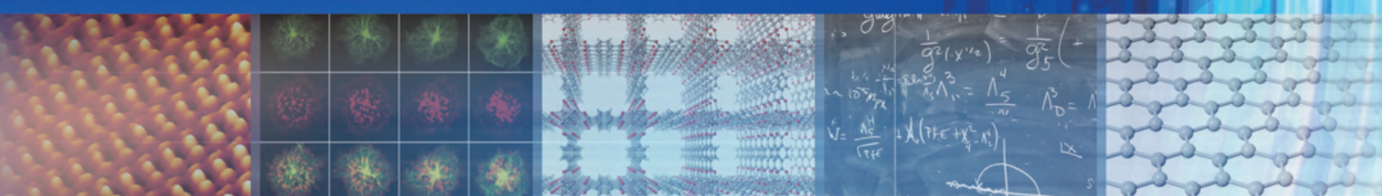
WPI

World Premier International
Research Center Initiative

10 Year Commemoration of the WPI Program



Circulating World's Best Brains

WPI

World Premier International Research Center Initiative

10 Year Commemoration of the WPI Program

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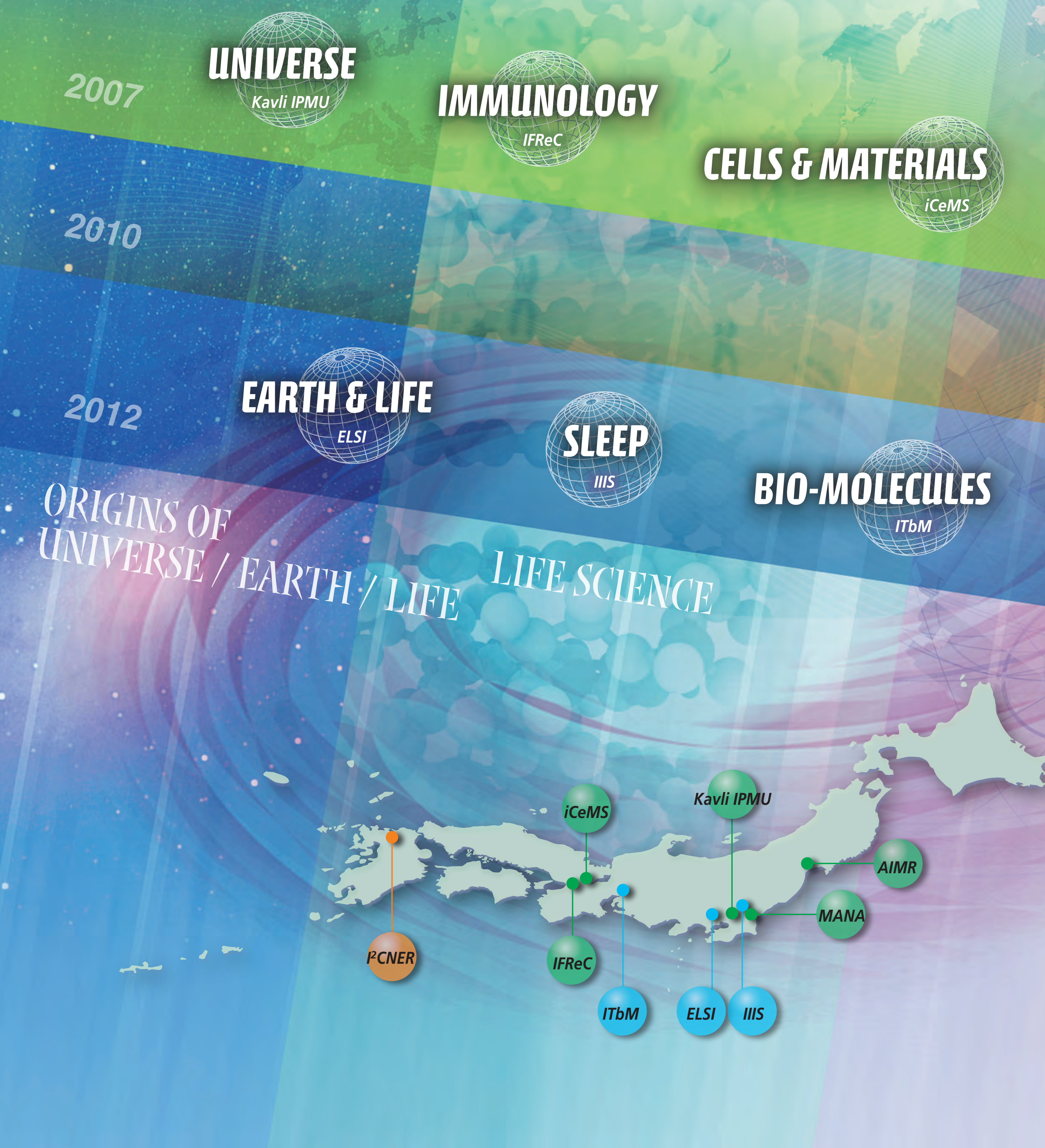

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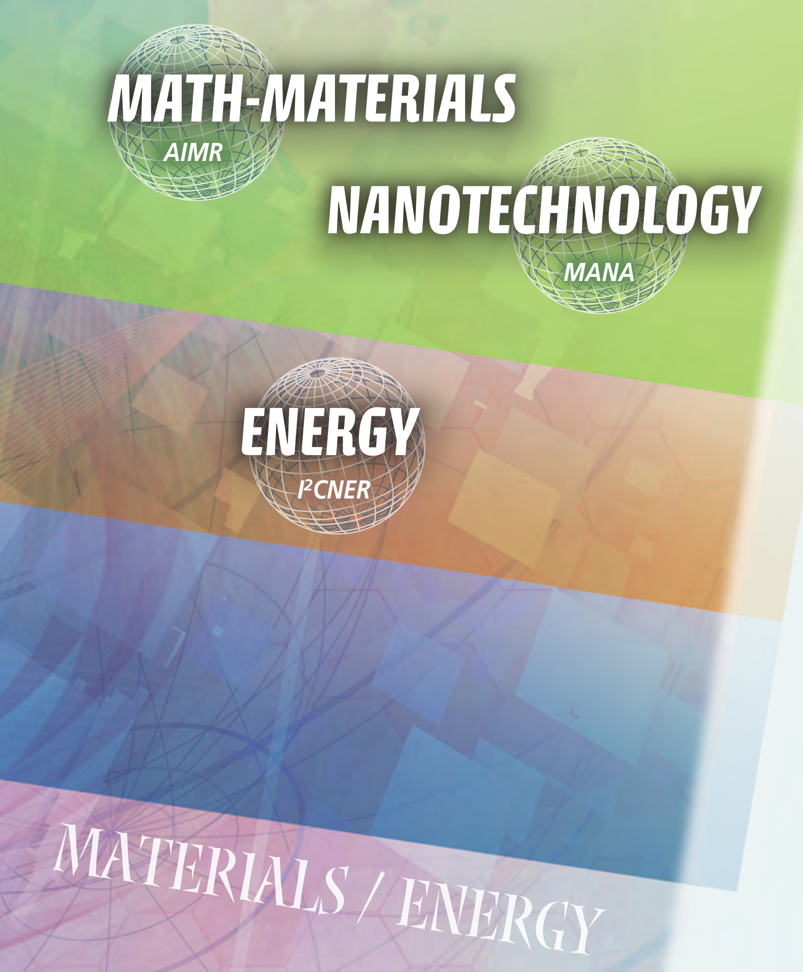


Message

The Objectives, Systems and History of the WPI Program

Effort and Achievement in Each Research Center

* The articles of centers selected in 2007 also provide ‘Research Paper’s Information’. The range of responsibilities of ‘Research Support Staff’ and ‘Administrative Staff’ described in the ‘Research Center’s Information’ is based on the report prepared by each center.

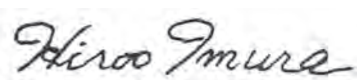
Message

The emblem of the WPI Program adopts the motif of a bird, symbolizing the program's driving concept of "upward flight. "Undaunted by today's turbulent global climate of twisting and turning winds, the bird flies on steady, azure wings through the sky. In its beak, it carries a seed of new innovation. This radiant dot over the "i" also serves to light the path ahead in pioneering the frontiers of scientific discovery.

wpi
World Premier International Research Center Initiative

*The ‘fiscal year' or ‘FY’ in the text is the Japanese Government fiscal year, which begins on April 1 and ends on March 31 of the following year.

On the 10th anniversary of the WPI Program



Hiroo Imura

Inaugural Chairperson of the Program Committee of the World Premier International Research Center Initiative, FY 2007-2015

Clark Kerr, the famous former chancellor of the University of California, once said that in every flourishing nation in history, there has been an outstanding university working on the cutting edge of global scholarship. Universities are places that pass on knowledge, cultivate it, and nurture those who go on to forge the future. It is essential that they possess groups of highly skilled researchers, research organizations, research facilities, and so on. These are referred to collectively as "Centers of Excellence" (COEs) and the best universities host multiple COEs that are world-famous. COEs can, of course, be found not only in universities, but also in independent research institutes and in the private sector.

Science and technology have become an important aspect of national policy since the latter half of the 20th century. One of the factors behind this has been the major structural changes in industry that occurred with increasing globalization. Organizations were established to provide advice on science and technology policy to governments, in order to further promote research activities. Efforts to proactively foster COEs are one example of this, and such efforts, referred to as "excellence initiatives," have become increasingly vigorous all around the world, particularly from the start of the 21st century.

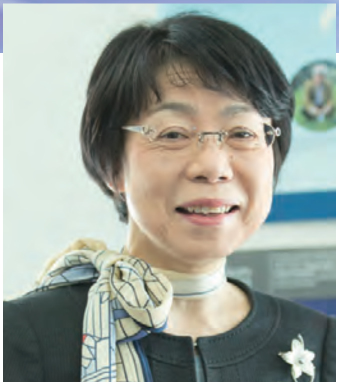
Several COE programs were launched in Japan as well in the 1990s, but they were not necessarily very successful. There are several probable reasons for this, including the fact that the grant periods were generally short, grants were used as research funds, and they did not receive university-wide support. Discussions were held at meetings of the Council for Science and Technology Policy (now the Council for Science, Technology and Innovation) to address this issue, and, as a result, the Ministry of Education, Culture, Sports, Science and Technology (MEXT) launched the World Premier International Research Center Initiative (WPI) as the ultimate COE program. I was appointed as the inaugural Chairperson of the WPI Program Committee at its launch in 2007.

Before the launch, the committee members based in Japan gathered to decide the basic policies of the WPI Program. Firstly, it was decided that the objective of the program would be to create organizations of worldwide renown that would become centers for global intellectual exchange. Naturally it would be necessary to have large numbers of overseas researchers working in these centers, and to achieve results on a level that would grab the world's attention. The decision was also made to ensure that approximately half of the members of the Program Committee would be non-Japanese academics. Secondly, instead of using government funds to cover research expenses, they should be used to build up the research centers by covering personnel costs etc., and that, provided that centers passed interim evaluations, they would in principle receive support for a 10-year period. Thirdly, these centers would differ from conventional Japanese organizations by being less hierarchical and more flexible, and the centers, including their administrative structures, would aim to become models for university reform. Fourthly, the heads of the host universities or research institutes would be required to support the WPI Program and take responsibility for sustaining the centers after government support ended. Fifthly, emphasis would be placed on proposals that sought to actively develop interdisciplinary and fusion research fields, which were expected to become areas with a wealth of research potential (this was later amended slightly to support any truly cutting-edge research, even if it did not necessarily involve the fusion of different fields). Lastly, a Program Director (PD) would be assigned to oversee the program, Program Officers (POs) would be assigned to each center, and annual site visits would be made to each center.

I believe it was extremely beneficial that we decided on these policies from the very beginning. Unlike conventional Japanese COE programs, global evaluation has been given emphasis. Furthermore, the PDs and POs have been passionate in their support for the creation of the centers, and have on occasion been prepared to provide harsh criticism. Support from host universities and other organizations has also been strengthened, with much effort being made to enhance research facilities. Moreover, large numbers of overseas researchers are now active at each of the centers and the resulting cosmopolitan atmosphere has, albeit gradually, begun to influence the host universities. As a result, the program is now widely recognized and appraised. The research performance of the centers, which is of course the most important factor for COEs, has earned an extremely favorable reputation, both in terms of objective performance indicators such as research publications, and in terms of the evaluations of the international members of the Program Committee. It therefore brings me great joy to see that the first decade of the program is regarded by so many as a success.

What is most important, however, is the program's future. First we need to look back and take stock of the last 10 years, hold discussions on our future vision for the program, and determine the path we need to take. Another important issue to consider is what requirements we should set for new WPI centers. We also need to decide what advice and support to give to centers that are no longer a part of the program. Moreover, in a reversal of situation in the aforementioned quote by Clark Kerr, it may be no exaggeration to say that the state of WPI and other COEs in Japan could even decide not only the future of scholarship in Japan, but also the prosperity or decline of the entire nation. This is the true aim of these proceedings that cover the first 10 years of activities, and I hope that as many people as possible will take time to consider the state of academia in Japan and the role of COEs in this.

Finally, I would like to express my gratitude to all of the Program Committee members; the PDs and POs; university presidents; everyone working at the WPI centers, especially center directors; MEXT; and the Japan Society for the Promotion of Science (JSPS).



WPI and the revitalization of research in Japan

Yayoi Komatsu

Director-General of the Research Promotion Bureau, MEXT

Ten years on from the launch of the WPI Program, each of the WPI centers has developed into an organization that is regarded extremely highly globally. This is all due to the deeply enthusiastic counsel and advice provided by the Program Committee, especially former Program Committee Chairperson Hiroo Imura and present Chairperson Ryoji Noyori; the committed support provided by the PDs and POs; the outstanding research capabilities and leadership of the directors of each center; and the continued assistance provided by the presidents of the host institutions, and I would like to express my sincere gratitude to them all for their efforts.

2016 marks the tenth year of the planned government support and there have been lively discussions amongst stakeholders in the program regarding its future direction. The discussions have covered issues such as how to maintain and further develop the outstanding achievements of each center to date; whether or not the burden placed on the host institutions is too heavy; the fact that it would be a waste not to feed research results back into the host institutions and into other universities and R&D organizations; thoughts on the establishment of new centers; how many WPI centers are ultimately necessary in Japan; and so on.

With regard to centers for which government support is ending, the host institutions have fortunately indicated their resolve to appropriately position the centers and work to maintain them. While the government will do everything it can to provide support, the government also has high expectations for efforts on the part of host universities and organizations to fully incorporate and internalize the valuable research results. The government is also planning to launch a program to create an environment for other organizations to be able to utilize the knowledge built up by each WPI center, as assets shared by everyone in Japan.

It has been noted that in the same ten-year span, the global standing of Japan's universities in general, as well as Japan's scientific, technological, and academic research environments have experienced a relative decline. There can be no doubt that that poses a potential crisis for Japan's future. It is essential that we build on the achievements of the WPI Program to overcome this situation.

In FY 2016, we have been able to earmark funding for two new centers in our budgetary request for FY 2017. Although there is a need for further discussions by the Program Committee and other bodies regarding the total number of centers that will ultimately be required, I believe that we are slowly but surely advancing to the next stage of the program.

The WPI Program is targeted at basic research in the field of natural sciences. As can be seen from the example of artificial intelligence, these days technology itself is becoming closely intertwined with the very structure of society. I realize that people are already cognizant of this fact, but it is my hope that they will value the relationship between basic research and the development of contemporary society.

Through the further advancement of the WPI Program, MEXT is aiming to enhance the standard of Japan's academic and technological research, and enhance the international standing of Japan's universities and research institutes. I would like to express once again my gratitude to everyone involved in supporting and nurturing the WPI Program and request your continued cooperation with the program's future development and expansion.

Creating superlative knowledge through the WPI Program

Yuichiro Anzai
President of the Japan Society for the Promotion of Science

Superlative knowledge is created by the tireless creative and cutting-edge work of researchers in fields from the humanities and social sciences to natural sciences, and has contributed a great deal to the development of human society. In addition to seeking the truth, the work of these researchers to create this superlative knowledge also provides society with solutions and footholds from which to surmount the complex and diverse challenges facing Japan, and the importance of this work grows day by day.

The third mid-term plan of JSPS sets out four fundamental pillars. One of these pillars is creating diverse world-level knowledge. As the only funding agency in Japan supporting academic research, we promote research that creates diverse knowledge, within a world-class academic system. The WPI Program forms part of this pillar. Ever since the launch of the WPI Program, JSPS has worked in tandem with MEXT on the review and evaluation of each WPI center.

Programs that support relatively large-scale and long-term research are normally subjected to an interim evaluation a few years after the research begins, followed by a final evaluation in the year in which the research ends. However, what makes the WPI Program different is that it involves a more thorough plan-do-check-act (PDCA) cycle than has been the case in other such programs. Specifically, with the intention of creating world-leading research centers, WPI centers are continually improved through a review and evaluation process that involves not only interim and final evaluations, but also annual site visits by the Program Directors (PDs), as well as a Program Officer (PO) and working group members who are specially assigned to the WPI center in question. Furthermore, centers are evaluated by the Program Committee not only from a scientific perspective, but also in terms of the level of fusion, how global the center is, and the extent to which organizational reform is occurring.

Thanks to the considerable cooperation provided by the Program Committee members, the PDs, the POs, and working group members, who have devoted their precious time to carrying out annual evaluations and providing advice; and thanks, above all else, to the perseverance, the flexible response to daily changes occurring in global science, and the outreach activities of WPI researchers, especially the directors of each WPI center and the heads of their host institutions, research support staff, and administrative staff, each of the WPI centers was able to reach its respective targets. Moreover there have been many positive ripple effects from their research and other activities. This result is truly deserving of great praise.

In Japan we have a saying that a decade in the past is like ancient history, but there is nothing outdated about the WPI Program ten years on from its launch. Rather, it could perhaps be called an outstanding example to research organizations. It has tackled head-on the demands placed on contemporary academic research, namely, being "competitive, comprehensive, interdisciplinary, and international," and it has achieved impressive results in doing so. JSPS intends to continue working to ensure that each WPI center is able to shine yet brighter and that the ripple effects from the example they provide reach all corners of Japan. We look forward to your continued understanding and support for the academic research activities that underpin these efforts to create superlative knowledge.

How the WPI Program was born

Hiroshi Ikukawa

Deputy Director General, Bureau of Science, Technology and Innovation, Cabinet Office
Former Director, Planning and Evaluation Division, Science and Technology Policy Bureau, MEXT.

The inception of the WPI Program can be traced back to the target outlined in the third Science and Technology Basic Plan (for April 2006 to March 2011) to "create about 30 research centers that will be positioned as the world's top-class centers." During the subsequent process of deliberating on the implementation of the third Science and Technology Basic Plan, the Council for Science and Technology Policy (now the Council for Science, Technology and Innovation) requested that MEXT consider how to make this idea a reality.

I had only just returned to Japan after serving as the Counsellor for Science and Technology at the Embassy of Japan in the United States in order to assume the role of Director of the Planning and Evaluation Division at the Science and Technology Policy Bureau at MEXT, when the Director-General of the Science and Technology Policy Bureau at the time instructed me to take charge of putting the WPI plan into practice.

The first thing I did was to listen to the ideas of people working in related fields, particularly the permanent members of the Council for Science and Technology Policy. I recall that although there was a shared recognition of the need to create world-leading research centers in Japan in order to take Japan's science and technology to the next level, and also a strong intention to do so, there was a wide divergence in terms of specific measures and concepts.

Meanwhile, at the time, MEXT was already implementing a variety of different research center programs including the 21st Century Center Of Excellence Program, the Super COE Program, and the Advanced Interdisciplinary Research Areas Program. Therefore, frankly speaking, there was not much enthusiasm at MEXT for the launch of yet another such program, at least at the early stages. I recall that as discussions progressed, they centered on the idea that, if we were going to launch another research center program, it would have to be significantly different in content to previous programs, and that it ought to be bolder and have a strong impact.

In light of such circumstances, I began to engage in even more in-depth discussions with a large number of experts, including members of the Council for Science and Technology Policy, about the objectives of the program, if we were indeed to set up such a program. The discussions involved, among others, Dr. Hiroo Imura, former President of Kyoto University and former member of the Council for Science and Technology Policy; Dr. Ryoji Noyori, who was then President of RIKEN, Japan; and the late Dr. Yoji Totsuka, former Director of the High Energy Accelerator Research Organization. I would like to express my sincere gratitude to them for the passionate enthusiasm with which they engaged in the discussions.

During the course of the discussions, the framework of the program began to take shape. One of the ideas discussed was aiming to create "globally visible research centers," and centers that would function as hubs for "international brain circulation." To achieve this it would be necessary to realize high research standards and create outstanding world-class research environments that would encourage distinguished researchers from around the world to come and conduct research in them and thereby create a critical mass of outstanding researchers that would encourage yet more researchers to join in. There was also wide-ranging discussion on what fields of research ought to be targeted. It was suggested that in order to facilitate great achievements and the creation of new scientific domains, we should promote the fusion of different fields of research. It was also suggested that not confining target fields to the bounds of any single existing field would help encourage bold system reform. This led us to consider pursuing fields of fusion research.

I believe that what lay behind these discussions was a sense of crisis. When one looks at the United States, it is obvious the standard of their science and technology is extremely high. This is not simply because Americans are performing exceedingly well however. One major reason for their high standards is that outstanding researchers and students from around the world gravitate toward the United States with the hope of conducting research or studying there. Cognizant of this, we strongly felt that, in order to catch up with such countries and be able to compete with them, we had to create the kind of environment that would encourage outstanding researchers from around the world to gather in Japan.

Deliberations continued based on this line of thinking, and because of this, it did not become a program aimed at subsidizing research expenses. Rather, the program is structured such that subsidies are used to realize high research standards (by creating a critical mass of outstanding researchers), and to create an outstanding and world-class research environment. This was predicated on the idea that the high-caliber researchers who would gather at the research centers would be able to obtain the necessary research funds through competitive research grants.

The basic concept behind the WPI Program was to create world-leading research centers by forming groups of researchers of a level and scale that could be considered critical masses, consisting of core groups of researchers from the fields that the host organizations (universities, national R&D entities, etc.) specialized in, and additional high-caliber researchers recruited from outside the host organizations, including researchers from overseas. In addition, a world-standard research environment would be created including making English the official language used at the centers.

In order to encourage high-caliber researchers to come to Japan, it is necessary to address social issues such as education for their school-aged children, employment for their spouses, and providing housing and medical care. To that end, we coordinated with the Ministry of Finance and other bodies when preparing the budget for the program, in order to make it possible to use subsidies to fund a wide range of different expense items, including a variety of different allowances, and support by the administrative staff of each center.

The WPI Program requires that each center and their host organizations engage in very bold system reforms involving significant shifts away from conventional practices. The strong top-down management style is another important characteristic of the program.

One of the reforms involved forming a powerful program committee to encourage each center and host organization to steadily implement system reforms that would normally be considered difficult to accomplish, by not only selecting centers and carrying out ex-post evaluations, but also annual follow-ups. The well-known and highly esteemed Dr. Hiroo Imura chaired the Program Committee, and the other members of the committee were also prominent figures. Roughly 40% of the 15 committee members were foreign nationals, including the former Director of the National Science Foundation (NSF), the Director General of the European Organization for Nuclear Research (CERN), the President of the European Science Foundation (ESF), and the Chairman of Singapore's Agency for Science, Technology and Research (ASTAR). They each responded positively to requests to participate in the Committee.

We also introduced a PD/PO system, which, at the time, was still quite uncommon. The system we created ensured a certain amount of tension in the relationships that the PDs and POs have with the centers and their host organizations, while at the same time facilitating cooperation between them towards building the kinds of centers that the WPI Program was aiming for. We requested Dr. Toshio Kuroki, who at the time had just retired from his role as President of Gifu University, to become the PD, which he accepted. The PDs and POs engage in frank and open debate about how best to move the WPI Program forward and have worked together to help nurture it.

We recognized that a certain amount of time would be required to successfully implement this kind of bold system reform. Despite a large number of objections even from within MEXT, we set the support provision period at 10 to 15 years, substantially longer than the usual 5-year support period. The amount of subsidies to be provided to each center was also extremely generous at 1.35 billion yen (a budget request was made for 1.5 billion yen but it was reduced through the budjet negotiation process by 10% to 1.35 billion yen). When deciding the amount of subsidies to be provided, a thorough survey of top-tier overseas research centers was carried out to gain a sense of scale with regard to their budgets and personnel numbers, etc.

Ten years have now passed since the WPI Program shifted from vision to reality. That it has been able to grow and develop into a program that is highly regarded both in Japan and internationally is thanks to the devoted efforts of former Chairperson Dr. Hiroo Imura, current Chairperson Dr. Ryoji Noyori, and the other members of the WPI committee, as well as the PDs and the POs, especially Dr. Toshio Kuroki.

During this initial 10-year period, the program has been successful in creating globally visible research centers and hubs for "international brain circulation" that, 10 years ago, did not exist in Japan. During the second 10-year period, which we are now heading into, we will aim to further expand the reach of the system throughout Japan.

With the increasing globalization of science and technology, for Japan to overcome international competition and develop into a true global leader in science and technology, we will need to get the system of WPI more widely implemented throughout the country. I hope that the WPI Program will contribute greatly to further strengthening Japan's science and technology capabilities.

Creating world top-level research centers
- The ambition and success of the WPI Program -

Program Directors: Toshio Kuroki and Akira Ukawa

At first glance, the natural sciences appear to be progressing in a satisfactory manner in Japan, especially when one considers that since the start of the 21st century the country has produced the second highest number of Nobel laureates in the world. There are in fact, however, a large number of borders and barriers that are hindering progress and that need to be overcome.
The WPI Program was launched in 2007 with the mission of transcending the borders between disciplines and between nations, and the barriers between universities and science systems, to create research centers that are "internationally opened" and "globally visible." Now, ten years on from the launch of the program, the nine WPI centers have become world-leading research centers in their respective fields. Before explaining how well the centers are performing, we will provide an overview of the WPI Program's objectives, systems, progress, and outlook for the future.

Table of contents

List of WPI abbreviations

COE	: Center of Excellence	**PO**	: Program Officer
JST	: Japan Science and Technology Agency	**REI**	: Research Excellence Initiative
PD	: Program Director	**WG**	: Working Group
PI	: Principal Investigator	**WoS**	: Web of Science

1 Transcending borders and barriers

The global university rankings in 2015 were a shock for us. The Times Higher Education World University Rankings, the most reputable of the various university rankings that exist, had significantly lowered the rankings of Japan's universities. The University of Tokyo, which in 2014 had been ranked at 23rd, dropped to 43rd in 2016, and Kyoto University, which was ranked at 52nd dropped to 88th. What's more, only the University of Tokyo made it into the top 10 for Asia, and even then it only ranked 7th (Kyoto University was 11th). Universities in Singapore, China and Hong Kong occupied the top of the rankings for Asia.

In 2015, the Times Higher Education World University Rankings provided the following reason for the long-term decline of Japan's universities:

"Research depends on the free movement of both ideas and people, and countries that adopt a more closed stance pay the price in the end. This is a prime cause of the substantial long-term declines in the global position of research in both Japan and Russia."

To be honest, we didn't realize that Japan was being so harshly scrutinized. Since the start of the 21st century Japan has produced the second highest number of Nobel laureates after the United States. In spite of this, Japanese universities' global rankings are continuing to decline. Why is that the case?

One of the reasons may be that, as the Times Higher Education World University Rankings points out, Japanese universities are unable to transcend a variety of borders and barriers that hinder them. The Times Higher Education World University Rankings unknowingly pinpointed Japanese universities' key weakness.

It is this very problem that the WPI Program has been attempting to overcome. The mission of the program is to pursue fusion research, globalization, system reform, and establish research centers that transcend academic and national borders and systemic barriers. Creating research organizations that are well-regarded internationally requires more than just funneling in research funds.

It is by transcending borders and barriers that science in Japan will presumably be able to continue forging powerfully ahead toward the future. Over the last 10 years, the WPI Program has shown that this is possible.

2 The objective of the WPI Program

The objective of the WPI Program is to transcend borders and barriers, and develop Japan's research capabilities. At the time of its launch in 2007, the objective of the WPI Program was expressed in the following powerful terms in the application guidelines.

"To enhance the level of science and technology in Japan and continuously trigger innovation that serves as an engine for future growth, it will be necessary to boost the nation's basic research capabilities while strengthening its global competitiveness. To this end, Japan needs to create research centers in which world's finest brains gather, outstanding research results are generated, and talented young researchers are fostered. These centers should be highly innovative in both their concepts and practices, unfettered by conventional thinking."

"This program provides priority support for proposals aimed at creating world premier international research centers staffed at their core with the world's most leading researchers. By achieving a very high research standard and providing an excellent research environment, the centers should be 'globally visible research centers' being able to attract top-level researchers from around the world."

The WPI Program was indeed implemented in line with this ambitious objective. Ten years on, the WPI centers are living up to the expectations that were placed on them.

3 The WPI Program's systems

1) The ambitiousness of the WPI Program

It would be safe to say that the WPI Program is one of the most ambitious programs implemented thus far by the Ministry of Education, Culture, Sports, Science and Technology (MEXT). As its name—the World Premier International Research Center Initiative—suggests, the objective of the program is to create world top-level research centers in Japan. The kind of heated debate that occurred between government officials and others involved in the process during the planning stages of the WPI Program have been described in this document by Dr. Hiroo Imura (inaugural Chairperson of the WPI Program Committee) and Hiroshi Ikukawa (Former Director, Planning and Evaluation Division, Science and Technology Policy Bureau, MEXT and now Deputy Director General of the Bureau of Science, Technology and Innovation of the Cabinet Office).

Universities are extremely democratic organizations. The opinions of researchers are respected, and minority opinions are valued. This is necessary for the development of scholarship, but it sometimes stands in the way of reform, and universities risk being left behind by society. To make changes to the system, it is sometimes necessary to shift from conventional faculty council-led guidance and consensus-based operations to aspirational and powerful leadership.

However, creating this kind of research environment is certainly not an easy feat. First of all, the insular systems typical of Japanese universities need to be changed. The attitudes of not only researchers but also administrative staff need to be changed. A system in which research is conducted in English and support is provided to non-Japanese researchers needs to be established.

One way to implement this kind of reform is to create a kind of "special zone" within each university, and then draw upon the experiences gained through the use of such a special zone and expand them to cover the entire university. The aim of the WPI Program is not only to facilitate world-class research, but, in doing so, also change the nature of Japan's research systems and universities. In this sense, the WPI Program could be said to be a very ambitious program.

2) The WPI's missions

The "ambitions" (missions) of WPI can be categorized as follows: (Fig. 1)

1. Leading-edge research
2. Fusion research
3. Globalization
4. System reform

These four missions could be thought of as the WPI Program's slogans, so to speak. The four missions are always given emphasis, when explaining the WPI Program to people, when WPI centers are evaluated, and so on. The annual inspections through site-visits, interim evaluations, extension screenings, and final evaluations are conducted based on the four missions. We believe that the WPI Program has been able to produce results in line with its objectives because its missions have been clearly delineated, because WPI centers have been required to accomplish those missions, and because they have been used as a key performance indicator during follow-up reviews. Detailed information about each of the four missions is provided in sections 6 to 9 (p.20 to 26).

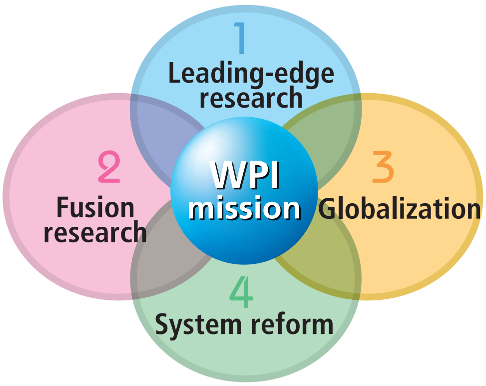


Fig. 1. The four WPI missions

3) Designing the WPI system

In order to put the clearly-defined principles explained above into practice, the system was, unlike conventional policies, designed to be ambitious and aggressive.

The WPI budget: To create world top-level research centers, sufficiently large budgets were required. The annual subsidy amounts approved in FY 2007 and FY 2010 for six WPI centers was 1.3 to 1.4 billion yen per center—an unprecedentedly large budget. In FY 2012, the three centers were established under a concept called "WPI Focus" on the basis of proceeding center-building funds, focusing on rather narrow research fields. Consequently, their subsidy was reduced to half (or less). The overall budget for the WPI Program was 9.44 billion yen in FY 2016.

Facility construction budget: 2 billion yen in facility construction subsidies were allocated to each WPI center following the approval of a supplementary budget request. With these funds each center was able to construct buildings with novel designs and carry out research "under one roof." Photos of each of the buildings are included in the pages explaining each center.

Research funds: WPI subsidies are basically provided for the purpose of creating research centers. Therefore, WPI subsidies cannot be used to fund research activities. Approximately 60% of WPI subsidies are in fact used to cover personnel costs for hiring researchers, post-doctoral researchers, and research support staff. An exception is allowed for startup research funds used by newly hired researchers, and funds used to advance fusion research, one of the missions of the WPI Program. For this reason, researchers at WPI centers carry out their research using externally sourced funds. WPI centers have in fact been very successful in procuring externally sourced funds.

WPI centers have also been noted for their success in procuring external funding other than public research funding.

- In 2012 IPMU (The University of Tokyo) became Kavli IPMU after receiving funding from the Kavli Foundation (United States), which primarily supports basic research in mathematics and physics. With the addition of "Kavli" to its name, IPMU has enjoyed increased international recognition.
- In 2015 ELSI (Tokyo Institute of Technology) received funding from the John Templeton Foundation (United States), which it is using to engage in international collaborative research.
- IFReC (Osaka University) concluded a 10-year, one billion yen a year comprehensive collaboration agreement with Chugai Pharmaceutical Co., Ltd. as a form of external funding that can be used from FY 2017 in the same manner as WPI funding.

These cases show that the WPI centers are highly regarded by the international research community and by industry, making them something of an exception amongst Japan's universities.

Support period: Building up WPI centers into world top-level research centers requires stable funding over a long period. For this reason, the centers are in principle supported for a period of 10 years. It is because the support was guaranteed for 10 years that the centers have been able to attempt the kind of challenging research that had hitherto not been possible.

It was decided that the support period could be extended for a further five years for particularly outstanding centers. Support provided over a period of 10 years + 5 years is unrivalled in length in any other such Research Excellence Initiative (REI; further explanation can be found in section 14) in the world. Information about the screening for the five-year extension is provided on p.20.

Target research fields: The application guideline issued at the time of the program's launch contained the following explanation:

"A field of basic research, including one aiming at the transition from basic research to applied research, in which a world-class research group currently exists in Japan. In principle, the field should be interdisciplinary, spanning or combining two or more of research areas."

The WPI Program's emphasis on basic research over applied research and the aim of fusing different fields also makes it unique amongst REIs. Note however that in the application guidelines for FY 2010, green innovation was designated as a research field, and selection was conducted from the perspective of applied research (p.18).

Although the WPI Program does not, in principle, position applied research and innovation as target areas of research, it is proud of and welcomes any research that results in the opening up of subsequent applied research that contributes to industry. There have in fact been cases in which WPI research has produced such results, and these will be explained in section 12 (p.27).

Center directors: Particular emphasis is given to selecting the right people to serve as center directors. To be able to promote their center globally and invite high-caliber researchers, center directors need to be researchers with a proven track record and an internationally visible "face."

Center directors are also required to provide powerful leadership regarding research activities and the management of their center. For this reason, any midstream replacement of a center director is debated by the WPI committee as a matter of great importance. Midstream replacement of center directors has occurred at two centers: AIMR and iCeMS (p.17 to 18).

Numerical targets: To become a world top-level international research center, a critical mass of researchers is required. The following numerical targets for WPI centers are indicated in the application guidelines:

- At least 20 world-class principal investigators (PIs)
- A total of at least 100 researchers including PIs, young researchers, and post-doctoral researchers
- A total of at least 200 staff members, including researchers, research support staff, and administrative staff.

Note however that for the "WPI Focus" center policy adopted in 2012, the numerical targets are roughly half of the targets above.

To become an international research center a certain proportion of the researchers need to be foreign nationals (or affiliated with overseas research organizations). The following figures are given as targets:

- At least 20% of PIs are from overseas
- At least 30% of the total number of researchers are from overseas
- Postdoctoral positions are filled through open international solicitations

As explained on page 23, these numerical targets have been achieved by almost all of the WPI centers.

English-language-based management: One of the conditions of being an international research center is that English is used as the official language. The WPI Program Committee meetings, site visits, other important meetings, materials and reports submitted to meetings, are all in English. In WPI centers, when there is even a single person present who is not proficient in Japanese, a switch is made to English, not only in meetings but also in daily conversations. What is important is that the center's operations are conducted in a transparent manner that transcends language barriers for all members, regardless of their nationality.

Therefore, all personnel, including not just researchers but also administrative staff, have to be conversant in English. All nine WPI centers in fact operate in English without any problems. This kind of program is unprecedented in Japanese universities. Some of the administrative staff who received English-language training have transferred within and without the host institutions and are spreading their experience.

Efforts by host institutions to maintain and sustain WPI centers: One of the most characteristic features of the WPI Program is the clearly-defined responsibility of the host institutions to make their own efforts to maintain and sustain WPI centers after the period of government support has ended. The application guidelines include the following:

"The host institution must clearly define the center's role within its own mid-to-long-term strategy and provide it comprehensive support accordingly." "The project proposal should not be limited to activities supported by the program grant, but should be both comprehensive and long-term in scope covering independent initiatives taken by the center, host institution, and partner institutions and include forecasted activities to be conducted after the grant period has ended."

This approach was taken in response to past lessons learned. When other past research promotion projects focused on creating research centers came to a conclusion, there was little of substance left.

The support and efforts of host institutions to maintain and sustain WPI centers have been repeatedly confirmed by the head of the host institution at the annual WPI Program Committee meetings. Indeed, in FY 2016 the host institutions of the four WPI centers for which budgeted support was to end promised to maintain the centers, each providing from their own resources hundreds of millions of yen of funding to ensure that facility maintenance costs, personnel costs, and so on are covered.

4) The WPI follow-up framework

The WPI Program has an unprecedentedly robust follow-up framework. It would be fair to say that it was because the follow-up framework is so thorough, that WPI centers have been able to produce world-class scientific results and achieve their missions.

Follow-up is provided through a two-stage review meeting process implemented by the four levels below.

Four levels:

- Program Committee (see p.14 to 15)
- Program Directors (see p.16)
- Program Officers (see p.16 to 17)
- Working Groups (see p.16 to 17)

Two-stage review process:

- Program Committee meetings
- Site visits (on-site reviews of centers)

Program Committee: The Program Committee deliberates on the WPI system, and selects and evaluates centers. At the time of the launch of the WPI Program, the committee consisted of 15 members with excellent insight into science and technology policy, including six foreign nationals from the United States, the United Kingdom, France, and Singapore. The inaugural Chairperson was Dr. Hiroo Imura (former President of Kyoto University).

Dr. Ryoji Noyori (currently Director-General of the Japan Science and Technology Agency's Center for Research and Development Strategy) was appointed as the WPI Program Committee Chairperson in FY 2016. In FY 2016 some of the committee members were replaced and the total number of members is now 19 (7 of whom are foreign nationals).

The Program Committee meets once a year to evaluate WPI centers. Following presentations by the heads of the host institutions and the WPI center directors, the Program Officers responsible for WPI centers provide reports on their site visits (see next section). In years when applications for new WPI centers are accepted, the Program Committee is responsible for selection. The Program Committee meeting usually takes two days. Additional Program Committee meetings involving committee members based in Japan are also held once or twice a year to debate various issues (Fig. 2).

Site visits: Each center is subject to an annual site visit (except in the 6th and 9th years following their establishment, Fig. 3). Site visit teams are made up of PDs, POs, working group members, MEXT officials, and members of JSPS. Members of the Program Committee also participate as observers.

Site visits occur over a two-day period. On the first day, the head of the host institution and the center director present reports, followed by reports from PIs, poster presentations by young researchers, and so on. On the second day, the research facilities are inspected, and discussions on future planning and more comprehensive matters are held. Program Committee meetings and site visits are both conducted entirely in English. Evaluation is based on the extent to which the four WPI missions (explained below in section 5) are being implemented. The most important evaluation criterion of all is the level of the science being carried out. POs prepare site visit reports (three pages long and written in English) based on compiled comments by PDs, POs, and working group members, and these are then submitted to the Program Committee.

