FY 2007 WPI Project Progress Report
World Premier International Research Center (WPI) Initiative

Host Institution	Osaka University	Host Institution Head	Kiyokazu Washida, President
Research Center	Osaka University Immunology Frontier Research Center	Center Director	Shizuo Akira, Research Institute for Microbial Diseases, Osaka University, Professor

Summary of center project progress

The aim of this program is to unveil the whole picture of dynamic immune system by employing a variety of imaging techniques to visualize the immune cells within live animals. We will attempt to improve an imaging technology, which allows us to track the dynamic behavior of immune cells and their communications more directly and understand how immune cells respond to non-self such as pathogens and cancers in vivo. Based on these basic studies, we will seek to develop new strategies for diagnosis and treatment of various diseases including infectious diseases, autoimmune diseases, allergy and cancer.
Following is a summary of center project progress at present.

1. Invitation of Principal Investigators:
We invited totally 18 Principal Investigators. 13 Principal Investigators are for Immunology Research Group, and 5 Principal Investigators are for Imaging Research Group.

2. Constituent members:
We employed postdocs and laboratory technicians for each of Principal Investigators.In some laboratories, research assistant professors have been employed. Priority is given to foreign researchers. Total number of researchers did not reach to the planned number, however, recruitment of researchers being employed by university budget into this project will be accelerated. To facilitate management in English, we employed English-speaking administrative staffs.

3. Cooperative institutions:
We made cooperative contracts with 6 overseas institutions and satellite contracts with 2 domestic institutions. We are keeping close contact with those researchers regarding research contents and plans through E-mail etc.
And also we are planning to send researchers to those cooperative institutions to promote research exchanges.

4. Administrative department:
Dr. Norio Furushiro, Administrative Director, heads the administration department. The administration department currently has two sections: accounting section and general affairs section. Each section has a senior supervisor with rich administrative experiences in the University, and several English-speaking personnel. The research management section will set up in 2008. It will consist of members with PhD degree. The section will deal with symposia, public information and issues relating to intellectual properties. We recruited personnel.

5. New research facility:
New facility will be constructed in March 2009 with Osaka University budget and external donation. 10-story building of 9,600m² space.

6. Animal experimentation facility:
We are planning to build an animal experimentation facility exclusively for WPI-IFReC in May 2009. This facility has 4 floors of 2,400m² area. The capacity is around 5,000 cages, which can keep approx. 20 thousand to 25 thousand mice.

7. Equipments:
We installed foundation equipments for advancing immunology and imaging research. (Flowcytometers, In vivo imaging system and others.)

8. Kick-off Symposium:
Kick-off Symposium was held on March 27- 28, 2008 in Osaka. 21 researchers, including Principal Investigators and researchers of cooperative institutions, presented the studies of their cutting-edge research. Approx. 800 people in total participated.

9. Recruitment of Specially Appointed Professors, Associate Professors and Postdocs:
Recruitment of researchers has been carried out on an international basis by posting advertisement on “Nature” journal, etc.

10. Acquisition of external funding:
Approx. 625 million yen.

11. Research achievement:
The study of innate immunity (DNA vaccine) was published in “Nature” journal. And also study of molecular mechanism of Herpes simplex virus infection appeared in “Cell” journal.

12. Public relations activity:
We established our website to get public widely informed about activities of the center.

13. Support from host institution: Osaka University assists this center by making every possible support for operation and research activities. Osaka University provides WPI-IFReC with resources that would be greater or equal to the WPI project grant.

1. Summary of center project

<Initial plan>

General plan of the project

The aim of this program is to unveil the whole picture of dynamic immune system by employing a variety of imaging techniques to visualize the immune cells within live animals. We will attempt to improve an imaging technology, which allows us to track the dynamic behavior of immune cells and their communications more directly and understand how immune cells respond to non-self such as pathogens and cancers in vivo. Based on these basic studies, we will seek to 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 expand by forming a linkage with domestic and overseas institutions that will function as satellites.

<Results/progress/alternations from initial plan>

In 2007, with main 18 Principal Investigators, we started researching to achieve our goal "Development of a new research technique through the fusion of immunology and imaging".

We also made 6 partnership contracts with 6 foreign institutions as well as satellite contracts with 2 domestic institutions. We are working together closely with them to develop our projects.

Especially, Immunology and Imaging research meetings will be held regurally to promote research.

In research environment Osaka University gives full supports by implementing institution reform that are necessary for formation of the Immunology frontier research center.

