NATIONAL LIBRARY OF MEDICINE

INTERVIEW PROJECT

INTERVIEW WITH

SHUN-ICHI HATA

Dr. Shun-Ichi Hata – Answers to Interview Questions

[Dr. Shun-Ichi Hata was not available for an interview in person, but generously answered the following questions via mail, in a letter dated July 28, 2004]

Biographical note

Shun-Ichi Hata received a BS in Chemistry from Tokyo Metropolitan University in 1960. He was a researcher at the Chugai Pharmaceutical Company for several years before getting his PhD from the Faculty of Pharmaceutical Science at the University of Kyusyu in 1969. Following this, he accepted a two-year post-doctoral research fellowship with Dr. Szent-Györgyi at the Institute for Muscle Research in Woods Hole, Massachusetts. He returned to Japan and to Chugai, as a senior researcher and later became head of research there. He contributed to the development of two kinds of gene-derived pharmaceutical products, EPO and G-CSF, both of which are still of great value in the Japanese market. From 1995 to 1997 he was director of research at Sugar-Chain Technology in Tokyo. Since his retirement in 1997, he has stayed busy as a medical writer and nature guide.

You were born in 1937, the same year in which Albert Szent-Györgyi won the Nobel prize for his work in identifying Vitamin C. When and how did you first learn of Szent-Györgyi and his research?

I am very surprised to know that Dr. Szent-Györgyi won the Nobel Prize in the same year I was born. I was not aware of this until receiving your questions. From 1963 to 1967 I had worked on my PhD thesis regarding a possible application of charge transfer complex in pharmaceutical science. As you may know, the concept of the complex is closely related to so-called electron donation and acceptance in chemical reactions. Initially, I found Szent-Györgyi's name and some of his research works in the literature of this field. This was the first I knew of him.

In 1969 you began a two-year postdoctoral fellowship in Szent-Györgyi's laboratory at Woods Hole, Massachusetts. Was that your first visit to the United States? Was it the first time you met Szent-Györgyi?

Yes, that was my first visit to the U.S. and the first time I met Szent-Györgyi himself.

What were you first impressions of Szent-Györgyi? Could you describe him? Was he as you had expected him to be, or were you surprised in any way?

When I arrived at Woods Hole on the bus, I was greeted by Szent-Györgyi, who was accompanied by a young lady. At that time, I was of course surprised at his friendly greeting, which I had not expected, and also by the fact that he seemed very young for his age. He was very healthy-looking, and carried my two large heavy trunks to his Cadillac by himself. Besides

this, he was very gentle-mannered and kindhearted. I stayed in a guest room at his big house on Penzance Point for two days after arriving.

Did your first impressions of him stay the same or did they change during the two years you worked with him?

These first impressions stayed much the same during those two years.

Who were some of the other people who worked in Szent-Györgyi's laboratory when you were there?

At that time several people were working in the laboratory: Dr. Laszlo Eguyd, Ms. Jane McLaughlin, Ms. Csilla Felker, Mr. Gary Taper, and three or four other technicians.

Could you describe your research there, the particular problems you were working on? (In his book *The Living State, with Observations on Cancer* (1972), Szent-Györgyi mentions some of your work on ketone aldehydes and other oncostatic extracts.)

First, Szent-Györgyi asked me to work on the research subject using polarography, by which he expected to clarify a possible role of chemical compounds including ketone aldehydes. When we did not obtain any promising results with this, he changed his mind and enthusiastically told me that tumor tissues may contain components which would show specific polarographic waves in terms of oxidation-reduction potential. So polarographic determination was made on extracted samples from many kinds of cancerous tissues including experimental animals as well as humans. As a result, we were able to confirm a polarographic wave which may be due to a specific component in cancerous tissues but not in any kinds of other normal tissues. The same wave was also found in urine samples from cancer patients. Szent-Györgyi was quite excited to find those, and then asked me to isolate that component which may be contained in tumor tissues. He very much expected that it would be specific to tumors Then we collected a large quantity of urine from cancer patients in order to purify the unknown component, which he believed to be there. However, our trial on the isolation ended unsuccessfully. Details of those investigations are summarized in four published papers.

How did a week spent in Szent-Györgyi's laboratory differ from a week spent in any other lab at Woods Hole? Was there a different or a special atmosphere in his laboratory?

It is difficult to answer this, because people in Szent-Györgyi's laboratory were working throughout the year at Woods Hole, while people in any other laboratory stayed there only from June to August. This makes it complicated to compare the two. Generally speaking, it would be possible to say that the atmosphere in the former was much more liberal in comparison to the latter.

