Self-Evaluation Report for Interim Evaluation
World Premier International Research Center Initiative (WPI)

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Research Center	Osaka University Immunology Frontier Research Center (IFReC)	Center Director	Shizuo Akira

Report Abstract

Over the initial period between FY2007 and FY2010, IFReC has made steady progress to establish itself as a WPI center true to its founding principles. Thus, while recognizing that further efforts are needed in various aspects, IFReC has well conformed to the main requirements of the WPI program as well as comfortably achieved the numerical targets stated in the program.

Science level

Even viewed objectively, the science ongoing at IFReC is considered to be of the internationally highest quality as indicated by the number of high quality publications and awards. In fact, according to the latest database (Thomson Reuters Essential Science Indicators for 2000 – 2010), the research groups of IFReC (Akira and others) has ranked Osaka University 1st in citation impact among the top 30 institutions in immunology all over the world. In addition, many principal investigators (PIs) have been invited to international symposia as plenary speakers. Among many awards given to IFReC researchers, notable are the Crafoord Prizes (2009) and the Japan Prizes (2011) to Kishimoto and Hirano and 2011 Canada Gairdner International Award to Akira. Another indication of the high quality of science at IFReC is that several government-sponsored grants of large scale have been obtained by PIs for last three years, which include JSPS-FIRST (Akira), JST-CREST (Hirano, Arase, Kurosaki and M. Ishii) and JST-PRESTO (Smith). These research funds have been very effective to boost the morale of all IFReC staff as well.

Globalization of the institution

We are confident that IFReC's international visibility in science has ever been increasing. As of March the 31st, 2011, the number of overseas PIs has reached 6 out of a total of 27, and the percentage of overseas researchers at all levels has reached 32% (56 non-Japanese out of a total of 173); clearing the WPI target of 30%. This is a major increase compared with 12% in April, 2008, of which the Kishimoto Fund Fellowships/ Scholarships program set-up in 2009 has been of great help. This program supports overseas researchers and students for short or long term stays at IFReC.

A marked increase in interest from overseas research institutions reflects our increasing international visibility. Thus, in addition to seven overseas partner institutions, we concluded academic cooperation agreements with Pohang University of Science and Technology, Korea (2009) and with the Indian Institute of Science Education and Research, Bhopal, India (2010). For the past three years, we received invitations exchange of scientific staff or for the future collaboration from the Ministry of Research, Science & Technology, New Zealand, the Dutch Innovation Platform and two overseas pharmaceutical companies.

International symposia of a large scale have been organized every year by ourselves (Immune Regulation: Present and Future, 2009; Immunology Forefront, 2010) or jointly with immunological institutions or societies in other countries (IFReC/Singapore Immunology Network (SIgN) joint symposium on Integrating Immune Networks with Immuno-Imaging, 2009; IFReC/Chinese Society for Immunology (CSI) joint Symposium, 2010).

To further step forward and foster young immunologists, IFReC and SIgN have reached an agreement to jointly organize a Winter School on Advanced Immunology every year, the first be scheduled in early 2012 in Japan.

Interdisciplinary research activities

We must admit that this item leaves the most room for improvement among the concepts stated in the WPI program, though efforts of collaboration have been made by imaging and bioinformatics researchers with immunologists. To construct a better platform for collaboration, we have introduced the "Research Support Program for Fusion of Different Fields", which provides IFReC's young researchers in different disciplines the financial support to start collaborative studies (15 research projects are now in progress). The projects are annually reviewed by IFReC PIs in a hearing open to all IFReC researchers. A series of the IFReC Interactive seminars has also been started. This is to

increase opportunities for researchers to interact with each other and to start their innovative collaborations.

These measures will become very effective now that the Integrated Life Science (ILS) building (2009) and the new IFReC building (2011) (see Research Facilities) were constructed. These two research buildings accommodate 18 laboratories (immunology, 11; imaging, 5; bioinformatics, 2), so that the core researchers of IFReC are now able to work under one roof, a most effective way to enhance the "Interdisciplinary research activities".

The opening of the Center for Information and Neural Networks (CiNeT) of the National Institute of Information and Communications Technology (NICT) and Quantitative Biology Center (QBiC) of the Rikagaku Kenkyūsho institute (RIKEN) (refer to Commitment of Host Institution) within walking distance from IFReC is scheduled in the near future. Both centers are headed by Yanagida. The main focus of CiNeT is the technological innovation allowing for the direct imaging of cellular activity, metabolism and systems analysis of cellular networks in the brain, while quantitative and comprehensive studies are performed to predict and control biological activities at QBiC. Although the missions and goals of these centers are different from those of IFReC, the methodologies and technologies are common to the three institutions, so that collaborations with these centers will help IFReC to advance interdisciplinary researches necessary for making breakthroughs in classical immunology.

Organizational reform

A top-down decision-making system, significantly different from the management systems in other faculties and institutions within the University, has been well understood through the whole organization of IFReC. Thus, the director makes major decisions of administrative matters, to which the Administrative Director gives full support by acting as a coordinator with the Deputy Directors and by executing management actions through the reformed administrative office, wherein the 'Research Management and Planning' office has been founded to which three PhD holders with research experience have been posted. This office is responsible for facilitating interdisciplinary researches, organizing symposia and seminars, outreach activities, etc.

Other aspects

Center Personnel Allocation: In this respect, IFReC has well cleared the targets of items requested by the WPI program (given in parentheses): the total number of PIs, 27 (10-20); total number of researchers and staff, 243 (about 200); the percentage of researchers at all levels from overseas, 32% (> 30%). Added to this, about 2/3 of the administrative staff are bilingual.

Research Facilities: The University constructed the ILS Building in 2009 to provide 11 IFReC PIs generous laboratory spaces. Next to this building, construction of a new IFReC research building was completed in March 2011, where 9 IFReC laboratories have moved in. This makes it possible for all of the full-time researchers of IFReC to assemble together. The radio-isotope experimental station and a part of the Core Instrumentation Facility of the Research Institute for Microbial Diseases (RIMD) are also set up in the new building. In addition to two animal resource centers of RIMD, the IFReC animal resource center for experiments with SPF animals was also constructed in 2009, so that researchers can use these animal resource centers for different purposes. Overall, international quality research facilities deserving to fundamental researches of immunology and infectious diseases in the 21st century, have now been established within the IFReC/RIMD complex.

Commitments of Host Institution: The University has duly fulfilled financial, administrative commitments and facility obligations to support the development of IFReC. The most significant are:

- Allocation of all indirect costs of the WPI budget to be at the disposal of IFReC
- Construction of the ILS building to provide PIs with generous laboratory spaces
- Financial support for the construction of the IFReC Animal Resource Center;
- Provision of a tenured position to invite Sakaguchi as a PI from Kyoto University
- Authorization of the center director to make top-down decision to reform the research environment, allowing PIs to devote more time to research
- Construction of Kasugaoka House (2010), accommodation of international standard for overseas researchers, where several IFReC researchers and their families are now staying
- Conclusion of collaborative research agreements with NICT (2009) and RIKEN (2010) to construct research centers in the University campus

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.

<Current status>

IFReC is now composed of 27 research groups (immunology, 16; imaging, 8; bioinformatics, 3), of which 10 groups (immunology, 7; imaging, 1; bioinformatics, 2) are accommodated in the Integrated Life Science Building (ILS building of a ten-storey, 9,258m^2) constructed in 2009. Construction of a new IFReC research building (a nine-storey, 6592m^2) next to the ILS building was completed in the end of FY 2010, where another 8 groups (immunology, 4; imaging, 4) open their laboratories. This gathering or integration of laboratories working under one roof is expected to facilitate the interactions of researchers in different disciplines. Their collaborative studies, regarding the comprehensive understanding of immune dynamism through directly visualizing immune cells within live animals and tracking the dynamic behavior of immune cells and their interactions, is also expected to benefit. Such activities of IFReC are well financed by competitive research funds acquired by the Director and other PIs and a generous donation from the Kishimoto Foundation.

Both domestic and overseas researchers are supported by an efficient administrative system of international standards, so that they are able to devote themselves to their studies.

<Future prospects>

While the gathering of the core IFReC researchers (see above) is expected to aid in the elucidation of the dynamic immune system through integrating the methodologies of imaging and bioinformatics with immunology; Forming productive and stimulating relationship between IFReC and other institutions of different disciplines will facilitate this further. Such collaborative relationships are expected to materialize in a few years. To obtain this, the University has recently concluded research agreements with both RIKEN and the NICT (see Section 9: Host institution's commitment). From these agreements, a RIKEN research institute, QBiC, and an NICT research center, CiNeT, will be constructed. Both QBIC and CiNeT will be headed by Yanagida.

In order to predict and regulate cellular events, quantitative and comprehensive analysis will be performed on complex biological systems at various levels at QBiC. At CiNeT, innovative studies will be conducted to visualize and directly measure the activity and metabolism of brain cells. Although the mission and goals of these centers are different from those of IFReC, the methodologies and technologies are common to all three institutions, and a collaboration of researchers at these centers is on the schedule, which will greatly favor the progress of IFReC to its goal.

In addition to these new plans, IFReC has not only been supported by the RIMD since it was launched in 2007,but also steadily established a collaborative partnership with RIMD through the sharing of experimental facilities such as the animal resource centers, the radioisotope experimental station and core instrumental facility. Since these two institutes are complementary to each other in terms of medical science: the Immunology focus of IFReC relates well to the infectious diseases focus of RIMD. Among the possible future plans the University has concerning IFReC, one is to reform IFReC as an IFReC/RIMD complex that systematically covers basic researches in immune dynamism to applied research such as the development of vaccines against various infectious diseases and cancers as described above in "Initial plan: General plan of the project". For this to be realized, further efforts must be made successfully by both sides for the research system reformation and improvement of the efficiency of the research administration under a comprehensive support of the University.

2. Center's Research Activities

2-1. Initial plan

<Research fields>

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)

<Research objectives>

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 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 within and outside the country. 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.

2-2 Research results to date

2-2-1 Center's research activities and results

Immunology Groups

Since IFReC launched as a WPI center, the immunology groups have continued to be productive in publishing high quality research achievements as easily recognized by the publication lists. The extensive collaboration with other groups, bioinformatics or imaging group started and several papers have been already published jointly (see for example, "Standley Systems Immunology"). Many immunology groups are now collaborating with imaging and bioinformatics groups to visualize the movement of molecules or cells they are dealing with, and to analyze the vast data obtained from microarray experiments and whole genome sequencing.

Akira Host Defense*:

The group showed that Atg16L1-deficient macrophages produced high amounts of IL-1b and IL-18 following stimulation with TLR4 agonist LPS. Atg16L1 is an essential component of the autophagic machinery responsible for control of the endotoxin-induced inflammatory response (Nature 456:264-8, 2008).
DNA vaccines induce adaptive immune responses through induction of type I IFN. Although a cytosolic sensor(s) that recognizes dsDNA and downstream signaling pathways are not well understood, the group found that the kinase TBK1 is essential in dsDNA-triggered type I IFN induction as well as eliciting adaptive immune responses by DNA vaccine (Nature 451:725-9, 2008).
The group found that autophagy-related proteins LC3 and Atg9a colocalized with STING after dsDNA stimulation. ATG9a negatively regulates dsDNA-mediated IFN production by preventing dynamic translocation of STING to TBK1-containing punctate (Proc Natl Acad Sci USA, 106:20842-6, 2009).
The group also found that IFN-inducible tripartite-motif (TRIM) 56 interacted with STING and targeted it for lysine 63-linked ubiquitination. TRIM56 is an E3 ubiquitin ligase that modulates STING to confer dsDNA-mediated innate immune responses (Immunity 33:765-76, 2010).
Zc3h12a is rapidly induced by stimulation with TLR ligands and contains a CCCH-type Zinc finger domain. Zc3h12a-deficient mice exhibited severe anaemia, and showed augmented serum immunoglobulin levels and autoantibody production. Zc3h12a-/- macrophages showed increased production of IL-6 and IL-12p40 following stimulation with TLR ligands. These showed that Zc3h12a negatively regulates TLR-induced inflammatory responses by affecting mRNA stability and prevents autoimmunity (Nature 458:1185-90, 2009).
Jumonji domain containing-3 (Jmjd3), a histone 3 Lys27 (H3K27) demethylase, was identified as one of TLR-inducible genes. The group demonstrated that Jmjd3 is essential for M2 macrophage polarization post helminth infection and chitin administration. Jmjd3 is also essential for proper bone marrow macrophage differentiation, and this function depends on demethylase activity of Jmjd3. The group showed that Jmjd3-mediated H3K27 demethylation is crucial for regulating M2 macrophage development leading to anti-helminth host responses (Nature Immunol. 11:936-44, 2010).

*The description is inclusive of Coban and K. Ishii, because both were senior staff of this laboratory until they became independent as PIs at the beginning of FY 2010.

Kinoshita Imunoglycobiology:

In order to understand molecular mechanisms of transport of GPI-AP from the ER to the cell surface, the group established a method to screen mutant CHO cells defective in GPI-AP transport (Nat. Cell Biol. 10:1135-45, 2009).
Using this method, the group obtained a mutant CHO cell, defective in ER-to-Golgi transport of GPI-AP. The group cloned the gene responsible for this mutant, termed PGAP5 and found that PGAP5 is a phosphoesterase that removes ethanolamine-phosphate side chain linked to the second mannose after attachment of GPI-anchor to protein. If this remodeling of the glycan part of GPI by PGAP5 does not occur, GPI-AP is not recruited to the ER-exit sites efficiently, resulting in delayed transport from the ER (Cell 139:352-65, 2009).

Kumanogoh Immunopathology:

The group found that plexin-A1-deficinet mice had impaired antigen-specific T-cell priming, in which DC trafficking from the peripheral tissues to the lymphatic was severely affected. The group found that plexin-A1 was localized at the trailing edge but not the leading edge of DCs during cellular migration in which Sema3A induced phosphorylation of myosin light chain to promote actomyosin contraction, resulting in increased DC velocity as these cells pass through the constricted area. Collectively, these findings not only demonstrate the involvement of semaphorins in DC trafficking, particularly the transmigration step, but also indicate that semaphorins uniquely function as immune cell guidance cues by regulating actomyosin contraction (Nat Immunol. 11: 594-600, 2010).

The group determined the crystal structure of plexin which would be critical information to develop semaphorin-targeted therapy (Nature 467:1123-7, 2010).

Arase Immunochemistry:

PILR is one of paired receptors that are mainly expressed on various immune cells. The group precipitated the PILRα ligand expressed on HSV-1 infected cells with PILRα-Ig fusion protein and analyzed the precipitant by mass spectrometry. The group found that the PILRα ligand expressed on HSV infected cells is glycoprotein B (gB) of HSV (Cell 132:935-44, 2008).

Kishimoto Immune Regulation:

The group found that the aryl hydrocarbon receptor (Ahr) negatively regulates inflammatory responses mediated by lipopolysaccharide (LPS) in macrophages. Ahr forms a complex with Stat1 and nuclear factor-kappa B (NF-kappaB) in macrophages stimulated by LPS, which leads to inhibition of the promoter activity of IL-6. Ahr thus plays an essential role in the negative regulation of the LPS signaling pathway through interaction with Stat1 (JEM 268(9): 2027-35). The group showed Ahr negatively regulates dendritic cell immunogenicity via a kynurenine-dependent mechanism (Proc Natl Acad Sci USA. 107(46):19961-6, 2010).

The therapies of anti-IL6R antibody (Tocilizumab) have been applied for various autoimmune diseases including Still's disease, Polymyalgia rheumatia, Giant cell arthritis, Spondyloarthrities, Relapsing polychondritis, Systemic sclerosis, Polymyositis and Uveitis. Tocilizumab showed significant therapeutic effect on all of these diseases (Arthritis Rheum. 61(12):1762-4, 2009. etc.).

Hirano Developmental Immunology:

The group found IL-17A together with IL-6 synergistically induces IL-6 gene expression in a manner dependent on both STAT3 and NF-γB. The "IL-6 amplifier" named by the group induces not only IL-6 but also many other inflammatory molecules including chemokines, which leads to chromic inflammation diseases such as F759 arthritis and EAE (Immunity 29:628-36, 2008).

The group found critical roles for Zn transporters in several biological processes including immune responses. Znt5 is selectively required for mast cell-mediated delayed-type allergic responses and has a significant role in PKC signaling (J. Exp. Med. 206:1351-64, 2009).

Miyasaka Immunodynamics:

The group found two interesting molecules apparently involved in lymphocyte extravasation from HEVs. One is autotoxin (ATX), which is highly and constitutively expressed in HEV ECs but not other types of ECs of other tissues (Am J Pathol 173:1566, 2008).

Another molecule involved in lymphocyte TEM (Trans Endothelial Migration) is nepmucin/CD300g. Nepmucin/CD300g is a type 1 membrane protein possessing a mucin domain and a V-type Ig domain, and is expressed in the vascular ECs of various tissues including those of HEVs in LNs, but not in PPs (J Exp Med 203:1603, 2006., FEBS Lett. 582:3018, 2008).

