Preface

Only a few instances in the history of biological research, and indeed in the history of science, were as dramatic and revolutionary as the birth and the first decades of molecular biology. Among the landmark discoveries that were made between the early 1950s and late 1970s were the establishment of DNA as the carrier of genetic information, the discovery of its double helical structure, and the identification of its semiconservative mode of replication. Of equal importance were the deciphering of the genetic code, the discovery of bacterial messenger DNA, the elucidation of the regulation of bacterial gene expression, and the identification of the basic components of the protein synthesis machinery. Several years later the split nature of eukaryotic genes and RNA splicing were discovered and recombinant DNA technologies came into wide use. At the same time methods were developed to determine amino acid sequences in proteins and nucleotide sequences in DNA. Structural molecular biology had its parallel triumphs with the determination of the three-dimensional structure of the proteins myoglobin and hemoglobin. Not less importantly than its concrete achievements, molecular biology instituted the principles of reduction and of mechanism as a way to explain biological phenomena.

This book describes selected key experiments in molecular biology in their historical context. Its intended readers are graduate students in the Life Sciences and the History of Biology as well as practicing scholars in both fields. Although today's practitioners of molecular biology are technically skilled and knowledgeable about current developments in their specific areas of research, many are unfamiliar with the origins and the recent history of their own field. In 1953, at about the time of the birth of molecular biology, André Lwoff wrote (Ref. 1, p. 271):

> *For many young scientists the future is more important than the past and the history of science begins tomorrow.*

More than four decades later, well after molecular biology had already become a full-fledged forefront discipline of life sciences, Benno Müller-Hill commented (Ref. 2, p. 1):

> *Molecular biology has no history for the young scientist. What happened ten years ago seems prehistoric and thus of no interest.*

Remarking on Müller-Hill's stance, Sidney Brenner opined[3]:

I hold the somewhat weaker view that history does not exist for the young, but is divided into two epochs: the past two years, and everything that went before. That these have equal weight is a reflection of the exponential growth of the subject, and the urgent need to possess the future and acquire it more rapidly than anybody else does not make for empathy with the past.

This situation of technical proficiency but unfamiliarity with the history of molecular biology is inverted to an extent among historians of biology. Books and articles by professional historians of science on the history of molecular biology go deeply into various historical, sociological, economic, political, personal, and philosophical aspects of the subject. Yet, oftentimes the concrete theoretical and technical particulars of critical experiments are taking a secondary place to the mentioned other aspects of the history of molecular biology.

This *Landmark Experiments in Molecular Biology* book grew out of an eponymous graduate course that I have taught at the Faculties of Medicine and of Biology of my own institution and at the Weizmann Institute of Science. Similar to Lwoff, Müller-Hill, and Brenner, it was also my experience that graduate students in molecular biology and younger senior faculty were largely ignorant of the historical roots of their own field. However, contrary to the assertions of Lwoff, Müller-Hill, and Brenner, I discovered that many among those who attended the course were keenly interested in the history of molecular biology. Although I had no similar direct contact with historians of science, it is likely that they may find complementing interest in detailed analyses of historically important experiments.

This volume attempts to address the needs of both practitioners and historians of molecular biology by combining a history of important junctures in the field with technical analyses of concrete key experiments. The book focuses on critical points at the prehistory and dawn of molecular biology (late 19th century to the 1940s) and during its golden age (1950s–1970s). By combining appraisals of the history and of the science of selected milestone experiments, this book offers molecular biologists a primer on the history of their field and presents historians of biology with technical analyses of critical experiments.

One common deficiency of texts on molecular biology is that they offer incomplete description of the evolution of ideas and of empirical findings. This was best put by Müller-Hill (Ref. 2, p. 1):

In the textbooks, almost everything is solved and clear. Most claims are so self-evident that no proofs are given. Old, classical experiments disappear. They are self-evident. Old errors in interpretation not mentioned. Who cares?

In this book I tried to provide a more realistic description of the nonlinear progression of molecular biology. Thus, theories and hypotheses that had

been proven incorrect are described alongside productive ones. Similarly, erroneous or lacking interpretations of experimental observations are examined side-by-side with ultimately fruitful interpretations.

Finally, even with its limited focus on landmark experiments, this book is definitively not comprehensive. The experiments that are described here were selected because of their fundamental contribution to our present understanding of key molecular elements of life. Yet, because of its limited space, this volume ignores many important theories and experiments. First, the book's main focus is on principal developments in the informational branch of molecular biology. Thus, except for some discussion in Chapter 5, "Discovery of the Structure of DNA" of the early phases of structural molecular biology, this volume does not cover advances in this equally important division of molecular biology. Second, due to its limited space, the book mentions only in passing or entirely omits cardinal discoveries in informational molecular biology. Among the many important developments that are not covered are the greatly influential operon model, mechanisms of regulation of gene expression and of enzyme action, the development and wide implications of the techniques of protein and DNA sequencing and of polymerase chain reaction, and the emergence of recombinant DNA and of cloning. The interested reader would certainly find material on these and additional facets of molecular biology in some of the books and articles that are listed in Chapter 1, "Introduction" of this volume.

Finally, it is a privilege to give thanks to individuals who made this book possible. I am indebted to my colleagues and friends, Drs Avram Hershko and Herman Wolosker, for patiently serving as a sounding board to my evolving ideas on different elements of this book. The able and dedicated help of members of the Elsevier/Academic Press editorial staff is gratefully acknowledged. Thanks are due to Jill Leonard, Senior Editorial Project Manager at Elsevier, for her early and sustained faith in this project. I am also grateful to the Editorial Project Managers who accompanied the book at its different stages of development: Elizabeth Gibson, Halima Williams, and particularly to Fenton Coulthurst and my Editor Melissa Read. Last but not least, in addition to a long list of my debts to her, I am grateful to Iris for standing by me throughout the often torturous writing of this volume.

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