Obituary

Wang Ying-lai (1907–2001)

Wang Ying-lai, a biochemist recognized as the first scientist to engineer synthetic insulin, died in his sleep on 5 May 2001 in a hospital in Shanghai, China. He was 93 years old.

Wang was born in 1907 in the remote village of Shanhou on the island of Jinmen (Quemoy), off the coast of Fujian, China. Although he lost his father at the age of two, and his mother when he was six, he pursued his education vigorously against all odds during a period of wars and political turmoil in China in the 1920s and 1930s. After graduating from Jinling University (now the University of Nanjing) with a degree in chemistry, he went to the University of Cambridge in 1938. His mentor, David Keilin, quickly recognized his talent, and Wang earned his PhD in 1941. He was invited to stay at Cambridge to teach and to continue his research at the Dunn Nutritional Laboratory, moving to Cambridge's Molteno Institute in 1944.

When the Second World War ended, Wang decided to return to China, against the advice of both Keilin and Professor Joseph Needham, the foremost historian of Chinese science. Wang's aim was to help the country to develop a world-class research base in science, and his first job was a research professorship at the Medical College of the National Central University. In 1948, he became a senior member of the Medical Research Institute of what was then the Academia Sinica (now the Chinese Academy of Science) — the most prestigious research institution in China. Shortly after the liberation of China in 1949, he was appointed deputy director of the newly established Institute of Physiology and Biochemistry of the Academia Sinica of the People's Republic of China.

From 1958 until he retired in 1984, Wang founded and headed the Institute of Biochemistry of the Academia Sinica in Shanghai. It was in this capacity, according to an essay he wrote in the *People's Daily* in 1991, that he recruited several prominent Chinese scientists who were until then working in other countries. Over several years he helped to plan and develop the national agenda for biochemistry and molecular biology. He also set up several national training programmes to recruit and train hundreds of young scientists. He founded, and was for many years the editor-in-chief of, China's premier journal, the *Journal of Biochemistry and Biophysics*.

Pioneer in the total chemical synthesis of biological molecules

By far the most significant of Wang's scientific contributions was the synthesis of crystalline insulin. This hormone, produced in the pancreas, controls the sugar content in the blood and is widely used to treat diabetes. Under Wang's leadership, scientists in the 'collaboration team on the synthesis of insulin' achieved the synthesis in 1965. Although similar attempts were being made in the United States and Europe, Wang's group was ahead of the game.

Beginning the project in August 1958, the first task of Wang's team was to synthesize the 20 amino acids — the fundamental building blocks of any protein. This enormous job also involved the separation of the D- and L-stereoisomers of each amino acid (only the L-isomers are found in proteins). Then, using these building blocks, the team produced the so-called A and B amino-acid chains of insulin. Wang later said that the greatest challenge was to align the six cysteine amino acids so that they would form the correct disulphide bonds — one within the A chain, and two between the chains. Any mismatch would lead to an inactive product. Biological assays and X-ray crystallography confirmed the authenticity of the chemically synthesized insulin.

The total synthesis of insulin from chemically synthesized amino acids represented a conceptual breakthrough in converting lifeless chemicals to a protein with biological activity. This was accomplished before the development of solid-state peptide synthesis, for which

R. Bruce Merrifield was to receive the Nobel Prize in Chemistry in 1984. In the 1970s, a team headed by Wang achieved the total chemical synthesis of another biologically significant molecule — a transfer RNA (tRNA), which is involved in protein synthesis *in vivo*. This led to Wang's lifelong interest in tRNA synthetases, the enzymes that produce tRNAs.

Despite Wang's successful work with insulin, China — soon in the throes of the ten-year-long Cultural Revolution and other political upheavals — effectively denied him the opportunity of being nominated for the Nobel Prize in Chemistry. During that period, scientists in China were abruptly banned from conducting research and from contact with researchers in other countries. Swedish scientist A. Tiselius (a member of the Nobel Prize committee) and Chinese-American Nobel laureate C. N. Yang independently suggested that Wang be nominated for the prize at that time. About the decade of lost opportunity, Wang said in an interview with the *Straits Times* of Singapore in 1986, "We were like the proverbial hare which took a long nap while others were not like the tortoise." Nevertheless, he won international acclaim in 1966, before the Cultural Revolution began, when he presented his findings on insulin at a European biochemistry conference in Warsaw. And in 1988, ten years after Deng Xiaoping introduced new policies of economic reform and openness, Wang was allowed to receive a special achievement award at the Miami Biotechnology Symposium.

Wang was a patriotic, humble and dedicated scientist. In his 1991 essay he wrote: "Science is the first productive force. To transform China into a modern socialist power, we must strengthen science and technology... This is the responsibility of every Chinese." Asked by the *Straits Times* about the honours he had received, he replied, "The honours should go to everyone in the team, including 30 members in our institute and many from five other institutes." Despite the hardship he endured during the Cultural Revolution, he harboured no bitterness.

He is survived by his two sons, Jia-hu and Jia-nan; his daughters-in-law, Huang Jin-pei and Zhang Hong-xia; and two grandchildren, Wei-zhen and Wei-xian.

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