of brain mechanisms for logical reasoning.	1	138	7	26	67	67	40	47	11	1	17	1	43	81		9	14	78	38	1	36	0	14	68	28	33	4	59	1	0	1	7	21	1			
			2	113	4	25	72	67	36	59	5	0	15	0	40	88		9	8	87	37	1	35	0	9	74	24	25	1	61	0	0	0	4	24	0			
			X	4	100	0	0	88	75	25	0	0	50	0	25	100		0	0	100	25	0	50	0	0	75	50	75	0	75	0	0	0	25	25	0			
66	Elucidation of the whole molecular mechanisms for synaptic plasticity in the mammalian brain. (e.g. hippocampal long-term potentiation and depression).	1	139	9	29	62	64	36	52	11	1	8	1	54	71		4	6	81	40	1	42	0	13	71	25	37	7	67	0	0	1	7	14	1				
		2	117	5	30	65	63	30	60	9	0	8	1	51	80		5	5	89	39	0	43	0	5	77	16	30	2	68	0	0	1	3	18	1				
		X	6	100	0	0	92	83	17	0	0	33	0	50	67		0	0	100	50	0	33	0	0	100	0	67	0	100	0	0	0	0	17	0				
Individuals	67	Become possible to cure senile dementia of Alzheimer type.	1	187	8	27	65	83	67	29	3	1	19	1	95	17		8	10	83	40	1	39	0	11	69	37	23	14	59	6	1	1	14	26	3			
			2	154	6	31	64	86	73	25	1	0	14	1	98	12		6	6	88	42	0	42	0	8	75	34	19	11	64	3	1	1	12	31	0			
			X	9	100	0	0	100	100	0	0	0	11	0	100	11		0	0	100	56	0	44	0	0	56	11	22	22	100	0	0	0	11	33	0			
	68	Elucidation of the cause of manic-depressive psychosis at the molecular level.	1	145	11	24	65	73	49	47	4	1	12	1	95	25		3	3	79	43	3	29	0	15	73	31	28	16	58	4	0	1	19	29	2			
			2	127	5	27	69	74	50	46	4	0	9	1	99	21		2	3	87	46	1	28	0	9	81	29	25	6	59	3	0	1	13	31	0			
			X	6	100	0	0	75	50	50	0	0	17	0	100	50		0	0	100	83	0	67	0	0	50	67	67	17	83	0	0	0	33	33	0			
	69	Elucidation of the cause of schizophrenia at the molecular level.	1	143	12	23	65	73	49	48	3	1	15	1	95	26		4	4	77	43	3	27	0	16	73	32	27	17	57	4	0	1	21	31	1			
			2	127	6	26	69	74	50	48	2	0	11	1	99	22		2	4	87	50	0	26	0	9	80	34	22	6	60	2	0	1	17	33	0			
			X	7	100	0	0	86	71	29	0	0	14	0	100	57		0	0	100	86	0	57	0	0	57	86	43	0	86	0	0	0	14	29	0			
	70	Widespread use of methods for controlling the immune system locally.	1	193	18	29	53	75	52	43	4	1	20	1	97	19		4	7	80	42	1	45	2	13	68	37	24	10	61	4	0	1	10	17	2			
			2	158	16	27	56	76	54	41	5	0	18	0	98	16		1	3	88	44	0	49	1	8	77	34	18	6	64	3	0	1	16	16	0			
			X	26	100	0	0	84	69	27	4	0	35	0	100	12		0	0	100	73	0	77	4	0	96	54	15	0	85	0	0	0	12	8	0			

(Note) See page 7 for the interpretation of the graphs.

