COLD SPRING HARBOR LABORATORY

ANNUAL REPORT 1972

COLD SPRING HARBOR LABORATORY

Cold Spring Harbor, Long Island, New York

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ANNUAL REPORT 1972

COLD SPRING HARBOR LABORATORY

COLD SPRING HARBOR, NEW YORK

DIRECTOR'S REPORT

Each year as I write this report I cannot help thinking of myself as an entrepreneur, scientist style. With more ideas to peddle than capital, I often must go before the general public for the financial support necessary to put our long-term projects into effect. And since like all other scientists we never can promise certain success, we must be regarded as a speculative venture which might run dry long before normal amortization. Moreover as this Laboratory's most tangible assets are its land which we would never consent to sell and some buildings not all of which are solid, the question is bound to be asked whether someday we might suddenly go the way of the Penn Central and provide future benefits only for the lawyers brought in to dispense the remaining pennies. Too easily I can understand why an outsider (granting agency) might carefully look us over only to decide that he (it) is more comfortable with the certainty of continuous dividends from a prestigious university, so much a national tradition that its future of being inundated with intelligent students is never in doubt.

In contrast we are a small body that cannot live on established ideas and stay alive. Unlike the audiences which face major symphony orchestras our constituents get restless when they listen to old truths and they will only be happy if they learn something new. So we can never long be comfortable with our past successes and only at great long-term peril can we treat them as if they were a prized Bacon or Gorky. Instead we must realize that what really matters is whether we provide an atmosphere for the importantly unexpected.

We certainly have in the past. Too many major discoveries have occurred here to be a matter of chance, leading us to suspect that a constant stream of visitors has a positive catalytic effect on an unhurried year-round research effort. And likewise, the existence of a productive year-round research group in the long run determines the nature of our visitors. Now as in the past, they come here because they think they will see here biology at its best and, hopefully, we do not often disappoint them. Prospectively we know we cannot hold a meeting on a dull topic or publish a so-so book or pick instructors below the quality of the subject they teach. And restrospectively, we must face up to the times where we have erred on the side of flatness and take steps to make the next year more lively.

Of course deciding what generates liveliness is not that easy. Clearly we aim to bring together people who gravitate toward difficult ideas, yet we must not overemphasize formal thinking per se. It would quickly bore us unless it can be directed toward a potentially soluable biological puzzle. So we must always have on hand people who see biology on its own terms and have the persistence to stick with an important problem if they think they have the means to solve it. Hopefully such people will also be well versed in the physical sciences, not being afraid of applying high powered mathematics or physics or chemistry. But they must also possess the perspective to realize that biology usually does not advance by formulas alone and that persistent as well as innovative experimentation is at the heart of most real achievements.

While our labs need not be plated with fancy chrome they have to be in tune with the complexity of modern molecular and cellular biology. While it sounds romantic to believe that great research is usually done on the shoestring, this is not generally the case. Most exciting results come from the better equipped labs. Thus we must never kid ourselves, even temporarily, into believing that the quality of our results is independent of the level of our research support. Even though adequate research money does not guarantee results it does make them possible. The recent upswing in money for cancer research most certainly increases the probability for a sensational result. And correspondingly if Congress gets bored with the

cancer problem believing that it has heard impending success too often proclaimed, our national output of "relevent cancer research" will soon decline.

We must also never forget that biology is a wildly unpredictable affair and too much consistency in our ways of thought can harm us. We often have to abruptly reject one train of thought and adopt another. One most dramatic turnabout occurred in the career of Albert Kelner who in 1948 was working here in a small lab on the first floor of Nichols. In studying how ultraviolet light caused mutations he was bothered by finding that on some days his ultraviolet light killed many more bacteria than on other days. Then suddenly he related his irreproducible results to whether the room lights were on or off. Many more bacteria were killed in the dark than in the light, an effect quickly shown as due to a reversal by visible light, of prior damage caused by the ultraviolet light. The unexpected manner of this discovery as of many equally important breakthroughs, led Max Delbruck to formulate the "principle of limited sloppiness." By this phrase he suggested that meticulously doing a given experiment in exactly the same way limits the variables which will be tested. When you don't know where you are going unintentional randomization does not really hurt. Once however something novel emerges, then it pays to quickly sort out the variables and think with all your might.

Our future productivity will also demand that we keep the average age of our staff low, perhaps no greater than 28-32, always remembering that some scientists not only remain perennially young but also know the fads of the past and where they don't lead. And it will always be necessary to maintain a wide degree of scientific and cultural diversity. A way of action which solves one problem may be totally unsuitable for the next one, yet most of us adopt a new style of research only with great reluctance. So we must never give too much influence to any one person no matter how talented, taking the long-range view that a new dominant approach is likely to play the second fiddle some 5-10 years later.

The temptation must also be resisted of growing too big. Now we can know everyone who appears on the scene, at least well enough to know whether his special talents may relate to anothers. As long as we have a year-round size range of no more than 40-50 scientists we are not likely to generate self-contained groups. But if we were to number more, our normal inhibitions from seeming too nosey will lead to fragmentation that not even the volley ball court can overcome.

We must also hold back the temptation to focus too much attention on the topic of the moment. Though many of us are now principally interested in the origin and nature of cancer cells we must also attract scientists who find other problems more to their liking. Only long-term dullness would likely result from a total commitment of this Laboratory toward cancer research. While now much of what is properly called cancer research is synonymous with modern molecular and cellular biology, this is unlikely to always be the case. In particular, if as we hope, the results of the next 10-15 years clarify many of the key molecular features of the human cell and their cancerous counterparts, many of our best younger biologists will move on to even more mysterious aspects of pure biology. Se we must not succumb to the immediate short-term advantages which could accrue from completely overlapping our aims with those of the National Cancer Institute.

In particular it seems wise to slowly increase our efforts in the area of neurobiology, a subject of unlimited intellectual challenges now largely hidden by the horrendous anatomical complexity of the vertebrate brain. Now thanks to major help from the Sloan Foundation we have a serious program aimed at encouraging new talent to tackle neurobiology at a fundamental level. Our resources however do not yet permit us to carry on research in this area on a year-round basis. Unfortunately it may not make sense to bank on sensible federal funding, of the semistable variety now accorded molecular and cellular biology that relate to cancer. There now exist so many viewpoints as to what should be the correct approach(s) to perception, memory, and learning, that much dissension exists as to which is good research and which can only be called crap. So we can never be sure that the review committees that pass out

the existing modest federal commitment toward neurobiology are not sometimes packed with vocal promoters of intellectual nonsense. For when that is the case even the best proposals may be shortchanged and go supported at levels too low for the emergence of significant new facts. Prudence suggests that we must find some stable private funds as a cushion to unpredictable fluctuations in federal support before we take a year-round plunge into this most inscrutable field.

We must also take caution that our enthusiasm for our current year-round programs does not lead us to bite off more than we can chew. We must not bring anyone here under conditions where he could not hope for the jackpot of an important discovery. Only if this remains possible will we be able to maintain our current high morale, our budget could not fall in half and we be the same place. Thus given that our proper functioning is intimately dependent on a continuous flow of federal funds, we cannot afford to take a hands-off attitude toward the national attitude toward science. It is all too much at the heart of our existence ever to be taken lightly. In particular we must realize that the American public only to a small degree now supports science because it represents an assault on ignorance and offers the possibility of understanding the deepest mysteries of human life. Instead the message it likes is that the new knowledge we obtain is continuously upgrading the quality of human life. So on the whole, our way of life exists because of a belief we will help our donors and it is hard to imagine that state ever changing. Science is now much too big an item in the federal budget to slip in unseen by the faceless inhabitants of the Office of Management and Budgets.

The real question thus is whether the science that we now do betters the human condition. From a narrow parochial view we fit the bill. Our work on tumor viruses together with that of corresponding laboratories throughout the world will someday clarify the nature of cancer and the means by which we can fight it. So we can ask for large sums of cancer money unhindered by inner doubts about out true sincerity. But other types of science are increasingly often producing nasty side consequences like radar controlled "surgical bombing" and massive long-term radioactive pollution due to the "peaceful atom." And so there are some people, not all far-out kooks, who believe that our very survival as a species may demand slowing down science until we can catch up with the inbalance that it has already created. This sentiment is bound to grow if the current decline in the quality of life within the United States continues. With it no longer possible to say that an increase in the gross national product leads to a better life, the need for more science will not much longer be easily accepted. There is thus no way of avoiding the problem that somehow we must redirect much of our efforts as scientists toward finding better ways of inhabiting the earth. This does not mean however that we stop being good scientists. We cannot throw out bad technologies without providing new ones and it would be surprising if this will occur without further developments in pure science itself.

The freedom will no longer exist however to sit in our particular cubby holes thinking that we are protected from future technological disasters by responsible actions from the wise men of our scientific establishment. Regretfully at this time no influential group of respected scientists exists equivalent to that which oversaw the development of the atomic bomb. Perhaps science has just gotten too big for any one group to believe they own it or perhaps the historical forces which seem to leave us without respected national leaders also are working upon science or maybe the seeming inability of either political party to respond to Vietnam by other means than bombs and slaughter has left no one of decency the capacity to remain close to the Washington stomach.

I thus see no choice but for each of us, no matter how overemployed, to also worry at the very practical level about how we can make our nation accept a set of national priorities that will lead to a social and physical environment that we can look forward to our children inhabiting.

For example we must see to it that new classes of safe pesticides are more than a slogan; find ways to remove the carcinogenic nitrate preservatives out of our preserved foods yet keep them

safe to eat; convince the medical profession that the overemployment of diagnostic X-rays may cause cancer as much as it allows us to cure; ask whether we should develop the artificial placenta or attempt to clone our domestic farm animals; argue that biological and chemical warfare makes sense only if one is objective in the indiscriminate obliteration of civilian populations, and see to it that future nuclear power plants are only sited hundreds of miles away from major population centers.

Only if we accept responsibilities like these will we have the opportunity to retain the optimism that has made the scientific life so rich and rewarding.

Highlights of the Year

First Year Under a Cancer Center Grant

The receipt of the first million dollar installment of our five-year center grant from the National Cancer Institute has had an immediate quickening effect on about all aspects of our year-round program. Demerec Laboratory "A" has now become totally renovated with Bob Pollack moving in February into a thoroughly modern laboratory for cell culture experimentation. He now shares the top floor with David Zipser who has moved up from the bottom floor, which is now largely reconstructed for more chemical type experiments by Richard Roberts. His newly completed hot room-chromatography complex compares well with the best of such facilities in newly built laboratories.

Equally important has been the increase in funds for support of our scientific personnel. As of January 1, 1973, it numbers some 14 staff scientists, 2 visiting scientists, 16 postdoctoral fellows, and 6 graduate students for total of 38. In comparison at this time last year, only 25 scientists were in residence. Growing even faster has been the science tempo itself. Though we know that work with animal cells starts up slowly and that we should not expect any results immediately, the necessary long period between the arrival of the first staff member and the appearance of publishable results was indeed frustrating for the James Laboratory group, most of whom came from research institutes already doing tumor virus research.

We must of course admit that as yet we cannot claim major breakthroughs of world shattering consequences for the cancer problem. That we are not alone in this regard we believe reflects not misguided research emphasis but the horribly difficult challenge that we and our sister laboratories have taken on. It would be nice to think new findings will quickly simplify the cancer problem but I fear this is not the case. We are in for a long ride that will even be longer if we do not accept the need for persistant intelligence and unmitigated hard work.

Construction of the West Addition to the James Laboratory

Work began last May on a new 1500 square foot annex to the James Laboratory that will provide us with expanded facilities for the growth of animal viruses. Now we are limited to a small room on the second floor of James that must be vacated when the animal cell courses take over the second floor for the summer. Then we can only grow viruses in highly makeshift conditions and so must of necessity slow down our research until the fall rolls around. When our new facilities become ready, hopefully by the end of March, we shall at least possess a set of rooms specifically designed for growth and isolation of viruses.

Additions to our Scientific Family

At the start of the fall Richard Roberts came to us from Harvard University where he was involved in RNA sequence studies. His arrival has given us badly needed chemical competence, long a deep gap in our total program. Also greatly strengthening us for the academic year 72-73 is the presence of Klaus Weber who came here on leave from Harvard University where he is a Professor of Biochemistry. Klaus, a master in the development and use of micromethods for protein structural analysis, will greatly speed up our effort to characterize the various proteins coded by the SV40 genome.

Regretfully we have lost the talents of Heinrich Westphal who moved to the National Institutes of Health at the end of the summer. His senior position in the James Laboratory is now filled by Phillip Sharp who came to us last year after several years at Caltech. Also greatly aiding our tumor virus group is Ulf Pettersson who brought to us from Uppsala a most needed knowledge of the adenovirus field.

Ahmad Bukhari, who first came here as a postdoc with David Zipser, now also has become a member of our scientific staff. His continued presence should help to maintain our lively interest in μ, a phage which he brought here from Larry Taylor's laboratory in Denver.

Expansion of our Neurobiology Summer Program

This year we expanded our neurobiology program to include a third course, the Behavioral Genetics of a Nematode, taught by Dick Russell of Caltech and Ruth Pertel of NIH. Many nematodes are characterized by nervous systems composed of only several hundred cells and they may represent an exciting new system for probing fundamental neurobiological problems. This challenge first taken up by Sidney Brenner in Cambridge, England, looks like it will spread to many other labs, so our course was designed to give these potentially hooked people a chance to learn more about the newest ways of working with these very small animals. We believe it was most successful and next summer we will again fill this third slot with a course designed to introduce a new animal system into the neurobiological repertoir.

Support for this course as for the ones on "Fundamental Principles of Neurobiology" and "Experimental Techniques" came from our Sloan Foundation grant. In order however to continue this program in succeeding years, we will need additional help hopefully in the form of long-term commitments either from some agency of the federal government or from private sources.

Continuing on successfully into its second year was our chromosome course this time given by Mary Lou Pardue and Charles Laird. Again it was given in Davenport which seemed shakier than ever and on occasions only breathing seemed to be required before the floor supporting our microscopes began vibrating. So this winter we are starting to rebuild Davenport, a task that will go over two years. To begin with, we are totally tearing up the basement, in particular lowering the floor by eight inches so that "six footers" can be accepted into our courses without risking their heads. On the first floor we shall provide space for an EM which we hope to be of a type where it can be integrated into our teaching programs as well as be employed year round for research on chromosome structure.

Upgrading of the Library

Susan Gensel, formerly the Science Reference Librarian at the University of California, Riverside, arrived here in March to take over the management of our Library from Guinevere Smith who retired after faithfully serving us for the past 43 years, first as a research assistant with Oscar Riddle of the Carnegie Institute staff and then for over 30 years as our Librarian. It is very clear that the rising uses of our Library now demands the services of a professional librarian and we feel we are most fortunate that we have been able to attract a person with Susan's abilities. More than 300 bound journal volumes and 325 books and series volumes were added to our collection over the past year bringing our total collection number to almost 25,000 volumes.

A New Generation of Laboratory Manuals

In July the first copies came off the press of "Experiments in Molecular Genetics" by Jeffrey Miller. Originating out of our bacterial genetics course which Jeffrey helped teach two summers ago, this book represents the first of what we hope will be a series of super laboratory

manuals designed to upgrade the teaching of modern biology as well as to provide innumerable guidelines for innovative research. We have set deliberately a low price of $11.95 to encourage course adoptions. If they occur in sufficient numbers, we may cover the heavy costs that we suspect a commercial publisher would never have incurred.

Throughout the year we have continued to upgrade the original manuscript for our tumor virus book, with again many different scientists joining in the project. Now we think we see the end of our effort and with the first eight chapters already in page proof, we hope to have it out by July 1 at the latest. At times this horrendous effort has seemed more than we could pull off and still do research in James. But since the need for a solid book on tumor viruses remains as compelling as ever, we have never had any real doubt but that we would finally bring it forth. Now we guess that it shall be some 700 pages in length, some three times longer than it would have been if we pushed our first manuscript through to book form.

Initiation by LIBA of a $250,000 Fund Drive

Warm and solid support from our local community has always been a vital ingredient in our existence. This support is officially channeled through the Long Island Biological Association (LIBA), a local philanthropic organization organized in 1924 for the express purpose of supporting the Laboratory. During the past year the directors of LIBA led by Dr. Edward Pulling made the very major decision to launch a fund drive for $250,000 to help achieve three very important objectives: 1) the building of the new addition onto James Lab, a project now estimated to cost approximately $100,000; 2) the winterization of Blackford Hall, a job long-dreamed of but never initiated because of costs estimated to exceed $100,000. In this task we will be also aided by a $30,000 gift from the Charles E. Merrill Trust; and 3) the acquisition of a nearby home sited on land effectively enclosed by our property and which will enable us to house some 10-12 additional people during the summer months.

