

Group 1	
Reviewers	Ito, Masao (RIKEN, Japan) Julien, Jean Pierre (McGill University, Canada) Kitamura, Yukihiko (Osaka University, Japan) Neher, Erwin (Max-Planck-Institute, Germany) Nilsson, Kenneth (Uppsala University, Sweden) Sonenberg, Nahum (McGill University, Canada) Toyoshima, Kumao (RIKEN, Japan) Tsumoto, Tadaharu (Osaka University, Japan)
Summarized by	Ito, Masao
<p><b>General Comments and Suggestions:</b></p> <p>While reviewing the twenty-three departments of Group 1, we were deeply impressed by the high standards and the extensive coverage of the topics presented to us. Through this review, we realize that the classic disciplines of medicine such as anatomy, physiology, biochemistry, pharmacology and pathology have been well reorganized during the past ten years around the methodology and conceptualization of modern biomedical research at molecular, cellular, system and cognitive levels.</p> <p>We used a five-grade rating system for evaluation (A: excellent, B: very good, C: good, D: fair, E: poor) of each of the four aspects of research, namely, originality, productivity, scientific impact and general aspect. Two assigned members of the review committee rated each of the 23 departments of group 1. The highest grade, AA, was given to 13 departments for originality, 11 for productivity, 7 for scientific impact, and 9 for general aspect. Hence, about one-half of the reviewed departments were deemed excellent. When we counted all of the AA, AB and BB grades, 19 departments were evaluated as excellent or very good for originality, 19 for productivity, 17 for scientific impact and 20 for general aspect. We conclude that most departments have chosen highly original research topics and conducted productive research with high scientific impact. These departments published numerous original papers in English, many of which appeared in highly prestigious journals. The heads of the departments are well-established leaders and are frequently invited to international symposia or lectures. We applaud the remarkable achievements of the reviewed departments and their heads, and wish that the Faculty of Medicine, University of Tokyo continues to lead in biomedical research worldwide.</p> <p>The research works we reviewed are mostly basic in nature. However, when the clinical implication was rated optionally, 16 departments were given at least one A grade. Therefore, we observe an outstanding clinical implication in the research we reviewed, even though its strength varies from department to department.</p> <p>We, however, note that six of the 23 reviewed departments received a low grade for one or more aspects. Three of them receiving C grades may require improvement of their research performance. Two departments received D grades, one for the relatively low productivity represented by the publication output and the other for the lack of innovative approaches. Another department received E grades because its research outcome was disappointing. We recommend that these three departments reconsider their research plans and strategies.</p> <p><b>Specific Comments and Suggestions for Research Activities in Each Field within the Group:</b></p> <p><b>I. Cellular Signaling, Molecular Biology, Cell Biology and Anatomy, Physiological Chemistry &amp; Metabolism, Integrative Physiology, Cellular &amp; Molecular Physiology, Neurophysiology, Cellular &amp; Molecular Pharmacology, and Molecular Neurobiology</b></p> <p>Modern medicine is firmly based on biomedical research that clarifies molecular, cellular and system mechanisms of a normal living body. The nine departments in field I constitute a major core of such research activities in the Faculty of Medicine, University of Tokyo. For the general aspect, four of them were rated with AA, another four with AB, and the remaining one with BB; hence, the nine departments of field I were all evaluated as either excellent or very good.</p> <p>Prof. Shimizu's group (Department of Cell Signaling) mainly focuses on an increasingly promising area, namely, lipid signaling. They cloned leukotriene A4 hydrolase, a key enzyme in the leukotriene biosynthesis, and successfully produced various types of gene-manipulated mouse deficient in the</p>	

leukotriene receptor, PAF receptor or cytosolic phospholipase A2, or mouse over-expressing the PAF receptor. Prof. Okayama's group (Department of Molecular Biology) targets the cell cycle control, differentiation control and anchorage-dependent growth, using the technology of the full-length cDNA cloning, which Prof. Okayama and Prof. Paul Berg reported in 1982 and revolutionized the field of gene cloning. This group continues to produce interesting results linking the cell cycle to oncogenesis. Prof. Hirokawa (Department of Cell Biology and Anatomy) heads a large dynamic group whose productivity has been truly outstanding. They have successfully analyzed motor proteins functioning in axonal and dendritic transport and identified most members of the kinesin gene family and clarified how they function as molecular motors. They have made several epoch-making discoveries; e.g., a deficiency in KIF1 B $\beta$  causes type 2A Charcot-Marie-Tooth neuropathy and KIF3 knockout leads to the loss of the right-left asymmetry in normal body formation.

Using gene manipulation, Prof. Kurihara's group (Department of Physiological Chemistry & Metabolism) discovered that endothelin (ET-1) is required for the formation of craniofacial and cardiac neural crest structures including brachial arches and great vessels, and that andrenomedullin (AM) is indispensable for vascular morphogenesis during the development and regulation of blood pressure by NO production. These provide the bases for their further work on the development of neural crest and vascular systems. Prof. Miyashita's group (Department of Integrative Physiology) takes the challenge of clarifying neural mechanisms of learning and memory, ingeniously combining molecular approaches with synaptic plasticity, microelectrode recording from monkey brains and fMRI imaging of human brains. They previously discovered specific memory neurons in the monkey ventral infratemporal cortex and more recently have shown that these neurons operate using the brain-derived neurotrophic factor (BDNF). They have recently demonstrated the top-down signals from the prefrontal cortex for retrieving memory from the infratemporal cortex. Prof. Mori's group (Department of Cellular & Molecular Physiology) developed genetic and imaging techniques for investigating specific neuronal connections that form the odor maps in the olfactory system, including the olfactory bulb, pyriform cortex and olfactory tubercle. Their work is now extended to clarify how specific connections are generated through neurogenesis by axonal recognition of target neurons.