PDs: One of the characteristics of the WPI Program is that it uses a PD/PO system and that PDs and POs play core roles in practical operations. Dr. Toshio Kuroki (President of Gifu University at the time, and now Special Advisor

List of current and former Program Committee members:

The international team of leading authorities of the WPI Program Committee

■ Committee members serving in FY 2016

Dr. Ryoji Noyori (Chairperson)
Director-General, Center for Research and Development Strategy, Japan Science and Technology Agency
Former President of RIKEN
Nobel Laureate in Chemistry (2001)
Field of specialization: Organic chemistry
Tenure: FY 2007-

Dr. Rita Colwell
(United States)
Distinguished Professor, The University of Maryland
Former Director of the National Science Foundation (United States)
Field of specialization: Microbiology
Tenure: FY 2007-

Dr. Richard B. Dasher
(United States)
Consulting Professor, Stanford University
Field of specialization: Technology management
Tenure: FY 2007-

Dr. Victor J. Dzau
(United States)
President, National Academy of Medicine (United States)
Field of specialization: Molecular medicine
Tenure: FY 2016-

Dr. Michinari Hamaguchi
President, Japan Science and Technology Agency
Former President of Nagoya University
Field of specialization: Tumor biology, biochemistry, cell biology
Tenure: FY 2016-

■ Committee members serving between FY 2007 and FY 2015

Dr. Hiroo Imura (former Chairperson)
Professor Emeritus and former President of Kyoto University
Former member of the Council for Science, Technology Policy (now the Council for Science, Technology and Innovation)
Field of specialization: Life sciences (endocrinology)
Tenure: FY 2007-2015

Dr. Robert Aymar
(France)
Senior Advisor, Atomic Energy Authority (CEA)
Former Director General, European Organization for Nuclear Research (CERN)
Field of specialization: Plasma physics
Tenure: FY 2007-2014

Professor Ian G. Halliday
(United Kingdom)
Professor Emeritus, University of Edinburgh
Former President of the European Science Foundation
Field of specialization: Theoretical particle physics
Tenure: FY 2007-2014

*The titles of committee members serving between 2007 and 2015 are current for that period.

Committee meetings are held every year to deliberate on WPI Program policies and implementation, select new WPI centers, and evaluate existing centers.
From FY 2017, the committee is also responsible for evaluating the WPI Academy.

Dr. Toshiaki Ikoma
Professor Emeritus, The University of Tokyo
President, The Canon Foundation
Special Advisor, Canon, Inc.
Field of specialization:
Semiconductor electronics
Tenure: FY 2007-

Professor Hiroto Ishida
Professor Emeritus, Kanazawa Gakuin University
Former Vice-Minister, Science and Technology Agency
Former Ambassador of Japan to the Czech Republic
Tenure: FY 2007-

Dr. Maki Kawai
Director General, Institute for Molecular Science, National Institutes of Natural Sciences
Former Executive Director, RIKEN
Field of specialization: Surface science, physical chemistry
Tenure: FY 2016-

Dr. Makoto Kobayashi
Honorary Professor Emeritus, High Energy Accelerator Research Organization (KEK)
Nobel Laureate in Physics (2008)
Field of specialization:
Theoretical particle physics
Tenure: FY 2008-

Dr. Kiyoshi Kurokawa
Professor Emeritus, National Graduate Institute for Policy Studies
Former President of the Science Council of Japan
Former Science Advisor to the Prime Minister of Japan
Field of specialization: Internal medicine
Tenure: FY 2007-

Dr. Chuan Poh Lim
(Singapore)
Chairman, Agency for Science, Technology and Research (Singapore)
Field of specialization: Research and innovation system and management
Tenure: FY 2007-

Dr. Hiroshi Matsumoto
Presiden, RIKEN
Former President, Kyoto University
Field of specialization: Space science, space radio engineering
Tenure: FY 2016-

Dr. Ryozo Nagai
President, Jichi Medical University
Former Director, The University of Tokyo Hospital
Field of specialization: Internal medicine
Tenure: FY 2014-

Dr. Michiharu Nakamura
Counsellor to the President and Advisor, Japan Science and Technology Agency
Former President, Japan Science and Technology Agency
Former Executive Vice President, Hitachi, Ltd.
Field of specialization: Materials and devices
Tenure: FY 2012-

Dr. Shinichiro Ohgaki
President, Japan Water Research Center
Former President, National Institute for Environmental Studies
Former Dean of the School of Engineering, The University of Tokyo
Field of specialization: Environmental and energy (environmental engineering)
Tenure: FY 2012-

Dr. Norihiko Suzuki
Chair of the Board/President, Akita International University
Field of specialization:
International management theory
Tenure: FY 2016-

Dr. Klaus von Klitzing
(Germany)
Director, Max Planck Institute for Solid State Research
Nobel Laureate in Physics (1985)
Field of specialization:
Solid-state physics
Tenure: FY 2016-

Dr. Harriet Wallberg
(Sweden)
Former President, Karolinska Institutet
Director General, Ministry of Health and Social Affairs, Swedish Government
Field of specialization: Biology, medicine
Tenure: FY 2016-

Dr. Jean Zinn-Justin
(France)
Scientific Advisor, Institute of Research into the Fundamental Laws of the Universe (IRFU/CEA)
Field of specialization:
Theoretical physics
Tenure: FY 2016-

Dr. Yuko Harayama
Deputy Director, Directorate for Science, Technology and Industry, Organization for Economic Co-operation and Development (OECD)
Field of specialization: Science and technology, innovation policy analysis
Tenure: FY 2012

Dr. Atsuo Iiyoshi
Chairman, Board of Trustees
Chancellor, Chubu University
Former Director General, National Institute for Fusion Science
Field of specialization: Plasma science and engineering, fusion science
Tenure: FY 2007-2011

Dr. Tsutomu Kimura
Advisor, National Institution for Academic Degrees and University Evaluation
Chairperson, Tokyo Metropolitan Government Board of Education
Former President, Tokyo Institute of Technology
Field of specialization: Geotechnical engineering, civil engineering
Tenure: FY 2008-2015

Mr. Yotaro Kobayashi
Former Chairman of the Board and Chief Corporate Advisor, Fuji Xerox Co., Ltd.
Former Chairman, Japan Association of Corporate Executives
Tenure: FY 2007-2011

Dr. Matthew T. Mason
(United States)
Professor, the Robotics Institute, Carnegie Mellon University
Field of specialization: Robotics
Tenure: FY 2007-2014

Dr. Hideo Miyahara
Former President, National Institute of Information and Communications Technology
Professor Emeritus and former President, Osaka University
Field of specialization: Information
Tenure: FY 2012

Dr. Yasuharu Suematsu
Honorary Professor and former President, Tokyo Institute of Technology
Laureate of the Japan Prize
Field of specialization: Semiconductor lasers for large-capacity and long-distance optical fiber communications
Tenure: FY 2007-2011

Dr. Masatoshi Takeichi
Director, RIKEN Centre for Developmental Biology
Field of specialization:
Developmental biology, cell biology
Tenure: FY 2012-2014

Dr. Yoji Totsuka
Director, Research Center for Science Systems, Japan Society for the Promotion of Science
Former Director-General, High Energy Accelerator Research Organization (KEK)
Field of specialization: High-energy physics
Tenure: FY 2007-2008

to the Research Center for Science Systems of JSPS) was appointed as a PD in 2008. In 2013 Dr. Akira Ukawa (Vice-President and Trustee of the University of Tsukuba at the time, and now Deputy Director of the RIKEN Advanced Institute for Computational Science) was appointed as a Deputy PD. PDs act as intermediaries between MEXT, the Program Committee, and WPI centers, providing advice to all parties from a researcher perspective.

POs: Researchers working in the fields of specialization of each WPI center were installed in each center as POs. The POs provide advice to their particular center on scientific issues, lead the annual site visits, prepare site visit reports, and submit reports to the Program Committee. Following Program Committee meetings, the POs visit WPI centers together with PDs to provide information regarding what was discussed at the meetings. The POs for each center are listed in the section below.

Working Groups: The research results of each WPI center are evaluated through peer review by leading researchers in the relevant fields, including Nobel laureates. Working Groups exist for this purpose and in principle consist of six members, three of whom are non-Japanese researchers. Working Group members participate in site visits and provide advice to WPI centers regarding their research results and the directions they are taking. Their opinions are compiled in site visit reports by POs. Working Group members for each WPI center are listed in the section below.

Program Directors (PD)
Program Officers (PO)
Working Group members (WG)

PD
Toshio Kuroki (FY 2007-)*
Special Advisor, Research Center for Science Systems of the Japan Society for the Promotion of Science
Former President of Gifu University
Professor Emeritus, The University of Tokyo
Field of specialization: Cell biology

Deputy PD
Akira Ukawa (FY 2013-)*
Deputy Director of RIKEN Advanced Institute for Computational Science
Former Vice-President (Planning and Evaluation, Information) and Trustee, University of Tsukuba
Field of specialization: Theoretical particle physics

* Since FY 2017, Dr. Ukawa has served as PD, while Dr. Kuroki has become Director of the WPI Academy.

One PD and nine POs (one for each WPI center) were appointed. From FY 2013, one Deputy PD was also appointed. Each WPI center has a Working Group consisting of five to six specialists in the fields in which the respective centers operate and these are each headed by the relevant PO and are established under the leadership of the Program Committee. In principle, roughly half of the members of each Working Group are foreign nationals.

* The titles of past POs are those current for the period concerned.

AIMR

PO : Yoshihito Osada
(FY 2007-)
Senior Visiting Scientist, RIKEN
Former Executive and Vice-President of Hokkaido University
Field of specialization: Polymer science, bio-related chemistry, polymeric materials

Working Group members
Yasuhiko Shirota
Hideo Hosono
Tomohiko Yamaguchi
Toyonobu Yoshida
Samuel M. Allen
Sir Colin Humphreys
Samuel I. Stupp

Past members
Hiroshi Kitagawa
Suresh Subra

KAVLI IPMU

PO : Ichiro Sanda
(FY 2007-)
Professor Emeritus, Nagoya University
Field of specialization: Theoretical particle physics, astrophysics, optical-infrared astronomy, theory of relativity and gravity, integrable systems

Working Group members
Hiraku Nakajima
Yutaka Hosotani
Tetsuji Miwa
Matthias Staudacher
Ian Shipsey
Anthony Tyson

Past members
Heisuke Hironaka
Hikaru Kawai
John Peacock
Tsuneyoshi Kamae

iCeMS
KYOTO UNIVERSITY
WPI Research Center

PO : Toru Nakano
(FY 2012-)
Professor, Graduate School of Frontier Biosciences/Graduate School of Medicine, Osaka University
Field of specialization: Epigenetics

Working Group members
Kazunori Kataoka
Yumiko Saga
Yoshiki Katayama
Toshio Suda
Alexander V. Kabanov
Paavo K. J. Kinnunen

Past members
Yoshiko Takahashi
Motomu Tanaka
Shigeki Mitaku
Masayuki Yamato
Toru Nakano
Sheng Ding
Leonard H. Rome
George Q. Daley

Past PO : Toshio Suda
(FY 2007- 2011)
Professor, Keio University School of Medicine
Field of specialization: Stem cell biology

4 WPI centers

As of FY 2016, the WPI Program consists of the following nine centers. Details about each center are provided from page 30 onwards. What follows is a brief overview.

WPI centers launched in 2007

The first request for applications attracted 33 applications from 22 research organizations. Following screening of the application documents and interviews, the following 5 centers were selected.

AIMR (p.30)
Tohoku University Advanced Institute for Materials Research
Center director: Motoko Kotani (Yoshinori Yamamoto until FY 2011)
Objective: To achieve new materials science research through the incorporation of mathematics.

Kavli IPMU (p.38)
Kavli Institute for the Physics and Mathematics of the Universe, The University of Tokyo
Center director: Hitoshi Murayama
Objective: To explain the origins and evolution of the universe through research incorporating mathematics and physics.

iCeMS (p.46)
Institute for Integrated Cell-Material Sciences, Kyoto University
Center director: Susumu Kitagawa (Norio Nakatsuji until the end of 2012)

WPI Osaka University iFReC

PO : Takehiko Sasazuki
(FY 2007-)
University Professor, Institute for Advanced Study, Kyushu University
President Emeritus of the National Center for Global Health and Medicine
Field of specialization: Immunogenetics

Working Group members
Hiroshi Kiyono, Kazuhiko Yamamoto, Günter J. Hämmerling, Hisataka Kobayashi, Philippe Kourilsky

Past members
Shigeo Koyasu, Kouji Matsushima, Haruo Kasai, Nagahiro Minato, Diane Mathis

IIIS — International Institute for Integrative Sleep Medicine

PO : Kozo Kaibuchi
(FY 2012-)
Professor, Graduate School of Medicine, Nagoya University
Field of specialization: Cell biology

Working Group members
Toru Takumi, Norio Ozaki, Noriko Osumi, Richard Neubig, Thomas Kilduff, Emmanuel Mignot

MANA — Nano Revolution for the Future

PO : Gunzi Saito
(FY 2007-)
Emeritus Professor, Kyoto University
Field of specialization: Development of molecular functional materials

Working Group members
Yoshinobu Aoyagi, Takehiko Ishiguro, Tadashi Matsunaga, Hiroshi Katayama-Yoshida, David L. Allara, Klaus von Klitzing

ELSI — Earth-Life Science Institute, Tokyo Institute of Technology

PO : Shoken Miyama
(FY 2012-)
Professor (Special Appointment), Office of the President, Hiroshima University
Former General Director of the National Astronomical Observatory of Japan
Field of specialization: Theoretical astronomy

Working Group members
Satoshi Yamamoto, Shin-ichi Kawakami, Mitsuyasu Hasebe, Edwin Turner, Antonio Lazcano, George D. Cody

I²CNER

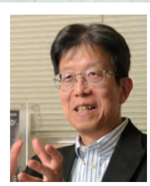
PO : Kazunari Domen
(Nov. 2014-)
Professor, School of Engineering, The University of Tokyo
Field of specialization: Catalytic chemistry, photocatalytic energy conversion

Working Group members
Koichi Eguchi, Shuichiro Hirai, Naoki Shikazono, Ellen Ivers-Tiffée, Dimos Poulikakos, David L. Greene

Past members
Kazunari Domen, Scott Samuelsen

Past PO : Nobuhide Kasagi
(FY 2010- Oct. 2014)
Principal Fellow, Center for Research and Development Strategy, Japan Science and Technology Agency
Field of specialization: Energy system engineering

ITbM Nagoya University



PO : Minoru Yoshida
(Jul. 2015-)
Chief Scientist, RIKEN
Field of specialization: Chemical genetics

Working Group members
Yasuhiro Aoyama, Ikuko Hara-Nishimura, Hiroaki Suga, Wilhelm Gruissem, Jonathan L. Sessler, Ben Shen

Past members
Minoru Yoshida

Past PO : Hiroo Fukuda
(FY 2012- Jun. 2015)
Professor, School of Science, The University of Tokyo
Field of specialization: Plant physiology/plant cell biology

Fig. 2. Program Committee Meeting

Fig. 3. Site visit (Site visit to ITbM in 2016)

Objective: To create new cross-disciplinary fields in meso-domains through the fusion of cell and materials sciences.

IFReC (p.54)
Osaka University Immunology Frontier Research Center
Center director: Shizuo Akira
Objective: To understand the dynamic network of the immune system in collaboration with imaging and informatics.

MANA (p.62)
International Center for Materials Nanoarchitectonics, National Institute for Materials Science
Center director: Masakazu Aono
Objective: To develop nanomaterials based on the new concept of nanoarchitectonics.

WPI center launched in 2010

In FY 2010 a request was made for green innovation-themed applications. Nine applications were received from nine research organizations, and following screening of the application documents and interviews, the following center was selected.

I²CNER (p.70)
International Institute for Carbon-Neutral Energy Research, Kyushu University
Center director: Petros Sofronis
Objective: To contribute to the creation of a sustainable society with a non-fossil-fuel-based energy system.

WPI centers launched in 2012

In FY 2012 a request was made for applications for "WPI Focus" centers with narrower research focuses. 15 applications were received from 13 research organizations, and following screening of the application documents and interviews, the following 3 centers were accepted.

IIIS (p.76)
International Institute for Integrative Sleep Medicine, University of Tsukuba
Center director: Masashi Yanagisawa
Objective: To elucidate the mechanisms of sleep and wakefulness and contribute to the alleviation of sleep disorders and related illnesses.

ELSI (p.82)
Earth-Life Science Institute, Tokyo Institute of Technology
Center director: Kei Hirose
Objective: To investigate the origins of life and Earth based on the idea that the origins of life are inseparable from the early stages of Earth's environment.

ITbM (p.88)
Institute of Transformative Bio-Molecules, Nagoya University
Center director: Kenichiro Itami
Objective: To create transformative bio-molecules with significant social impact through collaborative research into chemistry and animal/plant biology.

The following approaches were used when creating WPI centers:

- Establishment of new centers (Kavli IPMU, IIIS)
- Forming centers within existing parent organizations such as auxiliary research institutes, university departments, etc. (AIMR, iCeMS, IFReC, I²CNER).
- Creation of centers by a core group of relevant researchers within the host institution (MANA, ELSI, ITbM)

WPI centers' research fields: The research fields of the nine centers introduced above can be roughly grouped into the following three categories: 1. The origins of the Universe, Earth, and life; 2. life sciences; and 3. Materials/energy (Fig. 4). Kavli IPMU and ELSI engage in research into the origins of the Universe, Earth, and life. Such fields are expected to underpin the foundations of research activities in Japan by stimulating the intellectual curiosity of a wide range of people. WPI centers working in the life sciences field include IFReC (immunology), iCeMS (cell biology and materials science), IIIS (sleep research), and ITbM (chemistry and animal/plant biology). By delving deeper into basic research in their respective fields the centers are aiming to work toward applied research. Materials/energy are research fields that Japan already excels in. AIMR and MANA are following this tradition in working on basic research using a new strategy aimed at creating useful materials. I²CNER is working to tackle pressing energy-related issues facing contemporary society, and is aiming to help bring CO_2 concentrations in the atmosphere back into equilibrium. ITbM and iCeMS are pursuing research that integrates the fields of materials science and life sciences.

5 The WPI center evaluation system

1) Stringent evaluation

WPI centers are subjected to stringent evaluation with a robust follow-up system (p.13). Evaluation is conducted in two stages: Site visits and Program Committee meetings. Final evaluations are carried out by the Program Committee based on site visit reports, PD and PO comments, and presentations made to the Program Committee by the WPI center directors and the heads of host institutions. Evaluation results are published on the WPI Program website (JSPS and MEXT websites).

In addition to annual site visits and evaluation by the Program Committee, there is an interim evaluation in the fifth year, an extension screening in the eighth year for centers that apply for an extension beyond the ten-year support period, and a final evaluation in the tenth year.

2) Targets and evaluation standard

Evaluations focus on the extent to which WPI missions have been accomplished. That is, how well the following have been implemented: Leading-edge research, fusion research, globalization, and system reform.

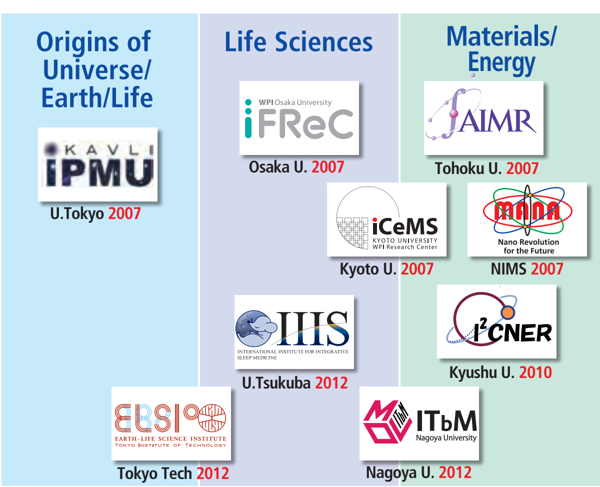


Fig. 4. The research fields of the nine WPI centers. These can be roughly grouped into the following three categories: The origins of the Universe, Earth, and life; life sciences; and materials/energy. ELSI, iCeMS, and ITbM engage in research that fuses multiple fields.

The primary form of evaluation used in science is peer review. This allows for the stringent evaluation of scientific work by other specialists in the same field (peers) with emphasis on the quality of the science, the extent to which it challenges accepted knowledge, its potential future contribution to science, etc. rather than simply relying on research performance indicators such as the impact factor of the journals in which the research is published and the number of citations.

The number of citations, investigated using the Thomson Reuters Web of Science (WoS) database (Fig. 5) is only used as reference information (to prevent this information from influencing evaluations, it is only disclosed to those making the evaluation after the evaluation has been made).

In the evaluations, accomplishment of the WPI missions is as important as the science involved. Since the outcomes of fusion research are inherently difficult to predict and since such research doesn't necessarily produce any results, no attempts are made to rush the researchers. Rather, it is the strategies aimed at moving ahead with fusion research that are subject to evaluation. The numerical targets for the number of researchers from overseas is used as a rough indicator for evaluating globalization. With regard to evaluation of system reform, particular attention is paid to the initiatives of the host institution.

When conducting interim and final evaluations, the publications of five world-class organizations of a similar scale are used as a benchmark with which to make comparisons. These benchmarks are also, however, used only as reference information.

The basic policy for evaluation is to conduct an absolute evaluation of each individual WPI center. Comparative assessment of centers based on relative evaluation is not conducted.

3) Interim evaluations

In the application guidelines it is clearly stated that "An interim evaluation will be carried out five years after the project starts. Projects may be revised or terminated early depending on the results of the evaluation." In accordance with this, WPI centers are subjected to interim evaluations five years after their launch. All of the currently active WPI centers have undergone interim evaluations.

- The five centers selected in FY 2007 had interim evaluations in FY 2011
- The single center selected in FY 2010 had interim evaluations in FY 2014
- The three centers selected in FY 2012 had interim evaluations in FY 2016

Interim evaluation results were distributed widely between S, A+, A, A-, and B. Centers that received A- and B evaluations made efforts to overcome the issues that were pointed out, and by the time of the extension screenings and final evaluations they had successfully overcome these (or were on their way to overcoming them). Interim evaluation results can be viewed by visiting the following website.

https://www.jsps.go.jp/english/e-toplevel/08_followup.html

4) Extension screenings

Extension screenings are explained in the application guidelines as follows:

The implementation period is "10 years, with possible 5-year extension for projects with outstanding results."

In accordance with this stipulation, the five centers established in FY 2007 applied for five-year extensions. In FY 2014 the Program Committee conducted extension screenings of these five centers. First of all, debates were held regarding the fundamental thinking behind the granting of extensions.

- The support period for the WPI Program is, in principle, ten years.
- "Outstanding," as stipulated in the regulations, applies only to truly exceptional cases, beyond even the WPI standard which is already of an extremely high level.

After settling on this basic concept, the Program Committee engaged in discussions and reached the following conclusions.

- It was concluded that all five centers had performed at a level that satisfied the requirements of the WPI both in terms of the level of science and accomplishment of the WPI missions, and had attained the "World Premier Status" that is the goal of the WPI Program.
- Amongst the five centers, it was Kavli IPMU that had proved exceptionally outstanding in all aspects of its performance, and a five-year extension for Kavli IPMU was approved.

5) Final evaluations

Final evaluations were conducted in FY 2016 for the four WPI centers for which budgetary support from the WPI Program would be coming to an end at the end of that fiscal year (AIMR, iCeMS, IFReC, and MANA). Kavli IPMU, meanwhile, was subjected to a tenth-year evaluation. All of the centers were evaluated highly as having maintained their "World Premier Status" since the time of the extension screenings.

http://www.jsps.go.jp/english/e-toplevel/data/08_followup/FY2016/FY2016 Follow up Report_E.pdf

6 WPI's achievements (1) Science

The science of the WPI centers is required to be at a world-class level. The first five centers have in fact produced internationally recognized work. Explanations of the outstanding performance of each of the centers are provided from p.30 onwards, with five to eight points explained for each center. The same information is also provided in the annual follow-up reports.

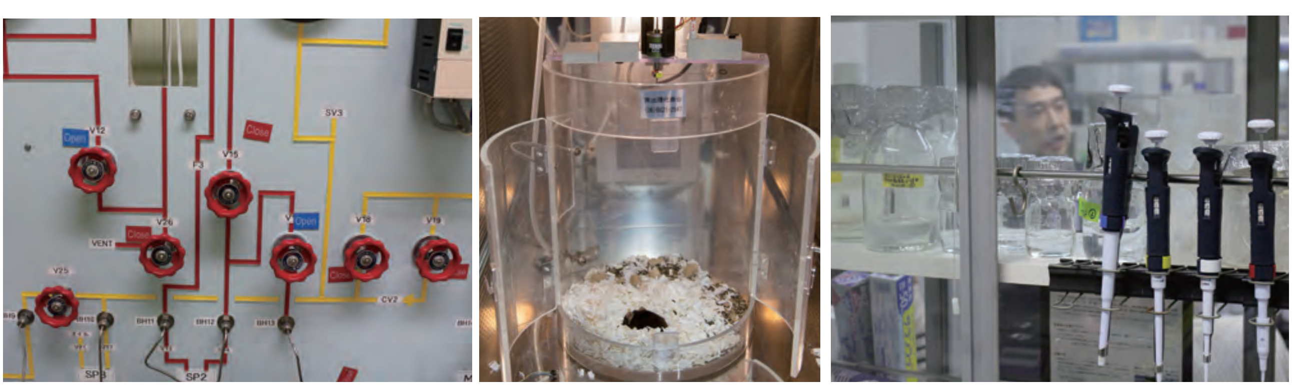
It was explained above that, although quantitative figures such as the number of citations etc. are investigated each year, this is only used as reference information. This kind of information is, however, certainly important when looking at the position of WPI centers in comparison with other research organizations around the world. The results of a survey of the Thomson Reuters WoS database is indicated in Fig. 5 below.

Publications

The numbers of published papers, the number in the top 1% and 10% of cited papers, and the number of internationally co-authored papers of the first five WPI centers are listed on the cover page of the center report documents. Between 2007 and 2015, the published papers of the first five centers totaled 10,932. The number of papers differed by field, and there tended to be a large number of materials-related papers, while there were fewer biology-related papers.

Top 1% papers

Exceptionally influential research papers are cited a large number of times by the authors of subsequent papers. The papers that are in the top 1% of cited papers can safely be



Research laboratories: I^2CNER (left), IIIS (middle), ITbM (right) said to be influential.

Internationally co-authored papers

International joint research is often pointed to as an indicator for globalization. Although Japan's performance in this regard, at 29.1%, is above the global average of 24%, it is considerably lower than the leading research countries in the West (the U.K., Germany, and France are over 50%). What is more, with the current growth rates, other Asian countries are catching up with Japan. Despite this, the internationally co-authored papers make up an average of 46.5% of the papers of the first five WPI centers (5,087 of 10,932). This gives an indication of how the WPI centers are positioned within international research networks.

Reference information: http://www.nistep.go.jp/wp/wp-content/uploads/NISTEP-RM239-FullJ.pdf (※Japanese only)

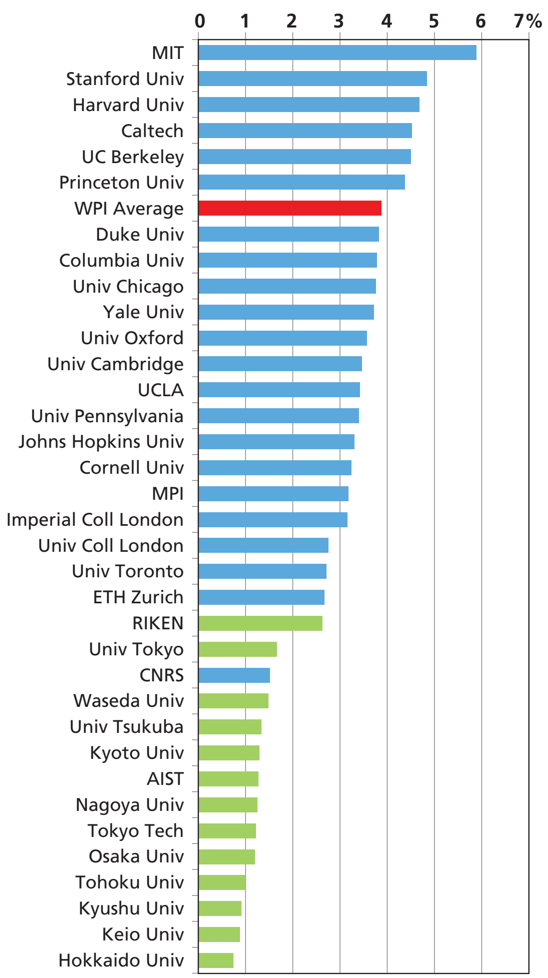


Fig. 5. The proportion of papers that are in the top 1% of cited papers of 36 leading research institutions (2007 - 2015) from Japan and around the world. The five WPI centers established in 2007 are ranked seventh among these research organizations. This comparison is made with the top 20 universities in the Times Higher Education World University Rankings plus the Max-Planck Institute (Germany), the Centre National de la Recherche Scientifique (France), 11 national and private Japanese research universities (the "RU11" universities), RIKEN, and National Institute of Advanced Industrial Science and Technology (AIST) (based on data from Thomson Reuters Corporation).

Awards

The number of awards won by researchers at WPI centers also clearly indicates the high standard of their work. WPI center researchers have won a large number of international and domestic academic awards including Nobel Prizes. The most prominent awards they have won are as follows:

Nobel Prizes: Two PIs at WPI centers have received Nobel Prizes: Dr. Shinya Yamanaka from iCeMS, who was awarded the Nobel Prize in Physiology or Medicine in 2012 for producing iPS cells, and Dr. Takaaki Kajita from Kavli IPMU, who was awarded the Nobel Prize in Physics in 2015 for the discovery of neutrino oscillations (Fig. 6).

WPI researchers have won famous international awards such as the Canada Gairdner International Award, the Lasker Award, the Robert Koch Prize, the Hermann Weyl Prize, the American Mathematical Society's Leonard Eisenbud Prize, etc. as well as top domestic prizes such as the Order of Culture, Person of Cultural Merit, the Medal with Purple Ribbon, the Japan Academy Prize, the JSPS Prize, etc. The award recipients are listed on the website below:

http://www.jsps.go.jp/e-toplevel/data/10thcommemoration-awardlist.pdf

Fig. 6. Takaaki Kajita (left, photo provided by Institute for Cosmic Ray Research, the University of Tokyo), Shinya Yamanaka (right)

7 WPI's achievements (2) Fusion research

Outstanding researchers congregate at WPI centers. There are those who say that it is therefore only natural that the centers produce outstanding research results. That is certainly true. However, it does not necessarily follow that truly revolutionary research and new fields of research can be produced simply by gathering together outstanding researchers. As indicated by the four WPI missions, the WPI Program demands transcendence of the various borders and barriers that hinder researchers. Just how much this contributed the development of the researchers' work is explained after the reports on each of the WPI centers.

One of the reforms required by the WPI Program is the second WPI mission of taking on the challenge of creating new fields of study through fusion research. Fusion research is not easy, however. Different fields of research use different technologies, concepts, and academic jargon. Fusion research needs to begin with the establishment of scientific dialogue. Making a success of fusion research requires a fusion strategy and a venue to carry out this fusion. The former could be referred to as a top-down aspect fusion research while the latter could be referred to as bottom-up fusion research.

Top-down strategic fusion research

Since the application guidelines explicitly stipulate fusion research, each of the WPI research centers drafted strategies as research institutes in a top-down manner in order to move forward with research that transcends the borders of different fields.

- AIMR is aiming to create new areas of materials science through the incorporation of mathematics.
- Kavli IPMU has, from the time of its establishment, stated that its goal is to fuse physics and mathematics at advanced levels.
- iCeMS is aiming to fuse cell biology and materials science.
- IFReC is producing a substantial volume of results through collaboration with traditional immunology researchers and RIKEN Quantitative Biology Center (QBiC, a molecular imaging research institute), and the Center for Information and Neural Networks (CiNet).
- MANA is working on fusing nanoscience and biology.
- I^2CNER's work to contribute to creation of a low carbon society is strongly influenced by integrated sciences.

With the WPI Focus application guidelines in FY 2012 on the other hand, there was not as much emphasis placed on fusion research, given the scale of the organizations and budgets involved. The centers ELSI and ITbM did however state their respective aims of fusing Earth/planetary science and life science, and animal/plant biology and synthetic chemistry, and they are currently producing significant results (described below). IIIS is conducting cross-cutting research across basic biology, experimental medicine, and pharmaceutical sciences, based on the theme of sleep and wakefulness.

Setting up a space for bottom-up fusion research

Even if fusion research policies are set in a top-down manner, it is the individual researchers who actually carry out the fusion research. Frank discussions between researchers provide them with stimulation and inspiration, and it is from this that new fields of research are created. It is not possible to predict however, when ideas will actually arise and what kinds of results can be achieved. In this sense, achieving fusion research is easier said than done.

What is important with bottom-up fusion research is establishing a system and a space that facilitate free debate and collaborative research. WPI centers have devised a variety of different methods to achieve this aim. These include creating "flat" organizations in which researchers are not pigeonholed in accordance with their particular fields, providing financial support aimed at promoting fusion research, and providing spaces where researchers can freely discuss issues between themselves. Several examples of this are listed below:

- An "interface" unit consisting of young mathematicians and theoretical researchers has been created at AIMR to work on incorporating mathematics into materials science (Fig. 7).
- Kavli IPMU makes participation in "teatime" discussions at 3pm every day an obligation for all researchers (p.44).
- iCeMS established a fusion research fund.
- IFReC established a fusion research unit and a fusion research fund, and uses a double mentor system to advance fusion research and nurture young researchers.
- MANA established a theorist unit.
- ITbM created "Mix-Labs" and "Mix-Offices" in which chemistry and biology researchers can carry out experiments and research in the same rooms.

Fusion research achievements

Just what fruits fusion research will bear cannot be predicted, and it always takes time to obtain results. However, through these kinds of steadfast efforts, fusion research began to bear fruit from the latter half of the ten-year support period.

- AIMR: The structure of glass, which had been considered a mystery for 50 years, was solved using mathematics (p.32).
- Kavli IPMU: Teatime debates between physicists, astronomers, and mathematicians led to the explanation of the magnification of a supernova as a result of the action of a gravitational lens (p.42).
- ITbM: Debates between plant biology and synthetic chemistry graduate students at the Mix-Lab led to development of a compound that can be used to

Fig. 7. A research presentation event at AIMR. New ideas arising in debates between young mathematicians and materials scientists lead to the creation of fusion research.

eradicate a parasitic plant called striga that has caused significant harm in Africa (p.90).

- Fusion research papers have begun to account for a large proportion of the papers published at iCeMS and IFReC. It is safe to say that fusion research at WPI centers is garnering attention around the world.
- AIMR publishes a series of mathematics and materials science monographs called "SpringerBriefs in the Mathematics of Materials" via Springer International Publishing, thereby playing a leading role in the field.
- ELSI has become known around the world as a research institute where collaborative research on Earth and the origins of life can be carried out, and five researchers left tenured positions in the United States to transfer to the Tokyo Institute of Technology and join ELSI.

At the time of the launch of the WPI Program, there were misgivings about the potential for success with fusion research, but it is now developing into one of the initiative's major attractions.

8 WPI's achievements (3) Globalization

Science is advancing rapidly, transcending disciplines and national borders. This progress is the result of interaction and friendly competition among researchers with different cultural backgrounds and ways of thinking.

However, Japan is significantly low down in global internationalization rankings. For example, in the three aspects of a university's international outlook as evaluated by the Times Higher Education World University Rankings (international staff, international students, and international research), Japan's universities all rank below 500th. In the midst of these circumstances, the WPI Program is helping Japan to achieve a breakthrough.

Proportion of researchers from overseas

The WPI Program's targets are maintaining the proportion of researchers from overseas in each center above 30%, and the proportion of PIs from overseas above 20%. As of FY 2016, almost all of the centers have reached these targets. The average for the nine centers is 41.2% for all researchers from overseas and 33.6% for PIs from overseas. Comparing these figures to the proportion of non-Japanese faculty in Japan's 86 national universities (a mere 4.6% according to the 2015 School Basic Survey) clearly demonstrates just how high they are.

There are more than 20 full time PIs from overseas at WPI centers. Many of these PIs say they have chosen to work at WPI centers because it is at WPI centers that they are able to pursue the research, e.g. interdisciplinary study, they themselves want to pursue. This is presumably evidence that the quality of WPI centers and their drive to open up new fields of research is garnering worldwide attention.

WPI centers are hubs for "global brain circulation"

Young researchers grow and develop by polishing their capabilities in post-doctoral and fixed-term positions. All WPI centers carry out recruitment in an open manner on a worldwide basis. All centers receive applications from around the world and in some centers, 90% of applications are received from overseas. Some centers select ten-odd post-doctoral researchers each year from a pool of several hundred applicants.

Over the last decade, a large number of young researchers from a wide range of countries have produced research results at WPI centers before going on to careers in universities and research organizations around the world. For example, of the 139 post-doctoral researchers who have conducted research at Kavli IPMU since its launch, 44 have left to take on positions at cutting-edge research institutes around the world. Becoming a researcher at WPI centers is now considered to be a path to a promising career.

On the other hand, the fact that young Japanese researchers have not been venturing overseas in recent years has become an issue. WPI centers are also focusing efforts on providing young researchers with opportunities to travel abroad for their development.

Each WPI center hosts an annual international conference. In addition to the conferences, which attract hundreds of participants, the centers also hold a large number of workshops focused on fusion research and other cutting-edge themes. For example, a "Winter School" held by IFReC in collaboration with the Singapore Immunology Network has fostered a large number of cutting-edge immunologists. The centers are also proactive in inviting leading and young up-and-coming researchers for short- and long-term visits, with each center hosting hundreds of such visitors every year.

WPI centers have become dynamic places where

Fig. 8. IFReC's malaria infection/immunology research group. Researchers from several countries are conducting research under the direction of PI Cevayir Coban (center).

researchers gather from around the world to discuss the latest research results before moving on again (Fig. 8). It is safe to say that WPI centers are fulfilling the initial objective of functioning as hubs for "global brain circulation."

Creating a cosmopolitan research and living environment

Historical, geographical, and cultural interaction is actively pursued in Europe and the United States. Such countries also have a high degree of affinity with English, the global lingua franca. Japan, however, is lagging significantly in each of these areas. In Japan, the linguistic, geographic, and cultural hurdles are high, and it is certainly true that Japan is at a disadvantage in overcoming them.

Each WPI center is devising different approaches to overcome such barriers. With the transition to English as the official language of WPI centers, the centers have pushed forward with a range of initiatives including switching to the use of English in meetings and documents, helping with research applications, employing bilingual administrative staff, and providing English-language support to help solve a range of issues relating to research funding, contracts and employment. In addition to this, strenuous efforts are also being made to provide housing, medical, and educational support to researchers from overseas and their families to help ensure a smooth transition to life in Japan.

WPI centers are fostering knowhow regarding how to provide international research and living environments and foster the necessary personnel to do so. This is also a fruit of the globalization mission, and an important asset that should be disseminated widely amongst Japan's universities.

Globally visible research centers (questionnaire survey)

One of the objectives of the WPI Programs is to create globally visible research centers. Are WPI centers widely recognized by researchers around the world? Are they the kinds of research centers that researchers want to join? Questionnaire-based surveys were carried out among researchers around the world in 2009 and 2011 to find the answers to such questions.

The surveys were conducted among 1,000 researchers (for each WPI center) who had published papers in journals related to the research fields of the five WPI centers as well as 30 leading researchers in each of the centers' respective fields. Despite being conducted only two and four years after the launch of the WPI Program, the results of both surveys indicated that the initiative was globally recognized. The results of the 2011 survey are shown below.

- Half or more of researchers were aware of the WPI center active in their particular field.
- Approximately half (48.3%) of researchers appraised the level of science at WPI centers as being "outstanding."
- The majority of researchers (79.1%) indicated that they were interested in participating in the research activities of WPI centers (including as dual appointment participants).

Although there was a certain amount of divergence amongst results for the various WPI centers, the survey showed that, only four years after the launch of the WPI Program, the centers had already become globally visible research centers. Details can be found in the follow-up reports for FY 2010 and FY 2011.

9 WPI's achievements (4) System reform

To further develop scientific research in Japan, would it be sufficient to simply provide an endless supply of research funds? Of course, research cannot be carried out without funds. However, it is also not the case that the mere provision of funds would achieve dramatic improvements in research in Japan. The environment surrounding research activities also needs to be changed

Overseas researchers: IFReC (left), I^{2}CNER (middle), and IFReC (right).

at the same time. Universities themselves also need to change.

As was stated in the application guidelines, one of the important missions of the WPI Program is to encourage universities to change themselves by promoting self-driven initiatives such as the implementation of system reforms.

For example, the hierarchy in Japanese universities headed by professors sometimes ends up hindering the free development of ideas by young researchers. It is often the case in Japanese universities that faculty councils wield the power to block reform. The barriers between universities and between departments are hard to overcome and little progress has been made with encouraging interaction beyond these barriers. Conservative teaching staff block system reform. The use of English cannot take root.

The fact is that some of those involved in developing science and technology-related policies are feeling irritated about the lack of progress being made with university reforms.

It was against this background that some looked at the launching of the WPI Program as a kind of seed from which university reform could develop, and the WPI centers are living up to such expectations.

The leadership of WPI center directors

While Japanese universities have until now been operated based on the consensus of faculty councils, WPI centers are required to operate in accordance with the leadership of their directors. All of the WPI centers do in fact operate in line with this policy. The burden of responsibility placed on the directors is therefore a heavy one.

The leadership of the directors manifests itself in many ways.

- Under the leadership of its director, mathematician Dr. Motoko Kotani, AIMR is aiming to use mathematics to open up new areas of materials science.
- Based on an idea by Dr. Hitoshi Murayama, the director of Kavli IPMU, all of the center's researchers gather every day at 3pm for "teatime" discussions, in which they write mathematical formulae on blackboards and engage in discussion. The words of Galileo "the laws of Nature are written in the language of mathematics" are displayed in the room in which the teatime discussions are held (see photo on p.45).
- ITbM's "Mix-Lab" concept, which allows chemistry and biology researchers to carry out experiments in the same laboratory, was created based on an idea by director Dr. Kenichiro Itami.

These endeavors have all produced tangible results.