Heading this very important effort is Mr. Robert Olney, ably supported by Mrs. Ward C. Campbell, Dr. Bayard Clarkson, Mr. Edward W. Kozlik, Mr. Angus P. McIntyre, Dr. Edward Pulling, and Mrs. Alex M. White. Already they have received pledges of over $100,000 allowing us to start the new addition to James and to begin installing the heating system for Blackford. And it is their hope to have in-hand pledges for the remaining sum within the next year. The thoughtful planning and the countless solicitations toward potentially interested friends represent an immense labor of love toward us and is most deeply appreciated by all members of the Laboratory.

Again during early June a number of LIBA members held dinner parties for the speakers at the Annual Symposium. Through their gracious efforts our 60 such visitors, many from outside the United States, enjoyed most relaxing interludes away from the intensity of a week of scientific discussions. We wish to thank Mr. and Mrs. Arthur M. Crocker, Mr. and Mrs. Robert Darrell, Mr. and Mrs. David Ingraham, Mr. and Mrs. George Lindsay, Mr. and Mrs. Ralph Maffei, Mr. and Mrs. Robert Olney, Mr. and Mrs. Walter Page, Mr. and Mrs. Franz Schneider, Mrs. Alex M. White, and Mr. and Mrs. William A. Woodcock.

Preventing the Commercialization of Cold Spring Harbor

We must never forget that a real ingredient in our past success has been our location at Cold Spring Harbor. It is what brought us here in the first place and still is a major reason why we have so little problem in recruiting new staff or course instructors. Initially there were many equally beautiful harbors along the North Shore of Long Island but now we are the only one which retains the flavor of the days when Indians fished along its shores. Without constant concern however it will fall victim to the commercialization now attendant on our neighboring harbors. Then we would lose the advantages not only of its inherent beauty, but also of the effective seclusion so vital to the spirit of our many meetings and courses. Fortunately this

Laboratory is not alone in its desire to preserve Cold Spring Harbor for posterity and it is our hope that the newly arisen ecological awareness will create an atmosphere where we together with our neighboring towns can promote the development of long-range plans that will keep Cold Spring Harbor among the showplaces of the Long Island North Shore. To this end our Board of Directors has established a Harbor Committee led by Bill Woodcock to work out plans that will meet the needs of ourselves and our neighbors as well as Long Island as a whole.

Tennis Returns to Bungtown Road

When I first came to the Laboratory in 1948 it was possible to play tennis on a court located near the water between Davenport and Jones. Already then this somewhat clay court gave rise to many unexpected bounces and not many complaints were voiced when a sewage treatment facility took over its site during the summer of 1964. Since then, to play tennis it has been necessary to go to the Cold Spring Harbor High School courts, a car-requiring event which frequently ended in the frustration of finding all the courts in use. Thus the building of new courts on our land has long been an objective of our many tennis playing addicts and we have very openly sought out potential tennis-loving donors. Success came with Manny Delbruck again arising to the occasion and sparking the construction near the beach parking lot of two courts of modern composition surface that should require very little maintenance. The record rain fall of this year kept us from having them ready for the past summer program and play could only begin late in September. Almost immediately there began heavy use and we expect there will be constant play on them next summer.

The Firehouse Reborn

When the village of Cold Spring Harbor acquired its first brick firehouse in 1926, the old wooden one dating from the middle of the 19th century was put up for auction. Hearing of this, Reginald Harris, then Director of the Biological Laboratory, put in a bid of $50 and so the

Firehouse arrives at Cold Spring Harbor Laboratory

firehouse became Laboratory property. After being towed across the harbor it came to rest next to Davenport Laboratory where it was used for the next 45 years as a summer dormitory of three apartments. Its inhabitants, particularly those who came back there year after year, came to appreciate its simple charm, even those dwelling in the basement flat that all too often was inundated by rain storms that gave it several inches of water. Last year we decided it was time for winterization, using the occasion to give it picture windows looking onto the inner harbor. Now that the job is done, again using the very considerable talents of Jack Richards and our building staff, we are most pleased, as are its inhabitants, particularly those on the upper floors who have quite breathtaking views, particularly in the evening hours.

Cash Reserves Remain All Too Low

This year our combined operating and capital budgets reached a record total of $2,600,000 reflecting the expansion of research and teaching efforts as well as many vital improvements in the quality of our physical plant. We have continued the policy of the past years that first priority for use of free money is toward improvements in our physical plant which still is marked by many buildings essentially unchanged over the past 50 years. So our cash reserve remains very small in relation to our cash flow and it is only knowing we have the superb talents of our Administrative Director, William Udry, that we are able to go ahead so rapidly.

Unrestricted Gifts are a Necessary Component of Our Well-Being

Failure of overhead to cover all the true expenses of our many research programs and our lack of even a small endowment means that our continued prosperity depends on the sustained help from local neighbors, charitable foundations, scientific alumni, industrial sponsors, and participating institutions. Only the fact that their gifts reached a record level last year allowed the continuation of our transformation from a dilapidated relic of early American science into a productive blend of the past and the very new. We thus hope very much that this coming year will witness the continuation of so many forms of real support.

If so, our outlook will continue that of high optimism.

December 31, 1972 *J. D. Watson*

MOLECULAR BIOLOGY OF TUMOR VIRUS

J. Sambrook
E. Allet
J. Ashton
M. Botchan
D. Day
F. Falcoz-Kelly
R. Greene
T. Grodzicker
A. Jackson
W. Keller
R. Lancaster
M. Lurye
J. Maroney
G. McKenna
A. Merrill
B. Miller
C. Mulder
B. Ozanne
U. Pettersson
B. Root
P. Sharp
W. Sugden
N. Sullivan
A. Vilkas
. Wendel
H. Westphal
T. Wilson

The work of the tumor virus laboratory has been concentrated on the molecular biology of simian virus 40, avian leukosis virus, and the human adenoviruses.

Transcription in vivo

For several years the pattern of SV40-specific RNA synthesis found in different in vivo and in vitro conditions has been perplexing. During productive infection some viral RNA sequences appear early and are synthesized throughout the growth cycle; others can be detected only after the onset of viral DNA synthesis (Oda and Dulbecco, 1968; Aloni et al., 1968; Sauer and Kidwai, 1968; Martin and Axelrod, 1969a). SV40-specific RNA sequences are also present in transformed cells (Benjamin, 1966) but there has been disagreement about the fraction of the viral genome that is transcribed. On the one hand saturation hybridization experiments show that RNA sequences representing the entire viral genome are present (Martin and Axelrod, 1969b); on the other, competition hybridization experiments suggest only that portion of the genome which is expressed early in lytic infection is transcribed (Oda and Dulbecco, 1968; Aloni et al., 1968; Sauer and Kidwai, 1968; Tonegawa et al., 1970; Sauer, 1971). Part of the difficulty in solving this discrepancy has been the inability to prepare separated strands of the viral DNA. However, Westphal (1970) showed that RNA transcribed from SV40 DNA in vitro by *E. coli* RNA polymerase (cRNA) was highly asymmetric and he suggested that it could be used to prepare separated strands of viral DNA. This turns out to be true. When denatured unit length single-stranded SV40 DNA was incubated in the presence of excess cRNA, about 50% of the DNA was converted into DNA-RNA hybrids which could be separated from unhybridized DNA by chromatography on hydroxylapatite. The two DNA fractions were shown to be the complementary strands of SV40 DNA and were used in hybridization experiments to determine the pattern of viral transcription under different in vivo and in vitro conditions. During lytic infection about 30% of the sequences of one strand (E strand) of viral DNA are transcribed both before and after viral DNA synthesis. The transcript of the other strand only appears at late times during lytic infection and corresponds to the 70% of the sequence of the complementary strand (L strand). Similar results have been reported by Khoury et al. (1972) and by Lindstrom and Dulbecco (1972). In different lines of transformed mouse cells the pattern of transcription was found to vary quite widely but considerably more RNA sequences were transcribed from the early DNA strand in all the transformed cells than in permissive cells supporting lytic infection. This must mean that at least some of the viral RNA present in transformed cells contains "anti-late" sequences. "Anti-late" RNA would not have been detected in competition hybridization experiments (Oda and Dulbecco, 1968; Aloni et al., 1968; Sauer and Kidwai, 1968), but it would have appeared in direct saturation experiments (Martin and Axelrod, 1969b) and this probably accounts for the conflicting results obtained with the two hybridization systems. In addition to "early" and "anti-late" RNA sequences some, but not all, lines of transformed cells contain RNA sequences complementary to the "late" strand of viral DNA.

These data are consistent with the following model of SV40 transcription in transformed cells. In transformed cells we know that the viral and host DNAs are covalently linked (Sambrook et al., 1968). In order to preserve intact the functions necessary to maintain transformation, we propose that the integration of the viral DNA into the host DNA involves a break somewhere in late viral genes. It may be that in different transformants the viral DNA is broken at different sites in the late portion of the genome, and that the extent of transcription of the early DNA strand depends on the exact position of the integration site within the viral genome. Clearly this model can be stringently tested by mapping the breakage point of integration of viral DNA in cell lines which show different amounts of transcription (see below).

Although the factors that modulate the transcription of SV40 DNA in different permissive and non-permissive cells are entirely unclear, we have been able to identify the polymerase responsible for the synthesis of viral RNA at late times during lytic infection. Nuclei were isolated from infected monkey cells and conditions affecting the synthesis of SV40-specific RNA were investigated. The results show that a polymerase whose properties (salt-dependence, cation requirement, α-amanitin sensitivity) are identical to those of host cell DNA-dependent RNA polymerase II is responsible for the synthesis of both "early" and "late" sequences of SV40 RNA.

Transcription in vitro

a) The purification and partial characterization of RNA polymerase II from KB and HeLa cells has been completed. The subunit structure of the enzyme appears similar to those found for the rat liver and calf thymus enzymes (Weaver et al., 1971; Kedinger and Chambon, 1972); in SDS-polyacrylamide gels, three polypeptides of 220,000, 140,000, and 35,000 daltons are invariably found to correlate with the activity applied to the gel (see Fig. 1). A fourth subunit

8.75% SDS-acrylamide gels of myosin (gel number 1 with a mol wt of 220,000 daltons) and KB RNA polymerase II (gel number 2). Bands *a*, *c*, and *d* correspond to the 220,000, 140,000 and 35,000 dalton mol wt subunits. *b* is the variable (170,000 dalton mol wt subunit); *e* is the running front, and *f* is a contaminant lost on further purification by isoelectric focusing.

may be running with the gel front and a fifth subunit of 170,000 daltons is found in varying amounts. Rutter's group believes that this last subunit is a degradation product of the 220,000 dalton polypeptide. The weight of the complete active enzyme is approximately 500,000 daltons as determined by velocity centrifugation in sucrose gradients. This approximate molecular weight is consistent with the active molecule being composed by one of each of the four subunits as proposed by Weaver et al. (1971).

During the course of purification the enzyme becomes increasingly unstable. This instability can be avoided in part by beginning with large amounts of cells (100g or more) and working as rapidly as possible. The purified enzyme is stable when stored at $-80°C$. The purified preparations do not contain detectable nucleases, kinases, or other polymerases. RNA polymerase II uses denatured DNA more efficiently than native DNA as a template. RNA polymerase II from HeLa and KB cells and *E. coli* RNA polymerase transcribe ϕX174 single-stranded DNA in similar ways. All three enzymes synthesize an RNA-DNA hybrid and with limiting template can displace the RNA from the hybrid.

Purified RNA polymerase II from KB cells has been used to transcribe SV40 in vitro. The extent of transcription is sensitive to both the form of the template and the cation used. Optimal synthesis occurs with SV40 form I DNA as template in the presence of 0.0015–0.002 M Mn^{++}. Compared with form I DNA, virion form II DNA and linear SV40 DNA obtained by cleavage with the R_1 restriction enzyme (see below) are poor templates. However, 0.005 M $MgCl_2$ stimulates preferentially RNA synthesis on these relaxed templates. The SV40-specific RNA made under optimal conditions hybridizes to 100% of the E strand and to 75% of the L strand of SV40 DNA.

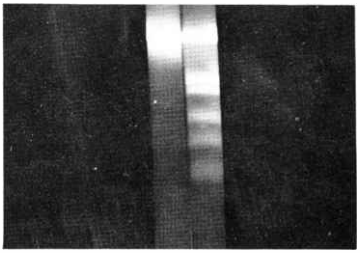
b) In cooperation with Dr. Hajo Delius we have continued work aimed at mapping promotor site(s) for *E. coli* DNA-dependent RNA polymerase on SV40 DNA. A new technique of electron microscopy was employed to visualize nascent RNA chains on unique linear duplex SV40 DNA, generated by endonuclease $R \cdot R_1$. This linear DNA was a less efficient template for *E. coli* RNA polymerase than SV40 DNA form I. Mapping of RNA chains attached at various positions to the linear template revealed one preferred site for RNA initiation located 0.16 fractional length from the $R \cdot R_1$ cleavage site. Another site appeared to be located near the middle of the linear DNA. Experiments are in progress to determine the number of chains of RNA synthesized by *E. coli* RNA polymerase from form I DNA and linear and relaxed covalently closed SV40 DNA by sequencing the γ-labeled products.

Restriction Enzymes

Bacterial restricting endonucleases are known to introduce double-stranded scissions at specific sites in DNA (see review Meselson et al., 1972). We have continued to study the action of several restriction enzymes on SV40 and adenovirus DNAs.

a) *A new assay for restriction enzymes* Certain enzymatic and physical treatments of DNA produce chemical changes at only a limited number of sites in the polymer but cause vast changes in the molecular weight or the configuration of the DNA. Two classic examples are the conversion of closed circular DNA containing negative superhelical turns into relaxed circular DNA after the hydrolysis of a single phosphodiester bond and the cleavage of high molecular weight duplex DNA into unique fragments by restriction endonucleases. The conventional assay for such events has been sedimentation velocity centrifugation. However this method is too expensive and laborious to use for routine assays during enzyme purification except in a few special circumstances.

The major variables which determine the rate at which DNA molecules migrate through gels under the influence of an electrical force are the length and configuration of the DNA



1.0mg of adenovirus 2 DNA untreated (left) or treated (right) with R_1 endonuclease was electrophoresed for 2hr through 1.4% agarose in the presence of 0.5mg/ml ethidium bromide. The gels were photographed using uv light and the specific cleavage products are easily visible.

chains. We have adapted agarose gel electrophoresis techniques to make them as routine and convenient as possible for assaying restriction endonucleases. Agarose (1.4%) was chosen as a gel matrix because it does not require polymerization and is relatively insensitive to the ionic strength (.01-0.5 μ) of the sample buffer. The agarose gel tubes (14 cm × 0.6 cm ID) are slightly tapered at one end to prevent the gel from sliding out. The running buffer is 0.04 M Tris pH 7.8, 0.005M sodium acetate, 0.001 M EDTA and contains 0.5 μg/ml ethidium bromide. At this concentration of dye about half of the binding sites for ethidium bromide on DNA are saturated and the fluorescent yield of the bound dye is enhanced 600-fold over that of free molecules. After electrophoresis (5 mA/get) the DNA can be seen as a bright red fluorescent band when the gel is placed onto a short wave ultraviolet lamp. As little as 0.05 μg DNA can be detected visually; the fluorescent bands can be photographed to provide a permanent record (see Fig. 2). The complete procedure is rapid (2 hr) and reproducible, requires no dripping of gradients or counting of radioactive isotopes, has much greater resolution than velocity centrifugation, and can be used to assay many samples simultaneously. We use the technique routinely to monitor for restriction activity during enzyme purification, to determine the restriction pattern produced by different enzymes on different DNAs, and to purify the specific DNA fragments of viral DNAs after treatment with restriction enzymes.

b) *Restriction of adenovirus type 2 DNA* In order to cleave the DNA of adenovirus type 2 we have used a restriction endonuclease from *E. coli* carrying the drug resistance transfer factor RTF-1 (endonuclease $R{\cdot}R_1$) (Yoshimori, 1971). This enzyme attacks duplex DNA by making single-stranded scissions in positions which are four bases apart thereby generating cohesive ends (Mertz and Davis, 1972; Hedgpeth et al., 1972).

