Y. Fukuuchi · M. Tomita · A. Koto (Eds.)

# Ischemic Blood Flow in the Brain

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Volume 6



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# Ischemic Blood Flow in the Brain

With 165 Figures, Including 8 in Color



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#### **Foreword**

This volume contains the proceedings of the sixth symposium of the Keio University International Symposia for Life Sciences and Medicine under the sponsorship of the Keio University Medical Science Fund. As stated in the address by the President of Keio University at the opening of the symposium, the fund was established by the generous donation of Dr. Mitsunada Sakaguchi. The Keio University International Symposia for Life Sciences and Medicine constitute one of the core activities of the fund. The objective is to contribute to the international community by developing human resources, promoting scientific knowledge, and encouraging mutual exchange. Every year, the Committee of the International Symposia for Life Sciences and Medicine selects the most interesting topics for the symposium from applications received in response to a call for papers to the Keio medical community. The publication of these proceedings is intended to publicize and distribute information arising from the lively discussions of the most exciting and current issues during the symposium. We are grateful to Dr. Mitsunada Sakaguchi, who made the symposium possible, the members of the program committee, and the office staff whose support guaranteed the success of the symposium. Finally, we thank Springer-Verlag, Tokyo, for their assistance in publishing this work.

Akimichi Kaneko, M.D., Ph.D.
Chairman
Committee of the International Symposia
for Life Sciences and Medicine

#### Preface

Stroke, especially ischemic stroke, is intractable. This Symposium was planned to investigate stroke from the most fundamental aspects of ischemic blood flow in the brain because stroke is essentially a disease of the vessels and/or blood flow. To ameliorate ischemic sequelae, manipulation of the deranged flow based on precise knowledge is considered crucial. The term "ischemic blood flow" in this Symposium was intended to mean not only sluggish flow which causes tissue ischemia, but also disturbed flow which occurs secondarily to ischemic tissue damage.

In response to our invitation, we were honored to have the participation of 20 distinguished guests from around the world. The titles of their papers led to a framework for the Symposium that covered the buffy coat (glycocalyx) of endothelial cells, the blood-brain barrier and permeability, gene expression, vascular reactivity, dysregulation, inflammatory deterioration, cortical spreading depression, edema, microvascular derangement, and pathology. Along these lines, *ad hoc* abstracts were called for. We received almost double the scheduled number of abstracts, from which 35 were selected. We must apologize to the authors of the remainder of the abstracts, which could not be included in the Symposium, not because of their quality but owing to the limitations imposed by our structured framework.

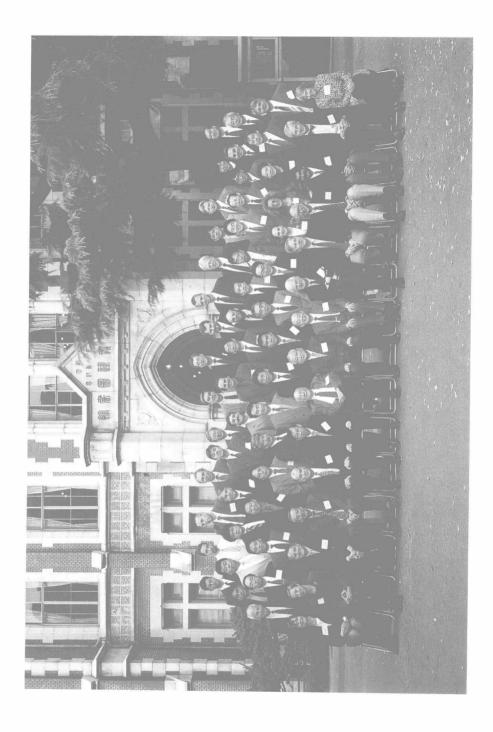
Through the kind cooperation of the participants, the Symposium ran very smoothly and enjoyed an at-home atmosphere with excellent presentations followed by fruitful discussions and thought-provoking comments. We were extremely satisfied with the Symposium, and the outcome was far better than we could have anticipated.

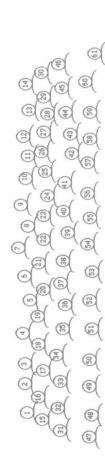
This book contains the papers from all 20 guest speakers plus the 35 explained above. We have not attempted to revise the manuscripts, because we thought that the thrust of the contents might shift if changes were requested. Instead, the reader can enjoy the unique, provocative questions and answers presented during the sessions in the "onsite discussions" following each paper. On examining the book, the reader may encounter new concepts, as well as rather unfamiliar or even disputable points. In such cases, the authors should be contacted directly. It would be much appreciated if any controversial issues could be reported to the Secretariat.