Prof. Takahashi's group (Department of Neurophysiology) conducts excellent cell-physiological analyses of synaptic transmission, using the unique preparation of the Calyx of Held, a synapse in the auditory pathway in which both presynaptic and postsynaptic compartments can be patch-clamped. This laboratory masters such a technically demanding task hardly like any other laboratories, worldwide. Works by Prof. Iino's group (Department of Cellular & Molecular Pharmacology) excels in its quantitative description of cellular processes related to IP<sub>3</sub>-induced calcium signals in neurons. They characterized different subtypes of IP<sub>3</sub> receptor playing different roles in various cell types. They have recently developed genetically encoded sensors for IP<sub>3</sub>. Prof. Mishina's group (Department of Molecular Neurobiology) is world-renowned for their contribution to the cloning of ion channel proteins, particularly in identifying diverse NMDA receptor subtypes and their functional roles. His group identified the delta 2 type of glutamate receptor, specifically located in cerebellar Purkinje cells. His group now attempts to combine mouse and zebrafish genomics to obtain insights into brain development and function.

## **II. Pathology, Molecular Pathology, Neuropathology, Forensic Medicine, Molecular Preventive Medicine, Microbiology, Immunology, and Neurosurgery**

The eight departments constituting field II are dedicated to disease-oriented research that identifies the causes of various diseases such as cancer, virus infections, heart or brain ischemia and Alzheimer's disease, aiming at developing innovative medical treatments. For the general aspect, five of them were evaluated as AA, another one AB, and the remaining two BB; hence, all of the eight departments of field II are evaluated as excellent or very good.

Prof. Fukayama (Department of Human Pathology) conducts high-quality "niche" research on Epstein-Barr virus-associated neoplasms and also on lung carcinoma. This area, however, needs to introduce more new methodologies of molecular pathology. Their decision to merge with the Division of Surgical Pathology of the University Hospital is reasonable and would allow more translational research. Prof. Miyazono (Department of Molecular Pathology) developed his earlier world class work with Prof. C. -H. Heldin to a new line of work on carcinogenic effects of the transforming growth factor- $\beta$  (TGF- $\beta$ ). He is in a position to reformulate traditional pathology to molecular pathology, and appears to need more resources and support. Prof. Ihara's group (Department of Neuropathology) focuses on molecular mechanisms underlying Alzheimer's disease pathogenesis, and has made important contributions to the field of amyloidogenesis with improvement of a method for quantifying amyloid  $\beta$  in human brains. Very recently,

they have discovered the  $\epsilon$  cleavage, distinct from the  $\beta$ - and  $\gamma$ -cleavage thus far established as the mechanism underlying amyloidogenesis in the brain. Prof. Yoshida's group (Forensic Medicine) works on reactive oxygen generation, lipid peroxidation, and injury and death of the myocardium or brain after ischemia reperfusion or intake of toxic substances, which are subjects closely relevant to forensic medicine. This group also aims to contribute to the legal aspects of forensic medicine, and to improve methods in forensic pathology. As an interface between the society and medicine, forensic medicine inevitably covers broad areas, but for this group, a more focused approach may enhance its research activity.

The works on the molecular pathogenesis of inflammatory and immune diseases of Prof. Matsushima's group (Department of Molecular Preventive Medicine) were deemed highly original, and if his presentation had been better organized, the rate would have been even higher. Prof. Nomoto (Department of Microbiology), known for his pioneering work on poliovirus, is now extending his group's research to clarifying the mechanisms underlying the shut-off host protein synthesis by poliovirus. His work provides a useful model for hepatoma development in hepatitis C virus (HCV) patients, which is expected to be applicable to other viral diseases as well. Prof. Taniguchi (Department of Immunology), renowned for his pioneering work on cytokines, impressed the reviewers by the remarkable breadth and depth, and groundbreaking significance of his group's research. It is hoped that the complex protein machinery in the immune system that his group uncovered will be further analyzed using novel technologies (for instance, cryoelectron microscopy). Prof. Kirino's group (Department of Neurosurgery) has made important contributions to research on cerebral ischemia as well as on genetic analysis of tumors. They demonstrated that the proteasome activity plays a key role in neuronal death after brief cerebral ischemia and that mice deficient in NR2A NMDA receptors are less vulnerable to ischemic insult. A major breakthrough is the finding that endogenous neuronal progenitors can be induced in situ to replace hippocampal neurons damaged after ischemia.

### **III. System Physiology, Bioimaging & Biomagnetics, Biosystem Construction & Control, Cognitive Neuroscience, Radiation Oncology, and Radiation Research Institute**

These six departments are grouped together because of their two common features, namely, they require large instruments and develop physical, rather than chemical, means for diagnosis and therapy. A general difficulty in establishing this research field III, in spite of its importance as an interface between biomedical research and clinical medicine, is reflected by the fact that the six departments received no A grade for the general aspect. Three of them, nevertheless, received BB, that is, "very good", but the remaining three received low scores reflecting problems in their research plans or strategies.

Prof. Ando's group (Department of System Physiology) studies the effects of shear forces on endothelial cells. The experimental device used to apply shear stress to cultured endothelial cells is valid, and it provides the basis for their attempt to identify a flow sensor, shear-induced changes in gene expression, and signal transduction in endothelial cells. The work, however, is still in a descriptive stage, and a more focused approach may benefit them. The transcranial magnetic stimulation (TMS) performed by Prof. Ueno's group (Department of Bioimaging and Biomagnetics) is in the front line of this field. Their finding that repetitive TMS facilitates regeneration or prevents damage to rat hippocampal neurons may have important clinical implications. The biological effects of strong static magnetic fields on mammalian cells are interesting, and studies of these effects should be expanded using advanced technologies of cell physiology, probably in collaboration with other departments. These basic studies may offer a basis for securing our health in environments where significant high-frequency electromagnetic waves emanate from an increasing number of commercial products such as mobile telephones. Prof. Imachi's group (Department of Biosystem Construction & Control) has inherited the long tradition of artificial heart engineering in the Faculty of Medicine, University of Tokyo, and extends it to develop an implantable total artificial heart (TAH) that has so far enabled an implanted animal to survive for 63 days. This group will benefit from collaborations with clinicians as well as cell biologists, particularly if, as is suggested in their future plans, they are going to start analyzing ES cells to generate whole organs. In view of the difficulty in heart transplantation, in particular in Japan, a rapid progress of the TAH project has a great social significance.