Adenoviruses contain linear duplex DNA with a molecular weight of about 23×10^6 daltons (Green et al., 1967). The DNA is not circularly permuted but the termini of each of its strands consist of complementary sequences which are inverted with respect to each other (Wolfson and Dressler, 1972; Garon et al., 1972). After adenovirus type 2 DNA has been digested with endonuclease $R{\cdot}R_1$, DNA fragments of six size classes are produced (1.1, 1.4, 1.7, 2.3, 2.7, and 13.6×10^6 daltons). The fragments can be resolved into six peaks after electrophoresis on agarose-ethidium bromide (see Fig. 1) or agarose-polyacrylamide gels. The six peaks each contain a unique segment of DNA because the sum of the molecular weights of the isolated fragments equals that of complete adenovirus DNA, because all peaks contain DNA segments in equimolar amounts and because each fragment exhibits a rate of renaturation that is inversely proportional to its molecular weight. The order of the fragments has been deduced by comparing partial denaturation maps of fragments with that of intact adenovirus 2 DNA, by electron microscopy of heteroduplex molecules of fragments and complete viral DNA, and by isolating the products of partial digestion of adenovirus 2 DNA. Currently we are studying the location of "early", "late" and "transforming" genes by hybridization of Ad2 DNA fragments with RNA synthesized in vivo. Similar studies are under way with the DNAs of other adenovirus serotypes and the adenovirus SV40 hybrid $Ad2^{++}ND_1$.

c) *Restriction of SV40 DNA* Work has continued on the action of endonuclease $R{\cdot}R_1$ on SV40 DNA. At the beginning of the year we knew that the enzyme cleaved SV40 DNA once (Morrow and Berg, personal communication). We have shown that the resulting linear DNA molecules are full length as judged by their sedimentation through alkaline sucrose gradients, by their electrophoretic mobility, and by direct observation in the electron microscope. The break in SV40 DNA occurs at a specific site as shown by analysis of partial denaturation maps and by heteroduplex mapping to the adenovirus-SV40 hybrid $Ad2^{++}ND_1$.

A low percentage of SV40 DNA molecules derived from plaque purified virus was found to be resistant to endonuclease R_1. The proportion of resistant molecules increases dramatically when the virus is grown at high input multiplicities for several passages. In collaboration with Rex Risser it was shown by heteroduplex mapping of $R{\cdot}R_1$-linear SV40 DNA molecules isolated from such a preparation that a high proportion of these molecules have a large deletion and a substitution at a specific site in the middle of the molecule. A second preparation shows

several deletions and substitutions located at many sites on the DNA molecules. The reason for this phenomenon is under investigation.

The effect of endonuclease $R{\cdot}R_1$ on circular dimers of SV40 DNA is being investigated to elucidate the mechanism of genesis of these dimer molecules.

We have recently discovered another restriction enzyme which cleaves SV40 DNA at a unique site. Danna and Nathans (personal communication) have reported that *Hemophilus parainfluenza* contains an enzyme which cleaves SV40 DNA in three places. During purification of this enzyme, we noticed another enzyme activity which eluted from phosphocellulose at a higher ionic strength than the Danna-Nathans enzyme. The second enzyme produces unit length linear molecules when closed circular SV40 DNA is used as a substrate. In acts on $R{\cdot}R_1$ SV40 linear DNA molecules to produce two DNA fragments, one being 25% and the other 75% of the length of SV40 DNA. The cleavage site is located at 9 o'clock on the SV40 genome (R_1 = 12 o'clock) as shown by heteroduplex mapping of unit length linear molecules against $Ad2^{++}ND_1$ DNA. The action of the enzyme on other DNAs is under investigation.

Replication of Adenovirus DNA

We have developed a method to isolate replicating viral DNA from KB cells infected with adenovirus type 2. Nuclei are isolated from infected cells which have been pulse-labeled with ^{3}H-thymidine. The DNA is extracted with phenol after digestion with pronase in SDS. The replicating DNA is purified by equilibrium centrifugation in CsCl and has the following properties: DNA which is pulse-labeled for short periods (2-5') bands 5-10 mg/cc heavier than mature adenovirus 2 DNA. Both replicating DNA which is pulse-labeled for long periods of time and DNA labeled with a short pulse followed by a long chase band as mature viral DNA. In order to investigate the cause of this increased density the replicating DNA has been digested with different enzymes. The single-strand specific nuclease from *N. crassa*, but not RNAse or pronase, decreases the density of the replicating DNA to that of mature adenovirus DNA. About 25% of the label in replicating DNA is solubilized by the single strand specific enzyme. Analysis by sucrose gradient centrifugation shows that replicating DNA sediments considerably faster (> 100S) than mature viral DNA through neutral gradients; alkaline gradients show DNA of full length and also shorter fragments. Electron microscopy has shown that most of the replicating DNA extracted by our method is present in large aggregates containing many single-stranded branches. Single molecules containing duplex DNA with one single-stranded tail are also observed.

Properties of Transformed Cells

a) Over the past year we have continued our efforts to elucidate the interactions of SV40 virus with 3T3 cells that result in transformation. Previously we had isolated variants resistant to killing by concanavalin A from a population of SV40 transformed 3T3 cells. These variants had reverted to an untransformed phenotype in some of their growth characteristics (Ozanne and Sambrook, 1971). In light of findings by Inbar and Sachs (1969) and Eckhart et al. (1971) which imply that a viral function is necessary for the maintenance of the transformed phenotype and sensitivity to the effects of concanavalin A, we examined the state of the SV40 genome in the concanavalin A resistant SV3T3 cells. We knew that the virus was present and functioning because the resistant variants contained T-antigen and the virus could be rescued from them, albeit at a lower efficiency than from the parental cells. By analyzing reassociation kinetics (Gelb et al., 1971) we have shown that the parent SV3T3 cells and the concanavalin A resistant variants contain the same amount of viral DNA per diploid quantity of cell DNA.

To study further the expression of the SV40 genomes in the revertants, we analyzed the SV40 specific RNA present in the concanavalin A resistant variants by hybridizing total cellular RNA to the separated strands of SV40 DNA (Sambrook et al., 1972). The parental SV3T3 cells contained RNA sequences complementary to 70% of the early strand of SV40 DNA and to 15-20% of the late strand of SV40 DNA. The concanavalin A resistant variants and the parental cells contained the same amount of the same SV40 RNA sequences. Currently we are examining whether the variants are sensitive to retransformation by other viruses.

b) We have investigated the action of cytochalasin B on normal and transformed cells and have shown that 3T3 cells respond differently to treatment with the drug than do their SV40-transformed derivatives.

Cytochalasin B inhibits cytoplasmic cleavage and a number of processes concerned with cell movement. Mitosis is unaffected so that cells treated with the drug become multinucleate (Carter, 1967). Although its precise mechanism of action is unknown, cytochalasin B is believed to interact either with microfilaments (Wessels et al., 1971) or directly with the plasma membrane (Estensen et al., 1971). We have found that cytochalasin B inhibits DNA synthesis in 3T3 cells very rapidly so that most of the cells become binucleated but do not undergo further nuclear division. Upon removal of cytochalasin B, cytoplasmic division resumes and even prolonged exposure to the drug (72 hr) does not markedly affect the viability of the cells. By contrast, SV3T3 cells continue to synthesize DNA in the presence of the drug, the number of nuclei per cell increases dramatically (up to 8/cell), and the ability of the cells to form colonies after removal of the drug is drastically reduced. The study is being extended to cells

transformed by other viruses and we are using the killing effect of cytochalasin B on SV3T3 cells to isolate cells which are resistant to the drug.

c) We have determined the amount of viral DNA in rat cells transformed by adenovirus type 2 using the method of Gelb et al., (1971). One copy of viral DNA was detected per diploid quantity of transformed cell DNA and most, if not all, of the sequences present in the viral DNA appear to be present in the transformed cells.

d) A biochemical method to determine the integration site of SV40 DNA in transformed mouse cells is being investigated. Because endonuclease $R \cdot R_1$ produces cleavage at one specific site in SV40 DNA (Mulder and Delius, 1972; Morrow and Berg, 1972) cleavage of transformed cell DNA with $R \cdot R_1$ should generate pieces of viral DNA covalently linked to host DNA. We have used the SV40-transformed mouse line SVT2 which contains about two copies of viral DNA per diploid quantity of host DNA (Gelb et al., 1971; Ozanne et al., 1972). High molecular weight DNA is extracted from the cells and is treated with endonuclease $R \cdot R_1$. After complete digestion the DNA consists of a heterogeneous population of molecules ranging in size from 1×10^6 to 1×10^7 daltons. The DNA is fractionated into different size classes by alkaline velocity centrifugation or by electrophoresis and each class is assayed for the presence of SV40 sequences by hybridization to ^{3}HcRNA. We have been able to detect SV40 sequences in DNA molecules of two size classes. Presumably these correspond to the "left" and "right" portions of the integrated viral genomes. We are currently mapping the segments of SV40 DNA in each size class by using cRNA complementary to the fragments of the SV40 genome produced by cleavage of SV40 DNA by a restriction enzyme from *H. influenzae* (Danna and Nathans, 1971).

RNA-primed DNA Synthesis and the Mode of Action of Ribonuclease H

As a by-product of RNA polymerase preparations from HeLa and KB cells, we have purified ribonuclease H (Stein and Hausen, 1969) and studies its mode of action. Because there was accumulating evidence for direct involvement of RNA in the initiation of DNA synthesis, we first asked whether DNA synthesis can be initiated in vitro by covalent extension of short stretches of RNA. This could be accomplished by using single-stranded circular DNA of phage ϕX174. In the presence of DNA polymerase II from KB cells or DNA polymerase from *M. luteus*, ribo-, and deoxyribonucleotide triphosphates, the addition of *E. coli* RNA polymerase results in a drastic stimulation of DNA synthesis. It was demonstrated that the newly synthesized DNA chains contain a short piece (20-50 nucleotides) of RNA at their 5′ ends which is linked via a 3′-5′-phosphodiester bond. These RNA-primers could be selectively removed from the product DNA by ribonuclease H implying a possible physiological role of this nuclease in RNA-primed DNA synthesis in vivo.

Molling et al. (1971) reported the presence of a ribonuclease H-like activity in partially purified avian myeloblastosis virus (AMV) DNA polymerase and suggested a role of this activity in the conversion of viral RNA into double-stranded DNA. We therefore investigated whether this viral RNase H activity is part of the viral DNA polymerase or a separate enzyme and compared it with the RNase H from host cells (chick embryos). The results so far obtained indicate that viral RNase H is inseparable from the DNA polymerase and is antigenically not related to host RNase H. Host RNase H is completely free of any DNA polymerase activity and differs functionally from the viral nuclease in its ability to cleave internal phosphodiester bonds in hybrid RNA covalently inserted into DNA. The viral enzyme by contrast requires hybrid RNA with free ends and seems therefore to be an exonuclease. Both cellular and viral RNase H produce 5′-phosphate-terminated mono- and oligonucleotides as degradation products. Work is now in progress to investigate a possible role of RNase H in viral RNA-directed DNA synthesis.

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MAMMALIAN CELL GENETICS

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The Demerec laboratory of the mammalian cell genetics section became operational in March, 1972. Since then we have followed three lines of work.

Reversion

The density-revertant line FISV101 maintains a monolayer by a contact-dependent inhibition of DNA synthesis. Apparently to this extent a revertant descended from a transformed cell can regain the regulation of cell division characteristic of the untransformed cell.

Density revertants of SV40-transformed 3T3 were isolated by means of agents that kill cells in mitosis or in S period. Serum-dependent revertants were isolated in low serum by agents that kill cells in S period. All serum-dependent revertants are also density revertant.

The amount and strand specificity of SV40 RNA was measured in our many different revertants. Although no general correlation was found between reversion and diminished transcription, the density revertant FISV101 appears to have less SV40-specific RNA than its transformed parent.

Attempts were made to recover SV40 virus from the different revertant lines. In all cases where virus could be recovered (4/11 lines), it was identical to wild-type virus.

In collaboration with S. Cram and H. Crissman of the Los Alamos scientific laboratory, we examined the DNA content per cell of many different transformed, revertant, and hybrid mouse cell lines in the Los Alamos flow microfluorometer. G1 peak model values for DNA per cell were higher than the transformed line in all 14 different lines examined. As a control, two transformed sublines that had survived the revertant selection procedures did not differ in DNA per cell from the original transformed line.

Transformation

The trypsin inhibitor TPCK has been reported to specifically inhibit the post-confluent proliferation of transformed cells. We found no difference between the response of 3T3 and SV3T3 cells to 50 μg/ml TPCK. The plating efficiency of both cells was reduced by more than 90%. Transformation frequency in TPCK was identical to untreated controls.

Transformation of 3T3 by SV40 was carried out in the continued presence of 0.5 mg/ml dibutyryl cyclic AMP. Whereas the untransformed 3T3 cells died in the presence of the drug, colonies of transformed cells grew well. The relation of this differential killing to the lower serum requirement of transformed cells is being tested.

SV40 transformed cells grow into colonies on top of monolayers of 3T3 normal cells. Surprisingly, growth of the transformed cells are inhibited by monolayers of their revertants.

Attempts to retransform revertant lines by DNA superinfection and by infection with DNA of other viruses have given negative results.

The transformation process itself is being investigated by comparison of eighty clones isolated from a single infection of 3T3 by SV40. These clones were picked without regard for morphology. They are being characterized with regard to their retention or loss of density-dependent, serum-dependent, and anchorage-dependent growth control. At the same time, these clones are being tested for the presence of viral T-antigen and for their ability to yield virus upon fusion with permissive cells. These experiments should allow correlations to be drawn among the various parameters currently in use to characterize transformation, without the preselection of minority cell types characteristic of standard transformation systems.

Enucleation

Using Prescott's technique of centrifugation in cytocholasin B, we enucleated monolayers of the epithelial line BSC-1 and of the fibroblastic line BHK21. These enucleate populations were removed from cover slips with trypsin and then replated. Both enucleated cell types spread out upon replating. Replated epithelial enucleates were epithelial and replated fibroblastic enucleates were fibroblastic. Ruffled membranes and cell movement also were re-established in both enucleated cell types.

After infection, newly synthesized poliovirus was recovered from enucleated BSC1 cells. This virus was fully infectious, indicating that polio virion assembly needs no nucleus.

Summer Visitors

During the summer months our laboratory was host to Dr. Jack Sheppard, University of Minnesota; Dr. Richard Goldsby, University of Maryland; and Dr. Robert C. Goldman, Case-Western Reserve University.

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PROTEIN SYNTHESIS

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C. Anderson
M. Anderson
P. Baum
J. Bruenn
P. Grisafi
P. Jeppesen
C. Kahn
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Transcription and translation of SV40 and polyoma DNAs.

Coupled transcription and translation of DNA from large plaque polyoma virus using a totally *E. coli* cell-free system yields a complicated mixture of polypeptides. The largest protein made accounts for about 3% of the total product and corresponds in size (47,000 daltons) and tryptic peptide pattern to the major virion protein of polyoma virus (with L. V. Crawford). We conclude that polyoma DNA encodes this main coat protein.

In the same system SV40 DNA stimulates synthesis of a mixture of polypeptides up to 60,000 daltons in molecular weight. None of these corresponds to the major virion protein of SV40 virus (48,000 daltons) as judged by size and fingerprint analyses. The reason for this obvious difference between SV40 and polyoma directed synthesis is now more clear. Whereas the *E. coli* RNA polymerase transcribes polyoma DNA rather symmetrically, it transcribes predominantly only the early strand of SV40 DNA. And in fact in the in vitro coupled system only early strand RNA can be found on the polysomes. Hence it is not surprising that the major virion gene which is presumably a late gene is not expressed in this system.

By using specific fragments of SV40 DNA produced by the *H. influenzae* restriction enzyme we can locate the regions of the DNA that give rise to the in vitro made polypeptides. Preliminary results show that fragments known to map in the early region account for the products. We conclude that this *E. coli* system is translating correctly at least some of the early region of SV40.

Fractionation of specific DNA fragments

Conditions have been worked out for optimal separation on gradient acrylamide gels of specific DNA fragments produced by the action of a number of restriction enzymes on lambda, SV40, T-7, and adenovirus DNAs.

