A tribute to Gene Goldwasser for *Experimental Hematology*

Eugene Goldwasser, who has made a lasting contribution to science and medicine, died from complications related to advanced prostate cancer at his home in Chicago on Friday December 17th, 2010. Generally regarded as the “father of EPO,” Gene’s laboratory at the University of Chicago succeeded, after 25 years of focused effort, in purifying firstly erythropoietin (EPO) from sheep and then human EPO. These achievements helped to launch the biotechnology revolution in the 1980s and improved the quality of life for millions of patients suffering from kidney disease and other anemic disorders.

Everyone who has heard of EPO knows that it is present in the body in miniscule amounts. After a long history of observation of the physiological response to high-altitude hypoxia and of the regeneration of blood after trauma, Carnot and Deflandre published observations in 1906 indicating that a humoral factor mediates the response to anemic hypoxia by stimulating red cell production. However, the Carnot feedback loop hypothesis was not generally accepted, and although Erslev and Stohlman and their colleagues provided conclusive evidence for the activity of EPO, its structure was unknown and had been variously described as a protein, a nonprotein, and a lipid.

Goldwasser embarked on this seemingly intractable problem with Dr. Leon Jacobson at the University of Chicago. Jacobson was interested in the suppressive effect of ionizing radiation on erythropoiesis and thought that EPO might be related to a putative radiation recovery factor. The rationale behind the study of EPO was that there seemed to be a humoral factor that caused an increase in erythropoiesis; this was interesting in its own right, so its isolation and characterization were an important endeavor. Inspired by recent advances in protein hormone purification and characterization, Goldwasser accepted Jacobson’s idea to recruit two medical students, Walter Fried and Louis Plzak, to their team in order to define the function of EPO. Goldwasser was confident that his laboratory, which specialized in standard fractionation methods, would be able to purify and characterize EPO within a matter of months. But it soon became clear that the validity of this assumption was under threat when they realized that the traditional assay for EPO activity, injecting animals and counting reticulocytes, was not only cumbersome, but was at best only semi-quantitative.

In parallel with ongoing studies on human EPO, Goldwasser and Charles Kung, who had joined the Laboratory in 1956 on the recommendation of the Professor of Botany, Lawrence Bogorad, persisted in working on EPO obtained from anemic sheep plasma. This had been made available through a contract with the Armour Pharmaceutical company, supported by National Institutes of Health funding awarded to Dr. Jacobson. This involved an eight-step process that achieved a 1 million-fold purification of the sheep EPO.

During this time, National Institutes of Health had also been funding the collection of urine from people with anemia due to hookworm infestation in Argentina and providing concentrates of this material to investigators. Dr. Chiba, who arrived in the Laboratory from Tokyo to work on the purification, found that these urine concentrates contained protease and sialidase activities that inactivate EPO, so they developed a harsh method of inactivating these enzymes with phenol, followed by precipitation with alcohol to ensure minimal loss of activity.

When progress in the purification of EPO seemed to have stalled, Dr. Takaji Miyake arrived in Chicago on Christmas Day 1975, carrying a package representing 2550 L urine. This had been obtained from a scheme instituted...
by Dr. Miyake and Dr. Kawakita to collect urine from patients with aplastic anemia in Kumamato City in Japan. Dr. Goldwasser, working with Kung and Miyake, systematically developed a protocol to enable them to purify about 8 mg pure human urinary EPO.

Working in the Goldwasser Laboratory in the 1980s was an exciting and formative experience for everyone. For a member of the laboratory staff, there was a strong sense of continuity of purpose. For a visiting fellow, it was edifying to be able to talk to Gene regularly, to be taught how to purify EPO first hand by Charles Kung, and do collaborative experiments with people like Ivan Rich, Nega Beru, Tania Weiss, and Nancy Pech. But the iconic memory is looking over Fran Wang’s shoulder to see the traces on the screen of the high-performance liquid chromatography instrument that she and Charles were using to separate out some of the highly purified fragments of the EPO protein. These valuable peptides would pave the way for cloning the EPO gene. Somehow it felt like history in the making, and that is indeed how it turned out.

This precious material was shared with Amgen, then a young biotechnology company, which developed a method to produce large amounts of recombinant EPO by genetic engineering. Sales of recombinant EPO now amount to billions of dollars a year for the major pharmaceutical companies, Amgen, Johnson & Johnson, and Roche. Most patients undergoing kidney dialysis are now given EPO, as well as many cancer patients who are suffering from anemia caused by chemotherapy.

Gene Goldwasser ran an outstanding laboratory. We know we will not be alone in finding in him an excellent mentor, both enthusiastic and inspiring. He never raised his voice but he always meant what he said. People from at least a dozen countries worked in Gene’s laboratory and everyone benefited from his knowledge and wisdom. Many of those have gone on to senior leadership positions in North America, Europe, and Asia.

Eugene Goldwasser was born in Brooklyn in 1922. During the Depression, his father’s clothing business failed and the family moved to Kansas City, MO. After high school and community college, he obtained a scholarship to the University of Chicago, where he obtained his bachelor’s degree and, in 1950, his doctorate in biochemistry. Dr. Goldwasser was the Alice Hogge and Arthur A. Baer Professor Emeritus of Biochemistry and Molecular Biology at the University of Chicago. He retired in 2002. Among many honors was his election as a Fellow of the American Academy of Arts & Sciences and the Prince Mahidol Award from Thailand for “outstanding performance and/or research in the field of medicine for the benefit of mankind.”

Gene’s love of science was always evident. He always spoke quietly and chose his words carefully, eyes twinkling as he explained something new. He combined this with a good, gentle sense of humor. Gene had a great love of literature and music. He was a voracious reader and was familiar with all the great Anglo Irish writers, especially Yeats, Shaw, Joyce, and Flan O’Brien. He loved music, everything from jazz to classical, but he had a particular passion for Bach.

Gene Goldwasser is survived by his second wife, Deone Jackman; three sons from his first marriage, Thomas, Matthew, and James; his two stepchildren, Tara and Tom Jackman; and seven grandchildren. His first wife, Florence Cohen, died in 1981.

EPO is now used to treat anemia in several million people each year. It has been a spectacular success when used appropriately for the treatment of patients with kidney disease and cancer. It has saved millions of blood transfusions. Gene’s own account of the EPO story, “A Bloody Long Journey,” is due to be published by xLibris shortly. He was an avid reader of The New York Times. How appropriate then that his favorite newspaper and many others around the world, including the Daily Telegraph in England, carried major obituaries for him.

Neither Gene Goldwasser nor the University of Chicago gained financially from his lifetime’s work on EPO. Neither submitted a patent. In his own characteristic way, Gene would maintain the altruistic position that the government had funded his research and that the taxpayers should receive the benefits of it. But many of his admirers have an entirely different view. Some of them have provided vivid and knowledgeable accounts of his achievements, with the aspiration that his work should be universally recognized in some way.

How fitting it would now be for those who have benefited from the use of EPO to endow a Chair at the University of Chicago in his memory. Such a memorial would at least help to ease the sense of loss ofGene Goldwasser, a wonderful colleague and friend to many.

Charles Kung
Terry Lappin