Takeda Mucosal Immunology:

The group showed an essential and direct requirement of ROP16 in parasite-induced Stat3 activation and the significance of a single amino acid replacement in the function of type II ROP16 of *T. gondii* (J. Exp. Med. 206:2747-60, 2009) .

The group showed that commensal bacteria-derived extracellular ATP acts on a unique subset of intestinal lamina propria dendritic cells to induce IL-6 and TGF-β leading to the development of Th17 cells in the intestine (Nature 455:808-12, 2008).

Kikutani Molecular Immunology:

The group found that immobilized Sema7A-Fc could stimulate cytokine production in monocytes and macrophages by binding to α1β1 integrin. The group showed that the interaction between Sema7A and α1β1 integrin is crucial at the effector phase of T cell-mediated inflammation (Nature 446:680-4, 2007).

Sakaguchi Experimental Immunology:

The group has shown that the transcription factor Foxp3 is specifically expressed in CD25+CD4+ naturally occurring Treg cells and that ectopic expression of Foxp3 can convert naïve T cells to Treg-like cells functionally and phenotypically. Foxp3 forms a large molecular complex involving NFAT and other transcription factors, co-activators, and co-repressors.

The group showed that Foxp3 bound to another transcription factor AML1/Runx1, thereby conferred suppressive activity to Treg cells (Nature 446:685-9, 2007).

The group prepared Treg-specific CTLA-4 conditional KO mice and showed that CTLA-4 play a crucial role in Treg-mediated suppression and that blockade of CTLA-4 can elicit autoimmune disease and allergy, enhance immune responses, including tumor immunity, via attenuating Treg-mediated suppression (Science 322:271-5, 2008).

The group showed that the expression levels of Foxp3 and CD45RA were instrumental for dissecting Foxp3+ T cells into three populations. This classification of Treg subsets was useful to assess Treg function in immunological diseases (Immunity 30:899-911, 2009).

Saito Cell Signaling:

Saito group revealed that TCR microcluster (MC) is the signaling complex responsible for mediating signal transduction of antigen-recognition signals in T cells and further that CD28-mediated co-stimulation is similarly regulated through MC in spatio-temporal manner. Analyzing the dynamics of CD28 and related signaling molecules upon T cell activation, CD28 is initially co-localized with TCR-MC and thereafter accumulated in the center of Immune synapse (cSMAC). CD28 recruits PKCθ and CARMA1 to the same area in cSMAC in order to induce sustained co-stimulation signal. The results demonstrated that cSMAC is not only TCR degradation site but also the active region for co-stimulation signals, and thus, T cell activation is regulated through spatially distinct regions for TCR- and co-stimulation signals (Immunity 33(3):326-39, 2010).

Kurosaki Lymphocyte Differentiation:

By crossing Erk1-/-Erk2flox/flox mice with Mx-Cre mice, the group found that Erkl and Erk2 kinases are essential in pre-BCR-mediated expansion as well as in the transition of pro- to pre-B cells. Activated Erk1 and Erk2 contribute to phosphorylation of transcription factors such as Elk1 and CREB and their activation, which in turn regulate genes involved in cell expansion such as Myc (Immunity 28:499-508, 2008).

To address the importance of calcium influx in physiological events such as mast cell activation, the group established STIM1 knockout mice and showed that STIM1-dependent calcium influx has a significant role in cellular outputs, leading to allergic responses, in physiological settings (Nat. Immunol. 9:81-8, 2008).

By crossing PLC-γ2flox/flox mice with Cγ1-Cre or ERT2-Cre mice, the group demonstrated that PLC-γ2 is critical for GC and memory B cell formation and, more importantly, that it is also required for memory B cell maintenance (J. Exp. Med. 206:681-9, 2009).

Jang Gastrointestinal Immunology:

Mouse CD11c+ LPCs consist of four subsets (CD11b- LPDC, CD11b+ LPDC, macrophage and eosinophils) distinguished by differential expression patterns of CD11c and CD11b. The group (Including Director Akira) has identified a subset of CD11chiCD11bhi LPDCs as TLR5-expressing cells. In response to flagellin, these LPDCs induced the differentiation of naive B cells into IgA+ plasma cells by a mechanism independent of gut-associated lymphoid tissue (GALT) (Nat Immunol. 9:769-76, 2008).

Imaging Groups

Imaging groups have revealed critical biological phenomenon especially in the field of immunology by using advanced imaging techniques they have originally established, and also developed novel imaging methodologies that should be conducive to making a noncontiguous breakthrough in classical immunology. State-of-the-art optical imaging techniques such as intravital multiphoton microscopy have been fully utilized to clarify complex dynamic systems in immunology and bone biology. Super high resolution microscopy, Raman microscopy, next-generation chemical probes, high-power MRI, and PET/SPECT have been developed by respective experts, and active collaborations in the frame of IFReC are currently ongoing, those would lead to the discovery of novel concepts in classical immunology.

Yanagida Single Molecule Imaging:

The immune system of an animal is a complex system composed of large numbers of multiple cells types interacting with each other directly or indirectly through intermediary molecules such as cytokines. One way to understand such complex biological systems is to make their numerical models. To this end, we are developing novel quantitative measurement technologies based on optical fluorescent microscopy, especially, the fundamental developments for current 3 years. Our developed super resolution microscopes overcome the fundamental diffraction limit of light, and one of them achieves simultaneously 120 nm spatial and 2 ms temporal resolutions that is world top level. Moreover, we succeeded in developing two new fluorescent proteins as environment indicator, which can detect the small structural change of target protein and pressure indicator, respectively. These technologies can be applied to various kinds of inflammations and becomes to be core technologies of IFReC next 2 years.

Seki Biomedical Optics:

Pushing the performance of a multiphoton microscope to its limit, the group developed the in vivo experiment system for visualizing immune cell dynamics in inguinal and popliteal lymph nodes, and spinal code (to be published). Along with development, the group started collaboration with Hirano Developmental Immunology group, projects (1) and (2), and with Miyasaka Immunodynamics group. (1) We unveiled that CD8+ and CD4+ T cells are different in migration property of from T cell zone through lymphatic labyrinth to follicle in T cell proliferation during homeostatic expansion, especially in a 48hrs period after transfusion. (2) We have reached a stage that at pathogenesis of experimental autoimmune encephalomyelitis, transmigration of disease-causing CD4+ T cells into spinal code is about to be visualized. (3) We are now able to well delineate a role of Autotaxin/lysophosphatidic acid in lymphocyte trafficking into draining lymph nodes, where it acts differently on transmigration and binding across/to high endotherial venules.

Yoshioka Biofunctional Imaging:

The group has made major advancement in noninvasive magnetic resonance spectroscopy (MRS) and magnetic resonance imaging (MRI) to measure temperature at various regions of human brain. Thus, the technique proved useful to detect the cerebral hemodynamic impairment in patients with unilateral chronic major cerebral artery steno-occlusive disease (Stroke 40: 3012-3016, 2009) and to identify patients at risk for post carotid CEA cerebral hyper-perfusion (Radiology 256: 924-931, 2010). Visualization of the cumulative activities of the neurons, such as learning and memory in rats is now also possible by the use of manganese-enhanced MRI (Neuroscience 167: 199-204, 2010). With further improvement, these techniques can be applied to measuring metabolic activities of lymph nodes and other lymphoid tissues of a whole live animal body. As a first step for visualization of immune reactions, the group demonstrated that an antibody-super paramagnetic iron oxide complex was a useful, target-specific contrast-enhancing agent for in vivo MR molecular imaging (Contrast Media Mol. Imaging 5: 18-22, 2010). With a newly developed probe prepared by Jin Nano-bio Materials Group (Chem Comm: 5764-5766, 2008), immune cells and lymph nodes were also visualized in vivo by dual-modal MRI and NIR fluorescence imaging technique.

Jin Nano-bio Materials:

In order to develop nano-bio probes for in vivo dual modal (fluorescence/ magnetic resonance) imaging, the group has synthesized Gd3+ functionalized quantum dots based on near infrared CdSeTe/CdS semiconductor nanoparticels (Chem Comm. 5764-66, 2008). Using this probe, the group showed the

capability of highly sensitive dual modal detection of the probe in vivo. The group has developed anti-HER2 antibody conjugated quantum dot probes for detection of breast cancer cells (Sensors, 9, 9332-9354, 2009). The group has also developed antibody-proteinA conjugated quantum dots (CdSe/CdZnS) for multiplexed fluorescence imaging of surface receptors in living cells (Mol. Biosys. 6, 2325-2332, 2010).

Masaru Ishii Biological Imaging:

The group succeeded in developing the techniques for imaging bone tissues in living animals that had been thought to be hard because of the surrounding hard mineralized tissues. Using the method, the group showed S1P-mediated chemotaxis of osteoclast precursors would be expected to contribute to their recirculation from endosteum to systemic blood flow, limiting formation of mature osteoclasts and reducing bone destruction. This study showed a novel concept in the field of bone biology and "osteoimmunology" (Nature 458: 524-8, 2009).
The group found that migratory behavior of osteoclast precursor monocytes in vivo is finely regulated by reciprocal activity of two types of S1P receptors, and manipulation of these receptor activities leads to the alteration of bone homeostasis. This is emerging as a novel therapeutic target against inflammatory bone-resorptive disorders, rheumatoid arthritis chief among them (J. Exp. Med., 207:2793-8, 2010).

Kikuchi Chemical Imaging Techniques:

Fluorescence imaging and MRI are powerful approaches to visualize the localization, dynamics and function of biomolecules in living cells and in vivo. So far, we created chemical probes for fluorescence protein labeling and ^{19}F-MRI. In the protein labeling project, protein tags called BL-tag and PYP-tag and their fluorogenic probes were developed. By utilizing these techniques, live imaging of epidermal growth factor receptor (EGFR) on cell surface was successfully achieved. In the ^{19}F-MRI project, probes consisting of ^{19}F and Gd^{3+} compounds were synthesized to detect the activity of hydrolytic enzymes. The principle of the probe design was newly developed and based on ^{19}F-MRI signal switch by the paramagnetic relaxation enhancement (PRE) of Gd^{3+}. The activity of enzymes (caspase-3, β-galactosidase, and β-lactamase) were successfully detected and imaged by the ^{19F}-MRI probes.

Smith Biophotonics:

In order to bring new imaging tools to immunology, we are focusing on label-free microscopy as well as selected probe-based methods as key technologies to advance the imaging capabilities in immunology experiments. We have now acquired all relevant equipment for Raman imaging and have begun experiments in imaging macrophage activation as well as other cell types. One particular problem which challenges all research in label-free image is the difficulty in obtaining signals. We have pursued two approaches to this problem, first we have made progress in developing algorithms and tools for large scale data processing of Raman images and have begun work on a database of cellular compounds to improve computer assisted signal extraction from the Raman images. We are additionally pursuing the use of gold nanoparticles for Raman scattering signal enhancement. Both nanoparticle and algorithmic methods may be combined with our Raman microscopy to produce time-resolved maps of the cell environment chemistry over time, and is being applied to the immune response in macrophage cell lines.

Hatazawa Nuclear Medicine:

Nuclear medicine imaging is now widely used for clinical diagnosis of the diseases and evaluation of therapy effect in patients. The aim of this group is first to fully visualize immune-system related phenomenon in humans using single-photon emission computed tomography (SPECT) and positron emission tomography (PET) with 2-deoxy-2-[F-18]fluoro-D-glucose (FDG) and other tracers. Clinical data is now being accumulated in patients with normal volunteers and patients with auto-immune diseases. Another aim is to develop scanners, radio-nuclides, and radiopharmaceuticals suitable for the study of immune system. We developed integrated PET/MRI for small animals (Yamamoto S, et al., Ann Nucl Med 2010), which elucidated metabolic changes without any morphological changes in transgenic mice. I-124 was produced to label specific lymphocytes and to trace their dynamics in humans with PET.

Bioinformatics Groups

There are currently three informatics labs at IFReC. As described below, these groups specialize in computational methods for image processing, macromolecular structure prediction, and genome-level analysis, respectively. In order to achieve productive collaboration between heterogeneous research

groups at IFReC, it is necessary for researchers to easily share their data, and to make use of modern data processing techniques. For example, in order to make optimal use of various new imaging methods it is necessary to be able to extract the relevant information from raw data in a computationally efficient manner. The same is true for structural and genomic data as well. Thus, in order to facilitate interdisciplinary studies of immune function, the informatics groups have been engaged in the development of novel computational methodologies for data processing and analysis.

Hata Information System:

Our group has developed novel imaging systems, methods for image processing, and parallel computing. These general methods have applications for imaging in general and for immunological imaging in particular. For example, using two ultrasonic array probes, we determined the bottom echo position of bone and imaged the brain surface (IEEE Int. Conf. on Systems, Man and Cybernetics, 1524-1529, 2010). We validated the performance of our novel image processing methodologies by analyzing the 3-D movement and orientation of knee implants using digital radiograph video images (Journal of Advanced Computational Intelligence and Intelligent Informatics, 14(2):122-127, 2010). We also developed a health monitoring system for the elderly with multi-sensors (Int. Journal of Applied and Computational Mathematics, 10(1):133-145, 2010). We have ported quantum chemical simulation methods and other applications to super scalar parallelization architectures (Cray-XT4 or higher1 and IBM-BlueGene/L2) and two types of GPUs (Cell Broadband EngineTM3 and NVIDIA-CUDA4).

Standley Systems Immunology:

The Systems Immunology Lab consists of computational researchers with various backgrounds, from physics, to biology, to computer science. Our main objective is to collaborate with IFReC immunology and imaging groups in order to facilitate various types of interdisciplinary research. However, we also aim to generalize our computational methods and make them available to the scientific community in the form of public servers (MAFFTash, Spanner, SeSAW), databases (MusVirus, IDD Navigator), or software (OSCAR). Our main collaborations are currently with the Host Defense, Lymphocyte Differentiation, and Mucosal Immunology labs. These projects include protein structure and function prediction (J. Exp Med 206: 2747-2760, 2009; Nature 458, 1185-1190, 2009), analysis of transcriptional and epigenetic regulation (Nature Immunol.11: 936-44, 2010), and mathematical modeling of post-translational regulatory networks.

Miranda-Saavedra Bioinformatics and Genomics

Our group has implemented and developed bioinformatics and genomics technologies (ChIP-seq and RNA-seq) to analyze the transcriptional changes that drive (i) the early development of the lymphoid system; and (ii) the (innate) anti-inflammatory response in macrophages. For the former, we have succeeded in purifying all the precursor cell types of the lymphoid system and are currently determining their epigenetic states with our own improved biochemical protocol that allows us to purify enough DNA for ChIP-sequencing from as little as 10^5 cells. Epigenetic information combined with (RNA-seq) expression data will allow us to build comprehensive models of early lymphoid development, which is severely impaired during senescence. For the second aspect of our research program, we have produced a high-quality description of the anti-inflammatory response network orchestrated by STAT3 in macrophages. The STAT3-dependent response appears to be highly complex and possibly a number of epigenetic transactions are associated with it. This is just a first step towards understanding the selective control of the anti-inflammatory response in macrophages.

2-2-2 Research Achievements

A. Refereed papers (published or accepted for publication)
Total: 513

FY 2007-2008	136	FY 2009	154	FY 2010	223

B. Invited lectures, plenary addresses (etc.) at international conferences and international research meetings
Total: 195

FY 2007-2008	66	FY 2009	53	FY 2010	76

C. General lectures at international conferences
Total: 37 oral 81 poster

FY 2007-2008	oral	poster	FY 2009	oral	poster	FY 2010	oral	poster
	9	9		5	10		23	62

D. Invited lectures at domestic scientific societies and research meetings
Total: 446

FY 2007-2008	139	FY 2009	139	FY 2010	168

E. General lectures at domestic scientific societies and research meetings
Total: 85 oral 86 poster

FY 2007-2008	oral	poster	FY 2009	oral	poster	FY 2010	oral	poster
	38	38		26	24		21	24

F. Books (e.g., scientific, specialized volumes)
Total volumes: 66

FY 2007-2008	22	FY 2009	11	FY 2010	33

G. Industrial property rights
Total: 25 registered 3 being processed

FY 2007-2008	registered	processed	FY 2009	registered	processed	FY 2010	registered	processed
	10	0		9	1		6	2

H. Major awards received (including those formally announced)

Total: 42

FY 2007-2008	11	FY 2009	11	FY 2010	20

2-3 Future Policy and Concrete Plans

<Research fields>
No change has been made from the initial plan.

<Research objectives>

In our initial plan (Section 2-1), bioinformatics was not emphasized. In the first three and a half years, a consensus emerged within the organization that cutting-edge computational methods are indispensable for advancing immunology and facilitating collaboration between immunology and imaging groups. The scientific mission of IFReC has been revised to reflect the importance of bioinformatics as follows:

"IFReC aims to comprehensively understand immune dynamism. To this ultimate goal, we are integrating imaging and bioinformatics technologies with experimental biology in order to study a wide range of phenomena at the molecular, cellular, tissue, and whole body levels. This integrated approach is not only providing a more systematic understanding of the immune system but is also targeted at medical applications through translational research. Advancement in our understanding of basic immunology improves medical strategies for body defense against infectious diseases and cancers, and diagnosis and treatment of immune-related diseases."

