

BIOLOGICAL EFFECTS OF POLYNUCLEOTIDES

Edited by
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and
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Biological Effects of Polynucleotides

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PREFACE

In recent years our horizons regarding the role of nucleic acids in biological systems have been expanded vastly by the finding that these molecules not only carry and transmit specific information but also can act as less specific triggers of antiviral factors and of immunological responses. The latter properties are of particular interest in terms of possible utilization in human and veterinary medicine and consequently led, in the last few years, to the development of a new research area that combines both fundamental and applied problems in a uniquely attractive way. Furthermore, the importance and the complexity of the problems has attracted investigators from many fields, including molecular biologists, virologists, immunologists, chemists, biophysicists, oncologists, pharmacologists, and clinicians. A discussion of new developments in this area of biological effects of polynucleotides, with particular emphasis on interferon induction and modification of immune responses, therefore, seemed a logical topic for one of the annual symposia that Miles Laboratories, Inc., has sponsored in recent years. The management of Miles accepted the suggestion with enthusiasm and thus once again earned the gratitude of the scientific community for sponsoring a catalytic meeting that was principally concerned with basic research problems and only tangentially with immediate applications. Springer-Verlag agreed to publish the proceedings of the meeting which was held at the Americana Hotel in New York City, June 4-5, 1970 and attracted an unusually large audience.

Many people have helped to make the meeting and this volume possible and we cannot possibly list them all. However, we would like to mention particularly and gratefully Dr. Walter Compton, President of Miles Laboratories, Inc., and Dr. Edward G. Basset of the Research Products Division of Miles who served as the symposium coordinator. We also are very grateful to Mr. Herbert Stillman, Production Manager of Springer-Verlag New York who helped efficiently in getting the present material between covers. Indispensable for the preparation of the discussions and for the numerous details involved in bringing continuity in style of the manuscripts have been

the long hours of work by Evelyn Sales of Johns Hopkins University, for which we are most indebted and thankful. Our special thanks, however, must go to the contributors who not only shared their findings and views with us but gave us permission to edit their discussions without seeing the finished product. We hope that by such editing we made the discussions more readable without harming the spirit and accuracy of the discussants' words.

February 1971

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INTRODUCTORY REMARKS*

Nearly 50 years ago James Cabell made the observation that "The optimist proclaims that we live in the best of all possible worlds; the pessimist fears this is true". We are being constantly warned of impending doom of our civilization and even of our species. Whenever a society becomes aware of a crisis that threatens its survival, there is immediately a search for the cause and cure of this crisis. During the past 10 years we have experienced a variety of thrusts in different directions, many of them labeled some kind of war: war on poverty, war on hunger, war on racial bigotry, and now war on pollution. It would seem that the American character can only respond to a challenge by taking the stance of a warrior going into battle to slay the enemy, an oversimplification of the issues which reduces the objective to a simple "victory". Certainly this posture has dominated our action in Vietnam.

In remarkable contrast to this single purposed approach to some of the major problems of our world today is the multivariant approach used so successfully during the past two decades in the fields of molecular biology. If there are "victories" in molecular biology, they are the creation of self-consistent models or the elimination of regions of ignorance; they are victories of understanding rather than of conquest. Nevertheless, molecular biologists have been under attack because of their "reductionist" approach to their subject, an attitude that has led to a framework of concepts that has become almost a dogma, replete with myths and the equivalent of sacred cows. It is a transformation of nineteenth century attitudes of physics into twentieth century biology. Such a condition, if it exists (and I think there is some evidence for believing that it does), provides the basis for the kinds of scientific revolution described by Thomas Kuhn. This can be very threatening to those whose careers and accomplishments are measured on the basis of a particular paradigm as well entrenched as that of molecular biology. But this is the inevitable price for the evolution of man's understanding of

* Presented at the banquet preceding the symposium.

his universe and of himself. It is clear that at some stage in the evolution of a science the reductionist's approach reaches a limit of detail and understanding or of suitable model constructs. At this point the holistic approach must become operational. Indeed, it is fair to conclude that the degree of maturity of a scientific field is often times reflected in the extent to which the model constructs reflect the holistic perspective.

