A Symposium Sponsored by THE JAMES W. McLAUGHLIN FELLOWSHIP PROGRAM University of Texas Medical Branch

An outstanding group of investigators consider the significant advances and pertinent information on both tissue and bacterial cell structure and their interrelationships

HOST-PARASITE RELATIONSHIPS IN LIVING CELLS

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Edward W. Dempsey

Rene J. Dubos

R. Dulbecco

Carl E. Georgi

Robert A. Good

John H. Hanks

Stuart Mudd

C. M. Pomerat

M. G. Sevag

Jerome T. Syverton

Harriet M. Felton

Each contributor was chosen because of his unique contributions in special disciplines and THE APPLICATION OF THE CONVENTIONAL FUNDAMENTAL SCIENCES TO THE DYNAMIC THREE-DIMENSIONAL ENVIRONMENT OF THE LIVING CELL.

Keynote articles on materials and methods employed in current investigations of tissue and cell physiology.

The role of the electron microscope in the study of both tissue and bacterial cell structure (many descriptive illustrations)

Current status of cytopathology (three pages of color plates)

Current concepts of tissue and bacterial cell physiology

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THE JAMES W. McLAUGHLIN FELLOWSHIP PROGRAM
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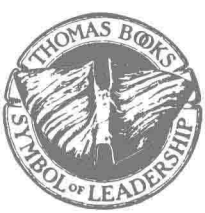

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PREFACE

CELL PHYSIOLOGISTS and microbiologists recently have been delighted with the reciprocal benefits produced by a common meeting in the fruitful study of viruses with the techniques of mass cell culture. The rewards which have accrued to date may represent only a small part of what may be available if interdisciplinary exchanges in the favorable atmosphere of willingness to yield "territorial sovereignty" can continue.

Investigators who know that their main preoccupation must remain focused on fundamental problems of cell morphology must at least show tolerance with those colleagues who would complicate their studies with the admixture of parasites and tissue cells. Admittedly, we need to know a great deal more about fine structure before reliable interpretations can be made concerning the presence of virus particles in, for example, a certain area of the endoplasmic reticulum. Conversely, microbiologists who call for bucketsfull of clone strain cells must show forbearance with workers whose interests lead them to a preoccupation with fibrogenesis, myelogenesis or pinocytosis. Success in the production of high viral titers from mass cell cultures in some quadrants has risked the development of a myopia concerning what may be learned of host-cell–parasite relationships with the use of tissue cultures.

In informal discussions on the evolutive history of cell culture methods, William Bloom refers to the development of a dichotomous tree. In his analogy, one group of branches derive from an arm which represents cell GROWTH. Here investigations on mitotic rates, nutrition and synthetic media are closely associated. Carrel's insistence on the maintenance of cell lines at rapid multiplicative rates was quickly supported by the work of Albert Fischer, L. E. Baker, and A. H. Eberling, and expanded by a brilliant group of contemporary students. Almost as a threatening shadow to shining exploits represented by Carrel's persistent chick heart culture, Alexander Maximow gave bedside care to a rela-

tively small number of cells which were encouraged to vegetate and decorate themselves without the responsibilities of intense proliferation. This attitude produced the other main branch—DIFFERENTIATION—of our tree with a parallel brilliant foliage of distinguished workers such as Ross Harrison, the Lewises, Giuseppe Levi and Honor B. Fell.

It has become a matter of practical pedagogy to employ this historical sketch to assist students in recognizing that there is a degree of specialization in the methods of cell culture appropriate to the study of GROWTH, in contrast to those which may primarily be directed at an analysis of DIFFERENTIATION. For example, the regeneration of Nissl substance cannot be expected if explanted nervous tissue is frequently cut and transferred to new situations. Chromophilic substance, neurofibrils and myelin are luxuries of a sedentary life! Conversely, mitotic activity in fibrocytes cannot be studied with profit without frequently imposing traumatic experience of subculture with due attention to the resulting high metabolic turnover.

For the microbiologist, cytological adventures in the establishment of replicate clone strains, the quest for a completely synthetic diet for particular species of elements, the production of massive quantities of cells with balance sheets describing the accompanying metabolic changes will remain of fundamental interest.

Similarly, the definition of submicroscopic cell architecture with the aid of electron microscopy correlated wherever possible with the dynamic records made available by phase cinematography of living systems increasingly will attract students of infection and immunity. In this realm of operation, much remains to be done to interest students in intracellular biochemistry. Inquiries directed at proving causal relations between the activity of mobile structures within the cell and demonstrable biochemical reactions are greatly to be desired. For example, are all mitochondria totipotent with respect to certain batteries of enzymes or are some of these bodies in special cytoplasmic loci dedicated to particular biochemical events? Individual differences between seemingly identical morphological cell types should not be a problem exclusively interesting to embryologists.