Cross appointments

One of the reforms developed within the WPI Program that has had a strong impact and that is becoming an important part of the university reform debate is the cross appointment system (also called joint appointments or double appointments).

The first example of this was Dr. Hitoshi Murayama, the director of Kavli IPMU. He first came to the University of Tokyo while on leave of absence from the University of California, Berkeley. Since he subsequently became an employee of both the University of California, Berkeley and the University of Tokyo, his two salaries were adjusted in response to the effort he was deemed to be devoting to each (i.e., a cross appointment). Dr. Petros Sofronis, the director of I^2CNER, also subsequently concluded a cross appointment contract between the University of Illinois and Kyushu University.

The introduction of cross appointments is a revolutionary system reform in that it increases the mobility of teaching staff. In fact, in the National University Reform Plan announced by MEXT in 2013, cross appointments were positioned as one of the pillars of university reform.

Administrative support departments

The WPI Program requires that WPI centers provide environments that are sufficiently conducive to research work.

- A support system to allow researchers to concentrate on research activities.
- A research and lifestyle support system for researchers from overseas.
- Since the official language of the centers is English, support staff who are able to work in English.
- Staff to host international research meetings that are appropriate for world top-level research centers.

To be able to support center directors both in terms of science and operations/management, selection of administrative directors is an important issue. Therefore all of the WPI centers have employed researchers from universities or private research institutions to act as administrative directors.

Up until now, administrative staff paid little attention to the globalization of university, and it has not been possible to provide sufficient support in English. The WPI Program is helping to change the nature of administrative staff in Japan.

Research support departments

Many of the WPI centers are also working on enhancing their research support departments.

- MANA has created the "MANA Foundry" which helps with research by supporting the production of research materials.
- ITbM has established support centers for molecular structures, its compound library, live imaging, and

peptides/proteins, each staffed with researchers with a PhD. These four centers are used as venues for integrating chemistry and biology and they have already helped with the discovery of a number of efficacious compounds.

Some universities in Japan that possess similar kinds of research centers are finding it difficult to maintain their support programs due to workforce reductions. This is one of the reasons for the weakening of Japan's scientific capabilities. Research at WPI centers is underpinned by these kinds of support centers and they provide a stable foundation for the pursuit of outstanding research.

10 Track records of WPI centers (5) Education

Training the next generation of researchers is another extremely important duty of advanced research centers like those participating in the WPI Program. Many such centers employ a double mentor system for training young researchers capable of contributing to the creation of new fields of study through engaging in fusion research.

One of the remaining issues is close coordination with graduate schools. Since WPI centers do not have conventional graduate schools as they were established independent of existing graduate schools, they are unable to confer degrees. This means that graduate students have to be dispatched from existing graduate schools to the center and some graduate schools are opposed to doing so. However with the recognition that WPI centers are now receiving, cooperative relationships between them and graduate schools are currently being built.

An exception to this is the University of Tsukuba. Thanks to its system of clear separation of faculty and educational bodies, which has been in place since the establishment of the university, IIIS is able to involve itself in the education of graduate students. The system used in the University of Tsukuba is starting to be adopted by other universities.

11 Track records of WPI centers (6) Outreach activities

During the budget screening that occurred in 2010, many scientific research projects including the WPI Program were in danger of having their budgets significantly reduced. Scientists were faced with the realization that their work was not adequately understood by politicians and the general public. This helped to remind us of the importance of not just concentrating solely on research activities but also engaging in outreach activities to communicate to the general public about the content and significance of their work.

Following this, each WPI center employed outreach staff and they now proactively engage in outreach activities.

In addition, the outreach staff of each center gather for meetings three times a year to ensure consistency in WPI outreach activities. Some examples of these activities are listed below:

AAAS (American Association for the Advancement of Science) Annual Meeting

Scientists from the United States and around the world gather at AAAS Annual Meetings, and WPI representatives have attended these since 2012. Each WPI center sets up a display booth to explain its research activities. Dr. Petros Sofronis, the director of I^2CNER, gave a talk on the WPI Program at the AAAS Annual Meeting held in Chicago in 2014.

Workshops for high school students

Every year WPI centers hold collaborative workshops for high school students to teach the next generation about the wonders of science. Students of high schools selected by MEXT as "Super Science High Schools" in particular are encouraged to participate in these workshops. Past workshops are listed below:

- Kyoto 2015 (hosted by iCeMS): "Science You Can Feel"
- Tokyo 2014 (hosted by Kavli IPMU): "Science Connecting Your Future"
- Sendai 2013 (hosted by AIMR): "Science Talk Live 2013"
- Tsukuba 2012 (hosted by MANA): "Enjoy World-Class

Workshops for high school students: Fukuoka 2011 (left and center), and Sendai 2013 (right)

Science "
- Fukuoka 2011 (hosted by I²CNER): "Cutting-Edge Science and Your Future"

The large numbers of high school students attending these workshops always participate enthusiastically and gather at the booths of the WPI centers asking for more detailed information. At the workshops in Tokyo and Sendai, high school students made presentations on research that they themselves had conducted, with students from Eleanor Roosevelt High School in Maryland, United States making presentations at the workshop in Sendai.

The "Science and Technology Festa" and the "Science Agora"

Each WPI center participated in the "Science and Technology Festa" events held by the government until FY 2012 and the "Science Agora" event held by the Japan Science and Technology Agency (in FY 2013) and set up display booths at both.

Outreach activities unique to each WPI center

Each WPI center carries out its own outreach activities, including, for example, talks aimed at general audiences, "science cafés," and the publication of handbooks.

The blogs of post-doctoral researchers visiting Japan also communicate in a direct manner about life in Japan and thereby contribute to globalization. Through these community-driven activities, the WPI Program is gaining the understanding of not only the researcher community but also their local communities.

12 WPI's achievements (7) Contribution to society

The WPI Program does not position applied research as a target activity. The intention is not, however, to denigrate applied research of course. Nothing delights us more than when basic research results lead to applied research, and then commercialization of technologies that prove useful in people's everyday lives. The research results of WPI centers do in fact get utilized in applied research. Below are some examples of this:

- AIMR's research achievements are widely recognized in industrial circles, and many companies have participated in consortia to work toward their commercialization. The fruits of AIMR's research are currently being commercialized by companies such as Toshiba, Hitachi, and NEC.
- iCeMS developed a probe that recognizes iPS cell differentiation and a company subsequently released this commercially.
- Based on IFReC's outstanding basic research results and successful track record with drug design, Chugai Pharmaceuticals has signed a comprehensive contract to support the operations of the center for ten years (see p.12). The center has also been involved in the establishment of several biotechnology startups.
- Like AIMR, MANA has also made substantial contributions to applied research. Of particular note is the atomic switch developed by MANA's director, Dr. Masakazu Aono, which was subsequently commercialized by NEC.
- I²CNER is working on the development of a device to produce hydrogen using solar energy.
- IIIS is collaborating with a pharmaceuticals company on designing sleep-related drugs.
- ITbM has produced results with applied research into catalysts and probes etc. Of particular note is the development and commercialization of a compound called Yoshimulactone that will help eradicate a parasitic plant called striga that has had a serious impact on agriculture in Africa (p.90).

Further details relating to the applied research and commercialization connected with each WPI center can be found at the website below:

http://www.jsps.go.jp/english/e-toplevel/17_contribution.html

13 Future plans for the WPI Program

In 2015 the WPI Program Committee submitted the two following policy requests to MEXT:

1. Continuation of the WPI Program

- The WPI Program should be continued.
- Further development of the WPI Program depends on the "metabolism of centers." A call for new WPI center applications should be made.

2. Support for centers for which the subsidization period has ended

- In light of the level of excellence attained by the WPI centers, a support scheme should be established for centers for which the subsidization period has ended.
- To maintain the vitality and brand recognition of the WPI Program, the establishment of a "WPI Academy" is recommended.

The Program Committee's recommendations are contained in the FY 2015 follow-up report.

Based on this, MEXT reported the following future vision at a meeting of the Program Committee in October 2016.

1. Call for new WPI center applications

- A call for applications for two new centers will be made in FY 2017. Further expansion of the WPI Program is targeted in FY 2018.

- The future aim is to establish a maximum of 20 centers.
- The new centers will be funded a maximum of 1 billion yen per year for 10 years (an extension system will not be established).
- The current four missions of the WPI Program will essentially be maintained.
- The target field will be basic research in the natural sciences. In FY 2017 consideration will also be given to application of mathematical and data sciences.
- If it is deemed necessary for the implementation of the initiative, the incorporation of humanities and social science perspectives may also be permitted.
- Organizations with host centers that are currently within the ten-year support period cannot submit applications.

In addition, for organizations hosting WPI centers launched in FY 2007, assurances regarding continued maintenance of the centers after the end of the support period is a precondition for application.

2. Establishment of the WPI Academy

- The WPI Academy is being launched as a new framework with which to fully establish, maintain, and develop the WPI brand.
- The academy will give particular focus to supporting "global brain circulation."
- The academy will operate laterally across all of the WPI centers to link them in a network.
- The academy will gather the accumulated experiences and achievements of WPI centers and work to share this information amongst them.

The future vision outlined above is based on the FY 2017 budgetary requests made at the time of a Program Committee meeting in October 2016. The manner in which the budgeting process proceeds may lead to alterations. The details will be determined following further debate amongst the Program Committee members that are based in Japan.

14 International trends relating to Research Excellence Initiatives

Policies aimed at enhancing the standard of research such as the WPI Program are not unique to Japan. Many other countries have also launched similar programs based on similar concepts. The following ideas are what lay behind this trend.

- Contemporary societies are knowledge-based societies.
- Global competition relating to the creation of new research results (knowledge base) and the securing of outstanding personnel is intensifying.
- The governments of each country are looking for more efficient ways to support the advancement of basic and applied sciences.

Against this background, more than two-thirds of OECD countries are using research excellence initiatives to create high-caliber research centers.

The following commonalities can be found in these initiatives:

- Long-term stable provision of funding in order to facilitate the implementation of ambitious research plans.
- The aim to create preeminent research centers.
- Facilitating more flexible approaches to research programs and operations.
- The directing of ripple effects toward the wider research community.
- Fostering of the next generation of outstanding scientists.

These common denominators are a perfect match with the aims of the WPI Program.

Research excellence initiatives around the world

Countries around the world are promoting research excellence initiatives based on the concepts above.

Japan: WPI
Germany: Excellence Initiative
France: Investments for the Future
Denmark: Investment Capital for University Research
Israel: Israeli Centers of Research Excellence
Spain: International Campus of Excellence
Russia: Project 5-100
Canada: Canada First Research Excellence Fund
United States: Science and Technology Centers
Australia: Competence Centers for Excellent Technologies
Chile: Millennium Science Initiative
China: 2011 Collaborative Innovation Centers
Republic of Korea: World Class University

As research excellence initiatives, these research organizations share common concerns. At the same time,

Musical performances at WPI centers: IIIS director Masashi Yanagisawa playing the flute (left), and Kavli IPMU director Hitoshi Murayama playing the double bass (right).

the particular circumstances of each country are also what lies behind their establishment.

- Japan's WPI Program positions globalization and university reform as part of its mission.
- One of the objectives of France's initiative is to bring together a diverse range of higher education organizations.
- Germany's initiative is aimed at channeling federal funds into higher education organizations that are supported by state governments, thereby strengthening them.
- Israel's initiative is seen as a method to encourage outstanding Israeli researchers to return home from overseas.

The WPI Program is a model for other research excellence initiatives

Launched in 2007, the WPI Program was the second to be launched after Germany's initiative (which was launched in 2006). The WPI Program has therefore garnered worldwide attention and is often cited as a role model for other research excellence initiatives.

In 2014, the OECD published a monograph on the state of research excellence initiatives called "Promoting Research Excellence." The journals Nature and Science have also made repeated mention of research excellence initiatives, including the WPI Program. International workshops relating to research excellence initiatives have been held four times: In 2010 (Bonn, Germany), 2013 (Jerusalem, Israel), 2015 (Tokyo), and 2016 (St. Petersburg, Russia). The workshop in 2015 was held in Tokyo in conjunction with the WPI's Program Committee and featured presentations from research excellence initiatives from seven countries. The WPI Program is drawing attention from around the world. We need to develop the WPI Program yet further in order to foster world-leading science.

Fig. 9. The OECD published a monograph in 2014 providing an overview of each country's research excellence initiative.

15 The WPI Program as the cornerstone for science and technology policies - In lieu of a summary

As a forward-thinking experiment, the WPI Program, with its world-class results, is positioned as a cornerstone of Japan's science and technology policies. In FY 2016 for example, the initiative was mentioned directly or indirectly in the following government policies (all cabinet resolutions).

- The Fifth Science and Technology Basic Plan
- The Comprehensive Strategy on Science, Technology and Innovation 2016
- The Japan Revitalization Strategy 2016

The Fifth Science and Technology Basic Plan

"STI activity has recently been expanded past national borders… [which] will have a great impact on Japan's international competiveness." (Chapter 1).

"Japan… [is] forming… world-class research center[s] that will attract leading researchers from throughout Japan and around the world." (Chapter 4)

The Comprehensive Strategy on Science, Technology and Innovation 2016

"The World Premier International Research Center Initiative (WPI), which creates research centers that attract leading researchers from throughout Japan and around the world… is steadily working to create research centers that serve as hubs for global brain circulation." (Chapter 3).

The Japan Revitalization Strategy 2016

"The Government will continue to promote World Premier International Research Center (WPI) initiatives to construct research centers where excellent talents will gather from all over the world, and consider a mechanism to horizontally deploy experiences and knowhow of such initiatives inside and outside the universities and introduce it in next fiscal year, given that those initiatives will produce distinguished results, including creation of new inter-disciplinary fields, personnel and salary reforms, and invitations of excellent researchers and solicitations for donation from outside of Japan." (Section 2. III).

As is repeatedly explained within the government's policy documents, there are great expectations that the WPI Program will continue to serve as the core of the government's science and technology policies. We, and others connected with the WPI Program, will continue to do everything in our power to live up to those expectations.

Director
Motoko Kotani

A Unique Research Center Where Mathematics Drives Materials Science Innovation

AIMR was established to bring together scientists in materials science, physics, chemistry and engineering – research fields in which Tohoku University holds a world-leading position – who can contribute to society by creating revolutionary new materials. Since its establishment in 2007, AIMR has consistently produced interdisciplinary "fusion" research achievements across different fields, utilizing atomic and molecular control. In 2011, a new policy was adopted of introducing mathematics into all areas of materials science research, aimed at making fusion research more dynamic. Since then, promoting collaboration between mathematicians and researchers in the fields of materials science, physics, chemistry, and engineering, AIMR has become the world's first research center fully devoted to fusion research between mathematics and materials science.

Research Center's Information (FY 2015)

Center Director: Motoko Kotani (up to FY 2011: Yoshinori Yamamoto)
Principal Investigators (PI): 28 (including 13 overseas researchers and 2 female researchers)
Other Researchers: 140 (including 74 overseas researchers and 13 female researchers)
Research Support Staff: 75
Administrative Division:
  Administrative Director: Masaru Tsukada
  Administrative Staff: 30 (percentage of bilingual staff: 90%)
Satellites and Cooperative Organizations: University of Cambridge, UK;
  University of California, Santa Barbara, USA; University of Chicago, USA;
  Institute of Chemistry, Chinese Academy of Sciences, China;
  University College London, UK; Tsinghua University, China; and others
URL: http://www.wpi-aimr.tohoku.ac.jp

Major Research Achievements

1 Using mathematics to shed light on materials science

The structure of metallic glasses was elucidated after remaining a mystery for half a century. This revolutionary fusion research, by materials scientists working with mathematicians (in the field of geometry), is emblematic of AIMR innovation.

2 Research advancing porous materials

Nanoporous metal, with countless nano-sized holes, was applied to development of highly efficient catalysts. Using nanoporous metal as a mold, technology was developed for fabricating three-dimensional nanoporous graphene that preserves the electron mobility of two-dimensional graphene. AIMR continues to dramatically advance the field of nanoporous materials science

3 Elucidation of new principle relating to magnetic properties and spin

A principle was conceived whereby magnetic waves (spin waves) are used to transport thermal energy in the desired direction. Moreover, a spin- and angle-resolved photoemission spectroscopy system (spin-ARPES) was developed achieving the highest resolution ever, and is being used to clarify the mechanisms by which material properties emerge. AIMR is advancing at the forefront of the magnetism and spin science.

4 Applications of multifunction hybrid materials and complex hydrides

Using supercritical water as the reaction solvent, multifunction hybrid materials were created without the use of hazardous substances. Discovering the excellent ionic conductivities of "complex hydrides", researchers applied these new materials to solid-state electrolytes for next generation rechargeable batteries. Creating new materials, AIMR is also pointing the way to potential applications.

5 Design of MEMS and biosensing devices

In the field of MEMS (Micro Electro Mechanical Systems), visible only with a microscope, a micromirror was developed using metallic glasses. Researchers also developed a noninvasive high-resolution imaging method using NanoSECM and related systems, and applied it to monitoring of living cells.

6 Oxide electronics endowing common, abundant materials with novel functions

Superconducting was realized by field-effect doping of oxides, which are basically insulators that do not conduct electricity. Moreover, researchers observed the fractional quantum Hall effect in oxide materials for the first time. The results of AIMR research led to the birth of a transparent superconductor.

Research Paper's Information

Number of Research Papers:	2,609
Top 10% Papers:	17.6%
Top 1% Papers:	2.4%
Internationally Collaborative Research Papers:	43.3%

(Database: WoS between 2007-2015)

The background is graphene.
Two-dimensional graphene consists of a single layer of carbon atoms arranged in a honeycomb lattice pattern.

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Blazing new trails at the forefront of materials science

The moment people start using a substance, it comes to be called a "material." The science of studying materials is known as materials science. The field of materials science, which seeks to make substances serve humankind in useful ways, crosses over a wide range of natural sciences including physics, chemistry, engineering, and life sciences. AIMR was established in 2007, bringing together researchers from this broad range of areas to advance fusion research and blaze new trails at the forefront of materials science.

In the first half of the decade since its founding, under the leadership of Director Yoshinori Yamamoto, a chemist, fusion research was carried out by people in the fields of materials science, physics, chemistry, engineering, and life sciences. Then in the second half, under current Director Motoko Kotani, a mathematician, fusion research was accelerated based on the policy of introducing mathematics into all areas of materials science research.

Today this policy has evolved further, moving in innovative directions with the aim of deriving common principles by describing various materials science phenomena and principles using mathematics, going on to mathematically predicting structures and other properties of previously unknown materials, and then actually creating these unknown materials.

Here we introduce some of the research results brought about by AIMR in each of the broad-ranging fields of materials science, starting with innovations achieved by introducing mathematics.

1 Using mathematics to shed light on materials science

Mingwei Chen (PI), Motoko Kotani (PI), Akihiko Hirata (Associate Professor)

A successful example of introducing mathematics into materials science is clarification of the structure of metallic glasses.

As is well known, the three states of matter are solid, liquid, and gas. Viewed at the nano scale, solids are made up of atoms packed tightly together in a regular pattern to form crystallized structures. In liquids, atoms are assembled close to each other but more disordered and free to move around. In a gaseous state, both the position and distance of atoms can change freely.

But are atoms arrayed regularly in all solids? Not necessarily. Glass, the material of windows and goblets, appears solid to the eye, but its atoms are not arranged regularly as crystals. They are disordered as in liquids.

Normally we tend to consider glass to be a "kind" of material. We think of the transparent material used for windows and drinking utensils as glass. In the world of science, however, the term "glass" is used rather as a material "state." The transparent material we call glass results from high-temperature melting of the main ingredients silicon and oxygen, followed by a cooling process, during which a "glass state" is reached in which the atoms have not had time to line up in an ordered array.

In the case of metal, when it is melted and then cooled, the atoms tend to become rapidly arranged in orderly arrays, forming crystallized structures. Under certain conditions, however, metal can become a solid without the atoms achieving an ordered arrangement. The resulting substance, while not transparent, is in glass state and is thus called metallic glass. Metallic glass is a new material exhibiting many times the strength of ordinary, crystallized metal. This is a material with many mysteries. The strength comes from the absence of crystal grain boundaries where fractures can occur, but the lack of order in the arrangement of atoms makes the structure difficult to characterize.

In 2013, a fusion research team of AIMR mathematicians and experimental scientists (materials scientists) succeeded in clarifying the structure of metallic glasses. First, experimental scientists identified a number of characteristic shapes (atom clusters) in which atoms are arranged in metallic glass, using electron diffraction. Then mathematicians analyzed the features of these atom clusters by means of a geometric method known as computational homology. While the existence of these atom clusters had been pointed out in the past, this was the first time anywhere that their structure was clearly determined. On the basis of these studies, researchers concluded that the arrangement of atoms in metallic glasses consists of clusters of icosahedra (polyhedra with 20 faces each) all distorted in the same way (Fig. 1).

How do metals, with their normal tendency to become crystallized structures, instead become glass with disordered atomic configurations? Hidden in what at first appear to be random atomic arrangements are distorted icosahedra, in large numbers and all similar to each other. However, regular icosahedra cannot completely fill up a three-dimensional space without forming gaps (they are not a space-filling polyhedron), making it theoretically impossible for them to form crystals. This leads to the conclusion that, because their atomic arrangement differs from that of crystal, they are hindered from crystalizing and remain in glass state.

In fact, the icosahedral structure of metallic glasses was theoretically predicted more than a half century ago; but direct confirmation could not be made despite

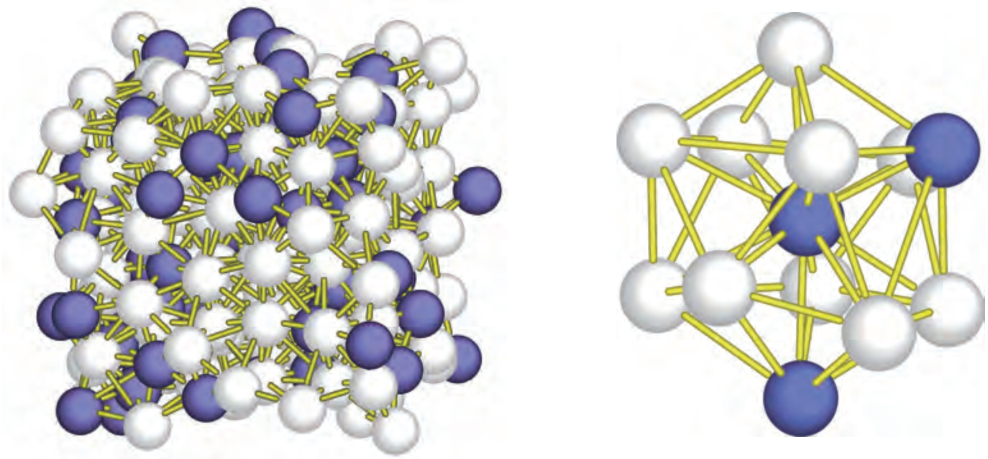


Fig. 1. Model of the atomic arrangement of metallic glass. The icosahedra structure hidden in what appears to be a disordered atomic structure of metallic glass (left) had long been predicted. This study revealed that the sequence of distorted clusters of icosahedra (right) prevent the glass state from crystallizing. The purple spheres in the figure are platinum (Pt) and the white spheres are zirconium (Zr).

attempts by numerous researchers. AIMR succeeded in verifying this hypothesis by combining the highest level of experimental techniques with leading-edge mathematics, settling discussions that had been waged for half a century. Optical fiber and other substances with glass structures are already widely used as practical materials. It is hoped that the knowledge gained from this elucidation of the structure of metallic glasses will lead to improvement of glass materials and development of new ones.

A. Hirata et al., Science 341, 376 (2013).

2 Research advancing porous materials

Mingwei Chen (PI), Yoshinori Yamamoto (PI), Naoki Asao (Professor), Takeshi Fujita (Associate Professor), Yoshikazu Ito (Associate Professor)

Materials with countless nano-sized holes are called nanoporous materials. AIMR scientists developed and applied technology for fabricating nanoporous metal (Fig. 2); moreover, using nanoporous metal as molds, they succeeded in developing new materials.

The process used for fabricating nanoporous metal is called dealloying. To make nanoporous gold, for example, first a gold-silver alloy is made, then the silver is dissolved in acid or the like, so that only gold remains. In the alloy state, gold and silver are mixed together at the nano level. The gold remaining after dissolving the silver is thus nanoporous, with very fine holes. The AIMR research team discovered that the nanoporous gold fabricated in this way acts as a catalyst to promote chemical reactions. Gold is an inactive substance resistant to corrosion, and was once thought not to function as a catalyst. Around 30 years ago, however, nanoparticulate gold was found to have catalytic activity. Thereafter, research on gold nanoparticle catalysts took off dramatically. The problem with gold nanoparticle catalysts is that their catalytic activity weakens as the nanoparticles agglomerate into larger particles. Solving this was a major research theme. The AIMR research team shifted their focus away from the gold nanoparticles that everyone had been studying, looking instead at nanoporous gold. Then they discovered that nanoporous gold had remarkable catalytic activity in the oxidization of organosilane compounds with water. In nanoporous gold, moreover, agglomeration does not occur as with nanoparticles. The high catalytic activity is retained and the catalyst can be re-used numerous times. Catalysts being essential to the chemical industry, nanoporous gold as a highly efficient catalyst is likely to contribute significantly to society.

AIMR is successfully using nanoporous metals like this to create completely new materials. Graphene is a substance consisting of a single layer of carbon atoms in a hexagonal honeycomb lattice structure. It became the object of public attention after the awarding of the 2010 Nobel Prize in Physics. Because of its very high electrical conductivity, graphene is expected as a

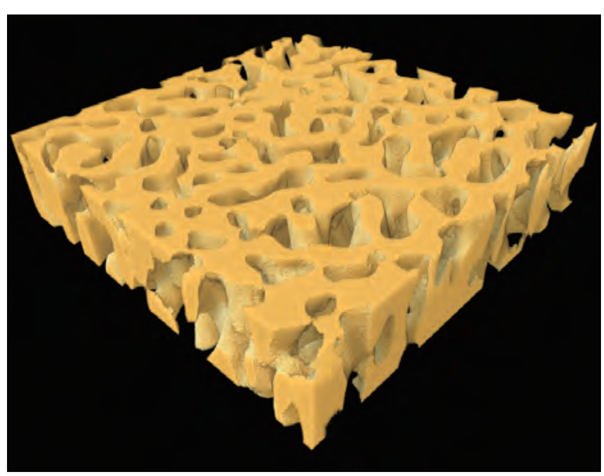


Fig. 2. Image of 3D nanoporous metal obtained by electron tomography using a transmission electron microscope

potential future replacement for silicon semiconductors and metal used in electronic devices today. Scientists have sought to create three-dimensional structures that maintain the high conductivity as demonstrated in two-dimensional graphene sheets, but none of the earlier attempts were successful. AIMR researchers, using the earlier-described nanoporous metal as a mold, developed a process for making a three-dimensional nanoporous graphene structure with high electron mobility. Graphene is grown by chemical vapor deposition on the surface of nanoporous nickel which is fabricated by a dealloying method. Then the nickel is dissolved leaving only graphene. Since this three-dimensional graphene preserves the properties of two-dimensional graphene, there are hopes for its application to electronic devices; but the discovery of its potential use as a catalyst for chemical reactions in hydrogen fuel cells has now suddenly become the focus of interest. Research is continuing toward enabling three-dimensional nanoporous graphene to contribute to hydrogen stations for fuel cell vehicles and to realization of the hydrogen society.

N. Asao et al., Angewandte Chemie International Edition 49, 10093 (2010).
Y. Ito et al., Angewandte Chemie International Edition 53, 4822 (2014).

3 Elucidation of new principle relating to magnetic properties and spin

Eiji Saitoh (PI), Takashi Takahashi (PI), Seigo Souma (Associate Professor)

AIMR has proven its excellence in the research area of magnetism and spin. One of the highlights is "spin caloritronics", which concerns interactions between spin and heat. By nature, heat flows from a hot place to a cold place and a control of the heat flow has been limited to a local heating and cooling. An AIMR joint research team has shown another way: a use of magnetic wave, a dynamics of spin, can control a heat flow in the desired direction. Applying this principle, it should be possible to develop heat flow control devices that transport thermal energy to places distant from the heat source, raising expectations for application to next-generation energy-saving devices.

Another remarkable achievement in this area is the development of a spin- and angle-resolved photoemission spectroscopy (spin-ARPES) system (Fig. 3) with the world's highest resolution. The system has been successfully applied to various novel materials for unraveling the mechanism and electronic states. To elucidate the mechanism of novel properties, it is essential to reveal the state of electrons, the fundamental basis of electronic properties. Photoemission spectroscopy is a powerful tool for this purpose. When materials are shone by light, electrons inside are emitted to outside from the surface (Einstein's photoelectric effect). By measuring the energy of photo-emitted electrons and comparing it with the energy of the light shone, one can estimate the binding energy of electrons in materials, namely the electronic state of materials. Of the three basic physical quantities of electron (energy, momentum, and spin), standard ARPES directly determines the first two quantities. To observe the last quantity (spin) which directly relates to the magnetic property of materials, AIMR researchers have developed a spin-ARPES system equipped with a mini Mott spin detector. The constructed spin-ARPES machine achieves the world's highest resolution. Using this spin-ARPES machine, they studied the electron

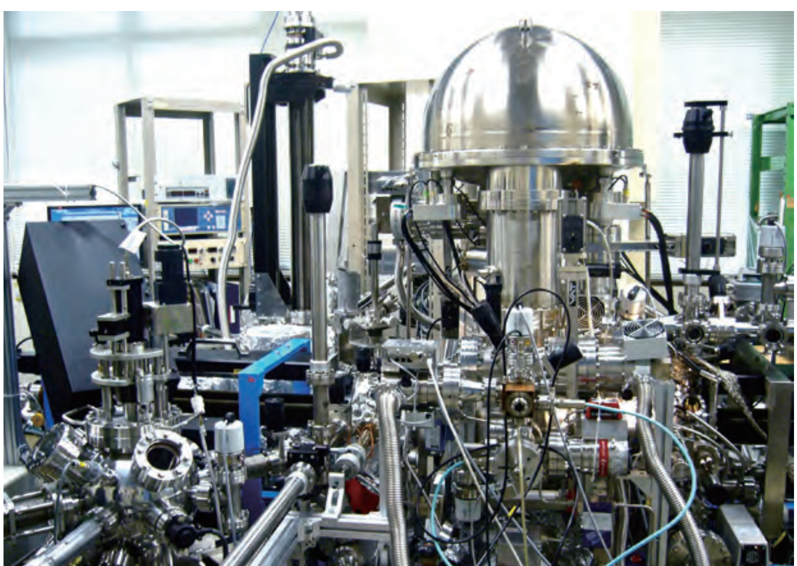


Fig. 3. Spin-ARPES system able to observe all three basic physical quantities of electrons (energy, momentum, and spin) in materials

states of various novel materials such as high-T_c superconductors and topological insulators.

By practical implementation of spin-based technology in personal computers and other electronic equipment, it is believed that energy savings of 80 percent can be achieved. The above studies, along with other spin-related studies pioneered by AIMR researchers in such areas as tunnel magnetoresistance effect and magnetic semiconductors, are major steps toward realizing the dream of energy-saving electronic equipment.

T. An et al., Nature Materials 12, 549 (2013).
Y. Tanaka et al., Nature Physics 8, 800 (2012).

4 Applications of multifunction hybrid materials and complex hydrides

Tadafumi Adschiri (PI), Shin-ichi Orimo (PI)

AIMR researchers are employing novel methods of materials science to create innovative materials with the potential for practical applications.

As one example, an AIMR research team discovered how to create multifunction hybrid materials without the use of hazardous substances, using supercritical water as a reaction solvent. At temperatures and pressure above the critical point, the state of materials turns into a supercritical phase that cannot be distinguished as either liquid or gas phase. Using water in supercritical state, the research team created CeO_2 nanocubes (cubic shape crystals of cerium oxide) of 10 nanometers or smaller (Fig. 4). The resulting CeO_2 nanocubes show higher catalytic activity at lower temperatures than normally seen in conventional catalysts. They are expected to be used for such applications as environmental cleaning and waste decomposition.

Another AIMR success was finding the excellent ionic conductivities of "complex hydrides" for next generation rechargeable batteries. Normally, liquid electrolytes are used in rechargeable (or secondary) batteries. The problem is that the liquid electrolytes become unsafe at high temperatures. Therefore, development of solid-state electrolytes has been socially desired. An AIMR research team discovered that, with the complex hydrides containing sodium, boron and hydrogen (stable salts substances such as $Na_2B_{10}H_{10}$), sodium ion conductivity at 100°C rises up to 100,000 times than that at room temperature. Research is continuing toward implementation of solid-state sodium rechargeable batteries using new complex hydrides with high ion conductivity even at room temperature.

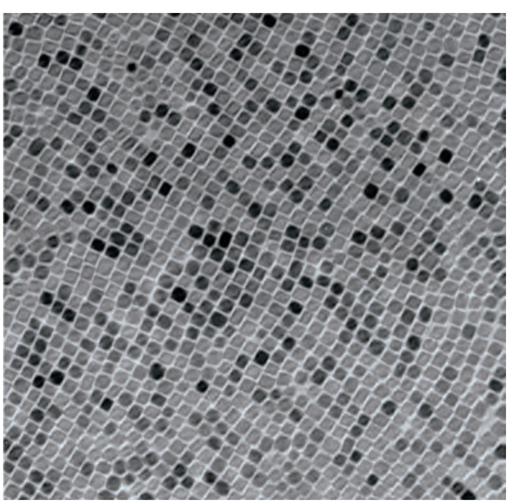


Fig. 4. Cluster of nanocubes fabricated by supercritical water thermal synthesis

J. Zhang et al., Nano Letters 11, 361 (2011).
T.J. Udovic et al., Advanced Materials 26, 7622 (2014).

5 Design of MEMS and biosensing devices

Masayoshi Esashi (PI), Thomas Gessner (PI), Tomokazu Matsue (PI), Yu-Ching Lin (Associate Professor)

AIMR has created highly innovative devices applying materials science knowledge. As examples, here we look at MEMS and biosensing devices.

MEMS (Micro Electro Mechanical Systems) are mechanical systems so small they can be seen only with a microscope. This is one of Tohoku University's strongest applied research fields. An AIMR fusion research team used metallic glass, which does not break even under large deformation, to support a silicon micromirror (Fig. 5). The micromirror can be mounted on an endoscope and used for beam scanning in optical coherence tomography (OCT) imaging of tissue. The encounter between materials scientists and device engineers gave birth to the novel result of MEMS using previously unimagined materials. As an example of a biosensing device, the voltage-switching mode scanning electrochemical microscope (VSM-SECM) developed by AIMR researchers is a special kind of microscope. Detection at cell surfaces of neurotransmitters, reactive oxygen species, and other short-lived chemicals that are released and consumed by cells had been a highly difficult challenge. AIMR researchers, using this special microscope, succeeded in acquiring high-resolution topographical and electrochemical images of living cells simultaneously by non-invasive (non-contact) imaging. Their next challenge will be to monitor the changes in neuron topography when neurotransmitters are released. These advances have wide-reaching implications for the future of medical care.

Y.-C. Lin, Y.-C. Tsai et al., Advanced Functional Materials 25, 5677 (2015).
Y. Takahashi et al., PNAS USA 109, 11540 (2012).

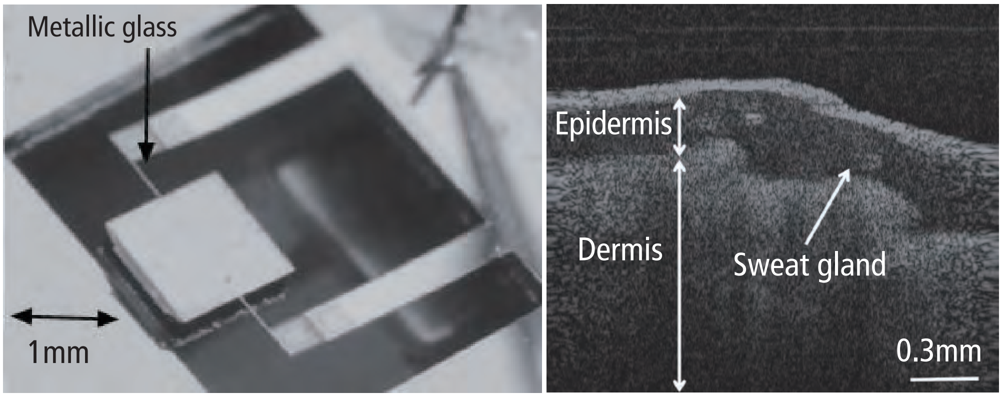


Fig. 5. Tomographic image of skin taken using a micromirror supported by metallic glass

6 Oxide electronics endowing common, abundant materials with novel functions

Masashi Kawasaki (PI), Taro Hitosugi (Junior PI)

Oxide electronics grew up rapidly as a research field soon after AIMR was established. Among the most important discoveries at AIMR, attracting the notice of researchers throughout the world, were superconductivity induced by field effect carrier doping and observation of the fractional quantum Hall effect in oxide materials.

When certain materials are cooled to very low temperatures, their electrical resistance rapidly drops to zero. This phenomenon is known as superconductivity. By making wires from superconductive materials, power transmission systems with very little energy loss can be realized, contributing greatly to solving the world's energy problem. The superconductors discovered up to now require cooling to reach the superconductivity state. As the search continues for materials that can achieve superconductivity at room temperature, besides the approach of looking for new materials, a breakthrough is being sought by coming up with a new way of inducing superconductivity. Here an AIMR research team has succeeded in establishing a brand new method, achieving superconductivity by field-effect doping of oxides.

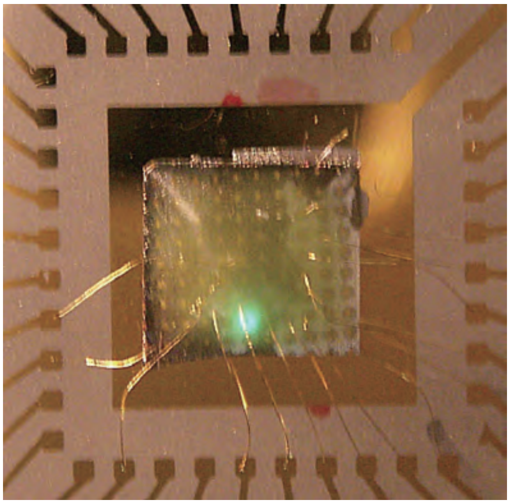


Fig. 6. Light from light-emitting diode made using zinc oxide material

Strontium titanate ($SrTiO_3$) is normally an insulator that does not conduct electricity. The team used field-effect doping to inject a large amount of electrons onto the surface of this oxide, inducing superconductivity. Previously, electron injection by doping with impurities had been tried, but the studies had been limited because very few oxides lend themselves to efficient impurity doping. Discovery of this new method suddenly broadened the search for superconductive materials, greatly impacting the world's materials scientists.

In addition to the above advances, AIMR researchers using zinc oxide confirmed the fractional quantum Hall effect in an oxide for the first time. This is a phenomenon in which electrical resistance take on values given by fractional times of a combination of fundamental constants of quantum mechanics. They also succeeded in developing high-luminance zinc oxide light-emitting diodes (Fig. 6). The key to both these achievements was the relentless effort of researchers to overcome the difficulties of controlling atoms on oxide thin films. A further accomplishment was creating transparent superconducting thin films of lithium titanates (spinel), exhibiting up to 70% transmittance of visible light. This was achieved by precise control of the atomic ratio. These research successes demonstrate the potential for creating highly functional electronics materials from oxides, which are abundant and found everywhere.

K. Ueno et al., Nature Materials 7, 855 (2008).
A. Tsukazaki et al., Nature Materials 9, 889 (2010).

The Path to Creation of Novel Scientific Fields

AIMR has produced a large and diverse array of remarkable research results, including those introduced above.

The number one reason that these accomplishments have been possible is that the center has attracted a large number of excellent world-class researchers. Tohoku University as the host institution has a long history of leading the world in materials science, and it is against the background of trust in this history that so many outstanding scientists have come to AIMR.

The second reason is the environment conducive to carrying out fusion research provided at AIMR, and many different innovative measures devoted to enabling its implementation. The center is equipped with the facilities and equipments for conducting world's top level research, and provides scientists appointed from outside Japan with extensive support for both research and living. It also holds various research events inside and outside the organization. The AIMR International Symposium is held annually, assembling scientists from more than 15 countries; many joint workshops are held with partner institutions from outside Japan; and interdisciplinary exchanges are encouraged in a wide range of materials science academic societies.

The third reason behind AIMR's success is the adoption of a clear policy and bold strategy of introducing mathematics into all areas of materials science research. Setting ambitious target projects that are highly compelling to researchers, research fusing mathematics and materials science has been carried out. Today research continues in AIMR on four target projects: Non-equilibrium Materials based on Mathematical Dynamical Systems, Topological Functional Materials, Multi-Scale Hierarchical Materials based on Discrete Geometric Analysis, and The Core Technology for Nano Energy Devices.

That the policy measures relating to the above three reasons could be carried out successfully is in each case due largely to AIMR being a World Premier International Research Center. Along with these measures, AIMR has consistently devoted energy to supporting and developing the young scientists responsible for the next generation.

