

**3 . Research Center Project** (in English)

Host institution	Osaka University
Head of host institution	Toshio Hirano, Osaka University, President
Research center	Immunology Frontier Research Center
Center director	Shizuo Akira, Osaka University, Professor (WPI IFReC)
Chief center-project officer(in October 2007)	Shizuo Akira, Osaka University, Professor (WPI IFReC)
Project summary	<p>· Briefly describe the general plan of the project.</p> <p>We aim to unveil the whole picture of the dynamic immune system by integrating the methodologies of bio-imaging and bioinformatics into immunology. Thus, we shall make every effort to improve these methodologies to track more directly the behavior and communications of immune cells within live animals and to understand their collective or systematic behavior in response to non-self, such as pathogens and cancers. Based on these basic studies, we shall seek to develop new strategies for the prevention, diagnosis and treatment of various immune-related disorders and diseases. To this ultimate goal, we shall establish the Osaka University Immunology Frontier Research Center (IFReC) consisting of 25 - 30 world-class principal investigators together with domestic and overseas institutions that will function as satellites or partners. A research-supporting and administrative system will be established to provide a research environment of international standards where all of IFReC researchers can devote themselves to research.</p> <pre> graph TD     UP[University President] --&gt; D[Director]     DD[Deputy Directors] --- D     IARB[International Advisory Review Board] --- D     D --- MC[Management committee]     D --- BR[Board of Representative]     AD[Administrative Director] --- AO[Administrative office]     AD --- CRG[Core Research groups]     AD --- CF[Common Facilities]     AD --- CI[Cooperative Institutions]     AO --- RPMO[Research Planning and Management Office]     AO --- GAS[General Affairs Section]     AO --- AS[Accounting Section]     CRG --- IG[Immunology groups]     CRG --- IAG[Imaging groups]     CRG --- BFG[Bioinformatics groups]     CF --- CIF[Core Instrumentation Facility]     CF --- ARC[Animal Resource Center for Infectious Diseases]     CF --- NAO[Network Administration Office]     CI --- RICA[RCAI RIKEN; Institute for Frontier Medical Science, Kyoto University; National Institute of Biomedical Innovation, etc.]     </pre> <p>Major changes from initial project plan:</p> <p>- In our initial plan, bioinformatics was not emphasized. Over the first four years, a consensus has emerged within the organization that cutting-edge computational methods are indispensable to advance immunology and facilitate collaboration between immunology and imaging groups. This is reflected as a change made in the plan.</p>