To date, research in immunology has been carried out mostly by *in vitro* methods, wherein immune cells are isolated from animals such as mice and individually examined using various methods of cell biology; similarly, immune-related molecules have traditionally been examined in isolation by biochemical and/or biophysical methods to reveal structure-function relationships. As a result of such studies, a number of immune cells and cytokines have been discovered, and signaling pathways in various immune responses have been outlined. It is no exaggeration to say that IFReC researchers have made great contributions to such advancement (Sections 2-2 and 6-iii).

However, the immune system of a mouse or a human is a complex system composed of large numbers of multiple cells types. Many of these cell types interact directly or indirectly through intermediary molecules such as cytokines. In addition, immune cells are generally in constant motion throughout the entire body and interacting with many types of tissue. We will reveal the dynamics of this cellular and molecular network through integration of biological, biochemical, and imaging data using information technology and complex systems simulations.

We cannot reach such an ambitious goal using an *in vitro* approach; instead, we must examine and analyze immune cells and molecules *in vivo*, as they naturally exist in a living organism. There already exist a number of *in vivo* methods; however, they are not yet as mature as the *in vitro*-based methods. Hence, one of our goals is to rapidly advance novel *in vivo* immunology methods. The first step in this process is to form fruitful collaboration between researchers with various theoretical and experimental backgrounds, and with proven experience in solving major problems in immunology. The collaborative spirit used to develop new *in vivo* methods is expected to generate not only breakthroughs in immunology, but also to strengthen more basic disciplines such as physics, chemistry, and information technology. Within this framework, we have set research objectives that can be shared by IFReC researchers. These can be divided into experimental and computational objectives as follows:

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

Three lines of innovation that are essential for experimental research to attain objectives a–c (above) are currently ongoing at IFReC. The first is a challenge to improve techniques of optical microscopy, where attempts are being made to push the performance of instruments to their limit by modifying the hardware and to visualize dynamics of cells in live animals and molecules in cells by using novel probes or reagents. The second is the development of probes suitable for "selective visualization of specific cells or molecules and to discriminate them from an ensemble of similar targets" and "detection of structural changes of immune-related molecules and organelles". Within a few years, several interesting observations could be made using these technologies. The third is

ambitious installment of cutting-edge instruments such as a Raman microscope and an advanced 11.7T MRI for minimally-invasive observations and measurements (the cost of purchasing these instruments has been covered by AKIRA FIRST project, see Section 7). None of these instruments have been used as is, but have been customized in hardware and software for improvement of their performance by experienced researchers, so as to optimize the technologies for immunology-based research purposes and/or experimental subjects. Although use of appropriate probes would be sometimes required, we could expect to be able to track certain immune cells in a whole animal (it is already possible at tissue levels) or molecules in a cell, and/or to directly measure cellular composition in immune cells.

Currently three bioinformatics groups are collaborating with immunology and imaging groups. The projects include topics such as structure/function prediction of proteins involved in immune responses, simulation of signal transduction cascades and transcriptional regulatory network in immune cells, and advanced data processing for imaging as described above (2-2-1). To effectively implement the above-mentioned objectives d-e, however, reinforcement of bioinformatics is both an important and immediately relevant issue at IFReC. In particular, information processing and systems-oriented studies should be strengthened. To this end, we have two concrete plans:

1) Improvement of computational facilities for the flow and availability of data from the imaging, informatics and immunology groups;
2) Reinforcement of human resources of computational research both in quality and quantity aspects.

As for the computational facilities, installment of new servers and network system are scheduled (see Section 5 - 6; Section 11-2 and -7). Our measure to reinforce the human resources includes:

2a) Recruitment of a few computational researchers with expertise in image processing, sequence analysis, systems-level simulations, and information technology;
2b) Seeking collaborators within Osaka University, since the University is one of the premier institutes for information science and technology research in Japan;
2c) Collaboration with CiNeT and QBiC (see Sections 1, 5 and 9), where several specialists of systems biology with experience in studying complex biological phenomena by computational analysis and network simulation are scheduled to join.

As can be seen from description above, fusion-oriented research between immunologists, imaging and bioinformatics experts is a prerequisite for ongoing projects at IFReC. This is a major background for introduction of the “Research Support Program for Fusion of Different Fields” in 2009 (see Sections 5 and 6).

Along with the effort to advance these basic studies, we are well aware of the importance to develop a means by which knowledge and experience accumulated with small animals are expanded to clinical studies. At present, IFReC laboratories are engaged in such translational activities. A typical case is a basic study of adjuvant development for vaccine in K. Ishii’s laboratory, collaborating with RIMD and NIBIO (see Section 4-2). Henceforth, however, IFReC should respond to the increasing demand of society by facilitating translational research committed by many more laboratories. In other words, while we are pursuing world-leading research in immunology, we should make practical steps towards improvements in society’s health, the ultimate goal of such translational studies. Several IFReC PIs belong to the medical school of the University and two of them have concurrent appointments with the University Hospital. Taking advantage of this fact, we are now planning to construct a consortium for clinical medicine-oriented immunology with those PIs as its core members. This aims to invite clinicians who are interested in clinical immunology and deeper investigation of clinical samples which are routinely collected in their treatment of patients suffering from immune–related diseases.

The first stage of the consortium is the creation of a firm platform for facilitating interactions between researchers in basic research fields and clinicians to exchange their views and opinions. Once a consensus is made, the next stage is the construction of a “clinical sample collection center” where invaluable samples such as blood and tissues removed during operations at clinical sites under patients’ informed consent are deposited, with detailed histories, which can be accessed by registered researchers. Incidentally, the database construction and data-mining team described above could make a good contribution to these activities. In this way, the researchers would then be able to examine or make use of invaluable clinical samples according to their research interests and for the clinicians to learn the results of such studies with leading-edge methods. We expect these collaborations between researchers in the basic

research fields and clinicians to lead a development of new clinical strategies for diagnosis and therapies of immune diseases.

IFReC is also aware of the importance to foster the next generation of young researchers because an undertaking in immunology research is endless. To provide a new educational and networking venue for young researchers all over the world, IFReC and SIgN have reached an agreement to jointly organize a Winter School on Advanced Immunology every year. The school will be held annually, with the location alternating between Japan and Singapore. In addition, we are now planning to establish a double mentor fellowship/scholarship program. This program is to support graduate students or young post-docs engaged in interdisciplinary projects under supervision by two PIs in different disciplines. It is also expected to literally facilitate interdisciplinary research at IFReC.

< Major changes >

No fundamental change has been made except for those described above.

3. Management

<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.

<Efforts to date and current state>

1) Composition of administrative staff

When IFReC was launched in 2007, Norio Furushiro was appointed as Administrative Director. He headed the administration department consisting of the accounting and general affairs sections. Each section had a senior supervisor with administrative experiences in the University and several English-speaking personnel.

In 2008, the research management section was set up with a newly employed associate professor, who was appointed to organize symposia, seminars and to be responsible for outreach activities.

In 2009, Takao Kodama was recruited as the new Administrative Director. Based on his long career of scientific research, as well as experience of research management and coordination, he reorganized the administrative department by reforming the former Research Management Section into the Research Planning and Management (RPM) office to facilitate fusion between the immunology and imaging groups and to act as a liaison with the University authorities.

In 2010, the Liaison Office was open within the framework of the RPM office to support researchers from abroad in various aspects such as immigration matters, providing a living support service as well as bilingual notices, announcements and helping with grant applications.

Composition of Administrative Staff

Office / Section	Professor	Associate Professor	Assistant professor	Other staff
Administrative Director	1	-	-	-
General Affairs	-	-	-	8
Accounting	-	-	-	7
RPM	1	2	1	6
Liaison	-	-	-	6 [a]
Total	2	2	1 [b]	23 [c]

a: consisting of three from General Affairs section, one from Accounting section and two from RPM office.
b: English native
c: Exclusive of staff from Liaison office; bilingual,14.

The posting of five personnel with research experience has enabled the smooth communication among researchers and supporting staff, close

	contact with the Administration Bureau of Osaka University and efficient coordination regarding the organization of seminars/symposia. In addition, 18 out of a total of 28 staff are bilingual, so that there is now little difficulty to use English as the primary working language, which has been highly appreciated by overseas researchers. The RPM office also covers: (a) outreach activities (b) management of matters related to intellectual properties such as material transfer actions and management of matters relating to the health safety of the IFReC organization (c) preparation of a database of information on external competitive research funds in English for overseas researchers' convenience. For each of these tasks, a person with PhD has been assigned (d) Purchase procedures for instrumentation
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 center Director makes major decisions, to which the Administrative Director gives full support by acting as a coordinator among the vice directors and by executing management actions through the reformed administrative office. The Administrative Director also acts as liaison between the director and trustees of the host institute and between IFReC and the MEXT/JSPS WPI office. Important matters such as annual budget and the appointment of PIs, or equivalent, are to be approved at the center management committee and the board of representatives.
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 It is operating in accordance with the initial framework. In addition, the Center's Director, Deputy Directors, Administrative Director and Trustees and Vice Presidents of the University hold briefings as needed.

< Future policy and concrete plans >

1) Composition of administrative staff

As described above, the personnel status of the administrative department is satisfactory not only in number but also as an organization as a whole. Its operation is efficient in its daily routines and flexible and able to smoothly deal with matters demanding speedy solutions, thus providing a good research environment for researchers to devote themselves to research. Although most of the staffs are talented in administration and/or English communication, we are determined to make more effort in staff development by furthering their skills in communication, symposium/seminar organization and outreach activities etc.

As for the outreach activities, we will cooperate with the Support Office for Large-Scale Education and Research Projects (See Section 9. Host Institution Commitments) and the Center for the Study of Communication-Design. We are also to improve the way matters relating to intellectual properties are handled by obtaining advice and suggestions from the Office for University-Industry Collaboration, respectively.

2) Decision-making system

This will be operated in the same way as before.

3) Allocation of authority between center director and host institution

This will be operated in accordance with the initial framework.

4. Researchers and center staffs, satellites, partner institutions

4-1. Number of researchers in the “core” established within the host institution

All members

	Goal set in proposal	Results at end of FY 2008	Results at end of FY 2009	Results at end of FY 2010	Final goal (Date: March 2017)
Researchers	147 < 47, 32%> [, %]	89 < 24, 27%> [18, 20%]	135 < 42, 31%> [26, 19%]	173 < 56, 32%> [35, 20%]	180 < 61, 34%> [38, 21%]
Principal investigators	22 < 5, 23%> [, %]	20 < 2, 10%> [0, 0%]	26 < 6, 23%> [1, 4%]	27 < 6, 22%> [1, 4%]	30 < 8, 27%> [3, 10%]
Other researchers	125 < 42, 34%> [, %]	69 < 22, 32%> [18, 26%]	109 < 36, 33%> [25, 23%]	146 < 50, 34%> [34, 23%]	150 < 53, 35%> [35, 23%]
Research support staffs	44	23	31	45	50
Administrative staffs	15	15	21	25	30
Total	206	127	187	243	260

Other matters of special mention

Matters related to this are described elsewhere: plans for achieving the Center’s goals, Sections 2-3, Section 6-iii), Section 8, and Section9; recruitment of new PIs, Section 6-ii).

Although IFReC has not yet established a concrete system for career paths, a mobilization/circulation of researchers is on an upward trend as indicated by the fact that a researcher who had spent 2 years at IFReC returned to be an assistant professor of his graduate school in his own country and that IFReC has recruited three researchers, a post doc, assistant professor and an associate professor from the Max-Planck Institute, NIH and UCSF, respectively. In addition, it is scheduled in FY2011 that Takeda (PI) is invited for a week of stay at Victoria University and the Maurice Wilkins Center, NZ, while an associate professor (University of Otago, NZ) is visiting IFReC for a week. Furthermore, we have a plan to send a post doc to the Institute for Systems Biology, Seattle, USA (see Section 4-2).

4-2. Satellites and partner institutions

<Initial plan>

i) Satellites (Make entry for each satellite.)

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.

<Collaboration to date>

i) Satellites (Make entry for each satellite.)

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

Dr Takashi Saito with one postdoc (Cell Signaling group)

Dr Tomohiro Kurosaki, four researchers, and two postdocs (Lymphocyte Differentiation group)

-Collaborative framework

Researchers at the center and RIKEN Research Center for Allergy and Immunology regularly hold a scheduled meeting to exchange ideas to improve the level of imaging technique. We offer employment expenses to hire several postdocs at RIKEN.

-Research Achievement

C-type lectin Mincle is an activating receptor for pathogenic fungus, Malassezia.

Standley and Baba are carrying out combined research.

Coauthored papers by Akira and Saito:

1. Dectin-2 recognition of alpha-mannans and induction of Th17 cell differentiation is essential for host defense against Candida albicans.
Saijo S, Ikeda S, Yamabe K, Kakuta S, Ishigame H, Akitsu A, Fujikado N, Kusaka T, Kubo S, Chung SH, Komatsu R, Miura N, Adachi Y, Ohno N, Shibuya K, Yamamoto N, Kawakami K, Yamasaki S, Saito T, Akira S, Iwakura Y. Immunity. 2010 May 28;32(5):681-91. Epub 2010 May 20.

2. C-type lectin Mincle is an activating receptor for pathogenic fungus, Malassezia. Yamasaki S, Matsumoto M, Takeuchi O, Matsuzawa T, Ishikawa E, Sakuma M, Tateno H, Uno J, Hirabayashi J, Mikami Y, Takeda K, Akira S, Saito T. Proc Natl Acad Sci U S A. 2009 Feb 10;106(6):1897-902. Epub 2009 Jan 26.

3. Cutting edge: TLR2 directly triggers Th1 effector functions.
Imanishi T, Hara H, Suzuki S, Suzuki N, Akira S, Saito T.
J Immunol. 2007 Jun 1;178(11):6715-9.

	Institution (2) Kyoto University, Institute for Frontier Medical Sciences -Role Kyoto University, Institute for Frontier Medical Sciences collaborates with IFReC to improve regenerative medicine, in particular by devising immunological methods to establish transplantation tolerance. -Personnel composition and structure Dr Shimon Sakaguchi, ten researchers, and four Laboratory technicians. (Experimental Immunology group) -Collaborative framework IFReC researchers and Kyoto University Institute for Frontier Medical Sciences held regular meetings to update on research activities to improve the level of regenerative medicine. We offer employment expenses to hire several postdocs to the institute. **Institution (3) The National Institute of Biomedical Innovation (NIBIO)** -Role NIBIO collaborates with IFReC to invent novel strategies and technologies to develop better and safer vaccines and their adjuvants. -Personnel composition and structure Dr Ken Ishii with three assistant professors (Vaccine Science Group) -Collaborative framework We concluded a satellite agreement in 2010 to promote collaborative researches to develop more efficient technologies for vaccines and adjuvants, ensuring their safety to higher level.
ii) Partner institutions (Make entry for each satellite.) 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,	ii) Partner institutions (Make entry for each satellite.) **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 Lammermann as postdoc financed by IFReC. Dr Lammermann attended the 4th IFReC international

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.

symposium (June 1-2, 2010) to give a presentation on “Dissecting leukocyte amoeboid motility in vitro and in vivo. For the year 2010, Dr Caren Aronin was supported by the Fund. In keeping with her bioengineering background, she explored the detailed cell biology of dendritic and T lymphocyte migration in 3 dimensional matrices using microfluidic devices to precisely control chemokine gradients, together with innovative multicolor studies to reveal the cytoskeletal changes associated with cell movement in such an environment and the forces involved in migration as assessed by displacement of fluorescent collagen strands.

Publications:

2010

Cannons, J.L., Qi, H., Lu, K.T., Ghai, M., Gomez-Rodriguez, J., Cheng, J., Wakeland, E.K., Germain, R.N., and Schwartzberg, P.L. Optimal germinal center responses require a multi-stage T:B cell adhesion process involving integrins, SAP and CD84. Immunity, 32: 253-265, 2010.

2009

1. Klauschen, F., Ishii, M., Qi, H., Bajénoff, M., Egen, J.G., Germain, R.N., and Meier- Schellersheim, M. Quantifying cellular interaction dynamics in 3D fluorescence microscopy data. Nat. Protoc. 4:1305-11, 2009.
2. Klauschen, F., Qi, H., Egen, J.G., Germain, R.N., and Meier-Schellersheim, M. Computational reconstruction of cell and tissue surfaces for modeling and data analysis. Nat. Protoc. 4:1006-12, 2009.
3. 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.

