Jikeikai Med J 2007 ; 54 : 23-4

# In Memory of Dr. Reiji Natori, President Emeritus of The Jikei University School of Medicine

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Dr. Reiji Natori, President Emeritus of The Jikei University School of Medicine, passed away on November 20, 2006. A special funeral ceremony was held at The Jikei University School of Medicine on December 22, 2006. About 1,200 people attended the ceremony to pay their last respects. This special issue is dedicated to Dr. Natori, who published three articles regarding skinned fibers in the first volume of Jikeikai Medical Journal in 1954. His work was recognized around the world, and skinned fibers have been used by many physiologists.

Dr. Natori graduated from The Jikei University School of Medicine in March 1936. After graduation, he joined the Department of Physiology (whose chairman at the time was Professor Seizaburou Uramoto) and started his research work. At the beginning, he measured action potentials in the respiratory center of the carp and in peripheral nerves. He became interested in the contraction of skeletal muscle fibers and intended to investigate the mechanism of muscle contraction at the myofibril level. He attempted to isolate myofibrils from other cellular components. At that time, the cell was considered the minimal functional unit, and dissociation of intracellular components from the cell was considered impossible. However, Dr. Natori attempted to peel off the cell membrane while leaving the myofibrils intact and undamaged. However, accomplishing this feat was quite difficult. If the cell membrane is damaged, the ionic barrier of the cell membrane disappears and the muscle fiber is irreversibly damaged. Dr. Natori created several solutions whose ionic composition was similar to that of the interior of the cell and attempted to remove the cell membrane of a skeletal muscle fiber in the solutions. Unfortunately, his attempts were unsuccessful.

In early spring 1949, Dr. Natori speculated that the intracellular environment might be maintained if the cell membrane were peeled off in oil. His idea was that oil covers the muscle fiber and that the intracellular environment could be maintained even though the cell membrane was removed. Thus, intracellular ionic condition should be maintained without the cell membrane. He took a bundle of skeletal muscle from the sartorius of a toad and placed it on a glass slide. After putting a drop of machine oil on the preparation, he dissected a single muscle fiber under a binocular microscope. He then peeled off its cell membrane. Contraction did not occur, and the myofibrils were well maintained even after the membrane was peeled off. This was how Dr. Natori created the skinned fiber (Natori's skinned fiber). His excellent idea had never been considered by other researchers. Professor Umazume, Chairman of the Department of Physiology (I), The Jikei University School of Medicine, describes the physiological importance of skinned fiber in this volume.

Dr. Natori presented his research about the skinned fiber at the annual meeting of the Physiological Society of Japan in 1949 and described the skinned fiber in a textbook (*Kinseirigaku* [Muscle Physiology]) in 1951. In 1954, Dr. Natori published three articles in the Jikeikai Medical Journal. These were the first articles reporting the skinned fiber in English. However, the skinned fiber was not known internationally, because the Jikeikai Medical Journal had a limited circulation. In 1957, Professor Hiroshi Kumagai (Professor of Department of Pharmacology, Faculty

of Medicine, The University of Tokyo) organized a symposium on "The Chemistry of Muscle Contraction" in Tokyo. Dr. Natori presented his research about the skinned fiber at the meeting. Scientists from the abroad were surprised at the various characteristics of the skinned fiber, especially its response to electrical stimulation and its mechanical properties.

In 1960, Dr. Natori visited Professor Sir Andrew Huxley (Nobel Prize Winner for Physiology and Medicine) at University College London and showed movies of the skinned fiber. Professor Huxley admired and praised the skinned fiber, which showed unexpected phenomena. Soon, the skinned fiber was known all over the world, and muscle physiologists began to use this preparation to study the mechanisms of excitation-contraction coupling and the properties of myofilaments.

The original method of skinning involves mechanical removal of the cell membrane with a fine surgical scalpel (mechanically skinned fiber). However, some detergents can be used to destroy the cell membrane while leaving the myofibrils intact. Detergent-treated skinned fibers are easier to prepare than are mechanically skinned fibers. On the other hand, Professor Iwao Ohtsuki (Professor Emeritus, Kyushu University School of Medicine ; now Visiting Professor of the Department of Physiology (II), The Jikei University School of Medicine) found that saponin produces pores in the cell membrane through which small molecules can pass without affecting the sarcoplasmic reticulum membrane. Saponin and other detergents are now used to prepare skinned cardiac and smooth muscle fibers, which are difficult to prepare mechanically. In particular, saponin is widely used for studies of the $Ca^{2+}$-handling mechanisms of the sarcoplasmic reticulum. Detergent- or saponin-treated skinned fibers are called chemically skinned fibers. Thus, skinned fibers are widely used for various experiments and are a powerful tool for the study of muscle physiology.

In the Department of Physiology (I) and (II) of The Jikei University School of Medicine, skinned fibers of skeletal, cardiac, and smooth muscles are now used to investigate the mechanisms of excitation-contraction coupling and mechanical properties of the muscle.

Thus, Dr. Natori made a tremendous contribution to muscle physiology by inventing the skinned fiber. For his contributions to science and culture, he was recognized as a person who had done distinguished service in the field of culture and awarded the Asahi Prize, the Order of Culture, and the Grand Cordon of the Order of the Sacred Treasure.

As a physiologist and the President of The Jikei University School of Medicine, I would like to pay my respects to Dr. Natori and his research. I hope that this issue will remind you of Dr. Natori's work in muscle physiology.

February 11, 2007