FY 2009 WPI Project Progress Report
World Premier International Research Center (WPI) Initiative

Host Institution	Osaka University	Host Institution Head	Kiyokazu Washida
Research Center	Osaka University Immunology Frontier Research Center	Center Director	Shizuo Akira

Summary of center project progress

In order to promote the WPI Immunology Frontier Research Center (IFReC) as an internationally recognized research institution, we took ambitious steps in 2009. These include: construction of a common work space and animal resource center; increasing the number of foreign researchers and improving facilities and support staff for all researchers; promotion of fusion between immunology, imaging, and informatics groups. These efforts have paid off in terms of world-class awards and publications. IFReC staff members at all levels will continue to make their best efforts with generous support from the host institution, Osaka University.

1. A common work space

The Integrated Life Science Building was completed in July, and 9 laboratories from different sites have gathered in one place. A new animal resource center is also in operation as of January, 2010. In addition, the construction of a new 9-story building has been approved in the FY2009 supplementary budget of the Japanese government. It will be completed by the end of FY2010.

2. Recruitment of new Principal Investigators

Dr Kazuya Kikuchi, an expert in the design of unique probes capable of visualizing live immune cells, joined the imaging group in August. Dr Diego Miranda-Saavedra, specialist in computational genomics and Bioinformatics, joined IFReC in January, 2010. They are expected to strengthen basic research, as well as promote fusion between different immunology, imaging, and informatics groups.

3. Further internationalization

We established the Junior PI Program for young research scientists, and we employed Dr Nicholas Isaac Smith and Dr Cevayir Coban. A Fellowship/Scholarship program has been set up with generous support by the Kishimoto Foundation for researchers and students from abroad. We organized or co-organized 5 international symposia (2 overseas meetings) and are planning to hold 2 symposia in the next fiscal year. We formed an Academic Cooperation Agreement with Pohang University of Science and Technology (POSTECH) and Indian Institute of Science Education and Research (IISER). The percentage of foreign researchers reached 31.1% as of the end of March 2010.

4. Promotion of fusion between immunology, imaging and bioinformatics

We launched the Research Support Program for Fusion of Different Fields to encourage young researchers from different backgrounds to collaborate with each other. Nine projects have been funded. Interactive seminars among research groups are held frequently, noteworthy of which are a series of Imaging-Immunology seminars organized by Drs Ishii and Fujii.

5. Improvement in research support system

The Research Planning and Management Office was established to strengthen relationships with researchers and research institutions abroad. Several international workshops were organized, and foreign researchers were recruited.

6. Major awards

Professor Akira was nominated as a foreign associate of the National Academy of Science of America, and designated as a Person of Cultural Merit. Professors Kishimoto and Hirano won the Crafoord Prize 2009. Professor Sakaguchi received a Purple Ribbon Medal.

7. High-impact publications

In 2009, IFReC scientists produced 154 papers, of which 13 were published in high-impact journals, further raising our global awareness: Cell (2), Nature (2), Nature Immunology (1), Nature Chemical Biology (1), The Journal of Experimental Medicine (4), Immunity (3).

8. Acquisition of external competitive funds

Support for IFReC research has also been obtained from the Funding Program for World-Leading Innovative R&D on Science and Technology (Professor Akira), JST-CREST (Professors Arase and Kurosaki), JST-PRESTO (Dr Smith) and MEXT Grants-in-Aid for Scientific Research (Drs Standley, Coban and Smith).

1. Summary of center project

<Initial plan>

General plan of the project

The aim of this project is to unveil the whole picture of a dynamic immune system by employing a variety of imaging techniques to visualize immune cells within live animals. We will also improve imaging technology, which allows us to track the dynamic behavior of immune cells and their interactions directly, and understand how immune cells respond to threats, such as those presented by pathogens and cancers in vivo. Based on these basic studies, we will develop new strategies for diagnosis and treatment of various diseases including infectious diseases, autoimmune diseases, allergy and cancer. To this end, we will invite 10-20 world-class principal investigators to Osaka University Immunology Frontier Research Center as core scientists in the project, and further expand by forming links with domestic and overseas institutions.

<Results/progress/alternations from initial plan>

The initial plan has not been changed, while we are making steady progress toward our ultimate goal.

1. **Internationalization**
   The percentage of foreign researchers at all levels reached 31.1% as of the end of March 2010. (42 non-Japanese out of all researchers of 135). This is a major increase compared with 15% in April, 2009. It should be pointed out that some non-Japanese researchers have successfully obtained competitive research funds from outside sources. Meanwhile, we have set up the Kishimoto Fund Fellowships / Scholarships to support foreign researchers and students for short or long stays at IFReC to promote future collaborations. In addition to two satellite institutions and seven partner institutions, we concluded an Academic Cooperation Agreement with Pohang University of Science and Technology (POSTECH) and Indian Institute of Science Education and Research (IISER) to exchange scientific staff. Thus, we can expect further increases in foreign researchers in 2010.

2. **Fusion of different scientific disciplines**
   We established a Support Program for Fusion of Different Fields, which is not only to support pre-existing collaborative projects (there were actually some as introduced at the last site-visit in February, 2009) but also to encourage young researchers to challenge new but difficult projects tasks, for which it would be otherwise hard to obtain financial support from outside sources. Nine projects are now running, which are expected to facilitate opening a new era of immunology as well as making breakthroughs in respective disciplines.

3. **Widening research scope to include bioinformatics**
   The Bioinformatics Group in 2008 proved to be effective in clarifying immune responses by utilizing genetic information, structural modeling, and systems-level analysis. In view of this, we will reinforce the Bioinformatics Group by employing a new PI (Dr Diego Miranda-Saavedra), who will clarify transcriptional networks in immune cells by collaborating with experimental immunologists at IFReC. He also will enhance and extend the work on characterizing kinases involved in host-pathogen interactions.

2. Research fields

<Initial plan>	<Results/progress/alternations from initial plan>
Name of the research field of the project Immunology and Bioengineering Relevant fields Biosciences, Precision and mechanical engineering Importance of the proposed research, including domestic and international R&D trends in the field and Japan's advantages The research on immune system, which is the host defense mechanism against external and internal threats, is therapeutically essential with regard to treating various diseases (infectious disease, allergy, inflammation, autoimmune disease, and immunodeficiency, etc.) in which the immune system takes part. Although numerous studies have focused on identification of cells and factors involved in the immune system, it still remains unclear how immune cells actually change in response to infections or in pathological conditions in vivo. Thus, it will be necessary to develop new imaging technology that tracks immune responses as well as a method to artificially control the immune response in the future. In foreign countries, unification of research on immunology and imaging technology has already started. However, both fields are still isolated and it has not become well integrated in Japan. Basic research on both immunology and imaging in Japan, especially Osaka University, is internationally at a very high level. Therefore, the first step to overcome the above-mentioned diseases is to establish a research center for immunology and imaging in Osaka University where domestic and overseas researchers can gather. Similar fields already exist in Japan or overseas Basel Institute for Immunology, Basel, Switzerland (1971-2001)	Name of the research field of the project Immunology, Bioengineering and Bioinformatics Relevant fields There are no alterations from the initial plan Importance of the proposed research, including domestic and international R&D trends in the field and Japan's advantages There are no alterations from the initial plan Similar fields already exist in Japan or overseas There are no alterations from the initial plan