2008

1. Germain, R. N., Bajenoff, M., Castellino, F., Chieppa, M., Egen, J. G., Huang, A. Y., Ishii, M., Koo, L. Y., and Qi, H.: Making friends in out-of-the-way places: How cells of the immune system get together and how they conduct their business as revealed by intravital imaging. Immunol. Rev. 221: 163-181, 2008.
2. Qi, H.*, Cannons, J.*, Schwartzberg, P.*, and Germain, R.N.* SAP-controlled T-B interactions underlie the formation of germinal centres. Nature,455:764-9, 2008.

Oral Presentation

・"From SAP-Less T Cells to Helpless B Cells and Back: In vivo Dynamics of Cell Cooperation and the Formation of Germinal Centers" BioSymposia symposium on Lupus Autoimmunity: Mechanism and Immune Regulation,

September 8-9, 2008, La Jolla, CA (HQ)
・“Visualizing Immune Cell Dynamics Using Intravital 2-photon Microscopy”, Yale School of Medicine, Microscopy Workshop & Symposium, June 2008, New Haven, CT (HQ)

Research collaboration with PI:
Dr Masaru Ishii, PI of IFReC has continuous research collaboration with Dr Germain’s lab. Ishii is the coauthor, with Dr.Germain, of the following articles:

1. Ishii M, Kikuta J, Shimazu Y, Meier-Schellersheim M, Germain RN. Chemorepulsion by blood S1P regulates osteoclast precursor mobilization and bone remodeling in vivo. J Exp Med. 2010 Dec 20;207(13):2793-8. Epub 2010 Dec 6. PMID:21135136
2. Mazzucchelli RI, Warming S, Lawrence SM, Ishii M, Abshari M, Washington AV, Feigenbaum L, Warner AC, Sims DJ, Li WQ, Hixon JA, Gray DH, Rich BE, Morrow M, Anver MR, Cherry J, Naf D, Sternberg LR, McVicar DW, Farr AG, Germain RN, Rogers K, Jenkins NA, Copeland NG, Durum SK. Visualization and identification of IL-7 producing cells in reporter mice. PLoS One. 2009 Nov 10;4(11):e7637. PMID:19907640
3. Klauschen F, Ishii M, Qi H, Bajénoff M, Egen JG, Germain RN, Meier-Schellersheim M. Nat Protoc. Quantifying cellular interaction dynamics in 3D fluorescence microscopy data. 2009;4(9):1305-11. Epub 2009 Aug 20.PMID:19696749[PubMed - indexed for MEDLINE]
Related citations
4. Ishii M, Egen JG, Klauschen F, Meier-Schellersheim M, Saeki Y, Vacher J, Proia RL, Germain RN. Sphingosine-1-phosphate mobilizes osteoclast precursors and regulates bone homeostasis. Nature. 2009 Mar 26;458(7237):524-8. Epub 2009 Feb 8. Erratum in: Nature. 2010 Jun 17;465(7300):966.
5. Germain RN, Bajénoff M, Castellino F, Chieppa M, Egen JG, Huang AY, Ishii M, Koo LY, Qi H. Making friends in out-of-the-way places: how cells of the immune system get together and how they conduct their business as revealed by intravital imaging.
Immunol Rev. 2008 Feb;221:163-81.

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

Dr Jan Liese was supported as a postdoc by IFReC (2008.4-2009.7.31). He conducted research on immunity related TLR, NK, and Dendritic cells during the supported period. Dustin Lab. switched the fund to Dr Sudha Kumari (2009.8.1-2010.3.31). She is engaged in research on Characterization of a novel molecular compartment modulating regulatory T cell function. A novel & unique signaling platform (iDPC) in Treg cells was identified & shown to be involved in recruiting GITR & PKC-θ, & activation of the NF-κB signaling pathway to a reduction of Treg function. Holding its position at the distal pole was also functionally important. Movement to the proximal resulted in a reduced suppressive function, similarly to that observed in Treg cells from patients with rheumatoid arthritis. Also, Dr Kumari attended the 4th IFReC international symposium and provided a presentation on "Role of PKC theta in regulatory T cell function".

Publications:

Alexandra Zanin-Zhorov, Yi Ding, Sudha Kumari, Mukundan Attur, Keli L. Hippen, Maryanne Brown, Bruce R. Blazar, Steven B. Abramson, Juan J. Lafaille, and Michael L. Dustin. Protein kinase C-theta mediates negative feedback on regulatory T cell function. Science. 2010 Apr 16;328(5976):372-6.

Oral Presentation:

・Selected for 20min talk entitled "compartmentalized molecular machinery in regulatory T cell function", in "Biology of recognition" meeting, Singapore. The meeting was organized by Cell press and Massachusetts general hospital and foundation IPSEN, 07 Oct 2010 - 09 Oct 2010.

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. Dr. Caneparo has been studying Gastrulation and Retro viral infection. Dr Thai V. Truong, postdocs at Dr Fraser's Lab, participated in the 4th IFReC

	international symposium and gave a presentation on “Light sheet microscopy-a versatile tool for 4-dimensional imaging”. **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. Drs Matteo Iannacone and Tiffany Horng at Andrian’s Lab. participated in the 4th IFReC international symposium and Innancone gave a presentation on “Lymph Node Subcapsular Sinus Macrophages Confer Resistance to CNS Invasion Upon Peripheral Infection with a Neurotropic Virus”. Horng gave a presentation on “Molecular Mechanism in Regulation of Innate Immune”. **Publications:** 1. “Differential kinetics of primary and secondary immune responses mediated by CD8 T lymphocytes in the bone marrow.” Irina B. Mazo, Matteo Iannacone, Golrokh Javid, Sarah E. Henrickson, Shawheen Saffari, Balimkiz Senman and Ulrich H. von Andrian (in preparation) 2. “Bone marrow is a site of hematopoietic/stem cell migration in adulthood and fetal development”. Irina B. Mazo, Steffen Massberg and Ulrich H. von Andrian. Review for Trends in Immunology (in preparation) 3. Iannacone M, Moseman EA, Tonti E, Bosurgi L, Junt T, Henrickson SE, Whelan SP, Guidotti LG, von Andrian UH.Subcapsular sinus macrophages prevent CNS invasion on peripheral infection with a neurotropic virus.Nature. 2010 Jun 24;465(7301):1079-83.PubMed [citation] PMID: 20577213, PMCID: PMC2892812 4. Boscacci RT, Pfeiffer F, Gollmer K, Sevilla AI, Martin AM, Soriano SF, Natale D, Henrickson S, von Andrian UH, Fukui Y, Mellado M, Deutsch U, Engelhardt B, Stein, JV. Comprehensive analysis of lymph node stroma-expressed Ig superfamily members reveals redundant and nonredundant roles for ICAM-1, ICAM-2, and VCAM-1 in lymphocyte homing.Blood. 2010 Aug 12;116(6):915-25. Epub 2010 Apr 15.PubMed [citation] PMID: 20395417 5. Beltman JB, Henrickson SE, von Andrian UH, de Boer RJ, Marée AF. Towards estimating the true duration of dendritic cell interactions with T cells.J Immunol Methods. 2009 Aug 15;347(1-2):54-69. Epub 2009 Jun

9.PubMed [citation] PMID: 19520083
6. Zheng H, Jin B, Henrickson SE, Perelson AS, von Andrian UH, Chakraborty AK. How antigen quantity and quality determine T-cell decisions in lymphoid tissue. Mol Cell Biol. 2008 Jun;28(12):4040-51. Epub 2008 Apr 21.PubMed [citation] PMID: 18426917, PMCID: PMC2423119
7. Henrickson SE, Mempel TR, Mazo IB, Liu B, Artyomov MN, Zheng H, Peixoto A, Flynn M, Senman B, Junt T, Wong HC, Chakraborty AK, von Andrian UH. In vivo imaging of T cell priming. Sci Signal. 2008 Mar 25;1(12):pt2.PubMed [citation] PMID: 18364513
8. Henrickson SE, Mempel TR, Mazo IB, Liu B, Artyomov MN, Zheng H, Peixoto A, Flynn MP, Senman B, Junt T, Wong HC, Chakraborty AK, von Andrian UH. T cell sensing of antigen dose governs interactive behavior with dendritic cells and sets a threshold for T cell activation.Nat Immunol. 2008 Mar;9(3):282-91. Epub 2008 Jan 20.PubMed [citation] PMID: 18204450, PMCID: PMC2698867

Oral Presentation:

・Kinetics of primary and secondary CD8 T cell-mediated immune responses in the bone marrow. Keystone symposia “Immunologic Memory and Host Defense”, Keystone, CO, February 2009.

・Kinetics of primary and secondary CD8 T cell-mediated immune responses in the bone marrow. Open Forum, Harvard Medical School, Department of Pathology, Boston, MA, February 2010.

・Role of bone marrow in T cell-mediated immune response during Multiple Myeloma. “Floor meeting”, Harvard Medical School, Boston, MA, March 2011.

・Role of bone marrow as hematopoietic and secondary lymphoid organ. Society of Toxicologic Pathology, Annual Meting, Denver, CO, June 2011 (upcoming).

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 M. Davis, Professor, Department of Microbiology and Immunology

-Collaborative framework

Davis Laboratory employed Dr Johannes B. Huppa as a Basic Science Research Associate financed by IFReC (2008.7-).

His two main research topics are:

1. Förster Resonance Energy Transfer (FRET) assay to measure TCR-ligand interactions in situ ; published in Huppa et al., Nature 463:963-967(2010)
2. High-Speed Photoactivation Localization Microscopy assay to resolve the architecture of the T cell plasma membrane at high resolution (20 nm) below he diffraction limit; published in Lillemeier et al., Nature Immunology 11, 90-97(2010)

Publications:

2010

1. Lillemeier B.F., Mörtelmaier M.A., Forstner M.B., Huppa, J.B., Groves,J.T., Davis, M.M. (2010) TCR and LAT are expressed in separate membrane domains and concatenate during activation. Nature Immunology11, 90-97
2. Huppa J.B., Axmann, M., Mörtelmaier M.A., Lillemeier B.F., Newell E.W, Brameshuber M., Klein L.O., Schütz G.J., Davis M.M. TCR-peptide-MHC interactions in situ show accelerated kinetics and increased affinity. Nature
3. Kuhns M.S., Girvin A.T., Klein L.O., Chen R., Jensen K.D., Newell E.W., Huppa J.B., Lillemeier B.F., Huse M., Chien Y.H., Garcia K.C., Davis M.M. (2010) Evidence for a functional sidedness to the ab TCR. Proceedings of the National Academy of Science U S A. 2010 Mar 16;107(11):5094-9.
4. Ebert P.J., Li Q.J., Huppa J.B., Davis M.M. (2010)
Functional Development of the T cell receptor for antigen.
Progress in Molecular Biology and Translational Science 92: 65-100

Oral Presentation by Johannes Huppa

・BIOSS Conference “Signaling meets Synthetic Biology”, Freiburg, Germany, September 2010

・Gordon Research Conference “Immunochemistry & Immunobiology”, Les Diablerets, Switzerland

・2nd international iFReC meeting Osaka, Japan, February 2009

・FASEB Meeting “Immunoeceptors”, New Haven, USA, August 2008

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.

Funds from this program have been used to support Dr. Tal Arnon in her studies on the role of GRK2-dependent S1P1 desensitization in controlling lymphocyte migration dynamics. Lymphocytes migrate from blood to tissue by following the concentration gradient of S1P using the receptor S1P1. These data showed that GRK2 was responsible for the desensitization of S1P1, thus negating the chemoattractant influence of SP1. This action, in part, helped illuminate the migratory mechanism employed by lymphocytes to move between areas of low and high S1P concentrations.

Publications:

2011

Tal I Arnon, Ying Xu, Charles Lo, Trung Pham, Jinping An, Shaun Coughlin, Gerald W Dorn, and Jason G. Cyster (2011) GRK2-dependent S1P1 desensitization is required for lymphocytes to overcome their attraction for blood. (submitted)

2009

1. Phan, T.G., Green, J.A., Gray, E.E., Xu, Y., Cyster, J.G. (2009) Immune complex relay by subcapsular sinus macrophages and noncognate B cells drives antibody affinity maturation. *Nat Immunol.* 10:786-93.
2. Phan TG, Gray EE, Cyster JG. *Current Opinion Immunology.* 2009 Jun;21(3):258-65.
3. Grigorova IL, Schwab SR, Phan TG, Pham TH, Okada T, Cyster JG. *Nature Immunology* 2009 Jan;10(1):58-65.

Oral Presentation:

Jesse A. Green, a student from the lab, presented at the 4th International Symposium of WPI-IFReC “Immunology at the Forefront” in Osaka. His talk was titled "S1P2 contributes to germinal center clustering and controls chronic germinal center homeostasis."

Oral Presentation by Jason Cyster:

・ 4th International Conference on B cells and Autoimmunity 4th International Conference on B cells and Autoimmunity; Nara, Japan, 2010

・International Congress of Immunology; Kobe, Japan, 2010

・1st International Kishimoto Foundation Symposium, Immune Regulation:

Present and Future ; Osaka, Japan, 2009
・38th Annual Meeting of the Japanese Society for Immunology ; Kyoto, Japan, 2008

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

IFReC concluded an Academic Cooperation Agreement with the Systems Biology in 2008. This Agreement aims at promoting cooperation in the fields of academic research between two institutions.
We plan to send a post doc to this institution in FY2011. The purpose is to make a coherent collaboration in order to unravel complex immune systems by creating and using systems approaches.

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

IFReC concluded an Academic Cooperation Agreement with POSTECH and established satellite Lab in POSTECH IBB recruiting eight IBB graduate students.

Two IBB graduate students visited IFReC and performed international collaborative research on the intestinal innate lymphoid cells (ILCs) with IFReC members during one month (from January28th, 2011 to 28th February, 2011).

IFReC and IBB faculty members developed new bio-imaging machine; combined two-photon microscopy and optical coherence tomography for in-vivo tissue imaging (Collaboraion with Drs. Kim KH, Doh JS; POSTECH, Korea).

IFReC is planning to held international workshop with IBB in this year.

Institution (9) Indian Institute of Science Education and Research (IISER), Bhopal

-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 an Academic Cooperation Agreement with the institute to further promote collaborative researches through exchange of information, materials and students.

Co-authored Publications:

2010

1. Pathogen recognition by the innate immune system.
Kumar H, Kawai T, Akira S. Int Rev Immunol. 2011 Feb;30(1):16-34.

2. NLRC5 deficiency does not influence cytokine induction by virus and bacteria infections. Kumar H, Pandey S, Zou J, Kumagai Y, Takahashi K, Akira S, Kawai T. J Immunol. 2011 Jan 15;186(2):994-1000.

3. The ubiquitin ligase TRIM56 regulates innate immune responses to intracellular double-stranded DNA. Tsuchida T, Zou J, Saitoh T, Kumar H, Abe T, Matsuura Y, Kawai T, Akira S. Immunity. 2010 Nov 24;33(5):765-76.

2009

1. Involvement of the NLRP3 inflammasome in innate and humoral adaptive immune responses to fungal beta-glucan. Kumar H, Kumagai Y, Tsuchida T, Koenig PA, Satoh T, Guo Z, Jang MH, Saitoh T, Akira S, Kawai T. J Immunol. 2009 Dec 15;183(12):8061-7.

2. Toll-like receptors and innate immunity. Kumar H, Kawai T, Akira S. Biochem Biophys Res Commun. 2009 Oct 30;388(4):621-5.

3. Poly I:C-induced activation of NK cells by CD8 alpha+ dendritic cells via the IPS-1 and TRIF-dependent pathways. Miyake T, Kumagai Y, Kato H, Guo Z, Matsushita K, Satoh T, Kawagoe T, Kumar H, Jang MH, Kawai T, Tani T, Takeuchi O, Akira S. J Immunol. 2009 Aug 15;183(4):2522-8.

4. Pathogen recognition in the innate immune response. Kumar H, Kawai T, Akira S. Biochem J. 2009 Apr 28;420(1):1-16.

5. Cutting Edge: TLR-Dependent viral recognition along with type I IFN positive feedback signaling masks the requirement of viral replication for IFN-{alpha} production in plasmacytoid dendritic cells. Kumagai Y, Kumar

	H, Koyama S, Kawai T, Takeuchi O, Akira S. J Immunol. 2009 Apr 1;182(7):3960-4. **2008** 1. TLR7-dependent and FcgammaR-independent production of type I interferon in experimental mouse lupus. Lee PY, Kumagai Y, Li Y, Takeuchi O, Yoshida H, Weinstein J, Kellner ES,Nacionales D, Barker T, Kelly-Scumpia K, van Rooijen N, Kumar H, Kawai T,Satoh M, Akira S, Reeves WH. J Exp Med. 2008 Dec 22;205(13):2995-3006. 2. TANK-binding kinase-1 delineates innate and adaptive immune responses to DNA vaccines. Ishii KJ, Kawagoe T, Koyama S, Matsui K, Kumar H, Kawai T, Uematsu S,Takeuchi O, Takeshita F, Coban C, Akira S. Nature. 2008 Feb 7;451(7179):725-9. 3. Cutting edge: cooperation of IPS-1- and TRIF-dependent pathways in poly IC-enhanced antibody production and cytotoxic T cell responses. Kumar H, Koyama S, Ishii KJ, Kawai T, Akira S. J Immunol. 2008 Jan 15;180(2):683-7. 4. Lymphocytoid choriomeningitis virus activates plasmacytoid dendritic cells and induces a cytotoxic T-cell response via MyD88. Jung A, Kato H, Kumagai Y, Kumar H, Kawai T, Takeuchi O, Akira S. J Virol. 2008 Jan;82(1):196-206. **2007** 1. Differential role of TLR- and RLR-signaling in the immune responses to influenza A virus infection and vaccination. Koyama S, Ishii KJ, Kumar H, Tanimoto T, Coban C, Uematsu S, Kawai T, AkiraS.J Immunol. 2007 Oct 1;179(7):4711-20.