Prof. Sugishita's group (Department of Cognitive Neuroscience) primarily focuses on the use of MRI and magnetoencephalography (MEG) in studies of human cognitive functions. Mapping of brain regions involved in writing and face recognition is the main contribution of this group. Since Prof. Sugishita will retire very soon, reformulation of the aim of the Department including a new research plan is essential for developing the important field of cognitive neuroscience. Prof. Suzuki's group (Department of Radiation Oncology) group focuses on two research subjects, 1) radiation-induced signal transduction and apoptosis, and 2) function of DNA protein kinases in double-strand-break repair and cell death. Their studies,

however, appear to have diverged beyond the capacity of a relatively small number of researchers in this group. It was also pointed out that not only the rather conventional approaches presently adopted but also innovative methods should be introduced. Prof. Kunio Shinohara' group (Radiation Research Institute) is so small that the scope of its activity is limited. They developed a new technology of soft X-ray microscopy that may have some potential, but its usefulness has yet to be demonstrated.

Group 2	
Reviewers	McCarley, Robert William (Harvard Medical School, USA) Ogihara, Toshio (Osaka University, Japan) Podolsky, Daniel K. (Harvard Medical School, USA) Saruta, Takao (Keio University, Japan)
Summarized by	Saruta, Takao
<p><b>General Comments and Suggestions:</b></p> <p>Group 2 consists of thirteen clinical medicine departments. They have different historical backgrounds, and the clinical and educational duties allotted to them also vary widely. Hence, their sizes and activity scales are not uniform, and the number of the faculty members and the staffs differ considerably. Regardless of the number of collaborators and the size of department, productive scientific research work with high originality has been conducted in each department within the framework of given conditions.</p> <p>One of the important tasks of clinical departments is to conduct research on the pathogenesis, pathophysiology, diagnosis, treatment, and prognosis of the diseases in each specialized area. The research activities of the majority of the thirteen departments that underwent external review are being conducted with well-defined objects and are considered satisfactory. It is well appreciated that in some of the thirteen departments, a highly organized translational medicine-oriented approach is being taken to correlate the research and the clinical activities.</p> <p>The majority of the staff of the departments that underwent review are highly motivated to act as the leading figures in this country through their clinical and research activities. The reviewers were impressed by the high academic motivation of the staff reflected in the official compendium that introduces their research activities. It is also impressive that numerous important publications in highly reputed journals have been made. In many instances, basic and clinical researches in these thirteen departments were performed in collaboration with basic science departments within the University of Tokyo, with other facilities in Japan, and also with some prestigious academic institutions outside this country. Undoubtedly, such collaborative works have been most rewarding. It should also be noted that these thirteen departments have received reasonably abundant academic grant moneys likely reflecting their superb academic achievements.</p> <p>It is concluded that the research activities in the departments of group 2 are highly satisfactory in general and that they should be encouraged to keep up with their current excellent performances. In some of the departments, however, the research activities have covered an excessively wide range of topics with rather scanty organization. It is advised that the research activities in such departments should be concentrated on a more limited number of topics in the future.</p> <p>In each of the departments in group 2, the staffs are expected to share various amounts of patient care duties and education. It is felt that the number of the staffs in each department should better be rearranged with careful consideration to the work loads that do not pertain directly to research activities: a larger number of staff personnel should be secured for the departments with greater patient loads and educational tasks to allow an adequate time for research activities.</p> <p>One final comment should be added to conclude this summary. This has been the first attempt to provide a comprehensive external review of the research activities of the Graduate School of Medicine of the University of Tokyo. Each of the professors was asked to make a presentation to the reviewers introducing the research activities of his department. The form and the method of the presentation had not been predetermined but were left to each of the presenters, resulting in presentations which differed considerably in organization, length, and technical quality. It is possible that this situation exerted some influence on the final evaluations made by the reviewers.</p> <p><b>Specific Comments and Suggestions for Research Activities in Each Field within the Group:</b></p> <p>1. DEPARTMENT OF INFECTION CONTROL AND PREVENTION: This department has made important contributions in the prevention and control of hospital infections within the university hospital as well as in other hospitals throughout Japan. It has also played an important role as the center of diagnosis and treatment of HIV-infection in this country. The research activities of the department have been focused on the prevention of MRSA infection, anti-HIV agents, and on basic mechanisms of hepatotropic viral infections. In view of the significance of the clinical and scientific contributions being made by this department, it is recommended that the number of its faculties</p>	

be increased in the future.

2. DEPARTMENT OF RADIOLOGY:

The department of radiology has played a leading role in diagnostic radiology, radiation oncology, and nuclear medicine in this country through multiple clinical research projects. Applications of magnetic resonance imaging and positron emission tomography in the diagnosis and studies on the pathophysiology of various diseases have yielded contributions highly valued internationally. The department is expected to continue its current research and clinical activities, and is also anticipated to extend its efforts to some newer fields of radiology including interventional radiology.

3. DEPARTMENT OF NEUROPSYCHIATRY:

Since 1994, when the ward and the ambulatory sectors of neuropsychiatry made the historical reunion, the members of this department have been remarkably productive in their research activities. In particular, their achievements in the study of post-traumatic disorders (PTSD) have been watched with keen interest. Application of neuroimaging techniques to the study of human neuropsychiatric disorders is another important contribution made by them. Basic research works using animal models are also being pursued. It is hoped that the department keeps up with its highly productive clinical and academic activities.

4. DEPARTMENT OF NEUROLOGY:

It is only six months since the current professor and chairman of this department took his office. The department, however, is already making new important contributions in the study of molecular mechanisms of neurodegenerative disorders under the superb leadership of the new department chairman. It is anticipated that the department will continue to play a leading role in the researches in molecular genetics and gene therapy of neurodegenerative disorders.