Division	Topic serial No.	Topic	Questionnaire round	Number of respondents	Degree of expertise (%)			Importance (index, %)				Expected effect (%)			Forecasted realization time					Leading countries (%)					Measures the government should adopt (%)					Life Science Potential problems (%)								
					High	Medium	Low	Index	High	Medium	Low	Unnecessary	Socioeconomic development	Resolution of global problems	People's needs	Expansion of intellectual resources						USA	EU	Former Soviet Union and Eastern Europe	Japan	Other countries	Do not know	Foster human resources	Promote exchanges among industrial, academic and government sectors and different fields	Upgrade advanced facilities and equipment	Develop a research base	Increase government research funding	Adjust regulations (relax/toughen)	Others	Adverse effect on the natural environment	Adverse effect on safety	Adverse effect on morals, culture or society	Other adverse effects
					2001	2006	2011	2016	2021	2026	Will not be realized (%)	Do not know (%)	USA	EU	Former Soviet Union and Eastern Europe	Japan	Other countries	Do not know	Foster human resources	Promote exchanges among industrial, academic and government sectors and different fields	Upgrade advanced facilities and equipment	Develop a research base	Increase government research funding	Adjust regulations (relax/toughen)	Others	Adverse effect on the natural environment	Adverse effect on safety	Adverse effect on morals, culture or society	Other adverse effects									
Individuals	71	Elucidation of the mutual regulatory mechanisms of the immune system, nervous system, and endocrine system, and utilization of such knowledge in the treatment of disease and promotion of health.	1	196	14	37	49	75	54	41	5	1	19	1	92	36		2	7	84	48	0	46	1	10	68	38	28	12	64	1	0	2	8	18	2		
			2	165	10	39	50	78	57	41	1	0	13	1	96	35		1	3	90	50	0	46	1	7	76	38	21	7	65	1	0	2	7	21	1		
			X	17	100	0	0	88	76	24	0	0	29	12	100	59		0	0	88	53	0	76	0	0	82	47	12	12	82	0	0	6	12	18	0		
	72	Scientific elucidation of the factors within daily life (eating habits, air quality, etc.) which influence the process of carcinogenesis.	1	239	14	33	54	79	61	33	5	1	16	18	95	23		2	8	77	40	1	57	0	13	64	38	21	15	59	3	0	7	6	16	2		
			2	197	11	31	58	83	68	31	2	0	11	14	97	19		1	3	86	38	1	63	0	9	71	36	17	10	64	4	0	6	4	18	1		
			X	22	100	0	0	91	82	18	0	0	14	14	91	36		0	9	100	50	5	86	0	0	77	55	23	14	73	9	0	14	5	18	0		
	73	Development of a complete in vitro embryo cultivation technique based on artificial placentas for small mammals.	1	127	10	25	65	50	18	54	21	7	29	20	50	34		8	13	61	34	1	23	0	25	56	37	32	6	46	6	0	9	12	41	2		
			2	102	8	26	66	54	18	62	18	2	29	14	58	33		6	6	75	35	0	26	0	17	64	32	27	2	47	4	0	5	8	44	0		
			X	8	100	0	0	75	50	50	0	0	38	0	63	75		0	13	100	75	0	63	0	0	88	50	13	13	63	13	0	13	25	63	0		
	74	Identification and classification by the molecular etiology of the genes related to diabetes, hypertension, and arteriosclerosis, typical geriatric diseases which exhibit multiple-factor hereditary traits.	1	221	17	31	52	83	68	26	4	1	20	1	93	32		1	5	87	52	1	45	0	7	64	29	23	38	62	2	0	1	21	23	2		
			2	180	16	32	52	88	77	22	1	0	16	1	98	26		0	3	94	54	1	49	0	3	73	22	18	34	66	3	0	1	16	29	1		
			X	28	100	0	0	95	93	4	4	0	21	4	100	29		0	0	100	71	0	64	0	0	75	11	18	43	57	4	0	4	11	32	0		