3. Research objectives

<Initial plan>	<Results/progress/alternations from initial plan>
Research objectives that the project seeks to achieve by the end of the grant period (in 10 years) Explore the technology of in vivo imaging of immune system. We aim to develop a new technology for visualization of immune cells in vivo through the merging of the two fields of immunology and bioengineering. This technology will enable us to understand the dynamics of immune	Research objectives that the project seeks to achieve by the end of the grant period (in 10 years) and Research plan to achieve the objectives, and any related past achievements by the host institution

system in normal and pathological conditions. New findings obtained through imaging of immune reactions will lead to development of new strategies for diagnosis and treatment for various immune diseases including autoimmune diseases, immunodeficiency, allergy and inflammation as well as for development of vaccines for pathogens and tumors. Research plan to achieve the objectives, and any related past achievements by the host institution We will attempt to develop new technology that can visualize the dynamics of the immune system at the level of one living cell. To this end, we will extensively invite world-class researchers in the fields of immunology and imaging. Through mutual interactions of both fields of researchers, we will attempt to design new probes suitable for MRI and multi-photon microscopy that can track one immune cell in vivo. We will apply those probes to visualize how immune cells respond to antigens and how immune cells behave in the pathological conditions like autoimmune diseases, allergy and inflammation. Based on the knowledge which we will obtain with this system, we will establish a new paradigm of in vivo immune response and apply the new theory for treatments of immune-related diseases. Notably, Osaka University is famous for immunology, especially innate and adaptive immunity and cytokine network that have been originally discovered by and extensively studied in this university. Osaka University has also conducted world-class research in the field of engineering. There is merit to perform collaborative work between immunologists and engineers as well as to invite researchers domestic and from overseas. Moreover, Osaka University has an MRI/NMR system (11.7T) with high resolution that is rarely housed in other laboratories of Japan, and which is indispensable for achieving our project.	Although there are no fundamental alterations from initial plan, we made minor revisions in order to enhance research in Bioinformatics. Extensive efforts have been made to form a unified, comprehensive, and dynamic view of immune mechanisms, from innate to acquired immunity. Toward this scientific goal, we are integrating methodologies from bioinformatics as well as cutting-edge imaging techniques with immunological research. Based on early successes in immunology-bioinformatics collaborative projects, we have decided to expand the number of bioinformatics gropes. We are confident that this effort will lead us to the identification of new biomolecules and their interactions. In addition, bioinformatics researchers are also collaborating with imaging groups to improve image processing techniques. Such basic work will enable us to control the immune system as a whole as well as at the cellular level, which will also impact the development of new vaccines against infectious diseases and cancers and new treatments for immune diseases, including autoimmunity. Toward this end, while aspiring to become an internationally visible and influential research center that attracts more world-class researchers, IFReC staff members at all levels are working together as a diverse, yet integrated team.

4. Management

<Initial plan>	<Results/progress/alternations from initial plan>
1) Composition of administrative staff Dr. Norio Furushiro, who is familiar with managements in English, will head the administration department. The administration department will have three sections: the research management section consisting of 2-3 members with PhD degree, and accounting section and general affairs section each consisting of a senior supervisor with rich administrative experiences in the University, and several bilingual or English-speaking full-time and part-time personnel. The research management section deals with planning and logistics of scientific meetings sponsored by the Research Center, public information and liaison, and issues relating to intellectual properties.	1) Composition of administrative staff **Administrative Director** : We recruited Dr Kodama, who has a long career of scientific research as well as its experience of management and coordination, as new Administrative Director in April. He supervises IFReC administrative department consisting of General Affairs Section, Accounting Section and Research Planning and Management Office. **General Affairs Section**: Section Leader with administrative staff - 7 persons **Accounting Section**: Section Leader with administrative staff - 8 persons **Research Planning and Management Office** : Office Leader with assisting staff - 6 persons (5 PhD holders). Note: This office is a reformation of the former Research Management Section. Posting academic staff with research experience as well as bilingual staff, this reformation has brought enormous effect on smooth communication among researchers and supporting staff, close contact with administrative bureau of Osaka University, and efficient coordination for holding seminars/symposia.
2) Decision-making system Center management committee consisting of center director (Chairman), administrative director and a few principal investigators will make mid-to-long term plan of the center based on advices by the International Advisory/Review Board. The center director, based on suggestions by the center management committee, will make decisions on major issues necessary for center's managements, such as researchers' salaries, appointment of new researchers and administrative director.	2) Decision-making system The Director makes major decisions, to which the Administrative Director gives support by acting as a coordinator among Vice Directors and Trustees of the host institute as well as of the WPI Initiative Program Committee. Important matters such as annual budget and appointment of PIs or equivalent are to be approved at the Center Management Committee and the Board of Representatives as needed.
3) Allocation of authority between center director and host institution 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 center's managements, such as researchers' salaries, appointment of new researchers and administrative director. The University president will make appointment of center director, determine the salary of center director and make evaluation of the center's performance.	3) Allocation of authority between center director and host institution Director, Vice Directors, Administrative Director and Trustees of host institute hold regular briefings.

5. Researchers and center staffs

i) “Core” to be established within host institution

Principal investigators

	At beginning	Planned for end of FY 2007	Final goal (around Apr. 2010)	Results at end of FY 2008	Results at end of FY 2009
Researchers from within host institution	10	10	10	11	15
Foreign researchers invited from abroad	1	2	5	1	2
Researchers invited from other Japanese institutions	6	6	7	8	9
Total principal investigators	17	18	22	20	26

All members

	At beginning	Planned for end of FY 2007	Final goal (around Apr. 2010)	Results at end of FY 2008	Results at end of FY 2009
Researchers <Number of foreign researchers among them and their percentage> [Number of female researchers among them and their percentage]	49 < 12, 24%>	82 < 25, 30%>	147 < 47, 32%>	89 < 24, 27%> [18, 20%]	135 < 42, 31%> [26, 19%]
Principal investigators <Number of foreign researchers among them and their percentage> [Number of female researchers among them and their percentage]	17 < 1, 6%>	18 < 2, 11%>	22 < 5, 23%>	20 < 2, 10%> [0, 0%]	26 < 6, 23%> [1, 4%]
Other researchers <Number of foreign researchers among them and their percentage> [Number of female researchers among them and their percentage]	32 < 11, 34%>	64 < 23, 36%>	125 < 42, 34%>	69 < 22, 32%> [18, 26%]	109 < 36, 33%> [25, 23%]
Research support staffs	28	34	44	23	31
Administrative staffs	9	15	15	15	21
Total	86	131	206	127	187

ii) Satellites <Initial plan> Institution (1) RIKEN Research Center for Allergy and Immunology -Role RIKEN Research Center for Allergy and Immunology contributes to improve imaging technique of the center. -Personnel composition and structure Takashi Saito, Cell Signaling research group Tomohiro Kurosaki, Lymphocyte Differentiation research group -Collaborative framework Researchers in the center and RIKEN Research Center for Allergy and Immunology visit each other and exchange information on a regular basis in order to improve the level of imaging technique. We offer employment expenses to hire several Postdocs to above institution.	<Results/progress/alternations from initial plan> There are no changes on the roles of the outside research institutions. Lymphocyte Differentiation research group (Dr Kurosaki) and Experimental Immunology research group (Dr Sakaguchi) have moved into the Integrated Life Sciences Building at Osaka University. It enabled the researchers to cooperate more closely with each other. Institution (1) RIKEN Research Center for Allergy and Immunology -Personnel composition and structure Dr Takashi Saito with one posdoc (Cell Signaling group) Dr Tomohiro Kurosaki and 8 other staffs (Lymphocyte Differentiation group) Institution (2) Kyoto University, Institute for Frontier Medical Sciences -Personnel composition and structure Dr Shimon Sakaguchi and 8 other staffs (Experimental Immunology group)
iii) Partner institutions <Initial plan> Institution (1) National Institutes of Health Institution (2) New York University Institution (3) California Institute of Technology Institution (4) Harvard Medical School Institution (5) Stanford University School of Medicine Institution (6) University of California San Francisco -Role Partner institutions contribute to improve imaging technique of the center. -Personnel composition and structure Ronald Germain, Deputy Chief, Laboratory of Immunology and Chief, Lymphocyte Biology Section, NIAID Michael Dustin, Professor, Skirball Institute of Biomolecular Medicine Scott Fraser, Director, Biological Imaging Center, Beckman Institute Ulrich H. von Andrian, Professor, Department of Pathology Mark Davis, Professor, Department of Microbiology and Immunology Jason Cyster, Professor, Department of Microbiology and Immunology -Collaborative framework Researchers in the center and above institutions visit each other and exchange information on a regular basis in order to improve the level of imaging technique. We offer employment expenses to hire several Postdocs to above institutions.	<Results/progress/alternations from initial plan> In addition to 7 partner institutions (initial 6 institutions together with Institute for Systems Biology joined in FY2008), we concluded Academic Cooperation Agreement with Pohang University of Science and Technology (POSTECH) , Korea and Indian Institute of Science Education and Research (IISER), India. Institution (1) National Institutes of Health -Role Joint research on imaging data analysis and modeling immune responses -Personnel composition and structure Dr Ronald N. Germain, Deputy Chief, Laboratory of Immunology and Chief, Lymphocyte Biology Section, National Institute of Allergy and Infectious Diseases (NIAID) -Collaborative framework The institute replaced Dr Hai Qi with Dr Tim Laemmermann as postdoc financed by IFReC. Dr Laemmermann will attend the 4th IFReC international symposium (June 1-2, 2010) to give a talk about his recent research. Their publications in 2009 are as follows: - Quast T, Tappertzhofen B, Schild C, Grell J, Czeloth N, Forster R, Alon R, Fraemohs L, Dreck K, Weber C, Lammermann T, Sixt M, Kolanus W. *Blood.* 2009 113(23):5801-10.