Proteins in cells

Pulse labeling of SV40 infected cells with ^{35}S-methionine showed that synthesis of three of the SV40 virion structural proteins could be readily detected on SDS polyacrylamide gels. The major virion protein (VP1) and the two minor species VP2 and VP3 could first be detected 12-15 hours after infection. Thereafter the rate of synthesis of these proteins increased. The turn on of this synthesis is contingent on DNA synthesis since addition of FUDR or cytosine arabinoside blocks it.

Fingerprinting of VP1 from labelled virions and the corresponding band from infected cells confirmed identification of this protein. Minor changes in the pattern of proteins made in infected cells at early times have also been observed and these are being examined in detail with respect to any relation to SV40 antigens and with respect to proteins made in the in vitro system from SV40 DNA.

The major protein of molecular weight 40,000 that we find in all cell lines was shown to be actin by comparison with purified rabbit muscle actin.

Acrylamide gels of labelled proteins from adenovirus infected cells shows 20-22 new proteins whose aggregate molecular weight accounts for 90-95% of the total coding capacity of the adeno DNA. This pattern is being compared to that produced by infection with the adeno-SV40 hybrid viruses with the hope of identifying the specific SV40 proteins.

SV40 and polyoma virion proteins

In collaboration with Dr. Bernard Hirt (Laussane) we are comparing the virion proteins of SV40 and polyoma. The 3-4 low molecular weight proteins (9,000-14,000) seem to be identical in the two viruses and preparations of host cell histones have these same proteins. We conclude that the virus merely picks these up from the host cell.

Comparison of the other virion proteins of SV40 with those of polyoma show no similarity in either size or tryptic fingerprints. With both, viruses VP1 and VP3 are structurally different proteins whereas VP2 in both cases may be a derivative of VP1.

Transcription and translation of lambda

Polypeptides synthesized in vitro from lambda DNA in a coupled system were further characterized. The mapping of the products has been done using various lambda derivatives. The specific effects of lambda repressor and termination factor were analyzed in detail.

Restriction enzyme RT-1 was shown to cut lambda DNA into six specific pieces which were then mapped by comparing the pattern of fragments from various deletion and substitution mutants. These fragments are now being used in transcription and translation studies.

Search for mutants with altered mRNA metabolism

Mutants of *E. coli* were selected for their ability to continue to express the *lac* operon long after a pulse induction under conditions where we predicted this might be due to prolonged lifetime of messenger. One of these mutants is being examined in detail. It does not appear to have unusually stable *lac* messenger as hoped but it has other unusual properties that may be of interest. After pulse induction of the mutant (which is partially constituative already) β-galactosidase is synthesized for many generations in synchronized steps. This also seems to result in synchrony of cell division. Since the mutation selected is on an episome (mapping near the lac operon) the possibility of wildly aberrant episome replication is being examined.

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ELECTRON MICROSCOPY

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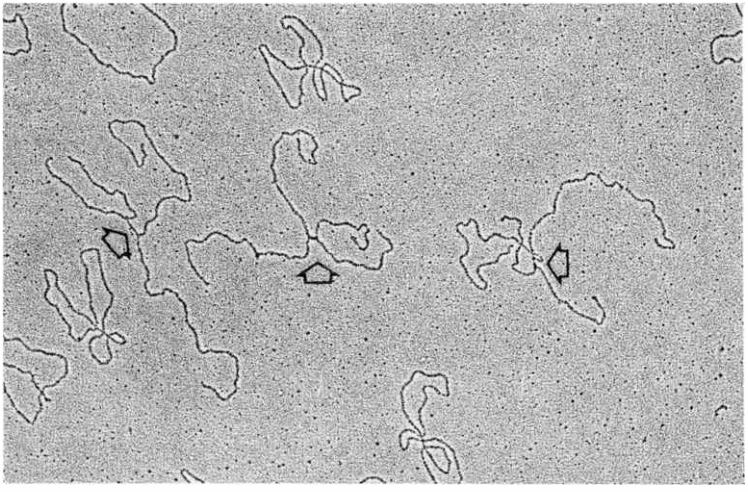
A WANG calculator system has been set up so that length measurements on nucleic acids prepared by the Kleinschmidt procedure can be done in a convenient and accurate way. The data are stored on tape and are easily available for plots of length distributions, plots of denaturation maps, and histograms derived from denaturation maps. This system proved to be of great help for the handling of a rather large amount of data accumulated in the course of the projects listed below.

Analysis of DNA treated with restricting endonucleases

Circular SV40 DNA is converted by restricting endonuclease $R \cdot R_I$ (Yoshimori, 1971) to linear molecules (Morrow and Berg, personal communication). Partial alkaline denaturation to 95% showed that the remaining double-helical DNA is located at a distance of 0.3 fractional lengths from one end of the linear molecules. (The micrograph shows three partially denatured molecules and circular fd DNA. The arrows point to the double-helical sections of the SV40 DNA). This proves that the enzyme breaks the DNA circle at a unique site, and produces a homogeneous population of linear molecules. The method of partial denaturation by Inman and Schnös has been modified so that gene-32 protein can be attached to the single-stranded parts of the DNA. This results in greater accuracy of the measurements of the denatured DNA.

The analysis of linear SV40 DNA produced by the restricting endonuclease P1 (in collaboration with R. Risser, N. Hopkins, and R. Davis) by partial alkaline denaturation showed that this enzyme can cut the circular DNA at any of at least four sites.



The difference in the action of the restricting endonucleases $R \cdot R_I$ and P1 has been confirmed using the alternate method of partially denaturing the linear molecules of SV40 with the help of a DNA-unwinding protein isolated from *E.coli* by Sigal and Alberts.

The molecular weights of the fragments produced by the action of endonuclease $R \cdot R_I$ on adeno-2 DNA and lambda-DNA respectively were determined by length measurements on samples mixed with standards of known molecular weight.

Analysis of in vitro transcription complexes

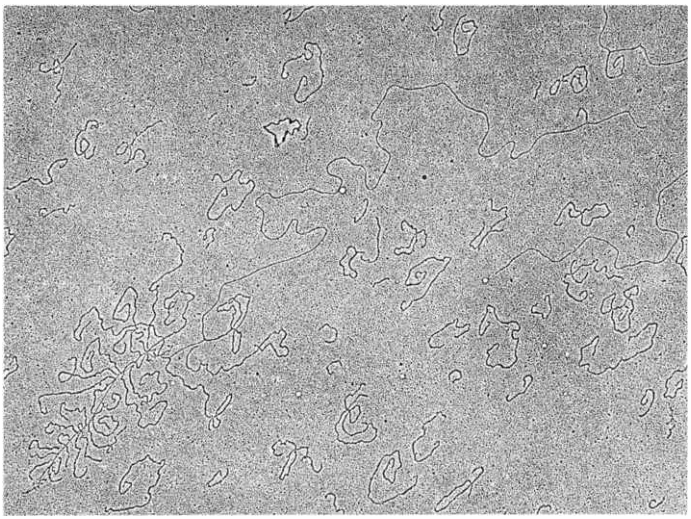
In collaboration with N. Axelrod transcription complexes of T7 DNA with *E.coli* RNA polymerase have been studied. The micrograph shows a transcription complex in which the RNA chains were coated and extended by gene-32 protein, followed by glutaraldehyde fixation and spreading by the Kleinschmidt procedure. This method makes accurate length measurements of the RNA still attached to the template possible. From these measurements a ratio of 870,000 daltons/μm RNA was derived. The position of the "early" promoter .014 fractional lengths from the left end of the DNA was confirmed and an additional weak promoter for *E.coli* polymerase on the right hand side of the molecule could be demonstrated. The method gives rather direct access to the determination of the position of promotor sites, the direction and rate of RNA synthesis, and of the frequency of initiation. It will be applied to the analysis of the more complex lambda transcription.

Partial denaturation of T5 DNA

Although the fine structure of the T5 denaturation maps obtained by partial alkaline denaturation is not very consistent, several characteristic regions in the DNA which melt only at high pH can be used to align the maps in an unambiguous way. The position of the single-strand nicks in the DNA, visible as free single-stranded ends in the denatured parts of the molecules, will be determined.

E. coli chromosome

In collaboration with Worcel and Burgi pictures of the *E. coli* chromosome isolated by sedimentation through high salt sucrose gradients (Stonington and Pettijohn, 1971) were obtained, which confirmed the result obtained by sedimentation analysis that most of the DNA in these complexes is present in the form of superhelical loops.



PUBLICATIONS

Allet, B., P. Jeppesen, J. Katagiri, and H. Delius. 1973. Mapping the DNA fragments produced by cleavage of lambda DNA with endonuclease R1. *Nature. In press.*

Alberts, B., L. Frey, and H. Delius. 1972. Isolation and characterization of gene 5 protein of filamentous bacterial viruses. *J. Mol. Biol.* 68:139.

Delius, H., C. Howe, and A. W. Kozinski. 1971. Structure of the replicating DNA from bacteriophage T4. *Proc. Nat. Acad. Sci.* 68:3049.

Delius, H., N. J. Mantell, and B. Alberts. 1972. Characterization by electron microscopy of the complex formed between T4 bacteriophage gene 32-protein and DNA. *J. Mol. Biol.* 67:341.

Pearson, P., H. Delius, and R. Traut. 1972. Purification and characterization of 50-S ribosomal proteins of *E. coli*. *Eur. J. Biochem.* 27:482.

MOLECULAR GENETICS

D. Zipser
B. Apte
E. Bade
A. Bukhari
M. Metlay
T. Razzaki
B. Shineberg
J. Sugrue

Studies of phage Mu messenger RNA hybridization showed that the overwhelming majority of messenger RNA comes from a single strand of the DNA of Mu. Thus operons appear to be on one strand.

The Mu prophage was mapped with the following results. All prophage have the same map, which is the same as the lytic phage map. The prophage can be inserted in either of two possible directions and anywhere in the *Escherichia coli* chromosome.

We have successfully identified and isolated β-galactosidase fragments which are terminated by the presence of Mu DNA in the *z* gene. These fragments are of importance because they can serve as a way of examining in detail the nucleotide sequence of the boundary between *coli* DNA and Mu DNA of inserted Mu phage.

We have done some work on the electron microscopy of Mu DNA which has, together with the results of other workers in the field, revealed some interesting though as yet unexplained structural features of Mu DNA.

Another result with Mu has been the finding that there is a one-to-one correlation between the orientation of the insertion of the Mu genome into the *lac* operon and the partial induction of the prophage by induction of the *lac* operon. Thus Mu pointing in such a way that its repressor end is toward the operator end of the *lac* operon is induced twentyfold by the addition of IPTG, whereas Mu pointed in the opposite direction is not affected by the addition of IPTG.

We have continued our work on the mechanism of polypeptide reinitiation fragment in the *z* gene. So far the only major result this year is that we have confirmed the phenomenon of "upstream suppression" in which reinitiation of polypeptide synthesis is suppressed if there is another initiation site closer to the operator end of the gene. Presumably the oncoming stream of ribosomes from the first initiation site prevents reinitiation at the second.

We have also continued to study the specific peptide degradation enzymes previously found in our laboratory. It will be recalled that these enzymes specifically degrade aberrant proteins. We have isolated mutants in the degradation system and have shown that the degradation system is extremely sensitive to cyanide and azide, thus showing that it is dependent in some way on energy usage. We are now trying to develop an in vitro system for the assay of these enzymes which specifically degrade aberrant proteins.

Mu Workshop

During the summer we held a workshop on phage Mu. To this workshop came a representative from each laboratory in the world working with Mu—about seven laboratories. The people at the workshop held seminars and exchanged their ideas and results on the biology of Mu phage. They also cooperated together in the laboratory to correlate studies on the genetic map of phage Mu, the complementation groups of Mu, and the nomenclature of the various genetic mutants that have been analyzed.

PUBLICATIONS

Bade, E. G. 1973. Asymmetric transcription of bacteriophage Mu-1. *Virology. In press.*

Bukhari, A. I., and D. Zipser. 1972. Random insertion of Mu-1 DNA within a single gene. *Nature New Biol.* 236:240.

Bukhari, A. I., and M. Metlay. 1973. Genetic mapping of prophage Mu. *Virology. In press.*

Zipser, D., A. I. Bukhari, and J. Zeldis. Random nonhomologous recombination. In *Advances in the Biosciences. Vol. 8.* Pergamon Press.

PROTEIN AND NUCLEIC ACID STRUCTURE

P. Greenaway
M. Kaplan
D. LeVine
B. Root

Studies on SV40

The aim of this laboratory is to chemically characterize the macromolecular components of SV40 particles.

Purified virions were dissociated in 1% (w/v) sodium dodecyl sulfate, pH 8, and the macromolecular components were separated by velocity sedimentation through sucrose gradients. Preparative sodium dodecyl sulfate-polyacrylamide gel electrophoresis is being used to obtain sufficient material for the chemical characterization of each capsid protein. Small amounts of O-phosphorylserine were detected in capsid protein preparations. Assays for the presence of a protein kinase in SV40 were negative and thus modification of the proteins occurred before or during capsid formation probably by a host-cell enzyme.

Uniformally ^{32}P-labeled SV40 DNA was digested with pancreatic deoxyribonuclease and the nucleotides produced were fractionated by ionophoresis on DEAE-ion exchange papers. Rather simple nucleotide fingerprints were obtained. The nucleotides were all small and thus only limited sequence

information was obtained. Pyrimidine tract analysis of SV40 DNA is currently in progress in an attempt to isolate long, unique oligopyrimidines.

The restriction enzyme from *Hemophilus influenzae* cleaves SV40 DNA into eleven unique fragments. These fragments were isolated by electrophoresis on polyacrylamide gels, dephosphorylated by treatment with bacterial alkaline phosphatase, and subsequently rephosphorylated at the 5'-terminus with polynucleotide kinase. The 5'-terminal mononucleotides were isolated by ionophoresis after total nuclease digestion of each fragment. The 5'-terminus of each fragment (the site of cleavage by the restriction enzyme) was guanosine. Sequence analysis of the nucleotides produced by partial nuclease digestion of the phosphorylated fragments is in progress.

Two deoxyribonucleoprotein complexes of SV40 were isolated after alkaline degradation of the virus. Complex electrophoretic patterns were observed after digestion of these complexes with the restriction enzyme from *H. influenzae*. It was concluded that the proteins present in the deoxyribonucleoprotein complexes protect SV40 DNA against endonucleolytic degradation. Further, it seems likely that this protection is due to a random association of the proteins with SV40 DNA. It is postulated that the mechanism of protection is simply one of limiting the accessibility of SV40 DNA to enzymic action.

Wheat-germ Agglutinin

Wheat-germ agglutinin binds nearly equally to both normal and transformed cells but only transformed cells are agglutinated. Wheat-germ agglutinin was purified to homogeneity by precipitation with ammonium sulphate and by chromatography on Sephadex G-75, sepharoseovomucoid and carboxymethyl cellulose. The agglutinin is a glycoprotein containing a single polypeptide chain with an approximate molecular weight of 23000. The protein was further characterized by N- and C-terminal studies, amino acid analysis and by peptide mapping. Equilibrium dialysis of the agglutinin against N-acetylglucosamine and N-acetylneuraminic acid indicated that the protein possibly contained both specific and nonspecific carbohydrate binding sites. It was proposed that the initial step in the agglutination of cells by wheat-germ agglutinin is the nonspecific binding of the lectin to sialic acid residues on the cell surface.

PUBLICATIONS

Greenaway, P. J. 1972. Possible error during assays for phosphorylatin of protein and nucleic acids. *Biochem. Biophys. Res. Commun.* 47:639.

Greenaway, P. J., and D. LeVine. 1973. Equilibrium dialysis of wheat germ agglutinin against N-acytil neuraminic acid. *Nature. In press.*

LeVine, D., and P. J. Greenaway. 1972. Purification and characterization of wheat germ agglutinin. *Biochem. J.* 129:847.

POST GRADUATE TRAINING COURSES

Summer 1972

Since its inception the postgraduate course program at Cold Spring Harbor Laboratory has aimed to meet the rather special need of training in new inter-disciplinary subjects that are either so new or so specialized that they are not adequately treated by universities. The intention is to provide intensive training in the most recent developments and techniques in each of the subjects so that it should be possible for the students to enter directly into research in the particular area.

