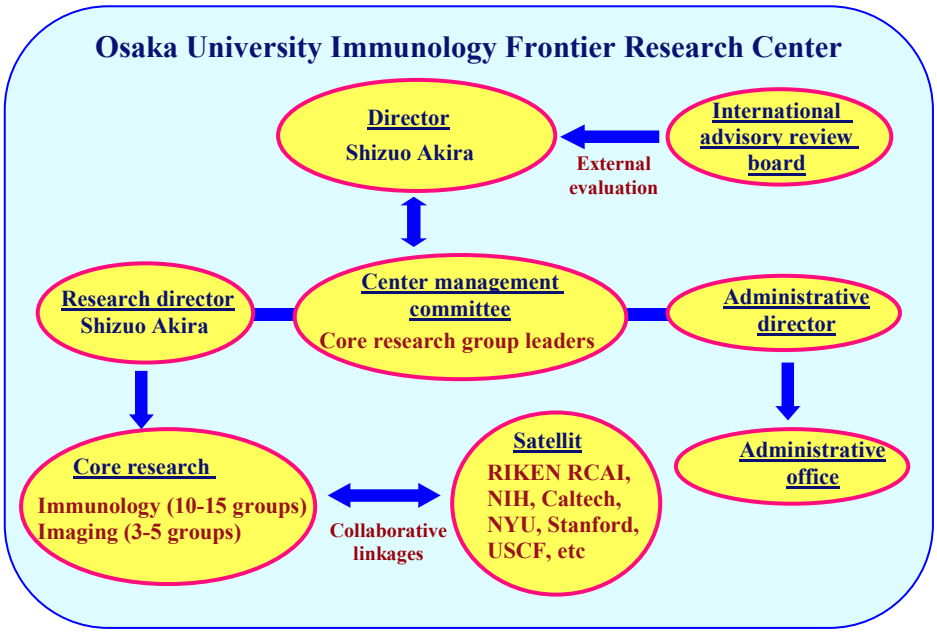
Research Center Project

Host institution name	Osaka University
Head of host institution	Kiyokazu Washida, President
Title of center project	Osaka University Immunology Frontier Research Center
Center name	Osaka University Immunology Frontier Research Center (IFReC)
Project summary	・ Briefly describe the 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. ・ Include a chart that illustrates the center's overall structure including its collaborative linkages with other domestic and foreign institutions, its system of external evaluation, and its management framework 

(1) Research fields

・ Fill in the name of the research field of the project.

Immunology and Bioengineering

・ Choose relevant fields from among ①－⑦ below, specifying the inter disciplinary field(s) that the project addresses.

Biosciences, Precision and mechanical engineering

①Biosciences, ②Chemistry, ③Material sciences, ④Electronics engineering and information sciences, ⑤Precision and mechanical engineering, ⑥Physics, ⑦Mathematics

・Describe the 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 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.

・If centers in similar fields already exist in Japan or overseas, please list them.

Basel Institute for Immunology, Basel, Switzerland (1971-2001)

(2) Research objectives

・Describe in a clear and easy-to-understand manner the research objectives that the project seeks to achieve by the end of the grant period (in 10 years). In describing the objectives, the following should be articulated in an easily understandable manner: What new domains are expected to be pioneered by fusing the target fields. In the process, what world-level scientific issues are sought to be resolved. What is the expected impact of the scientific advances to be achieved on society in the future.

○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.

・Describe concretely the 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.

(3) Management

i) Prospective center director

・ Fill in the name of the prospective center director, his/her age (as of 1 October 2007), current affiliation and position title, and specialties. Describe his/her qualifications to be the center director.

Name; Shizuo Akira
Age; 54
Affiliation and title; Professor, Immunology Frontier Research Center, Osaka University
Specialties; Immunology
Qualifications; Professor Shizuo Akira has been obtaining several big grants in Japan, including CREST, ERATO and 21 century COE, and he, as a project leader of these grants, has successively published so many papers concerning innate immunity with high citation. These findings clearly demonstrate that he has an ability to manage and organize a big grant program. Moreover, the fact that he has obtained several international awards and topped a list of highly cited researchers in the field of Immunology is attractive to many domestic and foreign researchers involved in immunology research as well as in the imaging research, and will make them participate in the establishment of this world-premier immunology center as principal investigators and satellite researchers.

・ Attach a biographical sketch of the prospective center director using Appendix 2.

・ How does the prospective center director intend to construct the center and what is his/her vision of objectives to be achieved? Provide a synopsis written by the prospective center director (free format).

