Eugene Goldwasser

(1922–2010)

Discoverer of the hormone that regulates the production of red blood cells.

Eugene 'Gene' Goldwasser made one of the outstanding advances in twentieth-century biomedicine. Through decades of effort, he purified and initially characterized the properties of the major hormonal regulator of red-blood-cell production — erythropoietin (EPO) — an advance that rivals the discovery of insulin in its importance. Goldwasser's work was instrumental to the large-scale production of recombinant EPO, which since the late 1980s has been used to induce red-cell formation, especially in anaemic patients with chronic renal disease.

Hundreds of thousands of people now benefit each year from this therapy, which has a multibillion-dollar annual market. Goldwasser himself — who died on 17 December 2010, from renal complications associated with prostate cancer — did not become rich. He was more captivated by the science than the money. Today, studies of EPO continue to provide breakthroughs in cytokine and receptor biology.

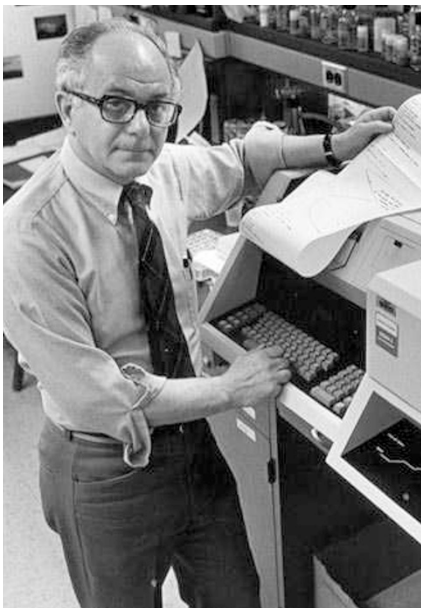
Goldwasser was born in Brooklyn, New York, in 1922, but the Depression forced his family to close their clothing business and move to Kansas City. In high school, Goldwasser's scientific interests were already keen, and landed him a scholarship at the University of Chicago, Illinois, for his undergraduate degree in biological sciences. Following two years of US army service as a biochemist working on anthrax at Fort Detrick in Frederick, Maryland, Gene returned to the University of Chicago and completed his PhD in biochemistry in 1950. As a postdoctoral fellow in Copenhagen he trained in cytophysiology — the study of the biochemistry of cells. In 1952 he returned to the University of Chicago. His initial studies there, at the Argonne Cancer Research Hospital, focused on new approaches to treating leukaemia.

HORMONE HUNT

The first clues to EPO's existence were found more than a century ago. This early work relied on highly variable measures of the number of mature blood cells, so the existence of such a substance remained contentious. In the 1940s, researchers had more precise measures of red-cell precursors, and named the proposed substance EPO; by the 1950s, more definitive results came from experiments using surgically conjoined rats and acutely anaemic animals. Still, no one knew exactly what was stimulating the formation of red blood cells.

In 1953, Goldwasser turned his attention to the EPO enigma. From 1956 to 1959, he worked aggressively and published 15 EPO-related papers, at a time when not everyone was convinced that EPO even existed. These included seminal studies published in *Nature* and *Science* showing that the kidney was a prime site of EPO production, and that cobalt could induce EPO production. He also developed a sensitive assay for EPO activity using a radioactive isotope of iron, which enabled the development of purification strategies.

Goldwasser originally estimated it would take him about six months to purify EPO.



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It took 17 years. EPO from any source existed in only vanishingly low quantities, and it tended to degrade during attempts at purification. In early studies, Goldwasser used litres of plasma from anaemic sheep, but even increasing the EPO concentration 1-million-fold didn't produce a pure sample. He tried many sources, and had some luck with urinary protein from anaemic Argentine patients with hookworm. A major breakthrough came on Christmas morning in 1975, when Goldwasser's colleague Takaji Miyake of Kumamoto University, Japan, hand-delivered a special gift: processed protein from more than 2,500 litres of urine from patients with aplastic anaemia. Others might have preferred fruit cake. Goldwasser and his colleagues used this unique gift to finally purify, in 1977, about 8 milligrams of human urinary EPO.

By the 1980s, other researchers began entering the field that Goldwasser had opened up. I joined Children's Hospital Boston and Harvard Medical School in Boston, Massachusetts, to work on EPO as a postdoctoral fellow. When I met Gene for the first time at a conference, he smiled and said: "It's nice to have you in the field, but should you not be in Chicago?" — working with him, in other words.

Goldwasser was captivated by EPO's basic science, but was also keenly aware of its potential clinical importance. In 1978, for example, he was involved with an early small clinical trial. At his university, he had initiated some paperwork for an invention disclosure, but this did not move forward. In the early 1980s, the idea of commercializing such work was quite new, as were the first biotechnology companies.

Goldwasser did agree to consult for a biotechnology company — Amgen. During the 1980s, some of the peptide fragments of human EPO were sequenced — a first step towards cloning the human EPO gene and producing clinically useful quantities of recombinant protein. As testimony to his excitement, Goldwasser unwittingly presented one such sequence at a national meeting. Fortunately for Amgen, the sequence turned out to have several mistakes, and no one else gained from the information. Amgen eventually took the lead in commercializing EPO.

Gene truly had a lifelong fascination for science. Had he chosen, he could have made great contributions in other areas of biochemistry: in 1953, for example, he published impressive work in *Nature* on nucleotide biosynthesis. From 1994 to 1998, he returned from retirement to chair the University of Chicago's biochemistry department, and continued his studies of EPO from 1998 to 2002, eventually retiring again at the age of 80. His unassuming nature, critical mind, collegiality and dedication — including to the Chicago Blackhawks ice-hockey team — will be greatly missed. ■

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