To do this we bring together a teaching staff from many laboratories around the world. These instructors direct extensive laboratory and lecture programs supplemented with a continuous series of seminar speakers which insures an up-to-date covering of current research work.

In addition to the continuing bacterial genetics, yeast genetics, cell culture, and animal virus courses and the tumor virus workshop, we have expanded into new areas: molecular cytogenetics, neurobiology, and a course on the behavioral genetics of a nematode. The three workshops included mu, phycomyces, and neurobiology.

1) ANIMAL CELL CULTURE—June 16-July 6

Major topics covered included phase microscopy, trypsinization, growth curves, saturation densities, cloning, cell synchrony, radioautography, mycoplasma testing, storage by freezing, suspension cultures, and lectin agglutination. Sendai virus-induced cell hybrids were produced between embryonic cells in primary culture and cell lines and chicken erythrocytes. Karyotypes were studied, utilizing students' peripheral lymphocytes, and student-produced hybrids by quinacrine mustard and Giemsa staining procedures. Fluorescence microscopy was used for the mustard-stained chromosomes and for detecting T-antigen in cells transformed with SV40 virus.

Some of the more special techniques covered were the histological detection of acetylcholinesterase activity in neuroblastoma cells, detection of surface antigens by means of hemadsorbtion, detection of immunoglobulin synthesis by plasmacytoma cells, and the effects of cyclic AMP on established cell lines and primary embryonic cells. In addition, photomicrography and media preparation were discussed.

INSTRUCTORS

Coon, Hayden, Ph.D., National Cancer Institute, Bethesda, Maryland
Roth, Stephen, Ph.D., The Johns Hopkins University, Baltimore
Webb, Glenda, M.A., The Johns Hopkins University, Baltimore
Vogel, Tikva, B.A., National Institutes of Health, Bethesda, Maryland

STUDENTS

Barry, Jack, Ph.D., Princeton University, Princeton, New Jersey
Berger, Hillard, Ph.D., The Johns Hopkins University, Baltimore
Cooper, Geoffrey, B.S., University of Miami, Florida
Croizat, Bernard P., Ph.D., Faculte des Sciences, Paris
Fairfield, Stephen A., Ph.D., Roche Institute of Molecular Biology, Nutley, New Jersey
Fleischer, Sidney, Ph.D., Vanderbilt University, Nashville, Tennessee
Fleischer, Becca C., Ph.D., Vanderbilt University, Nashville, Tennessee
Fulton, Chandler M., Ph.D., Brandeis University, Waltham, Massachusetts
Juliano, Rudolph L., Ph.D., Roswell Park Memorial Institute, Buffalo
Kutchai, Howard C., Ph.D., The Johns Hopkins University, Balitmore
Lever, Julia E., Ph.D., University of California, San Diego
Lund, Elsebet, Ph.D., University of Aarhus, Denmark
Monroy, Gladys H., M.S., Public Health Research Institute, New York City
Nissley, Peter S., M.D., National Cancer Institute, Bethesda, Maryland
O'Neill, J. Patrick, Ph.D., State University of New York, Stony Brook
Passarge, Eberhard, M.D., University of Hamburg, Germany
Perkins, John P., Ph.D., University of Colorado Medical Center, Denver
Ruoho, Arnold E., Ph.D., University of California, San Diego
Tartof, Kenneth D., Ph.D., The Institute for Cancer Research, Philadelphia
Wyche, James H., Ph.D., University of California, Berkeley

SEMINARS

Harry Eagle, Albert Einstein College of Medicine, *Cell culture parameters.*
Robert DeLong, Massachusetts General Hospital, *Brain cell specificity.*
Gordon Sato, University of California, San Diego, *Growth control.*
Stephen Roth, Johns Hopkins University, *Malignancy and morphogenesis.*
David Yaffee, Weizmann Institute, Rehovot, Israel, *Muscle cell culture.*
Martin Rechsteiner, University of Utah, *Protein transport via fusion.*

Elliot Levine, Albert Einstein College of Medicine, *Mycoplasma infection.*
Max Burger, Princeton University, *Malignant cell surfaces.*
I. Dawid, Carnegie Institution of Washington, *Mitochondrial DNA in hybrids.*
Robert Pollack, Cold Spring Harbor Laboratory, *Growth control.*
Michael Edidin, Johns Hopkins University, *Membrane fluidity.*
John Minna, National Institutes of Health, *Neuroblastoma hybrids.*
Tom Caskey, National Institutes of Health, *Mutagenesis in cells.*
Elizabeth Neufeld, National Institutes of Health, *Mucopolysaccharidosis in vitro.*
Imogene Schneider, Walter Reed Hospital, *Insect cell culture.*
Leo Sachs, Weizmann Institute, Rehovot, Israel, *Normal and neoplastic cells.*
George Johnson, National Institutes of Health, *Cyclic AMP and cells.*
Mathew Scharff, Albert Einstein College of Medicine, *Immunoglobulin synthesis.*

2) MOLECULAR BIOLOGY AND GENETICS OF YEAST—June 16-July 6

This course covered in detail the current techniques employed in the genetic analysis of yeast, including tetrad analysis, random spore analysis, complementation, mitotic recombination, and fine-structure mapping. Various types of chromosomal and mitochondrial mutants were isolated, and some of these were examined for protein synthesis, RNA synthesis, cytochrome content, UV sensitivity, enzyme levels, etc.

Several of the students undertook special projects, which included the isolation of hemin-dependent mutants and the genetic analysis of a usually wild strain of *Saccharomyces* that produced two-spored asci.

INSTRUCTORS

Fink, Gerald, Ph.D., Cornell University, Ithaca, New York
Lawrence, Christopher, Ph.D., University of Rochester, New York
Sherman, Fred, Ph.D., University of Rochester, New York
Rytka, Joanna, Ph.D., Polish Academy of Science, Warsaw

STUDENTS

Baskin, Leonard S., Ph.D., Stevens Institute of Technology, Hoboken, New Jersey
Blamire, John, Ph.D., Albert Einstein College of Medicine, Bronx, New York
Cryer, Dennis R., B.A., Albert Einstein College of Medicine, Bronx, New York
Goffeau, Andre, Ph.D., University of Louvain, Belgium
Heckman, Joyce E., B.A., Massachusetts Institute of Technology, Cambridge
Mason, Thomas L., Ph.D., Cornell University, Ithaca, New York
Mowshowitz, Deborah, Ph.D., Columbia University, New York City
Riggs, Arthur D., Ph.D., City of Hope National Medical Center, Duarte, California.
Rubin, Gerald M., B.S., Medical Research Council, Cambridge, England
Rytka, Joanna, Ph.D., Polish Academy of Science, Warsaw
Sebastian, Jesus, Ph.D., Brandeis University, Waltham, Massachusetts
Soll, Larry J., Ph.D., Harvard Medical School, Boston
Tipper, Donald J., Ph.D., University of Massachusetts Medical School, Worcester
Whitfield, Carolyn D., Ph.D., University of Michigan, Ann Arbor
Wickner, Reed B., M.D., Albert Einstein College of Medicine, Bronx, New York

SEMINARS

Robert K. Mortimer, University of California, Berkeley, *Genetic mapping in yeast.*
-- Genetic control of recombination and radiation sensitivity.
Leland H. Hartwell, University of Washington, *Genetic control of cell division in yeast.*
-- Integration of the cell cycle with the life cycle.
Donald D. Hurst, Brooklyn College, *Gene conversion and the mechanism of genetic recombination.*
Michael Esposito, University of Chicago, *Genes controlling meiosis and recombination in yeast.*
C. F. Robinow, University of Western Ontario, *Nuclear structure and behavior in yeast (I).*
-- Nuclear structure and behavior in yeast (II).
Calvin S. McLaughlin, University of California, Irvine, *Mutations and antibiotics that affect protein synthesis (I).*
-- Mutations and antibiotics that affect protein synthesis (II).
Julius Marmur, Albert Einstein College of Medicine, *Nucleic acids in yeast.*
Fred Sherman, University of Rochester, *Genetic control of cytochrome c in yeast (I).*
-- Genetic control of cytochrome c in yeast (II).
Christopher Lawrence, University of Rochester, *Genetic control of UV mutagenesis in yeast.*
Gerald R. Fink, Cornell University, *Observations on the "Killer" factor in yeast.*
-- The regulation of histidine biosynthesis in yeast.
Michael Vodkin, Cornell University, *The "Killer" phenomenon in yeast.*
Robert Lowenstein, Cornell University, *Nonmendelian inheritance of methionine auxotrophy in yeast.*
Michael Resnick, University of Rochester, *Radiation repair in yeast.*

3) BASIC PRINCIPLES OF NEUROBIOLOGY—June 16-July 6

An introductory course in neurobiology for research workers with no previous experience in the field. Subjects covered included action potential mechanisms, synaptic structure, and integration in the central nervous system. Developmental aspects of the nervous system were considered, as well as some aspects of the vertebrate central nervous system such as the cerebellum, the visual system, etc.

The three week course consisted of about thirty lectures, of which approximately half emphasized basic principles and classical experiments in the field; the other half described current research in neurobiology and were given by guest lecturers. Demonstrations were made to illustrate anatomical techniques, dissection, and the physiological properties of the electric eel, the leech, and hamster muscle. Students participated in the dissection of animals, histochemical staining, and elementary physiological recording.

INSTRUCTORS

Hudspeth, Albert J., Harvard Medical School, Boston
Kelly, James, Harvard Medical School, Boston
Kelly, Regis, Ph.D., University of California Medical Center, San Francisco
Nicholls, John, M.D., Harvard Medical School, Boston
Van Essen, David, Harvard Medical School, Boston

STUDENTS

Applebury, Meredithe L., Ph.D., Bell Telephone Laboratories, Murray Hill, New Jersey
Brandt, Bruce L., Ph.D., Stanford University, Stanford, California
Brenner, Hans R., University of Konstanz, Germany
Clay, John R., B.S., University of Rochester, New York
Culp, William J., Ph.D., The Salk Institute for Biological Studies, San Diego
Hastings, Stuart P., Ph.D., State University of New York, Buffalo
Haynor, David R., Ph.D., Harvard Medical School, Boston
Imada, Masaru M. I., Ph.D., Princeton University, Princeton, New Jersey
Kelly, Leonard D., Ph.D., The University, Leeds, England
Law, John H., Ph.D., University of Chicago
Loh, Peng Y., B.S., University of Pennsylvania, Philadelphia
Maccioni, Baraona R. B., Ph.D., University of Chile, Borgono
Mohler, Hanns H. P., Ph.D., Medical Research Council, Carshalton, England
Ort, Carol A., B.S., University of California, Berkeley
Pettigrew, Rona, B.S., University of New South Wales, Kensington, Australia
Safer, Daniel, B.A., Brandeis University, Waltham, Massachusetts
Siddiqui, M. A. Q., Ph.D., Roche Institute of Molecular Biology, Nutley, New Jersey
Streisinger, George, Ph.D., University of Oregon, Eugene
Vogel, Zvi, Ph.D., National Heart Institute, Bethesda, Maryland
Yanane, Tetsuo, Bell Telephone Laboratories, Murray Hill, New Jersey
Zweig, George, Ph.D., California Institute of Technology, Pasadena

SEMINARS

John Nicholls, Harvard University, *Introduction.*
-- Ionic basis of resting and action potentials.
-- Experimental evidence for that ionic basis.
-- Passive electrical properties of nerves.
-- Chemical and electrical synapses.
-- Permeability changes.
-- Quantal release of transmitters.
-- Leech neurobiology.
Albert J. Hudspeth and James Kelly, Harvard Medical School, Anatomy of nerve cells.
J. N. Ritchie, Yale University School of Medicine, *Ionic pumps.*
David Van Essen, Harvard Medical School, *Sensory transduction and adaptation.*
Motoy Kuno, University of North Carolina, *Spinal physiology (I).*
-- Spinal physiology (II).
Albert J. Hudspeth and Frank Werblin, University of California, Berkeley, *Retinal anatomy.*
R. Cone, Johns Hopkins University, *Retinal physiology (I).*
Frank Werblin, University of California, Berkeley, *Retinal physiology (II).*
M. Cowan, Washington University School of Medicine, *Development and morphology of CNS (I).*
-- Development and morphology of CNS (II).
-- Anatomy and physiology of the cerebellum.
-- Specificity and regeneration (I).
-- Specificity and regeneration (II).
D Hubel, Harvard University, *Retinal ganglion, LGN, simple cells.*
-- Complex and hypercomplex cells.
-- Binocular vision.
-- Deprivation.
Regis Kelly, University of California Medical Center, San Francisco, *Biochemistry of the nervous system (I).*
-- Biochemistry of the nervous system (II).
Gerald Fischbach, National Institutes of Health, *Nerve cells in culture.*
G. Szabo, University of California, Los Angeles, *Artificial membranes.*
Hugh Rowell, University of California, Berkeley, *Insect neurophysiology.*
Seymour Benzer, California Institute of Technology, *Drosophila neurobiology.*
E. Kandel, N.Y.U. College of Medicine, *Aplysia neurobiology.*
Stephen Kuffler, Harvard University, *Frog heart.*

4) ANIMAL VIRUSES—July 10-30

This course consisted of lectures, discussions, and laboratory exercises covering the following topics: Preparation of primary cell cultures; growth, cloning, and synchronization studies of continuous tissue culture cell lines; growth of virus stocks and their titration by plaque assay and hemagglutination; purification and electron microscopic examination of virions; determination of virus-specific macromolecules in infected cells by radioautography and cell fractionation techniques; assay of virus-induced and virion-associated enzymes, and effects of interferon and other inhibitors on virus replication.

Other topics covered were the analysis of events in the virus replication cycle by the use of *ts* mutants; translation of viral RNA by mammalian cell-free extracts, and electrophoretic characterization of in vitro products; virus-mediated oncogenic transformation, and cell fusion and karyotyping of hybrid and parental cell lines.

INSTRUCTORS

Kates, Joseph, Ph.D., University of Colorado, Boulder
Shatkin, Aaron, Ph.D., Roche Institute for Molecular Biology, Nutley, New Jersey
La Fiandra, Alba, Roche Institute for Molecular Biology, Nutley, New Jersey
Miller, Linda, University of Colorado, Boulder
Polisky, Barry, University of Colorado, Boulder

STUDENTS

Abrahams, Susan J., A.B., Columbia University, New York City
Avitabile, Allessandra, Ph.D., University of Naples, Italy
Bendis, Ina K., B.S., Albert Einstein College of Medicine, Bronx, New York
Brandner, Gerhard G., Ph.D., University of Freiburg, Germany
Buetti, Elena E. B., dip. Nat. Sci., University of Geneva, Switzerland
Caruthers, Marvin H., Ph.D., Massachusetts Institute of Technology, Cambridge
Chou, Iih-Nan (George), Ph.D., University of Illinois, Urbana
Cordaro, J. Christopher, Ph.D., The Johns Hopkins University, Baltimore
Incardona, Nino L., Ph.D., Florida State University, Tallahassee
Jelinek, Warren, Ph.D., Columbia University, New York City
Kahan, Eunice, Ph.D., Michigan Technological University, Houghton
Kamen, Robert I., Ph.D., University of Zurich, Switzerland
Lansman, Robert A., B.A., Stanford University, Stanford, California
Mangel, Walter F., Ph.D., University of California, Berkeley
Mora-Carrasco, Fernanco, M.D., Universidad de Nacional Autonoma, Mexico City
Rosenthal, Leonard J., Ph.D., Massachusetts General Hospital, Boston
Rozengurt, Juan E., Ph.D., Princeton University, Princeton, New Jersey
Smith, Kelvin E., Ph.D., Harvard Medical School, Boston
Veomett, George E., Ph.D., University of Colorado, Boulder
Weingarten, Murray D., B.Sc., Princeton University, Princeton, New Jersey

SEMINARS

D. Prescott, University of Colorado, *Cell cycle.*
— — DNA replication.
R. Perry, Institute for Cancer Research, Philadelphia, *RNA metabolism.*
Carel Mulder, Cold Spring Harbor Laboratory, *Structure of Ad-SV40 hybrid.*
H. Ginsberg, University of Pennsylvania, *Adenovirus.*
E. Pfefferkorn, Dartmouth College, *Arbovirus.*
J. Maizel, Albert Einstein College of Medicine, *Poliovirus.*
H. Lodish, Massachusetts Institute of Technology, *Protein synthesis.*
L. Prevec, McMaster University, Canada, *VSV.*
F. Rapp, Pennsylvania State Medical School, Hershey, *Herpesvirus and SV40-adeno hybrids.*
Hajo Delius, Walter Keller, Heiner Westphal, William Sugden, Cold Spring Harbor Laboratory, *Transcription of SV40 DNA.*
P. Choppin, Rockefeller University, *Myxo-, paramyxovirus.*
Brian McAuslan, Roche Institute of Molecular Biology, *Polyhedral cytoplasmic deoxyvirus.*
H. Hanafusa, New York Public Health Research Institute, *RNA tumor viruses.*
Thomas Benjamin, New York Public Health Research Institute, *DNA tumor viruses.*
Robert Pollack, Cold Spring Harbor Laboratory, *Cell hybrids.*
Clarence Colby, University of Connecticut, *Interferon.*
J. Hurwitz, Albert Einstein College of Medicine, *Reverse transcriptase.*
Joseph Kates, University of Colorado, *Poxvirus.*
Aaron Shatkin, Roche Institute, *Reovirus.*

5) BACTERIAL GENETICS—July 10-30

Students were introduced to the basic techniques involved in mutant isolation and characterization, genetic analysis, and the study of gene expression. Laboratory experiments in these areas were accompanied by lectures on relevant background material.