Related to but not identical with this is the increasing concern over the relationship of the models of molecular biology to man, his society, and his concerns. The phrase, "social relevance" included, for example, in the NSF program for Interdisciplinary Research Relevant to the Problems of Society (IRRPOS) reflects this concern. The present fiscal draught in the biomedical research field, especially in "nonmission-oriented areas", may be the consequence of misplaced priorities resulting from a misunderstanding of the significance of such research in the larger framework of man's world, but if so it is an inconsistent and illogical conclusion in the face of such priorities as the Vietnam adventure, the Apollo program, and the SST. But a more reasonable and, perhaps, modest explanation is an apparent irrelevancy of the goals of some of the fields of biomedical research with those of society. When the research does not appear to contribute to the solution or to alleviate the crises facing society, society ceases to support it or even tolerate it, especially if there is any suggestion that the research may contribute to the magnitude and complexity of these crises. One serious consequence, seen prominently in our rebellious younger generation, is the rejection of the rational methods of understanding and the growth of anti-intellectualism and "quickie" solutions. One of the major responsibilities of scientists and engineers today is to fight this trend by educating the public to the indispensable need for rational understanding, and by applying the methods of science and technology to the problems of man's troubled world.

It is true, although some would deny it, that science and technology in the present condition of mankind can only buy time, that is, delay the predicted catastrophes while man comes to grips with himself and his institutions. But time is a resource we can ill afford to squander or ignore. This Symposium, like its predecessors, constitutes a part of a sequence that reflects an attempt to provide a particular and timely perspective toward molecular biology and related biomedical areas of research; interdisciplinary in its content to emphasize a more comprehensive view of the topics and somewhat mission-oriented to indicate the relevancy of the topics to man and his society. The relevancy consists of the contributions of the fields of study toward and understanding of man and his world and the application of the information and concepts of these fields of study in the technologies employed in finding solutions to the problems of man.

It will become apparent in the following articles that there are several "socially relevant" areas but I would stress one in particular. One of the technologies that is answering the need for time is agriculture. Although I agree with the Paddocks and the Erlichs regarding the ultimate inability of agricultural technology to meet the demands for food as long as the world population increases exponentially, nevertheless, without the advances of agriculture the plight of the world would already be disastrous.

However, the problems of adequate food production, especially of protein, extend beyond high yields per acre through improved genetic strains and application of chemical fertilizers. Equally important are the competitors of man for the same food resources. Clearly the problem of pesticides and their impact on the ecology of the earth points out the fallacy of single-purposed approaches to problems of this nature. But similar complex problems looms on the horizon in the production of animal protein. As the world population of mammals and fowls increase at a rate faster than that of man, and their density and highly inbred character increases, the prospects for massive epidemics increase alarmingly. Contributing to this hazard are the modern methods for fast transportation which makes isolation increasingly difficult.

To put these remarks in perspective we could examine the economic cost. The recent foot-and-mouth disease outbreak in Great Britain cost that nation over \$ 300,000,000 just to eradicate it. It has been estimated that the annual loss in South America from this same disease is equivalent to the annual U.S. economic aid given there. Comparable losses occur in Africa and in Asia. Similar statistics can be cited for the poultry industry abroad and in the United States. Israel, which used to be an exporter of poultry products, is now an importer. These chronic losses are increasing at a time when the need for increased protein production is becoming critical.

What these considerations say, of course, is that the prevention of viral epidemics by methods other than those now employed (eradication by destruction of the diseased and exposed animals and isolation by quarantine) must be replaced by methods that directly attack the viral-host interaction. That challenge makes the topics of this Symposium particularly significant and relevant, a fact that has already been emphasized by Philip Handler in his defense for continued Federal support for basic biomedical research. If molecular biology is to develop beyond the model-building stage it appears to this observer that some of the best opportunities lie in the research studies represented by this assembled group of investigators.

June 3, 1970

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Part I

Template Effects and Their Modification