<Future Policy and Concrete Plans>

i) Satellites

At present, we have no plan to add new institutions. However, the satellite agreements with three institutions listed above will continue.

ii) Partner institutions

At present, we have no plan to add new institutions.

The research exchange agreement with six institutions listed above (institutions (1) to (6)) expires as of March 31, 2011, and its renewal negotiation is in progress. The partner agreements with three other institutions listed above will continue.

5. 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.

<Progress to date>

1) Environment in which researchers can devote themselves to their research

FY2007- FY2008:

When IFReC was launched in 2007, the administration department of IFReC , headed by Norio Furushiro, Administrative Director, only consisted of an Accounting and General affairs Sections, similar to other small research centers in the University. The department had two senior personnel with rich administrative experiences in the University and several English-speaking personnel who organized the Kick-off symposium and created the center's PR brochures, etc. However, it was soon realized that the research management section should be set up to provide the environment where researchers can devote themselves to their research. For this section, two personnel with PhDs were recruited in FY2008 to organize seminars and symposia, editing PR brochures and coordinating meetings between research groups. In April 2009, Takao Kodama, who has a long career of scientific research as well as experience of research management and coordination, took over as an Administrative Director. As a result of these appointments, the Director, Deputy Directors and staff in their laboratories have devoted far less time to bureaucratic work unrelated to their research.

FY2009- FY2010:

i) The former Research Management Section has been reformed into the Research Planning and Management office headed by the Administrative Director, to which a PhD holder with research experience and bilingual staff has 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 Administration Bureau of Osaka University and efficient coordination of planning seminars/symposia.

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

iii) The Liaison Office has opened within the framework of the RPM office to support researchers from abroad in various aspects such as Immigration

	matters, providing bilingual notices and announcements and helping with grant applications.
2) Startup research funding	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.	From the beginning, it has been one of the fundamental policies of the center's director that a start-up research fund is allocated to each PI from abroad for the first three years from WPI's direct budget. The total number of beneficiaries of this fund has reached five. To newly recruited PIs, some amount of the fund has also been given as a "set-up research fund". These funds were mostly spent to purchase necessary laboratory equipment. We introduced a "Research Support Program for Fusion of Different Fields" in 2009. The program is 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. Start-up budgets (¥3 million per year for 3 years) are provided for each project. The projects are annually reviewed by IFReC PIs in a hearing open to all IFReC researchers. 15 projects are now running, which are expected to facilitate a new era of immunology as well as making breakthroughs in their respective disciplines.
3) Postdoctoral positions through open international solicitations	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.	We have posted advertisements of postdoctoral positions on "Nature" journal and/or IFReC's website whenever we need to recruit.
4) Administrative personnel who can facilitate the use of English in the work process	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.	As described in Section 3 (Management: "Composition of administrative staff"), 18 out of a total of 28 staff are bilingual, there is now little difficulty to use English as the primary working language. In addition, an English native with post-doctoral research experience at IFReC will join the research planning and management office from 1 April, 2011, so that "the use of English in the work process" is to be literally an everyday routine.
5) Rigorous system for evaluating research and system of merit-based compensation	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.	The first meeting of the international scientific advisory board (ISAB) will be scheduled for the 19th and the 20th of May. The ISAB consists of 15 internationally leading scientists to conduct an in-depth evaluation of scientific activities at IFReC by reviewing PI's scientific activities based on their submitted progress report and interview. Each report shall be read by at least three separate reviewers. The ISAB report will be compiled by the end of June, well before the site-visit of the Working group. The center's Director will use the ISAB evaluation as a reference material to determine PIs' salaries and their contract renewal. Concerning the procedure for evaluation of other staff, standardized forms have been created specific to the position of the staff (it will be implemented in FY2011). Three forms have been generated to evaluate 1) the Specially Appointed Associate Professor/Assistant Professor/Lecturer, 2) Specially Appointed Researcher and 3) the Technician/Administrative staff. Points of evaluation range from the work performance and other areas such as: the involvement in the laboratory, research management, achievements, application/acquisition of external funds, progress in combined research projects and contribution to the WPI program. Points are relative to the staff's position. The evaluation data will be used as a reference material to determine staff salaries and their contract renewal.
6) Equipment and facilities, including laboratory space, appropriate to a top world-level research center	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.	As shown in the floor plan of the Integrated Life Science Building (ten-storey, 9,258 m^2) and the IFReC animal resource center (four-storey, 2482 m^2; 5000 cages for 25,000 SPF mice) constructed in 2009, construction of a new research building (nine-storey, 6,592 m^2) exclusively for IFReC was completed in the end of FY2010. Located next to the Integrated Life Science Building, it will facilitate interactions of IFReC researchers with each other in various fields and further promote their collaborative research. The facilities including the radio-isotope experimental station, core instrument facility, three animal resource centers are distributed between both IFReC and the RIMD and made available to all members of both institutes. In order to better organize and manage these facilities, an associate professor will be employed from April, 2011. Technicians will also be posted to operate certain equipment such as DNA sequencers, a new electron

microscope, cell sorters, mass spectrometer and DNA chip analysis on a commission basis.

A full list of all core equipment and facilities will be made available online to all members of staff in English and Japanese. All operational manuals will also be available in both Japanese and English. A new server and network system will be set-up to manage the flow and availability of data from the imaging, informatics and immunology groups.

Facilities in QBiC (section 9. Host institution's commitment) will be shared among the imaging and bioinformatics groups, which are expected to boost collaborative research for all of the researchers in IFReC.

7) International research conferences or symposia 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

FY 2007-2008: 2 meetings

Major examples (meeting title and place held)	Number of participants
Kick-off symposium of WPI-IFReC "Immunology and Imaging", Mar. 27-28, 2008, Osaka International Convention Center.	Domestic: 350 Overseas: 50
The 2nd International Symposium of IFReC "Dynamics of Immune Responses", Feb. 12-13, 2009, Icho-kaikan, Osaka University.	Domestic: 150 Overseas: 50

FY 2009: 5 meetings

Major examples (meeting title and place held)	Number of participants
International Symposium organized by JST & IFReC "Frontier Immuno-Imaging", May 11, 2009, Seminar room, Nano-biology building, Graduate School of Frontier Bioscience, Osaka University.	Domestic: 40 Overseas: 10
International Symposium "Immune Regulation: Present and Future", May 25-27, 2009, Osaka International Convention Center.	Domestic: 450 Overseas: 150
International Joint Symposium organized by SIgN & IFReC "Integrating Immune Networks with Immuno-Imaging", June 18-19, 2009, Singapore Immunology Network (SIgN), Singapore.	Domestic: 30 Overseas: 150

International Joint Symposium organized by IVI & IFReC “Regulation of Innate Immunity”, Sep. 18-19, 2009, International Vaccine Institute (IVI), Seoul, Korea.	Domestic: 20 Overseas: 70
International Workshop “Bioinformatics in Immunology”, Nov. 6, 2009, Taniguchi Memorial Hall, Integrated Life Science Building, Osaka University.	Domestic: 25 Overseas: 15

FY 2010: 6 meetings

Major examples (meeting title and place held)	Number of participants
The 4th International Symposium of IFReC “Immunology at the Forefront”, June 1-2, 2010, Icho-kaikan, Osaka University.	Domestic: 150 Overseas: 50
IFReC-New Zealand International Joint Workshop, June 17-18, 2010, Taniguchi Memorial Hall, Integrated Life Science Building, Osaka University.	Domestic: 25 Overseas: 15
International Symposium organized by RIKEN & IFReC “B cells and Autoimmunity”, Aug. 19-21, 2010, Nara Royal Hotel, Nara.	Domestic: 60 Overseas: 90
International Joint Symposium on Immunology organized by Chinese Society for Immunology & IFReC, Nov. 2-5, 2010, Xizi Hotel, Hangzhou, China.	Domestic: 25 Overseas: 35
International Symposium “The 2nd International Symposium on Integrated PET-MRI”, Jan. 28-29, 2011, Senri-Life Science Center, Suita, Osaka.	Domestic: 70 Overseas: 30
International Symposium organized by IFReC & FIRST Program AKIRA Project “Towards Comprehensive Understanding of Immune Dynamism”, Mar. 1-2, 2011, Senri Hankyu Hotel & Taniguchi Memorial Hall, Integrated Life Science Building, Osaka University.	Domestic: 150 Overseas: 50

<Summary of achievements to date>

As described above, we have successfully organized large scale international symposia every year, which has greatly enhanced “global visibility” of IFReC and much improved self-consciousness of the young researchers and administrative staff working for a WPI center.

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 Referring to advice and suggestions given every year by the WPI working group and the program committee, the executive board of IFReC consisting of the center Director, Deputy Directors and Administrative Director make plans to improve the research environment for both domestic and overseas researchers, so that they are able to devote themselves more to their research (see Section 5). Regarding the handling matters related intellectual properties and management of health and safety of IFReC, see Section 3. Management.

<Future Policy and Concrete Plans>

1) Environment in which researchers can devote themselves to their research
   See Section3. Management < Future policy and concrete plans >

2) Startup research funding
   We will continue to provide newly recruited overseas PIs start-up research funds for the first three years direct from the WPI's budget, as before.
   The "Research Support Program for Fusion of Different Fields" (see Section 5. Summary of center's research environment) will also be continued because it has proved effective in encouraging young researchers in different disciplines, and hence is expected to facilitate a new era of immunology as well as making breakthroughs in the respective disciplines.

3) Postdoctoral positions through open international solicitations
   We will continue to post advertisements of positions of postdoctoral fellows and technician on leading international journals such as Nature and IFReC's website.

4) Administrative personnel who can facilitate the use of English in the work process
   As of the end of FY2010, two thirds of administrative staffs are bilingual. A native speaker of English with research experience joined the RMP office (See section 3. Management) from April 2011. Without any doubt, this recruitment will not only facilitate the use of English in the work process but also make it possible for all bilingual staff to improve their English communication skill to a truly international level.

5) Rigorous system for evaluating research and system of merit-based compensation
   We have a plan to hold the ISAB meeting every two years, and will use a newly adopted system of staff evaluation. The evaluation data thus collected will be used as reference material to decide salaries and the renewal of employment of researchers and administrative staff.

6) Equipment and facilities, including laboratory space, appropriate to a top world-level research center
   As of the end of FY2010, 11 IFReC PIs have their laboratories in the Integrated Life Science Building, constructed in 2009. Next to this building, construction of a new IFReC research building was completed in March 2011, where 9 IFReC laboratories will move in. This makes it possible for 2/3 of IFReC researchers to assemble together. In this new building, the radio-isotope experimental station and a part of the Core Instrumentation Facility of the RIMD are also set up. Even so, an open space is still left for possible increase of laboratories in near future. In addition to two animal resource centers of RIMD, the IFReC animal resource center for experiments with SPF animals was also constructed in 2009, so that researchers can use these animal resource centers for different purposes.
   The center's director was selected as a recipient of the "Funding Program for World-Leading Innovative R&D on Science and Technology (FIRST Program) in 2009. Using this fund, several instruments such as a new DNA sequencer, a new model 11.7T MRI, an electron microscopes, cell sorters etc. will be purchased, so that instrumental facilities of IFReC will be made further substantial. Overall, international quality research facilities deserving of fundamental researches of immunology and infectious diseases in 21st century will be established within an IFReC/RIMD complex.

7) International research conferences or symposia held regularly to bring world's leading researchers together
   In addition to the international research conferences or symposia that should be held regularly to fulfill the requirement by the program committee, IFReC and SIgN have reached an agreement to jointly organize a Winter School on Advanced Immunology every year (http://ifrec-sign-winterschool.org/index.html) to provide a new educational and networking venue for young researchers from all over the world. The school will be held annually, with the location alternating between Japan and Singapore. In the first for the program, 2012, it will be held in Japan.

8) Other measures, if any
   Asking support from deputy directors and Administrative Director, the center director will continue to carefully examine advice and suggestions given by the working group and the program committee, which has proved indispensable for IFReC to establish its foundation in becoming a WPI center true to its founding principles.

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

<Initial plan and goals at the interim evaluation>

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.

<Current assessment>

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

Neither the principle nor criteria stated in the initial plan has been changed.

However, as a method of evaluation we have decided to hold the international scientific advisory board meeting (ISAB, see Section 5-5).

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

(a) Major contributions to main research areas:

List of publications, their citations, etc. are given in Section 2. The Center's Research Activities (major accomplishments of all PIs) are summarized in the subsection 2-2 "Research results to date".

Judging from these data, all PIs of IFReC can be regarded as leaders of their respective research fields not only before joining IFReC but also over the past four years.

Given below are the PIs appointed from April 2008 onward, who can be regarded as leading researchers in their respective fields.

-M. Ishii, imaging of immune cells in situ
-K. Kikuchi, development of chemical probes to give specific signals under specified environment
-N. Smith, Laser-Raman microscopy for imaging biomolecules without artificial labeling
-C. Coban, role of haemozoin in Malaria infection;
-D. Miranda-Saavedra, formation of transcriptional network during hematopoiesis
-K. Ishii, adjuvant innovation in vaccine development

(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).	(b) Creation of new research areas: All PIs have seemingly understood the importance of making breakthroughs by fusing different scientific disciplines and technology to open a new era of immunology. Thus, they have encouraged young researchers in their laboratories to apply for the program of "Research Support Program for Fusion of Different Fields" that was introduced in 2009; Fifteen projects are now in progress. Their interim evaluation, made last year, indicated that a few projects will be successful in creating of new research areas. The PIs listed above (a) who joined are expected to widen the scope of immune dynamism studied at IFReC since their backgrounds, and methodologies, are significantly different from that of the incumbent PIs. *The program provides financial support to start collaborative studies by IFReC young researchers in different disciplines. The projects are annually reviewed by IFReC PIs at a hearing open to all IFReC staff.
(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.	(c) Contribution to human life: The development of an Anti-IL-6 receptor therapy for inflammatory diseases based on basic research by Kishimoto has been used in clinical practice and proved very effective. Hatazawa is a specialist of nuclear medicine and responsible for diagnostic imaging at the University Hospital. He has been developing an integrated PET/MRI system, which is to create a new fusion of morphological and functional imaging. This technology is expected to become a powerful diagnostic means for various diseases. We understand the importance of reinforcing the lines that allow for basic research to be translated into benefits for human welfare. In view of this, we recruited C. Coban (2010) and K. Ishii (2010) as PIs, who are specialists of Malaria immunology and vaccine science, respectively. We believe that their creative interaction with other IFReC members will make a great step forward and contribution to human welfare.
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.	**iii) Goals to be achieved through the project (at time of interim and final evaluations)** Goals at time of interim - To keep the current levels and global standing of immunological research of this center. As described in Section 2, Center's Research Activities, the science ongoing at IFReC is of the internationally highest quality as indicated by

	number of high quality publications, invited lectures, plenary addresses etc. According to the latest database (Thomson Reuters Essential Science Indicators for 2000 – 2010), the research groups of IFReC (Akira and others) has ranked Osaka University 1st in citation impact among the top 30 institutions in immunology all over the world. This high quality of science is of course the major drive to increase the international visibility of IFReC. In fact, there has been a marked increase in interest from overseas research institutions towards IFReC. We have concluded academic cooperation agreements with Pohang University of Science and Technology, Korea (2009), and with the Indian Institute of Science Education and Research, Bhopal, India (2010). For the past three years, we have engaged in preliminary talks regarding the exchange of scientific staff and future collaboration from the Ministry of Research, Science & Technology, New Zealand, the Dutch Innovation Platform and two overseas pharmaceutical companies.
- To further grow new research areas that are opened by this center and make them major ones in the corresponding area.	- To further grow new research areas opened by this center and make them major ones in the corresponding area. At present, it is premature to say that any new research area has open as a direct result of the activities at IFReC over the past three years. This is because it is not an easy task to directly observe immune cell dynamics in live animal (see Section 2-3).
- To establish technical and theoretical basis of intravital and noninvasive single cell analysis of immune responses.	- To establish technical and theoretical basis of intravital and noninvasive single cell analysis of immune responses. We can see a bright future ahead owing to a recent development in non-invasive imaging techniques such as the whole animal imaging by MRI and molecular tracking by Raman microscopy underway at IFReC. In addition, other new imaging technologies and methodologies of systems biology will be brought in if successful collaborations of IFReC researchers are made with those at QBiC and CiNeT (see Section 1).
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.	Goals at final evaluation We have changed the goals at final evaluation as: - To establish the methodology for the visualization of multiple types of immune cells in live animals and immune-related molecules within single immune cells with good spatial and temporal resolution. - To integrate methodologies of bioimaging and bioinformatics into

	immunology for understanding of immune response and the dynamism of the immune network. <Current assessment>

<Future Policy and Concrete Plans>

As for criteria and methods for evaluation, no change seems to be needed. However, we are aware that the evaluation should be objective and fair as much as possible, and that if made properly it is beneficial not only to IFReC as a whole but also to individual researchers. For this reason, we will hold the International Scientific Advisory Board meeting every two or three years (See Sections 5 and 11) and review the publication of international databases, press releases and other media related to scientific evaluation.