The class carried out an extensive project on the isolation of λ transducing phages carrying different regions of the *Escherichia coli* chromosome, as well as small individual research projects. Daily seminars were presented by distinguished research workers.

INSTRUCTORS

Gross, Julian, Ph.D., University of Edinburgh, Scotland
Scaife, John, Ph.D., University of Edinburgh, Scotland
Taylor, Austin L., Ph.D., University of Colorado Medical School, Denver
Finnegan, David, Ph.D., University of Edinburgh, Scotland
Kenny, James, University of Colorado Medical School, Denver

STUDENTS

Burstin, Stuart J., A.B., New York University Medical Center, New York City
Cole, Patricia E., M. Phil., Columbia University, New York City
Fulcher, Carol A., B.S., University of Virginia, Charlottesville
Galloway, Denise A., B.S., Hunter College, New York City
Geiger, Hon R., B.S., University of Connecticut, Storrs
Heath, Harry E., III, Ph.D., University of Illinois, Urbana
Hess, Winand, B.S., Brandeis University, Waltham, Massachusetts
Jan, Lily, M.S., California Institute of Technology, Pasadena
Khachatourians, George G., Ph.D., Oak Ridge National Laboratory, Oak Ridge, Tennessee
Lipson, Edward D., Ph.D., California Institute of Technology, Pasadena
Lovely, Peter S., M.A., University of Oregon, Eugene
McCulley, Carol M., B.A., Medical University of South Carolina, Charleston
Merrick, Joseph E., Ph.D., State University of New York, Buffalo
Monnat, Raymond J., Jr., B.S., University of Wisconsin, Madison
Prasad, Chandan, Ph.D., National Institutes of Health, Bethesda, Maryland
Siler, Jack G., Ph.D., Wistar Institute, Philadelphia
Speedie, Marilyn K., B.S., Purdue University, Lafayette, Indiana
Taylor, Paula F. G., M.S., University of Vermont, Burlington
Town, Christopher D., Ph.D., Stanford School of Medicine, Stanford, California
Vogel, Arthur M., B.A., Cold Spring Harbor Laboratory

SEMINARS

C. F. Fox, University of California, Los Angeles, *Membrane structure and assembly.*
L. Soll, Harvard Medical School, *tRNA mutations: the anticodon and amino acid specificity.*
Jeffrey Miller, University of Geneva, *Translation re-initiations in* E. coli.
D. Dubnau, New York Public Health Research Institute, *Transformation in* R. subtilis.
Ross B. Inman, University of Wisconsin, *Phage* λ *replication.*
W. D. Donachie, University of Edinburgh, *Cell division in* E. coli.
M. Masters, University of Edinburgh, *Bidirectional replication in* E. coli.
K. Ippen, University of Pittsburgh, *Genetics of the sex factor, F.*
Masayasu Nomura, University of Wisconsin, *Ribosome structure and assembly.*
A. Newton, Princeton University, *Developmental genetics of* Caulobacter.
B. deCrombrugghe, National Institutes of Health, *Role of cAMP in transcription.*
Max Delbruck, California Institute of Technology, Phycomyces.
J. Dahlberg, University of Wisconsin, *Initiation of lambda transcription.*

6) EXPERIMENTAL TECHNIQUES IN NEUROBIOLOGY—July 10-30

The course focused on the marine snail *Aplysia californica,* whose nervous system consists of unusually large cells ranging from 50 μ to almost 1 mm in diameter, although some experiments were also done with the land snail, *Helix aspersa.* As a result of the large size of their cells, the technical problems involved in intracellular electrical recordings are considerably reduced. Equally facilitated are the problems involving dissection of individual neurons for biochemical and morphological studies.

Emphasis was placed on the following experimental techniques: intracellular recording of controlled membrane potentials, intracellular injection of ions, ionophoretic application of drugs, physiological and electrical stimulation of selected activities. These techniques were used in explaining the problems of resting potential, action potential, the sodium potassium pump, and ionic and pharmacological bases of synaptic transmission.

INSTRUCTORS

Ascher, Philippe, Ph.D., Ecole Normale Superieure, Paris
Kehoe, JacSue, Ph.D., Ecole Normale Superieure, Paris
Thomas, Roger, University of Bristol, England

STUDENTS

Arsenault, Molly, B.A., University of Colorado, Boulder
Brandt, Bruce L., Ph.D., The Salk Institute for Biological Studies, San Diego
Brenner, Hans R., University of Konstanz, Germany
Chun, Linda L. Y., B.S., Harvard Medical School, Boston
Haynor, David R., Ph.D., Harvard University, Cambridge, Massachusetts
Loh, Peng Y., B.Sc., University of Pennsylvania Medical School, Philadelphia
Streisinger, George, Ph.D., University of Oregon, Eugene
Sytkowski, Arthur J., M.D., National Heart and Lung Institute, NIH, Bethesda, Maryland
Yamane, Tetsuo, Ph.D., Bell Telephone Laboratories, Murray Hill, New Jersey
Zweig, George, Ph.D., California Institute of Technology, Pasadena

SEMINARS

Herbert Levitan, National Institutes of Health, *Biophysical control of membrane permeability.*
Henry Lester, Pasteur Institute, *ACh receptor at the neuromuscular junction.*
William Cottrell, University of St. Andrews, Scotland, *Synpatic transmitters in Helix.*
Donald Geduldig, University of Maryland, *Pump related conductances.*
Chris Ashley, University of Bristol, England, *Experiments on muscle cells with the Ca^{++}-sensitive light emitting protein Aequorin.*
Shigehiro Nakajima, Purdue University, *Muscle physiology: excitation-contraction coupling and electrophysiology of the T system.*
Harold Gainer, National Institutes of Health, *Correlative electrophysiological and protein synthetic studies on identifiable mollusc neurons.*

7) TUMOR VIRUS WORKSHOP—August 2-24

This course covered in depth the whole tumor virus field. It consisted for the most part of lectures and discussions. The final week of the course comprised the fourth annual Cold Spring Harbor meeting on tumor viruses, a meeting on the oncogenic papova viruses, and a meeting on the herpes viruses.

INSTRUCTORS

Hirt, Bernhard, Ph.D., Swiss Institute for Cancer Research, Lausanne
Weiss, Robin, Ph.D., Imperial Cancer Research Fund Laboratories, London

STUDENTS

Aviv, Haim, Ph.D., National Institutes of Health, Bethesda, Maryland
Axelrod, Nancy J., M.S., Harvard University, Cambridge, Massachusetts
Benz, Edmund W., B.A., Vanderbilt School of Medicine, Nashville, Tennessee
Burger, Armin, Ph.D., University of Freiburg, Germany
Cooper, Geoffrey M., B.S., University of Miami School of Medicine, Florida
Fey, Georg, M.S., University of Erlangen, Germany
Hilgers, Jo J., Ph.D., Netherlands Cancer Institute, Amsterdam
Klagsbrun, Michael, Ph.D., National Institutes of Health, Bethesda, Maryland
Kurth, Reinhard, M.D., Robert Koch Institut, Nordufer, Germany
Lopez, Ruben H., M.D., D.Sc., The Salk Institute for Biological Studies, San Diego
Medrano, Leandro, Ph.D., Massachusetts Institute of Technology, Cambridge
Mousset, Suzanne, Ph.D., Universite Libre de Bruxelles, Rhode-St. Genese, Belgium
Murphy, Helen, Ph.D., University College, London
Papas, Takis S., Ph.D., National Heart Institute, NIH, Bethesda, Maryland
Paulin, Denise, Ph.D., Institut Pasteur, Paris
Prage, Lennart V., Ph.D., Rutgers Medical School, New Brunswick, New Jersey
Rosenberg, Ralph A., M.S., University of Chicago
Shapiro, Stuart Z., B.A., Albert Einstein College of Medicine, Bronx, New York
Silberstein, Harvey, B.S., Albert Einstein College of Medicine, Bronx, New York
Tershak, Daniel R., Ph.D., Pennsylvania State University, University Park

SEMINARS

L. Prage, Rutgers University Medical School, *Adenovirus proteins.*
R. Bassin, National Cancer Institute, *Murine leukemia and sarcoma viruses.*
P. Tegtmeyer, Case Western Reserve University, *Genetics of DNA tumor viruses.*
E. Fleissner, Sloan-Kettering Institute, *Proteins of RNA tumor viruses.*
P. Duesberg, University of California, Berkeley, *RNA.*
Bradford Ozanne, Cold Spring Harbor Laboratory, *Agglutination by lectins.*
M. Weber, University of Illinois, *Membrane function in normal and transformed cells.*
R. Kurth, Robert Koch Institut, Berlin, *Tumor specific surface antigens.*
Robert Pollack, Cold Spring Harbor Laboratory, *Stable phenotypic reversion of the transformed state.*
F. Lilly, Albert Einstein College of Medicine, *Genetics of murine viral leukemogenesis.*
J. Hilgers, Netherlands Cancer Institute, *Mammary tumor viruses; Immunofluorescence techniques.*
Joseph Sambrook, Cold Spring Harbor Laboratory, *Cell surface.*
David Baltimore, Massachusetts Institute of Technology, *The DNA polymerase of RNA tumor viruses.*
H. Varmus, San Francisco Medical Center, *Nucleic acid hybridization of mammary tumor virus and host cell.*

8) MOLECULAR CYTOGENETICS—August 2-22

The 1972 Molecular Cytogenetics course began with considerations of classical cytological techniques and problems, and utilized a wide variety of plant and animal chromosome material, such as *Drosophila* polytene and *Triturus* lampbrush chromosomes, and meiotic chromosomes from pokeweed and grasshoppers.

This orientation in morphological, cytochemical, and microscopic techniques was followed by biochemical experiments designed to elucidate molecular organizations of eukaryotic genomes. These experiments involved in situ hybridization, renaturation kinetics, chromosome isolation and fractionation, and visualization of transcription in the electron microscope.

INSTRUCTORS

Laird, Charles, Ph.D., University of Washington, Seattle
Pardue, Mary Lou, Ph.D., University of Edinburgh, Scotland, and Massachusetts Institute of Technology Cambridge
Hutchison, Nancy, University of Texas, Austin

STUDENTS

Bachop, William E., Ph.D., Clemson University, Clemson, South Carolina
Calve, James P., M.A., University of Connecticut, Storrs
Cohen, Maurice, Jr., M.S., Oak Ridge National Laboratory, Oak Ridge, Tennessee
Davidson, Norman R., Ph.D., California Institute of Technology, Pasadena
Dusenbery, Ruth L., California Institute of Technology, Pasadena
Heywood, Janet L., B.A., Harvard University, Cambridge, Massachusetts
Kaback, David B., B.S., Brandeis University, Waltham, Massachusetts
Kasamatsu, Harumi, Ph.D., California Institute of Technology, Pasadena
Selander, Ritva-Kajsa, Ph.D., Folkhalsan Institute of Genetics, Helsingsors, Finland

SEMINARS

Bruce Nicklas, Duke University, *Mitosis: chromosome interactions with other chromosomes, the spindle, and experimenters.*
Barbara McClintock, Carnegie Institution of Washington, *Cytogenetics of plant chromosomes.*
Burke Judd, University of Texas, *Cytogenetics of polytene chromosomes.*
Hewson Swift, University of Chicago, *Cytochemistry of polytene chromosomes.*
Mary Lou Pardue, Massachusetts Institute of Technology, *Localization of the genes for 5 S ribosomal RNA and histone mRNA.*
Norman Davidson, California Institute of Technology, *Genetic sequences in nucleic acids by electron microscopy.*
Charles Laird, University of Washington, Drosophila *chromosomes.*
Carl Schildkraut, Albert Einstein College of Medicine, *DNA of fractionated mammalian metaphase chromosomes.*
Joseph Maio, Albert Einstein College of Medicine, *Fractionation of mammalian chromosomes.*
Aimee Bakken, Yale University, *Visualization of transcription.*

9) BEHAVIORAL GENETICS OF A NEMATODE—August 2-22

This new course consisted of discussions, defined laboratory exercises, and less well defined laboratory projects concerning the small soil nematode *Caenorhabditis elegans.* This animal's simple 200-cell nervous system, 3½ day generation time, and relative ease of culture make it well suited for genetic studies of nervous function.

Discussions centered on the functions, anatomy, and development of the nervous system. Defined laboratory exercises dealt first with culture (both axenic and monoxenic), storage, developmental synchronization, and mutagenesis; then with behavior, including spontaneous activity variations, normal modes of movement, and responses to environmental stimuli; and finally with altered behaviors of a variety of recently isolated mutants. The laboratory projects involved genetic and behavioral studies with some of these mutants.

INSTRUCTORS

Pertel, Ruth, Ph.D., National Institutes of Health, Bethesda, Maryland
Russell, Richard, Ph.D., California Institute of Technology, Pasadena
Dusenberry, David, Ph.D., California Institute of Technology, Pasadena



STUDENTS

Ash, John F., B.S., Stanford University, Stanford, California
Byerly, William L., Ph.D., Oberlin College, Oberlin, Ohio
Feiss, Michael, Ph.D., University of Iowa, Iowa City
Guthrie, Christine, Ph.D., University of Wisconsin, Madison
Herman, Robert K., Ph.D., University of Minnesota, St. Paul
Lewis, James A., B.S., University of California, Berkeley
Schildkraut, Carl L., Ph.D., Albert Einstein College of Medicine, Bronx, New York
von Ehrenstein, Gunter, M.D., Max-Planck-Institut fur experimentelle Medizin, Gottingen, Germany

SEMINARS

J. S. Parkinson, University of Wisconsin, *Bacterial chemotaxis.*
R. Wyman, Yale University, *Neural circuits and insect flight.*
C. Kung, University of California, Santa Barbara, *Behavioral mutants of* Paramecium.
R. Konopka, Stanford University, *Clock mutants and gynandromorphs in Drosophila.*
E. Mocagno, Columbia University, *Serial section neuroanatomy in the* Daphnia *visual system.*
S. Kater, University of Iowa, *Neurophysiology and genetics in a snail.*
J. Minna, National Institutes of Health, *Neuroblastoma cells in culture.*

10) WORKSHOPS

A) MU WORKSHOP July 10-31

As far as is known, all laboratories working with bacteriophage Mu were represented at the workshop. A very extensive and intensive exchange of information took place. Laboratory work included complementation tests between Mu amber mutants from different laboratories, and deletion mapping to confirm and extend the genetic map of prophage Mu obtained by different groups. Twenty-one cistrons of Mu were identified. The joint efforts resulted in elucidation of a comprehensive genetic map of prophage Mu. This map is expected to be published in Virology.

A meeting was held to devise and recommend a uniform Mu nomenclature. These recommendations also will be published.

There were no invited speakers. The workshop participants discussed the work of their laboratories in the general categories: genetic mapping of prophage and the vegetative genome, Mu-mediated insertions, DNA structure, and transcription. Participants in addition to those on the Cold Spring Harbor Laboratory staff are listed below.