・ If possible, attach a letter (s) of recommendation for the prospective center director from researchers with world-standard achievements in the subject field.

ii) Prospective administrative director

・Fill in the name of the prospective administrative director, his/her age (as of 1 October 2007), current affiliation and position title. Describe his/her qualifications to be the administrative director.

Name: Norio Furushiro
Age: 63
Affiliation: International Student Center, Osaka University
Position title: Director and Professor
Qualifications: Dr. Norio Furushiro, the Director of the International Student Center and Professor of Osaka University, is familiar with managements in English, and organization and administration system of Osaka University.

・Attach a CV of the prospective administrative director (free format).

iii) Composition of administrative staff

・Concretely describe how the administrative staff is organized.

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 two senior supervisors 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.

iv) Decision-making system

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

Center management committee consisting of 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 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.

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

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

The University president will approve the mid-to-long term plan of the center and the center director's decisions on major issues necessary for center's managements, such as researchers' salaries, appointment of new researchers and administrative director. The University president will make appointment of director, determine the salary of director and make evaluation of the center's performance.

(4) Researchers and other center staffs

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

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

	numbers		
	At beginning	At end of FY 2007	Final goal (Date: April, 2010)
Researchers from within the host institution	10	10	10
Foreign researchers invited from abroad	1	2	5
Researchers invited from other Japanese institutions	6	6	7
Total principal investigators	17	18	22

・Describe the concrete plan to achieve final staffing goal, including steps and timetables.

(At the beginning)

Ten Professors from within Osaka University (Shizuo Akira, Tadamitsu Kishimoto, Toshio Hirano, Masayuki Miyasaka, Hitoshi Kikutani, Taroh Kinoshita, Atsushi Kumanogoh, Kiyoshi Takeda, Hisashi Arase and Toshio Yanagida) will set up and start the Research Center with Shizuo Akira as the director. Two immunologists from RIKEN (Takashi Saito and Tomohiro Kurosaki) will join the center as Professors. Prof. Melchers, as a part-time principal investigator, will start preparation to set up research group while he will advise the director about organization of an international research center in Immunology based on his enormous experiences in organizing Basel Institute for Immunology for twenty years. Two members in imaging science (Yoshichika Yoshioka and Takashi Jin) will come to Osaka University and set up labs in space provided by the University. Junji Seki and Yutaka Hata will also join as a part-time principal investigator. Their labs will be located in the same building as Yanagida's lab and they will all together form "Imaging group".

(At the beginning of FY 2009)

When the new main research building is completed, Prof. Shimon Sakaguchi will join.

(By the beginning of FY2010)

We will recruit two, preferably young, principal investigators from abroad through international solicitation.

・Attach a list of principal investigators who are expected to join the center at the time of the application using Appendix 1. Place an asterisk (*) by names of the investigators considered to be ranked among the world's top researchers. Describe the policy and strategy for inviting the rest of PIs who are to be invited in the future.

We plan to invite two principal investigators from abroad by April 2010. We will invite highly active young investigators at Associate or Assistant Professor level. We will offer them full support including equipped research laboratory and office, 3-4 post-doc positions, 2-3 support staffs and 5-year research fund. Our strategy is to bring forth examples of foreign young principal investigators who are successful in research operation in Japan, in turn, to attract more foreign investigators of high potential. We also plan to actively recruit top-level researchers from abroad by providing higher salary and good research environment. While investigators who are considered as top-quality researchers will be strongly supported by the center,

investigators whose evaluation by the international advisory review board is low have to leave the center. This will increase the mobility of scientists as well as maintain and further upgrade scientific standards of the center.

・Attach a biographical sketch of each investigator using Appendix 2.

・As for the researchers invited from abroad or from other Japanese institutions, attach a letter of intent from each of them to join the center project (free format).

b) Total members

	Numbers		
	At beginning	At end of FY 2007	Final goal (Date: April, 2010)
Researchers (Number of foreign researchers among them and their percentage)	49 (12, 24%)	82 (25, 30%)	147 (47, 32%)
Principal investigators (Number of foreign researchers among them and their percentage)	17 (1, 6%)	18 (2, 11%)	22 (5, 23%)
Other researchers (Number of foreign researchers among them and their percentage)	32 (11, 34%)	64 (23, 36%)	125 (30, 34%)
Research support staffs	28	34	44
Administrative staffs	9	15	15
Total number of people who form the “core” of the research center	86	131	206

・Describe your concrete plan to achieve the final staffing goal, including steps and timetables.