	<p>- The research planning and management office has been established within the administrative office to cover a wide range of research supporting logistics to build a superb environment where all of IFReC researchers can devote themselves to research.</p>
<p>Mission statement and/or center's identity</p>	<ul style="list-style-type: none"> <li>· Briefly and clearly describe the mission statement and/or the project's identity as WPI center.</li> </ul> <p>IFReC aims to comprehensively understand immune dynamism. To this end, we shall integrate imaging and bioinformatics technologies with experimental biology in order to reveal spatio-temporal and/or the collective behavior of immune-related cells and molecules <i>in vivo</i>. This integrated approach will not only deepens our systematic understanding of the immune system but also facilitate basic research results to be targeted to medical applications through translational research. Thus, advancement in our understanding of basic immunology improves medical strategies for the body's defense against infectious diseases and cancers, and diagnosis and treatment of immune-related diseases.</p> <p>Along with these research efforts, we shall further improve the research administration system, which provides a research environment of international standard, where both domestic and overseas researchers can devote themselves to research.</p> <p>Through these endeavors, we shall establish the solid foundation for IFReC to be a truly internationally renowned research center.</p>
<p>(1) Research fields</p> <ul style="list-style-type: none"> <li>· Describe in simple words and phrases within one line the research field of the project.</li> </ul> <p>Immunology and Bioengineering</p> <ul style="list-style-type: none"> <li>· Choose relevant fields from among ①—⑦ below, specifying the interdisciplinary field(s) that the project addresses.</li> </ul> <p>①Biosciences, ②Chemistry, ③Material sciences, ④Electronics engineering and information sciences, ⑤Precision and mechanical engineering, ⑥Physics, ⑦Mathematics</p> <p>①Biosciences, ④Electronics engineering and information sciences, ⑤Precision and mechanical engineering</p> <ul style="list-style-type: none"> <li>· Describe the importance of the proposed research, including domestic and international R&amp;D trends in the field and Japan's advantages.</li> </ul> <p>Research on the immune system, which is composed of cells, tissues and organs to defend the body against invading microbial pathogens, is of fundamental importance in prevention, diagnosis and treatment of various immune-related disorders and diseases. Although numerous studies have focused on the identification of immune cells and their factors, it still remains unclear how they actually interact with each other <i>in vivo</i> in response to infections or in pathological conditions. Thus, it is of great and immediate importance to challenge such unsolved issues. Toward this end, it is necessary to develop new technologies that track immune responses, methods to artificially control immune responses by integrating imaging and informatics methodologies into immunology. This is nothing short of an attempt to make a breakthrough in traditional immunology. Immunology in Osaka University is internationally acclaimed in its highest quality. In addition, the University is also globally recognized as being among the foremost institutions regarding imaging and bioinformatics. Therefore, it is most pertinent to create a new research center for immunology in Osaka University where domestic and overseas researchers in those different disciplines come together to earnestly aim to achieve a "comprehensive understanding of immune mechanisms <i>in vivo</i>".</p> <ul style="list-style-type: none"> <li>· If centers in similar fields already exist in Japan or overseas, please list them.</li> </ul> <p>The National Institute of Allergy and Infectious Diseases, Bethesda, Maryland, USA</p>	
<p>(2) Research objectives</p> <ul style="list-style-type: none"> <li>· Describe in a clear and easy-to-understand manner the research objectives that the project seeks to achieve by the</li> </ul>	

end of the grant period. In describing the objectives, the following should be articulated in an easily understandable manner: What new domains are expected to be pioneered by fusing the target fields. In the process, what world-level scientific issues are sought to be resolved. What is the expected impact of the scientific advances to be achieved on society in the future.

We aim to Integrate imaging technology and bioinformatics into immunology to study the properties and functions of immune-related cells and molecules for a comprehensive understanding of immune dynamism. To date, research in immunology has been carried out mostly using *in vitro* methods, wherein immune cells are isolated from animals such as mice and individually examined using various methods of cell biology; similarly, immune-related molecules have traditionally been examined in isolation by biochemical and/or biophysical methods to reveal structure-function relationships. As a result of such studies, a number of immune cells and cytokines have been discovered, and signaling pathways in various immune responses have been outlined.

However, the immune system of a mouse or human is one composed of a large number of multiple cell types forming a complex network. Many of these cell types interact directly or indirectly through intermediary molecules such as cytokines. In addition, immune cells are generally in constant motion throughout the entire body interacting with many types of tissue. We will reveal the dynamics of this cellular and molecular network through the integration of biological, biochemical, and imaging data using information technology and complex systems simulations. This challenging endeavor is of importance not only to establish a new field of basic science but also to overcome various immune-related diseases. Furthermore, such developments will establish a solid foundation of medical immunology.

- Describe concretely the research plan to achieve these objectives.

#### <Research plan – General>

It is hardly possible to reach our ambitious goal of a “comprehensive understanding of immune dynamism” using an *in vitro* approach alone. Our alternative strategy is to examine and analyze immune cells and molecules *in vivo* as they naturally exist in a living organism. There already exist a number of *in vivo* methods; however, they are not yet as mature as the *in vitro*-based methods. Hence, one of our goals is to advance novel *in vivo* immunology methods. The first step in this process is to form fruitful collaborations between researchers with various theoretical and experimental backgrounds, and with proven experience in solving major problems in immunology. The collaborative spirit used to develop new *in vivo* methods is expected to generate not only breakthroughs in immunology, but also to strengthen more basic disciplines such as physics, chemistry, and information technology.

