NUCLEIC ACID RESEARCH

Future Development

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Preface

The coming together of scientists at meetings to discuss their newest experiments and ideas has long been an integral part of the "scientific scene." Through such meetings, we frequently hear of important new matters before they formally appear in print and, frequently, abruptly change our research directions. Equally important, we meet persons with common interests, often leading to collaborative efforts, which often quickly prove or deny our current ways of thinking. The failure to attend or to hold scientific meetings can have dire consequences, ranging from the persistence with research problems that already have been solved, to the failure to learn in time the new facts that would necessarily lead one to changing the ways we should look at a scientific question.

For many years after World War II, the United States alone had the resources to do science at its best and, correspondingly, served as the nucleus to which the best of the outside world's scientists of necessity had to visit. By the mid-1960s, however, the return of economic prosperity to much of Europe gave it again the opportunity to do first-rate science, with the creation of the European Molecular Biology Organization reflecting the fact that the traffic of biologists across the Atlantic was increasingly a two-way street.

Now with the emergence in so much of Asia of real economic prosperity, the possibility exists that Asia, like North America and Europe, will soon be doing molecular biology at its best. Toward this end, it now seems desirable to create the organizational structure that will promote the holding in Asia of high-level meetings and training courses in molecular biology. Toward this objective, in the spring of 1980, Professor Shiro Akabori, Professor Itaru Watanabe, and I invited Drs. Arthur Kornberg (Stanford), Niels Jerne (Basel), John Tooze (EMBO), Obaid Siddiqi (Bombay), and Ying Lai Wang (Shanghai) to come to Tokyo to join with us and Professors Takashi Sugimura (Tokyo), Hamao Umezawa (Tokyo), and Osamu Hayaishi (Kyoto) to help form the Asian Molecular Biology Organization (AMBO). There we jointly drew up plans for the holding in 1981 of several training courses (Monoclonal Antibodies and Flourescent Methods for the Study of Cell Structure), as well as the planning of a major symposium on "The Future of Nucleic Acid Research."

This volume reflects the proceedings of this symposium that came to be held in early December of 1981 in Kyoto. To say the least, it was most successful as reflected by the most distinguished list of scientists that accepted our invitations as well as by the enthusiasm of the audience that numbered more than 600 attendees. In choosing

the speakers, we sought for a balance of speakers from Asia and outside Asia. In this way, we could both illustrate the already superb quality of many Asian laboratories, as well as the need to invite distinguished scientists from the United States and Europe to give the meeting the high intellectual diversity that now marks DNA research on the world-wide scene.

The holding of the meeting required much intelligent planning, as well as major financial support. Here we are most indebted to Suntory Ltd. (Osaka) for the funds that enabled us to bring so many speakers from outside Japan. I also wish to emphasize the successful efforts of Professor Itaru Watanabe in finding the monies that enabled us to have in the audience leading scientists from South Korea, The Peoples Republic of China, Singapore, Indonesia, Thailand, Viet Nam, and the Philippines. Equally important has been the efforts of Professor Kiyoshi Mizobuchi in creating the secretariat needed in our use of the Kyoto International Conference Center, as well as functioning as the editor of this volume.

JAMES D. WATSON
April 8, 1982
Cold Spring Harbor Laboratory

Contents

CONTRIBUTORS ix
PREFACE xv

Introduction 1
Francis H. C. Crick

Part I STRUCTURE OF DNA AND CHROMOSOME AND INTERACTION OF NUCLEIC ACIDS WITH PROTEINS

Chemistry and Biology of Left-Handed Z DNA 11
Alexander Rich, Andrew H. J. Wang, and Alfred Nordheim

The Geometry of A, B, and Z DNA 35
Richard E. Dickerson, Benjamin N. Conner, Mary L. Kopka, and Horace R. Drew

Conformational Flexibility and Its Role in the Structure of DNA 61
V. Sasisekharan

Crystal Structure Studies on DNA Oligomers 79
M. A. Viswamitra, Z. Shakked, D. Rabinowich, O. Kennard, W. B. T. Cruse, E. Egert, and S. A. Salisbury

Nucleosome Structure and Chromatin Superstructure 91
A. Klug

Chromatin Fine Structure Analysis of the Histone Genes of *Drosophila melanogaster* 113
Abraham Worcel and Paul Schedl