5. DEPARTMENT OF CARDIOVASCULAR MEDICINE:

This department has been providing a comprehensive quality patient care in cardiovascular medicine. Many basic research works have also been conducted, including a series of internationally valued studies on the molecular biology of cardiac hypertrophy and cardiomyopathy. It is noteworthy that the members of this department are attempting intensively to integrate the research and clinical activities.

6. DEPARTMENT OF GASTROENTEROLOGY:

This department has been actively involved in the study of pathogenesis, treatment, and prevention of viral hepatitis and hepatocellular carcinoma that follows HCV infection, and it has undoubtedly played an internationally recognized leadership in these fields. Important basic researches on the relationship between Helicobacter pylori infection and gastric carcinoma have also been done. This department holds a well-organized system to undertake research works relevant to clinical gastroenterology. It is hoped that it extends its effort further to the study of gastrointestinal tract malignancies besides gastric cancer.

7. DEPARTMENT OF NEPHROLOGY AND ENDOCRINOLOGY:

The research works of this department have covered a surprisingly wide range of topics yielding many publications in the journals with high impact factors. However, it is the impression of the reviewer that the research activities of the department have been spread over an excessively wide range of topics. The department is advised to take a more organized approach in its research activities that enables strategic handling of the selected subject matters by the collaborative works of its members.

8. DEPARTMENT OF ALLERGY AND RHEUMATOLOGY:

The research activities of this department have been translational medicine-oriented, and have dealt with the pathogenesis of autoimmune disorders, basic immunology, and various clinical research works. The publications made in the journals of basic immunology with high impact factor ratings are impressive, although it is the opinion of the reviewer that more papers had better been submitted to the journals of internal medicine. The current research activity of the department, which is centered on the function of antigen-specific T lymphocytes, is anticipated to yield discoveries highly important in immunology and immunotherapy.

9. DEPARTMENT OF PSYCHOSOMATIC MEDICINE:

The members of this department have been actively involved in research on eating disorders and panic disorders. Unfortunately, however, it is the opinion of the reviewer that their research efforts have not always been most productive. Psychosomatic medicine should play an important role in our modern society. It is encouraged that the members of this department continue with their efforts to make publications in the journals with higher impact factor ratings and international reputations.

10. DEPARTMENT OF CLINICAL LABORATORY MEDICINE:

This department holds only two faculty members, both of whom serve concurrently as staff of the Clinical Laboratory Center. This situation should be somewhat limiting to the research activities of this department. The research works of this department, however, have covered a surprisingly wide range of topics. The reviewer is of the opinion that the research activities of this department should be concentrated on a more limited number of topics. An increase of the personnel of this department should also be seriously considered.

11. DEPARTMENT OF GERIATRIC MEDICINE/DEPARTMENT OF AGING RESEARCH:

This department was established in 1962 as the first geriatric medicine department of this country, and has been held as an ideal model of the provider of medical care for the aged and for research in geriatric medicine. The research works of the department have dealt with a wide range of topics including bone metabolism, atherosclerosis and respiratory diseases. The opinion was expressed that the research activities of this department had better been targeted on more selected subject matters relevant to geriatric patient care.

12. DEPARTMENT OF ORGAN PATHOLOGY, INTERNAL MEDICINE AND HEALTH SERVICE CENTER:

The members of this department are assigned to the health care of the faculty, the students and the employees of the University of Tokyo. Therefore, the time they can spend for research should not be too abundant. The research activities of this department have been focused on the molecular biology of cardiac dysfunction. The department is expected to be involved in researches that have relevance to mass health care.

13. DEPARTMENT OF PEDIATRICS:

Pediatric medicine is expected to cover a wide range of health issues of children, and this department has done a remarkable job to bring this expectation to effect. Many important papers, both basic and clinical, have been published in journals of high impact factor ratings. The department is expected to continue with its currently superb research activities. It is also hoped that it extends its activity to the study of mental health disorders of the children.

Group 3	
Reviewers	Kakita, Akira (Kitasato University, Japan) Kakizoe, Tadao(National Cancer Center, Japan) Nozawa, Shiro (Keio University, Japan) Park, Jae-Gahb (National Cancer Center, Korea) Shmelzeisen, Rainer (Albert-Ludwigs-University, Germany)
Summarized by	Kakita, Akira
<p><b>General Comments and Suggestions;</b></p> <p>The group 3 consisted of 17 departments in various clinical fields such as Surgical Sciences and part of Reproductive Developmental and Aging Sciences of the University of Tokyo Graduate School of Medicine. Five members of the review committee took part in the evaluation of these departments. Two of the 5 members reviewed one department and each referee independently reported his reviewing result of the research activities of each department.</p> <p>Through the entire review process, we were aware of and impressed by the fact that, under the circumstances of terribly busy clinical practice in the University Hospital, each department had spared no pains to performing basic as well as clinical research during the past decade, despite many restrictions on the time and money, the number of working staffs and research associates, and the installation for research activities as well, in each department. In general, there were no remarkable differences among the reviewed departments, although some departments had a long history as well as a bunch of research projects accumulated since their foundation, whereas others had been instituted only recently.</p> <p>Two assigned referees independently gave an assessment of the department after extensively reviewing a self-documentation on the outline of past accomplishment, present research activities and future prospect, as well as a hearing done for 2 days on research activities of each department. The referees used a five-graded scale for their evaluation (<i>i.e.</i>, A: excellent, B: very good, C: good, D: fair, and E: poor) for each of the following 5 categories: the originality, productivity, scientific impact, clinical impact, and general rating. The highest mark AA was given to 9 departments for the originality, to 7 departments each for the productivity, scientific impact and clinical impact, and to 10 departments for the general rating. All but one department obtained marks of CC and superior for the 5 categories; only one department obtained the mark CD for the category of clinical impact.</p> <p>To inclusively assess departmentis research activity, scores from 5 to 1 were given to the grades from A to E, respectively, and the sum of 2 refereeis scores in each category (<i>e.g.</i>, AA=10, AB=9, BB=8, etc.) was classified into three ranks defined as excellent (the score 8 or larger), ordinary (the score 6 or larger), and poor (the score less than 6). Thirteen departments were ranked as excellent and 4 departments as ordinary for the category of originality. For the productivity, 15 departments were ranked as excellent and 2 as ordinary. For the scientific impact, 13 were evaluated as excellent and 4 as ordinary. For the clinical impact, 13 departments were ranked as excellent and 3 as ordinary, whereas 1 department was ranked as poor. It may be noted that 15 of the 17 reviewed departments (88%) were ranked as excellent in the category of productivity, indicating that the prospects for further expansion of research activities in these departments are promising.</p> <p>Finally, looking at the assessment result for the category of general rating, 12 departments were ranked as excellent accounting for 70% of the 17 departments reviewed. Thus, it may be concluded that most department heads are well supervising their staff and fellow doctors including research associates, and are successfully directing their departments. For some of the remaining 5 departments ranked as ordinary, however, it would take a bit more time to make any progress in their current research activities. In addition, there was a suggestion from the reviewers to some of these departments that efforts might better be directed toward the institution and execution of well-designed research projects on more specific subjects with strong clinical impact, because these departments are regarded as clinical research units, in which not only basic research but also clinical research and practice are conducted daily, and also because newly established departments very often have several limitations to their research environment.</p>	