WORKSHOP PARTICIPANTS

Boram, William, B.S., University of California, San Diego
Couturier, Martine, Ph.D., Massachusetts Institute of Technology, Cambridge
Howe, Martha, Ph.D., Centro Degli Acidi Nucleici, Gruppo Regolazione, Rome, Italy
Hsu, Ming-Ta, B.S., California Institute of Technology, Pasadena
Martuscelli, Jaime, M.D., Instituto de Investigaciones Biomedicas, Mexico City
Nomura, Masayasu, Ph.D., University of Wisconsin, Madison
Schroeder, Walter, B.S., Institut fur Genetik, Cologne, Germany
Taylor, Austin L., Ph.D., University of Colorado Medical Center, Denver
Toussaint, Ariane, Ph.D., Universite Libre de Bruxelles, Rhode-St. Genese, Belgium
van der Putte, Piet, Ph.D., R.V.O.-T.N.O. Medical Biological Laboratory, Ryswyk, The Netherlands

VISITORS

Abelson, John, Ph.D., University of California, San Diego
Reznikoff, William, Ph.D., University of Wisconsin, Madison

B) PHYCOMYCES GENETICS WORKSHOP--July 6-August 31

The primary focus of the workshop was using genetic approaches to solve existing problems of behavoiral physiology and to develop new systems to a point where genetic analysis would become meaningful.

Enrique Cerda-Olmeda initiated a search for spontaneously-occurring dominant mutations. He successfully isolated several crystal violet resistant mutants and nystatin resistant mutants from heterokaryotic strains of *Phycomyces.* The fact that the resistant survivors are still heterokaryotic clearly demonstrates that the mutations he obtained are dominant to the wild-type allele. These mutations will be useful as genetic markers in complementation analysis. Cerda-Olmeda and Richard Sutter reinvestigated the optimal activation conditions for spore germination on acidified complete medium plates where *Phycomyces* mycelia grows as discrete colonies. It was found that a heat shock treatment was much superior to sodium acetate with respect to activation of spore germination on pH 3.3 glucoseasparagine-yeast extract plates. It had been reported previously that heat treatment and sodium acetate were equally effective at higher pH values.

Max Delbruck and Yno Jan conducted extensive mathematical and physiological investigations into the nature of the *Phycomyces* avoidance response. Mathematical models for the avoidance system suggest the emitter-absorber, presumably located in the sporangiophore growing zone, must be an exceedingly weak absorber and hence allows the derivation of an expression for the characteristic lifetime of the emitted molecule. Critical experiments have disproved the simple theory of a gas which is a growth inhibitor and is absorbed by barriers. The possibility that avoidance is caused by a gas which is reflected by barriers and

stimulates growth had been previously eliminated. Other experiments also have eliminated electrostatic polarizability of the sporangiophore as an important factor in avoidance. More complicated explanations for the effect must now be considered.

Ruth Dusenbery, Terry Leighton, and Walter Keller continued studies on *Phycomyces* RNA polymerase. An RNA polymerase activity similar to mammalian RNA polymerase I in chromatographic properties and inhibitor sensitivity has been isolated from early-log, mid-log, and late-log cultures of *Phycomyces*. Inhibitor experiments suggest the possibility of an activity similar to mammalian RNA polymerase II being present but unstable under the chromatographic conditions employed.

Leighton continued studies on spontaneously-occurring crystal violet resistant mutants. He found that a number of crystal violet resistant mutants of the (+) mating type *Phycomyces* are concomitantly altered in phototropic response in the wild-type and they display a normal avoidance response. Crystal violet resistant mutants of the (−) mating type are not blind at the light intensities tested. Leighton also found that nystatin and amphotericin B allow the selection of spontaneously-occurring resistant mutants. In addition, it was discovered that *Phycomyces* spores require a utilizable carbon source in order to initiate germination and outgrowth. It is hoped that this effect can be exploited to isolate spore germination and intermediary metabolism mutants.

Y. Jan and Enzo Russo studied chitin synthetase, an enzyme involved in *Phycomyces* cell wall deposition. It is thought this molecule may be a vector for the differential control of cell wall growth during behavioral responses. They have demonstrated that most of the enzyme activity is localized in the cell wall fraction. They characterized the assay system and the products formed by this enzyme. Polyoxin D, an antifungal drug, was found to be a very effective inhibitor of the enzyme. Cyclic AMP and theophylline also inhibit the enzyme. A large number of other compounds related to cyclic AMP and the enzyme substrate UDPG-N-acetyl-glucosamine, had no effect on chitin synthesis. Two *Phycomyces* behavioral mutants which have phenotypes suggesting transducer anomalies seem to have normal chitin synthetase activity. It is hoped that a continuation of these studies, augmented by chitin synthetase mutants, will allow an assessment of the role of this enzyme in the sensory output mechanism.

Sutter continued his studies on the relationship between trisporic acid (fungal sex hormones) accumulation and Carotene biosynthesis. He designed a procedure which should enable the selection of revertants from the existing β-Carotene mutants. Reversion analysis should clearly establish whether the existing mutants are single-site lesions and whether the observed decreases in trisporic acid production in these strains is due to a decrease in Carotene accumulation. Sutter searched for direct selection procedures which would facilitate the isolation of spontaneously-occurring trisporic acid biosynthesis mutants. A known inhibitor of trisporic acid accumulation, diphenylamine, appears to have the desired properties of such a selective agent.

COORDINATOR

Leighton, Terrance, Ph.D., University of California, Davis, and University of Massachusetts Medical School, Worcester

ASSISTANT

Foster, Susan, B.S., California Institute of Technology, Pasadena

WORKSHOP MEMBERS

Bergman, Kostia, Ph.D., California Institute of Technology and University of Seville, Spain
Cerda-Olmedo, Enrique, Ph.D., University of Seville, Spain
Delbruck, Max, Ph.D., California Institute of Technology, Pasadena
Dusenbery, Ruth L., Ph.D., California Institute of Technology, Pasadena
Foster, Kenneth, Ph.D., California Institute of Technology and University of Colorado, Boulder
Gamov, Igor, Ph.D., University of Colorado, Boulder
Jan, Lily, B.S., California Institute of Technology, Pasadena
Jan, Yno, B.S., California Institute of Technology, Pasadena
Reau, Patricia M., B.S., Institute of Biology, Freiburg, Germany
Russo, Vincenzo E. A., Ph.D., Max-Planck-Institut, Berlin, Germany



C) NEUROBIOLOGY

During the first two courses, JacSue Kehoe worked on the pharmacology of Aplysia synaptic transmission and Philippe Ascher and Roger Thomas worked on the effects of ammonium ions and osmotic challenge on the intracellular chloride and sodium activities of Aplysia neurons. Surprisingly, intracellular chloride always changed much more than sodium, suggesting that under hypo-osmotic conditions chloride ions leave the cell as water enters.

Thomas was joined by Robert Meech for the third course. Thomas spent the first part of the session attempting to perfect a new design of chloride-sensitive microelectrode. The main difficulty was finding the best sealant and procedure for sealing an etched and chlorided silver wire inside the end of a 1μ-tip pyrex micropipette with the terminal few microns of the wire exposed. The most promising sealant seems to be a cyanoacrylate adhesive, like Eastman 910 MHT.

Meech used some of the chloride-sensitive microelectrodes to calibrate his calcium chloride injections.

Thomas used pH-sensitive microelectrodes from Bristol and Cold Spring Harbor to measure intracellular pH in Aplysia neurons. As expected, the values were close to 7-2.

Meech also investigated the role of intracellular calcium in membrane responses of Aplysia neurons. Using a pressure injection technique he had earlier shown that calcium injection caused an increase in potassium conductance. Since it is known that calcium enters the cell during action potentials, it is possible that calcium is involved in the increase in potassium conductance occurring during the second phase of the action potential and after a burst of activity. By pressure injecting a calcium binding agent, EGTA, Meech was able to prolong action potentials and greatly reduce post-tetanic hyperpolarization, suggesting that calcium does indeed play an important role in these processes.

COLD SPRING HARBOR SYMPOSIUM ON QUANTITATIVE BIOLOGY

Our symposium each year gives us the opportunity to seek an exploding phase of biology and to bring together most of the key practitioners who may provide a signal point in the evolution of the subject.

With the emergence of the sliding filament model the field of muscle contraction has become in itself a major intellectual discipline, with its own well-defined objectives. On no occasion, however, since the sliding filament model was first presented has it been possible to bring together all the many people whose research directly bears on the molecular events underlying the contraction process. So it seemed most appropriate to devote this year's symposium to this theme.

In preparing this program, I greatly profited from the advice of Carolyn Cohen, John Gergely, Andrew Huxley, Hugh Huxley, and Andrew Szent-Gyorgyi. They suggested many more speakers than we could accommodate even in a very full week's program. So, regretfully, we were not able to include on the final program everyone who had something important to say. But, hopefully, the high level of animated discussion that occurred throughout the week allowed us to hear about all new facts of importance. It is our belief that this symposium volume will be of great value, not only in telling us about the current state of muscle research, but also in pointing out what problems remain to be solved.

Fortunately we were able to entice Albert Szent-Gyorgyi to open the program, thereby allowing us again to appreciate his vast contributions to the way we think about contraction. During the succeeding seven days, the formal program sessions were generally held in the mornings and evenings, with the afternoons reserved for more informal gatherings.

J. D. Watson

WEDNESDAY, JUNE 7th

PROTEINS I – SEQUENCE, SUBUNITS

Chairman: A. Weber, St. Louis School of Medicine, St. Louis

M. Elzinga and J. H. Collins, Boston Biomedical Research Institute; Harvard Medical School, Boston: "Amino Acid Sequence of Rabbit Skeletal Muscle Actin."

A. G. Weeds and G. Frank, MRC Laboratory of Molecular Biology, Cambridge, England: "Structural Studies on the Light Chains of Myosin."

S. Lowey and J. C. Holt, Children's Cancer Research Foundation; Harvard Medical School, Boston: "Immunochemical Approach to the Interaction of Light and Heavy Chains in Myosin."

P. Dreizen and D. A. Richards, State University of New York, Brooklyn: "Regulatory Role of Subunit Interactions in Myosin ATPase."

J. Kendrick-Jones, E. M. Szentkiralyi, and A. G. Szent-Gyorgyi, MRC Laboratory of Molecular Biology, Cambridge, England; Brandeis University, Waltham, Massachusetts: "Role of the Light Chains in the Regulation of Molluscan Muscle."

PROTEINS II – ASSEMBLY

Chairman: J. Lowy, University of Aarhus, Denmark

L. Szilagyi, M. Balint, and N. A. Biro, Eotvos Lorand University, Budapest, Hungary: "Studies on the Helical Segment of the Myosin Molecule."

M. Young, M. V. King, and D. S. O'Hara, Harvard Medical School; Massachusetts General Hospital, Boston: "Studies on the Structure and Function of the Rod Section of Myosin."

W. F. Harrington, M. Burke, and J. S. Barton, Johns Hopkins University, Baltimore: "Association Behavior of Myosin and its Significance in the Contractile System."

F. A. Pepe, Pennsylvania Medical School, Philadelphia: "Myosin Filament: Immunochemical and Ultrastructural Approaches to Molecular Organization."

G. W. Offer, King's College, London, England: "C-protein and the Periodicity in the Thick Filament Assembly."

THURSDAY, JUNE 8th

ATPASE I – CONTRACTION

Chairman: S. V. Perry, University of Birmingham, England

R. G. Yount, J. S. Frye, and K. R. O'Keefe, Washington State University, Pullman: "Mechanism of Inhibition of Heavy Meromyosin (HMM) by Purine Disulfide Analogs of ATP."

C. R. Bagshaw, J. F. Eccleston, D. R. Trentham, D. W. Yates, and R. S. Goody, University of Bristol, England; Max-Planck-Institute fur Experimentelle Medizin, Gottingen, Germany: "Transient Kinetic Studies of the Mg^{2+}-dependent ATPase of Myosin and its Proteolytic Subfragments."

C. Moos, State University of New York, Stony Brook: "Actin Activation of Heavy Meromyosin and Subfragment-1 ATPases. Steady-state Kinetics Studies."

E. Eisenberg and W. W. Kielley, NIH-NHLI, Bethesda, Maryland: "Interaction of Heavy Meromyosin (HMM) and Subfragment-1 (S-1) with Actin and ATP."

M. Barany and K. Baramy, Institute for Muscle Disease, Inc., New York City: "Proposal for the Mechanism of Contraction in Intact Frog Muscle."

ATPASE II – CONTRACTION

Chairman: H. E. Huxley, MRC Laboratory of Molecular Biology, Cambridge, England

Y. Tonomura, Y. Hayashi, and A. Inoue, Osaka University, Osaka, Japan: "Reaction Mechanism of Myosin-ATPase."
J. Koretz, T. Hunt, and E. W. Taylor, University of Chicago, Chicago: "Transient State Kinetic Studies on Myosin and Actomyosin ATPase."
J. Gergely and J. C. Seidel, Boston Biomedical Research Institute; Harvard Medical School, Boston: "Investigation of Conformational Changes on Spin Labeled Myosin-implications for the Molecular Mechanism of Muscle Contraction."
J. Botts, R. Cooke, C. G. Dos Remedios, J. A. Duke, R. M. Mendelson, M. F. Morales, T. Tokiwa, G. Viniegra, and R. G. Yount, University of California, San Francisco; Washington State University, Pullman: "Does a Myosin Cross-bridge Progress 'Arm-over-arm' on the Actin Filament?"
D. C. S. White, University of York, York, England: "Dynamics of Contraction in Insect Flight Muscle."

FRIDAY, JUNE 9th

REGULATION I – TROPONIN

Chairman: J. Hanson, King's College, London, England

S. Ebashi and I. Ohtsuki, University of Tokyo, Japan: "Rugulatory Proteins of Muscle with Special Reference to Troponin."
D. J. Hartshorne, Carnegie-Mellon University, Pittsburgh: "Studies on the Subunit Composition of Troponin."
M. L. Greaser and J. Gergely, University of Wisconsin, Madison: Boston Biomedical Research Institute, Boston: "Troponin Subunits and Their Interactions."
S. V. Perry, H. A. Cole, J. F. Head, and F. J. Wilson, University of Birmingham, England: "Localization and Mode of Action of the Inhibitory Protein Component of the Troponin Complex."
R. D. Bremel, A. Weber, and J. Murray, St. Louis School of Medicine, St. Louis: "Protein-protein Interactions in the Thin Filament during Relaxation and Contraction."

REGULATION II – THIN FILAMENTS

Chairman: S. Ebashi, University of Tokyo, Japan

F. Oosawa, Nagoya University, Nagoya, Japan: "Dynamic Properties of F-action and Thin Filament."
C. Cohen, D. L. D. Casper, D. A. D. Parry, J. P. Johnson, and K. M. Nauss, Children's Cancer Research Foundation; Harvard Medical School, Boston: "Tropomyosin-troponin Crystal Complex."
J. Hanson, V. Lednev. E. J. O'Brien, and P. M. Bennett, King's College, London, England: "Structure of Actin-containing Filaments."
A. G. Szent-Gyorgyi, W. Lehman, and J. Kendrick-Jones, Brandeis University, Waltham, Massachusetts: "Regulation in Molluscan Muscles: A Myosin Dependent Regulatory System."

SATURDAY, JUNE 10th

MUSCLE STRUCTURE I

Chairman: A. Miller, Zoology Department, Oxford University, England

F. D. Carlson, R. F. Bonner, and A. Fraser, Johns Hopkins University, Baltimore: "Intensity Fluctuation Spectra from Resting and Contracting Muscle."
M. K. Reedy, Duke University, Durham, North Carolina: "How Many Myosin Molecules per Cross-bridge? A Study of Insect Flight Muscle."
R. V. Rice, Carneigie-Mellon University, Pittsburgh: "Biochemical and Ultrastructural Studies on Vertebrate Smooth Muscle."
J. B. Leigh, K. C. Holmes, H. G. Mannherz, G. Rosenbaum, F. Eckstein, and R. Goody, Max-Planck-Institut fur Medizinische Forschung, Heidleberg, Germany: Max-Planck-Institut fur Experimentelle Medizin, Gottingen, Germany: "Effects of ATP-analogs on the Low Angle X-ray Diffraction Patterns of Insect Flight Muscle."
R. W. Lymn and H. E. Huxley, MRC Laboratory of Molecular Biology, Cambridge, England: "X-ray Diagrams from Skeletal Muscle in the Presence of ATP Analogues."