- Klauschen F, Ishii M, Qi H et al. *Nature Protocols.* 2009;4(9):1305-11.
- Klauschen F, Qi H, Egen JG, Germain RN et al. *Nature Protocols* 2009;4(7):1006-12.

Dr Masaru Ishii, PI of IFReC has been collaborating with Dr Germain's lab, and is the coauthor of the article.

Institution (2) New York University

-Role

Joint research on imaging intercellular interactions

-Personnel composition and structure

Dr Michael Dustin, Professor of the Skirball Institute of Biomolecular Medicine

-Collaborative framework

The university employed Dr Jan Liese as a Postdoc financed by IFReC last year. Dr Liese has been studying immunity related TLR, NK, and Dendritic cells.

Dr Sudha Kumari, a postdoc at Dr Dustin's lab, will attend the 4th IFReC international symposium to give a talk.

Institution (3) California Institute of Technology

-Role

Joint research on imaging the immune cell

-Personnel composition and structure

Dr Scott Fraser, Director of Biological Imaging Center, Beckman Institute

-Collaborative framework

The institute employed Dr Luca Caneparo financed by IFReC last year. He has been studying Gastrulation and Retro viral infection.

Dr Thai V. Truong, a postdoc at Dr Fraser's lab, will attend the 4th IFReC international symposium to give a talk.

Institution (4) Harvard Medical School

-Role

joint research on imaging the immune cell

-Personnel composition and structure

Dr Ulrich H. von Andrian, Professor of Immunopathology

-Collaborative framework

The school replaced Dr Sarah E. Henrickson with Dr Irina Mazo as postdoc financed by IFReC. Dr Matteo Iannacone, a postdoc at von Andrian's lab. will attend the 4th IFReC international symposium to give a talk.

The publication by postdoc in 2009 is as follows:

	- Beltman JB, Henrickson SE, von Andrian UH et al. *Journal of Immunological Methods.* 2009 Aug 15; 347(1-2):54-69. Institution (5) Stanford University School of Medicine -Role Joint research on single molecular imaging -Personnel composition and structure Dr Mark Davis, Professor, Department of Microbiology and Immunology -Collaborative framework The university employed Dr Johannes Huppa as a postdoc financed by IFReC last year. He has been studying immune imaging related T Cell Receptors, Immunological synapses and Bioinformatics. Dr Fleur Tynan, a postdoc at Dr Davis's lab, will attend the 4th IFReC international symposium to give a talk. Institution (6) University of California San Francisco -Role Joint research on imaging technique of intercellular interactions -Personnel composition and structure Dr Jason Cyster, Professor of Microbiology and Immunology -Collaborative framework The university replaced Dr Tri Giang Phan with Dr Tal Arnon as a postdoc financed by IFReC. Dr Arnon will attend the 4th IFReC international symposium to give a talk. The publication by postdoc in 2009 are as follows. - Phan TG, Green JA, Gray EE, Xu Y, Cyster JG. *Nature Immunology* 2009 Jul;10(7):786-93. - Phan TG, Gray EE, Cyster JG. *Current Opinion Immunology.* 2009 Jun;21(3):258-65. - Grigorova IL, Schwab SR, Phan TG, Pham TH, Okada T, Cyster JG. *Nature Immunology* 2009 Jan;10(1):58-65. Institution (7) Institute for Systems Biology -Role Joint research on imaging data analysis and modeling of immune responses -Personnel composition and structure Dr Alan Aderem, Director of Institute for Systems Biology -Collaborative framework Dr Stephen Ramsey, a leading bioinformatician at Dr Aderem's lab will attend the 4th IFReC international symposium to give a talk.

	Institution (8) Division of Life Science & Division of Integrative Bioscience and Biotechnology (IBB), Pohang University of Science and Technology (POSTECH) -Role Promotion of activities to enhance the educational cross-fertilization and academic research in immunology fields -Personnel composition and structure Dr Inhwan Hwang, Chairman of IBB, POSTECH -Collaborative framework We concluded Academic Cooperation Agreement with the institute to promote collaborative researches through exchange of information, materials and students. Institution (9) Indian Institute of Science Education and Research (IISER) -Role Promotion of activities to enhance the educational cross-fertilization and academic research in immunology fields -Personnel composition and structure Dr Vinod K Singh、IISER -Collaborative framework We concluded Academic Cooperation Agreement with the institute to further promote collaborative researches through exchange of information, materials and students.

6. Summary of center's research environment

<table>
<tr>
<td><Initial plan>
1) Environment in which researchers can devote themselves to their research
Research management section consisting of 2-3 members with PhD degree will be set up in the administration department. The research management section deals with planning and logistics of scientific meetings sponsored by the Research Center, public information and liaison, and issues relating to intellectual properties. The administration department also includes accounting section and general affairs section each consisting of a senior supervisor with rich administrative experiences in the University, several bilingual or English-speaking full-time and part-time personnel. These administration staffs will fully support researchers so that researchers do not have to spend their time in paper work and other administrative functions.

2) Startup research funding
Budget for equipments will be allocated to invite PIs from institutions outside Osaka University. Budget for consumables and supplies will also be provided to PIs from abroad so that those PIs are able to start research at maximum efficiency without losing time. To facilitate acquisition of competitive research grants from domestic funding sources, the research management section in the administration department will help PIs from abroad in application.</td>
<td><Results/progress/alternations from initial plan>
1) Environment in which researchers can devote themselves to their research
i) Establishment of Research Planning and Management Office
The former Research Management Section has been reformed into Research Planning and Management Office headed by the Administrative Director, to which a PhD holder with research experience and a bilingual staff have been posted. In addition, it has been arranged in such way that English-native researchers are asked to join when needed. The establishment of this office has improved communication among research laboratories, close contact with administrative bureau of Osaka University, and efficient coordination for planning seminars/symposia.

ii) Access to research grant information
To make foreign researchers accessible to a variety of public/private research grants proposed in Japan, we prepared application guidelines and formats in English and compiled them in database. This effort has, in part, contributed to acquisition of Grants-in-Aid for Scientific Research by foreign researchers not fluent in Japanese.