As has been stated by John Hanks, we have worshiped the role of antibodies, disregarding cellular metabolism. Stuart Mudd's insistence, based on the pioneer work of Max B. Lurie, that hormones may modify the role that macrophages may play in bodily defense, focuses attention not only on cell individuality, but on the plasticity of the intracellular environment. The richest dowry of this symposium may emerge from Rene Dubos's statement that: "Analysis of the phenomena of parasitism will become easier when techniques are available to study host-parasite relationships in tissue cultures under a wide range of biochemical circumstances."

When traveling at an altitude of 18,000 feet I often look down on a city with its central business area of tall buildings, its gridwork of suburban sections, perhaps a river with attending canals, fingerworks of railway sidings, fuel storage tanks and a clear periphery of open farmlands. Possibly wearied by previous hours at the microscope, I am wont to think that today we can appreciate the workings of a cell about as well as a Martian who could imagine, in a not-too-close view of our planet, that in the tall buildings there might be movement in the vertical direction surrounded by a crisscross of much horizontal activity. It is easy to drift into the construction of analogies in the division of labor related to the structural differentiation which we know exists in a distant city with the possible roles of juxtanuclear zone, mitochondria and the exoplasm! Since it is traditional in the study of parasitic relations to think of front lines of defense, infiltration, the destruction of communications and the paralyzing of organizational centers, our reverie provides easy access to analogies for those of us who have breathed the military air of the first half of the 19th Century. However, with the optimism deserving of a great age of scientific discovery, it becomes not unduly difficult to readjust our outlook and see that in the statements bound between these covers there is hope that our cell-city is in the process of being understood as a molecular society endowed with extraordinary capacities for cooperative effort, subject to terrible disequilibria, yet potentially capable of restitution to wholesome community harmony.

C. M. Pomerat

INTRODUCTION

THE University of Texas Medical Branch is very proud to be able to welcome all of you to the first James W. McLaughlin Symposium. We join in honoring the memory of a Professor of Medicine who served on this faculty from 1897 to 1905. It is known that he was a man "wise beyond his years" who had a particular interest in problems of infection. He apparently had some ideas that were considered at that time rather improbable, but which today are part of our standard fact information. Professor McLaughlin's son felt that his great respect and admiration for his father could best be shown by bequeathing to this school a substantial sum of money "to establish fellowships for the study of infection and immunity." We are happy today to have with us a group of great men whose lives have been dedicated to the pursuit of problems concerning these fields. The subject of host-parasite relationships as seen in living cells is a dynamic and exciting one and seems to be an appropriate theme for this first McLaughlin symposium.

The program will include eight formal keynote papers, to be presented by a group of outstanding investigators. Each will be followed by a short discussion period. The evening session will be very informal, and will be devoted to an interchange of ideas on the topics or questions which have arisen during the day. We are all looking forward to a most stimulating experience.

At this time I would like to introduce Dr. John Truslow our Dean and Executive Director, who has recently come to us from the Medical College of Virginia.

HARRIET M. FELTON

WELCOME

THANK YOU, Dr. Felton. It is a great privilege to welcome such distinguished visitors to Galveston as you have assembled for this unique symposium. I particularly enjoy the role of spokesman for the type of welcome for which Galveston is capable because I have had the experience so recently and so vividly myself as a newcomer.

This promises to be a thrilling experience for us all through the day. At a time when the pressures have been so great for applied and project investigation here is a biological field in which really basic research is being conducted. Here is a basically interdisciplinary effort and approach to a whole series of new problems in the area of the host-parasite relationship. We have with us today bacteriologists, anatomists, immunologists, and chemists; but my attention was drawn to the fact that there is not one of you here whose basic training has been in the definition of the discipline of pathology. There may be nothing very significant in this observation, for you are all pathologists by necessity; but there is a really important administrative aspect to several problems raised by this observation. Pathology must grow as a scientific discipline lest it lose its soul in menial service. To invite intra-departmentalism, however, is to invite budgetary chaos. This is however the normal medium of the Office of the Dean.

Ladies and gentleman, please proceed with your fine program.

JOHN B. TRUSLOW

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HOST-PARASITE RELATIONSHIPS IN LIVING CELLS

I. MATERIALS AND METHODS FOR THE STUDY OF HOST-PARASITE RELATIONSHIPS

MORNING SESSION

Moderator, Dr. Stuart Mudd

DR. FELTON: *To those of us who were trained in Philadelphia, Dr. Stuart Mudd, the moderator of our first session, is important for scientific and personal reasons and because he was and still is our teacher. Dr. Mudd is important to all of us because he is such a great man, he is such a tall man, and he has such a far-seeing eye. He has pioneered in that area of investigation which is indicated by the title of this symposium. We feel that no one could launch our program more appropriately.*

DR. MUDD: *First I should like to thank Dr. Felton and Dr. Truslow for getting together such a distinguished group of people to deal with these problems of protoplasm, and for the insights that we hope to gain into the living cell through many different approaches and disciplines. We will begin by hearing from Dr. Edward W. Dempsey of St. Louis who will discuss the "Role of the Electron Microscope in the Study of the Cells of the Host."*