MY WARM MEMORIES OF JAMES R. GILLETTE

(Received March 6, 2003; accepted March 26, 2003)

This article is available online at http://dmd.aspetjournals.org

It is a great pleasure to present my appreciation and memories of Dr. James R. Gillette at the National Institutes of Health (NIH, Bethesda, MD). In 1957, I engaged in the study of the metabolism of serotonin and catecholamine as a neuropsychiatrist at the Institute of Pharmacology, University of Milano, Italy. I met with Dr. B. B. Brodie, Chief, Laboratory of Chemical Pharmacology, National Heart Institute, NIH, in Milan, and he kindly invited me to his laboratory to study serotonin and catecholamine metabolism.

In fall 1958, during my studies of serotonin metabolism, I found by chance that the administration of chlorpromazine induced hepatic metabolism of pentobarbital. After that, I intensively engaged in studies on drug metabolism, especially the induction and inhibition, developmental and aging aspects, and sex-dependent differences of hepatic microsomal drug-metabolizing enzymes.

Throughout these studies, I realized that the field of drug metabolism research would become an important field of the medical sciences. I subsequently decided to continue my research on drug metabolism in Dr. B. B. Brodie’s laboratory in Bethesda, which was a mecca of drug metabolism research at that time and where Drs. J. R. Gillette, A. H. Conney, and J. J. Burns were working. At the end of August 1962, I left Milan and joined the Laboratory of Chemical Pharmacology at NIH in Bethesda to work with Jim Gillette. At that time, I was 32 years old and Jim was 35 years old.

My impression of Jim was of a pure and fervent scientist, and he was writing and correcting papers for his ideas everyday with his characteristic left-handed manner. Since I was an established scientist in the field of drug metabolism study, Jim kindly suggested to me “Ryuichi, you can do your research as you like by continuing your research in Milan.” Therefore, I began my research on the effects of some nonphysiological developmental and aging aspects, and sex-dependent differences of hepatic microsomal drug-metabolizing enzymes.

We found that starvation, adrenalectomy, hyperthyroidism, alloxan diabetes, morphine treatment, and formalin administration all decreased activity of MDME, such as hexobarbital hydroxylation and diabetes, morphine treatment, and formalin administration all decreased activity of MDME, such as hexobarbital hydroxylation and diuresis. Therefore, our results received considerable attention, and we realized from their results that phenobarbital most likely induced microsomal P450. We initiated studies to confirm this possibility, but unfortunately, the one dual-wave spectrophotometer at the Laboratory of Chemical Pharmacology was broken, and therefore we could not complete these studies.

A portion of our preliminary data was reported at the Federation Meeting in April 1964. During the preparation of a manuscript on our results, Dr. Sten Orrenius’ article was published in Biochemical and Biophysical Research Communications in June 1964 (Orrenius and Emster, 1964), and our exciting publication was no longer seminal for the field.

Dr. James Gillette was a fervent, kind, and warm scientist with splendid ideas, and he taught me many things during my 2-year stay in Bethesda.

Department of Pharmacology, School of Medicine, Keio University, Tokyo, Japan

Ryuichi Kato

References


Ryuichi Kato was born in 1930 in Hokkaido, Japan. He received his medical degree in 1954 from the Keio University School of Medicine. In 1957, he was a Visiting Fellow at the Institute of Pharmacology, University of Milan, Italy, and in 1962, a Visiting Scientist at the Laboratory of Chemical Pharmacology, NHI, National Institutes of Health, Bethesda, MD. In 1964, he became Section Chief of the Department of Pharma-