2) Startup research funding
- We allocated approx. 0.79 million dollars(=79 million yen) to Dr Kurosaki's laboratory and Dr Sakaguchi's laboratory respectively as their set-up budget necessary to locate their laboratories in newly built Integrated Life Science Building (completed in June 30, 2009).
- Set-up budget of 75 thousand dollars (=7.5 million yen) and start-up budget of 0.22 million dollars (=22 million yen) were allowed for Associate Professor Daron M. Standley's lab to launch his laboratory in the new building.
- Set-up budget of 0.15 million dollars (=15 million yen) and start-up budget of 0.13 million dollars (=13 million yen) were allowed for Associate Professor Jang Myoung Ho's lab to launch his laboratory in the new building.
- Start-up budget of 0.135 million dollars (=13.5 million yen) will be allocated to Associate Professor Diego Miranda-Saavedra who joined IFReC as of Janurary 16, 2010.
- Start-up budget of total 0.25 million dollars (=25 million yen) were distributed to 9 recipients selected for the "Research Support Program for Fusion of Different Fields". The program was set up in October 2009 aiming at creation of innovative research field through combination of immunology with imaging technologies and bioinformatics.
* Figures above are converted at the rate 1 U.S dollar=100yen</td>
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3) Postdoctoral positions through open international solicitations Postdocs will be hired through advertisement of positions on major journals, such as Nature and Immunity, and their home pages.	3) Postdoctoral positions through open international solicitations We posted advertisements of postdoc positions on “Nature” journal and IFReC’s website. In addition to the number stated in our previous progress report, we had approx. 150 applications for the positions, of which three applicants had been employed.
4) Administrative personnel who can facilitate the use of English in the work process Dr. Norio Furushiro, the Director of the International Student Center and Professor of Osaka University who is familiar with managements in English, will head the administration department. The administration department will have three sections: the research management section consisting of 2-3 members with PhD degree, and accounting section and general affairs section each consisting of a senior supervisor with rich administrative experiences in the University, several bilingual or English-speaking full-time and part-time personnel.	4) Administrative personnel who can facilitate the use of English in the work process As described above, the newly established Research Planning and Management Office functions independently from the administrative department and supports foreign researchers in various ways. The bilingual staff provides foreign researchers with English documents, and notices to make them share common information with Japanese researchers. The staff also assists paper work related to research such as making application for external funds as well as procedures necessary for daily life.
5) Rigorous system for evaluating research and system of merit-based compensation The center director will organize the International Advisory/Review Board consisting of several renowned immunologists. The International Advisory/Review Board will conduct evaluation of research groups’ performance every or every other year. The center director will determine principal investigators’ salaries based on the evaluation by the International Advisory/Review Board.	5) Rigorous system for evaluating research and system of merit-based compensation - The examination by the International Advisory Board is planed for 2011 to take an evaluation of IFReC scientific activities. - Annual review on research achievements and performance is to be held in IFReC and evaluation results will be reflected salary increase/decrease, promotion, etc. the following year. - Installment of new salary system is under negotiation with our host institution.
6) Equipment and facilities, including laboratory space, appropriate to a top world-level research center The main research building (nine floors and 9,400 square m) will be constructed by March 2009 with University budget and external donation, and 80% of its space will be used for the Research Center. After many of core research groups move into the new building, Osaka University will seek budget to renovate the old building these research groups are currently using.	6) Equipment and facilities, including laboratory space, appropriate to a top world-level research center i) Facilities The Integrated Life Science Building was completed in the end of July, 2009, and 9 laboratories, which were dispersed in different buildings of Research Institute for Microbial Diseases, RIKEN Research Center for Allergy and Immunology, and Kyoto University, moved into there and started their studies, so that we can anticipate increased opportunities for their members to meet and exchange their views with each other. In addition, a new animal resource center (an experimental station of infected animals) was also completed almost simultaneously. After installment of equipment and sterilization, it started operation from January 2010. - Furthermore, the construction of a new 9-story research building (a total

	floor space of 6,200 sq.m) of exclusive occupancy for IFReC has been approved in the FY2009 supplementary budget of the Japanese government, which will be completed by the end of FY2010. It is sufficiently spacious to accommodate most of IFReC PI's laboratories including those of Imaging group and junior PIs. Thus, the building will greatly facilitate collaborative studies between different laboratories and translational researches. It will also secure enough space for administrative department for its smooth and effective operation. ii) Equipment - We purchased animal breeding equipment to raise approx. 25,000 – 35,000 mice in 5,500 cages. - Major equipments such as DNA sequencer, Flow-cytometor, In-vivo imaging system, Confocal laser scanning microscope were newly installed.
7) International research conferences or symposiums held regularly to bring world's leading researchers together The Research Center will organize international research conferences independently or in connection with the annual Awaji International Forum on Infection and Immunity, which is organized since 2001 by the Research Institute for Microbial Diseases, Osaka University.	7) International research conferences or symposia held regularly to bring world's leading researchers together i) FY 2009 1. International Symposium "Frontier Immuno-Imaging", May 11, Osaka University (The total number of participants: ～60) 2. International Symposium "Immune Regulation: Present and Future", May 25-27, Osaka International Convention Center (The total number of participants-days, ～1000) 3. Singapore-Osaka, The 1st Joint SIgN-IFReC Meeting, June 18-19, "Integrating Immunology and Bio-imaging" at Singapore Biopolis, Singapore (The total number of participants-days, ～400) 4. International Symposium "Regulation of Innate Immunity", September 18 -19, International Vaccine Institute, Korea (The total number of participants-days, ～300) 5. International Workshop "Bioinformatics in Immunology", November 6, Osaka University (The total number of participants, ～40) ii) FY 2010 (Plan) 1. The 4th International Symposium of IFReC, June 1-2, Osaka University 2. The 1st China-Osaka Joint Symposium, November 3. "Guest society symposia" at annual meeting of The American Association of Immunologists in 2010
8) Other measures, if any Based on advices and/or suggestions by the International Advisory/Review Board, the center director will set up research environment suitable for international researchers.	8) Other measures, if any Implementation of new research systems resulted in acceptance of following researchers. - In this fiscal year, we accepted 3 students as Special Research Students, 2

	researchers as Kishimoto Fund Fellows, 2 students as foreign trainees (without financial support). - We provided two foreign research fellows with daily expenses.

7. Criteria and methods used to evaluate center's global standing

<Initial plan>	<Current assessment>
i) Criteria and methods to be used for evaluating the center's global standing in the subject field The following points will be evaluated not only quantitatively by numbers of publications, their citation and so on but also by external reviews of the reviewing committee that consists of internationally leading scientists in the corresponding fields. (a) Major contributions to main research areas: Are principal investigators of this center leading and advancing main research areas as major players in the corresponding fields? (b) Creation of new research areas: Are principal investigators of this center opening or creating new research areas in the corresponding fields? (c) Contribution to human life: Are there any accomplishments from this center, which have made great contributions to increases of 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 this center have been leading main research areas of the immunology field (Shizuo Akira in research of innate immunity; Shimon Sakaguchi in research of regulatory T cells; Tadamitsu Kishimoto and Toshio Hirano in research of cytokines), which are obvious from an enormous number of citations of their papers. Toshio Yanagida is also a pioneer of the single molecule imaging. (b) Creation of new research areas: Principal investigators of this center are currently opening new research areas (Takashi Saito in the single molecule imaging analysis of immune responses; Hitoshi Kikutani and Atsushi Kumanogoh in immune regulation by semaphorins). (c) Contribution to human life: Tadamitsu Kishimoto and his colleagues developed anti-IL-6 receptor therapy for inflammatory diseases, which is highly expected for treatment	Following is a list of research accomplishments and publications by IFReC staff. (1) Director Shizuo Akira was elected as the Foreign Associate of National Academy of Sciences (NAS) (May, 2009). (2) Professors Tadamitsu Kishimoto and Toshio Hirano won the Crafoord Prize 2009 (May, 2009). (3) Director Shizuo Akira was named a Person of Cultural Merit by the Japanese Government (October, 2009). (4) Director Shizuo Akira was awarded Hans Bloemendal Medal in Nijmegen Centre for Molecular Life Sciences (NCMLS) (November, 2009). (5) Dr Shimon Sakaguchi won a Purple Ribbon Medal (November, 2009). Total number of publications as of March 31, 2010 : 218 papers (immunology; 147, imaging; 59, bioinformatics; 12) High citation journals: Director Akira - Nature Immunology 10: 965-972 (2009) Director Akira - Cell 140(6): 805-20 (2010) Director Akira & Associate Professor Standley - Nature 458: 1185-1190 (2009) Dr Kinoshita - Cell 139(2): 352-365 (2009) Dr Kishimoto - The Journal of Experimental Medicine 206: 2027-2035 (2009) Dr Takeda - Cell 139(3): 485-498 (2009) Dr Takeda & Associate Professor Standley - The Journal of Experimental Medicine 206(12): 2747-60 (2009) Dr Hirano - Immunity 30(3): 447-457 (2009) - The Journal of Experimental Medicine 206: 1351-1364 (2009)

