

OBITUARY

Solomon Spiegelman 1914–1983

Professor Sol Spiegelman died on January 20, 1983. Spiegelman's career as a biologist spanned 40 creative years in which he had a profound impact on thinking and research in cancer. Spiegelman consistently demonstrated extraordinary insight into central issues of biology. He combined this perception with the unique ability to convert ideas into experimental reality. Spiegelman's contributions go well beyond his research accomplishments; as a teacher and colleague, he helped shape the development of an entire field.

His very first paper, published while he was still an undergraduate in 1937, asserts that cancer is a problem in cell population genetics and that rapidly dividing bacterial cells may provide a suitable experimental model. From this study of variation in bacteria, he concluded that mutation in bacteria obeys the same rules as in higher organisms. His work on bacterial variation was not accepted by leading geneticists of the period who held the view that "bacteria have no nucleus and therefore could have no genetics." This work provided an initial reflection of Spiegelman's foresight: he was not confined by preconceived dogma.

Spiegelman's efforts in molecular genetics focused on the RNA viruses, more specifically on the problems that RNA organisms encounter surviving in a universe of cells that use DNA as their genetic material and RNA as genetic messages. In a series of elegant experiments over 10 years, Spiegelman solved the problem as to how RNA phages exploit cellular information to survive and replicate in a host cell. Initial experiments on the life cycle of RNA and viruses led Spiegelman to reason that: (a) the injected RNA strand of the virus must serve directly as a message and be conserved during its translation into protein; (b) an enzyme should be found in cells infected with RNA viruses which is uniquely dependent on RNA to exhibit RNA-polymerizing activity; (c) RNA replicases must be specific since viral RNA replication had to proceed in cells replete with other cellular RNA molecules.

These predictions were confirmed by a series of elegant experiments in which he isolated the RNA replicase and characterized its functional properties. These studies immediately led to the important demonstration that the *in vitro* product was indeed biologically active; it was infectious. Spiegelman was thus the first to attain one of the major goals of modern biology, the "test tube synthesis" of biologically competent, replicating, and infectious viral nucleic acid.

These experiments then allowed Spiegelman to explore the evolution of a self-duplicating nucleic acid molecule outside a living cell. This situation mimics at least one aspect of early precellular evolution when environmental selection operates directly on the genetic material. These studies have led to the identification of increasingly simple replicating entities which provide simple models for understanding the mechanisms of replication and mutation.

During the course of these experiments, Spiegelman developed the formidable technology of DNA-RNA hybridization. It is recognized, perhaps best today, that molecular hybridization has been a most powerful tool in the successful development of molecular biology. It has been essential in analyzing the organi-

zation of the genome, in the study of differential gene expression, and most recently in the effective use of recombinant DNA technology.

More recently, Spiegelman changed fields, with the commitment that some laboratories with basic molecular biological expertise must begin to examine the problem of human cancer. In the early 1970's, with the aid of suitable animal models, Spiegelman began to explore the possible association of RNA tumor viruses with certain human neoplasias. His initial studies were prompted by the increasing awareness of the role of RNA tumor viruses in animal cancers and the assumption that human biology would not be so unique as to make animal studies completely irrelevant in human disease. Thus, sequences homologous to the RNA of the mouse mammary tumor virus were found in human breast cancer. Correspondingly, sequences homologous to the RNA of Rauscher leukemia virus were detected in RNA prepared from human mesenchymal tumors. More recent technologies clearly implicate the activation of endogenous cellular oncogenes homologous to known tumor viruses in certain human tumors.

Spiegelman then exploited these observations to develop a clinically useful diagnostic test for mammary cancer. To this end, an antigen immunologically related to a glycoprotein of the mouse mammary tumor virus has been identified in sections of human breast cancer. Prior to his death, Spiegelman was developing an assay that would meet the sensitivity levels required to detect this antigen in the body fluids of breast cancer patients. The development of such an assay would obviously be enormously powerful in the diagnosis and therapeutic management of human breast cancer.

Thus, Spiegelman's career had come full circle. In his earliest studies he suggested simple prokaryotic systems as a model for the study of human cancer; he developed such systems to generate the basic tenets of molecular biology and ultimately applied these principles to develop clinically useful diagnostic tests for human disease.

Born in 1914 in New York, New York, Professor Spiegelman received his Bachelor's degree from the City College of New York in 1939, his Master's from Columbia University in 1942, and his Ph.D. from Washington University in 1944.

For his scientific accomplishments, Spiegelman received honors and awards too numerous to recount here. His impact on biology does not result from his research accomplishments alone. He was a great teacher and colleague. Hundreds of students and fellows passed through his laboratory, each imbued with a critical sense and a love for science which characterized Spiegelman's own work. His impact on biology was indeed profound and is likely to continue to be felt for several decades.

Richard Axel
College of Physicians and Surgeons of Columbia University
Institute of Cancer Research
701 West 168th Street
New York, N. Y. 10032

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Richard Axel

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