	75	Widespread use of remote surgery systems utilizing virtual reality technology.	1	112	9	21	71	56	27	48	21	5	31	0	89	7		4	8	68	23	0	41	0	17	46	57	25	0	51	5	1	1	15	12	3		
			2	93	6	22	72	53	18	57	24	1	30	1	94	3		6	2	81	17	0	38	0	13	51	61	22	0	48	1	1	0	17	11	0		
			X	6	100	0	0	67	33	67	0	0	67	17	100	0		0	0	83	17	0	67	0	0	67	83	50	0	67	0	0	0	17	17	0		
	76	Widespread use of vicarious experience devices (using virtual reality technology) which allow bed-ridden patients to take vacations, etc.	1	96	9	20	71	48	16	46	32	5	30	0	90	6		5	1	60	17	0	40	0	22	30	60	20	1	36	2	1	1	8	24	3		
			2	81	7	21	72	47	10	59	28	2	31	1	94	1		2	0	69	11	0	41	0	21	35	64	11	4	41	1	1	0	7	30	0		
			X	6	100	0	0	46	17	50	17	17	67	17	67	0		0	0	67	17	0	67	0	0	33	83	33	0	50	0	17	0	17	33	0		
	77	Elucidation of the molecular mechanisms of flower bud differentiation in higher plants and its application in agriculture.	1	155	15	32	54	69	44	46	10	1	35	80	12	39		1	5	69	40	2	34	1	19	66	31	23	16	52	5	0	28	3	3	3		
			2	123	15	26	59	69	41	53	7	0	34	84	7	31		0	1	77	39	2	40	1	15	78	26	15	9	64	2	0	34	2	2	1		
			X	18	100	0	0	74	50	44	6	0	39	89	11	39		0	6	100	39	0	44	6	0	94	17	17	11	72	0	0	61	0	0	6		
	78	Practical use of technology for producing cloned individuals from the cells of livestock.	1	188	11	25	64	64	36	49	13	1	41	69	20	24		12	13	72	40	2	29	1	17	58	37	27	11	45	9	1	18	6	27	2		
			2	145	9	23	68	61	28	62	9	1	41	76	9	16		11	6	81	39	2	26	1	12	68	37	21	8	51	6	1	17	4	32	1		
			X	13	100	0	0	83	69	23	8	0	69	54	8	31		8	8	92	54	0	46	8	0	77	46	31	15	54	15	0	23	0	46	8		
79	Production of genetically engineered plants and microorganisms which are resistant to or able to reduce NOx, as a means of preserving the environment.	1	182	15	31	54	70	43	50	7	0	26	91	20	9		1	5	65	35	1	41	1	23	60	32	26	14	53	7	0	43	2	7	3			
		2	150	14	29	57	68	39	55	5	1	22	91	12	3		1	3	73	35	1	46	0	19	72	31	17	9	58	5	0	45	1	3	1			
		X	21	100	0	0	76	52	48	0	0	38	90	10	5		0	0	95	33	5	57	0	0	86	24	14	5	57	10	0	52	0	10	0			
80	Production of genetically engineered plants with high CO2 fixing ability, as a means of preserving the environment.	1	187	17	30	52	74	52	40	8	0	27	93	14	13		1	6	65	35	1	39	0	25	62	32	27	15	57	7	0	48	3	4	3			
		2	155	14	32	54	77	57	37	5	1	21	92	10	6		1	1	74	34	1	41	0	19	70	32	19	10	65	5	0	49	1	1	1			
		X	21	100	0	0	82	67	29	5	0	38	86	10	10		0	0	95	57	5	52	0	0	81	29	19	14	67	0	0	57	0	0	0			

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					2001	2006	2011	2016	2021	2026	Will not be realized (%)	Do not know (%)	USA	EU	Former Soviet Union and Eastern Europe	Japan	Other countries	Do not know	Foster human resources	Promote exchanges among industrial, academic and government sectors and different fields	Upgrade advanced facilities and equipment	Develop a research base	Increase government research funding	Adjust regulations (relax/toughen)	Others	Adverse effect on the natural environment	Adverse effect on safety	Adverse effect on morals, culture or society	Other adverse effects									
Individuals	81	Practical use of plants accumulating high amount of hydro-carbon as fuel sources.	1	141	11	34	55	66	42	39	16	3	33	92	11	9		11	13	55	29	1	20	3	28	52	36	21	15	42	6	1	33	3	4	4		
			2	120	7	33	61	68	45	42	12	2	33	96	6	3		7	8	68	31	1	23	4	22	66	37	14	12	52	2	1	43	1	3	2		
			X	8	100	0	0	72	50	38	13	0	38	88	13	0		13	0	88	25	0	25	0	0	75	25	0	25	38	0	0	25	0	0	0		
	82	Elucidation of the entire molecular mechanisms which generate the internal rhythms in organisms.	1	177	7	29	63	53	22	45	31	2	11	11	51	71		2	10	72	40	1	29	0	16	68	22	22	10	53	0	0	7	2	14	3		
