



Letter to the editor

Haruhiko Noda – First reporter of collagen fibrillar aggregates formed from solubilized rat tail collagen



Professor Haruhiko Noda was born March 3, 1922. He passed away on March 7, 2021. He graduated from The University of Tokyo in September, 1943, becoming associate professor in April 1958 and full professor in June, 1960 of the Department of Biochemistry and Biophysics, Faculty of Science, The University of Tokyo.

More than 20 former students and staff of Professor Noda's Laboratory (called "Noda Ken") attended his annual birthday parties at his home with excellent dishes, some of which were prepared by himself. Lately, KOKESHIYA restaurant near his home had been the gathering place for his birthday celebrations until his 97th birthday.

Although his primary field of study had been introduced as biophysical chemistry, Professor Noda had a wide range of interests; mathematics, statistics, neural sciences, genetics, molecular and cellular biology, material sciences, muscle sciences, and origin of life as well as regular biochemistry and biophysics. His interests further go on to languages and sometimes politics.

When I was his graduate student, I heard that Professor Noda's interest is collagen.

Professor Noda had written many reviews on collagen in Japanese. In fact, I got to know that most fundamental work for obtaining research funding from NIH was the study on bacterial collagenase that only degrades collagen but not the other proteins, and collagen could be degraded only by the collagenase but no other proteases. Professor Noda was famous for letting his students research freely, requiring only that students rationally explain their reasoning behind their research objectives.

Collagen had been known to be insoluble. At the time, the only information available on collagen structure was X-ray diffraction pattern and striated collagen fibrils imaged by EM. Collagen and other insoluble fibrils composing the organisms are called structural

macromolecules without any special biological activities comparable with enzymes, hormones, cytokines etc. which are found and isolated from the tissues by marking biochemical activities. Furthermore, many enzymes are extractable and purified with respect to their specific catalytic activities of biochemical reactions. In that sense, collagen could not be subjected to biochemical analysis.

Why did Professor Noda become interested in collagen? His first work on a possible ordered structure of collagen was conducted with Dr. Wyckoff in the United States. When Dr. Noda joined the Wyckoff laboratory, he discovered that solubilizing rat tail tendon in dilute acetic acid allows collagen to be solubilized with a rod-like structure; a length of about 300 nm.

The collagen solution aggregated with the structures that was neither unique nor random. The aggregate structures were versatile, depending on anion species, pH and other experimental conditions. Yet, some of the fibrous aggregates appeared by EM similar to the striated collagen fibrils *in vivo*. Professor Noda and his team concluded that reconstituted aggregates are related to collagen fibrils.

Based on his discovery the reconstruction of tissue-like structure *in vitro* was realized and applied to engineer artificial tissues like skin and dermis. Now, several products including Aprigraf and Dermagraft from Organogenesis are commercially available.

In later years, Professor Noda developed many personal relationships through his diverse interests, scientific and non-scientific matters. In particular, he was interested in the characteristics of Japan in comparison to other countries, especially the United States, where he had spent time for researching, and China, where he attended elementary and junior high schools in Shenyang. Shenyang is also where I have happened to be involved in research collaboration with Professor Ikejima to find out pharmacological roles of collagen and/or gelatin (denatured collagen).

The most impressive queries from Professor Noda when we were undergraduate students.

1. Automatic repair of the injury or recovery to the original structure.
2. Automatic formation of rather regular aggregates of living organisms.
3. Mechanisms of regulatory formation from a size of 1 nm–100 nm in order.

Professor Noda thought about collagen as one of the key materials to study in asking scientific questions or designing experiments on multicellular animals.

Professor Noda was also interested in the hypothesis that the origin of life may not be limited to earth. He conjectured that if

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organisms are made of *D*-amino acids instead of *L*-amino acids, which all proteins of earth organisms are made from, this would give us a proof for an alternative, non-earth-based origin of life.

I personally miss Professor Noda. I wish I could imagine what he would say to me in times that I feel lost.

Declaration of competing interest

The author declares that there is no conflict of interest.

Toshihiko Hayashi
*Nippi Research Institute of Biomatrix and Protein Engineering Project,
520-11 Kuwabara Toride-shi, Ibaraki-ken, 302-0017, Japan*

The University of Tokyo, Japan

Shenyang Pharmaceutical University, China

E-mail address: toshihikohayashi@jcom.home.ne.jp.

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