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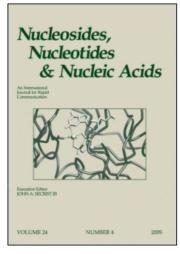
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## Nucleosides, Nucleotides and Nucleic Acids

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**Preface** 

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## **PREFACE**

As one of his first students, I feel greatly privileged to have been requested to write, as a representative of the editors, the preface of this special issue commemorating Professor Yoshihisa Mizuno's 75th birthday. It was in 1955, when the Faculty of Pharmaceutical Sciences was founded at Hokkaido University School of Medicine, that Dr. Mizuno joined the faculty from Kanazawa University where he had been awarded a full professorship in 1952 at the age of 33. His long involvement in nucleic acid chemistry, however, began at Hokkaido in a laboratory set in an abandoned wooden building, with Dr. Morio Ikehara and the late Tohru Ueda, both of whom later became leading nucleic acid chemists. Eiko Ohtsuka and myself were fortunate to be accepted in Mizuno's laboratory as students.

Although ten years had passed since the end of the World War II, almost every aspect of Japan (especially, science, industry and economy) was not quite recovered from the damage of the war. Neither sophisticated reagents nor expensive solvents were available to us. One of the major reasons Dr. Mizuno decided to devote the entire laboratory to nucleic acid chemistry was a rather ready accessibility to fresh brewery yeast from a nearby Sapporo Beer factory. Dr. Mizuno's first task was to optimize conditions for isolation of RNA from the yeast and efficient preparation of nucleosides from the RNA. Guanosine was easily obtained in pure crystalline form, but uridine, which was first crystallized by Tohru in the laboratory, was extremely difficult to isolate in a pure state. Fraction collectors were constructed by Akihiko Nomura, another of Mizuno's original associates, currently Professor at Fukui University. We all were excited by our own daily progress as well as publications

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by Todd, Khorana, B. R. Baker, J. A. Montgomery, R. K. Robins, Hitchings and Fox. We read Chargaff's "Nucleic Acids", and the chapters written by A. Bendich and Baddiley were especially useful. We had seminars twice a week, which started at 6:00 pm and lasted more than two hours. After each seminar, many of us went back to the bench. In early 1960's, 6-azacytidine, 1-(β-D-ribofuranosyl)-4-aminobenzimidazole (or 1,3-dideazaadenosine), 1- and 3-deazaadenosines were synthesized by several students under Mizuno's direct supervision. The ribose used in these syntheses was prepared from guanosine which was obtained by hydrolysis of RNA. Tohru and Eiko achieved the first synthesis of guanosine diphosphate mannose (GDPM). Morio with Eiko synthesized the first acyclo- or seco-nucleosides and their phosphates. One of the seco-nucleosides was later found in Nature. At about this time, Morio's purine-8-cyclonucleoside research was initiated with Hiroshi Tada. Akihiro Yamazaki, who later developed the famous cyclization reaction of AICAR leading eventually to guanosine, wrestled with thiopurine nucleosides, while Takuma Sasaki, currently Professor at Kanazawa University, was struggling to synthesize nucleotides by phosphorylation *via* anhydronucleosides

In 1960, Professor Mizuno took his first and only sabbatical leave for one year to work with Dr. Lorente de No at the Rockefeller Institute for Medical Research, where he isolated an imidazole derivative which appeared to be norhistidine from a large number of brains of cows and oxen. More than 30 years later, a nucleoside of a similar imidazole, "tele-imidazoleacetic acid riboside", was detected in rat brain and human cerebrospinal fluid.

In 1970, he was elected Dean of the Faculty. Three years later, he was re-elected, but refused to resume the elected position. As far as I know, Dr. Mizuno was the only professor who turned down deanship. He enjoyed chemistry with the least of administrative disturbances until his retirement in 1983 when he became professor emeritus. His chair was succeeded by Tohru, and then Akira Matsuda. The tradition of diligence established by Dr. Mizuno continued in the laboratory which he founded. Currently, Dr. Mizuno is Visiting

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Professor of Kitasato University. Once I met him at Kitasato. He looked really happy

working at the bench with young students . One of his starting materials, AICAR, was

supplied by Dr. Yamazaki of Ajinomoto Company. When I was his student, Dr. Mizuno was

very serious and stoic teacher who disciplined his students in very strict manner. If a student

did not follow his direction and made mistakes, he did not hesitate to yell at the student.

Mineo Saneyoshi, currently Professor of Nishi-Tokyo University, and myself were his regular

victims. Now, Dr. Mizuno is treating the Kitasato students as if he were their kind uncle

teaching in details with a smile.

For us friends and former proteges of Dr. Mizuno, it is really a timely and happy

occasion to celebrate his 75th birthday with the publication of this special issue of Nucleosides

and Nucleotides.

August 1995

K. A. W.

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