The administrative department fully supports researchers by leading by administrative director who is a researcher, setting English-speaking personnel and covering operation wider aiming to generate environment where researchers can concentrate on their research.

2. Research fields

<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 invading microbial pathogens, is therapeutically important with regards to treat various diseases (infectious disease, allergy, inflammation, autoimmune disease, and immunodeficiency, etc.) in which the immune system takes part. Although numerous studies have focused on identifications of cells and factors involved in the immune system, it still remains unclear how immune cells are actually changed in response to infections or in pathological conditions in vivo. Thus, it will be necessary to develop a new imaging technology that tracks immune responses as well as a method to artificially control the immune response in the future. In foreign countries, the uniting type of research on immunology and the imaging technology has already started. However, both fields are still isolated and it has not become uniting in Japan. The basic research on immunology in Japan, especially

<Results/progress/alternations from initial plan>

No alterations

Osaka University, is internationally in a very high level. Therefore, creating a research center for immunology in Osaka University in which domestic and overseas researchers gather that aims to image the immune system in vivo is important to establish not only an new field of basic science but also overcome the above-mentioned diseases.

Similar fields already exist in Japan or overseas
Basel Institute for Immunology, Basel, Switzerland (1971-2001)

3. Research objectives

<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 provide us to understand the dynamics of immune system in normal and pathological conditions. New findings obtained through imaging of the immune reaction 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 a new technology that can visualize the dynamics of 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 a world-top class research in the field of engineering. This is a merit to perform a 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 a high resolution that is rarely housed in other laboratories of Japan, which is indispensable for achieving our project.

<Results/progress/alternations from initial plan>

Aiming at fusion of immunology and imaging, we have started our research from the aspect of understanding what we want to measure as an existing immunology group, and what we are able to measure as an imaging group.

In the future, we will hold the seminars regularly to promote the research.

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** Dr. Norio Furushiro, Administrative Director, heads the administration department. The administration department currently has two sections: accounting section and general affairs section. Each section has a senior supervisor with rich administrative experiences in the University, and several English-speaking personnel. The research management section will be set up in 2008. It will consist of members with PhD degree. The section will deal with symposia, public information and issues relating to intellectual properties. We recruited personnel.
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** Osaka University allows the Director of the center to determine major issues by his top-down decision making. Some issues will be discussed with Center management committee and the board of representatives as needed. In future, the International Advisory Board will be held at the every other year.
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** Osaka University has approved the backup by including project of center in the mid-term strategic target. Osaka University allows the Director of the center to determine major issues by his top-down decision making.

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 (Date: month, year)	Results at end of FY 2007	April, 2008
Researchers from within host institution	10	10	10	10	10
Foreign researchers invited from abroad	1	2	5	1	1
Researchers invited from other Japanese institutions	6	6	7	7	7
Total principal investigators	17	18	22	18	18

All members

	At beginning	Planned for end of FY 2007	Final goal (Date: month, year)	Results at end of FY 2007	April, 2008
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 %>	52 < 8, 15 %> [7, 13 %]	69 < 12, 17%> [10, 15 %]
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 %>	18 < 1, 6 %> [0, 0 %]	18 < 1, 6%> [0, 0%]
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 %>	34 < 7, 21 %> [7, 21 %]	51 < 11, 22%> [10, 20 %]
Research support staffs	28	34	44	3	15
Administrative staffs	9	15	15	13	13
Total	86	131	206	68	97

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>** Kyoto University was added as a satellite. Institution (1) RIKEN Research Center for Allergy and Immunology **-Role** No alteration **-Personnel composition and structure** No alteration **-Collaborative framework** We concluded contract with above institution. We allocate staff to RIKEN Research Center for Allergy and Immunology and start actual exchange from FY2008. Institution (2) Kyoto University, Institute for Frontier Medical Sciences **-Role** Institute for Frontier Medical Sciences contributes to improve imaging technique of the center. **-Personnel composition and structure-** Shimon Sakaguchi, Department of Experimental Pathology, Institute for Frontier Medical Sciences **-Collaborative framework** We concluded contract with above institution. We allocate staff to Institute for Frontier Medical Sciences and start actual exchange from FY2008.
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**	**<Results/progress/alternations from initial plan>** **-Names of Institutions** No alteration **-Role** No alteration **-Personnel composition and structure** No alteration **-Collaborative framework** We are keeping close contact with those researchers of 6 cooperative institutions regarding research contents and plans through E-mail, etc. And also we are planning to send researchers regularly to each satellite to improve imaging technology and deepen research exchanges. Osaka University will offer employment expense for postdocs from April 2008. Agreements between the center and partner institutions are under discussion to realize these plans. We already have reached conclusion of contracts with 3 institutions and they are in the process. Conclusion of contracts between the center

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 expense to hire several Postdocs to above institutions.	and rest of 3 institutions are under discussion on final adjustment stage and will be agreed soon.

