OBITUARY

Harry V. Gelboin, 1929–2010

Harry V. Gelboin, PhD, passed away at his home on Tuesday, April 13 after a brief battle with cancer. Dr Gelboin was born in Chicago in 1929. He received a B.S. in Chemistry from the University of Illinois and a Ph.D in Biochemistry and Oncology from the McArdle Laboratory for Cancer Research at the University of Wisconsin, Madison where he studied under the guidance of James and Elizabeth Miller. Prior to his years at Wisconsin, he worked as a development chemist for the U.S. Rubber Company. Dr Gelboin came to the National Institutes of Health (NIH) in 1958 working with Louis Sokoloff and Giulio Cantoni at the National Institute of Mental Health and later became chief of the Laboratory of Molecular Carcinogenesis at the National Cancer Institute. From 2000, he was active as a Scientist Emeritus in the Laboratory of Metabolism.

During his career at NIH, Gelboin published >400 papers and received numerous awards, including four NIH Merit awards, a technology transfer award, an honorary D.Sc. degree, a Nakasone Lecture Award and a Claude Bernard Award. He shared his gifted intellect by giving numerous keynote lectures, organizing research conferences, sitting on several committees that evaluated research proposals and editing a number of books on chemical carcinogenesis. His work was highly cited, including an Institute for Scientific Exchange Citation Classic for his paper on development of the widely used fluorometric assay for aryl hydrocarbon hydroxylase. He held eight patents related to his research.

Dr Gelboin pioneered in early research on the mechanisms of microsomal enzyme induction. He showed that treatment of animals with the liver microsomal enzyme inducers phenobarbital and 3-methylcholanthrene stimulated the incorporation of amino acids into microsomal protein and increased the formation of messenger RNA needed for protein synthesis. He also demonstrated microsomal enzyme induction in cultured cells. Subsequent studies by many others used cultured cells extensively for research on mechanisms of enzyme induction.

Dr Gelboin made a number of key contributions central to our understanding of the metabolic basis for the activation and detoxification of drugs and carcinogens. These discoveries involved the discovery and definition of the role of cytochromes P450 (P450) in the activation of procarcinogens. As a graduate student with the Miller’s, Gelboin demonstrated the in vitro metabolism of aminazo dyes to intermediates that covalently bind to protein. At the NCI, he went on to demonstrate covalent binding of carcinogens to DNA that was dependent on their metabolic activation by microsomal enzymes, later determined to be cytochromes P450. These observations served as the foundation for the concept of in vitro activation of procarcinogens to electrophilic derivatives that damage DNA, which is the basis for the Ames test. Gelboin discovered 7,8-benzoflavone, a specific inhibitor of a P450 that metabolically activates polycyclic aromatic hydrocarbons (PAH) leading to inhibition of PAH toxicity, DNA binding, mutagenicity and tumorigenicity. Gelboin’s laboratory was the first to introduce high-performance liquid chromatography to the study of PAH metabolism, and with this methodology, he precisely defined the metabolic route for formation of the ultimate electrophilic metabolite of benzo[a]pyrene that reacts with DNA. He went on to determine the substrate and product stereoselectivity and regioselectivity of several P450s for PAH metabolism using purified and recombinant enzymes. Coincident with development of the fluorometric assay for benzo[a]-pyrene metabolism, he discovered benzo[a]pyrene induction of specific P450s involved in benzo[a]pyrene metabolism in cell culture and in vivo, the latter leading to the identification of the polymorphic aryl hydrocarbon receptor locus in mice. This provided clues to the genetic control of this induction through the aryl hydrocarbon or Ah locus in mice. He was among the first to express recombinant P450s at sufficient levels for determining the role of individual P450s in drug and carcinogen metabolism. Through use of purified and recombinant enzymes, he produced monoclonal antibodies to many rodent P450s and to almost all of the major human P450s involved in the metabolism of drugs and chemical carcinogens. These reagents have been distributed to academic labs around the world and are widely used by the pharmaceutical industry in preclinical drug development. His impact on the fields of chemical carcinogenesis, drug and carcinogen metabolism and P450s was enormous.

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Dr Gelboin has left behind a number of former colleagues and trainees now working at laboratories around the world, many of whom have achieved leadership positions in the areas of drug and carcinogen metabolism and who continue to carry out his legacy of scientific excellence.

Dr Gelboin was a true renaissance man. His keen intellect extended far beyond science. Outside of the laboratory, he enjoyed photography, gardening and writing short stories and poetry. He is survived by his loving wife, Marlena; four daughters: Michele, Lisa, Sharon and Tamara; and nine adoring grandchildren.

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