of various immunological diseases such as rheumatoid arthritis. **iii) Goals to be achieved through the project (at time of interim and final evaluations)** Goals at time of interim - To keep current levels and global standing of immunological research of this center. - To further grow new research area that were opened by this center and make them major ones in the corresponding area. - To establish technical and theoretical basis of intravital and noninvasive single cell analysis of immune responses. Goals at final evaluation - To establish the methodology of intravital and noninvasive single cell analysis of immune responses. - To combine the above methodology with basic immunological knowledge obtained by conventional immunology research of this center and to present new paradigm for understanding the immune network.	Dr Sakaguchi - Immunity 30(6): 899-911 (2009) - Immunity 31(4): 609-620 (2009) Dr Kurosaki - The Journal of Experimental Medicine 206: 681-9 (2009) Dr Yanagida - Nature Chemical Biology 5(6): 376-7 (2009) Associate Professor Ishii - Nature 458: 524-529 (2009) i) Approach from overseas research institution -Conclusion of Academic Cooperation Agreement with Pohang University of Science and Technology. (November 12, 2009) -Offer to have Immunology research exchanges and workshop from Ministry of Research, Science & Technology, New Zealand (November 4, 2009) -Research cooperation with Singapore Immunology Network ii) Site visits from overseas research institutions, opinion-exchange session - Netherlands Office for Science & Technology, July 8 -Professor Robert D. Sindelar, Dean of Faculty of Pharmaceutical Sciences, University of British Columbia, Canada, October 1 -M. D. Katz, College of Pharmacy, University of Arizona, October 20 -Dutch Innovation Platform, October 25 -International Advisory Council of Chugai Pharm. Co, February 18 iii) Inquiries for the opening of the researchers We have got 50 inquiries from overseas researchers as of the end of March 2010.

8. Securing competitive research funding

<Initial plan>	<Results/progress/alternations from initial plan>
i) Past record 2002: 6.76 million dollars or 811 million yen; 2003: 9.39 million dollars or 1.127 billion yen; 2004: 9.48 million dollars or 1.137 billion yen; 2005: 9.20 million dollars or 1.104 billion yen ; 2006: 9.60 million dollars or 1.152 billion yen; Average 8.88 million dollars or 1.066 billion yen. * Figures above are converted at the rate in 2007: 1 U.S dollar=120yen **ii) Prospects after establishment of the center**	Total amount of funds acquired by all IFReC researchers (135 persons) reached (12.4 billion dollars=1.24 billion yen) as of the end of this fiscal year. It consists of Competitive external funds (10.6 million dollars=1060 million yen), Private funds (0.19 million dollars=19 million yen), Donations (1.4 million dollars=140 million yen), Budget from Osaka University (0.27 million dollars=27 million yen). * Figures above are converted at the rate 1 U.S dollar=100yen

The specific measurements are as follows: 1) Indirect cost: 3.7 million dollars or 450 million yen. 2) Construction of main research building: 1.8 million dollars or 210 million yen. 3) Provision of other research space: 0.1 million dollars or 10 million yen. 4) Partial payment of Principal Investigators' salaries: 1.3 million dollars or 150 million yen. 5) University budget for Principal Investigators: 0.3 million dollars or 40 million yen. 6) Competitive Research Grants for Principal Investigators: 8.7 million dollars or 1.05 billion yen. 7) Facilitation of external donations: 0.8 million dollars or 100 million yen. Total: 16.7 million dollars or 2.01 billion yen. Notes: 1) Most of the Indirect cost from this project will be used for the Research Center. 2) The main research building (9,400 square m) will be constructed by March 2009 with University budget and external donation in total of 20.8 million dollars or 2.5 billion yen, and 80% of its space will be used for the Research Center for 9.5 years. (Annual contribution will be 20.8 million dollars or 2.5 billion yen x 0.8 / 9.5 = 1.8 million dollars or 210 million yen).	- Major research grants acquired this fiscal year i) Funding Program for World-Leading Innovative R&D on Science and Technology (Director Akira) ii) Grants-in-Aid for Scientific Research, Scientific Research(S) (Dr Kurosaki) iii) Research project: Etiological basics of and techniques for treatment of allergic and autoimmune diseases, JST CREST program: "Regulation of immune response and infection by paired receptors"(Dr Arase) "Development of new therapies for autoimmune diseases by regulating humoral immune system" (Dr Kurosaki) - Research Budget acquired by foreign researchers i) JST PREST "In-situ laser fabrication of nanoprobes inside living cells for analysis of biofunctions" (Dr Smith) ii) Grants-in-Aid for Scientific Research acquired by foreign researchers: 3 projects (among 15 recipients in IFReC) (Drs Standley, Coban and Smith) Research Planning and Management Office provides foreign researchers with sufficient help for paper procedures required for application as well as after acceptance.

9. Other important measures taken to create a world premier international research center

<Initial plan>	<Results/progress/alternations from initial plan>
Activities and initiatives to be taken after project funding ends After project funding ends and the project turns out to be successful, one possible initiative will be integration of the Immunology Frontier Research Center and Osaka University International Research Center for Infectious Diseases: the latter is a currently operating research center focusing on infectious diseases and will function complementally with the proposed Immunology Frontier Research Center. Such integration will include reorganization of related departments in Osaka University and will lead to the next generation world premier international research center. **Describe expected ripple effects** The Osaka University International Research Center for Infectious Diseases described above will be eventually reformed following the Immunology Frontier Research Center as a model of world-level research centers.	**Activities and initiatives to be taken after project funding ends** and **Describe expected ripple effects** There are no alterations from the initial plan

Other important measures to be taken in creating a world premier international research center **Global COE Program:** Project title: System Dynamics of Biological Function Outline: this project is planned to develop imaging technology, to analyze dynamics of various biological networks, and to perform modeling and simulation of such networks. Group leader: Toshio Yanagida Relationship: Toshio Yanagida, a group leader, is also a principal member of this center project. Both projects focus on imaging technology and mutually interact each other.	**Other important measures to be taken in creating a world premier international research center** **Global COE Program:** The same as in 2008 Development of a management system for intellectual property: We have recently named Dr Ken Ishii (associate professor of IFReC) as the person in charge of handling various matters related to intellectual property. His role is initially just a liaison for patent application and its prior consultation. With support by UIS, we will set up a more concrete management system for intellectual property and industry partnerships within 2010.