#### <Experimental and computational plans>

Well-armed with animal and instrumental facilities as described below (section 5), we will pursue:

- a) Selective visualization of multiple types of immune cells and molecules, hopefully simultaneous visualization and/or with good temporal resolution
- b) Non-invasive or at least side-effect free observation and measurements of cells and molecules
- c) Measurement of cellular activities and dynamics of immune-related substances in whole live animals
- d) Development of tools and expertise for processing, storing, and extracting useful information from large amounts of imaging and biological data
- e) Simulation and prediction of immune networks based on results obtained (as outlined above) both at the molecular and cellular levels

Three lines of innovation that are essential for experimental research to attain objectives a–c (above) are currently ongoing at IFRc:

- i) Improvement of techniques of optical microscopy: Attempts are being made to push the performance of instruments to their limits by modifying the hardware and to visualize the dynamics of cells in live animals and molecules in cells by using novel probes or reagents.
- ii) Development of probes suitable for “selective visualization of specific cells or molecules and to discriminate them from an ensemble of similar targets” and “detection of structural changes of immune-related molecules and organelles”.
- iii) Installment of cutting-edge instruments such as a Raman microscope and an advanced 11.7T MRI for minimally-invasive observations and measurements. These instruments will be customized in hardware and software for improvement of their performance by experienced researchers, so as to optimize the technologies for immunology-based research purposes

and/or experimental subjects.

In addition to on-going projects in bioinformatics groups (structure/function prediction of proteins involved in immune responses; simulation of signal transduction cascades and transcriptional regulatory network in immune cells; and advanced data processing for imaging), we have set two objectives for information processing and systems-oriented studies:

- i) Improvement of computational facilities for the flow and availability of data from the imaging, informatics and immunology groups;
- ii) Reinforcement of human resources of computational research both in qualitative and quantitative aspects.

#### **<Plans for Medical Immunology through Translational research>**

Since IFReC was launched in 2007, we have been well aware that the center is highly expected to contribute to improvements in society's health by clinical application of inventions/discoveries made through basic research. Hence, several IFReC PIs have been recruited from the medical school of the University, and two of them have concurrent appointments with the University Hospital. Furthermore, two new laboratories specialized in human immunology and immune diseases were set up in 2010 (Coban, malaria immunology; Ishii, K., vaccine science).

In order to more aggressively accelerate clinically oriented research, IFReC will make several practical steps:

- a) Support to on-going collaborative projects of IFReC researchers with clinical researchers at the medical school of the University
  - Multimodal (CT/PET/MRI) morphological and functional imaging for diagnosis of various diseases
  - Clinical application of a cancer vaccine and development of new biologics to treat autoimmune diseases such as rheumatoid arthritis in collaboration with pharmaceutical companies.
- b) Support collaborations with other institutions
  - Development of strategies to control chronic inflammatory diseases through revealing how dendritic cell subsets exert their immunostimulatory functions (RIKEN RCAI)
  - Development of stem cell-based immunotherapy including mesenchymal stem cells and intestinal stem-like cells that could ameliorate inflammatory bowel diseases by preferentially inhibiting the production of inflammatory cytokines. (Seoul St. Mary's Hospital and POSTECH)

In addition to supporting these on-going or scheduled projects, IFReC encourages their researchers to set up new projects with clear prospects for medical immunology. To construct a better platform for this, IFReC is now preparing to:

- c) Establish a consortium for clinical medicine-oriented immunology composed of PIs belonging to the medical school of the University as its core members. This is to invite clinicians who are interested in deeper investigation of clinical samples which are routinely collected during the treatment of patients suffering from immune-related diseases. Plans include:
  - Opening a clinical sample collection center in the IFReC research building for researchers to use the collected samples. Using the samples, research projects will be scheduled to search for bio-markers of immunological disorders such as systemic lupus erythematosus, juvenile idiopathic arthritis, and polymyositis/Dermatomyositis and to analyze the proteins or gene expression of immune-regulatory molecules of peripheral blood mononuclear cells of such patients to find therapeutic targets.
  - Discussion forums for clinical immunology research; participants include clinicians from local hospitals as well as IFReC researchers.
- d) Propose a joint project search for therapeutic molecular targets for immunological disorders and cancers for the Health Labour Sciences Research Grants in collaboration with NIBIO.