7. Securing competitive research funding

<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

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).

<Secured to date>

External competitive funds acquired by IFReC researchers from FY2007-FY2010 are summarized in a table below. The large increase of their total sum in FY2010 should be noted as this may be an indication of high the quality of science at IFReC. In addition, administrative staffs in the new Research Planning and Management Office of IFReC provide overseas researchers with sufficient help with administrative procedures that are required to be conducted in Japanese.

External competitive fund acquired during FY2007-2010.

CURRENCY:JPY

	FY2007(1/2 year)	FY2008	FY2009	FY2010	Total
Commissioned Research	317,663,860	675,919,933	382,100,824	396,744,284	1,772,428,901
Joint Research	10,280,991	17,139,800	26,919,618	43,661,740	98,002,149
Donation for Research	45,564,951	105,683,459	139,210,288	127,025,915	417,484,613
Grants-in-Aid for Scientific Research	115,595,225	408,342,538	673,182,993	993,943,153	2,191,063,909
Total	489,105,027	1,207,085,730	1,221,413,723	1,561,375,092	4,478,979,572

- Major external funds warranting special mention in recent two years :

i) Funding Program for World-Leading Innovative R&D on Science and Technology (Akira) almost 3 billion JPY for 5 years from 2009.
ii) Grants-in-Aid for Scientific Research, Scientific Research(S) (Kurosaki) 160 million JPY for 5 years from 2009.
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" (Arase) 350 million JPY for 5 years from 2009.
  -"Development of new therapies for autoimmune diseases by regulating humeral immune system" (Kurosaki) 350 million JPY for 5 years from 2009.
iv) The Special Coordination Funds for Promoting Science and Technology (Kishimoto, Kumanogo,Kikuchi, Masaru Ishii, Smith, Yoshioka and Standley) 142 million JPY for 5 Years from 2010.
v) Grants-in-Aid on Scientific Research on Innovative Areas (M. Ishii) 30 million JPY in 2010.

	- **Major Research Funds acquired by overseas researchers in 2009 and 2010.** i) JST PRESTO "In-situ laser fabrication of nanoprobes inside living cells for analysis of biofunctions" (Smith) 40 million JPY for 3 years from 2009. ii) Grants-in-Aid for Scientific Research acquired by overseas researchers: 3 projects (among 15 recipients in IFReC) (Standley, Coban and Smith) in 2009. iii) Grants-in-Aid for Young Scientist B (Coban) in 2010. Note it has recently been notified that Grants-in-Aid for Young Scientist have been awarded to 3 overseas researchers.

<Future Strategy>

Our strategy to secure competitive research funds consists of the following four plans:

1) Improve the skill of the staff at the RPM office, as well as other relevant administrative staff, to provide sufficient information and help for application and administrative procedures required to be conducted in Japanese;
2) English translation of information and manuals of major research funds for overseas researchers;
3) Establishment of internal pre-review system [a];
4) Compilation of successful proposals for reference in preparing external grant applications [b].
   a. A working group consisting of several researchers at associate professor, or higher level, will be established to read proposals by young oversea researchers for major external competitive funds such as MEXT Grants-in-Aid and give suggestions for improvement.
   b. This type of collection of the successful grant applications is useful for young researchers of little experience in such application.

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

<Initial plan>	<Measures taken to date>
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.	**Activities and initiatives to be taken after project funding ends** IFReC has been focusing all efforts to be established as a foundation WPI center. It would be, therefore, inappropriate and unreasonable at this time to attempt to protract any truly meaningful objective regarding said goal. As described in Section 9, however, the university has sought a way to support IFReC, not by ordinary financial or personnel assistance, but by a more research-oriented way. Thus, the university has continued negotiations with the National Institute of Information and Communications Technology（NICT）to conclude a collaboration agreement for fusion research. This was realized as an agreement of the “Brain/neural network-Information Communication” in 2009. Furthermore, a similar agreement of “Bio-system Dynamics” with Riken was established in 2010. Based on these agreements, two research centers, CiNeT of NICT and QBiC of RIKEN, will be open in the near future within walking distance from IFReC. Yanagida is appointed as the director of both centers. As can be seen from their names, technologies and methodologies of both centers are rather similar to those of IFReC. Hence, collaborations with these centers will be made in due course, helping IFReC to advance interdisciplinary researches necessary for initiating a new era of immunology. However, concerning the integration of IFReC with the International Research Center for Infectious Diseases (RCID), this will be left as a high possibility because as described elsewhere in this report (Sections 1, 5, 9, and 10), good partnership with the Research Institute of Microbial Diseases (RIMD), the parent body of both IFReC and RCID, has been built up through the sharing of research facilities such as animal resource centers, the radio-isotope experimental station and the Core Instrumentation Facility of RIMD.
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.	**Describe expected ripple effects** If the collaboration of IFReC with CiNeT and QBiC goes well in the near future regarding the successful integration of immunology with cutting edge-technologies of bio-imaging and bioinformatics, resulting in formation from a premier international research center, a reformation with RCID alone but rather RIMD as a whole would be realistic. * Continues <Future Policy and Concrete Plans> below.
Other important measures to be taken in creating a world premier international research center	**Other important measures to be taken in creating a world premier international research center**

Global COE Program:	**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.	The Global COE program (FY2007- FY2011) and IFReC started almost simultaneously in 2007. The program leader, Yanagida, is the PI of the "Single Molecule Imaging" group of IFReC as well; both sides have received benefit from each other. Cutting-edge technologies for real-time imaging and measurement of single biomolecules and cells have been pursued in several G-COE program-supported laboratories. The relationship between these two has the demonstrated benefits that can be yielded from such, as well as being a model for other imaging groups at IFReC.

<Future Policy and Concrete Plans>

In the next section (Section 9. Host institution's commitment), our stance to the items in this subsection is described because these should be considered in conjunction with the future policy of "Host institution's commitment"

However, it seems appropriate to stress that the major goals of IFReC and RIMD are complementary with each other: comprehensive understanding of immune dynamism, and better control and treatment of infectious diseases, respectively. If both institutions function together closely and systematically, an integrated life science center of global significance and presence could be established at Osaka University (Section 9" After the period of WPI project funding ends").

9. 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 aspect 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 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

<Progress to date>
-Provision in host institution's mid-to-long-term plan

During the latter half of the Osaka University Medium-Term Plan for the 1st period (1st MTP, FY2004 - FY2009), IFReC was selected as one of WPI research centers and started its operation. The 1st MTP stated its research objective at the University "to support development in science and industrial technology and flexibly handle research subjects of great urgency, such as applied and advanced research for human society and culture of the 21st century", which was in line with what the host institution of a WPI center should commit. In the Medium-Term Plan for the 2nd period (2nd MTP, FY2010 - FY2015), the research objective was further developed "to promote the world's top class research, advance knowledge in various research fields by fully utilizing the capacities of different research organizations of the university, and promote interdisciplinary research by establishing an innovation hub that supports both basic and applied research". This statement is a clear indication of the University's strong awareness of the reasons under which IFReC was selected, and it objective as a WPI center.

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. Notes: 1) Most of the Indirect research expenses from this program will be used for the WPI. 2)The main research building (9,400㎡ 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.	-Concrete Measures In general, the University has duly fulfilled various commitments to support IFReC's development as a WPI center, not only according to its 1st MTP as the initial plan given in the column on the left, but also by many aspects given in the 2nd MTP. (1) Competitive grants obtained by researchers participating in the project and in-kind contributions, etc. Among those listed in the column on the left, below are the most effective contributions the university has given IFReC in order to establish it's foundation enabling it to become a WPI center (for the initial period between FY2007 and FY2010). - Allocation of all indirect costs of the WPI budget to be at the disposal of IFReC. This has been of great financial support, allowing IFReC to afford various, and necessary expenses for the initial setting-up - Construction of the ILS building (2009) to provide core laboratory space of real international standard for all PIs - Finance support of construction of the IFReC Animal Resource Center for SPF animals, which together with two animal resource centers of RIMD, has made it possible for IFReC to use these centers for different experimental purposes - Provision of a tenured position to invite Sakaguchi from Kyoto University, who is an indispensable PI for IFReC to become a world-leading institution of immunology - Assignment of 2 administrative staff employed by the university budget

* 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.	As initially planned, the University has entitled the Center Director to manage and operate the center by making decisions regarding substantive personnel and budget allocation. However, important matters such as annual budget and appointment of PIs are to be approved at the Center Management Committee and the Board of Representatives. The Administrative Director is authorized to give full support to the Director by acting as a coordinator among Deputy Directors and executing management actions through the reformed administrative office. Thus, the director can literally make top-down decisions and reformation of research environments so that IFReC PIs can devote themselves to research.
(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.	This has been done as initially planned. That concurrent appointment of researcher who belonging to other departments to IFReC, and vice versa, can be made without any real difficulty.
(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 will	Most notable in this respect is the establishment of the Support Office for Large-Scale Education and Research Projects (LSERP) and the Office for International Planning and Programs (IPP). LSERP was established in 2009 for the purpose of improving support systems for obtaining large-scale education and research projects for Osaka University, in order to fortify the planning and strategic functions for such

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.	projects. This cannot totally be ascribed to the launching of IFReC in 2007, as a number of government- supported programs of large scale such as Global-COE programs have been underway. However, IFREC can be regarded as an organization with effective and efficient research support and administration. In fact, several personnel with research experience together with PhD and bilingual staff have been recruited to the administrative office of LSERP. The University had an office for international exchanges in academic research and education under the International Affairs Board. In view of the accelerating needs to further advance the level of research and education, the IPP was established in 2010. One of its goals is to promote research collaborations with scholars and institutions overseas and to share the research results for the benefit of the global society, which is almost exactly what is mentioned in the WPI program. In addition, IPP provides overall support to formulating plans and proposals for international exchange that can beneficial to IFReC. As for housing of international visiting professors and researchers, accommodation of international standard (Kasugaoka House), was constructed in 2010. Here, several IFReC researchers and their families are currently reside (part of the rent is subsidized from the WPI budget.) Due consideration has been made for other items listed in the column on the left.
(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.	(5) Accommodation of center's requirements for infrastructural support (facilities, e.g., laboratory space; equipment; land, etc.) The University constructed the Integrated Life Science building (ILS building of ten storey, 9,258m^2) in 2009 to provide 11 IFReC PIs sufficient spaces to set up their laboratories. Next to this building, construction of a new IFReC research building (nine-storey, 6592m^2) was completed in March 2011, where 9 IFReC laboratories will move into. This makes it possible for all of the full-time researchers of IFReC to assemble together. The University also supported the construction of IFReC animal resource center (four-storey, accommodating 25,000 SPF mice) in 2009, which together with the two animal resource centers of RIMD, has made it possible for researchers to use these animal resource centers for different purposes.

	The University has also made necessary arrangements for IFReC researchers to use equipment in other 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 The University concluded research collaboration agreements with NICT, (2009) and RIKEN (2010). Based on these agreements, two research centers, CiNeT and QBiC of RIKEN, which are within walking distance from IFReC, are scheduled in near future. The main focus at CiNeT is technological innovation for direct imaging of cellular activities, metabolism and systems analysis of cellular networks in the brain, while quantitative and comprehensive studies are performed to accurately predict and control complex biological phenomena at QBiC. Collaborations with these centers will be made in due course, helping IFReC to advance interdisciplinary researches necessary for open a new era of immunology.

<Future Policy and Concrete Plans>
-Provision in host institution's mid-to-long-term plan

As described above in the "Progress to date" of this section, the Medium-Term Plan for the 2nd period (2nd MTP, FY2010 - FY2015) of the University was laid down with a strong awareness of IFReC as a WPI research center. Thus, fully supporting IFReC to become a world class research center can be said to be among Osaka University's top priorities in the 2nd MTP.

-Concrete Measures

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

Arrangements to make all of WPI indirect costs from this project be at the disposal of IFReC will be continued.

From the beginning of FY2011, 4 administrative staff employed by the university budget will be assigned to IFReC, which will decrease in part the personnel expenses of IFReC.

Although difficult under the present financial situation of the university, negotiation will be continued between IFReC and the University to provide more tenured positions in order to attract and employ excellent researchers.

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

This will continue to be operated in the same way as before.

(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

This will be done as initially planned.

(4) Revamping host institution's internal systems to allow the introduction of new management methods (e.g., English-language environment, merit-based pay, top-down decision making) unfettered by conventional modes of operation.

In view of the important roles performed by members of the support systems in operation at IFReC, the University will make as much an effort as possible to reinforce the Support Office for Large-Scale Education and Research Projects through staff development in order to improve and enhance their administrative skills. Such efforts are also important with regards to the assistance the staff will provide with the application procedure of external competitive research funds. Toward this end, a person with both research and research administrative experience has already been assigned.

The University has an office for international exchanges in academic research and education under the International Affairs Board. In view of the accelerating needs to further advance the level of research and education, the IPP was established in 2010. One of its goals is to promote research collaboration with scholars and institutions overseas and share the research results for the benefit of the global society, which complements the aim of the WPI program well. In addition, IPP provides overall support to formulating plans and proposals for international exchanges that can be beneficial to IFReC.

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

This will be operated in the same way as up to now.

(6) Support for other types of assistance

See below (1. Over the next 5 years)

- What the host institution is /will do to support/sustain the operations of the center (include support activities already underway)?
1. Over the next 5 years

Within the framework of its 1st MTP (FY2004 - FY2009), as a major effort in the field of biological sciences, Osaka University already planned to establish a center for interdisciplinary research with the RIMD as the central core. To this end, through cooperation with the Institute of Medical Science, Tokyo University, RIMD established the International Research Center for Infectious Diseases in 2005. Supported by a MEXT-program, "Program of Founding Research Centers for Emerging and Reemerging Infectious Diseases", RIMD also established the Thailand-Japan Research Collaboration Center on Emerging and Re-emerging Infections in 2005. Along with these pursuits to develop institutions of pioneering research, IFReC was also successfully proposed and accepted as WPI research center in 2007.

Currently, in the second year of the 2nd MTP (FY2010 - FY2015), IFReC and RIMD are collaborating with each other. In addition to being located on the same premises, the advantage of this collaboration is that both institutes are complimentary to each other in terms of research fields: immunology and infectious disease medicine. Henceforth, the University actively supports the reformation of research organization that IFReC is now advancing, so as to expand it to RIMD. This is expected to lead:

a) Promotion of further internationalization of research groups
b) Further development and internationalization of the researcher support system
c) Further deepening of interdisciplinary collaboration between the IFReC and RIMD

Meanwhile, as a means to achieve an objective stated in the 2nd MTP, the University has continued its efforts to establish comprehensive collaboration and partnership with other public research organizations and companies beyond the usual types of joint research projects embarked upon. As a result, the University concluded a basic agreement with the National Institute of Information and Communications Technology (NICT) on an interdisciplinary research project on brain/neural network-information communication in 2009, and with RIKEN on the "agreement on promoting collaboration/cooperation" with an accompanying agreement on research collaboration concerning "bio-system dynamics" in 2010. The interdisciplinary/collaborative/cooperative researches based on these agreements are conducted at research centers on the university campus.

At the Center for Information and Neural Networks (CiNeT: construction of the new research building is to start in 2011), development of cutting-edge technology for directly measuring the activity and metabolism of neurons, and research focusing on the system analysis of cellular/neural networks cells is being performed. The QBC will start operating with Yanagida as the Director from April 2011 (located on the campus map) with the construction of a new building near the CiNeT building currently under way. Here, quantitative and comprehensive analytical biological research for the advancement and improvement of human welfare will be conducted.

The University is globally recognized as being among the foremost institutions regarding imaging technologies, such as the single molecule imaging (led by Yanagida), Raman spectroscopy (Kawata), electron microscopy (Namba), atomic force microscopy (Morita) and MRI (Yoshioka). With such superior cutting-edge technologies, the University plans to launch its "Imaging technology hub" project, which aims to become Japan's leading imaging technology center. In this plan, IFReC, CiNeT and QBiC and other research groups listed above will constitute its core. Developing such imaging technologies and establishing the research centers for applying these technologies to the fields of biological science signify the University's awareness of the importance of the IFReC's research objective, "comprehensive understanding of immune mechanisms", and its willingness to promote it.