Transposons as a Means to Clone the *White* Locus of *Drosophila* 125
W. J. Gehring, R. Paro and M. L. Goldberg

Poly(ADP-ribosyl)ation of Nuclear Proteins 143
Kunihiro Ueda, Masashi Kawaichi, Norio Ogata, and Osamu Hayaishi

Structural Models for DNA-Protein Recognition 165
Sung-Hou Kim

One Model for Protein Recognition of B-DNA Sequences Suggested by the Structure of Catabolite Gene Activator Protein 179
T. A. Steitz, D. B. McKay, and I. T. Weber

Part II GENE ORGANIZATION OF EUKARYOTES

Genetic Origins of B and T Cell Antibodies 197
Susumu Tonegawa, Yoshikazu Kurosawa, Bonnei Blomberg, Gunther Heinrich, Werner Haas, and Harald von Boehmer

Immunoglobulin Genes Move during Differentiation as Well as Evolution 213
Tasuku Honjo, Tohru Kataoka, Naoki Takahashi, Akira Shimizu, Shintaro Ueda, Masahiro Obata, Toshio Nikaido, and Shun-ichi Takeda

Solid-Phase Synthesis of Polydeoxyribonucleotides for Biological Applications 227
R. Bruce Wallace and Keiichi Itakura

Structure and Regulation of the Corticotropin β-Lipotropin Precursor Gene 247
Shigetada Nakanishi and Shosaku Numa

Structure and Expression of the Cloned Genes for Human Interferon-β 259
Tadatsugu Taniguchi, Shigeo Ohno, and Chikako Takaoka

Serine Proteases: A Tissue-Specific Multi-Gene Family 279
Anthony J. Mason, Robert I. Richards, and John Shine

Part III GENE EXPRESSION OF EUKARYOTES

The SV40 72 Base Pair Repeat: An Amazing Enhancer of Eukaryotic Gene Expression 291
R. Everett, R. Hen, P. Moreau, and P. Chambon

Structure and Function of Small Ribonucleoproteins from Eukaryotic Cells 309
J. A. Steitz, C. Berg, E. Gottlieb, J. A. Hardin, C. Hashimoto, J. P. Hendrick, M. Hinterberger, M. Krikeles, M. R. Lerner, S. M. Mount, I. Pettersson, J. Rinke, M. D. Rosa, and S. L. Wolin

The Structure and Regulation of Early Region 2 Encoding the DNA Replication Functions of Human Adenoviruses 319
Louise T. Chow, Jeffrey A. Engler, Mara Rossini, Richard A. Guilfoyle, Mark van Bree, and Thomas R. Broker

Expression of SV40 Large T Antigen in Bacteria 349
Tsu Hsun Kung and Robert Tjian

Transforming Genes of RNA Tumor Viruses 359
Hidesaburo Hanafusa and Tatsuo Takeya

Identification, Isolation, and Characterization of Human Transforming Genes 377
M. Wigler, K. Shimizu, M. Perucho, M. Goldfarb, and J. Fogh

Part IV GENE EXPRESSION OF PROKARYOTES

Flagellar Phase Variation in *Salmonella:* A Model System Regulated by Flip-Flop DNA Inversions 395
Tetsuo Iino and Kazuhiro Kutsukake

The Molecular Basis of Spontaneous Deletions 407
Alessandra M. Albertini, Michéle P. Calos, Murielle Hofer, and Jeffrey H. Miller

Versatile Expression Cloning Vehicles Using the Lipoprotein Gene of the *Escherichia coli* and Their Application 419
Masayori Inouye, Kenzo Nakamura, Sumiko Inouye, and Yoshihiro Masui

Structure, Function, and Biosynthesis of *E. coli* Elongation Factor Tu 437
Yoshito Kaziro

A Model for the Coordinate Regulation of Ribosomal Protein Synthesis 457
Masayasu Nomura and Dennis Dean

Part V DNA REPLICATION AND RECOMBINATION IN PROKARYOTES

Regulation of ColE1 DNA Replication 475
Jun-ichi Tomizawa

Enzyme Studies of ϕX174 DNA Replication: Structure and Function of dnaB Protein, an Essential Replication Protein in the Primosome 487
Ken-ichi Arai, Naoko Arai, and Naoki Nakayama

