Dr. Takashi Sugimura: A giant of chemical carcinogenesis

James E. Trosko[a,1]

It will be difficult to take the measure of the man, Dr. Takashi Sugimura, who died on September 6, 2020, since so much has been written about his persona and his status as an internationally recognized biochemical cancer researcher. It goes without saying that the scientific community has lost an extraordinary human being. However, at least he left us the shoulder of a giant on which to stand.

Sugimura was a graduate of the University of Tokyo, Faculty of Medicine, where he received his medical degree in 1949 and the degree of Doctor of Medical Science in 1957. He completed a postdoctoral fellowship at the Cancer Institute, Japanese Foundation for Cancer Research, and with that sterling education and experience, Sugimura became Chief of Biochemistry Division at the Research Institute, National Cancer Center, in Tokyo in 1962. Sugimura went on to serve as President of the institute from 1984 to 1991. While at the National Cancer Center, he also had an appointment with the Institute of Medical Science, University of Tokyo, where he worked from 1970 to 1985, advancing to the rank of Professor in recognition of his research and administrative acumen. He later served as President of Toho University from 1994 to 2000. In recognition of his international research impact, Sugimura was elected a recipient of the Japan Prize (1997), a Foreign Member of the Royal Swedish Academy of Sciences (1987), a Fellow of the American Association for Cancer Research, an Honorary Member of the Japanese Cancer Association, a Foreign Associate of the Institute of Medicine at the National Academy of Sciences (1994), President Emeritus of the National Cancer Center, and many other honorary awards and prizes.

While many others have already made tribute to him as to how he influenced the field of chemical carcinogenesis, I will try to add my own personal interaction with him over the early years when the two of us overlapped in research interests. To summarize Sugimura as an abstraction from a nonexperiential perspective would not serve him well. To do an assessment as a scientist and a human being can only be done, unfortunately, by dragging in some of my own background circumstances, which brought us together.

Takashi Sugimura. Image credit: The Japan Academy.

I first interacted with Dr. Sugimura via letters when he was the Chief of the Biochemical Division at the National Cancer Center in Tokyo. During the early 1970s, the fields of mutagenesis and carcinogenesis were being enhanced by new techniques to study the phenomenon of DNA damage and "error-prone DNA repair." The introduction of the Ames assay, an in vitro assay to detect chemicals that were associated with cancer, was the spark that excited Sugimura and was exactly the opportunity for him to exploit his skills. This discovery was a powerful tool with which Sugimura

[a]Department of Pediatrics and Human Development, College of Human Medicine, Michigan State University, East Lansing, MI 48824

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[1]Email: trosko@msu.edu.

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Sugimura and the author caught going to his favorite unagi (barbequed eel) restaurant, with him wearing his contagious smile. I later tried to reciprocate his friendship to me concerning our culinary interests and took him to my favorite okonomiyaki restaurant in Hiroshima.

could use his expertise, as a biochemist, to test if environmental chemicals and food ingredients might be mutagens that could "initiate" the cancer process. During that period of time, my collaborator, Dr. James E. Cleaver, and I demonstrated that cells from the skin cancer-prone human syndrome, xeroderma pigmentosum, could not repair the ultraviolet light damage to DNA and, subsequently, my laboratory showed that these ultraviolet-irradiated cells that survived had an increased frequency of mutations. However, soon afterward my laboratory showed that many chemicals associated with cancers were not mutagens in non-Ames assays. We had discovered a new nonmutagenic mechanism influencing the multistage, multimechanism of carcinogenesis.

It was in this context that Sugimura and I started to communicate via the mail and at scientific meetings. At an Environmental Mutagen Society meeting in the early 1980s, I gave a very controversial short talk in which I challenged the interpretations of the Ames assay and other mammalian assays to detect "mutagens." Right after that meeting, I met Sugimura in Japan and was immediately impressed with his scientific attitude. We had a most civil discussion of our disagreement about the strengths and weaknesses of these mutation assays, as well as the relevance of the so-called nonmutagenic or epigenetic toxins/toxicants.

Since Sugimura was genuinely concerned about nutrition and diets on the cancer process as a physician, he used his intellectual and technical skills as a biochemist to isolate and characterize food ingredients, in and on food, to determine their potential role in the carcinogenic process. He generously gave me some insights that I might test in my assay. In addition, at several international meetings, he and I would seek each other out, such as at the Princess Takamatsu meeting in Tokyo. There, Sugimura not only gave me an introduction to his favorite unagi restaurant, he also told me about Japanese culinary history, including fugu poison history, as well as other toxins and toxicants found in the Japanese diet.

Later, when I became the Chief of Research at the Radiation Effects Research Foundation (1990 to 1992) in Hiroshima/Nagasaki, Japan, we were able to work together more directly. I relied on his personal knowledge of the "cutting-edge" research in Japan at that time. With his warm personality, openness, and exuberance about science, I grew to depend on Sugimura's wisdom and knowledge, and he welcomed me into the scientific research community in Japan. Sugimura introduced me to so many of his students and colleagues that I knew that he trusted me as a scientist, as, of course, I trusted him. Sugimura invited me to give seminars at the National Cancer Foundation and made a real effort to link me with other Japanese scientists.

It was Sugimura's generosity that drew me to him and reminded me of my late mentor, Dr. Van Rensselaer Potter, another giant in the field of chemical carcinogenesis. I, unfortunately, never had the opportunity to experience with Sugimura those early formative years that made him such an engaging person, as well as a driven and committed scientist to help human beings with cancer. However, as Dr. Van Rensselaer Potter said, "humility with responsibility" ought to be a major driving force in scientific research. My experiences with Sugimura indicated that, before I ever met him, others had influenced this important trait in his core being. Sugimura was never motivated to seek national and international awards for the major scientific contributions that he published. His passion was to find scientific answers as to how to prevent or treat human cancers.

During all the exchanges we had, it seemed that Sugimura's serious objections to my ideas melted away: Not because of my own contributions to this field of chemical carcinogenesis, but because, like any good scientist, he was absorbing the international contributions to the delineation of the distinct mechanisms of "initiation," "promotion," and "progression" in chemical carcinogenesis. Equally important in our discussions about our disagreements with each other's thinking at the time, I think I convinced him that, while I never doubted the solid science he used as the basis for his results, I thought his acceptance of the prevailing universal interpretation of positive results of the Ames assay was immediately translatable to suggesting genomic mutations in human cells. Similarly, Sugimura challenged my interpretation of my assay to detect epigenetic tumor promoters and forced me to retest my results. It was this mutual agreement to disagree, in a very civil manner, that impressed me the most about his character. Sugimura soon realized that his basic research, as a biochemist, could now be used to outline how these unique food ingredients might be used to help distinguish the "initiation" or mutagenic step from the "promotion" or nonmutagenic step in chemical carcinogenesis. Sugimura's work significantly stimulated this area of research, not only in Japan but internationally.

After I left Japan in 1992, while he and I exchanged several ideas with each other (he constantly gave me insights for my research), I lost contact with Sugimura after his retirement and subsequent new post as President of Toho University.

As I look back, as do all scientists, to those who in one way or another not only helped us become better human beings, as well as contributors to the scientific community, Sugimura is one I will never forget. My one major regret is that I never told him that. I learned the lesson from him that you can disagree with another scientist's ideas or findings, but you do not have to impugn their integrity. Sugimura did so with astonishing grace.

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