The research methodologies at CiNeT and QBiC are closely related to the research at IFReC, which aims to make advances in immunology and achieve a "comprehensive understanding of immune dynamism" through integration of immunology with imaging and bioinformatics. Therefore, interactions and collaborations between researchers from these research centers as well as many other researchers at other graduate schools and laboratories are expected to increase, resulting in advancement in interdisciplinary research.

In addition to facilitating such interdisciplinary science, the University also encourages it by establishing a management system that allows for the flexible reshuffling of researchers and research support staff as well as smooth and efficient ways to share facilities and advanced equipment/devices. As part of this, in 2010, the University established the Support Office for Large-Scale Education and Research Projects (SOLER), a section under the direct control of the trustee in charge of research. In addition to operating as an office for research fund management, SOLER actively supports research and conducts outreach activities by appointing sufficiently experienced personnel. If the researchers of IFReC/RIMD, CiNeT and QBiC jointly apply for research projects supported by large competitive funds, it will also be actively supported by SOLER.

The University has also launched a Techno Alliance plan for promoting "Industry on Campus" stated in the 2nd MTP. The construction of a research building for that purpose was completed in March 2011. This building is equipped with facilities for conducting the latest research in diverse fields, where various research projects are jointly carried out by researchers from outside companies and researchers at the university to foster advanced human resources through industry-academia collaboration. This signifies the University's will to create an environment whereby the seeds produced by the basic research at the university facilitate next-generation technologies that meet new industrial and social needs. Therefore, through this Techno-Alliance plan, the University will provide a place for IFReC to bridge its basic and translational researches to develop new vaccines against infectious disease and cancers and treatments for immune-related diseases including autoimmune diseases.

2. After the period of WPI project funding ends

Well before the end of the WPI program implementation period, IFReC is expected to further its collaboration with QBiC and CiNeT and open up a new field in immunology by advancing the interdisciplinary research, which could make it rank among the world leaders of life science. On the other hand, RIMD is scheduled to proceed with the above-mentioned system reformation and reconstruction of its research support sections. This would bring a new horizon for IFReC and RIMD to restart as a single organization. This new organization is expected to be capable of systematically conducting a wide range of research from basic to applied, such as molecular details in immune responses to vaccine development.

The University is further expecting:

a) world class research development at CiNeT and QBiC;
b) deepening interdisciplinary research by the three research centers;
c) success in industry-academia collaboration by research teams at the Techno Alliance center to produce outcomes that meet social expectations.

If these all go well, the University will review the research center facilities, structure, budgets and personnel allocation to streamline the flow of data. Here, as the Techno Alliance center is flanked by CiNeT, QBiC and IFReC/RIMD research centers, this would allow the center to act as a virtual convergence point for basic research to be channeled for industrial translation.

10. Efforts to improve points indicated as requiring improvement by Program Committee and results of such efforts	
-Points specified as needing improvement (as noted in Item 3 “Points that need improvement” in the FY2009 follow-up results)	-Efforts to improve them and results
1. Strategic plans toward making a breakthrough in classical immunology.	1. Strategic plans toward making a breakthrough in classical immunology. The response to this point is described in Section 2-3.
2. Strategic advancement of imaging and informatics to be integrated into immunology.	2. Strategic advancement of imaging and informatics to be integrated into immunology. The response to this point is also described in Section 2-3.
3. Promotion of outreach activities.	3. Promotion of outreach activities. With our strong awareness of the importance of outreach activities, IFReC assigned the work to one of the staff (a PhD holder) of the Research Planning & Management Office in 2008, who has experience in science writing as well as research. He has been responsible for organizing IFReC symposia and seminars, publication of science reports since 2008. He is also in charge of matters related to items 4) and 11) of Section 11. With good support from the administrative office and strong link with IFReC researchers, he successfully organized several public events such as the science cafés and lectures for high school students to publicize the work and activities of IFReC. Note-worthy is the science café held in January, 2010, where Akira and Kurosaki held an informal scientific talk, which attracted a large audience. This particular event seems to be very effective in reaffirming the significance of outreach activities for many IFReC researchers. The success of the science café was followed by a marked increase in morale among the researchers; IFReC continues to make efforts to enhance its outreach activities. To achieve this, the appropriation of administrative staff and collaborations with other University organizations, such as the Communication Design Center, in order to exchange information and ideas on improving methods of science communication (See Section 9-4).

11. Efforts to improve points indicated as requiring improvement in the Project Progress Verification Report and results of such efforts

-Points specified as needing improvement (extracted from the FY2009 Project Progress Verification Report)

1) IFReC should generate a more explicit road map, including a mission statement, milestones and indicators. There should be a strategic discussion of the distribution of resources between immunology/ imaging and fusion projects.

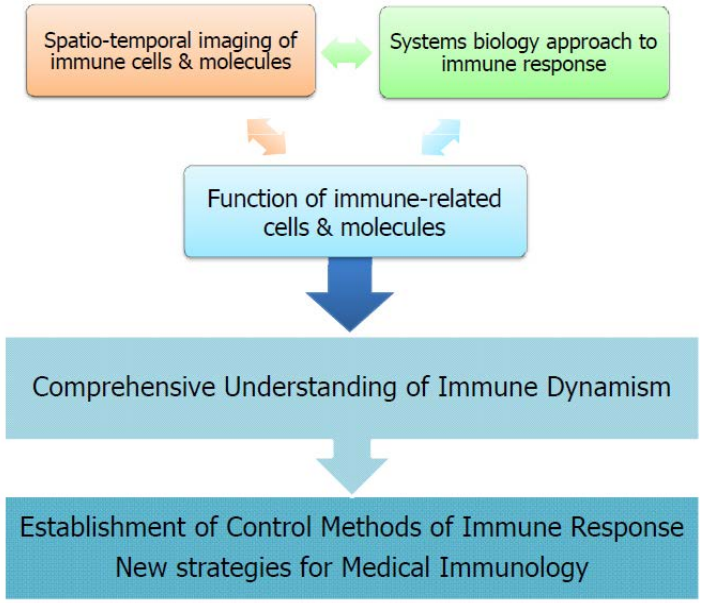

Fig. 11-1 The Scientific Goal of IFReC

-Efforts to improve them and results
*If you have already described these in other parts of this report, please indicate where for reference.

1) IFReC should generate a more explicit road map, including a mission statement, milestones and indicators. There should be a strategic discussion of the distribution of resources between immunology/ imaging and fusion projects.

We have reviewed our progress and scientific achievement over the initial three and a half years as a WPI center and reexamined criticisms, advice and suggestions raised during discussions with the WPI working group and the Program Committee. We have also taken into consideration the recent trend in the areas of life science relevant to us.

The results of our discussions are the basis of the “Future Policy and Concrete Plans” (Section 2-3) and the “road map” given below. Descriptions for the distribution of resources between immunology/imaging and fusion projects are also given in Section 2-3 and Sections 5 and 6.

The Road Map of IFReC

Mission statement IFReC aims to comprehensively understand immune dynamism. To this ultimate goal, we shall integrate imaging and bioinformatics technologies with experimental biology in order to study a wide range of phenomena (both in space and time) from the molecular to whole body levels. We believe this integrated approach not only deepens our systematic understanding of the immune system but facilitates basic research results to be targeted to medical applications through translational research. Thus, advancement in our understanding of basic immunology improves medical strategies for the body’s defense against infectious diseases and cancers, and diagnosis and treatment of immune-related diseases (Fig. 11-1).

Along with these research efforts, we shall further improve the research administration system, which provides a research environment of international standard, where both domestic and overseas researchers can devote themselves to research.

Through these endeavors, we shall establish the solid foundation for IFReC to be a truly internationally renowned research center.

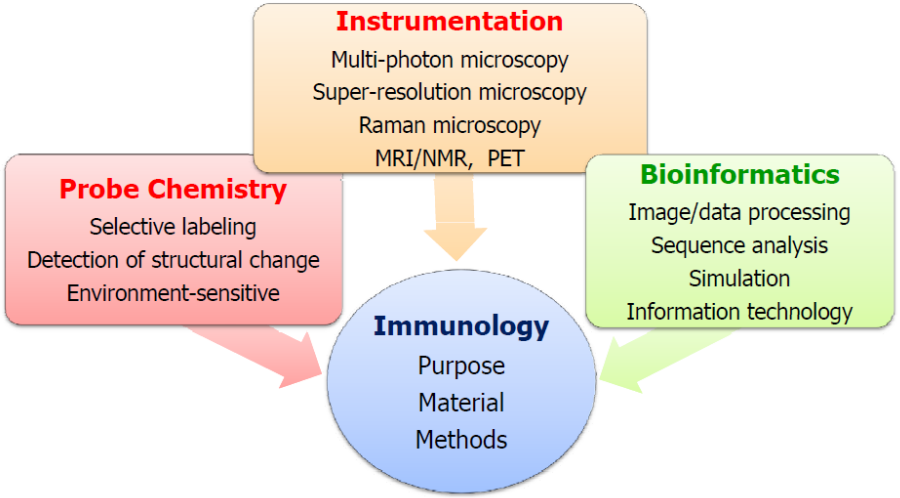

Fig. 11-2 Interdisciplinary Research at IFReC

Table 11-1 Methodologies for studying immune dynamism

Purposes	Methods	Targets
Dynamics of systems	Selective visualization	Molecules
	Tracking of movements	
	Network simulation	Cells
Properties of systems elements	Determination of structure	Molecules Supra-molecular assemblies Organelles
	Measurement of Metabolic state	Cells

Milestones and indicators

<Basic Research>

IFReC's scientific goal is to the 'comprehensive understanding' of immune dynamism through 'the 'integration' of imaging and bioinformatics technologies with experimental immunology (Fig. 11-2); Our understanding will be greatly deepened through successes made. Most of the instrumentation facilities are fully operational, and the optimization of the technologies, including progress towards the development of appropriate probes, is already being used in immunology-based research.

Well armed with animal and instrumental facilities as described above, we are attempting to unravel various aspects of molecular and cellular dynamics involved in immune responses by:

i) quantitatively examining structural, spatial and temporal properties of immune cells and molecules to understand the principles that govern individual reactions and interactions;

ii) simulating the dynamics of immune network systems, both at the cellular and whole body levels, based on the principles thus obtained to predict immune phenomena.

The methodologies employed by IFReC's researchers for the studies of immune phenomena are listed in Table 11-1.The complexity levels of purposes listed, and the organization hierarchy of the targets can be regarded as milestones for the research progress.

(a) Dynamics of systems

- Molecules in a cell: At present, only a few types of immune-related molecule can be visualized in a cell at any one time. Any further 'in cell visualization of molecules' is an advance towards the ultimate goal of the elucidation of signal-transfer molecular networks within an immune cell. Such advances will only be seen after progressive stages of development, with the eventual aim of visualizing more types of molecules simultaneously and a higher temporal resolution. Such progress is expected to be attained in a few years, with the eventual accumulation of such data being used to create comprehensive and insightful computer simulations.
- Visualization of individual cells *in vivo*: Only a few types of cells are currently able to be visualized at the tissue level. The facilities in already in place, or to be installed in the near future, will improve our experimental abilities to a stage where multiple types of immune cells can be visualized simultaneously. This advancement is difficult, but should be made in terms of spatial/temporal measurements to track the movement of cells with

different functions throughout the body. Accumulation of data from such studies will make it possible to simulate cellular dynamics in the body and ultimately find a way of controlling the immune response.

(b) Properties of systems elements

- Determination of structure: Currently structural information of protein molecules directly relevant to their functions can only be measured *in vitro*. Attempts will be made to directly determine structures of immune-related proteins, subcellular structures, and organelle, *in vivo*. This is important to further understand their states in an immune response. Such progress is, again, expected to be attained within a few years.
- Measurement of metabolic state: In addition to the intracellular structure, it is important to know the physiological state of immune cells when they are interacting with antigens and cytokines, or in direct contact with other immune cells. At present, measurement of cellular metabolic state by MRI is limited to an organ level with low time-resolution, which can be improved to tissue level in a few years.

<To Medical Immunology through Translational research>

To this end, IFReC encourages its researchers to engage in translational research, either as an individual effort or by collaborating with other institutions. In fact, several small scale collaborations between some laboratories and pharmaceutical companies are currently in progress. In order to facilitate the basic research results to be targeted towards medical applications, we have recently decided to construct a consortium for clinical medicine-oriented immunology as detailed in Section 2-3. Its approximate schedule is:

1) Preparatory committee meetings and discussions concerning the construction of a 'clinical sample collection center' to be held several times in FY2011;
2) Opening the center in order to collect samples from April, 2012;
3) IFReC's researchers to use the center's collections from mid 2012 onwards;
4) Forums for clinical immunology research to be held in the 2nd half of FY2012 onward.

<Research administration system>

The future plans, which can be regarded as milestones of our progress in systems reformation, are described elsewhere (Sections 3, 6, 7, and10). Those plans will mostly be materialized within FY2011 or in the 1st half of FY2012.

2) IFReC should present its plans concerning core facilities, including potential use of those of Osaka University.

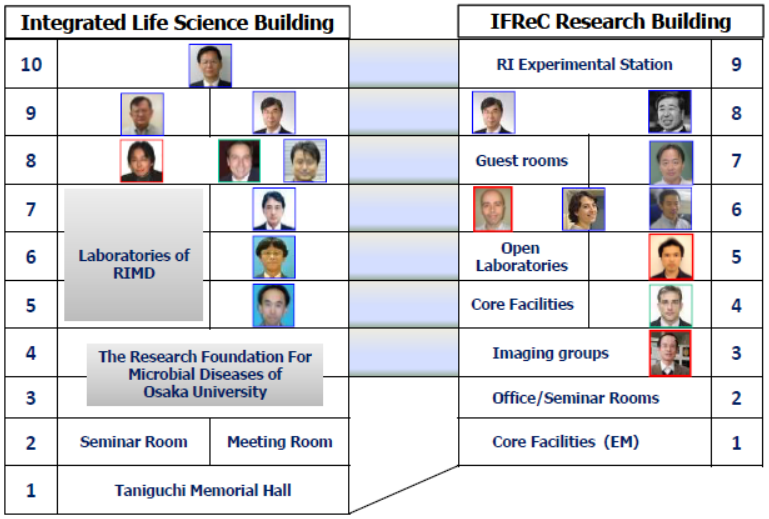

Fig. 11-3 The floor guide of IFReC research complex

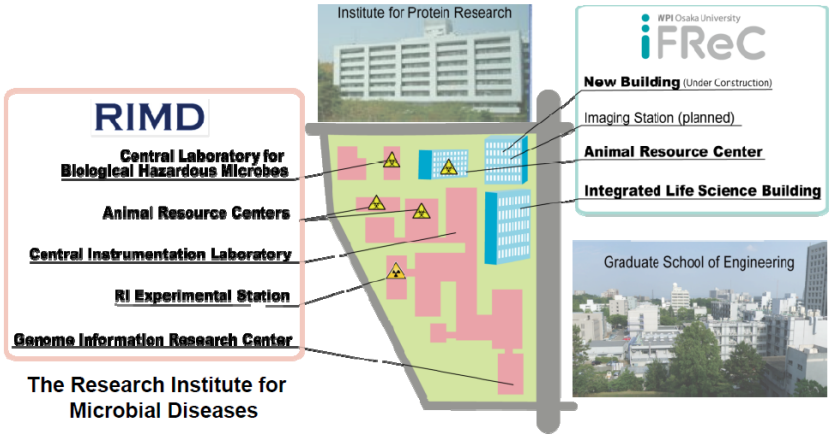

Fig. 11-4 IFReC/RIMD research complex

2) IFReC should present its plans concerning core facilities, including potential use of those of Osaka University.

In addition to the Integrated Life Science Building and the IFReC animal resource center constructed in 2009, construction of a new research building exclusively for IFReC was completed at the end of FY2010. Located next to the Integrated Life Science Building, it aims to facilitate interactions among IFReC researchers in various fields and further promote their collaborative research.

The core facilities, including the radio-isotope experimental station and part of the Core Instrumentation Facility of RIMD, will operate in the new IFReC building (Fig. 11-3). These facilities together with three animal resource centers are available to all members of IFReC and RIMD (Fig. 11-4).

An associate professor will be employed from April 2011 to better organize and manage these facilities. Technicians will also be posted to operate certain equipment such as the DNA sequencers, electron microscope, cell sorters, mass spectrometer and DNA chip analysis.

A full list of all core equipment and facilities will be made available online to all members of staff in English and Japanese. All operational manuals will also be available in both Japanese and English. A new server and network system will be set-up to manage the flow and availability of data from the imaging, informatics and immunology groups.

The Quantitative Biology Center (Section 9. Host institution's commitment) will collaborate with the imaging and bioinformatics groups. These facilities are expected to boost collaborative research for all of the researchers in IFReC.