### (3) Management

#### i) Center director

- Provide the name of the center director, his/her age (as of 1 April 2012), , specialties, and brief career profile(within 5 lines).

Name; Shizuo Akira

Age; 59

Specialties; Immunology

Profile; Ph. D., Osaka University, Graduate School of Medicine (1984)

Associate Professor, Institute for Molecular and Cellular Biology, Osaka University (1995)

Professor, Hyogo College of Medicine (1996-1999)

Professor, Research Institute for Microbial Diseases, Osaka University (1999-present)

Center director, Immunology Frontier Research Center, Osaka University (2007-present)

#### ii) Administrative director

- Provide the name of the administrative director, his/her age (as of 1 April 2012), and his/her brief career profile(within 5 lines).

Name; Takao Kodama

Age; 70

Profile; Ph.D., Nagoya University, Graduate School of Science (1970)

Associate Professor, Okayama University School of Dentistry (1981-1992)

Professor, Kyushu Institute of Technology (1992-2005)

Research Manager, Japan Science and Technology Agency (2005-2008)

Administrative director, Immunology Frontier Research Center, Osaka University (2009-present)

#### iii) Composition of administrative staff

- Concretely describe how the administrative staff is organized.

Dr Takao Kodama, who has a long career of scientific research as well as experience in research management and coordination, is in charge of the overall administration system of IFRc. The system is composed of three sections: the accounting section, the general affairs section and the research planning and management (RPM) office. Each of the former two sections is staffed with English-speaking personnel supervised by two senior staff with rich administrative experience in the University. The RPM office is headed by Dr Kodama, consisting of six PhD holders and several English-speaking personnel. The office is to make a research environment with smooth communication among researchers and support staff and close contact with the Administration Bureau of Osaka University by covering:

- (a) Organization of seminars and symposia
- (b) Outreach activities
- (c) Management of matters related to intellectual properties such as material transfer actions and management of matters relating to the health and safety at IFRc
- (d) Preparation of a database of information on external competitive research funds in English for overseas researchers' convenience. For each of these tasks, a person with a PhD has been assigned
- (e) Purchase procedures for instrumentation

#### iv) Decision-making system

- Concretely describe the center's decision-making system.

The center Director makes major decisions, to which the Administrative Director gives full support by acting as a coordinator among the deputy directors and by executing management actions through the reformed administrative office. The Administrative Director also acts as liaison between the director and trustees of the host institute and between IFRc and the MEXT/JSPS WPI office. Important matters such as annual budget and the appointment of PIs, or equivalent, are to be approved by the center management committee and the board of representatives.

v) Allocation of authority between the center director and the host institution's side

- Concretely describe how authority is allocated between the center director and the host institution's side.

The University president will approve the mid-to-long term plan of the center and the center director's decisions on major issues necessary for the center's management, such as researchers' salaries, appointment of new researchers and administrative director. The University president will appoint a director, determine the director's salary and evaluate the center's performance. In addition, the Center's Director, Deputy Directors, Administrative Director and Trustees and Vice Presidents of the University hold briefings as needed.

