The Structure of Nucleic Acids and Many Other Natural Products: Phoebus Aaron Levene

The Structure of Yeast Nucleic Acid. IV. Ammonia Hydrolysis

Phoebus Aaron Theodor Levene was born in Russia and attended school in St. Petersburg completing work for a medical degree from the Imperial Military Medical Academy in 1892. He was one of very few Jewish students admitted for medical studies, and with growing anti-Semitism in Russia and a desire for greater opportunities, Levene moved with his family to New York City. During the period from 1892 to 1905, he practiced medicine, recovered from tuberculosis, studied in Europe, and served as physiological chemist at the Pathological Institute of the New York State Hospitals. In 1905, he was appointed to a position as laboratory assistant with Dr. Simon Flexner at the Rockefeller Institute for Medical Research, later Rockefeller University. His talent in physiological chemistry was quickly recognized, and in 1907 he was made a Member of the Institute in charge of its Division of Chemistry. He served in this capacity until his death in 1940 (1).

Levene might best be described as a natural product chemist. He published over 700 papers covering a wide range of biological molecules including the chemistry of nucleic acids, proteins and amino acids, lipids and carbohydrates, glycoproteins, and amino sugars. He was an enormously important figure at the dawn of biochemistry and contributed greatly to the emergence of biochemistry in the United States.

The paper reprinted in this installment of Journal of Biological Chemistry (JBC) Classics represents a typical Levene paper with purification and chemical characterization of the nucleotides of yeast nucleic acids. His study, and others, used alkali to hydrolyze nucleic acid, and as a result, the study really focuses on RNA composition and structure because DNA is alkali-resistant. For these reasons, the nucleosides isolated from alkaline hydrolysis were AMP, CMP, GMP, and UMP. There was no TMP. (In the paper, these compounds are referred to as guanosinphosphoric acid, adenosinphosphoric acid, etc.)

Levene reviews the proposals that others, the groups of Thannhauser and of Jones, had made for the structure of nucleic acids and proceeds to discredit them. He then concludes, incorrectly, that the linkage between the bases is a phosphomonoester linkage between the ribose residues (see page 420). He adds confidently that now, “there is no doubt as to the polynucleotide structure of the yeast nucleic acid.” We know, of course, that the correct linkage is a phosphodiester. It is also interesting that he notes that earlier results published in 1917 by Thannhauser in Germany did not reach the United States until 1919, the end of World War I.

Among many awards, in 1931 Levene received the Willard Gibbs Medal of the American Chemical Society. In his acceptance address, “The Revolt of the Biochemist” he described his view of the future of biochemistry. “Thus step by step, one mystery of life after another is being revealed. Whether the human mind will ever attain complete and absolute knowledge of and complete mastery of life is not essential. It is certain, however, that the revolt of the biochemist against the idea of a restriction to human curiosity will continue. Biochemistry will continue to function as if all knowledge, even that of life, were accessible to human understanding. The past has taught that the solution of some problem always opens up a new one. New discoveries in physics, in mathematics, in theoretical chemistry, furnish new tools to biochemistry, new...
tools for the solution of old problems and the creation of new ones. So long as Life continues, the human mind will create mysteries and biochemistry will play a part in their solution” (1).

In addition to wide ranging and important research contributions, Levene was a great teacher (1). Of particular note, one of his collaborators on earlier nucleic acid papers was W. A. Jacobs who later became a distinguished alkaloid chemist at the Rockefeller University. Jacobs, in turn, was the research advisor of Lyman C. Craig, a distinguished biochemist, also at The Rockefeller University. A JBC Classic by Lyman C. Craig, the development of counter-current distribution methods, will be published in a future installment.

Levene was a member of the JBC Editorial Board for the first issue in 1905 and served for over 15 years. He was also a charter member of The American Society of Biological Chemists (ASBC).

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REFERENCES