3) The Center should make explicit its mechanisms of internal governance including procedures for evaluation of PIs and staff. It should prepare and distribute a document describing rules and responsibilities at IFReC, and get the signature of individuals joining IFReC to make sure they understand the Center's mission.	3) The Center should make explicit its mechanisms of internal governance including procedures for evaluation of PIs and staff. It should prepare and distribute a document describing rules and responsibilities at IFReC, and get the signature of individuals joining IFReC to make sure they understand the Center's mission. The mechanisms of internal governance have been described in a previous section of this report (Section 3 and 5). The procedure for staff evaluation and its use has also given in Section 5. It is felt that the availability and access to the rules and regulation of IFReC to the staff is adequate. The contract and labor manuals are sufficient for describing the rules. Staffs have not been asked to sign a mission statement as the institute's goals are considered to be widely understood to all members and newcomers. Instead, during the orientation of newcomers at the beginning of each fiscal year, the center director explains the outlines of the WPI program, mission and ultimate goal of IFReC, and the administrative director explains organization of IFReC and how it runs.
4) Documents for evaluation of IFReC by this committee (and others) should be standardized. Materials should contain, for each group: a scientific progress report, discussion of future plans, a description of any other important administrative/educational /etc contributions, and lists of personnel, grant support, publications and any honors, prizes, etc.	4) Documents for evaluation of IFReC by this committee (and others) should be standardized. Materials should contain, for each group: a scientific progress report, discussion of future plans, a description of any other important administrative/educational /etc contributions, and lists of personnel, grant support, publications and any honors, prizes, etc. As a scientific part of the evaluation, we compiled data from progress reports submitted by IFReC PIs. The progress report contains items such as current research and research collaboration, education and awards, a one-page research mission guide and a four-page brief outline of research outputs, publications and a list of presentations including invited lectures, research funds attained and patents. Submitted progress reports are used for the document evaluation and also as references to the evaluations via interview. Concerning the issue of evaluating PI's future plans, PIs will annually submit a document detailing their future plans.
5) IFReC needs to attract more female PIs. It might be helpful to invite more female speakers and other visitors.	5) IFReC needs to attract more female PIs. It might be helpful to invite more female speakers and other visitors. Although the number of female PIs has not changed since the last site visit by the WPI working group in January 2010, the number of female researchers has greatly increased every year: FY2007, 7; FY2008, 18; FY2009, 26; FY2010, 35.

	The number of female speakers invited to symposia, workshops and seminars organized by IFReC has also steadily increased: FY2008, 2; FY2009, 3; FY2010, 11. These trends indicate that IFReC is attracting female immunologists, hopefully resulting in the increase of future female PIs. We expect that the Day Care Centers within the premises of Osaka University (established in 2008) would improve researcher and student's child welfare, and thus to be effective to terms of recruitment.
6) The imaging scientists should work on being more cohesive, with close connections between the labs following different approaches, and hopefully. Some more physics/engineering assistance. IFReC should analyze the need for a super resolution optical microscope	6) The imaging scientists should work on being more cohesive, with close connections between the labs following different approaches, and hopefully. Some more physics/engineering assistance. IFReC should analyze the need for a super resolution optical microscope. The major strategy and concrete plans which are relevant to this point are described in Section 2-3. We are aware that to facilitate collaborations between researchers belonging to the imaging groups with those in different research fields, an increase in the opportunity for them to discuss their work and establish collaborations. Events like a symposium which was held in March, 2011 by the AKIRA Project (FIRST Program) allowed for such as this. Approximately 80 young researchers from the fields of imaging, informatics and immunology were divided into groups of 5-6 to facilitate in depth discussions. The opening of QBiC and CiNeT (see Section 9) is also expected to enhance collaborations of researchers in different disciplines. To meet the immunologists' specific needs, two scientists have already been transferred from IFReC to QBiC to improve equipment performance and to design new imaging probes. This collaborative effort also has the potential to development new methodologies and specialist equipment. To improve the cohesiveness of the Imaging groups, groups that were dispersed over the campus will relocate to the new building (See Section 1). To facilitate interdisciplinary collaborations, monthly seminars will be held by each lab in which a potential collaborator from a different research back ground will be invited to speak. Since its establishment in 2009, fifteen imaging and immunology collaborative research projects have been set-up. Nine such projects were initiated in 2009 and six in 2010 (See section 5). To further strength the instrumental facilities for imaging, a Raman-microscope, an electron-microscope and an 11.7T MRI will be purchased with a budget allocated by the FIRST Akira project, which will be set up in the new IFReC building. As for a super resolution optical microscope, a new

	instrument, the first one in IFReC, was recently purchased. It is now in operation in the Akira lab; preliminary data have already indicated at its usefulness in studying dynamic responses some immune cells to antigen stimulation.
7) Bioinformatics as presented may not be sufficient. A small group of international experts should be invited to evaluate whether the existing and planned bioinformatics resources match the future needs.	7) Bioinformatics as presented may not be sufficient. A small group of international experts should be invited to evaluate whether the existing and planned bioinformatics resources match the future needs. The major strategy and concrete plans which are relevant to this point are described in Section 2-3. From FY2009 to FY2010, the number of research staff belonging to Bioinformatics groups increased from 4 to 10. IFReC obtained a ¥33 million grant from the university to establish facilities to provide new servers and network system. This would make it possible to share research resources and data among the immunology, imaging and bioinformatics groups. The association with QBiC will also serve as a platform from which the researchers from the bioinformatics groups will be able to establish collaborations. An arrangement has been made to invite several internationally leading experts in bioinformatics to provide comments and advice for their current research as well as the future plans of the bioinformatics groups.
8) The center should send PhD students and young postdocs abroad to meetings and activities such as summer schools at least once a year.	8) The center should send PhD students and young postdocs abroad to meetings and activities such as summer schools at least once a year. IFReC's current position is to leave this decision at the discretion of the researcher's PI. However, IFReC has a specific program in place, the "Young Researchers Collaborative Support Fund", to encourage and financially support young researchers to attend conferences, or a collaborators laboratory abroad. For example; 30 young researchers participated the "IFReC/SIgN Symposium on Integrating Immune Networks with Immuno-Imaging" in FY2009. FY2010 saw the fund support 17 young researchers by allowing them to attend the IFReC/CIS joint symposium in Hanzhou, China. Also, an associate professor and a post-doc are visiting institutions in the USA for a short stay.
9) A Center retreat, preferably organized by young researchers, should be held annually to promote communication and interactions among researchers at IFReC.	9) A Center retreat, preferably organized by young researchers, should be held annually to promote communication and interactions among researchers at IFReC.

	The values such a retreat can offer, in terms of potential in-house collaborations and information exchange, are understood. However, at present, IFReC has no immediate plans to organize or fund such a retreat. It is felt that the current events held after international or internal symposiums provide sufficient opportunity for networking and collaborations to be established.
10) The website can be made more attractive to applicants by highlighting the Center's excellent imaging capabilities, describing core facilities and better highlighting programs supporting foreign scientists.	10) The website can be made more attractive to applicants by highlighting the Center's excellent imaging capabilities, describing core facilities and better highlighting programs supporting foreign scientists. The Research planning and Management office is now responsible for the website of IFReC (http://www.ifrec.osaka-u.ac.jp/). The major changes include: a) Information regarding the "Core Instrumental Facility" of RIMD and Osaka University that the researches of IFReC can use. Information regarding the installation of future equipment shall also be included b) Original data, particularly digital movies and images generated using IFReC's imaging tools will be available to be viewed from the site c) Information regarding the "Kishimoto Foundation Fellowship", an original fellowship program to support overseas researchers, is now available d) The website links the site for "Kasugaoka House", a housing complex built by Osaka University for overseas researchers. IFReC also gives financial supports to the researchers who reside at Kasugaoka house
11) Like other institutions, IFReC should prepare and distribute an annual scientific report.	11) Like other institutions, IFReC should prepare and distribute an annual scientific report. The Research Planning and Management Office of IFReC is now editing the "Annual Report FY2010". However, it should be mentioned that IFReC published two kinds of booklets on the center's activities in FY2008 and FY2009. The first one is called the "IFReC Profile", which introduces the research outline of each laboratory and was published both in English and Japanese. The second booklet is a 16-page "Annual Report", which gives brief summaries of the WPI Program and the yearly activity of IFReC. The "Report" was published only in English. The new "Annual report" is edited only in English. An editor/designer with knowledge and experience in biological research was chosen to improve the presentation. The "Annual Report of IFReC FY2010" is scheduled for publication at the end of June, 2011, so will not be available for this report.

12) An international scientific advisory board (ISAB) should meet before our next site-visit to carry out an in-depth evaluation of IFReC scientific activities	12) An international scientific advisory board (ISAB) should meet before our next site-visit to carry out an in-depth evaluation of IFReC scientific activities Although we established the ISAB when the center was launched in 2007, the board meeting has not yet been held, according to the suggestion made on the occasion of the first site-visit in 2008. In view of the importance of an objective, peer-review based evaluation of scientific activities at IFReC, we decided to hold the board meeting in 2011 (Section 5-5). However, the ISAB report will not be available prior to the writing of this report, but it will be compiled by the end of June, well in advance of the next site-visit.

12. Project Expenditures
- Fill out the below expenditure tables in order of FY 2007, 2008, 2009, 2010.
- When converting foreign to yen, give the exchange rate used.

FY2007 (the exchange rate used: JPY/USD=120)

i) Overall project funding

Cost Items	Details	Costs (10,000 dollars)
Personnel	Center director and Administrative director	11
	Principal investigators (no. of persons) : 9	47
	Other researchers (no. of persons): 48	55
	Research support staffs (no. of persons): 3	2
	Administrative staffs (no. of persons): 4	15
	Total	130
Project activities	Gratuities and honoraria paid to invited principal investigators (no. of persons): 0	0
	Cost of dispatching scientists (no. of persons): 8	9
	Research startup cost (no. of persons): 6	15
	Cost of satellite organizations (no. of satellite organizations): 2	0
	Cost of international symposiums (no. of symposiums): 1	13
	Rental fees for facilities	0
	Cost of consumables	50
	Cost of utilities	32
	Other costs	288
	Total	407

Ten thousand dollars

WPI grant		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:	57
Name of equipment: Two Photon Laser Scanning Microscopy Number of units: 1	Costs paid:	55
Name of equipment: BD FACSCalibur 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

Travel	Domestic travel costs	2
	Overseas travel costs	1
	Travel and accommodations cost for invited scientists (no. of domestic scientists): 2 (no. of overseas scientists): 6	3
	Travel cost for scientists on secondment (no. of domestic scientists): 3 (no. of overseas scientists): 1	1
	Total	7
Equipment	Depreciation of buildings	1
	Depreciation of equipment	6
	Total	7
Other research project	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

ii) Costs of Satellites and Partner institutions

Cost Items	Details	Costs (10,000 dollars)
Personnel	Principal investigators (no. of persons) : 0	
	Other researchers (no. of persons): 0	
	Research support staffs (no. of persons): 0	
	Administrative staffs (no. of persons): 0	
	Total	0
Project activities		0
Travel		0
Equipment		0
Other research project		0
Total		0

FY2008 (the exchange rate used: JPY/USD=120)

i) Overall project funding

Ten thousand dollars

Cost Items	Details	Costs (10,000 dollars)
Personnel	Center director and Administrative director	26
	Principal investigators (no. of persons): 14	111
	Other researchers (no. of persons): 67	278
	Research support staffs (no. of persons): 19	72
	Administrative staffs (no. of persons): 14	75
	Total	562
Project activities	Gratuities and honoraria paid to invited principal investigators (no. of persons): 0	0
	Cost of dispatching scientists (no. of persons): 4	3
	Research startup cost (no. of persons): 6	35
	Cost of satellite organizations (no. of satellite organizations): 6	27
	Cost of international symposiums (no. of symposiums): 1	13
	Rental fees for facilities	0
	Cost of consumables	2
	Cost of utilities	2
	Other costs	88
	Total	170
Travel	Domestic travel costs	1
	Overseas travel costs	1

WPI grant		1,262
Costs of establishing and maintaining facilities in FY 2008		521
Establishing new facilities (Number of facilities: 2 , 11,740 m²)	Costs paid:	521
Others		0
Cost of equipment procured in FY 2008		474
Name of equipment: Cell sorting system Number of units: 1	Costs paid:	46
Name of equipment: Multi-photon Laser Scanning Microscopy Number of units: 2	Costs paid:	168
Name of equipment: Development of machines for imaging in vivo Number of units: 1	Costs paid:	27
Name of equipment: Extension of MRI channel Number of units: 1	Costs paid:	11
Name of equipment: Highly secured isolated containment type animal casing unit Number of units: 1	Costs paid:	27
Name of equipment: Individually ventilated caging system for experimental animals Number of units: 1	Costs paid:	49
Name of equipment: P2A/BSL2 animal breeding and experimentation system Number of units: 1	Costs paid:	16
Others		130

	Travel and accommodations cost for invited scientists (no. of domestic scientists): 0 (no. of overseas scientists): 0	0
	Travel cost for scientists on secondment (no. of domestic scientists): 5 (no. of overseas scientists): 2	1
	Total	3
Equipment	Depreciation of buildings	27
	Depreciation of equipment	227
	Total	254
Other research projects	Projects supported by other government subsidies, etc.	52
	Comissioned research projects, etc.	628
	Grants-in-Aid for Scientific Research, etc.	350
	Total	1,030
Total		2,019

ii) Costs of Satellites and Partner institutions

Cost Items	Details	Costs (10,000 dollars)
Personnel	Principal investigators (no. of persons): 1	
	Other researchers (no. of persons): 7	
	Research support staffs (no. of persons): 3	
	Administrative staffs (no. of persons): 1	
	Total	64
Project activities		34
Travel		1
Equipment		104
Other research projects		110
Total		313

FY2009 (the exchange rate used: JPY/USD=100)

i) Overall project funding

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	□ 9
	Total	843
Project activities	Gratuities and honoraria paid to invited principal investigators (no. of persons): □	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

Ten thousand dollars

WPI grant	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

	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		2,779

Name of equipment:Cray System
Number of units: 3 Costs paid: 4

Others 35

ii) Costs of Satellites and Partner institutions

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

FY2010 (the exchange rate used: JPY/USD=100)

i) Overall project funding

Cost Items	Details	Costs (10,000 dollars)
Personnel	Center director and Administrative director	31
	Principal investigators (no. of persons): 20	185
	Other researchers (no. of persons): 126	515
	Research support staffs (no. of persons): 37	170
	Administrative staffs (no. of persons): 20	103
	Total	1,004
Project activities	Gratuities and honoraria paid to invited principal investigator (no. of persons): 0	0
	Cost of dispatching scientists (no. of persons): 3	9
	Research startup cost (no. of persons): 3	15
	Cost of satellite organizations (no. of satellite organizations): 2	0
	Cost of international symposiums (no. of symposiums): 2	9
	Rental fees for facilities	1
	Cost of consumables	10
	Cost of utilities	31
	Other costs	392
	Total	467
Travel	Domestic travel costs	1

Ten thousand dollars

WPI grant 1,350

Costs of establishing and maintaining facilities in FY 2010 1,246

Establishing new facilities: IFReC research building
(Number of facilities: 1, 6,592m²) Costs paid: 1,246

Cost of equipment procured in FY 2010 139

Name of equipment:Spot UV Curing Equipment
Number of units: 1 Costs paid: 5

Name of equipment:X-Ray System
Number of units: 1 Costs paid: 15

Name of equipment:Individually Ventilated Cage System
Number of units: 1 Costs paid: 13

Name of equipment:Expansion equipment to ODINS (Osaka Daigaku Information Network System)
Number of units: 1 Costs paid: 8

Name of equipment:NIR Multi Channel Photo Detector
Number of units: 1 Costs paid: 6

Name of equipment:RF Coil for 11.7 Tesla NMR
Number of units: 1 Costs paid: 9

Name of equipment:Digital Signage
Number of units: 1 Costs paid: 9

Name of equipment:Access Control System for IFReC research building
Number of units: 1 Costs paid: 15

Others 59

	Overseas travel costs	7
	Travel and accommodations cost for invited scientists (no. of domestic scientists): 0 (no. of overseas scientists): 15	8
	Travel cost for scientists on secondment (no. of domestic scientists): 10 (no. of overseas scientists): 12	7
	Total	23
Equipment	Depreciation of buildings	178
	Depreciation of equipment	622
	Total	800
Other research pro□ ects	Projects supported by other government subsidies, etc.	58
	Comissioned research projects, etc.	485
	Grants-in-Aid for Scientific Research, etc.	339
	Total	882
Total		3,176

ii) Costs of Satellites and Partner institutions

Cost Items	Details	Costs (10,000 dollars)
Personnel	Principal investigators (no. of persons): 1	
	Other researchers (no. of persons): 8	
	Research support staffs (no. of persons): 2	
	Administrative staffs (no. of □ ersons): 1	
	Total	80
Project activities		0
Travel		1
Equipment		0
Other research projects		105
Total		186