AIMR: Looking Ahead

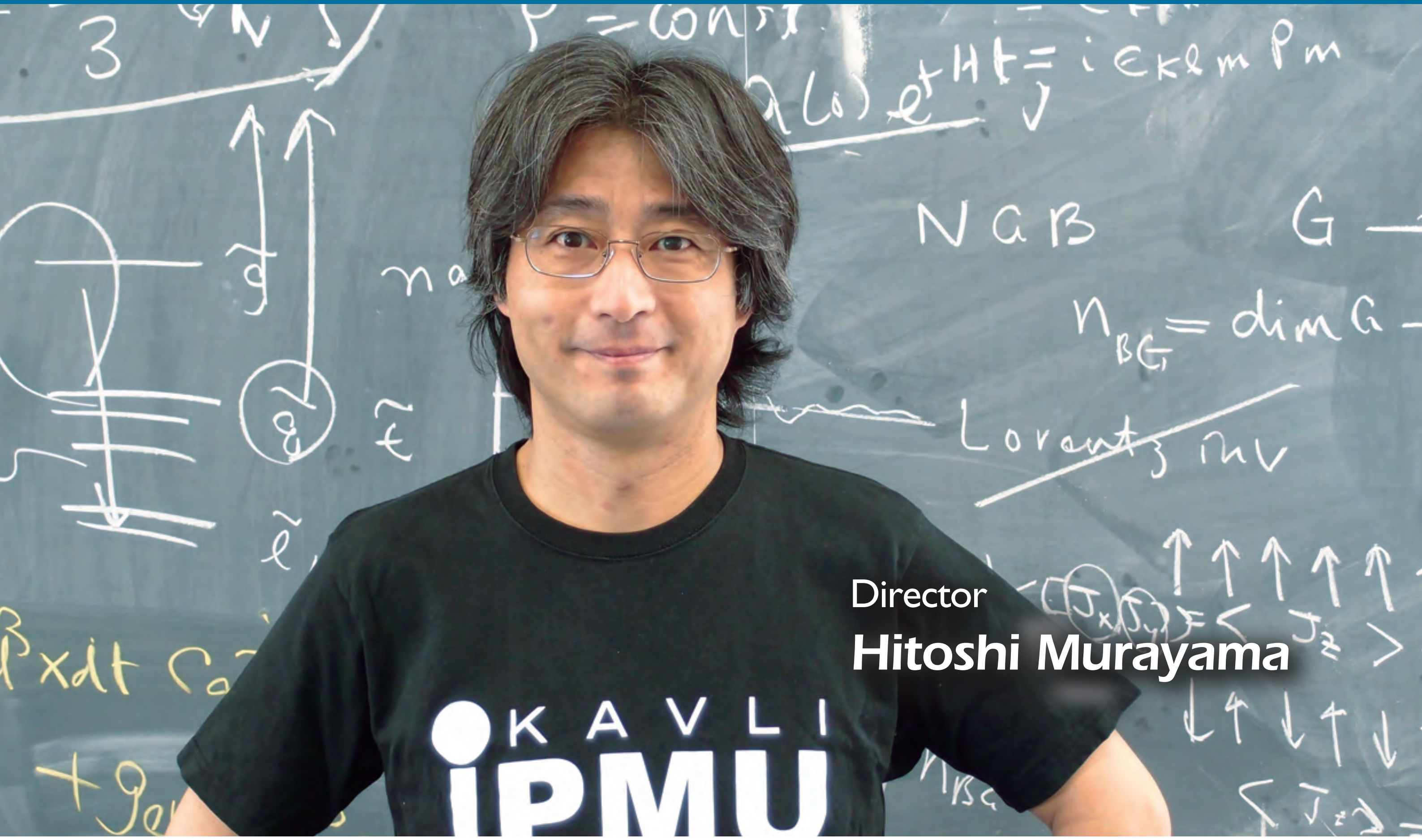
Throughout its ten-year history, AIMR has continued to encourage and support young scientists willing to take up the challenge of interdisciplinary fusion research. In fact, young researchers from different disciplines, who would have few chances to become acquainted at an ordinary university or research institution, can frequently be seen talking to each other at Tea Time or debating at workshops, as they transcend the wall between disciplines. It is not hard to imagine that they will further advance the results that have emerged from such interchanges, and in the future will themselves create new fields of science. The fact that there are ambitious young scientists who grew up, transcended the walls between disciplines, and went out to the world, is the largest accomplishment of AIMR as a research center, and the core of the organization (Fig. 7).

Fig. 7. Director Kotani with young AIMR scientists.
They will go on producing research results by transcending the walls of nationality, gender, and academic fields

The goal of AIMR as an organization today is to create and give root to new materials science that enables prediction of new functions based on collaboration between mathematics and materials science. To bring about a completely new academic field and a brand new science, AIMR will continue to steadily produce research achievements. It will also nurture scientists who will create the future.

Osamu Shimizu (AIMR)

Kavli Institute for the Physics and Mathematics of the Universe



Challenging the mysteries of the Universe through leading collaborations in mathematics, physics, and astronomy

Under the World Premier International Research Center Initiative (WPI), the Institute for the Physics and Mathematics of the Universe was established in 2007. Five years on, the institute received an endowment from The Kavli Foundation, and was renamed the Kavli Institute for the Physics and Mathematics of the Universe (Kavli IPMU), The University of Tokyo Institutes for Advanced Study. As of April 2015, the institute includes 85 full time researchers, half of whom are from overseas. In total, about 250 mathematicians, physicists, astronomers, including those with other affiliations, and graduate students are collaboratively engaged in uncovering the mysteries of the Universe.

■ Research Center's Information (FY 2015)

Center Director: Hitoshi Murayama
Principal Investigators (PI): 19 (including 5 overseas researchers and one female researcher)
Other Researchers: 240 (including 86 overseas researchers and 10 female researchers)
Research Support Staff: 31
Administrative Division:
  Administrative Director: Tomiyoshi Haruyama
  Administrative Staff: 10 (percentage of bilingual staff: 30%)
Satellites and Cooperative Organizations: University of California, Berkeley, USA; Steklov Institute of Mathematics, Russia; TRIUMF, Canada; Princeton University, USA; Laboratoire d'Astrophysique de Marseille, France; ASIAA, Chinese Taipei; and others
URL: http://www.ipmu.jp/en

Major Research Achievements

1. **Subaru unravels the mystery of star explosion observed by Tycho Brahe in 16th Century**
By studying the surrounding dust of a supernova remnant, researchers captured the light echoes of star explosion seen by Tycho Brahe, thereby established that it was a Type Ia supernova.

2. **Galaxy cluster observation hints at cold dark matter evidence**
Observations by Subaru Telescope's Suprime-Cam led to a discovery of new evidence that dark matter distribution around galaxy clusters agree with the prediction of the cold dark matter model.

3. **Curve counting theories and derived categories**
Using abstract counting theories of objects (derived categories), certain rules that govern curve counting in six dimensions were proved.

4. **Discovery of new discrete parameters of gauge theories**
Gauge theories were shown to have new discrete parameters hitherto unnoticed, with which the phases and the dualities can be studied in more detail.

5. **Nature's magnifying glass playing tricks on a supernova — discovery of a galaxy serving as a gravitational lens —**
A supernova appearing 30 times brighter than normal is found to have been magnified by a foreground galaxy acting as a gravitational lens.

6. **T2K Experiment shows muon neutrinos transforming into electron neutrinos**
Evidence of muon neutrino to electron neutrino transformation is captured for the first time by shooting muon neutrino to a detector 295 km away.

7. **New theory suggests that dark matter behaves like Yukawa particle**
New theory of SIMP (Strongly Interacting Massive Particle) as candidate of dark matter was proposed. SIMP has properties very similar to the pi meson, often called Yukawa particle.

8. **Secondary polytopes and the algebra of the infrared**
Mathematical theory of secondary polytopes proposed by Kapranov in 1990s can be used to explain the lower energy limit of physical theories.

Research Paper's Information

Number of Research Papers:	2440
Top 10% Papers:	27.0%
Top 1% Papers:	3.8%
Internationally Collaborative Research Papers:	66.5%

(Database: WoS 2007-2015)

Blackboard in Director Hitoshi Murayama's office at the Kavli IPMU

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Email : inquiry@ipmu.jp

Research Goals

What is the Universe made of? How did the Universe begin? What is the fate of the Universe? What are the rules governing the Universe? Why do humans exist in the Universe? These are the universal questions of mankind. Kavli IPMU is trying to uncover these mysteries of the Universe through the collaboration of mathematicians, physicists, and astronomers (Fig.1).

1 Subaru unravels the mystery of a star explosion observed by Tycho Brahe in the 16th Century

Ken'ichi Nomoto (PI)

An international team of astronomers, including Kavli IPMU, Max-Planck-Institute for Astronomy in Germany, and the National Astronomical Observatory of Japan, carried out spectroscopic analysis of light echoes observed by the Subaru Telescope around a supernova remnant. This analysis established that the light echoes are from the supernova originally seen in 1572 by Danish astronomer Tycho Brahe, and confirmed that it was a typical Type Ia supernova.

A "new star" observed by Tycho Brahe, teacher of Kepler, in detail in 1572 is considered as a supernova. The remains of the explosion are observable today and are referred to as Tycho's supernova remnant. However, the nature of the explosion has been a puzzle.

The international team observed a "dust cloud" about 3 degrees away from the direction of Tycho's supernova remnant using the Subaru Telescope. When the explosion occurred, the emitted light should have flown out in all directions. Some of the light would have traveled directly to Earth to be observed by Brahe 436 years ago. But astronomers have long hypothesized that some of the light may have reflected off nearby dust particles in dust clouds, delaying their observation on Earth. The "cloud" observed by the team precisely correspond to those "echoes" of light.

Nomoto's team also succeeded in analyzing the spectrum of the light echo, and confirmed that the supernova that Brahe had seen was a Type Ia supernova.

O. Krause et al.: Nature, 456, 617, 2008.

2 Galaxy cluster observation hints at cold dark matter evidence

Masahiro Takada (Professor)

An international team of researchers from Academia Sinica of Republic of China (Taiwan), the University of Birmingham, Kavli IPMU and Tohoku University used the Subaru Prime Focus Camera (Suprime-Cam) at the Subaru Telescope to collect observational data of 50 galaxy clusters, and successfully measured the mass density distribution of dark matter in the region of the galaxy clusters. By way of gravitational lensing effect,

Fig. 1. Group photo taken at the Kavli IPMU 9th Anniversary event (credit: Kavli IPMU).

the team determined the dark matter distribution, and found new evidence that it matched the prediction of the cold dark matter model (CDM).

CDM describes dark matter as particles that interact with each other and with other matter only via the force of gravity. Unlike other particles such as neutrinos, these particles have small thermal velocity, thus the name cold dark matter.

There are two quantities which characterize dark matter mass distribution. One is the total mass of dark matter contained in a galaxy cluster. The other is a concentration parameter, which describes how dark matter density changes from its dense center to its lower density edges. Even with galaxy clusters with the same amount of matter, those with the most matter at the center of its cluster will have a higher concentration parameter.

CDM is regarded as the most promising model of dark matter. Observations so far, however, have reported high concentrations of dark matter not compatible with CDM predictions.

According to the new results, the average mass distribution of dark matter has a conspicuous peak at the center, and is symmetrical. The observed mass distribution of the galaxy cluster is well aligned with the prediction of the cold dark matter model.

N. Okabe et al.: ApJL, 769 no.2, 35, 2013

3 Curve counting theories and derived categories

Yukinobu Toda (Associate Professor)

Superstring theory (Fig.2) is based on the idea that our Universe is made up of the familiar 4 dimensions of space and time, and extra dimensions, namely the minute 6-dimensional space. Researchers have wondered how many 2-dimensional curved surfaces exist on the 6-dimensional space. There may be an infinite number of curves, but if we specify the shape and volume, we can regard them as finite sets. It has been conjectured that a certain set of rules must exist that governs the numbers counting such curves. This is an interesting problem for both mathematicians and physicists.

Yukinobu Toda of Kavli IPMU successfully proved the regularity conjecture of the curve counting rule using an abstract notion of mathematics called derived categories.

A derived category can be thought of as a community of objects called sheaves. Derived categories were originally introduced from a technical motivation of pure mathematics, but they are now being studied for their insight into D-branes in superstring theory, and their effect on geometric properties.

Fig. 2. Superstring theory is a popular candidate which may connect the macro world described by Einstein's general theory of relativity, and the micro world described by quantum mechanics (illustration by Tomiyoshi Haruyama).

Using derived categories, it becomes possible to study some peculiar objects. Toda found it was possible to count the number of such objects, and that certain rules govern them. He also linked this 6-dimensional object with a 2-dimensional curved surface, and proved the existence of curve counting regularities.

Thanks to this result, Toda was invited to speak at the International Congress of Mathematicians in South Korea in 2014; they only meet once every four years.

Y.Toda: JAMS, 23 no.4, 1119, 2010

4 Discovery of new discrete parameters of gauge theories

Yuji Tachikawa (Professor)

The four fundamental interactions of nature are i) the electromagnetic force, ii) the force that binds quarks to make protons and neutrons, called the strong force, iii) the force responsible for radioactive decay, called the weak force, and iv) the force that keeps planets in orbit around the Sun, which is gravity. Gauge theories are used to describe the first three, and are specified by a few parameters, including the coupling constant specifying the strength and the theta angle related to its topology. The coupling constants and the theta angles have been known since the 1970s.

In 2013, Yuji Tachikawa at Kavli IPMU, Nathan Seiberg at the Institute for Advanced Study in Princeton, and Ofer Aharony at the Weizmann Institute of Science in Israel found and studied the effects of additional discrete parameters necessary to fully specify a gauge theory. Their research has incorporated the concept of topological phases, which is actively studied in condensed matter physics, into elementary particle theories. An interesting aspect of these works is that they use mathematical techniques already developed in the 1970s but not utilized in theoretical physics until very recently.

O. Aharony et al.: JHEP. 1308, 115, 2013

5 Nature's magnifying glass playing tricks on a supernova – Discovery of a galaxy serving as a gravitational lens

Robert Quimby (Visiting Scientist)

The research team led by Robert Quimby of Kavli IPMU has uncovered how a galaxy acted as a gravitational lens to magnify the brightness of a Type Ia supernova by 30 times (Fig. 3).

Through observations, the team discovered a galaxy located between the supernova, named PS1-10afx, and the Earth. The gravity of this galaxy caused a "gravitational lens effect" which collected light from the supernova, just like a magnifying glass, and this made PS1-10afx appear to shine much brighter than normal supernovae.

When PS1-10afx was first discovered in 2010, its color and light curve matched that of a typical Type Ia supernova, but its brightness was greater than normal. Thus scientists debated two interpretations:I. It was a new type of supernova; II. A gravitational lens was magnifying a Type Ia supernova to make it look brighter. The second interpretation was first suggested by Quimby and his team in 2013. The eventual discovery of the intervening galaxy strengthened this interpretation. It is also the first case documented that shows strong gravitational lensing having such an effect on a Type Ia supernova.

This discovery originated from a tea time discussion between Quimby, an astronomer, and a mathematician and a physicist as described below.

R.M.Quimby et al.: Science, 344(6182), 396, 2014

6 T2K Experiment shows muon neutrinos transforming into electron neutrinos

Mark Hartz (Project Assistant Professor), Mark Vagins (Professor)

The international T2K (Tokai to Kamioka) collaboration has made a definitive observation of muon neutrino to electron neutrino transformation. Their observation was the world first in which they were able to capture a neutrino with a unique flavor that started with a different flavor at its production point.

The T2K experiment (Fig. 4) involves the production of a muon neutrino beam at J-PARC (Japan Proton Accelerator Research Complex), located in Tokai village on the east coast of Japan. The beam is aimed at and detected in the gigantic Super-Kamiokande underground detector (Fig. 5) in Kamioka, 295 km (185 miles) west of Tokai. An analysis of the data from the Super-Kamiokande detector collected between January 2010 and April 2013 showed that, of 532 neutrino candidate events synchronized with the expected arrival time of the J-PARC beam, 28 events produced electrons, indicating the interaction of an electron neutrino. This proves that a fraction of the muon neutrinos in the beam transformed (oscillated) to electron neutrinos over the 295 km distance from Tokai to Kamioka.

Kavli IPMU joined the T2K collaboration in May 2013, which today includes Professor Mark Vagins and Project Assistant Professor Mark Hartz. Hartz has especially played a significant role in analyzing the neutrino oscillation data in this discovery.

T2K Collaboration: PRL, 112, 061802, 2014

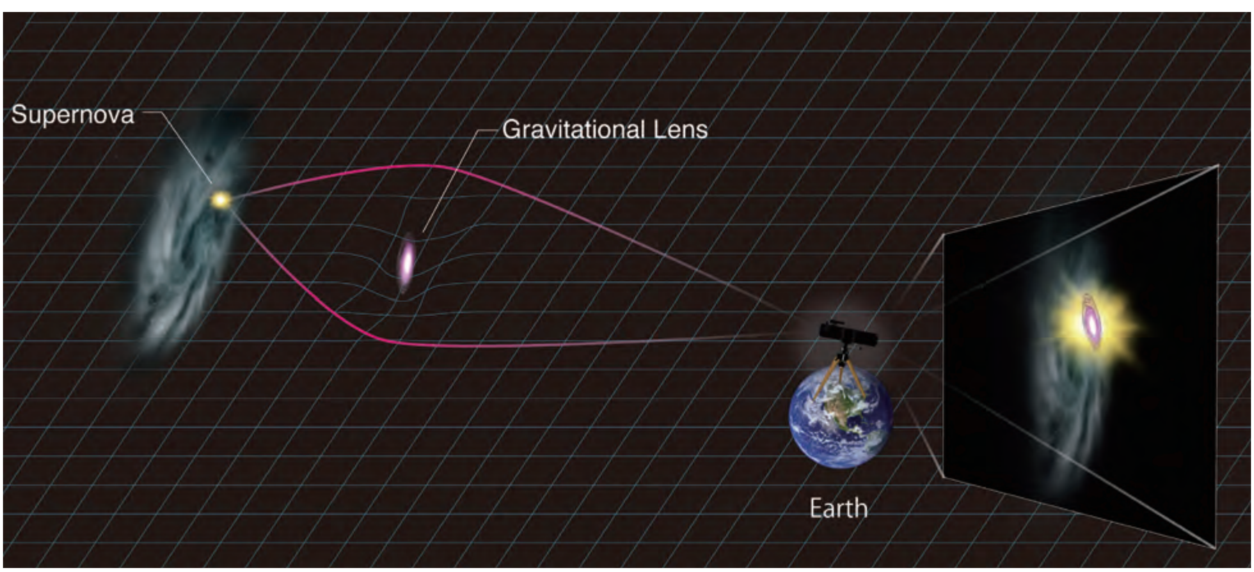


Fig. 3. The gravity of a galaxy situated between a supernova and Earth creates a magnifying glass that makes the supernova appear brighter.

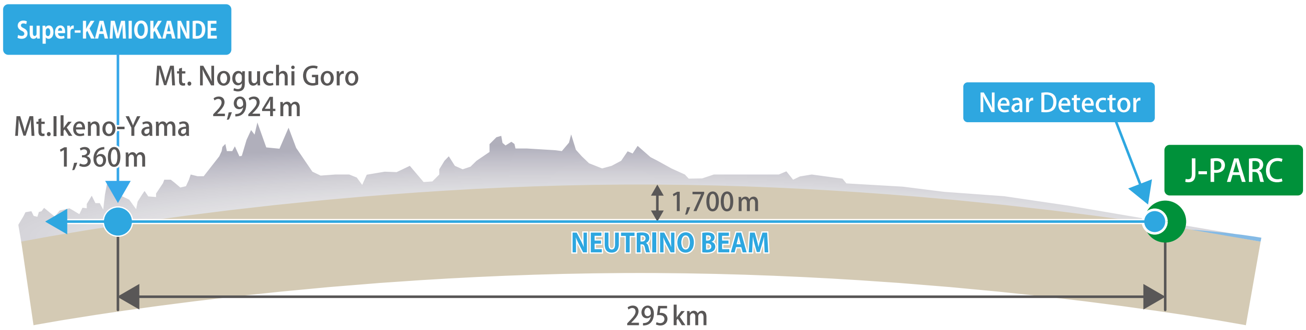


Fig. 4. T2K Experimental set up (diagram courtesy of the T2K Collaboration / KEK)

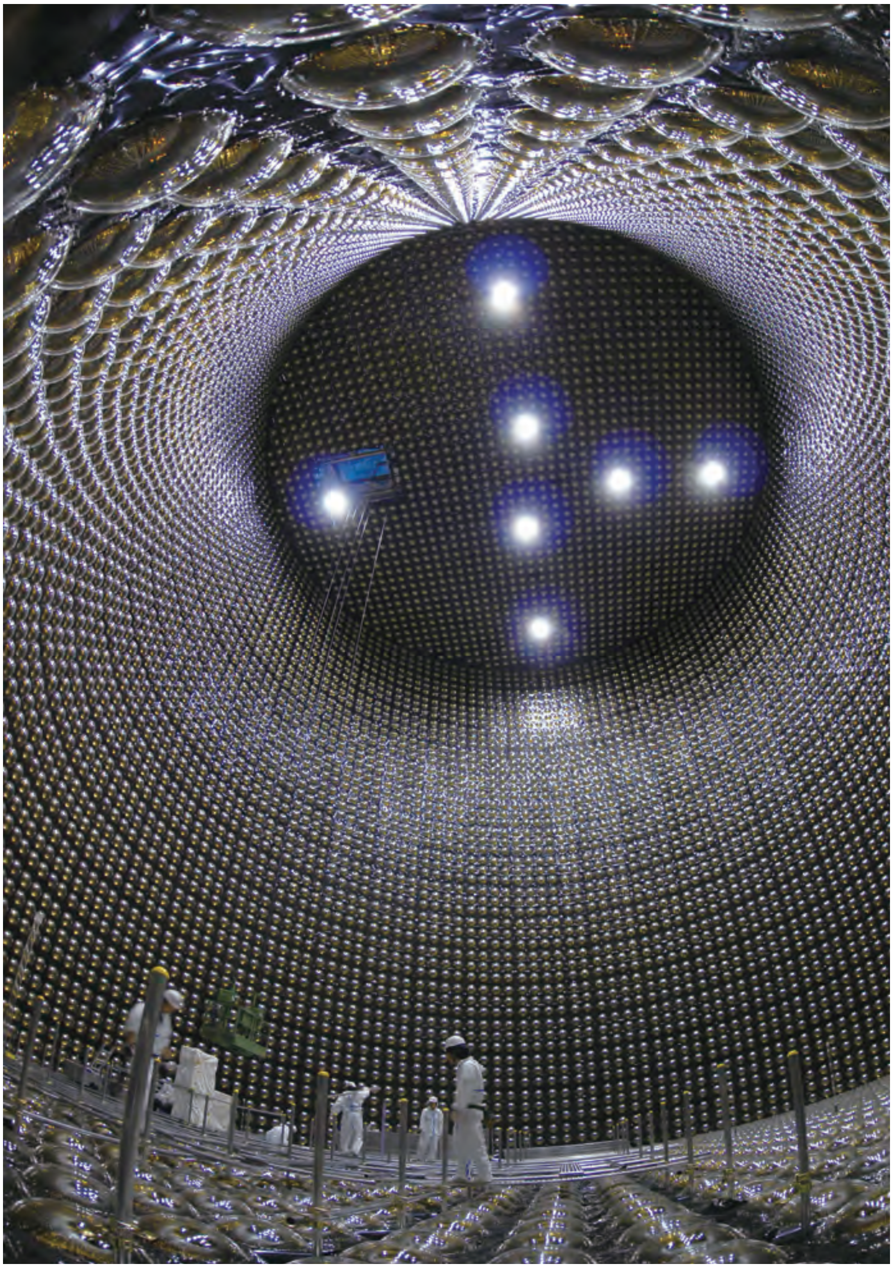
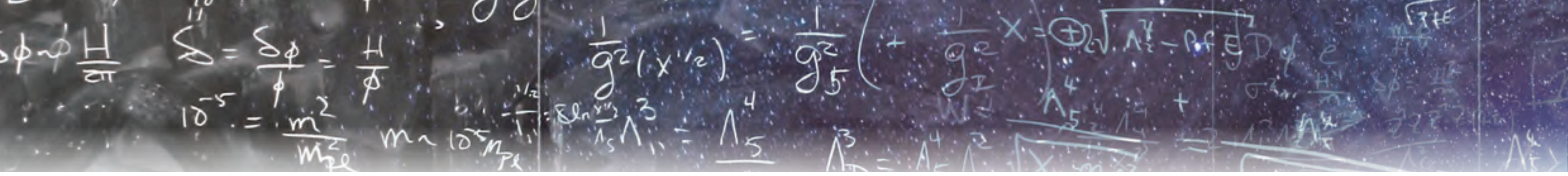


Fig. 5. Inside the Super-Kamiokande detector (Aug 2005 – July 2006). (Photo courtesy of Kamioka Observatory, Institute for Cosmic Ray Research, the University of Tokyo)



7 New theory suggests that dark matter behaves like Yukawa particle

Hitoshi Murayama (PI)

A new theory developed by a team including Director Hitoshi Murayama, Yonit Hochberg of the University of California, Berkeley, and others says that dark matter, which is supposed to occupy 80% of matter in the Universe, acts remarkably similar to the Yukawa particle, a subatomic particle named pi meson and first proposed by Japan's first Nobel Laureate Hideki Yukawa in 1935.

Dark matter is the agent keeping galaxies, our solar system together. Yet no one has been able to observe it, and it has often been regarded as a totally new exotic form of matter with significantly different properties than particles scientists know about today, such as super-symmetric particles or a particle moving in extra dimensions of space beyond the four predicted by superstring theory.

However, Murayama and his team proposed that dark matter particles are SIMPs (Strongly Interacting Massive Particles), which are similar to pions (Fig. 6).

The properties of pion is precisely described by the concept of "spontaneously broken symmetry" which was proposed by 2008 Nobel Laureate Yoichiro Nambu in 1961. The new theory points out that the properties of Yukawa particles based on Nambu's theory fit with those of dark matter. This theory also has deep connection with topology in mathematics.

Y. Hochberg et al.: PRL, 115, 021301, 2015

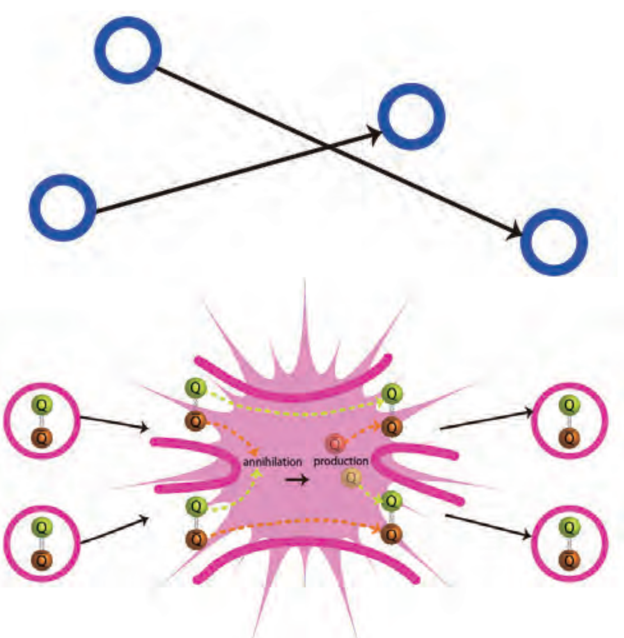


Fig. 6. The difference between dark matter as proposed by conventional theories (upper diagram) that assume dark matter particles pass through one another without affecting the other, and as SIMP (lower diagram) that assume dark matter particles act like pions and do interact with one another upon collision.

8 Secondary polytopes and the algebra of the infrared

Mikhail Kapranov (Professor)

Just as a circle is described by the equation $x^2 + y^2 = 1$, the study of figures given by polynomial equations is called algebraic geometry. On the other hand, geometry which deals with simpler shapes such as polygons, polyhedra and their triangulation is called combinatorial geometry.

By way of a method called tropical geometry, it is possible to obtain combinatorial geometric information from an algebraic geometry problem. Such relations were found by Kapranov et. al. in the study of secondary polytopes of higher dimensional hyper-geometric differential equations.

In 2014, Kapranov et.al. found further that such secondary polytopes can be applied to the study of the infrared limit in quantum field theory, e.g., the description of a Lie algebra structure.

M. Kapranov et al.: arXiv: 1408.2673, 2016

Interdisciplinary research and internationalization

Kavli IPMU has a tea time. Every day at 3pm, researchers from different fields and projects take time to relax, and exchange ideas and stories during the tea time (Fig. 7). This, the institute believes, leads to better opportunities for making new discoveries.

A prime example is a tea time discussion between an astronomer, a physicist and a mathematician. Robert Quimby and his fellow researchers followed up by publishing a paper that provided a clear explanation to a recent mystery surrounding a supernova that had appeared 30 times brighter than normal.

In addition to tea time, Kavli IPMU offers a very international environment. As of March 2016, the institute has more than 150 full time researchers, staff and graduate students, as well as more than 100 affiliated researchers. Many of these faculty and postdocs come from overseas. The institute also hosts tens of international scientific meetings every year, attracting 800 visitors for seminars and research discussions annually, half of whom are visiting from overseas.

Kavli IPMU is operated according to international standards; postdoc recruitment is done at the same time as those institutions in the US and Europe; annual salaries are paid by year at the same level. These two factors make Kavli IPMU a competitive choice internationally.

Fig. 7. Tea time inside Kavli IPMU

Hitoshi Murayama speaks at UN Headquarters for Science for Peace and Development Today and Tomorrow

Director Hitoshi Murayama delivered a speech at the "Science for Peace and Development" held at the United Nations Economic Social Council in New York on 20 October 2014. The talk was part of a special event commemorating CERN's 60th anniversary: "CERN: Sixty Years of Science for Peace and Development – The role of science and scientific intergovernmental organizations in bringing people and cultures together," hosted by the United Nations Economic and Social Council, and jointly sponsored by the Permanent Representatives of France and Switzerland (Fig. 8).

Talking after Nobel Laureate Carlo Rubbia and the former Secretary General of United Nations Kofi Annan, Murayama emphasized the need to create places where people can share a common goal in pursuing science. He said this idea was the basis of Kavli IPMU, effectively making the institute known to a worldwide audience.

To read the full speech (English) go to:
http://www.ipmu.jp/en/node/2050

Marina Komori (Kavli IPMU),
Motoko Kakubayashi (Kavli IPMU)

Fig. 8. Director Hitoshi Murayama giving a speech at the UN (photo courtesy of UN Photo / Evan Schneider)

A Research Institute to Expand Knowledge by Integrating Cell and Material Science

The mission of iCeMS is to create new chemicals for the elucidation and control of cellular functions. We are also committed to developing sophisticated cell-inspired materials, which can contribute solutions to problems such as disease diagnosis/treatment and environmental pollutant cleanup. iCeMS' research horizons extend far beyond the borders of any single existing field. We therefore conduct our research by crossing different perspectives from multiple fields of study (interdisciplinary research) such as biology, chemistry, physics, engineering and mathematics. Researchers at iCeMS share ideas and inspire each other as they work together to pursue their research objectives.

Research Center's Information (FY 2015)

Center Director: Susumu Kitagawa (up to 2012:Norio Nakatsuji)
Principal Investigators (PI): 25 (including 6 overseas researchers and 3 female researchers)
Other Researchers: 149 (including 44 overseas researchers and 34 female researchers)
Research Support Staff: 124
Administrative Division:
- **Administrative Director:** Shinji Tomita
- **Administrative Staff:** 27 (percentage of bilingual staff: 50%)

Satellites and Cooperative Organizations: Gifu University, Japan; National Centre for Biological Sciences (NCBS), India; Institute for Stem Cell Biology and Regenerative Medicine (inStem), India; UCLA California NanoSystems Institute (CNSI), USA; Heidelberg University, Germany; Vidyasirimedhi Institute of Science and Technology (VISTEC), Thailand; and others
URL: http://www.icems.kyoto-u.ac.jp/en/

iCeMS
KYOTO UNIVERSITY
WPI Research Center

Major Research Achievements

1 Successful regulation of the fate of neural stem cells by light technology

The oscillatory expression of the transcription factor Mash1 leads to maintenance and proliferation of neural stem cells, while steady Mash1 expression induces neuronal differentiation. We control such Mash1 expression dynamics by light technology to enable regulation of the proliferation and differentiation of neural stem cells.

2 Epigenetics drive cancer development

Cancer cells harbor changes in epigenetic modifications. However, the contributions of altered epigenetic modifications to cancer development remains to be fully understood. Taking advantage of properties of iPS cell technology, we demonstrate that epigenetic regulation can drive particular types of cancer.

3 Cell-inspired porous materials

The simultaneous implementation of "selection" and "storage" of matter is a basic aspect of compartmentalization within cells. We create artificial materials called porous coordination polymers (PCPs) that efficiently and inherently store and select small molecules. However, we seek to mimic cellular systems that do this in massively sequential ways and have developed several strategies to control sequential storage and selection in such cell-inspired compartments.

4 Mechanisms of ABC proteins involved in optimal health maintenance

ABC proteins maintain optimal health in several ways, including eliminating various toxic compounds from cells and generating HDL-cholesterol. We reveal the functional mechanisms of ABC proteins by determining 3D-structures and visualizing them at the single molecule level.

5 Generation of functional oocytes from mouse pluripotent stem cells

We succeeded in inducing mouse embryonic stem cells (ESCs)/induced pluripotent stem cells (iPSCs) into primordial germ cell-like cells (PGCLCs). When aggregated with embryonic ovarian somatic cells and transplanted in mice, the PGCLCs differentiated into oocytes that contributed to fertile offspring.

6 Chemical tools for programming stem cells

Realization of regeneration therapy requires new technologies that coax stem cells to differentiate or behave as we desire. We have developed several such cell-controlling technologies by combining chemistry and cell biology.

Research Paper's Information

Number of Research Papers:	1,477
Top 10% Papers:	25.4%
Top 1% Papers:	4.3%
Internationally Collaborative Research Papers:	22.2%

(Database: WoS between 2007-2015)

The background images are human iPS cells and porous coordination polymers (PCPs) with a jungle gym-like molecular structure.

Yoshida Ushinomiya-cho, Sakyoku, Kyoto Japan 606-8501, Japan
Phone: +81-75-753-9753
Email: info@icems.kyoto-u.ac.jp

Research Background

Biological phenomena are explainable as an integration of chemical reactions. If we can precisely explain these phenomena by the principles of chemistry, it should be possible to imitate and reproduce cellular functions using chemical substances.

The idea to explain cellular functions by chemistry per se is not necessary a new concept. In the classic research discipline of biochemistry, cellular functions are illuminated at the molecular level starting with proteins; whereas, in molecular biology, cellular functions are approached by studying DNA.

In contrast, cell biology developed to understand the entire living organism starting with cells. This field has bloomed into embryonic stem (ES) cell and induced pluripotent stem (iPS) cell research. The attempt to unveil the secrets of cellular functions by beginning from proteins and DNA, and the effort to explain living organisms starting from cells, have both contributed to the development of pharmaceutical and biotechnology industries.

Taking the next step in the history of cellular function study, iCeMS now focuses on the "mesoscopic" point of view. This is neither "macroscopic", like observing cells in the field of cell biology, nor "microscopic", like investigating proteins and DNA in the fields of biochemistry and molecular biology, but somewhere in the middle of these two. This region, which ranges from a few tens to a few hundreds of nano meters (1 nano meter is one billionth of a meter) is the border that separates life and material. We believe that by studying this boundary region, we can understand the vital activity of cells as the chemical reactions of materials and ultimately mimic the functions of living organisms using materials. In this way, we can contribute to treating diseases and promoting a healthy society.

Research Purpose

The purpose of iCeMS is to expand current knowledge by approaching this unexamined border between life and materials. To be more precise, we try to design and utilize novel materials to better understand and control cellular functions. Our future goal is to develop unique, cell-inspired materials to apply to problems, such as the diagnosis and treatment of diseases or the purification of environmental pollutants.

To approach this challenge, iCeMS researchers of various specialties, such as biology, chemistry, physics, mathematics, and engineering, collaborate to integrate their knowledge. Cells produce various chemical substances and utilize them to maintain vital activity. The behaviors of these materials change dynamically both temporally and spatially inside cells. Therefore, development of various visualization techniques and modeling approaches, along with analysis systems to understand complicated cellular activities using physical and chemical approaches, are required to create novel materials to regulate cellular functions. The representative research areas in our institute can be divided into 3 areas: A: Nucleus information, B: Membrane compartments, and C: Cell communication. (Fig1,2)

Achievements

A: Nucleus information

The nucleus of a cell regulates the storage and utilization of cellular information. Our challenge at iCeMS is to unveil the mechanisms of the dynamic remodeling of the nucleus structure, which is accompanied by proliferation, initialization, reorganization, and the readout of genetic information. To do this, we aim to develop techniques to visualize

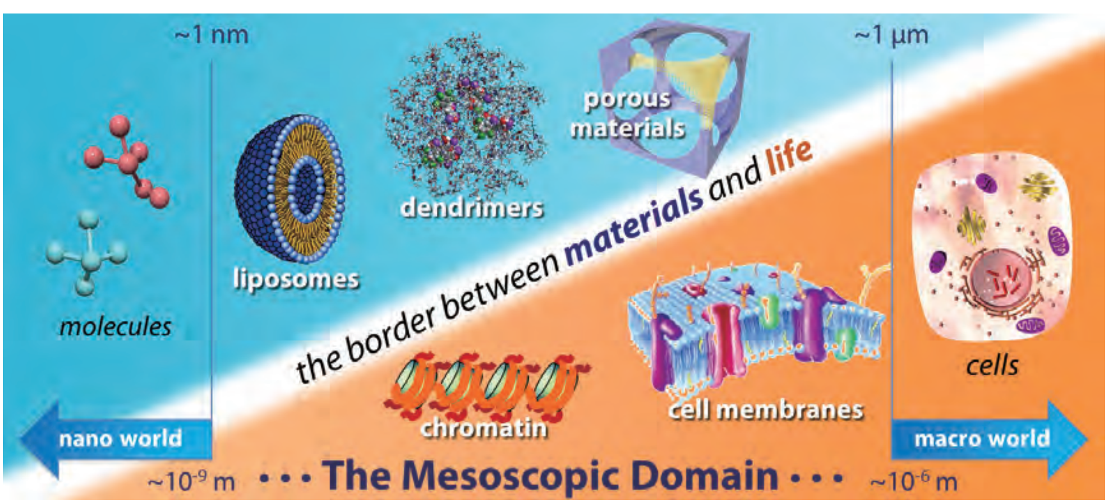


Fig. 1 Mesoscale region: The border between materials and life (from 10^{-9} m ~10^{-6} m)

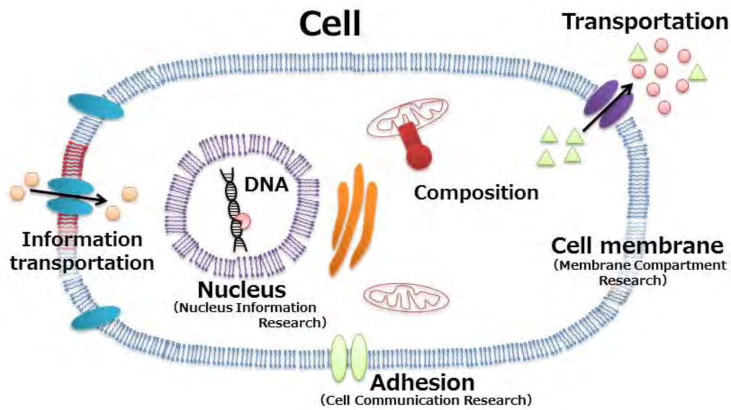


Fig. 2. A model of cells and cell functions as they related to the research areas of iCeMS

and control information transformation inside the nucleus using light-responsive materials and functional molecules.

1 Successful regulation of the fate of neural stem cells by light technology

Ryoichiro Kageyama (PI)

Neural stem cells have the ability to give rise to various types of neurons while proliferating. However, the technology to control this capability has not been established. Time-lapse imaging of gene expression at the single-cell resolution revealed that the expression of the transcription factor Mash1 is oscillatory in neural stem cells but steady in differentiating neurons. Furthermore, control of Mash1 expression dynamics by light technology showed that this oscillatory expression leads to the proliferation of neural stem cells, while steady expression induces neuronal differentiation. This light technology now enables us to control the fate of neural stem cells at will. This opens the way to regulate endogenous neural stem cells, a feat which has been difficult until now. Even in the adult brain there are neural stem cells, although they are mostly dormant. If we can induce such endogenous neural stem cells to proliferate and differentiate into neurons using our light technology, we can apply this method to developing therapies for various neural disorders.(Fig.3)

Kageyama, R et al., Science 342, 1203 (2013)

2 Epigenetics drive cancer development

Yasuhiro Yamada (Professor)

Cancer is believed to arise primarily through the accumulation of genetic mutations. Research shows that cancer cells also harbor changes in epigenetic modifications. However, the contribution of altered epigenetic modifications to cancer development remains to be fully understood.