6. Summary of center's research environment

<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. **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. **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	**<Results/progress/alternations from initial plan>** **1) Environment in which researchers can devote themselves to their research** Dr. Norio Furushiro, Administrative Director, heads the administration department. The administration department currently has two sections: accounting section and general affairs section. Each section has a senior supervisor with rich administrative experiences in the University, and several English-speaking personnel. It provides the environment where researchers can devote themselves to their research. The research management section will be set up in 2008. It will consist of members with PhD degree. The section will deal with symposia, public information and issues relating to intellectual properties. We recruited personnel. Although research management section will be set up in FY2008, existing administrative department succeeded to plan and manage holding Kick-off symposium in FY2007, establishing center's website and publishing PR brochures, etc. without using time and work of researchers. **2) Startup research funding** A start-up research fund is allocated to laboratories to establish research structure. Allocation of the fund is done through the top down decision by the director. **3) Postdoctoral positions through open international solicitations** Recruitment of Postdocs has been carried out by posting advertisements on "Nature" journal (world edition) and our website. **4) Administrative personnel who can facilitate the use of English in the work process** Dr. Norio Furushiro, Director of International Student Center and Administrative Director of IFReC, takes a leading part of administrative department.

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.

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.

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.

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.

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.

The administrative department has two sections: accounting section and general affairs section each consisting of a senior supervisor with rich administrative experiences in Osaka University, and several English-speaking personnel who have over 850 TOEIC score. The department helps foreign researchers, manages partnership with research institutions in abroad, public relation activities and organizes symposia in order to make center as a world top research institution. The administrative department fully supports researchers so that they can concentrate on their research.

5) Rigorous system for evaluating research and system of merit-based compensation

The center organizes the International Advisory Board consisting of immunologists from domestic and international institutions. The International Advisory Board will conduct evaluation of research groups' performance every other year from FY 2008. The Director determines salaries of Principal Investigators and other staffs based on evaluation by the International Advisory Board and evaluation system of the Center.

6) Equipment and facilities, including laboratory space, appropriate to a top world-level research center

Constitution of the main building for research began in Jan. 2008. 10-story building of 9,600m² space.

Constitution of the building for animal experimentation is scheduled to start in Aug. 2008. 4-story building of 2,400m² space.

The center mainly purchased equipments necessary for imaging research.

7) International research conferences or symposiums held regularly to bring world's leading researchers together

The center organized Kick-off Symposium of WPI-IFReC on the theme of "Immunology and Imaging" on March 27-28, 2008. 21 premier investigators gave speeches at the symposium. It had approx. 380 attendances on 27th and approx. 350 attendances on 28th.

8) Other measures, if any

Support Office for International Students and Scholars that assists foreign researcher's entry into Japan and residence, etc. started its operation.

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

<Initial plan>

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 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.

<Current assessment>

The center organized International Advisory Board consisting of immunologist from domestic and international institutions. The International Advisory Board will start evaluation of research groups every other year in FY 2008.

The center established International Advisory Board based on the approval of total 7 members (5 foreign members and 2 Japanese members). The 1st International Advisory Board committee will be held at the end of FY2008 or FY2009. The members of International Advisory Board are as follows;

-Jeffrey Ravetch
（Professor, Laboratory of Molecular Genetics and Immunology, The Rockefeller University）
-Richard Locksley
（Professor, Departments of Medicine and Microbiology/Immunology, University of California, San Francisco）
-Anne O'garra
（Head, Division of Immunoregulation, The National Institute for Medical Research）
-Lewis Lanier
（Professor and Vice Chair, Department of Microbiology & Immunology, University of California, San Francisco）
-Shimon Weiss
（Professor, Department of Chemistry and Biochemistry, University of California, Los Angeles）
-Kiyoshi Takatsu
（Invited Professor/Endowed Chairs, Department of Immunobiology and Pharmacological Genetics, Graduate School of Medicine and Pharmaceutical Sciences for Research, University of Toyama）
-Kayo Inaba
（Professor, Graduate School of Biostudies, Kyoto University）

- 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.	