			2	145	3	33	64	50	15	55	27	2	8	6	47	75		1	3	82	39	1	23	0	12	82	17	19	6	57	0	0	3	2	21	1		
			X	4	100	0	0	38	0	75	0	25	0	0	50	75		0	0	100	25	0	50	0	0	75	0	50	0	100	0	0	0	0	25	0		
	83	Elucidation of the neural mechanisms of sleep and dreams.	1	118	3	19	78	48	16	48	36	1	8	2	69	62		6	9	65	30	2	29	0	25	69	19	25	5	49	0	0	1	12	19	2		
			2	99	1	22	77	48	12	57	30	1	7	0	72	66		5	5	78	28	1	30	0	17	84	14	21	3	56	0	0	1	12	25	0		
			X	1	100	0	0	50	0	100	0	0	0	0	100	0		0	0	100	0	0	0	0	0	100	0	0	0	100	0	0	0	100	0	0		
	84	Complete elucidation of the molecular mechanisms of development and differentiation.	1	242	23	32	45	71	48	40	11	0	15	13	48	81		5	14	86	56	1	40	0	6	73	22	26	22	66	1	0	5	6	21	3		
2			201	21	31	47	71	48	44	8	1	10	7	46	84		7	8	92	60	0	41	0	3	82	16	21	12	68	1	0	3	4	25	1			
X			43	100	0	0	82	67	28	2	2	14	12	47	91		7	5	98	81	0	65	0	0	93	23	26	19	70	0	0	2	2	23	5			
85	Elucidation of the environmental and genetic factors which determine the sizes and shapes of trees.	1	130	10	23	67	55	22	54	24	1	22	78	8	47		5	10	55	39	2	25	2	27	58	23	22	19	50	0	0	24	2	8	4			
		2	108	9	19	71	56	19	67	13	1	14	77	5	44		4	6	72	38	1	25	1	19	76	18	17	14	54	1	0	28	1	6	1			
		X	10	100	0	0	75	50	50	0	0	30	80	10	20		0	0	100	40	0	20	0	0	80	20	40	10	70	0	0	50	0	0	0			
86	Elucidation of the neurobiological basis for emotion.	1	118	8	25	67	56	22	59	18	1	8	2	66	62		2	14	71	36	4	27	0	22	71	19	29	8	54	2	0	0	17	26	2			
		2	102	5	25	70	57	20	69	11	1	6	0	71	68		4	9	76	36	3	24	0	19	80	19	25	2	57	1	0	1	14	30	2			
		X	5	100	0	0	70	40	60	0	0	20	0	100	60		0	0	80	40	0	40	0	20	100	60	0	20	100	0	0	0	20	60	0			
87	Elucidation of physiological effects of gravity-free state and development of measures for preventing deterioration in biological functions caused by the weightless state.	1	92	0	29	71	42	9	48	36	7	14	11	51	48		5	10	85	22	16	11	0	11	48	32	38	2	51	1	0	7	2	8	1			
		2	82	0	28	72	45	10	53	34	4	11	9	59	54		5	5	88	22	18	10	0	5	62	29	37	0	62	1	0	7	1	7	1			
		X	0	-	-	-	-	-	-	-	-	-	-	-	-		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-				
88	Development of technologies for breeding and cultivating organisms in (cosmo) space.	1	116	5	24	71	43	14	38	41	7	29	47	13	34		7	7	82	15	14	12	0	11	47	34	30	3	48	0	2	16	4	3	3			
		2	99	3	23	74	43	12	42	42	4	23	61	6	34		1	3	87	17	15	11	0	7	55	31	21	3	58	0	2	20	2	1	1			
		X	3	100	0	0	75	50	50	0	0	67	67	0	0		0	0	67	67	0	0	0	0	67	33	33	0	67	0	0	0	0	0	0			
89	Development of perfect testing procedures to replace testing on animals.	1	193	18	27	55	71	48	42	8	1	41	20	64	24		20	13	64	40	1	27	0	22	52	37	22	8	49	7	0	6	5	20	2			
		2	166	14	27	58	71	46	45	7	2	40	16	70	20		18	5	72	47	1	25	0	19	64	35	16	4	58	7	0	2	5	22	0			
		X	24	100	0	0	79	67	25	0	8	58	33	58	29		38	0	79	63	0	50	0	17	63	50	8	0	79	13	0	0	8	29	0			
90	Widespread use of novel educational curriculums through the elucidation of the physiological and psychological mechanisms of independence formation, personality development, etc. in humans.	1	79	1	19	80	69	48	33	18	1	32	1	56	43		9	16	57	33	1	14	0	29	62	30	25	4	47	8	0	0	16	46	3			
		2	68	0	25	75	75	55	35	9	0	31	1	60	40		10	10	68	38	0	12	0	25	68	25	16	1	50	6	1	0	9	40	0			
		X	0	-	-	-	-	-	-	-	-	-	-	-	-		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-				

(Note) See page 7 for the interpretation of the graphs.