Induced pluripotent stem cell (iPSC) technology can actively modify epigenetic regulation without affecting the genomic information. We developed a murine system in which iPS cells can be established through the forced expression of reprogramming factors in vivo. We demonstrated that transient expression of reprogramming factors in vivo results in the development of kidney cancers that exhibit global changes in epigenetic modifications. We next established iPS cells from kidney cancer cells. Notably, kidney cancer-derived iPS cells gave rise to non-

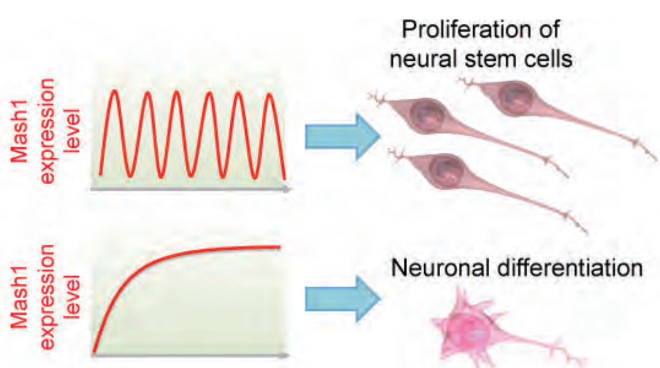


Fig.3. By using the light-responsive protein GAVPO, we can switch on and off the Mash1 expression with blue light and dark conditions. With this method, we can induce oscillatory and steady expression of Mash1, which activates proliferation of neural stem cells and neuronal differentiation, respectively.

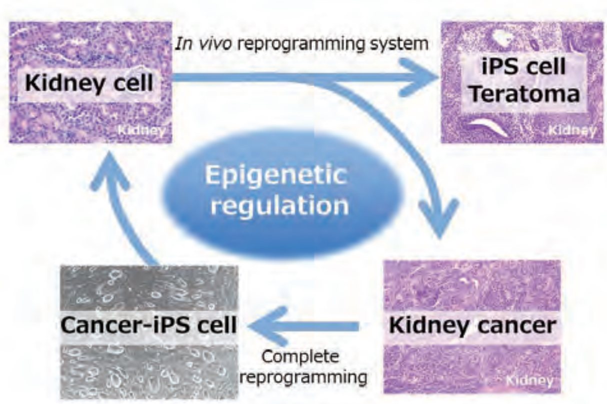


Fig.4. Epigenetic regulation controls the fate of cancer cells

neoplastic kidney cells in mice, proving that they did not undergo irreversible genetic transformation. These findings suggest that epigenetic regulation associated with iPSC derivation may drive the development of particular types of cancer and could be a potential target for cancer treatment. (Fig.4.)

Yamada, Y et al. , Cell 156, 663 (2014)

B: Membrane compartment

Cellular membranes coordinate the selection and concentration of materials and information inside and outside of cells. In other words, membranes regulate signal conversion, energy conversion and material exchange flowing from the inside to the outside of cells and vice versa. At iCeMS, we aim to clarify the principles of these membrane-region reactions and are developing environmentally-sensitive molecules and molecular assemblies to regulate the above-mentioned conversion reactions by light, heat, or magnetic stimuli.

3 Cell-inspired porous materials

Susumu Kitagawa (PI),
Shuhei Furukawa (Associate Professor)

The simultaneous implementation of "selection" and "storage" of molecules and ions is a basic aspect of compartmentalization within cells, which regulates the balance of substances inside cells. We create artificial materials called porous coordination polymers (PCPs), which possess a structure of billions of nanosized pores that efficiently and inherently store and select small molecules. Our group's key achievement is to realize the synthesis of transformable pores in a fashion similar to proteins. Our new PCPs transform their structure when incorporating target molecules, giving rise to high molecular selectivity. One of the important industrial applications of this type of transformable pore structure is to selectively trap carbon monoxide molecules.

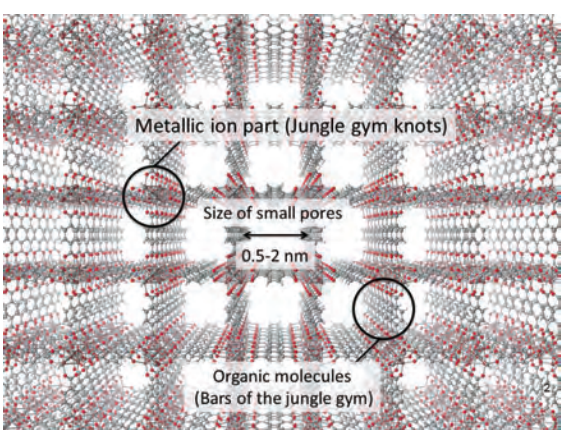


Fig.5: Crystal structure of one example of a porous coordination polymer (PCP). It possesses a jungle gym-like molecular structure and inherent voids as nanosized pores.

Generally, these PCP materials are fabricated as micrometer-sized crystalline powders; however, with new mesoscale chemistry, we can shape materials into a variety of morphologies. For instance, shaping PCPs into a hollow box structure, like a cell membrane, allows for controlling internal molecular balance to improve the selection efficiency for target organic molecules. (Fig.5)

Furukawa, S et al. , Science 339, 193 (2013)

4 Mechanisms of ABC proteins involved in optimal health maintenance

Kazumitsu Ueda (PI)

Membranes define the boundaries of all cells of the body and separate the intra- from the extra-environment. ABC proteins function on cellular membranes as transporters, which eliminate various toxic or nonessential compounds from cells and maintain optimal health. Collaboration among iCeMS research groups have revealed several functional mechanisms of human ABC proteins that contribute to improving health.

The mechanism of the multidrug exporter MDR1, an ABC protein that eliminates various structurally unrelated toxic compounds from cells, has been unclear for a long time. By determining the 3D-structure of MDR1 at the highest resolution we have revealed its mechanism.

Cholesterol is an indispensable component of our bodies, whose concentration is elaborately regulated. Furthermore, 'good' cholesterol (HDL) is invaluable in preventing heart disease. We have also established the mechanism of ABCA1, a key protein for HDL generation, by observing its movement on membranes at the single molecule level.

In humans 48 ABC proteins play important physiological roles. Functional defects are related to

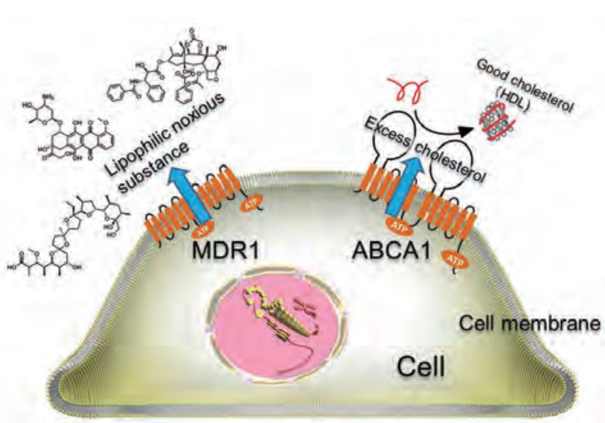


Fig.6 ABC proteins help maintain optimal health by eliminating toxic compounds from cells and generating HDL-cholesterol.

various diseases, such as atherosclerosis, diabetes, gout and Alzheimer's disease. Improving the understanding of ABC protein structures and mechanisms through this work at iCeMS will help the prevention and cure of these diseases.(Fig.6)

Ueda, K et al., Proc. Natl. Acad. Sci. U. S. A. 111, 4049 (2014)

C: Cell communication

The proliferation from stem cells to specific tissues in multi-cellular organism is a process that is strictly controlled by cell-cell and/or cell-material interactions. At iCeMS, we strive to decipher these mechanisms to design and create scaffolding materials at the molecular level. This allows us to regenerate the structure and functions of organs such as the brain, cardiac muscle, and the reproductive system.

5 Generation of functional oocytes from mouse pluripotent stem cells

Mitinori Saitou (PI)

The germ cell lineage differentiates into spermatozoa and oocytes and contributes to new individuals, thereby transmitting genetic information to new generations. Understanding the mechanism of germ cell development contributes to the development of reproductive medicine/technology, stem cell biology, and regenerative medicine.

iCeMS has been investigating germ cell development using the mouse as a model organism. Based on this achievement, iCeMS succeeded in inducing mouse embryonic stem cells (ESCs) and induced pluripotent stem cells (iPSCs) into primordial germ cell-like cells (PGCLCs). When transplanted into neonatal testes lacking endogenous germ cells, PGCLCs contributed to spermatogenesis and fertile offspring. Similarly, when PGCLCs were aggregated with embryonic ovarian somatic cells and transplanted in mice, the PGCLCs differentiated into oocytes that, upon fertilization and transfer to foster mothers, led to fertile offspring. These findings are the first to demonstrate the feasibility of generating germ cells in culture dishes. (Fig.7)

Saitou, M et al., Science 338, 971 (2012)

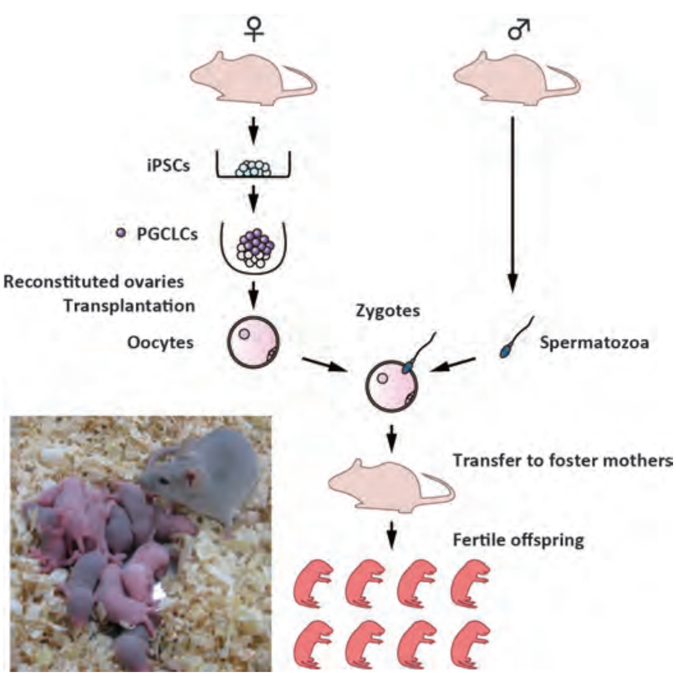


Fig.7. Offspring from oocytes generated from pluripotent stem cells.

6 Chemical tools for programming stem cells

Motonari Uesugi (PI)

Realization of regeneration therapy requires new technologies that coax stem cells to behave as we desire. iCeMS has developed many such cell-controlling technologies by combining chemistry and cell biology.

Regeneration therapy requires a large amount of iPS cells. iCeMS developed a material that permits mass production of iPS cells, and we initiated a collaboration with the industry sector to develop their automated culture. After production, the next step is to coax the resulting iPS cells to differentiate into clinically useful cells. From iCeMS's collection of 70,000 chemicals (chemical library), we discovered chemical compounds that coax iPS cells to become heart muscle cells and pancreatic βcells. These chemical tools have now been used by researchers all around the world.

One of the major problems encountered in regeneration therapy is the low survival of transplanted cells. iCeMS has developed a chemical compound that impairs detachment-induced cell death, known as anoikis, to improve cell engraftment. This promising chemical has now been licensed to industry. Another hurdle in stem cell therapy is the tumorigenic risk of residual, undifferentiated stem cells. The collaboration of chemists and biologists at iCeMS has enabled the development of several chemicals that eliminate residual iPS cells.

These fruits from multidisciplinary research activities in iCeMS result in chemical tools that serve both regeneration therapy and basic research.

Uesugi, M et al., Cell Reports 2, 1448-1460 (2012)

Unique Achievements by iCeMS as a WPI Center

(1) Interdisciplinary Research Environment

Problems of modern society, such as global warming, environmental pollution, disease and aging, are often too complex to be adequately tackled by a single academic discipline. An interdisciplinary approach, crossing different perspectives from multiple fields of study, is essential to generate breakthrough solutions (Fig. 8 & 9).

Since its inception, iCeMS has tailored its organization and facilities towards the goal of cell-material science integration. In conventional faculties and departments of Kyoto University, researchers from different laboratories seldom see each other or have friendly discussions about their studies. That is why iCeMS adopted an interdisciplinary architecture in its facility design. Having open offices with no private rooms and open laboratories with shared experimental equipment means that every researcher is surrounded by people from other research areas. This research climate has acquainted members across all laboratories and specialized domains, nurturing an atmosphere in which researchers feel free to consult with those in other specialties about a problem they cannot solve or to ask for measurements or other specialized tasks they need for their research. Even casual greetings and subsequent chats can sometimes offer a fresh perspective or inspiration for future research.

In addition to the environmental arrangements described above, iCeMS promotes further interdisciplinary collaboration with its annual overnight retreat for all members. Participating researchers discuss possible solutions to their common challenges, submitting ideas based on their respective expertise. The retreat also invites suggestions for interdisciplinary projects for young researchers. These activities help researchers understand each other's work, appreciate their differences, and stimulate each other intellectually to find new inspiration.

As fruits of these approaches, iCeMS has presented 537 interdisciplinary papers compiled by multiple laboratories, out of a total of 1,477 papers published to present. It has also fabricated over 2,000 synthetic compounds for use in various sectors, contributing to the further advancement of interdisciplinary research.

(2) Realizing a True International Setting

True internationalization does not progress until there is a critical mass of foreigners seen on a daily basis. Pointing to similar critical mass adoption, tools such as the telephone and the Internet flourish only when their users represent over 15% of the population. iCeMS currently has 44 international members, which account for 30% of the total. In contrast, the average ratio at Kyoto University is 7–8%. Meetings and seminars at iCeMS are all conducted in English, and most documents are written in English and Japanese, side by side. Half of iCeMS' administrative staff members are bilingual, and each laboratory has a bilingual secretary. iCeMS' researchers (and students) naturally improve their communication skills through everyday interaction with overseas colleagues. These interactions yield even greater cooperation as researchers are able to have deeper discussions and understanding. Moreover, iCeMS has an Overseas Researchers Support Office to assist international members in having a comfortable life in Japan. All these efforts have allowed iCeMS to successfully remove language and cultural barriers and to achieve an environment in which all members can pursue their research regardless of nationality—in other words "true internationalization."

(3) An Environment to Focus on Research

Most graduate schools and research institutes have small "non-research" budgets, which often forces faculty members, especially younger ones, to do less relevant jobs along with their own research. iCeMS, in contrast, has successfully established an environment that allows researchers to focus on research by utilizing WPI funds as described below.

a) Shared Equipment Support Office: Full-time technicians undertake time-consuming maintenance of much of the laboratory equipment owned by iCeMS.

b) Research Support Staff: Well-experienced support staff are indispensable for a research institute to

Fig. 8 A researcher running an experiment

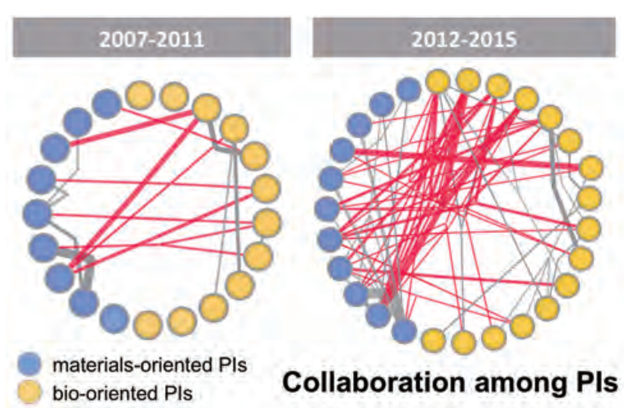


Fig. 9 Interdisciplinary collaboration among PIs

procure budgets of hundreds of million yen. iCeMS hires support staff who specialize in cell and material sciences as specially appointed Professors. Their paperwork assistance in budgetary requests contributes to the successful acquisition of large amounts of competitive research funds.

(4) Outreach Activities for Social Recognition

With the Social Communication Group (SCG) established upon its inception, iCeMS has constantly stressed that researchers should not only educate but also dialogue with the public to foster a view of "science in society." Towards this, the SCG has developed diverse programs to inform the public about the content and concepts of iCeMS's innovative research. Examples of these programs include the Science Café; "Hands on with Stem Cells!" classrooms for high school students/teachers (which received the Commendation for Science and Technology from the Minister of Education, Culture, Sports, Science and Technology in 2014); and "iCeMS Caravan" active learning classrooms on "the mechanism (karakuri) of study" for high school students (the iCeMS Caravan held at Nagasaki Prefectural Goto High School was broadcast by NHK). SCG also implements various projects to familiarize the public with science, including the "iCeMS Art Exhibition" (covered by the Kyoto Shimbun newspaper and other media), which exhibited fashion designs featuring synthetic compounds developed by iCeMS and cell micrographs. (Fig. 10)

Fig. 10 Juichi Yamagiwa, President of Kyoto University, delivering his lecture at the WPI joint symposium in December 2015

(5) Establishment as a "Globally Visible" Research Institute

iCeMS has an Overseas Affairs and Planning/Public Relations section for worldwide dissemination of its research accomplishments. This section engages in various public relations activities, including press release assistance, manuscript preparation, and utilization of EurekAlert! and other international news distribution services, to globally and effectively convey iCeMS research achievements. Furthermore, iCeMS is the first Japanese university to join the "edX" massive open online course run by a consortium of universities, including MIT, Harvard and over 20 world-leading universities. For this course, Prof. Motonari Uesugi, Deputy Director of iCeMS, gave a free lecture in English titled "The Chemistry of Life", which was delivered worldwide to about 26,000 registered students. Such global-scale dispatches of information about iCeMS' vision and interdisciplinary research achievements, establishes it as an attractive institute for researchers from around the world.

Future Outlook

The research theme of iCeMS has hitherto been, "can we chemically describe cellular processes and create materials to control them?" From now on, while continuing our present research, we will also work with the theme, "can we reproduce cellular structures with materials?"

Renowned Nobel physicist Richard P. Feynman once wrote, "What I cannot create, I do not understand." In other words, only in the process of creation can we achieve true understanding. Replication of cellular functions with designed materials should be possible once a full understanding of such cellular processes has been achieved. We therefore simultaneously advance analysis and synthesis, applying the resulting higher level of knowledge to further research towards the creation of new materials and technologies, including the following:

a) Materials for Cell Membrane Functions: Development of catalytic materials mimicking the complex yet efficient mechanisms of the cell membrane (e.g. material transformation, production)

b) Gas biology: Creation of "gaseous medicine" for storage and as-needed retrieval of gas molecules such as carbon monoxide and nitric oxide. Once considered toxic, these gases have proven to be efficacious in cells and act on various diseases when used in small amounts

c) Artificial photosynthesis: Study of efficient methods to realize plant photosynthesis, a light-mediated chemical reaction that converts atmospheric carbon dioxide into carbohydrates, through utilization of porous or other materials as regulators

d) Energy Storage in Cells: Creation of materials that mimic a living systems' ability to sort and store energy-bearing ions and molecules and of materials that unlock the energy storage potential of carbon dioxide, carbon monoxide, methane and other gases

Shinji Tomita (iCeMS)

Immunology Frontier Research Center

The pursue of fundamental immunology research and elucidation of immune diseases

Immunology is a field of research that studies the mechanism of the host defense system protecting our bodies from microbial infections. The immune system is essential for eliminating pathogens, and its disorder causes various illnesses such as autoimmune diseases and allergy. Osaka University has a long and distinguished history in immunology researches. IFReC has selected excellent researchers from Japan and overseas, and has actively incorporated imaging science and bioinformatics into immunology. IFReC aims to overcome immune-related diseases by clarifying the whole picture of the immune system.

Research Center's Information (FY 2015)

Center Director: Shizuo Akira
Principal Investigators (PI): 27 (including 5 overseas researchers and 1 female researcher)
Other Researchers: 100 (including 35 overseas researchers and 15 female researchers)
Research Support Staff: 66
Administrative Division:
- **Administrative Director:** Nobuo Sakaguchi
- **Administrative Staff:** 39 (percentage of bilingual staff:54%)

Satellites and Cooperative Organizations: Institute for Frontier Medical Sciences, Kyoto University, Japan; RIKEN Center for Integrative Medical Sciences, Japan; National Institute of Biomedical Innovation, Health and Nutrition, Japan; Seoul St. Mary's Hospital, Catholic Medical Center, Korea; Indian Institutes of Science Education and Research, India; Maurice Wilkins Centre, The University of Auckland, New Zealand; Pohang University of Science and Technology, Korea
URL: http://www.ifrec.osaka-u.ac.jp/en/

WPI Osaka University
iFReC

Major Research Achievements

1 **New models for immune regulations**
"Brake" and "Accelerator" for the regulation of inflammation.

2 **Regulatory T cell (Treg); an important immune regulator**
New concepts of immune regulation and therapies for various diseases.

3 **Fighting with parasites**
Infection by parasites is still an enormous problem of the world.

4 **Toward the novel vaccine developments**
Basic principle of vaccination revealed by latest researches.

5 **Guts are important organs for immunity**
The gut is a fertile field for immune reactions.

6 **Observation of Immune cells by MRI**
MRI performance at IFReC reached a stage where each immune cell is visualized.

7 **Dynamic observation of osteoporosis**
Newly developed fluorescent dye and 4D imaging enabled to depict the state of individual osteoclasts.

8 **Neural activity affects immune reactions**
"Illness starts in mind" is truth in some aspects.

Research Paper's Information

Number of Research Papers:	1,090
Top 10% Papers:	27.3%
Top 1% Papers:	5.3%
Internationally Collaborative Research Papers:	46.4%

(Database: WoS between 2007-2015)

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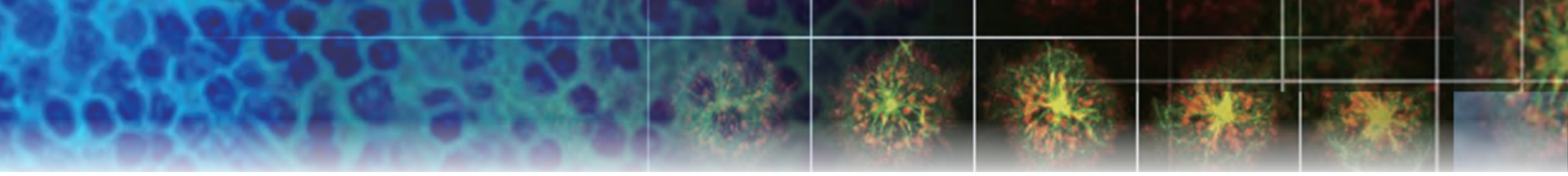
3-1 Yamadaoka, Suita, 565-0871 Osaka, Japan
Phone: +81-6-6879-4275(General Affairs),
+81-6-6879-4917(Accounting),
+81-6-6879-4777(Research Planning & Management)
Email: ifrec-office@ifrec.osaka-u.ac.jp

Background Picture: Microscopic images of mouse spleen where lymphocytes mature and "Immune synapse" formed on a T lymphocyte



Introduction

Immunology has made significant advances since the 19th century. Scientists such as Edward Jenner, the pioneer of the small pox vaccine and Louis Pasteur, who discovered treatments for rabies and other infectious diseases, appear frequently in textbooks. After these pioneer researches, immunology has achieved tremendous discoveries by continually introducing advanced scientific techniques. For example, developments in culturing methods led to the isolation of pathogens such as cholera, typhus and dysentery. Optical microscopy permitted the identification of pathogenic microbes and electron microscopy led to confirmation of the existence of viruses. Immunology attained its success by incorporating the techniques of microbiology, genetics, and computer science.

Research into infection and immunology at Osaka University began with Ogata Koan, the founder of Tekijuku and promotor of the smallpox vaccine in Japan. Later, in the 1960's, researchers inspired by Yuichi Yamamura, Professor of the Medical School, became the core of immunology studies at Osaka University. One of the peaks of that research was the discovery of interleukin-6 (IL-6) by Tadamitsu Kishimoto. Kishimoto's group clarified that IL-6 is implicated as an essential factor in inflammatory response of the immune system. In the 1990s, Shizuo Akira and others determined that innate immune cells such as dendritic cells detect pathogens by a receptor protein group called Toll-like receptors and elucidated the mechanism causing inflammation after infection. At this stage, most immunology researches were undertaken with T cells that had been isolated from the body. As such, it was not possible to draw conclusions on how immunity operated within the complex system of a living organism.

IFReC has advanced research with the aim of controlling immune response to pathogens and autoimmune diseases as well as cancer since its inception as a WPI center in 2007. We aim to determine the dynamism of individual immune cells and further elucidate live immune response of the whole body. This requires visualization (imaging) to track the infinite movements of cells during a living immune response. Technology to analyze the simultaneous and diverse responses is also vital. IFReC is advancing interdisciplinary research to probe these new realms by promoting and encouraging a team of excellent researchers combining immunology, bioimaging and bioinformatics.

Following is a sample of the remarkable results published by IFReC researchers over the past 10 years.

1 New models for immune regulations

Shizuo Akira (PI), Tadamitsu Kishimoto (PI)

The human body functions through the activities of various proteins. Cytokines (cell-to-cell mediators) are a group of proteins that have a vital role in immune response. They are produced inside cells based on genome information. In other words, mRNA is read (transcribed) as a messenger from the DNA in the nucleus, and then the cytokine proteins are produced in the cytoplasm (translated) and subsequently secreted from the cell.

If the mRNA of an inflammatory cytokine such as IL-6 is stabilized, the inflammationwas expected to continue; if it becomes unstable, then the inflammation was expected to recede. The discovery of this mechanism, at the level of mRNA, that finely controls inflammatory response was first in the world and was demonstrated by two independent approaches (Fig.1).

Regnase-1, discovered by Shizuo Akira, is an enzyme that diminishes the protein causing inflammation after transcription. If Regnase-1 activity is strong, it defeats the mRNA inflammation gene and suppresses the inflammatory response. In other words, it is an inhibiting factor for inflammation. Arid5a, discovered by Tadamitsu Kishimoto, binds to the mRNA of the proteins that cause inflammation and eventually regulate the inflammatory response. It is an accelerator of inflammation.

Matsushita et al. Nature 458, 1185 (2009).
Masuda et al. PNAS 110, 9409 (2013).

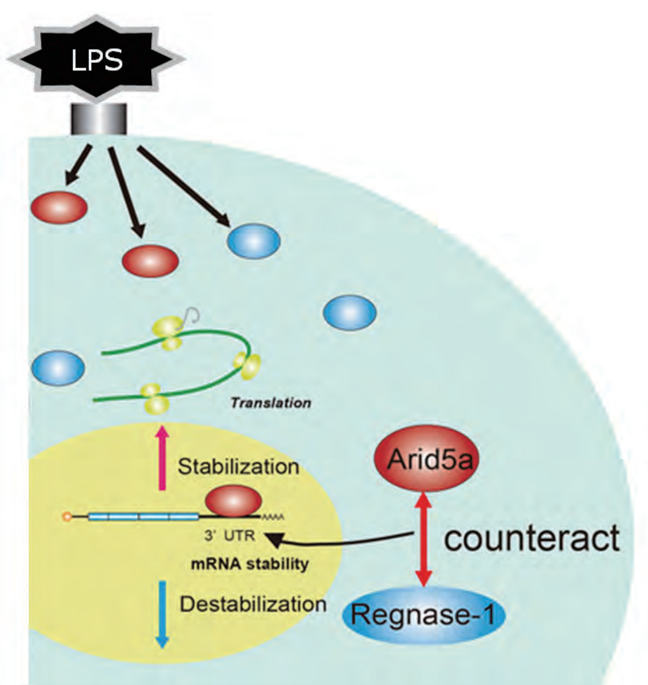


Fig. 1 Regnase-1 and Arid5a are "Blake" and "Accelerator" for inflammation respectively.

2 Regulatory T cell (Treg); an important immune regulator

Shimon Sakaguchi (PI)

Lymphocytes are the main player of acquired immunity that specifically recognize pathogens and remember the pathogenicity of them. T-lymphocytes (T cells) are known as the command center of immunity and are vital for control of immune response. T cells, during cell differentiation, express proteins called T cell receptors that have an infinite repertory of antigen specificity at the clonal level through genomic DNA recombination of the T cell receptor genes. This is the reason that the immune system can specifically identify enormous kinds of pathogens however, a substantial number of T cell clones express the receptor that responds to self. Most of the self-reactive T cells are removed in the thymus while some remain. A long-term puzzle in immunology is the question of "How are the T cells that attack the self inhibited?"

Sakaguchi discovered that some of the helper T cells, which are a type of lymphocyte, have that function: He called them regulatory T cells. The discovery caused a global sensation and raised interest in this field.

Sakaguchi's group found that the role of regulatory T cells in the human body is to suppress autoimmune response (autoimmune diseases). In a healthy person, damage to the self is prevented by making self-reactive killer T cells immunologically unresponsive (allergy). Namely, they elucidated the importance of regulatory T cells in immunological tolerance (Fig. 2).

Sakaguchi's group discovered that regulatory T cells derive from the same cells as normal helper T cells and various gene expression patterns are controlled by acquired factors (epigenetic information). Regulatory T cells occur not only in innate immune response but also under acquired immune response. If this condition is utilized to enhance the function of regulatory T cells, it would be possible to safely suppress autoimmune disease through immunoregulation. In contrast, weakening regulatory T cells could raise specific immune function toward cancer cells. Immune regulation, as explained, has become a realistic option for treatment of various diseases.

Maeda et al. Science 346, 1536 (2014).
Ohkura et al. Immunity 37, 785 (2012).

3 Fighting with parasites

Masahiro Yamamoto (PI), Cevayir Coban (PI)

In a hygienic, advanced nation such as Japan, infection by parasites is rare but if we look at the rest of the world it is an enormous problem. For example, there are over 200 million malaria patients a year and 2 million deaths (WHO 2013). Most parasites are multicellular organisms compared to viruses and bacteria with a minimum unit or a single cell. Parasites are large and cannot be eliminated by a simple reaction from a living organism. Once parasites enter the body they survive by using the energy and nutrition of the host. They also extend their existence as parasites by keeping the host alive. In Japan, infection is usually due to domestic pets we keep, overseas travel, swimming in a dirty river or eating uncooked food.

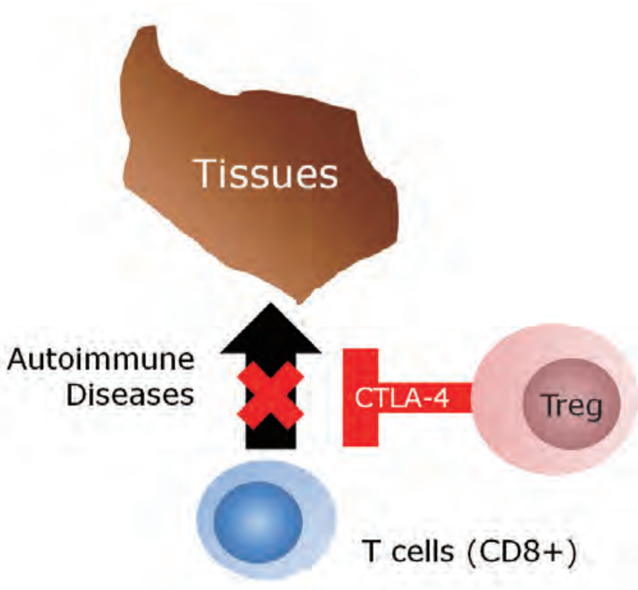


Fig. 2 Usual immune suppression by Tregs.

Amongst these, Toxoplasma can cause lethal encephalopathy and myocarditis in weakened patients. Infection from eating insufficiently heated meat and touching cat feces has been confirmed. The parasite is of concern for pregnant women as infection can cause miscarriage and hydrocephalus in newborns.

Yamamoto's group found that Toxoplasma directly activates the cells of the host (infected mouse) that assembles neutrophils (white blood cells) in inflammatory response at the site of Toxoplasma infection. Toxoplasma opportunistically uses the assembled neutrophils for its survival and to spread throughout the body. It uses the immune response of the organism like the capture of the Trojan horse and takes advantage to spread infection from the original site to the rest of the body (Fig. 3).

Ma et al. J Exp Med 211, 2013 (2014).
Zhao et al. Cell Host & Microbe 15, 551 (2014).

4 Toward the novel vaccine developments

Tomohiro Kurosaki (PI), Ken Ishii (PI)

The rule of infection that states; "once one has had an infection it is harder to get it again" is recorded as far back as Ancient Greece. Later research showed that many illnesses are caused by microbe infection and after a first infection the organism becomes resistance to further infection. Furthermore, it was found that the injection of an attenuated microbe can create the same resistance as a prior infection. This knowledge led to our current vaccines.

The nature of vaccines is to leave a memory of illness in the immune system to enable quick resistance upon a second infection. How this immune memory is created and how vaccines work best is still largely a mystery. Kurosaki's group used a mouse model to elucidate that the decreased expression of a protein called Bach2 in B cells is the primary factor for generating memory B cells, which are the main immune cells that govern immunological memory, in order to respond quickly upon re-infection and release antibodies. Bach2 temporarily suppresses the differentiation of B cells into antibody producing cells after contact with an antigen (bacteria, virus). Once Bach2 has decreased, memory B cells rapidly differentiate into antibody producing cells in large numbers after a second contact with the antigen. The over-suppression of Bach2 causes hyper-activation of memory B cells into antibody secreting cells, potentially resulting in allergy and autoimmune disease. Understanding the function of memory B cells is vital to developing effective vaccines against diseases such as influenza.

Ishii Ken's group is investigating additives or adjuvants that raise the effectiveness of vaccines. The most often used adjuvant to date is alum, an aluminum compound. Alum adjuvants, once taken up into the immune cell induce the cell's death. It has been found that the unwound double-helix structure DNA, then released from the host cell, revitalizes natural immunity and is indispensable for the vaccine effect. The released DNA activates a protein called interferon regulatory factor (IRF3), and subsequently causes the allergic reaction with IgE antibody as a side effect of adjuvants. However, the antibody reaction with IgG that is a main effect of the vaccine is unaffected. This research is expected to lead to the development of new adjuvants that suppress the excessive release of DNA and vaccines with fewer side-effects.

Kometani et al. Immunity 39,136 (2013).
Marichal et al. Nat Med 17, 996 (2011).

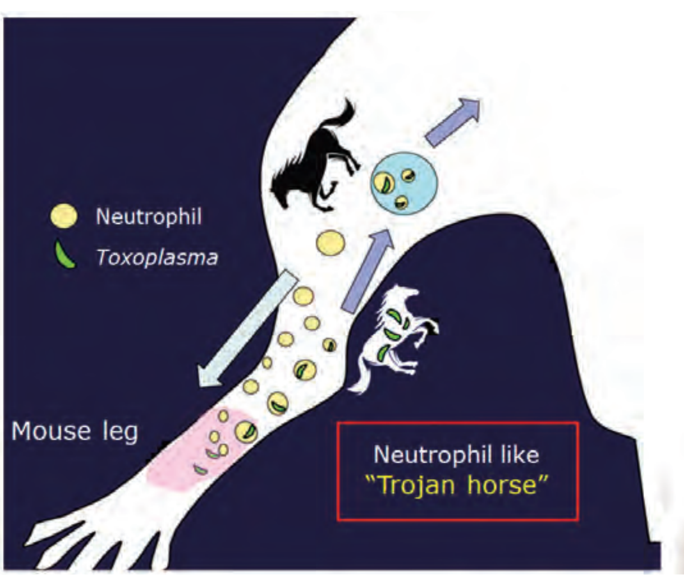


Fig. 3 "Trojan horse strategy" by Toxoplasma gondii.

5 Guts are important organs for immunity
Kiyoshi Takeda (PI)

A large quantity of microorganisms lives in our intestines in the form of intestinal bacteria. The number exceeds the total number of human cells constituting our whole body. This assembly of intestinal bacteria is also known as microflora. Meanwhile, the gut is also gaining attention as a fertile field for immune reactions as a variety of good and microorganisms pass through from the outside.

Takeda's group found that in a mouse lacking a protein called Lypd8, which is abundant in the epithelial cells of the intestine, many intestinal bacterial penetrate to the inner mucous layer resulting in more severe enteritis than a wild-type mouse. They revealed that Lypd 8 binds specifically to intestinal bacteria with flagella and prevents bacterial invasion by suppressing motility (Fig. 4).

In addition, the group found that lymphoid tissue present in the appendix, which was thought to be redundant in humans, is important for production of the antibody protein IgA known to play an important role in mucosal immunity as it is involved in the control of intestinal bacteria. Namely, it is now considered that the appendix is an important organ for the suppression of inflammatory bowel disease caused by an imbalance of intestinal bacteria. Thus, the claim that the cecum is redundant is refuted from an immunological standpoint.

Okumura et al. Nature 532, 117–121 (2016).
Masahata et al. Nat Commun 5, 3704 (2014).

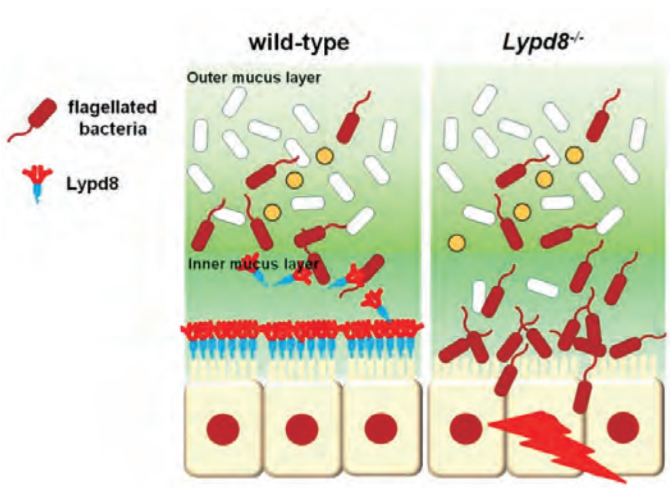


Fig. 4 Important function of Lypd8 in gut homeostasis.

6 Observation of immune cells by MRI
Yoshichika Yoshioka (PI)

Nuclear Magnetic Resonance Imaging (MRI) is an analytical method capable of photographing and stereoscopically displaying the inside of a human body. It is based on a completely different principle from X-ray CT. Improvements to electromagnetic coils and peripheral equipment has dramatically improved MRI performance. It has now reached a stage where each immune cell can be visualized.

Yoshioka's group has successfully continuously observed macrophages (phagocytes) in the mouse brain using the world's highest level MRI installed at IFReC (Fig. 5).

In mice injected with lipopolysaccharide (LPS), which causes inflammation, macrophages in the brain increase over time peaking after several days. However, after one week it returned to normal as if nothing had happened. It was surprising that so many immune cells were present in the brain without direct invasion of toxin into the brain. Thereafter, MRI imaging has been further enhanced with three-dimensionalization and time resolution capability, the world of immunity that could be observed previously is being revealed in living animals.

Mori et al. Sci Rep 4, 6997 (2014).

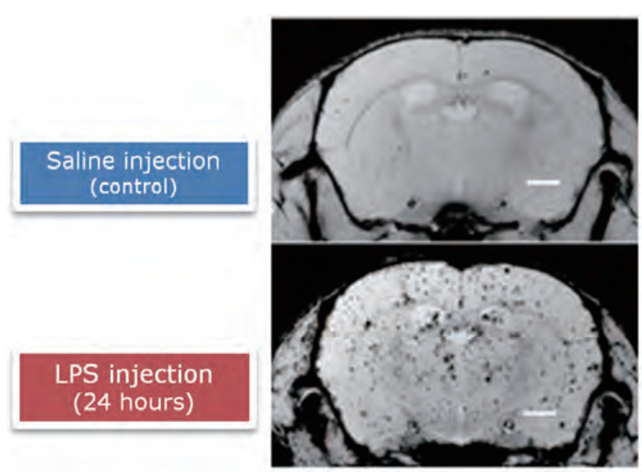


Fig. 5 Macrophages appearing in the brain in response to the toxin.

7 Dynamic observation of osteoporosis

Masaru Ishii (PI), Kazuya Kikuchi (PI)

The constituents of our body are replaced daily by metabolism on a daily basis. Bones are no exception, bones are formed by osteoblasts while osteoclasts destroy and consume bones. Osteoporosis occurs when osteoclasts, a type of immune cell, excessively destroy bones and this balance breaks down.

Masaru Ishii's group and Kikuchi's group are collaborating to investigate this function of osteoclasts by using their proprietary live imaging technology. Initially, multiphoton microscopic imaging was only able to show osteoclasts as "shiny particles". Eventually, however, individual shapes and movements became apparent. Furthermore, using the newly developed functional fluorescent molecule and 4D imaging (three-dimensional + time), they are able to depict the activity of individual osteoclasts, that is, "how actively they consume bone, do they take rests?" (Fig. 6).

These results are only achievable at IFReC with the combination of immunology, microscope system and multiple imaging technologies such as the development of fluorescent dye. Based on such data, control of the activity balance of osteoclasts could lead to new treatment strategies for bone-destroying diseases such as osteoporosis and cancer metastasis. If we can control the activity balance of osteoclasts based on such data, it will be a new strategy to treat bone destruction due to osteoporosis and cancer metastasis.

Maeda et al. Nat Chem Biol 12, 579 (2016).

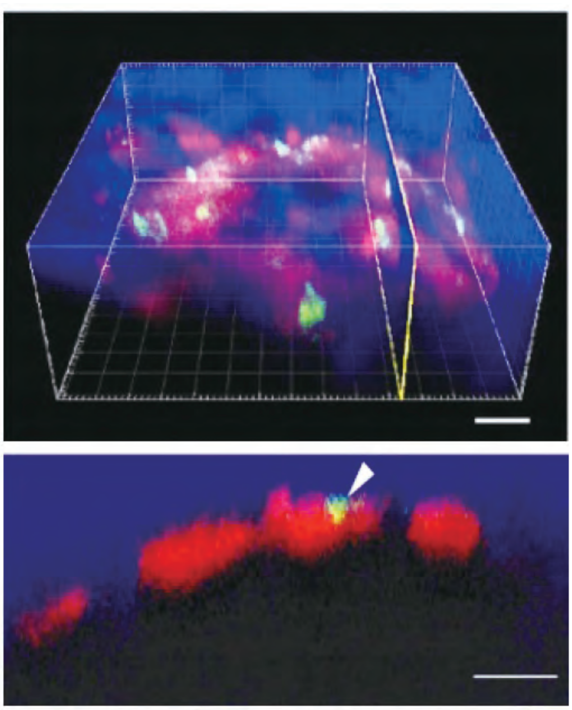


Fig. 6 Direct 4D imaging of bone-eating osteoclasts.

