OBITUARY

This communication is written to the scientific community worldwide to honor and celebrate the life and contributions of Professor Setsuro Ebashi, a Pioneer of muscle research, who died on 17 July 2006 at the age of 83 years. This news saddened all who were privileged to know him. Indeed, Setsuro Ebashi was an exceptional scientist and he had an outstanding personality.

Setsuro Ebashi was born in Tokyo on August 31 1922. In September 1944, he graduated Doctor of Medicine from the Faculty of Medicine of the University of Tokyo where he spent most of his professional life. In June 1954, he obtained the title of Doctor of Medical Sciences (Ph.D.) from the same University. From January to December 1959, he stayed as Guest Investigator of the Rockefeller Institute in the Laboratory of Fritz Lipmann, Nobel Laureate in Medicine. In May 1959, he was offered the Chair of Pharmacology at the Faculty of Medicine of the University of Tokyo and kept this position of Professor until March 1983. From May 1971 until March 1983, he was in charge of the Chair of Biophysics at the Faculty of Sciences of the University of Tokyo. After retiring from the University of Tokyo where he became Professor Emeritus, he was offered a professorship in the National Institute for Physiological Sciences in Okazaki. In April 1985, he became Director-general of the National Institute for Physiological Sciences and left this position in March 1991, being nominated as President of Okazaki National Institutes. When retiring from this position, he became Professor Emeritus of the National Institute for Physiological Sciences in March 1993.

Setsuro Ebashi gave early proof of his scientific mettle. While preparing his Ph.D. thesis under the supervision of Professor H. Kumagai, he purified choline-acetylase and he took special pride in the discovery of a “relaxing factor”, which in the presence of adenosine triphosphate (ATP), relaxed glycerinated muscles of rabbits. Later, he found that this factor existed in particulates with Mg$^{2+}$ activated-ATPase. He demonstrated that the fractions that strongly took up Ca$^{2+}$ in the presence of ATP consisted of fragmented sarcoplasmic reticulum, suggesting a regulatory function for the calcium pump of the sarcoplasmic reticulum. W.H. Hasselbach and Anne-Marie Weber who explained how the endoplasmic reticulum (ER) could accumulate Ca$^{2+}$, confirmed the importance of intracellular Ca$^{2+}$ pumps associated with the endomembranes. In the meantime, the first indications of ER-residing regulated ion channels, which could provide a means of Ca$^{2+}$ release, were reported, namely by Clara Franzini-Amstrong.

Published online in J-STAGE doi: 10.1254/jphs.OTJ06001X
Setsuro Ebashi is internationally acclaimed for the discovery of troponins. In the early 1940’s Heilbrunn in the United States and Kamada in Japan demonstrated the role of Ca\(^{2+}\) as a contraction signal. Setsuro Ebashi showed in the early 1960’s that the Ca\(^{2+}\) signal is correctly interpreted by muscle only when tropomyosin and troponins are present. Specifically, actomyosin prepared from pure preparations of actin and myosin (thus containing no tropomyosin and troponins) was observed to contract when ATP was added, even in the absence of Ca\(^{2+}\). However, actomyosin prepared directly from whole muscle would contract in the presence of ATP only when Ca\(^{2+}\) was added. Clearly the muscle extracts contained a factor that conferred Ca\(^{2+}\) sensitivity to actomyosin. The factor turned out to be the tropomyosin-troponin complex. Ebashi’s concept of calcium receptor protein was extended to other cell types for instance with calmodulin, which is playing a role in various cellular regulations from muscle to nervous cells.

Setsuro Ebashi presented a clear picture for factors regulating onset and offset of Ca\(^{2+}\) signal in skeletal muscles. Later on, he reported that Ca\(^{2+}\)-related regulatory processes were different in the various types of muscles. This elucidation of the calcium ion’s role in mechanisms that regulate muscle contraction-relaxation and the demonstration of differences among muscles paved the way to studies of the pharmacological control of Ca\(^{2+}\) signal that emerged as a therapeutic principle. A byproduct of his research included studies related to alterations of calcium regulatory mechanisms and proteins dysfunctions in muscle pathologies such as muscular dystrophy and malignant hyperthermia.

