TRANSFER AND EXPRESSION OF EUKARYOTIC GENES

Edited by
HAROLD S. GINSBERG
HENRY J. VOGEL

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College of Physicians and Surgeons
Columbia University
New York, New York

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Sol Spiegelman*

(1914–1983)

This symposium, "Transfer and Expression of Eukaryotic Genes," is dedicated to the memory of Sol Spiegelman, who died on January 21, 1983. The volume documents the rapid progress in our understanding of gene structure and function. As such, this dedication is particularly appropriate for Spiegelman had a profound impact on our thinking and research in molecular biology.

Spiegelman's 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 mode. 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. These studies allowed Spiegelman to accomplish one of the major goals of modern biology, the "test tube synthesis" of biologically competent, replicating, and infectious viral nucleic acid. Spiegelman then used this *in vitro* system to explore the evolution of a self-duplicating nucleic acid molecule outside a living cell. This *in vitro* 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.

*Commemorative remarks delivered at the symposium on Transfer and Expression of Eukaryotic Genes.

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. He was also among the first to demonstrate that reverse transcriptase could be used to copy cellular as well as viral messenger RNA's. These procedures have been essential in analyzing the organization 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 1970s, 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.

Prior to his death, Spiegelman was developing 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. 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.

Sol Spiegelman's career as a biologist spanned forty creative years in which he 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.

Richard Axel