10. Host institution's commitment

<Initial plan> -Provision in host institution's mid-to-long-term plan Osaka University has from the start been committed to its mid-term strategic target as a university emphasizing research, aiming to produce unique and high quality results at the forefront of research. Notably, Osaka University is strongly focusing on "accomplishing high-level research results and playing a crucial role in the establishment of the World Premier International Research Center (WPI)". Osaka University will further encourage the study of Advanced Science and Technology fields to maintain its system of research practice. The provisions of the mid-term strategic plan were set to accomplish the goals of the plan under the existing implemented systems. If the proposal with Osaka University is selected as one of the "WPI" programs, the University will give the top priority to develop "Osaka University Immunology Frontier Research Center" and subjoin in the mid-term strategic plan as effective measures to fulfill the research quality and research results. In addition, Osaka University will support the WPI for maintaining the research enforcement system. The WPI will be supplemented in the mid-term strategic plan. Osaka University in its mid-term organization planning (2004-2009) described and published that one of the University's specific targets is the establishment of the Research/Education Center of Excellence in Microbiology and Immunology. The educational aspects of this planning is taking place through the 21st Century COE program entitled, "Combined program on Microbiology and Immunology" (2003-2007). This 21st Century COE program will be followed by a new proposal to the Global COE	<Results/progress/alternations from initial plan> -Provision in host institution's mid-to-long-term plan Osaka University mentions in its second mid-term goal and mid-term plan for FY 2010 to FY 2015 that "the university will organize and promote large scale intensive research projects in order to explore academic fields necessary to solve complex social and global issues characteristic in the 21st century".

program. The research aspect of the planning consists of two parts. One focuses on infectious diseases. Osaka University established the “Osaka University International Research Center for Infectious Diseases” in 2005 including setting up the Research Collaboration Center on Emerging and Reemerging Infections in Thailand as a branch. The other part of the research aspects is to propose the “Osaka University Immunology Frontier Research Center” with its focus being Immunology as the “World Premier International WPI (WPI) Initiative”. The two Centers will be functionally complimentary. If the proposal with Osaka University is selected as one of the WPI Initiative programs, formation of the WPI will be the top priority in the mid-term strategic target and plan, and Osaka University will give full support by implementing institutional reforms that are necessary for formation of the WPI and improving the research systems.	
-Concrete Measures (1) Competitive grants obtained by researchers participating in the project and in-kind contributions, etc.	-Concrete Measures (1) Competitive grants obtained by researchers participating in the project and in-kind contributions, etc.
Osaka University will assist the WPI to perform every possible support for operation and research activities of WPI. Osaka University will provide support to the WPI resources that would be either greater or equal to the WPI project grant. The specific measures are as follows: 1) Indirect research expenses: 3.7 million dollars or 450 million yen. 2) Construction of main research building: 1.8 million dollars or 210 million yen. 3) Provision of other research space: 0.1 million dollars or 10 million yen. 4) Partial payment of principal investigators’ salaries: 1.3 million dollars or 150 million yen. 5) University budget for principal investigators: 0.3 million dollars or 40 million yen. 6) Competitive research grants for principal investigators: 8.7 million dollars or 1.05 billion yen. 7) Facilitation of external donations: 0.8 million dollars or 100 million yen. Total: 16.7 million dollars or 2.01 billion yen for each year. Notes: 1) Most of the Indirect research expenses from this program will be used for the WPI. 2)The main research building (9,400 m2 of space) will be constructed by March 2009 with University budget and external donation in total of 20.8 million dollars or 2.5 billion yen, and 80% of its space will be used for the WPI	- All WPI indirect costs from this project will be used for IFReC. - Osaka University provided total 2.4 million dollars (=240 million yen) as start-up budget with seven laboratories invited from other institutions. - Personnel expenses for researchers who have co-current positions in IFReC and other department in the university are provided by Osaka University’s management expenses grant - 1.2 million dollars (=120 million yen) was allocated for movement and facility installment into the Integrated Life Science Building. - A tenure position was provided by Osaka University. The allocation of this secured position enabled us to invite Dr Sakaguchi from Institute for Frontier Medical Sciences, Kyoto University in next fiscal year. * Figures above are converted at the rate 1 U.S dollar=100yen

for 9.5 years. (Annual contribution will be 20.8 million dollars or 2.5 billion yen x 0.8 / 9.5 = 1.8 million dollars or 210 million yen. * Figures above are converted at the rate in 2007: 1 U.S dollar=120yen	
(2) System under which the center's director is able to make substantive personnel and budget allocation decisions	(2) System under which the center's director is able to make substantive personnel and budget allocation decisions
The WPI will be recognized as a department within the university. Osaka University will provide the center director with the entitlement to manage and operate the WPI. The center director is entitled to make decisions regarding substantive personnel and budget allocation as are the Deans and Directors in other faculties in Osaka University. An Administrative Director will support the center director and he will be responsible for office management so that the Director's decisions are kept to the bare essentials. Osaka University will support the center director's research environment.	Osaka University allows the Director to decide employment and annual salaries of staffs which are normally restricted by university regulations. Moreover, Director is authorized to make discretionary decision on budget use, start-up budget size, etc.
(3) Support for the center director in coordinating with other departments at host institution when recruiting researchers, while giving reasonable regard to the educational and research activities of those departments	(3) Support for the center director in coordinating with other departments at host institution when recruiting researchers, while giving reasonable regard to the educational and research activities of those departments
When a researcher from a different department in Osaka University joins the WPI as a full time researcher, Osaka University will support the replacement by indirect research expenses and/or other expenses. If a researcher at other departments in Osaka University is working concurrently at the center, he or she will be exempted from educational work. Osaka University will support resource sharing/exchange between the WPI and other departments.	It is operating according to the initial framework.
(4) Revamping host institution's internal systems to allow introducing of new management methods (e.g., English-language environment, merit-based pay, top-down decision making) unfettered by conventional modes of operation	(4) Revamping host institution's internal systems to allow introducing of new management methods (e.g., English-language environment, merit-based pay, top-down decision making) unfettered by conventional modes of operation
To maintain the excellent research environment for the WPI, the center will apply the existing employment system of Osaka University, including the annual salary system. If the present employee system of Osaka University does not fit in with the operation of the center, then Osaka University will consider revising and supplementing the present internal system of Osaka University. The new system should be flexibly operated. Osaka University	Annual review on research achievements and performance was held in IFReC and evaluation results will be reflected to salary increase/decrease, promotion, etc. of following year. Items below are under negotiation with our host institution. -Installment of new salary system for IFReC

will support the WPI's enforcement to endorse the system and its operation as follows: ・The WPI will ensure that the retirement allowance to be paid to the hired researcher is based on the total years of service to the center and other institutions. ・The Housing of International Visiting Professors will be arranged by WPI and there is no need to pay neither the security deposit nor key money. ・To hire exceptional researchers, their salaries can be changed from the existing system depending on his or her ability. ・High English ability administrative staff will be hired from both inside and outside the University. There will be on-the-job training after their employment. The aforementioned items will undergo examination as necessary by related departments of Osaka University.	-Giving titles peculiar to IFReC staff -Not setting any limitations on the terms of employment in the case that employees are transferred to different organization after termination of WPI program. -Making it possible to offer tenure positions in order to attract and employ excellent researchers
(5) Accommodation of center's requirements for infrastructural support (facilities, e.g., laboratory space; equipment; land, etc.)	(5) Accommodation of center's requirements for infrastructural support (facilities, e.g., laboratory space; equipment; land, etc.)
A new research building of nine floors with 9,400m² of space will be constructed by March 2009 for the Research Center. Osaka University will also provide laboratory space on the campus to accommodate research groups, which will join the Research Center before the new research building is completed. After many of the core research groups move into the new building, Osaka University will seek funds to renovate the old building these research groups are currently using. To meet the space requirements for an animal facility for newly coming research groups, Osaka University will construct a new block of animal facilities and provide it for the Research Center's use.	- The Integrated Life Science Building was completed in the end of July, 2009, and 9 laboratories, which were dispersed in different buildings of Research Institute for Microbial Diseases, RIKEN Research Center for Allergy and Immunology, and Kyoto University, moved into there and started their studies, so that we can anticipate increased opportunities for their members to meet and exchange their views with each other, which will facilitate their collaboration. In addition, a new animal resource center (an experimental station of infected animals) was also completed almost simultaneously. After installment of equipment and sterilization, it started operation from January 2010. - Furthermore, the construction of a new 9-story research building (a total floor space of 6,200 sq.m) of exclusive occupancy for IFReC has been approved in the FY2009 supplementary budget of the Japanese government, which will be completed by the end of FY2010. It is sufficiently spacious to accommodate most of IFReC PI's laboratories including those of Imaging groups and junior PIs. Thus, the building will greatly facilitate collaborative studies between different laboratories and translational researches. It will also secure enough space for administrative department for its smooth and effective operation. The Department of Facilities at Osaka University gave us support in making layout of this building. - Osaka University Kasugaoka House, accommodation for foreign researchers, is under construction and is planned to be finished in June 2010. IFReC residence at the accommodation will receive expenses support