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. **ii) Prospects after establishment of the center** 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 program 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	**i) Past record** No alteration **ii) Actual performance of FY2007** The specific performance was as follows: 1) Employment cost：736,517dollars = 88,382,000 yen 2) Business promotion cost：3,422,749 dollars = 410,729,886 yen 3) Business trip cost：14,345 dollars = 1,721,480 yen 4) Equipment cost：7,743 dollars = 929,162 yen 5) Research project cost：5,208,765 dollars = 625,051,865 yen Total：9,390,119 dollars =1,126,814,393 yen Although we initially indicated figures of annual prospects, actual performance of FY 2007 is that of half year from October 2007 to March 2008. Notes: 1) All of the Indirect cost from this program will be used for the Research Center. 2) Construction cost for the main research building (10-story building of 9,600m² space) : 20.8 million dollars = 2,500,000,000 yen 3) The center borrowed 8.75 million dollars = 1,050,000,000 yen by using university lending system and will start construction of building for animal experimentation.

billion yen x 0.8 / 9.5 = 1.8 million dollars or 210 million yen).	

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. **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.	No alterations

10. Host institution's commitment

<Initial plan> **-Provision in host institution's mid-to-long-term plan**	**<Results/progress/alternations from 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	Osaka University established backup system for the center based on "accomplishing high-level research results and playing a crucial role in the establishment of the WPI" in the medium term target and the medium term plan.

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" projects, 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 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 projects, 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.

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.

-Concrete Measures

(1) Competitive grants obtained by researchers participating in the project and in-kind contributions, etc.

Osaka University supplies facilities of university for the center in order to support activities of the center.

The specific performance was as follows:

1) Employment cost：736,517dollars = 88,382,000 yen
2) Business promotion cost：3,422,749 dollars = 410,729,886 yen
3) Business trip cost：14,345 dollars = 1,721,480 yen
4) Equipment cost：7,743 dollars = 929,162 yen
5) Research project cost：5,208,765 dollars = 625,051,865 yen

Total：9,390,119 dollars =1,126,814,393 yen

Although we initially indicated figures of annual prospects, actual performance of FY 2007 is that of half year from October 2007 to March 2008.

Notes:

1) Most of the Indirect research expenses from this program will be used for the WPI.

2)The main research building (9,400 m^2 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 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.

(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.

(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.

(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 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.

Notes:

1) All of the Indirect cost from this program will be used for the Research Center.

2) Construction cost for the main research building (10-story building of 9,600m² space) : 20.8 million dollars = 2,500,000,000 yen

3）The center borrowed 8.75 million dollars = 1,050,000,000 yen by using university lending system and will start construction of building for animal experimentation.

(2) System under which the center's director is able to make substantive personnel and budget allocation decisions

Osaka University allows the Director of the center to determine employment and annual salaries of staffs by his top-down decision making. The budget of the center will be allocated intensively in proportion to the condition and research progress of the center.

(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

Osaka University treats the center as a special department. Osaka University established special regulations on personnel, etc. for the center. The administrative board of the university also promotes to get acknowledgement of center's position in the university. Osaka University also started to consider institutionalization of system for academic staffs to make them concentrate on research being exempted from other works such as education and administrative 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

Osaka University established special regulations on personnel as special measures for WPI project to support flexible employment. We are making regulations in English.

・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.

(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.

(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".

(5) Accommodation of center's requirements for infrastructural support (facilities, e.g., laboratory space; equipment; land, etc.)

Osaka University started to construct a new research building to support the center by using accumulated surplus and donation. It also plans to construct a new building for animal experimentation completed around the same time. Osaka University also installed a lending system in the university. It enables the center to refund the construction cost in 8 years by using its indirect expenses.

(6) Support for other types of assistance

Osaka University started 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.

11. FY 2007 funding

(Exchange Rate: JPY/USD=120)