(4) Researchers and other center staffs, satellites, partner institutions

i) The "core" to be established within the host institution

a) Principal Investigators (full professors, associate professors or other researchers of comparable standing)

	Numbers		
	At beginning	At end of FY 2011	Final goal (Date: March, 2017)
Researchers from within the host institution	10	14	15
Foreign researchers invited from abroad	1	2	3
Researchers invited from other Japanese institutions	6	11	12
Total principal investigators	17	27	30

- Describe the concrete plan to achieve final staffing goal, including steps and timetables.
- Attach a list of principal investigators using the Appendix. Place an asterisk (\*) by names of the investigators considered to be ranked among the world's top researchers. Describe the policy and strategy for inviting the PIs who are to be included after 1 April 2012.

b) Total members

	Numbers		
	At beginning	At end of FY 2011	Final goal (Date: March, 2017)
Researchers	49 < 12, 24% >	173 < 53, 31% > [ 35, 20%]	180 < 61, 34% > [ 38, 21%]
Principal investigators	17 < 1, 6% >	27 < 6, 22% > [ 1, 4%]	30 < 8, 27% > [ 3, 10%]
Other researchers	32 < 11, 34% >	146 < 47, 32% > [ 34, 23%]	150 < 53, 35% > [ 35, 23%]
Research support staffs	28	61	50
Administrative staffs	9	29	30
Total number of people who form the "core" of the research center	86	263	260

- Enter the total number of people in the columns above. In the "Researchers" column, put the number and percentage of overseas researchers in the < > brackets and the number and percentage of female researchers in the [ ] brackets.
- Enter matters warranting special mention, such as concrete plans for achieving the Center's goals, established schedules for employing the main researchers, particularly principal investigators.

To increase the number of female principal investigators, IFReC is to:

- Invite more female speakers to IFReC-organized scientific meetings.
- Make and use a reservoir of female talented young researchers of international level, exploiting the fact that a number of young female students and post-doctoral fellows participated in the Winter School held in January, 2012, who had been selected among many contesting applicants (see page 9, Hold international research conferences).
- More aggressively publicize the University's support systems for gender equality in planning and promotion ((5). Research environment ○ Other measures to ensure that top-caliber researchers from around), which would be effective to terms of recruitment.

ii) Collaboration with other institutions

- If the "core" forms linkages with other institutions, domestic and/or foreign, by establishing satellite functions, Provide the name of the partner institution(s), and describe the role of the satellite functions, personnel composition and structure, and collaborative framework between the host institution and the said partner institutions (e.g., contracts to be concluded, scheme for resource transfer).

Domestic

- RIKEN Research Center for Allergy and Immunology
- Kyoto University, Institute for Frontier Medical Sciences
- The National Institute of Biomedical Innovation

- If some of the principal investigators will be stationed at satellites, attach a list of these principal investigators and the name of their satellite organizations using the Appendix.

Not applicable

- If the "core" forms organic linkages with other institutions, domestic and/or foreign, without establishing satellite functions, provide the names of the partner institutions and describe their roles and linkages within the center project.

Domestic

None

Overseas

- Institute for Systems Biology (Alan Aderem, Director) Seattle, USA
- Pohang University of Science and Technology (Inhwan Hwang, Chairman, Division of Life Science & Division of Integrative Bioscience and Biotechnology), Pohang, Korea
- Indian Institute of Science Education and Research (Vinod K Singh, Director), Bhopal, India
- The University of Auckland (P. Rod Dunbar, Director, Maurice Wilkins Center), Auckland, New Zealand
- The Catholic University of Korea Seoul St. Mary's Hospital (Tae-Kon Hwang. President). Seoul, Korea

Researchers in the center and these satellite/partner institutions will visit each other and exchange the information to upgrade the scientific standard of both sides. These interactions will provide an environment for the training of young immunologists and facilitate integration of different scientific disciplines.

( 5 ) Research Environment

- Concretely describe measures to be taken to satisfy each of the requirements outlined below, including steps and timetables.

- Provide an environment in which researchers can devote themselves exclusively to their research, by exempting them from other duties and providing them with adequate staff support to handle paperwork and other administrative functions.

