



Professor Toshiaki Osawa

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Toshiaki Osawa was born on November 10th, 1930, in Maebashi, Gumma Prefecture in Japan. After attending Seikei Junior College in Tokyo from 1947 to 1950, he was accepted at the Faculty of Pharmaceutical Sciences of the University of Tokyo where he obtained his B.S. in 1953 and his Ph.D. in Pharmaceutical Sciences in 1960. For the last three years of his graduate studies, he was appointed Research Assistant at the School of Medicine of Tokyo Medical and Dental University.

Toshiaki Osawa's interest in carbohydrate chemistry and biochemistry was influenced by his thesis director, Professor Shichiro Akiya, with whom he stayed as research assistant at Tokyo Medical and Dental University after obtaining his doctoral degree. This interest led him to spend two years, from 1962 to 1964, as Research Fellow in the Laboratory for Carbohydrate Research at Massachusetts General Hospital and Harvard University Medical School, Boston, under the direction of Roger W. Jeanloz. During his stay, Osawa devised a practical synthesis of muramic acid and of some of its naturally occurring derivatives, as well as the synthesis of a disaccharide of *N*-acetylmuramic acid and *N*-acetylglucosamine which provided the basis for the determination of the chemical structure of the bacterial peptidoglycan. Subsequently, Osawa returned to the School of Medicine of Tokyo Medical and Dental University as Assistant Professor and, in 1967, he joined the Faculty of Pharmaceutical Sciences at the University of Tokyo as Associate Professor. He was promoted to the rank of Professor in 1971 and, in 1989, he assumed the function of Dean of the Faculty of Pharmaceutical Sciences.

Prior to his stay in Boston, Osawa had started in 1960 the study of lectins, some time before their biological importance had been fully recognized. He purified the lectin of *Sophora japonica* by biochemical methods and, in a paper published in the journal of his university, discussed the sugar-binding specificity on the basis of steric conformation. This early work was one of the main incentives for his interest in the synthesis of oligosaccharides, which he pursued actively on his return from Boston. The use of oligosaccharides and glycopeptides having well established structures for the determination of the specificity of lectins led to his first attempt at studying systematically the structure of oligosaccharides with lectins.

In the following years, Osawa and his group characterized lectins and isolectins from more than fifty plants, most of them being leguminous, and they determined their sugar-binding specificity not only with mono- but also with oligo-saccharides. For these studies, synthetic oligosaccharides and glycopeptides representing important domains of glycoprotein molecules were synthesized as well as isolated from plant and animal tissues. The most important impact of this work for the study of lectins was the development of a quantitative binding-inhibition assay for the determination of the structure of carbohydrate chains at the surface of cells, thus demonstrating that lectins can differentiate between chains having closely related structures.

The structure of the lectin molecule itself was also one of the early interests of Osawa. In the late 1960's, he began an investigation of the anti-H lectin, demonstrating in 1969 the existence of two anti-H lectins in the seed of *Ulex europaeus*, one having an L-fucose specificity, the other having a di-N-acetylchitobiose specificity. Later, he isolated these lectins from other sources, as well as a third anti-H lectin, specific for lactose, which was purified. Further work in this field involved the determination of the sequences of amino acids and the identification of the sugar- and metal-binding sites by computer graphic analysis based on the amino acid sequence. Very recently, Osawa and his group initiated the DNA cloning of these and other lectins.

Toshiaki Osawa was one of the first biochemists to study the modifications of the sugar chains at the surface of the tumor cell by use of specific lectins. He characterized the specificity of the lectins that are able to activate lymphocytes, as well as the structures of the glycoproteins at their surface. The specificities of mitogenic lectins were elucidated with immobilized glycopeptides obtained from T-cell-derived lymphoma cell lines. This work started Osawa's interest in lectin receptors on cell membranes and in the interaction between lectins and lymphocytes, which results in a modification of the fluidity of the membrane, for which he suggested a mechanism. Along similar lines of interest was the isolation of a macrophage lectin acting as a tumor-adhesive factor which Osawa and his group purified, cloned the gene, and determined the primary structure. They also isolated a collagen receptor responsible for platelet aggregation and a lymphotoxin receptor, and they used fluorescence-labeled lectins to study the modifications of the sugar chains of T-cell CD 45 antigen during the pathological progress of a model autoimmune animal. In another practical use of lectins, they determined the basic structure of the sugar chains of various glycoproteins, including human glycophorin, with immobilized lectins, such as concanavalin A-Sepharose, wheat germ agglutinin-Sepharose, and erythroagglutinin PHA-E-Sepharose.

In order to kill selectively cancer cells, Toshiaki Osawa was one of the first immunochemists to prepare immunotoxins by coupling toxins, such as ricin, to lectins that are relatively specific for some cancer cells. Along lines similar to those developed at the Weizmann Institute of Science by Nathan Sharon, Osawa's group used lectins for the fractionation of immune cells, such as the suppressor T-cell, the helper T-cell, and cytotoxic cells.

For his study of the mechanism of activation of lymphocytes, Osawa prepared a monovalent concanavalin A, which allowed him to demonstrate that cross-linking of membrane receptors is essential for activation, and he proposed two signal theories. This led to the discovery of the lymphokine IL-2, which was followed by the isolation of a GTP-binding protein related to the phosphatidyl-specific phospholipase, a key enzyme in the transmission of the activation signal. Already in 1971, Osawa and his group had started the study of the lymphokine released by lectin-stimulated lymphocytes. In order to produce large amounts of lymphokine, the lectin-stimulated T-cell was fused with T-cell-derived hybridoma selected by emetine and actinomycin D treatment. A lymphotoxin was also purified and produced in large amounts by recombinant techniques. More recently, Osawa's group has been involved in the chemical synthesis of a

macrophage-chemotactic factor, and in the purification of a macrophage-migration inhibitory factor and of a macrophage-activating factor.

This extensive research activity has been recognized by awards from the Pharmaceutical Society of Japan and of the Naito Foundation, and by the election of Toshiaki Osawa to the presidency of the Japanese Biochemical Society and to membership in the Executive Committees of the Pharmaceutical Society of Japan, of the Japanese Society of Immunology, and of the Japanese Society of Carbohydrate Research. Osawa has also been active in the publication field, as an Editor and Managing-Editor of the *Journal of Biochemistry (Tokyo)*, Editor of *Microbiology and Immunology*, and *Journal of Pharmacobio-Dyn (Tokyo)*, Managing-Editor of the *Chemical and Pharmaceutical Bulletin*, and on the editorial board of several periodicals. He has been invited to write numerous reviews, chapters, and books (in Japanese) on lectins, and in 1988 he gave a plenary lecture at the 14th International Carbohydrate Symposium on "Application of Lectins in the Structural Study of Glycoproteins."

Professor Osawa has a very keen sense of humor, greatly appreciated by his colleagues, his associates, and his students. When he was younger, he was an active mountain climber, and in recent years he has shifted his physical activity to the practice of golf. He was an active skier and would invite his associates and graduate students to spend a few days with him in the Japanese Alps in Winter. One of us (RWJ) was fortunate to attend one of these get-togethers, and participate in the very congenial atmosphere of a communal meal around a wide circular table with an open-fire in the middle to warm our feet and to take part in the traditional mashing of the rice on New Year's day. Retirement comes very early for professors at the University of Tokyo, but fortunately for the science of "lectinology", Professor Osawa will move to another prestigious research institution where all his friends wish him many successful endeavors.

Isamu Matsumoto
Roger W. Jeanloz