

# Obituary for the late Yasuo Ihara

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Professor Yasuo Ihara, who guided a number of researchers including myself to a career in research on AD, passed away on June 10, 2023. He was 78 years old.

It was the 1990s, over 30 years ago, when I got into Alzheimer's disease (AD) research via basic research on proteolysis. The motivation for this was my encounter with Professor Ihara. At that time, Prof. Ihara was Chairman of the Department of Neuropathology, Faculty of Medicine, University of Tokyo (located in Hongo, Tokyo), and I was a research scientist at the Tokyo Metropolitan Institute of Medical Science (located in Komagome, Tokyo). Prof. Ihara and I were involved in proving the hypothesis that the chemical structure of A $\beta$ , which had been established as a causative agent of AD, was different from what was thought at the time. I performed experiments by myself every day, and once a week I brought the data from Komagome to Hongo by bicycle. The discussions often lasted over two hours; it was a dreamy time, and truly the happiest period in my research career. I co-authored the research with Prof. Ihara and published it in *Neuron*,<sup>1</sup> which later led to development of donanemab by Lilly<sup>2–4</sup> and has been approved by FDA.

I can confidently say that I would not be where I am today without my encounter with Prof. Ihara. In total, he and I published 12 papers together in English<sup>1,5–15</sup> and one review in Japanese.<sup>16</sup>

After that, we continued to interact not only in research but also in the management of the Japan Dementia Research Society. However, after Prof. Ihara retired from the University of Tokyo and moved to Doshisha University in Kyoto, his health gradually deteriorated, and finally he had to receive hospital treatment, meaning that opportunities to see him diminished. The fact that visits were restricted due to the COVID-19 pandemic was also an obstacle. Professor Ihara's wake was held on June 12, and his funeral ceremony was held on June 13,

2023. Researchers around the world requested live streaming, so with the permission of his close family members, we shared the live information and recordings on Zoom. Prof. Ihara was one of the first researchers in the world to discover that tau protein is a component of neurofibrillary tangles.<sup>17,18</sup> He also pioneered in elucidation of the serial cleavages of APP C-terminal fragment by  $\gamma$ -secretase.<sup>15,19</sup> Everyone involved in AD research has heard of him. It is exactly as if "a giant star has fallen".

In addition to his research, he was instrumental in reforming and developing the Japanese Dementia Research Society. June 10th became the saddest day for me. I sincerely pray for the repose of his soul.

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Photo by TC Saido.

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