	from IFReC. - Imaging groups are provided research spaces, facilities and equipments from Graduate School of Frontier Biosciences. - IFReC staff who hold co-current positions in Graduate School of Medicine/Graduate School of Frontier Biosciences are provided facilities and equipments from those faculties.
(6) Support for other types of assistance In addition to the above, Osaka University will start a new “one stop service office” for international researchers and students in 2007. This all-in-one service aims to improve both the research and living conditions for visitors from abroad. Information including the research and daily life on campus and in the surrounding area has already been released on the web information service site “GCN-Osaka & Worldwide”. This “one stop service office” does not only function as an information center, but also aims to reduce the burdens placed on international researchers and students related to immigration, by offering substantial support services such as visa application on their behalf. Osaka University has established three Overseas liaison offices for Education and Research in San Francisco (U.S.A), Groningen (The Netherlands) and Bangkok (Thailand). Their central task is to collect and transmit information, and scout highly talented researchers. All the faculties and overseas offices of Osaka University will assist the WPI so as to become the “World Premier International Research Center”.	(6) Support for other types of assistance Support Office for International Students and Scholars in Osaka University expanded its range of assistance in visa application and housing. IFReC can receive further benefits from this expansion. The Department of Research Promotion at Osaka University and IFReC always work together to operate WPI program. The department provides us with generous assistance to set our research plans.

11. FY 2009 funding

i) Overall project funding

(Exchange Rate: JPY/USD=100)

Cost Items	Details	Costs (10,000 dollars)
Personnel	Center director and Administrative director	31
	Principal investigators (no. of persons):19	161
	Other researchers (no. of persons):94	419
	Research support staffs (no. of persons):30	133
	Administrative staffs (no. of persons):17	99
	Total	843
Project activities	Gratuities and honoraria paid to invited principal investigators (no. of persons):0	0
	Cost of dispatching scientists (no. of persons):2	4
	Research startup cost (no. of persons):7	240
	Cost of satellite organizations (no. of satellite organizations):2	0
	Cost of international symposiums (no. of symposiums):2	40
	Rental fees for facilities	1
	Cost of consumables	4
	Cost of utilities	3
	Other costs	317
	Total	609
Travel	Domestic travel costs	1
	Overseas travel costs	2
	Travel and accommodations cost for invited scientists (no. of domestic scientists):7 (no. of overseas scientists):7	4
	Travel cost for scientists on secondment (no. of domestic scientists):5 (no. of overseas scientists):9	5
	Total	12
Equipment	Depreciation of buildings	70
	Depreciation of equipment	451
	Total	521
Other research projects	Projects supported by other government subsidies, etc.	26
	Comissioned research projects, etc.	376
	Grants-in-Aid for Scientific Research, etc.	392
	Total	794
Total		2779

Ten thousand dollars (Exchange Rate: JPY/USD=100)

WPI grant for FY 2009	1,350
Costs of establishing and maintaining facilities in FY 2009	2,451
Establishing new facilities: Integrated Life Science Building (Number of facilities: 1, 9,258m²) Costs paid:	1,273
Establishing new facilities: Animal Resource Center for Infectious Diseases C (Number of facilities: 1, 2,480m²) Costs paid:	508
Establishing new facilities: New research building (Number of facilities: 1, 6,200m²) Costs paid:	670
Cost of equipment procured in FY 2009	629
Name of equipment: Specific Pathogen Free Rodent Maintaining System Number of units: 2 Costs paid:	441
Name of equipment: In-Vivo Imaging System Number of units: 2 Costs paid:	44
Name of equipment:DNA Sequencer Number of units: 2 Costs paid:	41
Name of equipment: Flow Cytometry System Number of units: 1 Costs paid:	22
Name of equipment: Flow Cytometer Number of units: 1 Costs paid:	10
Name of equipment: Laser illuminator unit Number of units: 1 Costs paid:	9
Name of equipment: Motorized Inverted Microscope Number of units: 1 Costs paid:	9
Name of equipment: High-Performance Liquid Chromatography Number of units: 1 Costs paid:	5
Name of equipment: Micro Ultracentrifuge Number of units: 1 Costs paid:	5
Name of equipment: Objectivelenz unit Number of units: 1 Costs paid:	4
Name of equipment: Cray System Number of units: 1 Costs paid:	4
others	35

ii) Costs of Satellites and Partner institutions

(Exchange Rate: JPY/USD=100)

Cost Items	Details	Costs (10,000 dollars)
Personnel	Principal investigators (no. of persons):1	
	Other researchers (no. of persons):9	
	Research support staffs (no. of persons):3	
	Administrative staffs (no. of persons):1	
	Total	76
Project activities		0
Travel		1
Equipment		0
Other research projects		132
Total		209

12. Efforts to improve points indicated as requiring improvement in follow-up review and results of such efforts

-Points specified as needing improvement

According to the above comments as well as the site-visit report, the following points should be considered to meet the WPI Program objectives:

1. **Breakthrough in both immunology and imaging by fusion of the two disciplines**
2. **Inclusion of genomics and structural biology**
3. **Internationalization.**

Other comments and suggestions made up in follow-up review

1. Achievements of Science

Fusion of immunology and imaging is positively evaluated:

- Very interesting work and excellent progress is being made. The fusion of imaging and immunology being done is impressive and the awards given the scientists are laudable.

- WPI Program brings strong expectations for collaborative research. IFReC should develop additional measures to develop culture strongly committed to collaborative research, especially to bring the imaging and immunology groups closer together. It is the excitement of marrying these two fields that secured WPI funding.

- The group has been making steady progress in many aspects; strong collaboration with imaging groups within Osaka University, provision of support in preparing infrastructure as Osaka University on the whole, recruitment of overseas researchers and so forth.

At the same time, some problems of fusion with imaging are pointed out:

- Quality of research is very high. “Fusion” of research is in progress. However, the synergistic effect by founding this new institute is not clear.

- The fusion of immunology and imaging is very difficult, because immunologists use imaging for research and because imaging researchers may become slaves. They may need some strategies to promote super science between immunology and imaging.

-Efforts to improve them and results

The three points that IFReC should consider to meet the WPI Program objectives are arranged forms of many concerns and suggestions (**C&S**s) from *a* to *g* as raised by the working committee led by PO Professor T Sasazuki after the site visit on February 4, 2009:

a: Further advances in globalization
b: Research development of the human immune system
c: Reinforcement of Bioinformatics
d: Further advances regarding the fusion of different research areas
e: Recruitment of more foreign researchers at all levels
f: Concern about average age of PIs
g: Better use of the internet to promote IFReC

To take appropriate measures to deal with them, IFReC submitted a tentative version of “The Three-Year Program” to the PO. In its acceptance at the WPI follow-up committee (held on March 17, 2009), the program was discussed and approved at the Center Management Committee on March 27, 2009. The Three-Year Program consists of two sub-programs and several feasible plans :

1) **Junior PI Program:** This program is in direct response to ***a***, ***c***, ***f*** and indirect to ***b*** of **C&S**s.
2) **A support program to fuse the different research areas:** This program supports young researchers who belong to at least two of IFReC’s research groups (Immunology, Imaging and Bioinformatics). Screening and verification must be conducted. This program is in direct response to ***d*** and indirect to ***b*** of **C&S**s.
3) **Small-scale symposia:** In addition to the international symposium held every year, small-scale symposia or workshops covering the three different research areas will be organized once or twice a year. IFReC invites young researchers from home and abroad. These efforts are in direct response to ***a*** and ***d*** of **C&S**s.
4) **Improving the IFReC website:** More dynamic images like immune system cells or cytokines should be posted. More regular updates of IFReC accomplishments and activities are needed too. Moreover, administrative procedures in detail should be uploaded. These are in

- I am a bit concerned that informatics and imaging may be viewed primarily as providers of technology services to the immunologists, rather than as partners in the establishment of a fundamentally new approach to the topic areas. The imaging and informatics PIs and other researchers in these areas need to have an impact back on their primary fields.