(At the beginning)

Thirty or more researchers at levels of Assistant Professors and post-doctoral fellows, at least eleven of them being foreign researchers, will be hired in seventeen research groups. About 30 technicians and secretaries will be hired and nine of 15 administrative staffs will be hired. In total, the Research Center will be consisted of 86 or so members at the beginning.

(At the end of FY2007 or the beginning of FY2008)

The number of researchers at levels of Assistant Professors and post-doctoral fellows will be increased to 50 or more. Among them 19 or more will be foreign researchers. We will also hire 10 graduate students as Research Assistants (Four of them will be foreign students). The total number of technicians and secretaries will be increased to 34. The administrative department will become fully staffed with 15 members. Total number of members in the Research Center will be 130 or so at the beginning of FY2008.

(By the beginning of FY2010)

Three more principal investigators (one from Kyoto and two from abroad) will join the center by this time. More researchers at levels of Assistant Professor and post-doctoral fellow will be hired for these new research groups and other groups, and the total number of researchers at these levels will be 90-100. We will hire 20 more Research Assistants. Total number of support staffs will be 44. In total, the center will have about 200 members. We will recruit highly capable non-Japanese scientists from Asian countries as well as Japanese female scientists with high priority throughout the program.

ii) Collaboration with other institutions

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

Domestic

RIKEN Research Center for Allergy and Immunology

Overseas

NIH (Ronald Germain, Deputy Chief, Laboratory of Immunology and Chief, Lymphocyte Biology Section, NIAID)

New York Univ. (Michael Dustin, Professor, Skirball Institute of Biomolecular Medicine)

California Institute of Technology (Scott Fraser, Director, Biological Imaging Center, Beckman Institute)

Harvard Medical School (Ulrich H. von Andrian, Professor, Department of Pathology)

Stanford University School of Medicine (Mark Davis, Professor, Department of Microbiology and Immunology)

University of California San Francisco (Jason Cyster, Professor, Department of Microbiology and Immunology)

The center will provide each satellite lab costs to hire several postdoctoral fellows. Researchers in the center and satellites will regularly visit each other and exchange the information to upgrade the scientific standard in imaging. These interactions will provide an environment for the training of young immunologists. We will attempt to have strong connections with various molecular imaging programs in addition to these satellites, in which more innovative researches will be expected.

・If some of the principal investigators will be stationed at satellites, attach a list of these principal investigators and the name of their satellite organizations using Appendix 1, and provide a biographical sketch of each using Appendix 2.

Not applicable

・If the “core” forms organic linkages with other institutions, domestic and/or foreign, without establishing satellite functions, fill in the names of the partner institutions and describe their roles and linkages within the center project.

(５) Research Environment

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

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

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 two 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.

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

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.

ⅲ) As a rule, fill 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.

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

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 two senior supervisor with rich administrative experiences in the University, several bilingual or English-speaking full-time and part-time personnel.

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

The director will organize the International Advisory Board consisting of ten-odd renowned immunologists. The International Advisory Board will conduct evaluation of research groups' performance every or every other year. The director will determine principal investigators' salaries based on the evaluation by the International Advisory Board.

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

The main research building (ten floors and 9,600 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.

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

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. In this forum, 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.

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

Based on advices and/or suggestions by the International Advisory Board, the director will set up research environment suitable for international researchers.

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

・Describe concretely the following points.

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

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.
- 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.

(7) Securing research funding

i) Past record

・Indicate the total amount of research funding (e.g., competitive funding) secured by principal investigators who will join the center project. Itemize by fiscal year (FY2002-2006) taking into account the percentage of time each will devote to research activities at the center vis-à-vis the total time they spend conducting research activities（"Effort ②" in Appendix 2）. For example, if this percentage is 70%, then 70% of his/her research funds can be counted in calculating the total amount of research funds.

Past record of competitive research grants for Principal Investigators

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

・ Based on the past record, describe the concrete prospects for securing resources that match or exceed the project grant.
・ Calculate the total amount of research funding (e.g., competitive funding) based on the percentage of time the researchers devote to research activities at the center vis-à-vis the total time they spend conducting research activities（"Effort ②" in Appendix 2）. Be sure the prospects are realistically based on the past record.

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.

Others

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

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.

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

- If one or more of the projects applying for Global COE program have some connections with this research center project, list the project title(s) , outline(s), group leader(s) and the relationship(s) with this project.

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.