We cannot adequately express our gratitude to Dr. Mitsunada Sakaguchi, an alumnus of the School of Medicine, Keio University, for his generous donation which made possible the creation of the Keio University Medical Science Fund. We are also

grateful to the Committee of the International Symposia for Life Sciences and Medicine for selecting the present topic as the 6th Keio University International Symposium. We would like to take this opportunity also to express our deep gratitude to the Symposium secretaries, Hiroshi Ohin, Junko Shimane, and Sachiko Hosokawa. They have coped with a tremendous volume of work before, during, and after the Symposium, often under a very tight schedule. We all were impressed by their skill and patience.

February 2000 Yasuo Fukuuchi Minoru Tomita Atsuo Koto





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### **Opening Remarks**

Professor Yasuhiko Torii President, Keio University Chairman, Keio University Medical Science Fund

#### Ladies and Gentlemen:

Speaking for everyone at Keio University, it is a great pleasure to welcome all of you to the 6th Keio University International Symposium for Life Sciences and Medicine. I am particularly grateful to the distinguished medical scientists who have traveled such long distances to participate in this meeting. I hope you have overcome jet lag. Actually, I myself came back from Europe just the day before yesterday, and had to get to work right after my return.

The major subject of this year's symposium is "Ischemic Blood Flow in the Brain." Although remarkable progress and breakthroughs are reported almost every day in the research fields of brain function, metabolism, and blood flow, it is also true that there are still many victims who suffer from stroke sequelae. In this regard, I believe that it is an opportune moment to hold a symposium at Keio University related to the subject. All speakers kindly accepted our invitation to contribute to this symposium on ischemic blood flow in the brain, and I feel certain that this unique meeting will prove both exciting and successful.

In Japan we have 622 universities, including 99 national, 66 municipal public, and 457 private universities. Keio was founded in 1858 by Yukichi Fukuzawa and is the oldest university in the country. Fukuzawa was a pioneer in the modernization of Japan. He was an enlightened man and was a member of the very first mission of the Tokugawa Shogunate government to the United States in 1860 and to European countries in 1862. Before that time, the Shogun had closed Japan's doors to the outside world in a period of self-isolationism lasting almost 300 years, until the American Commodore Perry knocked on our door. Fukuzawa realized during his visit to the United States and Europe as a member of the official Japanese mission that education was crucially important and inevitable in the future of Japan. How highly his achievements are valued by the Japanese Government is reflected in the fact that his portrait is printed on the 10,000-yen note issued by the central bank. Thus, Keio has its origins in international exchanges; indeed, international exchanges such as this symposium have been one of the most important academic and social missions of Keio University since its foundation.

In the fall of 1994, Dr. Mitsunada Sakaguchi, an alumnus of the class of 1940 of our medical school, donated five billion yen, approximately 50 million dollars, to the university. He expressed the wish that his fund should be used to encourage research in

life sciences and medicine at Keio University and to promote worldwide advancements in life science. I fully agreed with his proposal and thus launched the Keio University Medical Science Fund in April 1995. The International Symposia for Life Science and Medicine have been organized as one of several projects supported by the fund. This year, Dr. Sakaguchi made an additional donation of two billion yen.

We are now witnessing the dawn of the 21st century and the third millennium. We realize that society faces many problems from this century that will be carried over into the next. Many new and unknown difficulties also await us in the new century. I believe that exploring new horizons in life sciences is one of the most vital tasks facing us at the dawn of the 21st century. It is equally important to ensure that the knowledge gained through such pursuits will be used in a way that brings genuine happiness to humankind.

It is thus more than a pleasure, indeed it is an honor, for me to be able to meet the distinguished medical researchers and clinicians from world-renowned institutions who kindly gathered here, and to share in a frank and valuable exchange of views. I am also grateful for the efforts made by the organizing committee, chaired by Drs. Yasuo Fukuuchi and Minoru Tomita, who have devoted themselves to ensuring that this symposium is an auspicious and enjoyable event. I do hope that the meeting will prove a truly fruitful and productive one for you all.

Let me close by wishing everyone gathered here further success in their research and clinical work. Thank you very much.

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