### **Specific comments and suggestions to each subspecialty group of Departments in group 3:**

#### **1. Surgery**

Cardiothoracic Surgery; Gastrointestinal Surgery/Surgical Metabolism and Nutrition and Endocrine Surgery; Hepato-Biliary-Pancreatic Surgery/Artificial Organs and Transplantation; Urology, and Surgical Oncology

For the category of general rating, all 5 departments in this group were ranked as excellent with the average score of 8.8 (ranging from 7 to 10) in accordance with the scoring system defined above. It thus appears that their research activities are to be favorably evaluated as excellent.

Department of Cardiothoracic Surgery (Takamotois group) has made remarkable contributions to the field of thoracic and cardiovascular surgery especially in aortic valvular and coronary artery bypass surgeries, and thoracic surgery as well. In general, very good clinical setting-oriented research projects have been conducted to date. It is expected that many patients in the clinic would benefit from their continuous research activities.

Dept. of Gastrointestinal Surgery (Prof. Professor Kaminishiis group) has focused its research interests on the pathophysiology and carcinogenesis of the gastrointestinal tracts system. The development of a model for creating chronic gastric ulcer, which was published in Gastroenterology, may be assessed as an exceedingly unique and creative work. Also, a series of experiments related to *Helicobacter pylori* infection and its eradication are very interesting. Research efforts in the future may better be exerted to vigorously continue the investigation on the carcinogenesis of gastric cancer.

Dept. of Hepato-Biliary-Pancreatic Surgery/Artificial Organs and Transplantation (Prof. Makuuchiis group) has introduced and standardized the systematic subsegmentectomy of the liver, which is emerging as the most significant idea in recent hepatic surgery, especially in cirrhotic livers. Prof. Makuuchi also proposed the concept of preoperative portal vein embolization in the event of extensive hepatic resection in patients with hilar bile duct cancer to minimize the postoperative hepatic dysfunction. Most of all, he and co-workers are the first in the world to have performed adult-to-adult living related liver transplantation (LRLT), and have greatly contributed to improving the surgical techniques as well as the post-transplant outcomes. Thus, their accomplishment may be favorably evaluated as excellent and their endeavor to develop the hepatic surgery be respected, although they appear to attach too much importance to clinical issues.

Dept. of Urology (Prof. Kitamurais group) has made good contributions to the understanding of multifocal carcinogenesis in the urinary bladder and also to the development of dendrite cell immunotherapy for patients with metastatic cancer. Moreover, a series of studies on urinary polyoma virus JC virus for the past decade have a great impact on the development of the diagnostic as well as therapeutic modalities. These excellent findings, which had originated from well designed clinical as well as experimental studies, were recognized by several good international journals, and the results of this research is expected to contribute to the advancement of the clinical urologic fields. There was a suggestion that these studies on the carcinogenesis of urinary system should be continued and the knowledge obtained from this research should be further directed toward clinical applications in the future.

Dept. of Surgical Oncology (Prof. Nagawaís group) has made a contribution to furthering not only basic sciences such as immunology, molecular biology, and genomics, but also clinical oncology. It provides comprehensive evaluation, diagnosis, treatment and management for adult patients with both general and oncologic surgical problems, in the ambulatory as well as inpatient settings. Among many excellent studies of this department, the study that lateral nodes dissection is not necessary for patients with lower rectal cancer undergoing preoperative radiotherapy is considered really important and very useful for treating patients with advanced rectal cancer. These outstanding works would provide clinicians and practitioners with valuable and novel ideas for managing patients. Prof. Nagawaís ardor for scientific knowledge and quality care of the patients should continue to be held.

#### **2. Sensory and Motor System Medicine**

Dermatology; Plastic and Reconstructive Surgery; Oral and Maxillofacial Surgery; Orthopedic Surgery; Ophthalmology; Otorhinolaryngology, Head, and Neck Surgery; Rehabilitation Medicine

For the category of general rating, six of the 7 departments in this group gained the full mark, AA, or were ranked as excellent (the average score of 10 in accordance with the scoring system). The remaining 1 Department was assessed as ordinary, or as good with the mark, CC.

Department of Dermatology (Prof. Tamakiis group) appears as a well-structured, young

department showing good cooperation with other departments in the University, and also appears very productive as indicated by its publications with a very high impact factor. This can be considered as a successful transition from research to clinic. This group has shown a strong focus in the research front with increasing applications of research results for clinical diagnosis. It has incorporated both cytokines research and immunological research into the clinical realm. Research into the basic mechanisms of immunology is applicable not only to Dermatology but to Cell Biology in general. Results of the research work on metastasis of melanomas are similarly applicable to the mechanisms of metastasis in other malignancies. Constructive criticism would be aimed at the application of the results of research works to the treatment of diseases in addition to the expanding molecular, enzymatic, and immunological diagnosis of dermatological disorders. It is believed, however, that the direction of its perceptive studies would eventually incorporate these goals towards actual clinical treatment of diseases.