As described above (3), the Research Planning and Management office headed by the Administrative Director deals with planning and logistics of scientific meetings, public information and liaison, and issues relating to intellectual properties, etc. Several PhD holders with research experience and bilingual staff have been posted. Together with general affairs and accounting sections, this office fully supports researchers so that they do not have to spend their time on paper work and other administrative functions.

- Provide startup research funding as necessary to ensure that top-caliber researchers invited to the center do not upon arrival lose momentum in vigorously pursuing their work out of concern over the need to apply immediately for competitive grants.

Each PI from abroad is allocated a start-up research fund for the first three years from the WPI's direct budget. To newly recruited PIs from domestic institutions, some amount of the fund is also given as a "set-up research fund". In order to facilitate a new era of immunology as well as making breakthroughs in related scientific disciplines, "The Research Support Program for Fusion of Different Fields" is available to young researchers. The program is to encourage them to challenge new but difficult project tasks, for which it would be otherwise hard to obtain financial support from outside sources. Start-up budgets (3 million yen per year for 3 years) are provided for each project. The projects are annually reviewed by IFReC PIs in a hearing open to all IFReC researchers.

- As a rule, fill postdoctoral positions through open international solicitations.

In principle, postdocs will be hired through advertisement of positions in major journals, such as Nature and Immunity, and the IFReC web-page.

- Establish English as the primary language for work-related communication, and appoint administrative personnel who can facilitate the use of English in the work process.

It is one of the IFReC's administration policies that at least two thirds of the total staff be bilingual, using English as the primary working language. In addition, there exists the Liaison Office as a virtual organization within the framework of the RPM office to support researchers from abroad in various aspects such as immigration matters, providing a living support service as well as bilingual notices, announcements and helping with grant applications.

- Adopt a rigorous system for evaluating research and a system of merit-based compensation. (For example, institute a merit-based annual salary system primarily for researchers from outside the host institution. As a basic rule, the salaries of researchers who were already employed at the host institution prior to the centers' establishment are to be paid by the host institution.)

The director will organize the International Scientific Advisory Board (ISAB) consisting of internationally renowned scientists in the fields of immunology, bio-imaging and bioinformatics. The Board will conduct an evaluation of the research groups' performance every other year. The center's Director will use the ISAB evaluation as reference material to determine PIs' salaries and their contract renewal.

Concerning the procedure for evaluation of other staff, standardized forms have been created specific to the position of the staff. Three forms have been generated to evaluate 1) the Specially Appointed Associate Professor/Assistant Professor/Lecturer; 2) Specially Appointed Researcher; and 3) the Technician/Administrative staff. Points of evaluation range from the work performance and other areas such as: the involvement in the laboratory; research management; achievements; application/acquisition of external funds; progress in combined research projects; and contribution to the WPI program. Points are relative to the staff's position. The evaluation data will be used as reference material to determine staff salaries and their contract renewal.

- Provide equipment and facilities, including laboratory space, appropriate to a top world-level research center.

About 50% of the space of the Integrated Life Science Building (ten-storey, 9,258 m<sup>2</sup>) constructed in 2009 are allocated for the use of IFReC. Located next to this building is the IFReC animal resource center (four-storey, 2482 m<sup>2</sup>; 5000 cages for 25,000 SPF mice, constructed in 2009) and the IFReC research building (nine-storey, 6,592 m<sup>2</sup>, constructed in 2011). The close proximity of these buildings will facilitate the interactions of IFReC researchers of various fields with each other, and further promote their collaborative research.

The facilities including the radio-isotope experimental station, core instrument facility and three animal resource centers that are distributed between both IFReC and the Research Institute of Microbial Diseases and made available to all members of both institutes. In order to better organize and manage these facilities, an associate professor and a few technicians are posted.