Albert Szent-Györgyi did not hold any formal academic appointments in the United States, yet many people describe him as an excellent teacher and lecturer. What were your own experiences with him as a teacher? What did he teach you, and how did he teach you?

Regarding how to proceed with research programs, Szent-Györgyi liked to value his own intuition more than anything. One day he said in our laboratory meeting that "most people say everything should be logical. But I don't like to think in this manner." I am quite sure that this may be true in the case of great scientists like him, but as for other average ones, it is not the case. In the latter, it might be too risky to think in his way. Those are what I had been taught by him during the stay.

Szent-Györgyi once said that Abiochemistry is a lovely game of refined cookery, very fit for the amusement of big children. He suspected that many chemists loved their work because it was fun to mix solutions, heat them, and watch them change. Did Szent-Györgyi seem to be enjoying himself in this way when he worked? He said that he suspected that his Areally good colleagues also had this attitude about their work. Do you think that is true, or was he describing something that was true mostly for himself?

It seemed to me that he was really enjoying himself at his work, in the process of seeing his scientific ideas growing into something new scientific discovery. In this sense, what you have mentioned in this question was true mostly for himself.

Do you recall any examples or instances when you observed Szent-Györgyi -- playing or enjoying himself at his work? On the opposite side, did you ever see him frustrated at his work?

I was very surprised to see that even while shaking a test tube in an experiment, there was a look of enjoyment on his face. In fact, I never saw him frustrated at his work.

Szent-Györgyi believed strongly that science transcended cultures and national boundaries. But culture can influence culture sometimes. For example, when Szent-Györgyi came to the United States in 1947 he discovered that finding money for his research was a problem. Funding agencies required that a researcher should predict what he is likely to find, in order to justify spending the money. This is nonsense, Szent-Györgyi said, because research means going into the unknown. As a result, he couldn't bring himself to apply for research grants.

Did he ever speak to you about this? Is your own view of grant applications similar to or different from Szent-Györgyi's?

During my time at Woods Hole, he said nothing to me about his financial difficulties in terms of research grants. But I was somewhat aware of it. Regarding his famous remark that "research means going into the unknown," I am convinced that in fact this was an important philosophy in

his scientific work. I gained a clear understanding of this point, though he did not speak to me specifically about it. Regarding my own grant applications, I would prefer to take Szent-Györgyi's position, but that would be very difficult, so I've had to do things differently.

In his biography of Szent-Györgyi, *Free Radical*, Ralph Moss said (p. 214) about Szent-Györgyi, who was in his late seventies when you worked with him. In Japan he might have been declared a living treasure and given the means to continue research, but in the United States he struggled for funding. Do you agree with Moss's observation?

I do not agree with Moss's observation. In Japan too, a scientist in his late seventies, even a Nobel Prize winner, is confronted with severe limits in regard to research funding, if he wants to work further as a "genuine researcher" and not just at an honorary post.

Szent-Györgyi set a very high standard of dedication and commitment for the scientist. In 1943 he wrote, *Scientific research is a passion. The real scientist is driven by this passion and is ready to bear privation and, if need be, starvation rather than let anyone dictate to him which direction his work must take.* He was willing to make great sacrifices to continue his work. Did he ever speak to you about this? When you worked with him, what examples did you see of his unusual degree of dedication to his work?

He did not say anything to me about this during the time I worked with him, nor did I see an unusual degree of sacrifice on his part.

Your years at Woods Hole coincided with years of great political conflict in the United States, mostly about the Vietnam war but also about civil rights, nuclear weapons, and other issues. Szent-Györgyi had very strong opinions about these issues, and he also was very outspoken. Did he ever discuss such matters in the lab? Did he discuss them with you, in or out of the lab?

No, he did not discuss such things with me or the others, in or out of the lab.

What contacts did you have with Szent-Györgyi after your fellowship? Did you ever speak with him? Did you ever see him again?

I corresponded with him for a time after my fellowship. In one letter he wrote, "electrostatic force weakens as intermolecular distance increases, but friendly feeling between the two becomes tighter in contrast." I did not see him again, and I regret to say that my second visit to Woods Hole was after his death.

In his long career as a scientist in Europe and in the United States, Szent-Györgyi made two different kinds of contributions B one was *what* he discovered; the other was *the way that he discovered it.* That is, one was the *substance* of his work, the other was his *style and his attitude* about research. Which of these two had the greatest influence on you? Which

do you think had the greatest influence generally, on others and in the field of biochemistry?

I agree with you entirely about his two kinds of contribution to the world. That is to say, one is the substance and the other the style and attitude in his research. As for myself, the latter has had the greatest influence. Furthermore, I really believe that the latter has also been the biggest one upon people not only in the field of biochemistry but in all kinds of scientific fields, including biology as well as medicine.