8 Neural activity affects immune reactions

Kazuhiro Suzuki (PI)

Have you ever come down with a cold as soon as a period of stress is over? The connection between the nervous system and immunity is fascinating but it seems difficult to prove academically.

Kazuhiro Suzuki's group found that noradrenaline secreted by stimulation of the sympathetic nerve, which is an autonomic nerve, suppresses the release of lymphocytes from the lymph node (they are retained in the lymph node). The autonomic nerve plays an important role to maintain the balance of the body when it is having cold sweats and panting in times of nervousness. In this study, the group succeeded in demonstrating that information from the nervous system affected the function of the immune system (Fig. 7).

Furthermore, it was found that in a mouse model of multiple sclerosis, an autoimmune disease of the nervous system, nervous system signals hindered the arrival of lymphocytes at the site of inflammation. That is, inflammation (immune reaction) was suppressed to some extent when nerves were in tension.

Nakai et al. J Exp Med 211, 2583 (2014)

The future of IFReC

In the 10 years since its establishment, IFReC has achieved steady results to high international acclaim. Osaka University was ranked No. 1 in the world (number of citations per paper) in "Research Institution Ranking in the 10 Years (Immunology Field)" published by Thomson Reuters in 2014. IFReC researchers make a significant contribution to this ranking. In addition, comparing IFReC article citation data with several top laboratories in Europe and the United States, it was indeed the world's leading research institute of immunology.

Some of the major awards received since establishment include; The Keio Medical Science Prize (Akira and Sakaguchi), Person of Cultural Merit (Akira), The Asahi Prize (Sakaguchi), The Canada Gairdner International Award (Akira and Sakaguchi), The Crafoord Prize (Kishimoto and Hirano), and The Japan Prize (Kishimoto and Hirano). As of 2016, four IFReC members; Akira, Sakaguchi, Nagata and Kishimoto are foreign members of the American Academy of Sciences this is very rare for research institutions around the world.

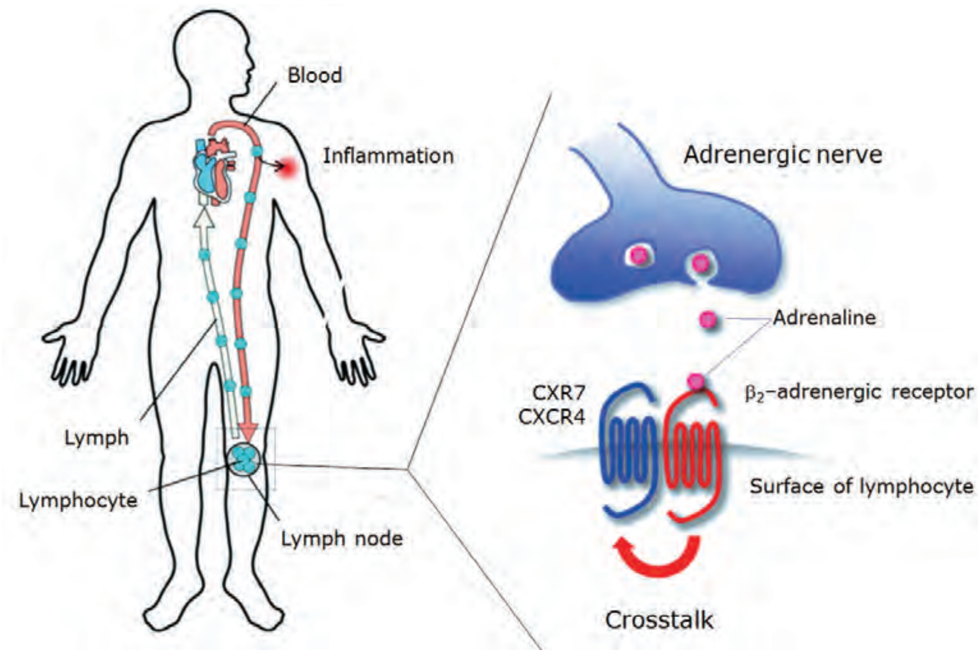


Fig. 7 Neuronal excitation affects immunity.

Promotion of integrated research in IFReC has become the foundation of significant developments in fundamental immunology research and has produced many excellent results. In the field of multiphoton excitation microscope and MRI imaging, the results obtained were as mentioned above. The results exceeded initial expectations due to advances in technological innovation during this period.

In addition to this, many researchers are developing research that incorporates bioinformatics, and it has already become a major trend in IFReC, including multiple papers published in Cell, Nature and their sister journals. In IFReC, fusion research of immunology with imaging and informatics is no longer a goal but a natural part of our daily research method.

There is no doubt that this research system has achieved the "environment in which researchers from different fields gather under one roof" promoted by the WPI program.

The research environment of IFReC is an achievement that could not exist without the WPI program. In 2017, IFReC, with a variety of financial support including from private companies, will increase human resources and extend research concepts and diversity. Even then, the devoted efforts of IFReC researchers who emphasize basic research will continue.

In addition, IFReC will continue as a WPI center to make new approaches to continuing to disseminate excellent research results to the world. The fusion with bioinformatics made it possible to comprehensively analyze research data. It will become possible to make data analysis, which until now has depended on human effort, far more reliable and it will be possible to apply it to ultra-high resolution analysis images etc. The development of AI technology as an artificial brain is also expected to advance quickly. The trend of scientific research in the world will develop with these technological innovations meaning young talented persons will be essential for the future of IFReC. Therefore, IFReC hopes to expand as a center that can provide a wide field for collaborative research. We will advance the Open Innovation Laboratory Concept which aims to gather the intelligence of industry and academia with international researchers in various fields. It will be a place for the circulation of global brains that focuses the power of young people. IFReC will continue its activities as a WPI center in line with the currently proposed Open Campus Initiative of Osaka University.

Jun Sakanoue (IFReC), Catherine Nakamichi (IFReC)

International Center for Materials Nanoarchitectonics

Toward a better global future: Pioneering a new paradigm in materials development on the basis of "nanoarchitectonics"

MANA's purpose is to pioneer a new paradigm in nanotechnology by proposing and developing the novel concept of "nanoarchitectonics." Nanoarchitectonics is a system of material architectural technology that enables free creation of new material functions by controlling the arrangement and interactions of nano-sized units. Aiming at new materials that will support next-generation technologies in various fields, including energy and the environment, information and communications, and medicine, MANA has attracted global attention for its world-class research in the five fields of Nano-Materials, Nano-Systems, Nano-Power, Nano-Life and Nano-Theory.

Research Center's Information (FY 2015)

Center Director: Masakazu Aono
Principal Investigators (PI): 18 (including 8 overseas researchers and 2 female researchers)
Other Researchers: 179 (including 96 overseas researchers and 36 female researchers)
Research Support Staff: 10
Administrative Division:
  Administrative Director: Tomonobu Nakayama
  Administrative Staff: 18 (percentage of bilingual staff: 100%)
Satellites and Cooperative Organizations: University of California, Los Angeles, USA; Georgia Institute of Technology, USA; University of Tsukuba, Japan; French National Center for Scientific Research (Centre national de la recherche scientifique, CNRS), France; University of Montreal, Canada; University College London, UK; and others
URL: http://www.nims.go.jp/mana/

Nano Revolution
for the Future

Major Research Achievements

1 Oxide nanosheets for next-generation electronic devices through nanoarchitetonics

MANA discovered high-k dielectric nanosheet with 1 ～ 2nm thickness using functional oxides such as Titanium oxide. A high-performance thin-film capacitor having the world's smallest size and the highest performance was successfully developed by stacking these nanosheets, nanosheet architectonics.

2 Atomic switch with synaptic operations of remembering and forgetting

The world's first "synaptic element" was successfully developed by using an "atomic switch" that forms a conducting path by transfer of metal atoms (ions) when a voltage is applied. This element autonomously reproduces the distinctive remembering/forgetting neural operations of the brain.

3 Development of electron microscope for *in-situ* measurement of nanomaterial functions

An "*in-situ* property measurement instrument" was developed by combining techniques for precise manipulation of individual nanomaterials with the outstanding high resolution performance of the transmission electron microscope (TEM). The relationship between nanostructure and physical properties of nanomaterials was successfully clarified by using this instrument.

4 Ultra-high sensitivity, ultra-compact nanomechanical sensor realizing "mobile olfaction"

An ultra-small sensor, "Membrane-type Surface stress Sensor (MSS)," which enables detection of various molecules with extremely high sensitivity was successfully developed. An industry-academia-governmental joint research framework, the "MSS Alliance," was launched to realize practical application and industrial standardization of olfactory IoT sensor systems.

5 Discovery of mechanisms for enhanced performance of thermoelectric materials

The importance of the interaction of charge carriers and magnons as a mechanism by which magnetism improves thermoelectric performance in $CuFeS_2$ magnetic semiconductor system materials was discovered. Performance enhancement was also realized by synthesis of nanosheets of thermoelectric materials.

Research Paper's Information

Number of Research Papers:	3316
Top 10% Papers:	37.1%
Top 1% Papers:	7.8%
Internationally Collaborative Research Papers:	46.2%

(Database: SCOPUS database, Elsevier B.V.)

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Phone: +81-29-860-4709
Email: mana@nims.go.jp

The world's thinnest superconductor: ordered metal atoms on a silicon surface

To continue sustainable development, the human race requires tireless pioneering of advanced technologies that achieve innovations in the food, resources and energy production, information processing and communication, medical diagnosis and treatment, and improvement and preservation of social infrastructure and the environment. However, many of these technologies will not be realized without proper new materials. In the last 30 years nanotechnology has achieved remarkable growth. But in recent years further evolution is required to enable nanoscale observation and manipulation of materials and making many important contributions to the development of new materials. Advancing beyond observation and manipulation, novel technologies are required that enable creation of materials with the desired functions by combining and assembling nano-scale materials.

However, because nanomaterials exhibit properties that are unimaginable in everyday world, realizing these technologies is no simple matter. For this reason, MANA is engaged in research aimed at establishing those technologies under the concept that we have named "nanoarchitectonics," which enables creation of new material functionalities by controlling the arrangement and interactions of materials in nano-sized units. MANA is also developing innovative new materials on the basis of nanoarchitectonics in diverse fields, which we hope will result in great advances in the nanotechnology of the 21st century.

1 Oxide nanosheets, new solution to future nanoelectronics

Takayoshi Sasaki (PI), Minoru Osada (PI)

Nanosheets for next-generation electronic devices

As electronics continue to decrease in size, new classes of materials are necessary to continue this downsizing trend. Two-dimensional (2D) nanosheets, which possess atomic or molecular thickness and infinite planar lengths, have been emerging as important new materials due to their unique properties. In particular, the development of exotic 2D systems such as graphene and inorganic nanosheets has provided new possibilities and applications in nanoelectronics.

Among various inorganic nanosheets, oxide nanosheets are important and fascinating research targets because of the innumerable varieties of layered oxide materials with interesting properties such as electrical conductivity, superconductivity, high-κ dielectricity, ferroelectricity, ferromagnetism, etc. MANA is working on the creation of oxide nanosheets and the exploration of their novel functionalities towards applications. For example, MANA discovered high-κ dielectric nanosheets, an important material platform for ultra-small electronic devices, exhibiting the highest permittivity (ε_r = 210~320) ever realized in all known ultrathin (<10 nm) dielectrics.

The world's smallest, highest performance capacitor made from "nano building blocks"

MANA also developed the world's smallest, highest performance capacitor by "nanosheet architectonics."

Capacitors based on dielectric thin films are a key component of electronic devices, where they provide essential functions such as storing electrical charge, and blocking direct current while allowing alternating currents to propagate. Because capacitors are essential in our electronic equipments such as cell phones, personal computers, etc., extensive efforts are directed at the developments of high performance capacitors with smaller size and higher capacitance. But current technology with multi-layered ceramic capacitor (MLCC) has almost reached its limit in terms of materials and processing, which in turn limits the performance that manufacturers can achieve. In response, the researchers have gone to the nanoscale, but "nanocapacitors" are not easy to make.

MANA developed a LEGO-like approach, and applied it to make high-performance ultrathin capacitors. MANA used conductive RuO_2 and dielectric $Ca_2Nb_3O_{10}$ nanosheets as core device components. By using solution-based assembly, MANA created a sandwich consisting of layers of two different types of oxide nanosheets to produce an ultrathin capacitor. The new capacitor has a stable capacitance density (~30μF/cm^2), which is 1,000 times higher than that of currently available commercial products despite the thickness of 30 nm, a 50 times reduction compared to MLCC.

MANA also utilized high-κ dielectric nanosheets as building blocks in the LEGO-like assembly, and successfully developed various functional nanodevices such as field effect transistors, artificial ferroelectrics/

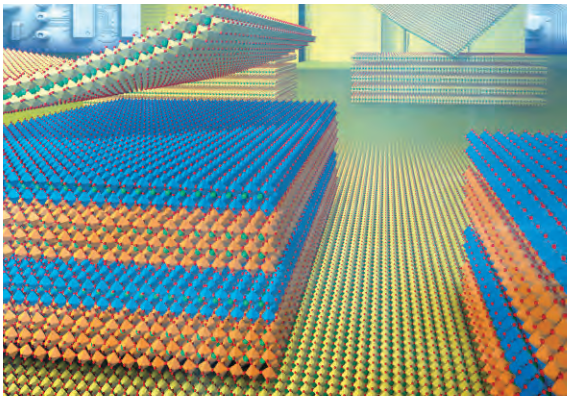


Fig. 1 Image for device fabrication process by nanosheet architectonics. Sophisticated functionalities of nanodevices can be designed through the selection of nanosheets and precisely controlled over their arrangement.

multiferroelectrics, metamaterials, actuator crystals, etc. Our work is a proof-of-concept, showing that new functionalities and nanodevices can be made from "nanosheet architectonics."

M. Osada et al., Advanced Materials, 24, 210, 2012.
C. Wang et al., ACS Nano, 8, 5449, 2014.

2 Atomic switch with synaptic remembering and forgetting operations

Tsuyoshi Hasegawa (PI), Kazuya Terabe (PI), Masakazu Aono (PI)

"Atomic switch" – the world's smallest mechanical switch

An "atomic switch" is a switching device that operates through the transference of metallic atoms/ions and a redox process, which occur when a voltage is applied.

The world's first atomic switch (Fig. 2) was invented by MANA Director Masakazu Aono, et al. The switch has a structure in which a gap of approximately 1 nm exists between the tip of a silver sulfide needle and a platinum surface, which function as electrodes. By controlling the voltage applied to the needle, chemically-reduced silver atoms precipitate in the gap, resulting in contact between the electrodes, and the device is switched "on." The device is switched "off" when oxidized silver ions return to the needle and the gap between the electrodes is reestablished. It requires an extremely small amount of electrical power to start up, and realizes on-off operations depending on whether or not only a few atoms are present in the gap.

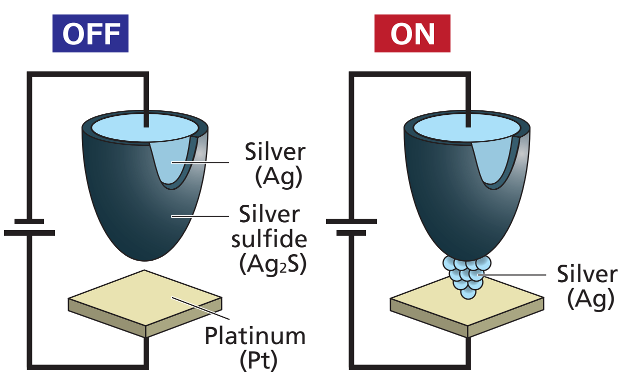


Fig. 2 Schematic diagram of an atomic switch that switches "on" when silver atoms are discharged from a silver sulfide needle.

Realizing synapse elements with atomic switches

MANA researchers are pursuing the world's first demonstration experiment after discovering that the atomic switch operates as a "synaptic element" that autonomously reproduces neural activities in the brain, which are characterized by "remembering necessary information" and "forgetting unnecessary information."

Synapses are junctions that form between the nerve cells (neurons) that make up the neural circuits in living organisms. When the action potential of a neuron reaches a synapse, a neurotransmitter is released and a synaptic potential is generated and transmitted as the action potential of the next neuron. Synaptic connections where this stimulus occurs frequently are strengthened, and as a result, memory is strengthened. In other words, "remembering necessary information" and "forgetting unnecessary information," which are the distinctive features of the brain, are thought to correspond to changes in the strength of synaptic connections.

The atomic switch displays behavior that corresponds closely to these changes in the strength of synaptic connections in the brain. When an electrical signal is input frequently, a stable conducting path (bridge) is created between the electrodes by the efficient precipitation of silver atoms. Conversely, the conducting path disappears over time when the frequency of input is low. Thus, the higher the signal input frequency, the thicker and more stable the bridge becomes (Fig. 3).

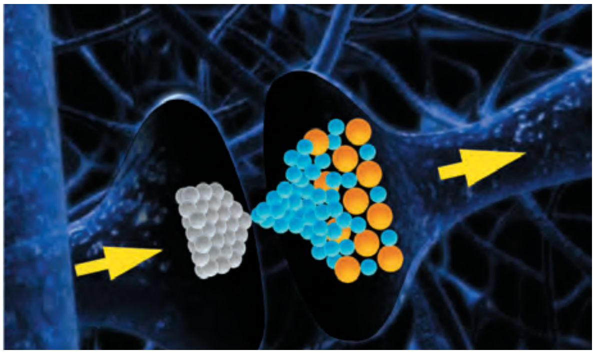


Fig. 3 Schematic diagram of an atomic switch with synaptic operation. When an electrical signal is input, a bridge is formed between the electrodes by precipitation of silver atoms from the electrode on the right.

The road to an artificial brain

Since it has been pointed out that existing computers will not be able to cope with the future demand for higher performance and diversification, attention has been focused on the development of neural circuit/brain-type computers. Artificially reproducing the synaptic functions of brain neural circuits is essentially important, and the synaptic function has already been reproduced by complex circuits and software, however, this approach requires a drive program that has been designed in advance. In contrast, research has shown that circuits that incorporate the synaptic elements developed by MANA can create calculation functions without advance operational design. In the future, progress is expected in research toward the realization of artificial intelligence materials that become more intelligent (learn and grow) with experience.

T. Hasegawa et al., Advanced Materials, 22, 1831, 2010.

T. Ohno et al., Nature Materials, 10, 591, 2011.

3 Development of electron microscope for *in-situ* measurement of nanomaterial functions

Yoshio Bando (PI), Dmitri Golberg (PI)

The difficulty of measuring nanomaterials

In materials science, nanomaterials have attracted the greatest interest over the past several decades. Nano-sized materials display different physical properties than those of the bulk (i.e., those states in which a substance exists in a large quantity to some degree), including mechanical, electrical, thermoelectric, electrochemical, magnetic, piezoelectric, photoelectric, photoelectromotive properties and others. While it is expected to be possible to obtain a variety of functions by combining nanomaterials and various technologies, a precise grasp of the nature of nanomaterials is extremely important in the stage of actual applications.

In measurements of the physical properties of nanomaterials to date, it was possible to investigate the surface form by the scanning electron microscope (SEM), scanning tunneling microscope (STM), atomic force microscope (AFM) and other techniques, but a detailed knowledge of the internal structure was still out of reach. As a result, it was unclear how the measured property data were influenced by nano-level conditions, namely, the shape, the crystal structure, elemental distribution and defect structure of the nanomaterial. In fact, some scientific papers reported very different property data, and this was a serious hurdle to the practical application and industrial use of nanomaterials.

New *in-situ* property measurement instrument

To overcome the hurdles caused by measurement techniques, MANA developed an instrument which makes it possible to manipulate individual nanomaterials while performing observation by high resolution transmission electron microscopy (HRTEM). This enabled *in-situ* measurement of physical properties, which simultaneously captures the changes in properties and changes in the material structure at the nano-level. With this instrument, it is possible to acquire enlarged images with magnification of 2 x 10^6 times and observe deeply into the crystal structure of nanomaterials. In addition to applying voltage, resistance heating, electrostatic charge, bending, tension, peeling, and light irradiation, it is also possible to measure mechanical, electrical, thermal and optical properties while manipulating the sample with nanometer precision. By using an STM probe (for measurement of electrical characteristics), AFM cantilever (for measurement of mechanical properties) and optical fiber (for measure of photoelectric/photovoltaic properties) in combination with the conventional HRTEM specimen holder, the new instrument has made it possible to measure diverse properties of more than 50 different nanomaterials, including nanotubes, nanowires, nanosheets, graphene and nanoparticles.

Toward elucidation of the causal relationship between structure and physical properties

Analysis by the *in-situ* property measurement instrument is innovative, in that it is possible to investigate the physical properties of individual nano-level structures by utilizing its extremely high spatial resolution, temporal resolution and energy resolution, which could be obtained only with HRTEM. As another important attraction, *in-situ* measurements are also possible in real-time, at each step in the structural changes of nanomaterials.

Utilizing this technique, MANA has already realized elastoplastic analysis, measurement of the electron transport property, etc. of nanomaterials, for example, when bending or tension is applied (Fig. 4). In the future, more active use of this *in-situ* property measurement instrument will make it possible to clarify the relationship between the nanostructure and physical properties of nanomaterials and open new

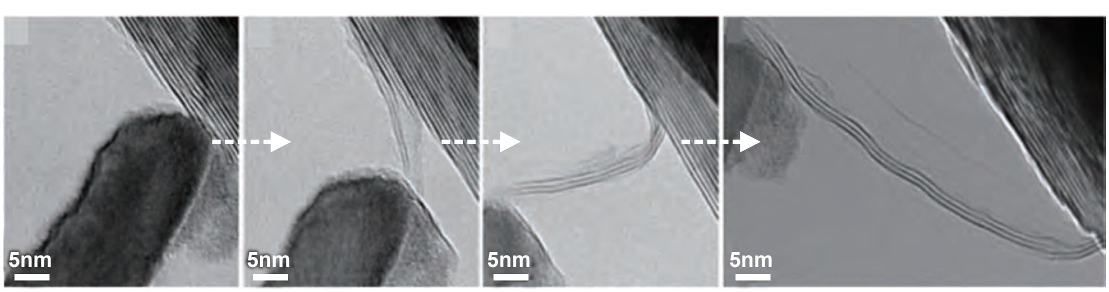


Fig. 4 HRTEM images showing the dynamics of the Scotch tape method of peeling atomic layers. It is possible to peel 3 atomic layers from a layered MoS_2 single crystal by skillfully manipulating the metal probe in the *in-situ* property measurement instrument.

paths in the development of nanomaterial applications.

D. Golberg et al., Advanced Materials, 24, 177, 2012.
D. M. Tang et al., Nature Communication, 5, 3631, 2014.

4 Highly sensitive and compact nanomechanical sensor realizing "mobile olfaction"

Genki Yoshikawa (Group Leader)

Development of a new sensor –"MSS"

Practical application of molecular sensors that can detect and identify various types of molecules has been desired in various fields, including foods, medicine, healthcare, security and the environment science. Nanomechanical sensors, which are one type of molecular sensors, detect surface stress induced by target molecules adsorbed on receptor layers coated on the sensor surface. Nanomechanical sensors can be very versatile because various materials including organic, inorganic and bio molecules can be utilized for receptor layers. However, it was difficult for conventional nanomechanical sensors to satisfy both high sensitivity and compact system, which had been a long-standing challenge for over 20 years. Through the fusion of four basic sciences *i.e.* structural mechanics, materials science, crystallography and electric circuit science, we developed a new nanomechanical sensor called the "Membrane-type Surface stress Sensor (MSS)," which achieved both high sensitivity and compact size. The MSS has a sensitivity more than 100 times higher than that of conventional cantilever-based piezoresistive nanomechanical sensors, and realizes the integration of more than 100 sensor elements in 1 cm^2.

The MSS also possesses a number of other outstanding features: Compatibility with mass production (1$ per chip in future) and integration based on conventional semiconductor microfabrication technology, low power consumption (1 mW or less per sensor element), quick response (response time can be less than a few seconds depending on the conditions) and thermal, electrical and mechanical stability. These practical features of the MSS provide the opportunities for various applications to mobile or IoT devices, contributing to safety and security in daily life in the areas such as freshness/quality control of foods, health management, environmental monitoring and security control.

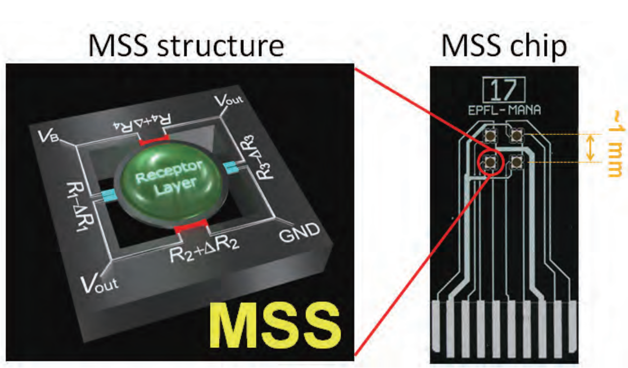


Fig. 5 Left: Schematic illustration of the MSS structure. Surface stress generated by the adsorption of target molecules on the receptor layer is detected electrically with high efficiency by piezoresistors embedded in the four surrounding bridges. Right: Optical microscope image of an MSS chip.

The possibility of a mobile "olfactory sensor"

One of the most important applications of the MSS is an artificial olfactory sensor. We have already demonstrated the identification of various specimens by smell including meat, spices, perfume and beverages. In a joint research between the Swiss Federal Institute of Technology in Lausanne, the University of Basel and MANA, cancer patients were identified through breath analysis using MSS. Research is now underway to explore a variety of applications including reliable cancer diagnosis with small stress to patients, personal diagnosis of daily monitoring of health, and mobile olfactory sensing (Fig. 6).

Fig. 6 Application as a mobile olfactory sensor device for monitoring health conditions by analyzing exhaled breath.

Moves toward practical application and standardization

With the aim of social implementation of MSS as a sensor system, six organizations including NIMS (parent institute of MANA), Kyocera, Osaka University, NEC, Sumitomo Seika and NanoWorld jointly launched an industry-academia-governmental joint research framework called "MSS Alliance" in September 2015. This alliance focuses on the integration of various cutting-edge technologies towards reliable odor analysis system and industrial standardization.

G. Yoshikawa et al., Nano Letters, 11, 1044, 2011.
F. Loizeau et al., Proceedings IEEE MEMS, 26, 621, 2013.

5 Discovery of mechanisms for enhanced performance of thermoelectric materials

Takao Mori (PI)

The importance of development of thermoelectric materials and related issues

Only about 1/3 of the primary energy (petroleum, coal, gas, etc.) used by humankind is effectively utilized, and most of the remainder is simply lost as waste heat. For this reason, high expectations are placed on solid-state thermoelectric material devices which convert waste heat directly into useful electricity by using the phenomenon called the Seebeck effect, whereby a temperature difference is converted to voltage.

At present, thermoelectric devices have not reached wide practical application due to the inadequate performance of the thermoelectric materials. To begin with, in power generation by thermoelectric materials, it is necessary to create a temperature differential in the material, and also to extract electric current. However, it is generally difficult to realize a condition in which current flows but heat does not, i.e., maintaining the temperature differential, and thereby, achieving high performance in a thermoelectric material. As an additional challenge, the main components of conventional high performance thermoelectric materials are scarce, expensive and/or toxic elements such as bismuth (Bi), tellurium (Te), lead (Pb), silver (Ag), hafnium (Hf), etc.

Therefore, MANA is pioneering the mechanisms for achieving high functionality in compounds of elements that are more abundant in nature in order to contribute to wide-ranging practical application of thermoelectric materials.

Nanoarchitectonics of thermoelectric materials

Focusing on the difference in the mean free paths of phonons and charge carriers, suppressing thermal conduction may be realized by more selective scattering of phonons. In recent years, this method has enjoyed worldwide popularity for achieving high thermoelectric performance. Because the design of a proper nanostructure is the key for the success of this idea, MANA established a nanoarchitectonics approach in which nanosheets of thermoelectric materials are synthesized and utilized, resulting in improved thermoelectric performance.

This is a simple method that uses little energy, and is expected to be applicable to a wider range of thermoelectric materials in the future. Furthermore, dramatically improved performance can be expected if nanosheets can be assembled in a high-order structure designed by nanoarchitectonics (Fig. 7).

The search for new principles

The nanostructuring of thermoelectric materials is a powerful method for achieving high thermoelectric performance. It is also extremely important to discover new principles for improving the figure of merit, which expresses the performance of thermoelectric materials. MANA discovered that $CuFeS_2$ shows high thermoelectric performance even at around room temperature. Toxicity is not a problem with the component elements of this material, namely, copper (Cu), iron (Fe) and sulfur (S), and the material itself exists in abundance in nature in the form of a copper iron sulfide mineral called chalcopyrite. The magnetism of the material can be adjusted by controlling the content of Fe, and MANA research has shown that it is possible to improve thermoelectric performance by appropriate adjustment of the coupling of the charge carriers and magnons (Fig. 8). (A magnon is a quasiparticle related to the oscillations of the magnetic moment of electrons in a magnetic body.)

C. Nethravathi, et al., Journal of Materials Chemistry A, 2, 985, 2014.
R. Ang et al., Angewandte Chemie, 54, 12909, 2015.

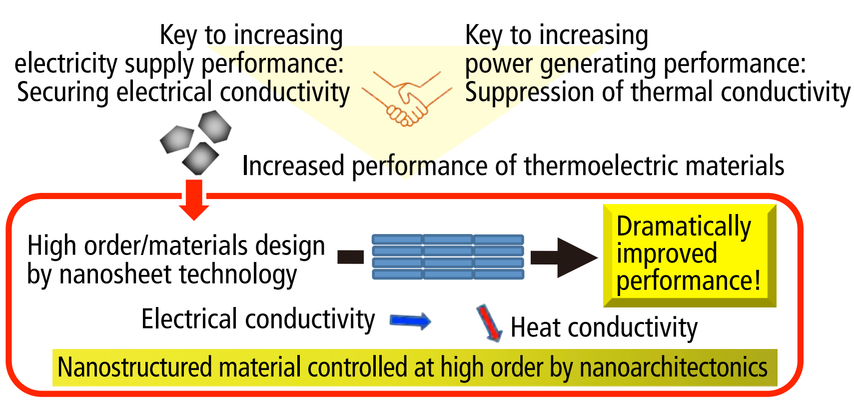


Fig. 7 Realization of high thermoelectric performance by utilizing nanostructures. Securing electrical conductivity and suppressing heat conductivity are achieved simultaneously through nanoarchitectonics utilizing nanosheet technology, and a dramatic improvement of thermoelectric performance is achieved.

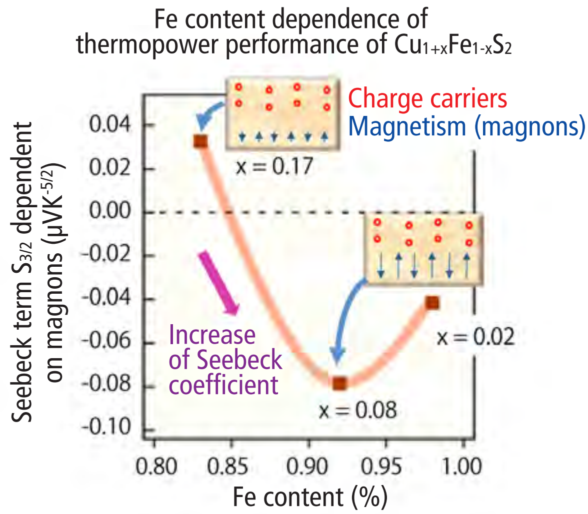
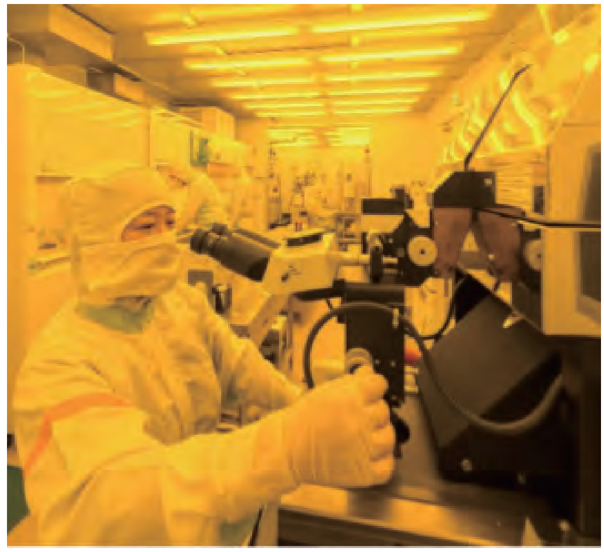


Fig. 8 Change of thermopower performance (change of Seebeck term $S_{3/2}$) when the coupling contributions of charge carriers and magnons are adjusted by controlling the iron content of the magnetic semiconductor $Cu_{1+x}Fe_{1-x}S_2$. In this figure, the optimum coupling is realized and improvement of thermopower performance is observed at x=0.08.

MANA to date, and outlook for the future

MANA grew into a world-class research institute in the field of nanotechnology with the support of the WPI program (WPI: World Premiere International Research Center Initiative). This is also proof that the missions of WPI were indeed on target. One of the missions of the WPI is "Fusion." Basic research begins with individual research and frequently advances to high level research as a result of the formation of a group of researchers or a "trend" of research. MANA additionally gave birth to "dynamic research" that produces world-class research results by encouraging a fusion of research activities, ideas and concepts which are already at a high level. The mission of the WPI also includes "Globalization." In this respect as well, MANA has demonstrated a fusion effect, in the form of a high level of research, by introducing different cultures and thinking in a front-line research center in Japan, thereby creating a new research environment. While the five outstanding research achievements described above are all results of such fusion effects, MANA has also cultivating a large number of other germinal ideas for research.

From the outset, MANA realized that the fusion and globalization would not progress by simply gathering researchers from different fields and from different countries. Before the WPI program, the National Research Institute for Materials Science (NIMS), with the support of Japan's Ministry of Education, Culture, Sports, Science & Technology (MEXT), had operated the International Center for Young Scientists (ICYS). The ICYS established a system for accepting and fostering outstanding young scientists from around the world and accumulated experience in coping with the "culture shock" that accompanies internationalization. Based on that experience, MANA has become the most globalized international research center in Japan by conducting various unique programs that encourage globalization and fusion under the auspices of WPI. As one result, in terms of the level of its research results, MANA now ranks with the top research institutes in other countries such as Harvard University and MIT. At present, half of the researchers working at MANA are non-Japanese. MANA is continuing to promote cutting-edge research through cooperation among young researchers who have gathered here from Japan, other Asian countries, Europe, USA and Oceania.



Young researchers who have come to MANA from around the world cooperating in an experiment in a cleanroom

MANA is also extremely active in collaboration with overseas research institutes, and the international network of nanotechnology research centered on MANA is growing steadily. As just one example, more than 250 young scientists who gained experience at MANA are now spreading their wings in countries throughout the world.

At MANA, this successful experience is deeply engraved in our hearts. In achieving unique and high level of research results as one of the world's top research centers, MANA learned that dynamic operation of a research center is necessary and indispensable for realizing fusion and globalization. While continuing to spread this essence of MANA to NIMS as a whole, and to all of Japan, we also intend to play an active role as a "catalyst hub" for nanotechnology research by bringing together the best scientific brains from around the world.

Tomonobu Nakayama (MANA)

International Institute for Carbon-Neutral Energy Research

Grand Highway for a Carbon-Neutral Energy Society

I²CNER's mission is to contribute to the advancement of low carbon emission and cost-effective energy systems, and improvement of energy efficiency. The array of technologies that I²CNER's research aims to enable includes Solid Oxide Fuel Cells, polymer membrane based fuel cells biomimetic and other novel catalyst concepts, and production, storage, and utilization of hydrogen as a fuel. Our research also explores the underlying science of CO_2 capture and storage or the conversion of CO_2 to a useful product. Additionally, central to I²CNER's mission is the establishment of an international academic environment that fosters innovation through collaboration and interdisciplinary research (fusion).

■ Research Center's Information (FY 2015)

Center Director: Petros Sofronis
Principal Investigators (PI): 26 (including 10 overseas researchers and 1 female researcher)
Other Researchers: 140 (including 70 overseas researchers and 17 female researchers)
Research Support Staff: 53
Administrative Division:
  Administrative Director: Shunichi Masuda
  Administrative Staff: 21 (percentage of bilingual staff: 81%)
Satellites and Cooperative Organizations:
  University of Illinois at Urbana-Champaign, USA; and others
URL: http://i2cner.kyushu-u.ac.jp/en/

I²CNER

Major Research Achievements

1 Development of organic-inorganic perovskite solar cells with long lifetimes

The accumulation of lead originating from the breakdown of perovskite crystals upon reaction with water and oxygen was identified as a major mechanism leading to the degradation of organic-inorganic perovskite solar cells under operation. Device lifetime was extended by 17 times using a unique method to suppress this degradation mechanism.

2 Development of polymer-coated, highly durable carbon nanotube-based fuel cells

A new polymer electrolyte fuel cell cathode catalyst, in which the carbon nanotubes were doubly-coated with two different polymers, has been shown to be at least 100 times more durable than the conventional catalyst. In addition, this technology allows the smallest possible platinum particles to be used, leading to an overall reduction in the amount of platinum in the fuel cell.

3 Atomic level surface analysis with low energy ion scattering

The surface composition of perovskite, which had excellent oxygen molecule dissociation (catalytic activity), and is used as an air electrode, was analyzed at the atomic level using a new surface analysis method (the Low Energy Ion Scattering method). Degradation of cell performance was identified, and durability of the cell was improved.

4 Small Molecule Activation

An "Artificial molecular catalyst that can extract electrons from the hydrogen molecule (H_2) via a hydride ion (H^-)" was developed by mimicking a natural enzyme, hydrogenase. Furthermore, molecular fuel cells that make use of this molecular catalyst were successfully built.

5 Modeling of CO_2 behavior for safe and efficient CO_2 storage

A quantitative estimation of CO_2 saturation in rock was obtained using digital rock physics to investigate the behavior of CO_2 inside the rock, and conditions for effective CO_2 storage were clarified.

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Images shown in the background show blue emissions from a plasma plume during the pulsed laser deposition and observation of CO_2 behavior in natural rock.

Results of the research

The International Institute for Carbon-Neutral Energy Research (I^{2}CNER) of Kyushu University aims to promote advanced basic science research that will enable low carbon emission, highly efficient, and economically effective energy systems. As an Institute, we aspire to lead the way toward realizing an environment-conscious and sustainable society.

In an effort to create innovative solutions that will pave the way to the future, the Institute also addresses many major issues that currently hinder the realization of future clean energy societies.

1 Development of organic-inorganic perovskite solar cells with long lifetimes

Chihaya Adachi (PI)

Solar cells are currently garnering a lot of serious attention because they provide a promising solution to the growing concern over energy resources. A major advantage of solar cells is that no CO_2 is emitted through the power generation process, but this is offset to a certain extent by the substantial amount of power that is used and the amount of CO_2 that is emitted during the fabrication of the devices themselves.

In recent years, a class of solar cells called "perovskite solar cells" has drawn considerable attention because of their strong potential to achieve both a low carbon footprint and a high power conversion efficiency. Perovskite solar cells are composed of a mixture of organic and inorganic layers, and get their name from the crystalline perovskite layer that is used to absorb light.

The solar-to-electrical power conversion efficiency of perovskite solar cells is already greater than 20%, which is good enough for practical applications, but the devices degrade quickly under operation, which poses a major obstacle to commercialization. I^{2}CNER has set the goal of extending the lifetime–the time by which a device's efficiency decreases by a certain amount–while also increasing the conversion efficiency by clarifying and eventually elucidating the degradation mechanisms in perovskite solar cells.

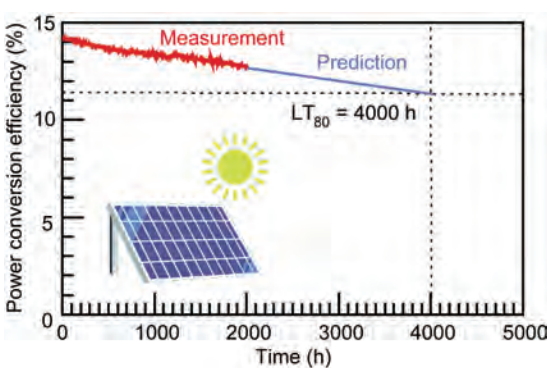

Fig. 1: Lifetime of a perovskite solar cell with benzoquinone added to the perovskite film

The dominant sources of degradation are thought to be water and oxygen from the atmosphere. To verify this, we produced prototype cells in a nitrogen environment free of water and oxygen, and compared them with those fabricated in an ambient atmosphere. The prototype cells were illuminated in the laboratory with simulated sunlight to measure the time until the conversion efficiency decreased to 80% of the initial, or a lifetime referred to as LT_{80}.