In addition, cutting-edge instruments such as a Raman microscope and an advanced 11.7T MRI for minimally-invasive observations and measurements have been installed at the expense of the



AKIRA project from the Funding Program for World-Leading Innovative R&D of Science and Technology budget. These instrument's hardware and software have been customized by experienced researchers to improve their performance so as to optimize the technologies for immunology-based research purposes and/or experimental subjects. Although use of appropriate probes would be sometimes required, we can expect to be able to track certain immune cells at the whole animal level (it is already possible at the tissue level) or molecules in a cell, and/or to directly measure cellular composition in immune cells.

A full list of all core equipment and facilities will be made available online to all members of staff in English and Japanese. All operational manuals will also be available in both Japanese and English.

- Hold international research conferences or symposiums regularly (at least once a year) to bring the world's leading researchers together at the center.

IFReC will organize international research conferences, workshops or symposia at least once a year. In addition, to provide a new educational and networking venue for young researchers all over the world, IFReC and SigN have reached an agreement to jointly organize a Winter School on Advanced Immunology every year. The school will be held annually, with the location alternating between Japan and Singapore.

- Other measures to ensure that top-caliber researchers from around the world can comfortably devote themselves to their research in a competitive international environment, if any.

Osaka University has established the Gender Equality Promotion Office to provide career support and encouragement for young scholars who will be next-generation researchers through the following:

- Implementation of a Research Supporter System to support female researchers who are having difficulty in securing time for research due to child birth, child-rearing, or nursing-care. This support is practiced by the University's Human Resource Bank that employs individuals who are studying at or have graduated from a graduate school in the same field and deploys these individuals as research assistants to researchers.
- Sharing information about research on gender equality through setting up a research network connecting in-campus faculty, staff at gender equality program divisions in local communities, gender equality promotion offices in companies and gender equality promotion offices at research institutions and universities throughout Japan.

The activities of this office will be expected to be beneficial for IFReC to increase the number of female PIs and junior researchers.

Referring to advice and suggestions given every year by the WPI working group and the program committee, the executive board of IFReC consisting of the center Director, Deputy Directors and Administrative Director make plans to improve the research environment for both domestic and overseas researchers.

#### (6) Indicators for evaluating a center's global standing

- Describe concretely the following points.

##### i) Criteria and methods to be used for evaluating the center's global standing in the subject field

- (a) Major contributions to main research areas: Are principal investigators of IFReC leading and advancing main research areas as major players in their respective fields?
- (b) Creation of new research areas: Are principal investigators of IFReC opening or creating new research areas in the corresponding fields?
- (c) Contribution to human welfare: Are there any accomplishments from this center, which have made great contributions to increase the quality of human life in various ways such as developing therapeutic or diagnostic means of diseases?

##### ii) Results of current assessment made using said criteria and methods

###### (a) Major contributions to main research areas:

Principal investigators of IFReC have been leading main research areas of the immunology field (Akira in research of innate immunity; Sakaguchi in research of regulatory T cells; Kishimoto in research of cytokines), which is obvious from the enormous number of citations of their papers. Yanagida is also a pioneer of the single molecule imaging. In addition to these original PIs, most of the PIs appointed from April 2008 onward can be regarded as leading researchers in their respective fields.

(b) Creation of new research areas:

The collaboration of immunology groups with imaging and bioinformatics groups has gradually started to visualize the movement of molecules or cells they are dealing with, and to analyze the vast data obtained from microarray experiments and whole genome sequencing since IFRcC was launched four years ago. To systematically enhance such collaborations, as a WPI center we introduced the "Research Support Program for Fusion of Different Fields" (2009). A total of 15 projects have been supported, a few of which have already been jointly published by different research groups and some others have reached the stage ready for publication. The program will be succeeded by the "Double Mentor Program" which is to encourage PhD students and young post-docs to engage in research projects jointly planned by senior researchers in different disciplines.