His seminal research attracted a large number of research fellows and associates, a pattern that was to continue after his move from Tokyo to Okazaki. Those developed their own field, so allowing Japanese research to be a leader in the scientific world. At the risk of leaving out numerous such associates, who benefited from his creative critical scientific approach, I would mention the following that are well known in the fields of skeletal muscle and cardiovascular research as well as neurosciences: Masanori Otsuka, Makoto Endo, Yosiaki Nonomura, Tomoh Masaki, Iwao Ohtsuki, Yoshiki Hotta, Yasuo Ogawa, Eijiro Ozawa and Takeyuki Wakabayashi.

Setsuro Ebashi has accepted international responsibilities: for the period 1978 – 1981, he was President of the International Union for Pure and Applied Biophysics (IUPAB), but his major international activity has been devoted to IUPHAR, the International Union of Pharmacology (now International Union of Basic and Clinical Pharmacology). He has organized and chaired the Eighth World Congress of Pharmacology held in Tokyo in July 1981. This Congress is considered as a model due to its perfect organization and the high quality of its scientific program. Some years later, Setsuro Ebashi was elected President of IUPHAR, for the period 1990 – 1994 and officiated as Immediate Past-President until December 1998. During this office, he devoted himself to fund-raising for IUPHAR. Due to his action, the Japanese Pharmacological Society initiated an increase of Member Societies contributions to IUPHAR with the purpose to allow the establishment and the development of scientific research activities operated by the Union such as the Receptor Characterization and Classification that is now becoming a major Receptor database.

Setsuro Ebashi, who was awarded the Order of Cultural Merit (Bunka-Kunsho), received numerous major honors from diverse scientific and civic organizations and from academies throughout the world. A few of these that are especially: in 1965 the Prize of Yamaji Science-promoting Foundation, in 1968 the Asahi Prize (issued by Asahi Newspaper Publ. Co.), in 1972 the Imperial Prize of the Japan Academy. In 1999, he was awarded the International Prize for Biology for outstanding developments in biomedical sciences and fundamental developments in the field of calcium’s role in the physiological regulation of skeletal muscle. The Prize’s presentation ceremony was held at the Japan Academy in Tokyo, with Their Majesties the Emperor Akihito and the Empress Michiko in attendance. At the ceremony, Emperor Akihito delivered an Imperial Message.

Setsuro Ebashi was Member of the Japan Academy and Foreign Member of several Academies including: the Deutsche Akademie Leopoldina, the Royal Academy of Medicine of Belgium, the American Academy of Arts and Sciences, the National Academy of Sciences (USA), the Academia Europaea and the Royal Society, London. He was also Honorary Professor of Shanghai Institute of Biochemistry, Chinese Academy of Sciences.

Bob Furchgott introduced me to Setsuro Ebashi in 1969. Since, I met him several times either in Tokyo and Brussels or at scientific meetings elsewhere in the world. I met him more regularly during the period 1990 – 1998 when he was in office for IUPHAR. He was a modest person with a very rich and complex personality. As a Scientist, he proved to be
rational and imaginative. He had a great memory even for small details; this allowed him to identify existing connections between facts apparently disparate. His scientific creativity was enhanced by his rejection of any dogmatism. As President of IUPHAR, he distributed cautiously various charges in order to include his Colleagues in the process of decision. As already mentioned, he had devoted himself to fund-raising, therefore, he took active part with Karl Netter, Treasurer of the Union, in discussions on financial contracts, being firm with the other party in order to defend the interests of IUPHAR. In such circumstances, he appeared sometimes imposing. In private gatherings he was friendly and humorous, he could eventually be slightly ironic. I remember when I told him about the biography of Yukio Mishima written by the famous novelist Marguerite Yourcenar, his mouth curved into an ironic smile and he asked me if I did consider that Mishima’s novels really described Japanese people. In fact, Setsuro Ebashi was unusual in his being very outspoken; when he was critical about something or somebody he said so. He was among the most cultured scientists I have met, able to sing *a capella* chorals of J.S. Bach. In Brussels, he asked to visit gothic churches for their stained glass windows.

When writing on Setsuro Ebashi, it is not possible to forget his wife who has provided a great support to him. In the first years, she was efficiently active in his laboratory. At the end of his life, she has been vigilant, keeping an affectionate environment and maintaining contacts with his friends abroad.

Setsuro Ebashi made many life-long friendships. His many friends from the different continents will dearly miss him.

Théophile GODFRAIND
Past-President of IUPHAR.