Whereas LT_{80} was at most 230 hours for the cells fabricated in an ambient atmosphere, LT_{80} increased to as long as 570 hours when the cells were made in a nitrogen environment. Thermally stimulated current measurements revealed that the cells produced in an ambient atmosphere had a large number of hole traps, i.e., positive charges that cannot move freely, and further analysis indicated that parts of the perovskite ($CH_3NH_3PbI_3$) had decomposed into CH_3NH_3I, PbI_2, and Pb. Thus, the efficiency degradation comes from the decomposition of perovskite in the presence of water and oxygen from the atmosphere, and hole traps formed by Pb produced after perovskite decomposition appear to play a particularly strong role in the reduction of efficiency.

Since we expect that the most likely source of Pb is the chemical reduction of Pb^{2+} created by the decomposition of perovskite, we developed a method to suppress this reduction by adding a small amount of an oxidizing agent called benzoquinone into the perovskite film. With the proper selection of benzoquinone concentration, the generation of hole-trapping Pb was controlled and the LT_{80} extrapolated from experimental measurements was extended to over 4,000 hours (Fig. 1).

These lifetimes are 17 times longer than those of conventional cells, and are the longest reported values to date. Furthermore, the addition of benzoquinone resulted in the formation of larger perovskite crystals, leading to an increase in conversion efficiency of about 30%. This research represents a major step toward the realization of perovskite solar cells with high conversion efficiency and long lifetimes for practical applications.

C. Qin et al: Adv. Mat., 28, 446, 2016

2 Development of polymer-coated highly durable carbon nanotube-based fuel cells

Naotoshi Nakashima (PI)

The fuel cells which have been used in "ENE FARM" (a home-use fuel cell cogeneration system) and fuel cell vehicles are an extremely clean electricity supply that generates electric power and water through the reaction between oxygen (i.e., air) and hydrogen with the help of catalysts. Polymer electrolyte fuel cells, in particular, in which a polymer membrane allows hydrogen ions to pass through and acts as the electrolyte membrane, are considered to be the most promising fuel cells because of their small size, light weight, and high energy efficiency.

However, since platinum is used as the catalyst, driving up the overall device cost, the reduction of the amount of platinum used in the device and an increase in durability are important challenges.

In order to adsorb (or support) the nanometer-sized platinum particles on the catalyst, a conductive carbon material, carbon black, has been used. Carbon black poses a challenge, since it has a lot of chemically defective areas that cause functional degradation, although it supports platinum particles very well.

To resolve this dilemma, I^2CNER's goal is to replace carbon black with carbon nanotubes (CNTs), which have almost no chemically defective sites. However, it is more difficult for CNTs to support platinum particles, and hence it is not simply a matter of switching from carbon black to CNTs.

Despite this difficulty, I^2CNER has succeeded in supporting platinum particles by applying a thin polymer coating, polybenzimidazole (PBI), which has a strong affinity with the CNTs, to the surfaces of the CNTs. The schematic drawing of PBI-coating and platinum particle deposition on the CNTs is illustrated in the upper portion of Fig. 2. It can be said that PBI is playing the role of "double-sided tape" because it can be adsorbed strongly on the surfaces of the CNTs and at the same time, it can support platinum particles.

In Fig. 2, the durability of conventional fuel cells (shown by black dots), in which carbon black is used as the catalyst to support platinum particles, is compared with the durability of the fuel cells based on the PBI-coated CNTs (shown by red squares) to which platinum nanoparticles are deposited. The durability test based on the FCCJ protocol for the cells was carried out, in which high potential (1.5V) was applied in order to cause the carbon degradation/corrosion. In contrast to the distinctive degradation of the carbon black-based catalyst, the PBI-coated CNT-based catalyst shows almost no degradation and its durability is dramatically higher (Reference 1).

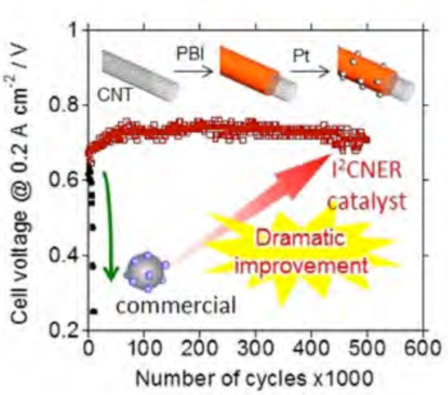

Fig. 2: Durability of fuel cells (cell voltage vs. durability cycling). Scheme of PBI coating is illustrated in the upper portion of the figure; black dots indicate durability of fuel cells with carbon black catalyst; and red squares indicate durability of fuel cells with PBI-coated CNT-based catalyst.

In addition to the above, the size of the platinum particles can be minimized with this new technology, leading to an overall reduction in the amount of platinum (Reference 2). This is, so to speak, a "trump card" for lowering the overall cost of the fuel cell.

These results indicate a strong possibility that this type of fuel cell (cells with the PBI-coated CNT-based catalyst) could be a promising next-generation fuel cell, and they have the potential to contribute to the wide-spread utilization of fuel cells in the near future.

M. R. Berber et al: Scientific Reports, 5, article number 16711, 2015
I. H. Hafez et al: Scientific Reports, 4, article number 6295, 2014

3 Atomic level surface analysis using the low energy ion scattering method

Tatsumi Ishihara (PI)

Solid Oxide Fuel Cells (SOFCs), in which the oxide ion conductor is a commonly used electrolyte that does not need to be humidified, is one type of fuel cell that is expected to be widely used in the future. Since SOFCs can operate at high temperatures, they do not require expensive precious metal electrodes, such as platinum, and achieve a high energy conversion efficiency. For these reasons, SOFCs are expected to have a wide array of practical applications.

In general, SOFCs use an oxide ion conductor as the electrolyte, with an oxide (i.e., perovskite) with high electrical conductivity acting as the air electrode (cathode) and a nickel-based metal acting as the fuel electrode (anode).

The lanthanum strontium cobalt ferrite (LSCF) perovskite used as the oxygen dissociation catalyst for air electrodes is susceptible to chemical reactions with substances from the air, such as sulphur, which causes the oxygen dissociation activity to degrade over time. This is one of the most difficult roadblocks in the development of SOFCs. In order to resolve this issue, I^2CNER analyzed the aging (change with time) and spatial distribution of LSCF (perovskite-type oxide) composition in the vicinity of its surface using the latest analysis method (i.e., the low energy ion scattering, or LEIS method) and investigated the relationship between the composition of the outermost surface and the stability of the air electrode catalyst.

It was found that strontium, which was an additive to LSCF, tends to segregate on the surface as the temperature increases, and that strontium oxide was formed within a relatively short period (2 hours). The perovskite-type oxide is the chemical compound whose chemical formula is expressed as ABO_3 (where A and B are cations of different ionic sizes). In the case of LSCF, the A ion is lanthanum and strontium ions, and the B ion is cobalt and ferrite ions, and it has been assumed that A, B, and O ions are uniformly distributed on the surface. However, this assumption was proven to be entirely incorrect through a detailed analysis of the catalytic LSCF surface. The composition of LSCF in the vicinity of the surface was investigated in detail using LEIS, and it was found that in the outermost layer (most surface one atomic layer of LSCF), the A ion is segregated and that the strontium ion in particular is occupied at the outermost surface layer (Fig. 3).

The above findings observed in this research clearly revealed that the degradation of catalytic activity at the air electrode caused by a reaction with a very small amount of impurities was closely related to the changes in surface composition. We have succeeded in finding an approach to improve the catalytic activity and durability of fuel cells by controlling the concentration of strontium that causes the activity to degrade. With this approach implemented, air electrode catalysts that can operate stably for long periods of time should be developed, which has the potential to lead to commercial viability for the SOFC.

J. Druce et al: Energy & Environmental Science, 7, 3593, 2014
A. Staykov et al: Chem. Mater., 27, 8273, 2015

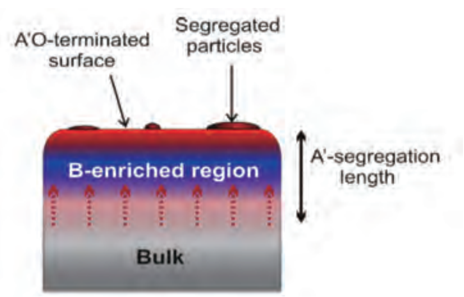

Fig. 3: Surface structure of perovskite oxides was clearly revealed by this research. A ions in the perovskite composition are concentrated in the uppermost surface and some of them have an island structure. Under the uppermost surface, there are regions that are abundant in B ions. Any one of these regions has a thickness of 3 to 5 atomic layers and, inside of (or under) these regions, the oxide is composed of ions (ABO_3).

4 Small Molecule Activation
Seiji Ogo (PI)

Small molecules such as H_2 (hydrogen molecules), O_2 (oxygen molecules), H_2O (water molecules), N_2 (nitrogen molecules), and CO_2 (carbon dioxide molecules) can be used effectively as energy sources when they are activated by oxidation and reduction. This process is called "Small Molecule Activation" and it is an area of research that has been gaining popularity rapidly in recent years. This report describes the results of I^{2}CNER research that is focused on the activation of hydrogen and oxygen molecules.

In nature, activation of the hydrogen molecule is achieved by a metalloenzyme, namely, hydrogenase. Hydrogenase plays a major role in many natural energy conversion systems. Under mild conditions, hydrogenase reversibly oxidizes the hydrogen with Fe and Ni, which is given by the following reaction equation: "$H_2 \rightleftarrows H^+ + H^- \rightleftarrows 2H^+ + 2e^-$". To date, no artificial catalyst has been developed that can catalyze this reaction. However, researchers at I^{2}CNER were the first in the world to succeed in developing "molecular catalyst extracting electrons (e^-) from the hydrogen molecule (H_2) via hydride ions (H^-)" by mimicking hydrogenase (Fig. 4 and Reference 1).

In addition, we are also the first in the world to have demonstrated that the oxygen molecule can be activated by making only minor changes to the molecular catalyst used to activate the hydrogen molecule, and that the peroxide species can be synthesized (Reference 2). In the peroxide species, the oxygen molecule is bound to an Fe center whose oxidation number is 4.

The key in designing the molecular catalyst is to configure the ligands surrounding the Fe center such that "they can withdraw the electron from the Fe center (Fig. 4)." Using this approach, the molecular catalyst can activate hydrogen molecules. We have also clarified that the molecular catalyst capable of activating oxygen molecules can be designed by "donating an electron to the Fe center."

By further deploying these approaches, we were successful in producing the first-in-the-world "molecular fuel cells" by making use of complexes (metal ions having molecules and ions bound) that activate hydrogen and oxygen molecules as the anode and cathode catalysts, respectively. This type of molecular catalyst can be manufactured less expensively than the platinum catalyst that is used as the electrode catalyst of fuel cells, with an added advantage being the ease with which the catalysts are designed. This type of catalyst has the potential to accelerate the development of precious-metal-free molecular fuel cells.

Ogo, S., et. al: Science 339, 682, 2013
Kishima, T., et. al: Angew. Chem. Int. Ed. 55, 724, 2016

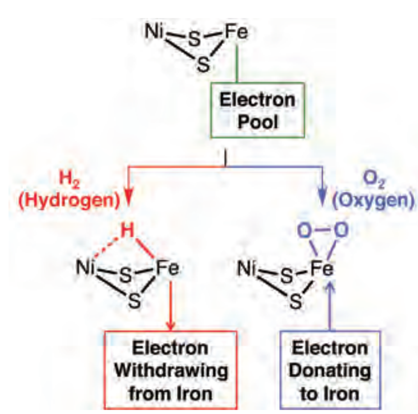

Fig. 4: Mechanism to control the activation of hydrogen (H_2) and oxygen (O_2). Fe: Ferrite, Ni: Nickel, S: Sulphur

5 Modeling of CO_2 behavior for safe and efficient CO_2 storage

Takeshi Tsuji (PI)

Carbon Capture and Storage (CCS) is a technology that can be used at a source which emits a large amount of CO_2, such as a coal-fired power station, to separate CO_2 and store it deep underground. The technology is well-known for its potential to reduce CO_2 emissions quickly in the near future. The storage of CO_2 does not require the construction of large, artificial underground spaces (e.g., tunnels). Instead, CO_2 is stored in the pore space of rocks (i.e., gaps in between the particles that make up rocks). Geologic strata in which a lot of pore spaces exist are called reservoirs. The porosity (i.e., a fraction of the pore volume over the total volume) of reservoirs is usually 20 to 30%. In ideal CO_2 reservoirs, CO_2 can be injected and stored using a small number of wells. However, around the Japanese Islands, the number of ideal reservoirs for CO_2 injection is limited, and thus, it is necessary to store CO_2 efficiently. As part of their efforts to develop ideal strategies for storing CO_2 underground, I²CNER researchers have developed a new approach making use of a novel approach called digital rock physics, which will allow them to consider specific factors, such as the geology of the Japanese islands or the limited number of reservoirs, when identifying potential CCS sites.

Using high-resolution CT equipment, we extracted the fine structure of pores in rocks at resolutions on the μm scale, which has allowed us to create a fine and precise digital (numerical) model of rocks. We have analyzed this model using the lattice Boltzmann fluid simulation method and precisely simulated and visualized CO_2 behavior as it runs through various networks of pores that exist inside rocks (Fig. 5).

Using the above-mentioned fluid simulation method, the behavior of CO_2 has been calculated under various reservoir conditions, and the amount of CO_2 (saturation) stored in the rock pores was investigated. It was found that saturation of CO_2 can be clearly estimated using two parameters: capillary number and viscosity ratio (i.e., ratio of CO_2 viscosity to water viscosity). The capillary number is a dimensionless parameter represented by surface tension and viscous forces. The capillary number and viscosity ratio are influenced by the conditions of reservoirs and the method used to inject CO_2 into the reservoir. Therefore, using the lattice Boltzmann method, it is possible to identify the conditions that allow for extremely efficient CO_2 storage. Furthermore, it could be possible to control CO_2 behavior in addition to the storage capacity. This technology is expected to contribute to the widespread use of CCS technology.

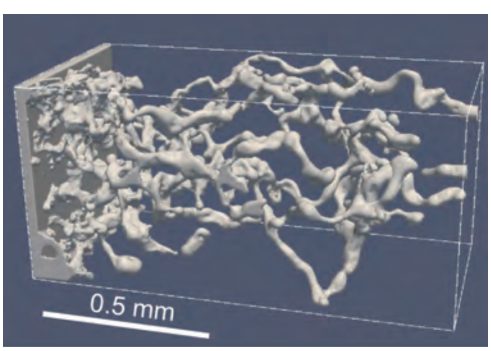

Fig. 5: CO_2 behavior running through rock pores. In this figure, only the injected CO_2 is color-coded in white, whereas formation water and rocks (solids) are shown as transparent. Conditions to effectively store CO_2 should be clarified by calculating CO_2 behavior under various conditions.

T. Tsuji et al: Advances in Water Resources, 95, 3-15, 2016
F. Jiang et al: Water Resources Research, 51, 1710, 2015

The unique influence of the only American WPI Director

When I²CNER was established in 2010, Professor Petros Sofronis (Ph.D.) of the University of Illinois became the first American to serve as the Director of a WPI Institute. Since the foundation of the Institute, we have held ourselves to the highest international operational standards, and our official language has been English.

In addition to creating a research environment that attracts some of the world's top researchers, we have adopted rigorous personnel performance evaluation systems based upon those used in the top US academic institutions. The Institute has also contributed to the cultivation of global human resources; implemented an efficient top-down decision-making system; sponsored international symposia which have attracted world-authorities in various fields; and cultivated some of the world's most cutting-edge fusion research efforts. All of these efforts by the Institute are expected to have widespread positive effects within Kyushu University, which will help increase KU's overall global recognition.

Thanks to the unceasing effort and dedication of Director Sofronis, I²CNER has created a unique network of research institutes and universities throughout the world. Most notable are the Institute's ongoing interactions with the United States Department of Energy (DOE) and the California Air Resources Board (CARB), among others.

As a world leading energy research institute, I²CNER aims to serve as a hub for accelerating the transition to a carbon-neutral energy society by promoting the circulation of ideas, information, and scientists in the area of energy research; expanding its basic science efforts; and proactively promoting the fusion of disciplines, including mathematics, sociology, and computational science, to create new research domains.

Shunichi Masuda (I²CNER)

International Institute for Integrative Sleep Medicine

Sound sleep for everyone in the world ~ Solving the mystery of sleep ~

We spend nearly one-third of our lives asleep. Although sleep is a quite common phenomenon in vertebrates including human beings and other animals, it still remains one of the greatest mysteries in today's neuroscience. Masashi Yanagisawa's discovery of neuropeptide "orexin," which plays important roles in sleep/wake regulation, opened a new era of sleep science, and led to the elucidation of neural circuits and neurotransmitters controlling sleep/wakefulness. However, there are two major and important questions unanswered; why do we sleep, and what are fundamental mechanisms that regulate sleep/wakefulness (i.e. what is "sleepiness")?
IIIS, a unique world-premier institute specialized in the fundamental studies on sleep medicine, was established to uncover the mystery of sleep, and to develop therapeutic means for sleep disorders and associated metabolic syndromes and/or mental disorders.

■ Research Center's Information (FY 2015)

Center Director: Masashi Yanagisawa
Principal Investigators (PI): 22 (including 8 overseas researchers and 2 female researchers)
Other Researchers: 29 (including 10 overseas researchers and 13 female researchers)
Research Support Staff: 11
Administrative Division:
 Administrative Director: Toshio Kokubo
 Administrative Staff: 17 (percentage of bilingual staff:71%)
Satellites and Cooperative Organizations: University of Texas Southwestern Medical Center, USA; University of California, Berkeley, USA; Akita University, Japan; RIKEN Brain Science Institute, Japan; Japan Aerospace Exploration Agency (JAXA), Japan; Kyoto University, Japan; and others
URL: http://wpi-iiis.tsukuba.ac.jp/

IIIS
INTERNATIONAL INSTITUTE FOR INTEGRATIVE SLEEP MEDICINE

Major Research Achievements

1 Discovery of genes regulating sleep/wake network

Yanagisawa/Funato laboratory discovered mouse mutations affecting sleep/wake, and identified responsible genes. This will be a huge first step to uncover the entire signaling network of sleep/wake regulation, potentially leading to diagnostic and therapeutic targets for sleep disorders and related diseases.

2 Development of the orexin receptor agonist

Nagase's group developed a compound that acts as orexin receptor agonist, which significantly induces wakefulness and ameliorates narcoleptic symptoms in model mice. This finding holds intriguing implications for developing remedies for the sleep disorder.

3 Why do we dream? Exploring the role of REM sleep

Hayashi and his colleagues identified the brain region switching REM/NREM sleep, and developed a transgenic mouse whose REM sleep can be manipulated arbitrarily. They found that REM sleep enhances the slow wave during NREM sleep, which is important for memory formation and restoration of brain function.

4 The 'pacemaker' cells for the circadian rhythm

Researchers identified specific neurons that function as pacemakers of the circadian rhythm in the suprachiasmatic nucleus (SCN). Those neurons play an important role in synchronizing the circadian rhythm via the intercellular neurotransmission.

5 Discovery of a novel neural network connecting wakefulness and memory regulation

Greene *et al.* revealed that dopamine released from neurons in the locus coeruleus (LC) plays an important role in the hippocampus in memory retention. LC is known to control wakefulness, and found to be important for regulating memory as well.

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Background: Large-scale sleep recording system for mice

Sleep is an essential behavior that everyone experiences everyday and it takes up one-third of the entire lifetime. However, the very fundamental mechanisms of sleep still remain unknown. While underlying principles of sleep has been a complete black box, its medical and social importance is clear. Healthy, natural sleep is essential for maintaining our mind and body fitness, and lack of sleep causes severe economic loss every year. Masashi Yanagisawa (Director of IIIS) discovered a neuropeptide "orexin", which plays an important role in sleep/wake regulation, opened up the avenue of sleep science, and greatly contributed the development of sleep medicine. However, the questions of how is sleep/wake regulated, why two sleep phases – rapid eye movement (REM) sleep and deep NREM sleep – exist, what is the neural substrate for "sleepiness", and even why we have to sleep, remain unanswered.

International Institute for Integrative Sleep Medicine (IIIS) in University of Tsukuba, launched in 2012, focuses on sleep neurobiology and aim to solve one of the biggest black boxes of today's neuroscience. IIIS gathered prominent scientists globally from various research fields contributing to neurobiology of sleep, to elucidate the fundamental principles of sleep/wake regulation, and develop new strategies to diagnose and treat sleep disorders as well as closely associated metabolic /mental disorders.

1 Discovery of genes regulating sleep/wake network

Masashi Yanagisawa (PI), Hiromasa Funato (PI)

The principles of regulating sleep/wakefulness are still in a black box. Substantial mechanisms of 'sleepiness' in our brains or the mechanism to determine daily sleep amount are completely unknown. Yanagisawa/Funato laboratory has been tackling this great mystery by using forward genetic screening, in which researchers explore mutagenized animals showing characters or phenotypes of interests.

They scrutinized sleep behaviors by examining electroencephalogram (EEG) and electromyography (EMG) of more than 8,000 randomly mutagenized mice to seek for individuals with sleep/wake abnormalities, resulted in the discovery of two important gene mutations in two pedigrees: *Sleepy* and *Dreamless*. They found that *Sleepy* pedigree has a mutation in the Sik3 gene, whereas *Dreamless* pedigree has a mutation in the Nalcn gene.

SIK3 is a kinase and has a protein kinase A (PKA) phosphorylation site in the middle part, which is deleted in *Sleepy* mutant. This PKA phosphorylation site is well conserved in roundworm *C. elegans* and in fruit fly *D. melanogaster*, and also found to regulate sleep-like behaviors in those animals. It is quite interesting that the sleep-like behaviors of invertebrates are also regulated by the same molecular mechanism via SIK3 orhologues as in vertebrates. Sleep-deprived mice (i.e. mice with increased 'sleepiness') showed an increased phosphorylatation in the kinase domain, which regulates enzymatic activity of SIK3, suggesting that SIK3 comprises the intracellular signal transduction of 'sleepiness'.

NALCN is an ion channel, and one of amino acids in transmembrane region is changed due to the *Nalcn* mutation. The mutation causes increased ion conductance through the channel and increases the activity of REM sleep-terminating neurons in the brain stem, which leads to REM sleep reduction.

The *Sik3* and *Nalcn* genes have never been annotated with sleep behavior, and this milestone discovery will give a huge impact on future sleep studies. The researchers will be keen to elucidate intercellular signal transduction pathways involved in switching between wake and sleep or between REM sleep and NREM sleep, and the entire network of sleep/wake regulation.

Funato et al.: Nature 539: 378 , 2016.

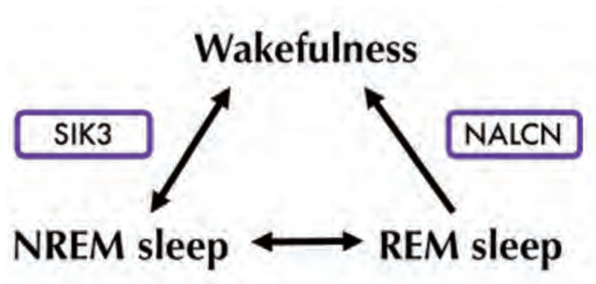


Fig. 1 Sleep states regulated by two proteins discovered in this study. SIK3 determines the amount of NREM sleep, whereas NALCN regulates the termination of REM sleep.

2 Development of the orexin receptor agonist regulating wakefulness

Hiroshi Nagase (PI), Masashi Yanagisawa (PI)

In 1998, Yanagisawa and his colleagues revealed that the neuropeptide orexin and its receptor play central roles in maintaining and stabilizing wakefulness, and their deficiencies in brain cause a serious sleep disorder narcolepsy, in which patients experience excessive daytime sleepiness that may occur at any time. The discoveries of orexin and its receptor promoted research for developing a new type of drug that specifically inhibits the receptor (i.e. antagonist). On the other hand, the development of a small molecule mimicking orexin (i.e. agonist), which promotes wakefulness and may potentially be useful as a therapeutic agent for narcolepsy, has been hampered by several technical reasons.

Hiroshi Nagase, a professor of IIIS, and his colleagues successfully developed a potent compound that promotes wakefulness and remedies narcolepsy in mouse models in collaboration with Yanagisawa. They screened more than 250 thousand compounds to discover multiple candidate molecules that show activities on type 2 orexin receptor, which plays an important role in regulating sleep/wakefulness. Through designs and syntheses of more than 2,000 derivatives from those candidates followed by pharmacological assays, they found key structures that are relevant to the agonistic activity. Further optimization resulted in a small compound named YNT-185, with high activity and selectivity on type 2 orexin receptor. Both intracerebroventicular and intraperitoneal administrations of this compound significantly induced wakefulness in mice, and also ameliorated narcoleptic symptoms in model mice. They are accelerating the research to obtain more potent compound, which will lead to the specific cure for narcolepsy through animal and clinical studies.

Nagahara T et al.: J. Med. Chem. 58(20): 7931, 2015.

3 Why do we dream? Exploring the role of REM sleep

Yu Hayashi (PI)

REM sleep, the phase where dreams occur, was found in more than 60 years ago, but its function was a long mystery. Since REM and NREM sleep are observed only in vertebrates and Aves, those two phases have been considered to be involved in higher brain functions. The amount of REM sleep increases during neonatal period and immediately after learning, though the role of REM sleep has been unknown due to the paucity of means to effectively inhibit REM sleep. Also, the neural basis of switching between REM and NREM sleep is largely unknown.

Yu Hayashi and his colleagues used genetic engineering techniques in mice to identify neural cells that play a central role in switching between REM and NREM sleep. They manipulated those cells with the cutting-edge technologies to increase/decrease the amount of REM sleep and analyzed the effects.

When REM sleep was genetically manipulated, a brain activity termed delta activity was affected during the subsequent NREM sleep. Delta wave, another phenomenon unique to vertebrates and Aves, is known to enhance synaptic plasticity and contribute to learning and memory formation. Delta waves appear most frequently during NREM sleep. In this study, they found that elongated or shortened REM sleep resulted in correspondingly larger or smaller delta waves in the following NREM sleep. These results suggest that

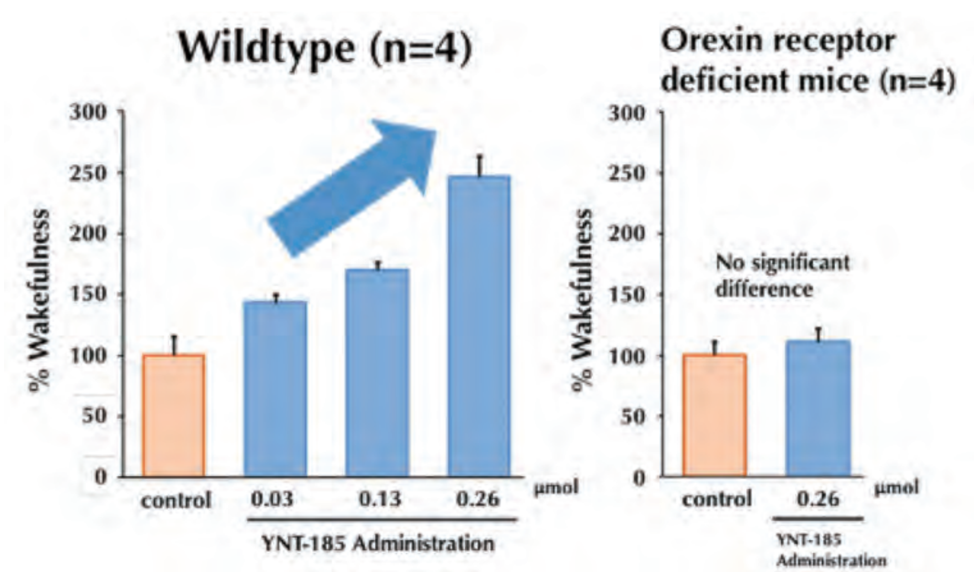


Fig. 2 YNT-185 increases the level of wakefulness in dose-dependent manner in wildtype mice, whereas no effects in orexin receptor deficient mice.

REM sleep enhances delta waves in the subsequent NREM sleep and it contributes to learning and memory consolidation.

They also succeeded in identifying neural progenitor cells in the fetus that postnatally become the neurons that function as the REM/NREM sleep switch. Interestingly, these progenitor cells not only generated neurons involved in REM/NREM sleep switching but also generated neurons involved in sleep/wake switching. This is the first discovery of a common developmental origin for cell governing switching between various brain states. It may further provide insights to how animals with REM sleep evolved from animals with more primitive sleep.

Hayashi Y et al.: Science 350(6263): 957, 2015.

4 The ‘pacemaker’ cells for the circadian rhythm

Masashi Yanagisawa (PI), Joseph Takahashi (PI)

Circadian rhythms, the 24-hour processes controlling sleep/wake cycles, are generated by the suprachiasmatic nucleus (SCN) in the hypothalamus of the brain. SCN controls biochemical, physiological and behavioral processes, and is regulated by feedback processes by multiple genes. SCN contains approximately 20,000 neurons secreting more than 100 neurotransmitters, neuropeptides, cytokines and growth factors, and these molecules are known to synchronize the length and phase of circadian rhythms. However, scientists have been unable to pinpoint which of those neurons are involved in time-keeping mechanisms.

Yanagisawa, Takahashi and their colleagues focused on a group of SCN neurons that express a neuropeptide, neuromedin S (NMS). By using cutting-edge genetic technologies in mice, they succeeded in constructing a system to reversibly manipulate circadian clocks of NMS-expressing neurons at arbitrary timing to remotely control their behavioral rhythms, and revealed that; (1) elongating period in NMS-producing neurons by overexpressing the molecular clock $Clock^{\Delta 19}$ lengthens periods of SCN- and behavioral circadian rhythms, (2) the loss of molecular clocks in NMS (*Bmal1*, *Per2*) causes losses of SCN- and behavioral rhythms, and (3) inhibition of neurotransmissions from NMS cells abolishes SCN and behavioral rhythms. Those results clearly suggest that NMS expressing neurons, which comprise about 40% of neurons in SCN, act as master pacemakers to regulate circadian clocks. The findings may offer molecular targets for the diagnosis and treatments of circadian dysfunction in the future.

Lee IT et al.: Neuron 85: 1086, 2015.

5 Discovery of a novel neural network connecting wakefulness and memory regulation

Robert W. Greene (PI)

Both in humans and animals, episodic-like memory is enhanced when something new or emotionally salient occurs shortly before or after memorizing (memory encoding). Dopaminergic neurons originating in the ventral tegmental area (VTA) are thought to play important roles in this process, called novelty effect.

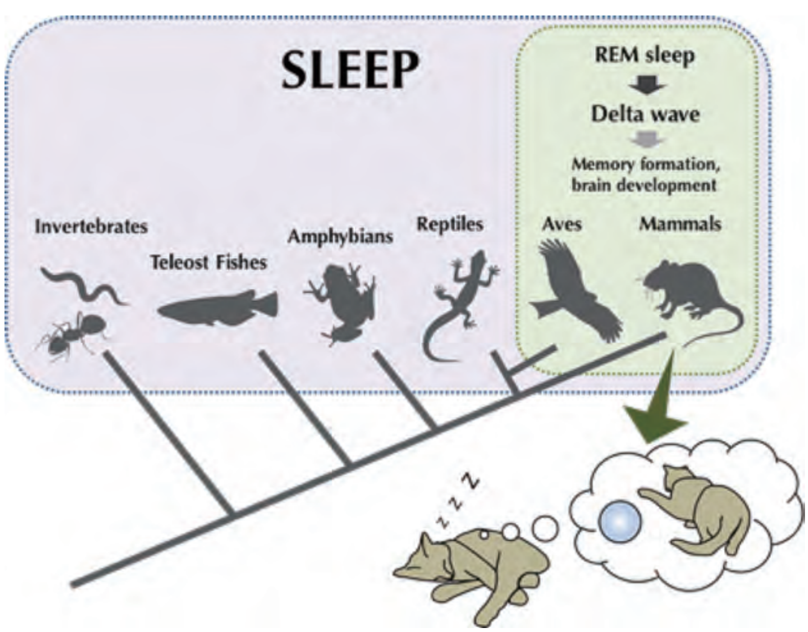


Fig. 3 REM sleep induces delta waves and thus may enhance memory consolidation, learning and brain development in vertebrates and Aves.

Dopamine and noradrenaline are monoamine neurotransmitters and both are biosynthesized from the same amino acid, tyrosine. Dopamine is a precursor of noradrenaline and essential for its biosynthesis. Tyrosine hydroxylase-positive (TH^+) neurons in locus coeruleus (LC) are thought to mainly release noradrenaline and regulate higher function (e.g. wakefulness) by projecting to various parts of brain from LC. This study showed that TH^+ neuron is not only noradrenergic but dopaminergic, and it also regulates memory by the projection to hippocampus.

Greene and his colleagues used memory task experiments and the technique to control activities of specific neurons with light (called optogenetics) and revealed that: (1) the firing of noradrenergic neurons in LC occurs in novel environment and dopamine is released, (2) noradrenergic neurons in LC project more densely to hippocampus than neurons in VTA, (3) optogenetic activation of noradrenergic neurons in LC mimics novelty effect, and (4) the blockade of VTA does not affect novelty effect-related memory enhancement.

Those results suggest that dopamine, released from noradrenergic neurons from LC, not VTA, mediates the enhancement of memory after encoding. Neurons in LC are long believed to be noradrenergic, but this study showed a new role as dopaminergic neurons projecting hippocampus. It is quite interesting that LC, which has been thought to play central roles in controlling wakefulness, also plays a critical role in regulating memory mediated by dopamine.

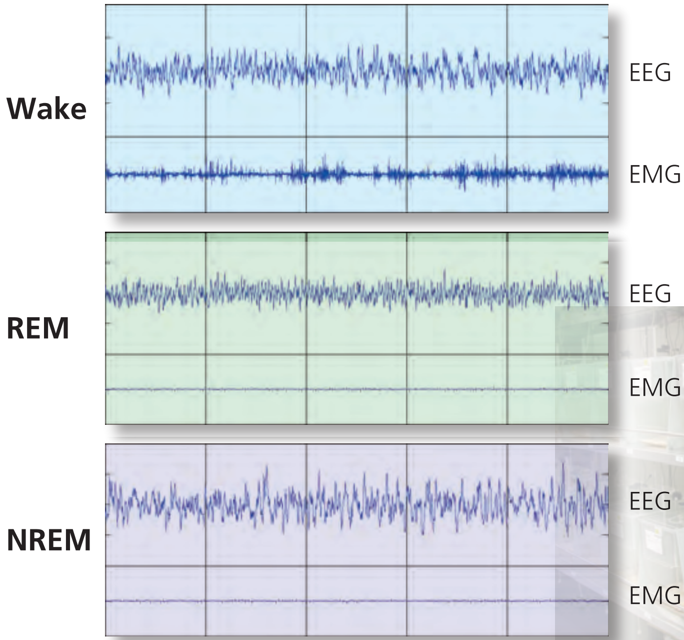
Takeuchi T et al.: Nature 537 (7620): 357, 2016.

Predominant Features of IIIS

Based on Yanagisawa's 20-plus-year experience at the University of Texas Southwestern Medical Center, IIIS has been challenging to establish the best and unique sleep research center in Japan, by learning from the merits of academic systems and organization in the U.S. "department" style. IIIS has accomplished a free and vigorous atmosphere pioneering traditional Japanese-style research organizations, in which flexible and timely appointment of independent PIs regardless of their age and career stage with necessary startup package, a flexible and dynamic allocation of floor space for each laboratory, and sharing of large facilities or capital equipment among laboratories.

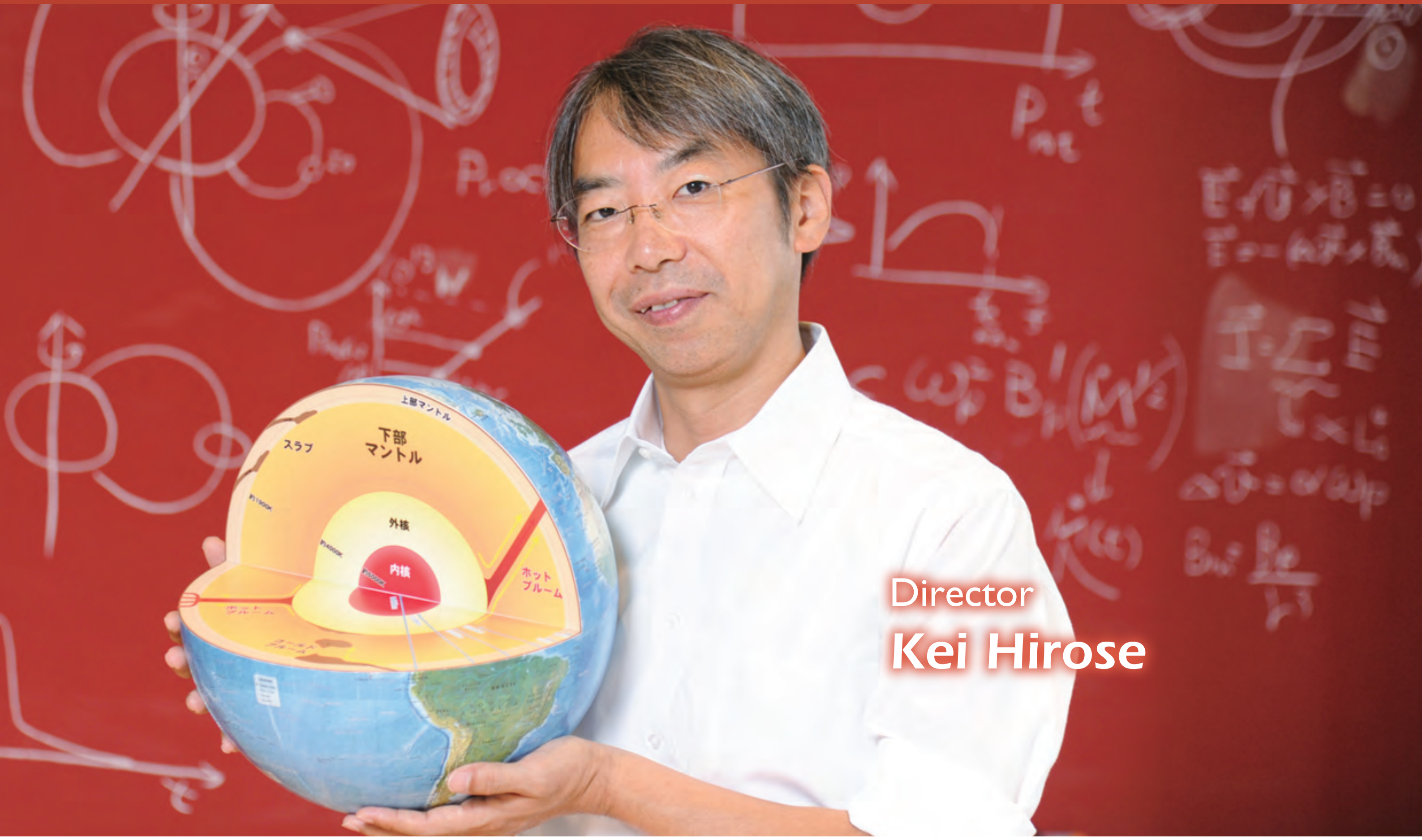
Following the concepts above, IIIS aims to establish a highly ambitious and novel research field, "sleep science", by integrating basic biology, experimental medicine and pharmaceutical science, under Yanagisawa's strong leadership as the driving force.

Masataka Sasabe (IIIS)



Representative EEG/EMG patterns for 3 sleep stages (left) and the sleep recording room implemented in IIIS Building (right).

Earth-Life Science Institute



Seeking to Discover the Origins of the Earth and Life

The Earth-Life Science Institute (ELSI) is a unique research institute that seeks to discover the "origins of the Earth and life" through an integrated interdisciplinary approach that brings together top-level domestic and international researchers in fields such as Earth science, life science, and planetary science. ELSI's research attempts to answer questions such as how the Earth formed in the solar system, how life originated on Earth, and how life and the Earth arrived at their present forms. Furthermore, ELSI also considers how life might exist in other planetary systems based on this understanding of how the Earth and life on Earth originated.

EARTH-LIFE SCIENCE INSTITUTE
TOKYO INSTITUTE OF TECHNOLOGY

Research Center's Information (FY 2015)

Center Director: Kei Hirose
Principal Investigators (PI): 17 (including 7 overseas researchers and 1 female researcher)
Other Researchers: 59 (including 20 overseas researchers and 17 female researchers)
Research Support Staff: 30
Administrative Division:
  Administrative Director: Motonori Hoshi (from FY 2016: Takashi Sakurai)
  Administrative Staff: 23 (percentage of bilingual staff: 91%)
Satellites and Cooperative Organizations: Ehime University, Japan; Japan Aerospace Exploration Agency (JAXA), Japan; Japan Agency for Marine-Earth Science and Technology (JAMSTEC), Japan; Princeton University, USA; Harvard University, USA; and others
URL: http://www.elsi.jp/en/

Major Research Achievements

1 Refinement of the giant-impact hypothesis that explains the formation of the Moon

It is currently believed that the Moon was formed after a proto-planet collided with the Earth. If the giant-impact hypothesis is correct, however, then why is the elemental composition of the Moon roughly the same as that of the Earth? This question can be resolved with advanced numerical simulations.

2 Water equivalent to 80 times the amount of water in today's oceans existed when the Earth was formed

High-pressure experiments on mantle material reveal that there must be large quantities of hydrogen in the Earth's core. Although the Earth gained a large amount of water during its formation (80 times the current amount of water in the oceans), the land surface was not fully submerged when life emerged on the Earth probably because most of this water had been absorbed by the core.