(c) Contribution to human welfare:

The development of an Anti-IL-6 receptor therapy for inflammatory diseases based on basic research by Kishimoto has been used in clinical practice and proved very effective. Hatazawa is a specialist of nuclear medicine and responsible for diagnostic imaging at the University Hospital. He has been developing an integrated PET/MRI system, which is to create a new fusion of morphological and functional imaging. This technology is expected to become a powerful diagnostic means for various diseases. We understand the importance of reinforcing the lines that allow for basic research to be translated in to that which may be of benefit to human welfare. In view of this, we recruited C. Coban (2010) and K. Ishii (2010) as PIs, who are specialists of Malaria immunology and vaccine science, respectively. We believe that their creative interaction with other IFRcC members will make a great step forward and contribution to human welfare.

iii) Goals to be achieved through the project (at time of final evaluation)

- (a) To establish methodologies to quantitatively examine structural, spatial and temporal properties of immune cells and molecules in vivo.
- (b) To simulate the dynamics of immune network systems, both at the cellular and whole body level, by combining the data thus obtained in order to present new paradigms for understanding the immune network.
- (c) To open a new vista for clinical immunology through translational development of the basic research results.

(7) Securing research funding

Future prospects

- Describe the concrete prospects for securing resources that match or exceed the project grant.
- Calculate the total amount of research funding (e.g., competitive funding) based on the percentage of time the researchers devote to research activities at the center vis-à-vis the total time they spend conducting research activities. Be sure the prospects are realistically based on the past record.

We have mainly obtained the following budgets other than WPI budgets in FY2011 and expect nearly the same amount will also be ensured after FY2012 onwards.

- 1) Competitive Research Grants obtained by researchers: 1.82 billion yen
- 2) Personnel expenses provided by management expenses grant of Osaka University to employ researchers who have concurrent positions at IFRcC and other department in the university: 217 million yen
- 3) Personnel expenses financed by Kishimoto Foundation Fellowships/Scholarships: 50 million yen

Others

- Describe activities and initiatives to be taken after project funding ends.

One possible initiative will be the integration of IFRcC and Osaka University International Research Center for Infectious Diseases (IRCID). Since IRCID is currently operating as a research center focusing on infectious diseases, it will functionally complement IFRcC. Meanwhile IFRcC has established good partnership with the Research Institute of Microbial Diseases (RIMD), the parent body of both centers, through the sharing of research facilities such as animal resource centers, the radio-isotope experimental station and the core instrumentation facility. Thus the new organization is expected to be capable of systematically conducting a wide range of research from basic to applied, such as molecular details in immune responses to vaccine development.

As described in "**5. Host Institution's Commitment**", Osaka university has concluded collaborative agreements with the National Institute of Information and Communications Technology (NICT) and

with Riken. Based on these agreements, two research centers, the Center for Information and Neural Networks (CiNeT) of NICT and the Quantitative Biology Center (QBiC) of RIKEN have been opened near IFReC. Professor Yanagida, an IFReC Deputy Director, has been appointed as the director of both centers. Technologies and methodologies of both centers are rather similar to those of IFReC, so collaborations with these centers will be made in due course and helping IFReC to advance interdisciplinary research necessary for initiating a new era of immunology. If both institutions function together closely and systematically with the IFReC/RIMD complex, an integrated life science center of global significance and presence could be established at Osaka University.

- Describe expected ripple effects (e.g., how the research center project will have trailblazing components that can be referred to by other departments in the host institution and/or other research institutions when attempting to build their own top world-level research centers).

If the collaboration of IFReC with CiNeT and QBiC is successful in integration of immunology with cutting edge-technologies of bio-imaging and bioinformatics, momentum would rise in researchers of other bioscience-related departments of Osaka University, as the University is among the foremost institutions regarding cutting-edge technologies including Raman spectroscopy, electron microscopy, atomic force microscopy, etc.

- Describe other important measures to be taken in creating a world premier international research center, if any.

As it is obvious that the whole environment should be favorable for IFReC to become a WPI center, in particular, for integration of different research fields, we are expecting the University to make the effort to:

- (a) Support world class research development at CiNeT and QBiC
- (b) Facilitate industry-academia collaboration by research teams at the Techno Alliance center to produce outcomes that meet social expectations