Prof. Harii and co-workers (Dept. of Plastic and Reconstructive Surgery) have shown exceptional ability to lead the vanguard in the still emerging field of reconstructive surgery. They have introduced new surgical procedures and also have incorporated new techniques into the reconstruction of muscle and bony structures for cancer patients. In addition, they have pursued new research leads into the molecular basis of disease as well as the possibility of stem cell differentiation into tissues for skin and hair replacement. Their outstanding research has had extremely strong impact on Plastic Surgery, and their excellent articles that appeared in high-ranked journals have been appreciated worldwide. This clinical as well as basic research should be continued in cooperation with other departments. In particular, the possible use of epidermal and mesenchymal stem cells for replacement of various surface structures holds increasing promise for the future. Optimization of their transformation and shaping/molding are topics for continuing research. Moreover, their focus on the genetic basis of congenital anomalies related to plastic/reconstructive surgery is commendatory. These supportive suggestions reconfirm the general positive trend of research carried out by this Department.

Department of Oral and Maxillofacial Surgery (Prof. Takatoís group) has taken multi-pronged or multidisciplinary approaches to both clinical and basic research studies that are very commendable. On the clinical front, in expanding the horizons of maxillofacial surgery, multidisciplinary approaches hold promise for broadening treatment options for patients with deformities or tumors of the oral region. On the research front, the collaborations with various academic as well as corporate groups are broad and varied, and continue to shape the future for reconstructive oral and maxillofacial surgery. The broad diversification of research is to be lauded. This department has exhibited the delicate balance in stewardship necessary to finesse the strengths obtained from both corporate and academic collaborations. This department has shown a similar approach to translational research; the diversification of oral reconstructive surgery to regenerative technology and development are exemplary and show strong promise for the future.

Dept. of Orthopedic Surgery (Prof. Nakamuraís group) has done outstanding research in the field of orthopedics, especially of bone destruction, osteoclastogenesis in such areas as rheumatoid arthritis, senile osteoporosis, and spinal cord or neuronal injuries. The departmentís research targets are very clear, and excellent results of those research works were published in several prestigious international journals including *Nature*. These results have been quite useful in the clinical orthopedic settings. This work is believed to serve as a firm basis for deepening our understanding about orthopedic research. Studies on the pathogenesis of osteoclastogenesis and therapeutic tools for damaged spinal cord should be better continued in the future.

Dept. of Ophthalmology (Prof. Araieís group) has shown a strong focus on both the clinical and basic research forefronts of glaucoma pathophysiology and treatment. In clinical research, the pharmacokinetic evaluation and determination of pharmacological characteristics of various treatment modalities for glaucoma are substantiated. In basic research, the investigations into the underlying molecular biology and pathophysiology of glaucoma are similarly tangible foundations for future treatments. It may appear that this department attaches too much importance to the evaluation of various treatment modalities for glaucoma; an expansion of these developments and applications to other ophthalmologic disorders is strongly suggested. Similarly, the research focus of the department is strongly directed toward glaucoma and related fields; collaborations with other fields of basic research would be a welcome addition to its research portfolio. In this respect, the forays into corneal transplantation using regenerative medicine and amniotic cell replacement are innovative and very promising.

Dept. of Otorhinolaryngology, Head and Neck Surgery (Prof. Kagaís group) has shown a strong propensity for developing the products of research into innovative therapeutic modalities. On the clinical forefront, this department continues to expand the pathophysiological understanding of the various sensory organs while incorporating new treatment strategies towards malignancies. On the research forefront, the

group continues to focus on the basic underlying mechanisms of disease that may lead to future clinical applications. Its work continues to be both broad in scope and deep. Its applications of research harvests to clinical treatments, especially in new substitutive modalities for the sensory organs, are intuitive and original. Prof. Kaga seems to have taken strong leadership in publishing various articles as lead author during his tenure; it is laudatory that he demonstrates the initiative in publishing to junior members of the department.

Recognized as a new-borne department in clinical medicine field, the Department of Rehabilitation Medicine (Prof. Eto's group) has been focusing its studies on the field of geriatric and stroke rehabilitation. This group is especially interested in the functional and motor behavioral assessment of geriatric and brain-disordered populations, and has published several good relevant articles. In addition to committing themselves to clinical studies, Prof. Kaga and co-workers have recently broadened their research spectrum to cover animal experiments, tissue and biomechanical studies. Because Prof. Eto has a strong standing in the field of rehabilitation for geriatric people, research should better be continued in this field. Moreover, it may be recommended that this department should institute a couple of more specific research theme in this particular field of clinical medicine.

### **3. Vital Care Medicine**

Anesthesiology; Emergency and Critical Care Medicine

The reviewers gave the mark BC each to these departments for the category of general rating, which is favorably evaluated as good or ranked as ordinary (the average score of 7 each) according to the scoring system.

Department of Anesthesiology (Prof. Hanaoka's group) has concentrated its energies mainly on the topics and themes that were closely connected to the anesthesiology, namely, respiration and circulation, pain management, muscle relaxation, development of new devices and techniques for anesthesia, mechanisms of anesthesia, shock, and perioperative quality of life control. Above all, the establishment of the guideline for postoperative pain management using local anesthetics combined with narcotics via epidural catheter to the epidural space may be noted as a remarkable accomplishment of this department. However, because of the multidisciplinary nature of research activities that this department is involved in, the objectives of basic as well as clinical research tend to be obscure and ambiguous. Therefore, it may be recommended that this department should institute much clearer objectives in the research field.