3 Inference of the synthesis of hydrocarbons on early Earth before life emerged

It has been discovered that the water of the hot springs in the Hakuba region of Nagano prefecture contains methane gas that was synthesized inorganically. These kinds of chemical reactions could have created organic compounds on the early Earth, which could have then led to the emergence of life.

4 Using computational chemistry to determine the optimal materials for creating life

Almost all living organisms on Earth use only 20 different amino acids. Computational chemistry can be used to decipher the reasons why these 20 variations were selected.

5 Searching for the origins of life by creating artificial cells

ELSI researchers have developed a technique for incorporating synthetic proteins into artificial membranes resembling cell membranes. Not only does this research help deepen our understanding of how actual cells function, it can also promote applications in fields such as medicine and industry.

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The background image shows Earth as viewed from outside the atmosphere (CGI).

Background and objectives of research

The Earth was formed approximately 4.6 billion years ago in a disk of gas and dust surrounding the primordial Sun. The collision between the Earth and another small planetary body that formed the Moon (giant impact) is believed to make the surface of the Earth covered with hot magma (magma ocean), which then gradually cooled.

The Earth and its life forms have been mutually influencing each other while continuously evolving. Over the course of 4.6 billion years of history on this planet, geomagnetism has been generated by the formation of the core, oxygen has been supplied due to the emergence of living organisms capable of photosynthesis, continents have formed and moved due to mantle convection, and the entire planet was once covered with ice (the Snowball Earth). These changes in the environment have greatly influenced the evolution of life.

Recent astronomical observations have shown that numerous planets exist in our universe with favorable conditions for life, just like Earth. The research into the origins of life on Earth is also the quest to discover whether or not life may exist elsewhere in the universe.

Life originated somewhere on the early Earth. Although the processes that resulted in life are still not clear, the basic sequence of events must have included the composition of organic substances from inorganic substances, polymerization of these substances into peptides, the formation of primordial RNA and cell membranes, and the subsequent generation of primitive life forms.

The Earth-Life Science Institute (ELSI) is a research institute that seeks to find answers to the following four questions that have challenged humanity over the ages (A, B, C, and D in Fig. 1).

A. Origin of the Earth: How was the Earth formed in the solar system, why does it have water, and what was the early atmosphere like? Important information can also be obtained by exploring asteroids and Mars by spacecraft.

B. Origin of Life on Earth: When, where, and how did life originate, and what were the genomes of early life like?

C. Evolution of the Earth and Life: How did changes in the planet Earth affect its ecosystem, how did changes in the solar system and nearby interstellar space affect Earth's environment, and why is there oxygen in the Earth's atmosphere?

D. Life in the Universe: Understanding the origins of the Earth and its life can shed light on the answers to questions such as how unique our planet is in the universe, and what steps should be taken in order to search for extraterrestrial life.

At ELSI, many researchers work closely together to achieve an integrated understanding of these four questions while deepening each researcher's own field of specialty. The main findings of this research are summarized below.

1 Refinement of the giant-impact hypothesis that explains the formation of the Moon

Shigeru Ida (PI)

The giant impact hypothesis, which claims that the Moon was formed by the ejected material from a collision between the Earth and a proto-planet of a similar mass to Mars, is gaining support. According to previous numerical simulations based on this hypothesis, the Moon was formed mostly from material from the proto-planet itself. Then the Earth and the colliding proto-planet should have had different compositions. However, both the Earth and the Moon have similar elemental isotopic ratios, and this has been a mystery. ELSI researchers worked at revising and improving the techniques used for these simulations and found that there were problems in the methods previously used to handle discontinuous boundaries between the Earth's core and mantle or its surface and outer space.

According to our giant impact simulations using a new numerical computation technique that can correctly handle discontinuity between the core and mantle, the proto-planet that collided with the Earth can be smaller

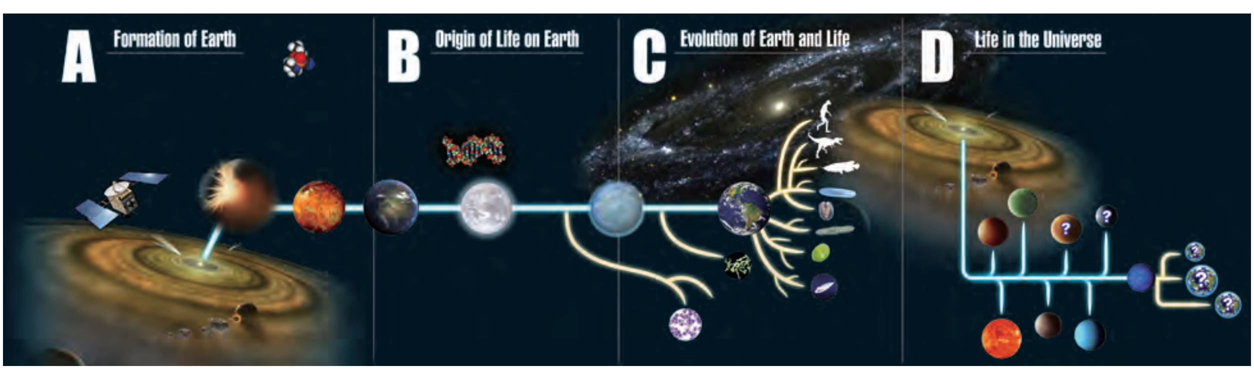

Fig. 1 Main research topics of ELSI.

than it was thought. The amount of material that was ejected from the Earth and went into forming the Moon can also be greater (see Fig. 2). This may explain why the elemental isotopic ratios of the Earth and the Moon are so similar.

Although our new computational technique still cannot perfectly handle the boundary between an astronomical body and the space outside, further development in the future will make it possible to attain clues regarding the origin of the Moon and also regarding the surface environment of the early Earth when life originated.

N. Hosono et al., Icarus; vol. 271, p.131, 2016

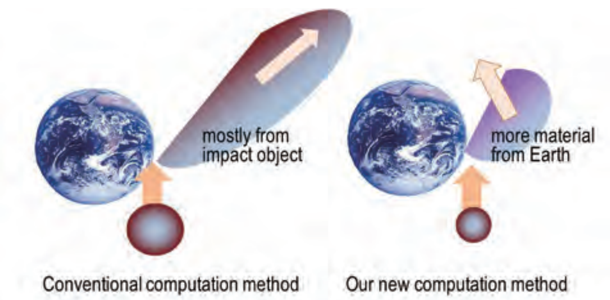

Fig. 2 Comparison between old and new giant impact simulations.

2 Water equivalent to 80 times the amount of water in Today's oceans existed when the Earth was formed

Kei Hirose (PI)

2,900 km below the surface of the Earth is the border between the mantle, which is comprised of rock, and the outer core, which is liquid comprised of iron alloy. Since the lower mantle is solid, its temperature must be cooler than the melting temperature of the mantle's material. The outer core, which is located just underneath the mantle, must also be cooler than this temperature in order for contacting mantle not to melt. On the other hand, the outer core temperature must be hotter than the melting temperature of the core's material. Since the melting temperature of iron alloy is highly dependent on its impurity composition, the temperature of the outer core places limitations on its possible chemical composition.

Fig. 3 Diamond anvil cell that reproduces an ultra-high pressure state

At SPring-8, a large synchrotron radiation facility of RIKEN, the researchers of ELSI have placed mantle material into a high-pressure, high-temperature environment (equivalent to what exists in the depths of the Earth at greater than one million atmospheres) in order to check for evidence of melting (see Fig.3). Through these experiments, ELSI's researchers discovered that the melting temperature of the mantle just above the core is at least 400°C cooler than previously estimated, at approximately 3,300°C.

The melting temperature of pure iron is approximately 3,900°C at the outermost portion of the core, but the melting temperature of the liquid part of the core (the outer core) is cooler than this by more than 600°C due to impurities. Therefore, the core must contain approximately 0.6% of hydrogen by weight. If this amount is converted to water, it implies that the Earth acquired a huge amount of water during its formation, equivalent to 1.6% of the planet's total mass (approximately 80 times the current amount of water in the oceans). This conclusion is also consistent with the recent theory about the formation of the solar system. The submergence of land by huge amounts of water can be avoided because this water sank below the surface and into the core.

For his series of accomplishments, including this research, Director Kei Hirose was awarded the Fujihara Award in 2016.

R. Nomura et al, Science; vol. 343, p.522, 2014

3 Inference of the synthesis of hydrocarbons on early Earth before life emerged

Ken Kurokawa (PI)

Hot spring environments including rock called serpentinite are one of the promising candidates for the origin of life. Only a trace amount of serpentinite is exposed on the surface of the Earth today, but this was the most common type of rock on the bottom of the

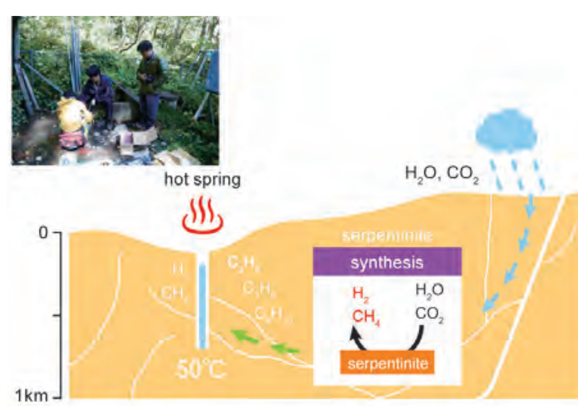

Fig. 4 Collecting samples from a hot spring in Hakuba (left); Schematic diagram showing hydrocarbon synthesis on the surface of serpentinite.

ocean immediately after the planet formed. This rock reacts with water, generating a highly concentrated hydrogen gas that may have produced the energy and organic compounds necessary to kick-start life. Hot springs with this kind of special environments are located in the Hakuba region of Nagano prefecture, and ELSI's researchers have been investigating these hot springs since 2010.

The gases from these hot springs, which have a temperature of approximately 50° C, include hydrogen, methane, and other hydrocarbons. Since methane (CH_4) contains about the same amount of deuterium as the water in the hot springs, the hydrocarbons in the hot springs must have been synthesized from the water there.

Research into these hot springs has shown how previously unknown inorganic chemical reactions could have synthesized the hydrocarbons from which life arose. Similar chemical reactions may have created organic material on early Earth, thereby leading to the origin of life. This is one of the findings of the Grant-in-Aid for Scientific Research on Innovative Areas project "Hadean Bioscience," which began in 2014 with Ken Kurokawa as the leader.

K. Suda et al, Earth and Planetary Science Letters; vol. 386, p.112, 2014

4 Using computational chemistry to determine the optimal materials for creating life

H. James Cleaves (Associate Professor)

In spite of the fact that the number of amino acids that exist in this world is extremely large, almost all living organisms on Earth use only 20 of them. Why were these 20 types selected?

In order to answer this question, ELSI researchers computed trillions of different possible amino acid structures comprised of the five elements that form amino acids (carbon, hydrogen, oxygen, nitrogen and sulfur). The researchers entered these combinations into a database, and then narrowed down to approximately 2,000 candidate amino acids that can exist in a stable form in the Earth's environment. There are 100 million ways of randomly selecting 20 different amino acids from this group, but there are only six other sets that can provide more diversity in generated proteins than the 20 amino acids used in living organisms. Furthermore, the 20 amino acids used in living organisms have the lowest energy requirement for their generation than the other six groups. In other words, the living organisms use these 20 amino acids due to their superior energy efficiency, implying that this is the result of natural selection.

Ilardo et al, Nature Scientific Reports; vol. 5, article no. 9414, 2015

5 Searching for the origins of life by creating artificial cells

Yutetsu Kuruma (Associate Professor)

Researchers around the world are trying to create artificial cells that self-replicate. One of the keys to accomplishing this task is the creation of an artificial cell membrane. A cell membrane is a lipid membrane that separates the interior of the cell from the outside world, with a variety of embedded protein molecules called "membrane proteins" that control the movement of material in and out of the cell.

ELSI's researchers and their partners have developed a protein synthesis system called "the PURE system." Its components are 36 different enzymes individually isolated from cells and purified ribosomes. They have used this system in a range of different applied research projects. For instance, they have succeeded in synthesizing membrane channels that can move proteins outside a cell, and incorporated these channels into artificial membranes. These achievements not only helped to deepen our understanding of the mechanisms working in the actual cells, but also they will lead to practical applications in medical and industrial fields.

H. Marubayashi et al, Angewandte Chemie; vol. 53, p.7535, 2014

Y. Kuruma & T. Ueda, Nature Protocol; vol. 10, p.1328, 2015

Research at ELSI satellites

Ehime University's Geodynamics Research Center (GRC) is conducting research as a satellite of ELSI, with approximately ten members including the Director, Professor Tetsuo Irifune. GRC's research into the Earth's deep interior complements the work of ELSI at Tokyo Institute of Technology which conducts ultra-high-pressure experiments of several million atmospheres. GRC, on the other hand, is more interested in high accuracy data by using samples of larger size under pressures of less than one million atmospheres. GRC also studies material properties under high temperature and pressure conditions that are not accessible in experiments, by performing the so-called "first-principle" calculation which is based on the fundamental principles of quantum mechanics. There is plenty of water on the Earth's surface, and some of the water is carried to the mantle in the form of hydrous minerals by plate subduction. Although such minerals were thought to reach the depth of at most 1,000 km into the mantle, GRC's researchers have shown that by phase transitioning to a newly discovered "phase-H state" of hydrous mineral, water may be transported even deeper. Starting in 2015, the Grant-in-Aid for Scientific Research on Innovative Areas project "Interaction and Coevolution of the Core and Mantle: Toward Integrated

Deep Earth Science" has been pushing forward even further with this research with GRC's Professor Taku Tsuchiya (affiliated researcher of ELSI) as the leader.

Professor Jack Szostak, 2009's recipient of the Nobel Prize in Physiology or Medicine and an authority in synthetic biology, is the leader of the ELSI satellite placed under the Harvard University Origins of Life Initiative, where he is conducting research together with ELSI's research scientist Albert Fahrenbach. In order to validate the hypothesis that an "RNA world" existed on Earth before cells appeared, this research project is exploring topics such as the conditions that would be required for RNA to efficiently replicate even without the existence of enzymes (enzymes are required for DNA to replicate).

The Princeton University satellite is located at the Institute for Advanced Study, and is being conducted under the leadership of the ELSI professor Piet Hut, who is an authority in astrophysics. In addition to astrophysics, this satellite is also pursuing a wide range of research topics including computer science and cognitive science.

Fusion and globalization in ELSI

Research institutes where scientists specializing in planetary science, earth science, and life science work together on a diverse range of research topics, such as the origins of the Earth and of life, are extremely rare throughout the world. Solving big problems like this will require new ideas. Therefore, ELSI does not have a hierarchical structure; all researchers are on an equal footing, no bosses. Communication between researchers is an important driving force for fusion between fields (see Fig. 5), and the ELSI buildings have open spaces called the Lounge and the Agora for exchanging ideas (see Fig. 6).

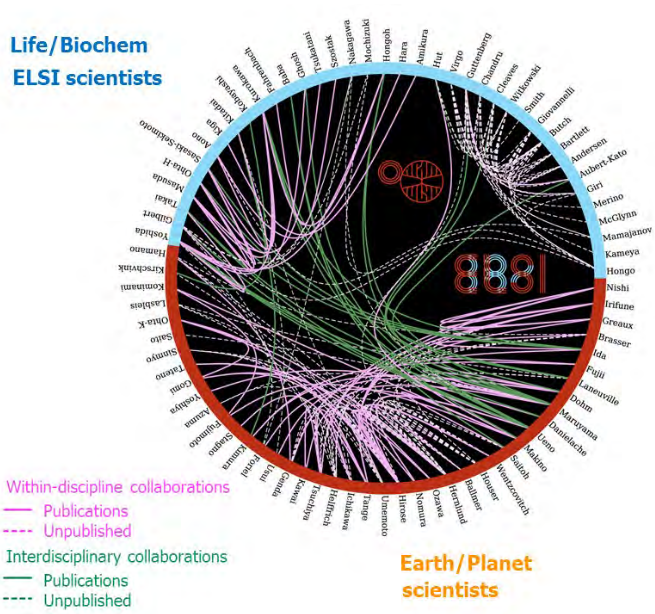

Fig. 5 Fusion in research on Earth and life sciences

Fig. 6 Discussion in front of a chalkboard in the Agora

Approximately 40% of ELSI's 70 researchers are from outside Japan, including seven principal investigators. Of these, geophysicist John Hernlund is a Vice Director who has brought in excellent researchers from overseas by e.g. advertising the institute at international conferences. As a result, ELSI is also well known internationally, and 90% of applicants to the open recruitment come from overseas. The astrophysicist Piet Hut is also the Head of the Program in Interdisciplinary Studies, Institute for Advanced Study, Princeton. Thanks to his activities in interdisciplinary sciences, ELSI was awarded funding of $5.5 million (approximately 670 million yen) from the John Templeton Foundation in the US for the period between July 2015 and March 2018. ELSI applied this funding toward the start of its EON project (ELSI Origins Network), which is aimed at strengthening and expanding a network that connects origins of life researchers from around the world, with ELSI acting as a hub. EON's budget is not being used to purchase equipment, but rather to hire young researchers, promote exchanges, and hold international workshops.

In order to create environments for research and everyday life that are as comfortable as possible for international researchers, a secretary is assigned to about every 10 researchers and provides with one-stop services (the same service is also offered for Japanese researchers). In the administrative office is a dedicated life adviser who provides support for immigration and local procedures. Japanese language lessons are also held on a weekly basis for international researchers. We hope that this comfortable research environment becomes widely known and attracts excellent researchers, thereby enhancing our international reputation.

Takashi Sakurai (ELSI)

Director
Kenichiro Itami

Change the world with molecules: Innovative interdisciplinary research between animal/plant biology and synthetic chemistry

The Institute of Transformative Bio-Molecules (ITbM) at Nagoya University is an international research center that creates a new research field through the integration of cutting-edge synthetic chemistry and animal/plant biology research. ITbM aims to develop molecules that change the way we live, i.e. "transformative bio-molecules", in order to "understand", "see", and "regulate" biological systems, and address urgent social issues on the environment, food production and medical technology.

ITbM Nagoya University

Research Center's Information (FY 2015)

Center Director: Kenichiro Itami
Principal Investigators (PI): 11 (including 4 overseas researchers and 2 female researchers)
Other Researchers: 54 (including 18 overseas researchers and 15 female researchers)
Research Support Staff: 34
Administrative Division:
  Administrative Director: Tsuyoshi Matsumoto
  Administrative Staff: 12 (percentage of bilingual staff: 50%)
Satellites and Cooperative Organizations: ETH-Zürich, Switzerland; Queen's University, Canada; University of Washington, USA; University of Southern California, USA; NSF Center for Selective C-H Functionalization, USA; RIKEN Center for Sustainable Resource Science, Japan; and others
URL: http://www.itbm.nagoya-u.ac.jp

Major Research Achievements

1 Development of molecules that promote plant growth

Succeeded in discovering that plant growth is controlled by the opening/closure of stomata. Solutions to environmental and food production issues are expected to be derived by improvement in plant growth through the development of molecules that can control the number and opening/closure of stomata.

2 Development of molecules to combat the parasitic plant *Striga*

Achieved the development and commercialization of a fluorescent molecule "Yoshimulactone", which acts as a tool to elucidate the parasitic mechanism of the parasitic plant *Striga* that causes huge damage to the agricultural production in Africa.

3 Development of molecules to control plant reproduction

Accomplished for the first time in identifying the structure and function of long-sought key molecules, "LURE" and "AMOR", which are involved in the reproduction of plants. This outcome may eventually lead to full elucidation of the mechanism of plant reproduction.

4 Development of molecules to regulate the circadian clock of animals and plants

Gained access to molecules that can control the biological clock rhythm, and identified highly active molecules through structure activity relationship studies. Regulation of the circadian clock in animals and plants is expected to lead to the improvement of food production and development of drugs to treat sleep disorders in humans.

5 Development of molecules to visualize biological systems

Established synthetic routes for highly photostable and environmentally responsive fluorescent dye molecules, which are essential tools for live cell imaging that can be used to elucidate the various mechanisms occurring in biological systems.

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Background image: Photo of leaves. Leaves contain stomata, which are small holes located on the surface that allow gas exchange.

Aim of ITbM

ITbM aims to create a new interdisciplinary field of research through the integration of forefront synthetic chemistry and animal/plant biology, as well to deliver bio-functional molecules that will greatly change the way we live, i.e. "transformative bio-molecules". Humans have generated various transformative bio-molecules up to now. Representative examples in the pharmaceutical field are the well-known antibiotic, *Penicillin*, and the anti-influenza drug, *Tamiflu*. At ITbM, chemists and animal/plant biologists achieve full collaboration by breaking the walls between their fields, and work together to develop molecules that can solve various social issues, including the environment and food production, as well as contribute to advances in medical technology.

1 Development of molecules that promote plant growth

Toshinori Kinoshita (PI), Keiko Torii (PI), Kenichiro Itami (PI)

Plants have stomata, which are small pores located on the surface of leaves that control gas exchange with the external environment. Stomata are the primary inlet and outlet for the uptake of carbon dioxide (CO_2) and transpiration of water, respectively. During the day, plants open their stomata (Fig. 1a) and absorb CO_2 from the atmosphere to carry out photosynthesis and create nutrients necessary for their growth. In addition, stomata are responsible for adjusting the water content in leaves, i.e. stomata close when the water content is low (Fig. 1b) to protect the plant from water loss. Stomata are also involved in the global water regulation, with data suggesting that all water in the atmosphere pass through the stomata every half-year.

As stomata are essential for plant growth, ITbM's researchers figured that by being able to control the number and opening/closure of stomata, they would be able to produce plants with drought resistance, increase plant growth and reduce the amount of CO_2, a greenhouse gas, from the atmosphere.

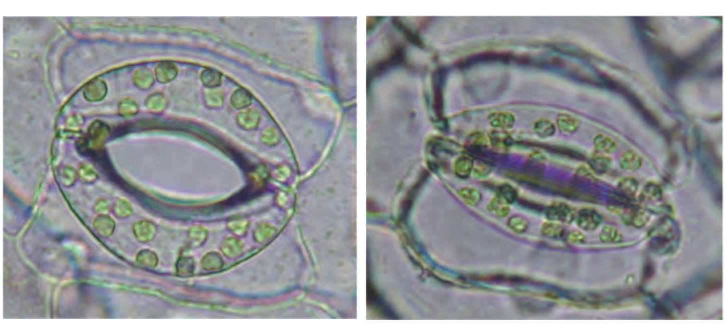


Fig. 1 Plant stomata in: (a) open state, (b) closed state

When the guard cells of the stomata are illuminated with sunlight, phototropins (photoreceptors) respond to the blue light and activate the plasma membrane proton pump (H^+-ATPase), eventually leading to stomatal opening. Using a model plant, *Arabidopsis thaliana*, plant biologists at ITbM have selectively increased the amount of H^+-ATPase in the guard cells of the stomata. In comparison to the wild type, the researchers found that this led to an approximately 25% and 15% increase in the amount of stomatal opening and CO_2 uptake (photosynthesis), respectively. As a result, a 1.4-1.6 times increase in plant weight was observed, thus indicating that the control of stomata was essential for plant growth.

ITbM aims to contribute towards solving food, energy and environmental issues by developing this technique to enable an increase in the production of food crops and plants for bio-fuels, as well as reduce the amount of CO_2 in the atmosphere with plants.

Y. Wang, et al: Proc. Nat. Acad. Sci. USA, 111, 533, 2014.

2 Development of molecules to combat the parasitic plant *Striga*

Toshinori Kinoshita (PI), Kenichiro Itami (PI), Takashi Ooi (PI)

Striga is a parasitic plant that causes drastic damage to agriculture in parts of Africa, Asia and Australia. This parasite is also known as witchweed from its beautiful purple-pink flowering (Fig. 2). *Striga* is a major threat for food crops, such as rice, corn and sugarcane as it infests the host crop plant through its roots by depriving them of their nutrients and water. The host plant eventually withers, leading to yield losses in approximately 40 million hectares of land, worth over 10 billion U.S. dollars, which affects over 100 million people. Therefore, an effective antidote for this situation is critical to ensure global food security.

Striga is known to detect host crop plants from a class of plant hormones called strigolactones, which are released by plants for their own growth. Yet, the full mechanism on how *Striga* detects strigolactones has been unclear up to now. Based on the hypothesis that *Striga* possesses a protein receptor to detect strigolactones, ITbM's chemists and biologists worked together to develop a molecule, "Yoshimulactone green (YLG)", which shows green fluorescence upon binding to a strigolactone receptor (Fig. 3). Using YLG, the research team was able to directly observe how the molecule interacts with the receptor during *Striga* germination by live cell imaging. The development of YLG was an interdisciplinary outcome that arose from 3 young researchers from ITbM, and the molecule was

Fig. 2 A crop field infested by *Striga*
(Photo by: Professor Abdel Gabar Babiker, Sudan University of Science and Technology)

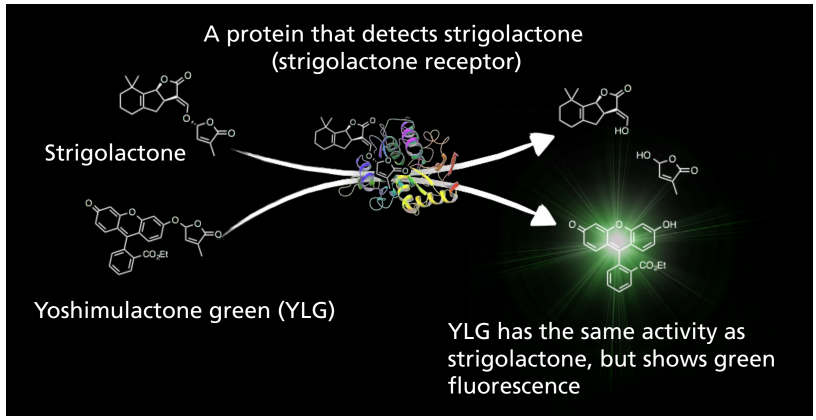


Fig. 3 Reaction mechanism of Yoshimulactone green (YLG): YLG exhibits a similar activity to strigolactone. Upon binding to a strigolactone receptor, the molecule is decomposed to release a molecule that shows green fluorescence.

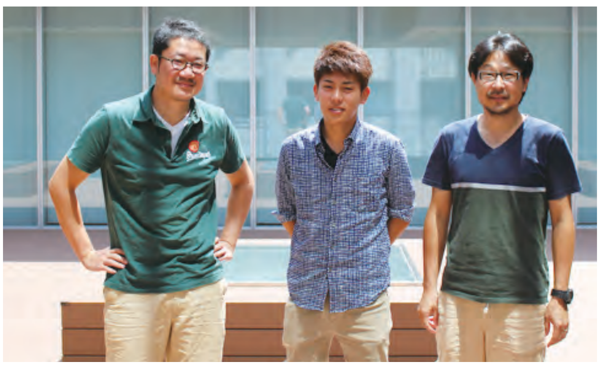


Fig. 4 YLG development team. From the left: Dr. Shinya Hagihara, Mr. Masahiko Yoshimura, Dr. Yuichiro Tsuchiya

named after the graduate student Masahiko Yoshimura, who designed and synthesized the molecule (Fig. 4).

The outcome of this research is an important step forward for elucidating the parasitic mechanism of *Striga*. YLG is now commercially available (from TCI Co., Ltd.) and can now be used by researchers around the world, which is expected to accelerate *Striga* research.

Y. Tsuchiya, et al: Science, 349, 864, 2015.

3 Development of molecules to control plant reproduction

Tetsuya Higashiyama (PI), Kenichiro Itami (PI), Jeffrey Bode (PI)

Rapeseed plants are known as the main ingredient for rapeseed oil and are essential for our daily life. Rapeseed originally occurred from the natural crossing of different species, and is a successful example of crossbreeding. However, most organisms have a barrier known as reproductive isolation in order to maintain their own species, which therefore makes fertilization between different species a rather difficult event. Clarification of the mechanism for reproductive isolation is considered as the key to bring about successful crossbreeding. In 2012, ITbM's plant biologists have shed light on this unresolved mystery of 140 years by identifying an attractant molecule, a "LURE" peptide, which is secreted from within the plant's ovule to attract the pollen tube. When pollen pollinates on the pistil, a pollen tube grows towards the ovule. The synergid cells located next to the egg cells within the ovule secrete LURE and guide the pollen tube towards it (Fig. 5). The pollen tube that reaches the synergid cell releases its sperm cells, which fertilizes the egg cells. The structure of LURE depends on the plant species and is known to have an important role in the conservation of species.

Moreover, ITbM's plant biologists have also found that ovules secrete a molecule that activates the pollen tubes for fertilization. The researchers named the molecule "AMOR", taken from the Latin word meaning "love" and "cupid", which brings together the female and male organs together. AMOR is a large glycoprotein, which contains a sugar chain characteristic for plants. Through the collaboration between biologists and chemists, ITbM's team chemically synthesized a disaccharide molecule containing two sugar units, which is similar to the two units located at the terminus

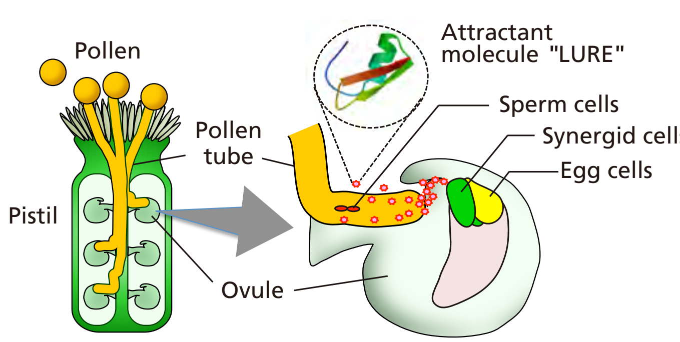


Fig. 5 Pollen tube guidance by the attractant molecule "LURE" in *Arabidopsis thaliana*.

of AMOR. Studies showed that this disaccharide exhibits the same properties as AMOR, and this key molecule is expected to be released soon on the market.

These discoveries are expected to increase the plant's fertilization efficiency and seed production, which may eventually lead to increased success in the crossbreeding of plants.

H. Takeuchi et al: Nature, 531, 245, 2016.
A. G. Mizukami et al: Curr. Biol., 26, 1091, 2016.

4 Development of molecules to regulate the circadian clock of animals and plants

Takashi Yoshimura (PI), Steve Kay (PI), Kenichiro Itami (PI), Stephan Irle (PI), Florence Tama (PI)

Our bodies contain a circadian clock, which regulates various daily rhythms, such as sleep/wake rhythm, hormone secretion, and metabolism. Disruption of the circadian rhythm may lead to sleep disorders, obesity, and other lifestyle diseases as well as mental disorders. Therefore, studies are being carried out to develop molecules that can control the circadian clock and relieve related disorders.

Based on the discovery of a period-lengthening molecule, KL001, by Kay's group in 2012, ITbM has carried out research to synthesize related molecules by synthetic chemistry and theoretical calculations. Through structure-activity relationship studies, ITbM's team succeeded in designing new molecules that show strong period-lengthening activity. These molecules are considered to act by targeting cryptochrome, which is a clock protein responsible for regulating the circadian clock.

This research is expected to lead to further understanding of disorders related to the circadian clock along with the development of potential treatments. In addition, the circadian clock has been reported to be the key factor for seasonal reproduction in animals, and application of this research towards the control of animal reproduction may lead to a potential increase in food production.

T. Oshima, et al: Angew. Chem. Int. Ed., 54, 7193, 2015.
J. W. Lee, et al: ChemMedChem, 10, 1489, 2015.

5 Development of molecules to visualize biological systems

Shigehiro Yamaguchi (PI), Tetsuya Higashiyama (PI), Cathleen Crudden (PI)

Bioimaging is an essential technique to study the localization and movement of molecules in living cells. Advances in the development of multipotent fluorescent dyes and super resolution microscopy have largely opened up the field of bioimaging. In particular, **st**imulated **e**mission **d**epletion (STED) microscopy (2014 Nobel Prize in Chemistry) has up to ten times higher resolution in living cells with respect to conventional microscopy. In addition, this technique enables nanoscale visualization of biological systems, such as organelles and proteins within cells, which has been difficult by previous techniques. Yet, the gradual degradation of fluorescent dyes bound to proteins, when exposed to the high intensity light necessary for super resolution microscopy has been a major obstacle for long-term observations.

To overcome this issue of reduced resolution in STED imaging due to photodegradation, ITbM's chemists and biologists developed a new fluorescent dye, "C-Naphox" that has enhanced photostability relative to conventional dyes (Fig. 6a). C-Naphox has demonstrated to be extremely photoresistant with almost no degradation of fluorescence even after prolonged STED imaging in live cells. Conventional fluorescent probes usually decompose after a few hours of irradiation, but the fluorescence of C-Naphox in HeLa cells persisted and remained unchanged even after 50 recordings under STED conditions.

The research team has also succeeded in developing a fluorescent molecule with a similar structure to C-Naphox that can change its color by detecting the polarity of the surrounding environment in biological systems. The dye molecule shows a color spectrum from red to green depending on the polarity of the organic solvent, in which it is dissolved in (Fig. 6b). Upon treatment of the cell with the dye, selective uptake of the dye by a lipid droplet is observed, and green emission is observed.

(a)
(b)

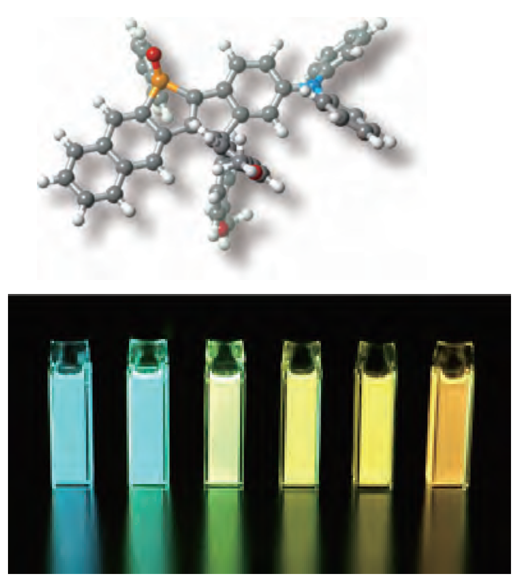


Fig. 6 (a) Structure of a new photostable fluorescent dye "C-Naphox"
(b) A fluorescent molecule that changes its color depending on solvent polarity

ITbM's chemists and biologists are working together to develop probe molecules and techniques applicable for STED microscopy. Some of the fluorescent probes developed at ITbM are commercially available as LipiDye, and their use in bioimaging is expected to accelerate biological research.

C. Wang et al: Angew. Chem. Int. Ed., 54, 15213, 2015.
E. Yamaguchi et al: Angew. Chem. Int. Ed., 54, 4539, 2015.

As a WPI center

Within 4 years since its establishment, ITbM has been generating a number of significant results from its interdisciplinary research. This is a result of an intensive collaboration between synthetic chemistry and animal/plant biology on top of the high caliber of each researcher. ITbM started under the call of the center director, where ITbM's PIs, who are rising stars in the fields of chemistry and biology, gathered in the same spirit. Driven by the need to integrate different disciplines, ITbM's researchers have come together to start new research projects and are sharing the excitement of integrative studies, which would have been difficult in a single research group or field alone.

ITbM's interdisciplinary research is greatly accelerated by ITbM's unique research environment called "Mix Labs" and "Mix Offices". These "Mix" spaces have been created to remove the walls between research groups and integrate researchers from different fields so that they can carry out research in the same space. ITbM's research center is built under this "Mix" concept. The effect of mixing has generated more results than initially expected, with the faculty, postdoctoral researchers, and graduate students forming their own research teams, proposing their original research projects and generating interdisciplinary research outcomes (Fig. 7).

ITbM has set up 4 sub-centers that promote ITbM's research: Molecular Structure Center, Chemical Library Center, Live Imaging Center and Peptide Protein Center. Each sub-center has a coordinator, who not only assists analytical measurements, but also actively participates in research projects to promote interdisciplinary research.

ITbM involves many researchers from overseas. Active exchange of researchers, especially graduate students, with overseas cooperative organizations, including USA, Canada, Switzerland and Germany, is being carried out. In addition, ITbM organizes many international meetings on a regular basis and hosts 3 international awards, 2 in organic chemistry (Nagoya Medal and Hirata Award) and 1 in biology (Tsuneko and Reiji Okazaki Award), which helps in building international networks.

Fig. 7 A fume hood in the Mix Lab for conducting chemistry experiments.

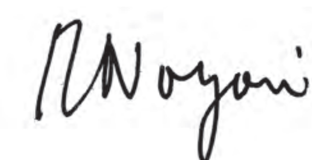
ITbM's Administrative Division also plays a role in promoting interdisciplinary research and international collaborations. ITbM provides support in English and help in the daily lives of overseas researchers. What makes ITbM different from the usual Japanese university administrative system is the presence of the Research Promotion Division and the Strategic Planning Division within the center. These 2 divisions consist of researchers with a background in ITbM's related fields (chemistry and biology), and provide seamless support for ITbM, through managing intellectual properties, help in presenting/exchanging research results, public relations and outreach, as well as social implementation of scientific outcomes.

ITbM's female scientists are receiving high recognition for their active performance, which is reflected in the number of awards and honors received by the faculty as well as graduate students. Nagoya University has been supportive for promoting female leaders, and provides nurseries and after-school care for children to create an environment for female researchers to be able to continue their research. These endeavors have been recognized by the international community, in which Nagoya University was selected as one of the ten leading global universities that lay out concrete commitments and begin charting their progress toward achieving gender parity (HeForShe IMPACT 10×10×10 University Parity Report). ITbM benefits from this environment and provides support for female scientists.

The outcomes and measures taken by ITbM are strongly supported by the WPI program and by Nagoya University. ITbM will continue its challenge in cutting edge research under this support and by the strong leadership of the center director.

Tsuyoshi Matsumoto (ITbM), Ayako Miyazaki (ITbM)

Further development of the WPI Program



Ryoji Noyori

Chairperson of
the Program Committee of
the World Premier International
Research Center Initiative

As is clear from the three Nobel Prizes in science won by Japanese researchers in recent years, individuals within Japan's science community are continuing to produce highly regarded research results, but this will not be adequate if Japan wishes to remain a powerful world leader.

Over the last decade, the WPI Program's aim has been to create optimal research centers of a global standard. This is because it is organizations with a strong presence that attract the world's best intellectuals, and the honing of skills that arise from competition between these people opens up new horizons in science. This in turn inspires subsequent generations, and encourages their growth and development. Happily, the program has proved successful in this regard, thanks to the commendable leadership of the directors of each of the WPI centers, the comprehensive support provided by the heads of host institutions, the able evaluation work of the Program Committee, which is composed of domestic and overseas experts, and above all, the unwavering resolve of the Ministry of Education, Culture, Sports, Science and Technology to work toward system reform.

Five WPI centers were accepted into the program in FY 2007: AIMR, IPMU, iCeMS, IFReC, and MANA. All five of the centers were able to meet the standards imposed by the WPI Program: World-leading research, creation of fusion areas, creation of an international research environment, and system reform of research organizations. In doing so they have built up WPI as a global brand. I^{2}CNER, the center accepted in FY 2010, is pursuing green innovation. Meanwhile, the three centers accepted in FY 2012—IIIS, ELSI, and ITbM—which were slightly smaller in scale, can also be said to have been successfully operated with clearly defined focuses, and they are expected to make further progress still. Based on their historical backgrounds, Japan's universities face conditions that make the pursuit of fusion research difficult. Research environments that are more liberating than those found in existing organizations were created at WPI centers, and, I am glad to say, they more closely resemble ideal research environments. That the centers have contributed to the creation of personal networks, with top-caliber personnel congregating in them, before spreading out across the world, is another fruit of the WPI Program. What is most important is that the knowledge and experience accumulated through the program is shared with all of Japan's universities and research institutions, thereby contributing to an enhancement of the overall standard in the country.

Nevertheless, we certainly must not rest on our laurels. Universities need to move with the times and society can change rapidly. Although the primary focus of the program is to advance basic scientific research, as hubs for the world's best minds, they will need to be sure to pioneer intellectual activities that are in step with the times.

The world is highly diverse. Contemporary society is driven by the domestic and international movement of people, and the activities of groups built around a particular purpose. Our aims are to enrich people's lives, create a safer country, and sustain civilized society. Creating new social values requires the integration of wide-ranging areas of knowledge and wisdom, and ensuring the diversity of personnel is therefore crucial. Ensuring the stable continuity of Japanese society requires the fostering of both international competitiveness and international cooperation, and we must participate proactively in "international brain circulation." How should we respond to the 2030 Agenda for Sustainable Development adopted by the U.N. General Assembly? Solving and alleviating the serious issues that threaten humanity, such as global warming, environmental degradation, increased risk from natural disasters, reduced "ecosystem services," depletion of energy resources, and infectious diseases, as well as Japan's massive public debt, declining childbirth rate, and ageing population, will require multifaceted wisdom, consensus building, and collaborative international efforts aimed at drafting and implementing concrete policies. In what ways can Japan's scientific community contribute to the solution of issues as diverse as these?

We are heading toward the second stage of the WPI Program. WPI centers need to look squarely at the overwhelming changes occurring in the world while operating as optimal research centers that Japan can be proud of. I would like all stakeholders to help identify issues, provide advice, and closely follow the future developments of the WPI Program.

World Premier International
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