Cost Items	Details	Costs (ten thousand dollars)
Personnel	Center director and Administrative director	11
	Principal investigators (9 persons):	47
	Other researchers (48 persons):	55
	Research support staffs (3 persons):	2
	Administrative staffs (4 persons):	15
	Total	130
Project activities	Gratuities and honoraria paid to invited principal investigators (none):	0
	Cost of dispatching scientists (8 persons):	9
	Research startup cost (6 persons):	15
	Cost of satellite organizations (2 organizations):	0
	Cost of international symposiums (one time):	13
	Rental fees for facilities	0
	Cost of consumables	50
	Cost of utilities	32
	Other costs	289
	Total	408
Travel	Domestic travel costs	2
	Overseas travel costs	1
	Travel and accommodations cost for invited scientists (2 of domestic scientists): (6 of overseas scientists):	2
	Travel cost for scientists on secondment (3 of domestic scientists): (1 of overseas scientists):	1
	Total	6
Equipment	Depreciation of buildings	1
	Depreciation of equipment	6
	Total	7
Other research projects	Projects supported by other government subsidies, etc.	15
	Comissioned research projects, etc.	362
	Grants-in-Aid for Scientific Research, etc.	144
	Total	521
Total		1,072

Ten thousand dollars (Exchange Rate: JPY/USD=120)

WPI grant for FY 2007		602
Costs of establishing and maintaining facilities in FY 2007		830
Establishing new facilities (Number of facilities: 1 , 9,600m²)	Costs paid:	784
Repairing facilities (Number of facilities: 2 , 355m²)	Costs paid:	46
Others		0
Cost of equipment procured in FY 2007		394
Name of equipment: Cell sorting system Number of units: 2	Costs paid:	102
Name of equipment: In vivo imaging system Number of units: 1	Costs paid:	60
Name of equipment: Flowcytometer Number of units: 4	Costs paid:	56
Name of equipment: Two Photon Laser Scanning Microscopy Number of units: 1	Costs paid:	56
Name of equipment: BD FACSalibur HG Flow Cytometry System Number of units: 1	Costs paid:	13
Name of equipment: Confocal Laser Scan Microscope Number of units: 1	Costs paid:	13
Others		94

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

-Points specified as needing improvement

1. Innovation of Japan's scientific structure could be achieved if more creativity was introduced into this team.
Participants with other backgrounds-- e.g. genomics, physics, mathematics--may provide unexpected new frontiers in "classical" immunology research. Particularly, genomics should be made a strong component.
To open up this discussion it may be meaningful to hold a brainstorming conference with specialists in these fields. Needless to say, genome-environment interaction is of great importance for developing immunological disorders.

2. This center should advance diversity by having special programs, fellowships, and positions for women.
Japan has some extremely intelligent, capable women medical scientists and their careers could be advanced significantly but more importantly, Japan would benefit from their discoveries, new products, new medical based industries, jobs and a strengthened economy.

3. Expansion of the participation of researchers from Japan ("out of Osaka") and various Asian countries is needed.

4. It is recommended to implement exchanges and avoid inbreeding tendencies typical of Japanese academic institutions. Thus, a policy must be developed to encourage incoming and outgoing scientists.

5. The biggest weakness of this application is the passive attitude toward attracting international researchers.
In order to meet WPI goals, it is important to establish the international environment from the very beginning, not wait for research results. In that sense, the center needs more foreign PIs. Ways should be devised to invite more top-level senior researchers from abroad. A more active recruiting system should be set up. For example, if it establishes very prestigious highly remunerative visiting fellowships, Osaka could attract really top scientists from overseas.

6. There should be a stronger focus on training immunologists since the need worldwide for competent immunologists is significant.

-Modifications included in the revised proposal for FY2007

1. We will hold international research conferences or symposia. In these events, we will often include a brainstorming session by inviting top scientists in other research areas, including genomics, physics and mathematics, which may provide unexpected new frontiers in immunology research. Especially, genomics is an important component since genome-environment interaction appears to be linked to immunological disorders.

2,3. We will recruit high capable non-Japanese scientists from Asian countries as well as Japanese female scientists with high priority throughout the program.

4. We will actively support world top-level researchers.
- We started flexible employment system and international environment by hiring Researchers and Postdocs through advertisement of positions on major journals, such as "Nature".
- We are fostering young researchers to Principal Investigators level.

5. We plan to actively seek top-level foreign researchers to hire with generous salary and excellent research environments.

6. Collaborations with domestic and international institutions will give good effect on young researchers.

7. Collaborations with research institutions with top-level imaging science will lead to innovative advancement in science.

8. Effort of Dr. Yanagida in WPI-IFReC was increased to 25%.

-Progress in FY 2007

We hired 10 female scientists and 9 scientists from Asian countries. We hired 5 Japanese scientists from outside of Osaka University.

7. The center should have stronger connections with external molecular imaging programs. The program at Osaka University is strong, but it needs to show more collaboration with groups that may be examining other modalities or have other approaches. 8. Given the importance of imaging to this project, Prof. Yanagida should increase his time commitment.	