Division	Topic serial No.	Topic	Questionnaire round	Degree of expertise (%)			Importance (index, %)				Expected effect (%)			Forecasted realization time				Leading countries (%)					Measures the government should adopt (%)					Potential problems (%)								
				Number of respondents	High	Medium	Low	Index	High	Medium	Low	Unnecessary	Socioeconomic development	Resolution of global problems	People's needs	Expansion of intellectual resources	Will not be realized (%)	Do not know (%)	USA	EU	Former Soviet Union and Eastern Europe	Japan	Other countries	Do not know	Foster human resources	Promote exchanges among industrial, academic and government sectors and different fields	Upgrade advanced facilities and equipment	Develop a research base	Increase government research funding	Adjust regulations (relax/toughen)	Others	Adverse effect on the natural environment	Adverse effect on safety	Adverse effect on morals, culture or society	Other adverse effects	
Groups	91	Development of technologies which dramatically improve photosynthetic ability in order to increase food production.	1	183	17	33	49	83	68	30	2	1	38	96	14	15		4	14	70	40	2	40	1	19	64	40	25	16	62	2	1	43	2	5	3
			2	149	15	32	52	86	73	23	3	1	38	93	7	8		2	7	79	44	2	44	1	13	73	38	17	12	70	2	1	47	1	4	2
			X	23	100	0	0	93	87	13	0	0	48	87	0	13		0	4	96	48	4	52	9	0	87	30	13	13	70	0	0	35	0	0	4
	92	Practical application of breeding techniques for plants resistant to dry and saline conditions aimed at desertification prevention.	1	180	14	30	56	62	35	45	18	2	30	94	12	12		1	9	61	33	2	35	4	23	57	36	27	17	57	2	1	44	1	3	3
			2	148	11	30	58	61	30	55	14	1	25	95	7	4		1	4	74	34	1	38	5	17	69	39	14	9	67	1	1	44	0	1	1
			X	17	100	0	0	79	65	24	12	0	29	94	0	0		0	0	94	41	6	53	18	0	65	24	18	6	59	0	0	47	0	0	0
	93	Emergence of experimental evidence of the evolutionary mechanism of organisms.	1	216	12	29	59	48	18	43	35	4	5	14	10	92		13	16	66	40	3	26	0	20	64	16	24	21	53	0	0	7	2	27	4
			2	177	10	25	64	47	14	49	34	2	4	5	7	95		11	15	75	45	3	20	0	15	77	9	19	18	58	1	0	5	1	32	1
			X	18	100	0	0	78	61	28	11	0	11	11	17	100		11	11	94	61	0	39	0	6	78	11	33	22	61	0	0	0	0	33	0
	94	Advancement of the analysis of the human genome diversity regarding individual races, and the elucidation of the origin and phylogeny of human being.	1	235	10	26	64	44	13	42	37	8	3	6	22	87		2	11	80	49	1	32	0	11	55	14	17	43	47	2	2	1	18	49	2
			2	196	11	23	66	45	11	49	37	3	1	4	15	95		2	8	84	48	1	28	0	10	71	9	10	45	54	2	2	1	13	55	0
			X	22	100	0	0	60	32	50	14	5	0	5	18	95		0	0	100	68	0	36	0	0	82	14	18	41	64	0	0	0	14	59	0

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