RNA Priming for Discontinuous DNA Chain Elongation and for Replication Origin of *Escherichia coli* 509
Tuneko Okazaki, Yuki Kohara, Tohru Ogawa, Kinya Yoda, Asao Fujiyama, Tetsunori Seki, Tatsunobu Hozumi, Takako Kitani, Hachiro Yasuda, and Takaaki Miyasaka

Recombination Activities of *Escherichia coli* RecA Protein: Synapsis and Strand Exchange 535
Charles M. Radding, Chanchal DasGupta, Anna M. Wu, Roger Kahn, and John Flory

DNA Supercoiling and DNA Topoisomerases 549
James C. Wang

Summary 567
S. Brenner

INDEX 571

Introduction

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The title of this symposium "The Future of Nucleic Acid Research" indicates that we are going to discuss both present nucleic acid research and future prospects. Molecular events in the eukaryotic nucleus, which is the focus of attention of this sort of molecular biology at present, will be emphasized.

We are well into the beginning of a second revolution in molecular biology, that associated with the term recombinant DNA. At present it is possible to take an organism like man, which has a haploid number of 3 x 10^9 base pairs, and by selecting one gene, just a few thousand bases, or one part in a million can obtain enough of that material to do useful things with it, such as sequencing the DNA. What is very obvious is that in a diploid organism there are only two molecules of that DNA per cell. Seven years ago it would have been impossible to do that with so little DNA. This is now done on a daily basis, because of the new and powerful techniques which have come into use in the last few years. Some are the usual techniques, with suitable modifications—chromatography, radioactivity, nucleic acid hybridization, and so on. However, there are two very powerful methods which have been at the basis of recombinant DNA. One, which distinguishes it from conventional organic chemistry, is the extensive use of enzymes to perform chemical jobs that we want done. The second is the use of biological magnification. Using this process, one molecule is magnified to obtain enough for many purposes. These new developments are behind many of the things discussed in this volume.

There are a number of problems with which we are confronted. A major dithionite is the nature and the control of eukaryotic genes. What happens in prokaryotes is fairly well understood. This is not yet true in eu-

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karyotes, since neither what is meant by a gene in eukaryote nor the control mechanisms are yet known. In addition, whereas in prokaryotes there is only what might be called a sensible amount of DNA, in eukaryotes (at least in many of them) there seems to be an excessive amount of DNA, and we are not at all clear what all of this extra DNA is doing. Closely related to that is the actual act of expression of the gene. RNA transcription and nuclear processing is much more elaborate that might have been guessed a few years ago.

This volume does not include details about protein synthesis, although nucleic acid in both messenger RNA, ribosomal RNA, and transfer RNA is involved. The emphasis is more on nucleic acid in other roles.

Of great import is the interaction between nucleic acids and proteins and, in particular, the interaction of DNA with proteins in many different contexts. Specific problems arise out of these general ones.

Molecular biology and recombinant DNA have attracted much attention in the press, at least in the United States. The study of DNA is concerned not only with academic problems but also with its applications:medical problems, such as, cancer and also a number of industrial problems, such as, production of molecules of insulin, interferon, and so on, that are used as drugs in medicine or in new methods of diagnosis. There are also agricultural problems, such as obtaining energy from biomass. For industrial chemicals, such as, fructose, the problem is whether they can be made cheaply enough by methods involving recombinant DNA. Most of these problems will involve the construction of new organisms which may be used either as organisms or as a source of enzymes. One of the major difficulties is how to stabilize these enzymes. As at the beginning of any other technological revolution, it will be the applications that we have not thought of which, in 10 years, will probably be the most striking. There are also other problems which must be considered on a much wider scale in the future. For example, how does an organism like *E. coli* arrange its complete organization and how do all the controls work together in a global manner. We do not know enough about *E. coli* to see how the factory really runs. There are also the more extensive fields of embryology and of neurobiology and, eventually, those of evolution and natural selection. It is because nucleic acid is at the foundation of all these subjects that future work in this area is bound to have enormous importance for the future of biology as a whole.

In this volume, the general structure of DNA is presented first. This is due to another technical advance not yet mentioned—the chemical synthesis of DNA. Astonishing strides have already been made. For example, there is the synthesis of a large stretch of DNA, much longer than one would ever have thought could have been done, by the workers at ICI. Small pieces of DNA, about six or ten or twelve base pairs long, are now available in sufficient quantity and purity that they can be crystallized.