- I was originally very impressed with the plans to integrate immunology with imaging in particular. The reports do not give the impression that this is happening at the level of defining research challenges and problems. I am afraid it will even be reduced to the purchase of commercial imaging microscopes.

- Excellent progress, but the collaboration or ways to take advantages of the project originally outlined in the application between immunology and imaging (which is a technology) are not clear and not effectively implemented.

Importance of the fields of genomics and structural biology is suggested:

- Greater attention to genome sequencing and structural biology is needed. If these disciplines are not included, the work will not be truly interdisciplinary. Also opportunities for major new discoveries will be lost.

- Genomics is a major area that needs to be included in the research effort.

2. Implementation as a WPI Research Center

The follow-up committee members pointed out that more efforts are needed for internationalization.

- WPI Program is an opportunity to develop high international profile. It is not clear that IFReC leadership is really taking advantage of this opportunity.

- Although efforts are being made to increase overseas researchers in the group, further improvement is needed in this respect.

- The project has made a strong start toward internationalization and achieving global recognition. However, it is unclear what sort of a strategic plan underlies the specific activities.

direct response to ***a*** and ***g***, and indirect to ***e*** of **C&S**s.

5) **Developing a management system to handle intellectual property:** This point was made at the last site visit. This is indispensable for pursuing translational research.

Program	FY2009	FY2010	FY2011	FY2012
1) Junior PI Program	First half: Planning (Budget, Space) Open recruitment for FY2009 Second half: To accept a maximum of 1 Junior PI The total number of Junior PI: maximum 1	First half: To draw up a plan Open recruitment for FY2010 Second half: To accept a maximum of 2 Junior PIs The total number of Junior PIs: maximum 3	First half: To draw up a plan Open recruitment for FY2011 Second half: To accept a maximum of 2 Junior PIs The total number of Junior PIs: maximum 5	Review and evaluation The total number of Junior PIs: maximum 5
	Qualification PI: 10 to 15 years after earning a doctoral degree, presumably around 40s Possible Candidates: Associate Professors, Assistant Professors, Postdoctoral Fellows including those in overseas cooperative institutions Term: 5 years Personnel Support: 1 Postdoctoral Fellow and 1 Technician Financial Support: Start-up cost for the initial fiscal year; maintenance grant for the second fiscal year or later			
Program	FY2009	FY2010	FY2011	FY2012
2) Research Support Program for Fusion of Different Fields	First half: Planning (Budget, Criteria for selection, etc.) To draw up a plan Open recruitment for research projects at IFReC for FY2009 Second half: 2 research projects will be selected and commence	First half: To draw up a plan Open recruitment for research projects at IFReC for FY2010 Second half: 2 research projects will be selected and commence The total number of projects: maximum of 4	First half: To draw up a plan Open recruitment for research projects at IFReC for FY2011 Second half: 2 research projects will be selected and commence The total number of projects: maximum of 6	Review and evaluation The total number of projects: maximum of 6
	Term: 3 years Financial Support: roughly equivalent to Grant-in-Aid for Scientific Research of MEXT (B) (Kakenn-hi Kiban-B)			

Recruiting of young researchers and organizing symposia are suggested:

- Need to inject young researchers both from Japan and also internationally into the center – an important issue to consider is to give more independence to promising young investigators.
- Has the WPI project attracted more and more Japanese young scientists and graduate students and fellow from major universities of Japan?
- There need to be more aggressive plans for promoting interdisciplinary collaborations, e.g. more joint seminars, informal coffee discussions, and also multidisciplinary public programs. It will be good to invite other groups / departments in Osaka University to participate in many of these programs.
- IFReC has strategically positioned itself to be visible internationally and should continue to invest in this effort – including co-hosting a symposium in Singapore.
- New partnership with Pohang University of Science and Technology (Postech) and Institute for Systems Biology (ISB) is a way to show visibility of the new center.

Program	FY2009	FY2010	FY2011	FY2012
3) Symposia and Workshops	Two International Symposia in Japan and abroad have been fixed. Small-scale symposia and workshops are under consideration.	International Symposium (Japan) Small-scale symposia and workshops	International Symposium (Japan) Small-scale symposia and workshops	International Symposium (Japan) Small-scale symposia and workshops
4) Development of a manage-ment system for intellectual property	First half: To build a consensus within IFReC with the Office of University-Industry Collaboration, Osaka University Second half: To establish a Management section to handle intellectual property	To establish a Management section regarding intellectual property and to start essential activities regarding industry partnerships including the recruitment of researchers from industry		

Results

Junior PI Program: The first candidate of Junior PI is Dr Nicholas I Smith (previously an assistant professor of Graduate School of Engineering, Osaka University) was employed as a lecturer from June 1, 2009. He is a specialist of Raman microscopy, which enables visualization of intracellular nano-structures without labeling them by chemical or genetic engineering methods. He is now collaborating with bioinformatics groups (Dr Standley) and immunologists (Dr Akira) to image the immune response in macrophages and has been promised personnel and financial support as described in the above Table. We expect that his contribution will significantly increase the impact of imaging fusion on IFReC. This addresses the concern that imaging groups are used only as technicians by immunologists. Another junior PI is Dr Cevayir Coban (previously an assistant professor of Research Institute of Microbial Diseases, Osaka University), who was joined IFReC as an associate professor in January, 2010. She is a specialist of malaria immunity, aiming to better understand the role of host innate immune responses to malaria parasites by using mouse malaria models and genetically-modified mice. Her studies are expected to

development of new strategies such as new drugs or vaccines to combat malaria that is responsible for the deaths of over a million people each year.

Research Support Programs for Fusion of Different Fields: Upon invitation of IFReC researchers to apply this program, 9 proposals were accepted. Of these, 4 were headed by young imaging researchers, and 3 additional proposals were co-authored by imaging researchers. By fostering creative, collaborative research proposals, this program is one of our responses to the concern that imaging groups are used by immunologists. The budget is roughly equivalent to that given by MEXT Grant-in-Aid for Scientific Research (B) for one-year.

Symposia and Workshops: In 2009, IFReC organized or co-organized four international symposia, of which two were held abroad (Singapore and Seoul). Also held was an international workshop "Bioinformatics in Immunology" (November 6, Osaka University), which was held to promote the fusion of immunology, imaging and bioinformatics. In addition, a number of laboratory-organized seminars were held with visiting scientists as speakers. We have a plan to organize two international symposia in 2010 , of which one will be held in China.

Development of a management system for intellectual property: In order to cope with this point, we asked the Office for University-Industry Collaboration of Osaka University (UIC) to give us some advice. As a result, we have recently named Dr Ken Ishii (associate professor of IFReC) as the person in charge of handling various matters related to intellectual property. His role is initially just a liaison for patent application and its prior consultation. With support by UIC, we will set up a more concrete management system for intellectual property and industry partnerships within 2010. The necessity of this is obvious, because as many as 15 patent applications have been made by IFReC with high potential of generating seeds researchers since its establishment in 2007, indicative of IFReC with high potential of generating seeds for translational research.

Other efforts to meet the points that need improvement: Professor Hatazawa organized the 1st Clinical Immuno-Imaging Conference to be held on December 18 at Osaka University, which can be appreciated as IFReC's first step toward *development of research on the human immune system.*

We have made a considerable *improvement in our website*. The pages are designed to appeal visually our latest research and recent activities to the viewer, including the information about new project, "Research Support

	Program for Fusion of Different Fields" (see above). Special pages have been set up to show the exciting and latest research through multimedia presentation. In addition, we have set a platform for IFReC staff so that they can obtain most of the information supplied by administrative office, such as social insurance, guide-book for foreign researchers, and working regulations, etc. It is also possible to download various documents from the website.