Dept. of Emergency and Critical Care Medicine (Prof. Yahagi's group) has only a small working staff serving as clinicians and surgeons at both the Emergency Center and the Critical Care Center. In spite of this awfully terrible condition, they not only have seen more than 17000 patients per year at the Emergency Ctr., but also have been engaged in many programs in a wide range of subjects related to basic researches as well as practical problems. Particularly, their works on the structural parts involved in activation and inactivation of Na channel that appeared in *Nature* (1989), and the clinical use of electrolyzed water (*Artificial Organs*, 2000) are considered very commendable. Their curiosity to as well as enthusiasm for research should not be discouraged from now on, and it is further suggested that they may better direct their research interest toward more basic/scientific subjects.

### **4. Obstetrics and Gynecology**

Obstetrics and Gynecology; Gynecologic Surgery

Both of these 2 departments gained the mark AA, or a full score of 10, for the category of general rating. Thus, it appears that their research activities should be assessed and ranked as excellent.

In the Department of Obstetrics and Gynecology, Prof. Taketani has shown strong leadership in supporting both diversification and specialization in his department. His research and clinical applications for treatment of endometriosis are particularly noteworthy as well as his clinical prowess into the various assisted reproductive technologies. To be noted is the fact that, in basic research field, this department has been at the forefront of endocrinology and has expanded the knowledge of the underlying mechanisms of folliculogenesis and gametogenesis. Clinically, this department has recently shown strength in the field of fetomaternal medicine; this is believed to be a strong focus for the department in the future. In addition, it is expected that the fruits of these basic research works in endocrinology would find their way into clinical practice and technologies in the future.

Prof. Tsutsumi (Dept. of Gynecologic Surgery) has shown very active administration in both the clinical and basic research forefronts. This department has continued to lead the field in the application of

endoscopic surgery for gynecologic disorders. Especially, research works of this department on the determination and surgical indications for lymph node spread in gynecologic malignancies are noteworthy. In basic research, several works in molecular endocrinology and reproductive biology are very unique and intuitive. Any critical suggestions may not be necessary for this department. The work on environmental estrogens and reproductive biology are perspective and influential; similar collaborations of Prof. Tsutsumi's expertise in reproduction with experts in other fields may be recommended for the future.

## **5. Pediatric Sciences**

### **Pediatric Surgery/Pediatric Oncology**

Dept. of Pediatric Surgery (Prof. Hashizume's group) has concentrated its research interests on subjects in the following three areas, namely transplantation, developmental biology of congenital anomalies and fetal surgery, and immunology of intestine. The idea of tracheal occlusion was very interesting, although the clinical relevance was a little bit obscure. It may be recommended that the department should concentrate its resources on experiments more related to clinical activities. In addition, considering the very small departmental staff, it may be suggested to select and institute a couple of much clearer research objectives; experiments on beta-catenin, for example, seem to be too much.

Group 4	
Reviewers	Aoki, Yoshiki (Nagasaki University, Japan) Holzemer, William L. (University of California, San Francisco, USA) McGarvey, Stephen (Brown University, USA) Ueda, Reiko (Okinawa Prefectural Collage of Nursing, Japan)
Summarized by	Aoki, Yoshiki
<p><b>General Comments and Suggestions:</b></p> <p>Group 4 includes three research areas encompassing fifteen different departments. The three research areas are: 1) Social Medicine with two departments; 2) Health Sciences and Nursing with eight departments; and 3) International Health with five departments. Four reviewers were assigned to Group 4. Two reviewers evaluated the academic achievements of seven departments of Social Medicine and International Health, while the other pair evaluated eight departments within Health Sciences and Nursing. Evaluation followed the methods used by Groups of 1, 2 and 3. One reviewer assigned to Group 4 performed evaluations based solely on documents prepared specifically for this external review by the University of Tokyo.</p> <p>Inter-reviewer rating variation for the evaluation was relatively small among the group scores for all departments. Of the fifteen departments of Group 4, twelve received the highest or second highest ratings, AA, AB or BB. These results indicate that, on the whole, the Graduate School and Faculty of Medicine, Tokyo University, assumes a leading role in research on Social Medicine, Health Sciences and Nursing, and International Health in Japan, while some departments are regarded world leaders.</p> <p>A few departments within Health Sciences and Nursing received somewhat moderate or lower ratings. Although these departments are encouraged to strengthen the quality and quantity of their research, it may be that some, especially those belonging to Health Sciences or Nursing, have not been adequately evaluated by the methods of the present external review.</p> <p><b>Specific Comments and Suggestions for Research Activities in Each Field within the Group:</b></p> <p><b>Subgroup I; Department of Public Health, Department of Medical Informatics and Economics</b></p> <p>Subgroup I includes the Department of Public Health and the related Department of Medical Informatics and Economics. Both departments have published often in well-regarded, peer-reviewed journals. Accordingly, they are recognized as excellent or very good (AB, BB).</p> <p>Public Health must embrace a wide range of interdisciplinary research. The research areas targeted by Department of Public Health are all essential topics, and are of special significance to Japan. Prof. Kobayashi's group (Department of Public Health) presented research activities of high quality in varied, significant disciplines. This includes work on disabled elderly care system, tobacco control policy, the supply of physicians and their demographic and geographic distribution, cardiovascular disease risk factors, sarin poisoning, and other subjects. The long life expectancy and reduced birth rate has brought about a revolution of health policy in Japan. The academic achievements of Department of Public Health indicate that Prof. Kobayashi is making a significant contribution to an appropriate health policy for a changing Japan.</p> <p>The department of Medical Informatics and Economics currently has large service component as part of its overall mission in addition to its usual routine scholarly activities. Research interests within the Department of Medical Informatics and Economics are basic to technical innovation in medical science and health care in this country. Prof. Ohe's group (Department of Medical Informatics and Economics) has initiated research on the development of a hospital informatics system and standardization of medical information exchange. His group provides a useful information to medical staffs.</p> <p><b>Subgroup II: Four departments relevant to Health Sciences and four departments relevant to Nursing Sciences.</b></p> <p>Health Sciences: Department of Mental Health, Department of Social Gerontology, Department of Biomedical Ethics, Department of Biostatistics</p> <p>Beyond traditional Health Science two new research fields, Biomedical Ethics and Biostatistics. These have developed to reflect recent thinking about the social context of the conduct of research and newly required research methods in health research. Anticipating that biomedical ethics and biostatistics will be essential to the evolving Japanese system of medical education across the many school of medicine in the near</p>	

future, Tokyo University has assumed a leading role in these new areas of investigation. The decision to establish these departments was a visionary one. Many useful papers have appeared in peer-reviewed journals. However, scientific productivity of one department appears to be only moderate or low. Three departments are given the mark of excellent or very good (AB, AB, BB) and one is rated as score of good (CC).

Prof. Kurita (Department of Mental Health) significantly contributes to the diagnosis and treatment of pervasive developmental disorders. He is encouraged to continue promoting research reaching out to collaborators in nursing and other fields of healthcare.

Professor Kai's group focuses on health for the elderly, exploring fundamental human capacity, social support exchange, as well as the functional impact of home visiting and activities outside of the house. Gerontology today is a multidisciplinary field and, although worthwhile, the scope of current efforts here is too broad to be adequately addressed by the limited staffing now available. Professor Kai is encouraged to sharpen his focus within the areas of functional capacity and quality of life for the aged.

Prof. Akabayashi (Department of Biomedical Ethics) is investigating the development of social consensus, functions, and responsibilities of the ethical committee. He should play a vital role in developing a national code of biomedical ethics.

Prof. Ohashi's group (Department of Biostatistics) assumes a supportive role in clinical trials, admirably serving the biostatistical needs of various principal investigators. Beyond this worthwhile activity however, the department is challenged to become more engaged in their primary role, the development of new statistical methodology for biomedical research, clinical trials, and epidemiology. They are also encouraged to lend their supportive expertise to research areas other than clinical trials.

Nursing Sciences: 1) Department of Advanced Clinical Nursing/Nursing Administration, 2) Department of Adult Nursing/Terminal and Long-term Care Nursing, 3) Department of Family Nursing, 4) Department of Community Health Nursing.

The professors of nursing have taken the national lead in nursing administration, in adult, terminal, and long-term care nursing, and in family and community health nursing. There are some research areas which do not appear to fit into the mission of the respective department. Many papers, published only in Japanese, would have a greater impact if incorporated into the English language literature. Two departments are given a mark of excellent or very good (AB, BB), while two are rated as good (BC, CC).

Prof. Kanda's group (Department of Advanced Clinical Nursing/Nursing Administration) studies the national nursing workforce, with particular emphasis on staffing ratios as predictors of healthcare quality. They also address the measurement and improvement of quality of nursing care. This work has impacted national healthcare policy in hospital staffing ratios.

Prof. Kazuma's group (Department of Adult Nursing/Terminal and Long-term Care Nursing) has made an impressive use of the concentric circle model in research on muscle mass, exercise and fatigue. Her focus on nursing care in an outpatient setting is an exciting development that is strongly encouraged.

Prof. Sugishita's group (Department of Family Nursing) demonstrates national leadership in family nursing. They have published useful investigations in such diverse areas as acupuncture, elderly quality of life, and physiological nursing care actions. However, little attention has been given to the family per se. The department is encouraged to address both family and pediatric nursing.

Prof. Murashima's group (Department of Community Health Nursing) offers useful insights into the care delivery system, quality of care in the community health, and governmental policy. There appear to be many opportunities for collaboration with the Department of Social Gerontology in the area of health for the elderly and with Nursing Administration in the areas of seamless hospital-community discharge.

### **Subgroup III: Department of International Community Health, Department of Human Genetics, Department of Developmental Medical Sciences, Department of Human Ecology, Department of Biomedical Chemistry**

Subgroup III includes five departments whose interests focus on the field of International Health. It covers a wide range of medical and epidemiological considerations, arising in both the developed and developing world. International Health must embrace the continuing and widening economic and political disparities that underlie poor health in developing nations. The research orientation of the chairman of each department is clear and appropriate and the research subjects targeted by each of the five departments are of high priority in the field of International Health.

Even though Japan lacks a long history in research of International Health, the chairs of these five departments, in their respective disciplines, have made considerable achievements in international health. All departments have numerous publications in recognized journals. Two departments are recognized with the highest scores, AA, and three are given a commendable AB.

Prof. Wakai's group (Department of International Community Health) has made significant progress in the socio-economic, behavioral and biological basis of health using epidemiological and public health analytic techniques. Prof. Wakai is an effective advocate for the theoretical and applied aspects of International Health.

Prof. Tokunaga's group (Department of Human Genetics) addresses some crucial areas of human genetics, including anthropogenetic studies of associated populations, their histories, and the genetic basis of disease. Their studies show that molecular genetics is a powerful tool with significant implications not only for International Health, but also more broadly for the future of biomedical science.

Prof. Ushijima's group (Department of Developmental Medical Sciences) has done extensive work on molecular epidemiology of diarrheal diseases and on social epidemiology in maternal child health. Such a program, linking basic science with maternal and child health, is an admirable innovation.

Prof. Ohtsuka's group (Department of Human Ecology) has made strides within a theoretical framework linking environment, socioeconomic factors and human populations. Their studies are characterized by holistic and multi-disciplinary approaches.

Prof. Kita's group (Department of Biomedical Chemistry) has demonstrated that basic research, including molecular biochemistry represents a powerful set of tools holding great potential for public health intervention. Their works on respiratory chains of eukaryote mitochondria and prokaryote cells may well lead to promising new treatments for parasitic diseases.

Achievements to date clearly identify the University of Tokyo as a promising center of excellence in the research of International Health. Nevertheless, close, inter-disciplinary and trans-disciplinary collaborative efforts have not yet matured. We strongly recommend that these departments interact with one other more effectively in order to develop their potential for world-class research in the field of International Health.