MUSCLE STRUCTURE II

Chairman: K. C. Holmes, Max-Planck-Institut fur Medizinische Forschung, Heidelberg, Germany

E. M. Rome, King's College, London, England: "Structural Studies by X-ray Diffraction of Striated Muscle Permeated with Specific Ions and Proteins."
J. E. Haselgrove, MRC Laboratory of Molecular Biology, Cambridge, England: "X-ray Evidence for Conformational Changes of the Actin and Myosin Containing Filaments."
J. Lowy and P. J. Vibert, University of Aarhus, Denmark: "X-ray Studies of a Molluscan Smooth Muscle."
H. E. Huxley, MRC Laboratory of Molecular Biology, Cambridge, England: "Factors Controlling the Movement and Attachment of the Cross-bridges in Muscle."
P. Armitage, A. Miller, C. D. Rodger, and R. T. Tregear, Oxford University, England: "Structure and Function of Insect Muscle."

SUNDAY, JUNE 11th

SARCOPLASMIC RETICULUM
Chairman: W. F. M. M. Mommaerts, California Medical Center, Los Angeles

A. Martonosi, R. Boland, and R. A. Halpin, St. Louis School of Medicine, St. Louis: "Biosynthesis of Sarcoplasmic Reticulum (SR) Membranes and the Mechanism of CA Transport."
D. H. MacLennan, University of Toronto, Canada: "Resolution of Proteins of the Sarcoplasmic Reticulum."
L. D. Peachey, Univeristy of Pennsylvania, Philadelphia: "Electrical Events in the T-system of Frog Skeletal Muscle."
B. M. Twarog and Y. Muneoka, Tufts University, Medford, Massachusetts: "Control of Excitation and Relaxation in a Molluscan Catch Muscle."
M. Endo, Purdue University, Lafayette, Indiana: "Length-dependence of Activation of Skinned Muscle Fibers by Calcium."

MYOGENESIS
Chairman: R. T. Tregear, University of Oxford, England

R. D. Goldman, Case Western Reserve University, Cleveland, Ohio: "Evidence Regarding the Functions of Cytoplasmic Fibers in Non-muscle Cell Motility."
A. O. Jorgensen, G. Morris, E. Buzash, and S. M. Heywood, University of Connecticut, Storrs: "Synthesis of Muscle Proteins."
J. D. Etlinger and D. A. Fischman, University of Chicago, Chicago: "M and Z Band Proteins of Rabbit Myofibrils."
D. Yaffe and H. Dym, Weizmann Institute of Science, Rehovoth, Israel: "Gene Expression During Formation of Contractile Muscle Fibers in Cell Cultures."
H. Holtzer and J. W. Sanger, University of Pennsylvania, Philadelphia: "Aspects of Myogenesis."

MONDAY, JUNE 12th

CONTRACTILE PROTEINS IN TISSUES OTHER THAN MUSCLE
Chairman: F. Oosawa, Magoya University, Japan

D. Bray, MRC Laboratory of Molecular Biology, Cambridge, England: "Cytoplasmic Actin: a Comparative Study."
T. D. Pollard and E. D. Korn, NIH, Bethesda, Maryland: "Interaction of Acanthamoeba. Myosin with Muscle Actin and Native Tropomyosin."
J. A. Spudich, University of California, San Francisco: "Purification and Properties of Platelet Actin and its Interaction with Cytochalasin B."
A. Stracher, J. Abramowitz, M. N. Malik, C. Mahendran, and T. C. Detwiler, State University of New York, Brooklyn: "Studies on the Contractile Proteins of Blood Platelets."
R. S. Adelstein and M. A. Conti, NIH, Bethesda, Maryland: "Isolation of Muscle Proteins from Non-muscle Sources."

ENERGETICS
Chairman: A. F. Huxley, University College, London, England

C. Gilbert, K. M. Kretzschmar, and D. R. Wilkie, University College, London, England: "Heat, Work and Chemical Change During Muscular Contraction."
N. A. Curtin and R. E. Davies, University of Pennsylvania, Philadelphia: "Mechanical and Chemical Properties of Muscle During Stretching."
R. C. Woledge, University College, London, England: "*in vito* Calorimetric Observations Relevant to the Interpretation of Muscle Heat Production."
F. J. Julian, Boston Biomedical Research Institute, Boston: "Molecular Explanations for the Effect of Calcium on Both Force and Speed in the Activation of Contraction."
R. H. Abbott, A. R. C. Unit of Muscle Mechanisms, Oxford, England: "Does Calcium Affect the Rate Constants of Muscle?"

TUESDAY, JUNE 13th

MECHANICAL PROPERTIES
Chairman: D. R. Wilkie, University College, London, England

J. Pybus and R. T. Tregear, University of Oxford, England: "Estimates of How Long and How Hard Myosin Heads Pull on Actin and How Many Do So at One Time."
R. J. Podolsky and A. C. Nolan, NIH-NIAMD Bethesda, Maryland: "Cross Bridge Properties Derived from Muscle Contraction Transients."
A. F. Huxley and R. M. Simmons, University College, London, England: "Mechanical Transients and the Origin of Muscular Force."
H. E. Huxley, MRC Laboratory of Molecular Biology, Cambridge, England: "Summary."



SUMMER MEETINGS

The Cell Surface Meeting was organized by Brad Ozanne; Tumor Virus Meeting by Phillip Sharp, and Herpes Virus by Bernard Roizman of the University of Chicago. These meetings were partially supported by a grant from the National Cancer Institute and the American Cancer Society.

Ernesto Bade and Carl Anderson organized the two Phage Meetings.

Abstracts of these meetings were shipped to all who subscribe to the Laboratory's Abstracting Service.

CELL SURFACES MEETING

Attended by 79 participants

FRIDAY, JUNE 2

Chairman: B. W. Burge, Massachusetts Institute of Technology, Cambridge

S. Dales, Public Health Research Institute of the City of New York: "Membranes of the Poxviruses and their Host Cells."

D. B. Rifkin and R. W. Compans, Rockefeller University, New York City: "Influence Virus as a Model System for the Labeling of External Membrane Proteins."

R. W. Compans, F. R. Landsberger, J. Lenard, and P. W. Choppin, Rockefeller University, New York City: "Viral Membranes: Structure, Assembly, and Interaction with Cells."

J. Kaplan, Harvard Medical School, Boston: "Viral Membrane Biogenesis."

J. P. Segrest, I. Kahane, and V. T. Marchesi, NIH-NIAMD, Bethesda, Maryland: "Molecular Anatomy of Human Erythrocyte Glycophorin."

M. Bretscher, MRC Laboratory of Molecular Biology, Cambridge, England: "Lipids of the Red Blood Cell Plasma Membrane."

J. P. Revel, P. Hoch, and S. Smith, California Institute of Technology, Pasadena: "Morphology of Cell Surfaces."

SATURDAY, JUNE 3

Chairman: W. J. Grimes, University of Arizona, Tucson

P. W. Robbins, Massachusetts Institute of Technology, Cambridge: "Tumor Virus Transformation of the Cell Surface."

I. A. MacPherson and D. R. Critchley, Imperial Cancer Research Fund Laboratory, London, England: "Glycolipids of the NIL Hamster Cell Line."

M. L. Pearson*, G. Yogeeswaran‡, R. K. Murray‡, B. D. Sanwal*, F. A. McMorris†, and F. Ruddle†, *Department of Medical Cell Biology and ‡Biochemistry, University of Toronto, Canada; †Yale University, New Haven, Connecticut: "Glycosphingolipids of Mouse Neuroblastoma Cells and Neuroblastoma XL Cell Hybrids."

P. T. Mora, NIH, Bethesda, Maryland: "Amino-sugar Incorporation into Cell Membranes in Spontaneously and in Virally Transformed Mouse Cells."

R. Sheinin, Ontario Cancer Institute, Toronto, Canada: "Biochemical Comparisons between the Surface of Normal and Virus-transformed 3T3 Mouse Fibroblasts."

W. T. Shier, Salk Institute, San Diego, California: "Comparison of Cell Surface Glycoproteins from Normal and Tumor Cells."

G. Walter, H. Werchau, Z. Ben-Ishai, and R. Dulbecco, Salk Institute, San Diego, California: "Surface Alteration in Polyoma Transformed BHK Cells."

AFTERNOON SESSION

Chairman: R. Sheinin, Ontario Cancer Institute, Toronto, Canada

S. Roseman, Johns Hopkins University, Baltimore: "Synthesis of Glycoproteins and Glycolipids by Multiglycosyl-transferase Systems and their Potential Role in Intercellular Adhesion."

S. Roth, Johns Hopkins University, Baltimore: "Surface Glycosyl Transferases and Acceptors on a Variety of Cultured Mouse Cells."

W. J. Grimes, University of Arizona, Tucson: "Glycosyl Transferases from Normal and Transformed Cells."

H. P. Schnebli, Friedrich Miescher-Institute, Basel, Switzerland: "Protease Inhibitors as Selective Growth Inhibitors for Transformed Cells."

T. Humphreys, P. Henkart, C. B. Cauldwell, and S. Humphreys, University of Hawaii, Honolulu: "Characterization of Cell Surface Components Participating in Species Specific Aggregation of Marine Sponge Cells."

H. B. Bosmann, Rochester Medical School, New York: "N-acetyl Neuraminic Acid on Cell and Organelle Surfaces."

SUNDAY, JUNE 4

Chairman: I. A. MacPherson, Imperial Cancer Research Fund, London, England

L. Sachs, Weizmann Institute of Science, Rehovoth, Israel: "Membrane Changes Associated with Malignancy."
K. D. Noonan and M. M. Burger, Princeton University, Princeton, New Jersey: "H-Con A Binding to Normal and Transformed Cells."
B. Ozanne, Cold Spring Harbor Laboratory: "Selection and Characterization of Con A Resistant SV3T3 Cells."
J. R. Sheppard, Colorado Medical School, Denver: "Cyclic AMP and the Control of Cellular Growth."
P. W. Wright, NIH-NCI, Bethesda, Maryland: "Tumorigenecity and Antigenecity of SV40 Transformed Mouse Cell Lines."
M. J. Weber, University of Illinois, Urbana: "Glucose Transport in Normal and in RSV-transformed Chick Cells."
R. Kurth, H. Gelderblom, and H. Bauer, Robert Koch-Institut, Berlin: "RNA Tumor Virus Directed Cell Surface Antigens."

AFTERNOON SESSION

Chairman: P. W. Wright, National Cancer Institute, Bethesda, Maryland

J. Konisky, University of Illinois, Urbana: "Studies on the Colicin Ia-receptor Interaction."
D. Allan and M. J. Crumpton, National Institute for Medical Research, London, England: "Nature of the Lymphocyte Membrane Receptor for PHA Mitogen."
F. Miller, State University of New York, Stony Brook: "Role of Cell Surface Oligosaccharide Units in Blastogenic Stimulation of Human Lymphocytes."
G. V. Bennett, M. Hollenberg, and P. Cuatrecasas, Johns Hopkins Medical School, Baltimore: "Insulin Interactions with Inverted Adipocyte Membrane Vesicles."

FOURTH TUMOR VIRUS MEETING

Attended by 134 participants

WEDNESDAY, AUGUST 16

ENDONUCLEASE RESTRICTION

J. F. Morrow and P. Berg, Stanford Medical Center, Stanford, California: "Restriction Enzyme Cleavage of SV40 DNA."
J. E. Mertz, R. W. Davis, and P. Berg, Stanford Medical Center, Stanford, California: "Characterization of the Cleavage Site of the R$_1$ Restriction Enzyme."
H. Delius and C. Mulder, Cold Spring Harbor Laboratory: "Restricting Endonuclease R$_1$ Cleaves SV40 DNA at One Unique Site."
C. Mulder, U. Pettersson, H. Delius, and P. A. Sharp, Cold Spring Harbor Laboratory: "Cleavage of Adenovirus Type 2 DNA into Six Unique Fragments by Endonuclease R$_1$."
E.-S. Huang, J. Newbold, M. Edgell, C. Hutchison, and J. S. Pagano, University of North Carolina, Chapel Hill: "Analysis of SV40 DNA with the New Restriction Enzyme, Endonuclease Z."
P. Beard, J. F. Morrow, and P. Berg, Stanford Medical Center, Stanford, California: "Cleavage of SV40 DNA by S1 Endonuclease."
D. A. Jackson, R. H. Symons, and P. Berg, Stanford Medical Center, Stanford, California: "Covalent Insertion of the Galactose Operon of *E. coli* into the Genome of SV40."
W. R. Kidwell, R. Saral, R. G. Martin, and H. L. Ozer, NIH-NCI, NIH-NIAMD, Bethesda, Maryland; Worcester Foundation, Worcester, Massachusetts: "Characterization of an Endonuclease Associated with SV40 Virions."
R. Risser, Harvard University, Cambridge, Massachusetts: "P1 Endonuclease Restriction of SV40 DNA."

THURSDAY, AUGUST 17

TRANSCRIPTION

Y. Aloni, Weizmann Institute of Science, Rehovoth, Israel: "Extensive Symmetrical Transcription of SV40 DNA in Virus Yielding Cells."
R. Weinberg, Z. Ben-Ishai, and J. Newbold, Salk Institute, San Diego, California: "SV40 Messenger RNAs."
U. Lindberg, T. Persson, and L. Philipson, Uppsala University, Uppsala, Sweden: "Adenovirus Messenger RNA in the Lytic Cycle."
R. Wall, Columbia University, New York City: "Processing of Adenovirus 2 Messenger RNA from Large Nuclear RNA in Transformed Cells."



M. Brunner and H. Raskas, St. Louis University, St. Louis: "Processing of Adenovirus RNA Prior to Release from Isolated Nuclei."
M. Blangy, M. Vogt, and R. Dulbecco, Salk Institute, San Diego, California: "Transcription and Hybridization Properties of Polyoma DNA Oligomers."
E. Buetti, University of Geneva, Switzerland: "Late Polyoma-specific RNA on Polyribosomes of Infected Mouse Cells."
M. H. Green and R. J. Shmookler, University of California, San Diego: "Searching for the Polyoma Transcription Complex in Mouse Cells."
W. Doerfler and L. Philipson, Uppsala University, Uppsala, Sweden: "Isolation of a DNA-RNA Complex from KB Cells Infected with Adenovirus Type 2."

REPLICATION

G. C. Fareed and N. P. Salzman, NIH, Bethesda, Maryland: "Mechanism for SV40 DNA Chain Growth."
P. Bourgaux and D. Bourgaux-Ramoisy, Universite de Sherbrooke, Canada: "Unwinding of Replicating Polyoma Virus DNA."
A. R. Hunter, B. R. Francke, and W. Eckhart, Salk Institute, San Diego, California: "*in vitro* Synthesis of Polyoma DNA."
R. Jaenisch and A. Levine, Princeton University, Princeton, New Jersey: "Mechanism of Formation of SV40 Catenated and Circular Dimers."
M. Girard and A. Manteuil, Institut de Recherches sur le Cancer, Villejuif, France: "Relationship between Transcription and Replication of SV40 DNA."
P. Tegtmeyer, Case Western Reserve University, Cleveland, Ohio: "SV40 Replicon."
A. J. van der Eb, State University, Leiden, Netherlands: "Intermediates in Adenovirus Type 5 DNA Replication."
U. Pettersson and H. Delius, Cold Spring Harbor Laboratory: "Some Properties of Replicating DNA from KB Cells, Infected with Adenovirus Type 2."
G. D. Pearson, Oregon State University, Corvallis: "Adenovirus Replication Complex."

FRIDAY, AUGUST 18

GENETICS

W. Eckhart, Salk Institute, San Diego, California: "Polyoma Gene Functions."
W. R. Folk, Imperial Cancer Research Fund Laboratories, London, England: "Induction of Viral DNA Synthesis in Polyoma Transformed BHK 21 Cells."
M. Fried, Imperial Cancer Research Fund Laboratories, London, England: "Properties of a Temperature Sensitive Mutant (TS-C) of Polyoma Virus."
J. A. Robb, University of California, San Diego: "SV40-induced Cell Death in BALB/3T3 Cells and Its Prevention by Dibutyryl Cyclic Adenosine 3',5'-Monophosphate."
J. F. Williams, M. R. C. Virology Unit, University of Glasgow, Scotland: "Temperature-sensitive Mutants of Adenovirus Type 5."
M. J. Ensinger, F. E. Rubinstein, and H. S. Ginsberg, University of Pennsylvania, Philadelphia: "Temperature-sensitive Mutants of Types 5 and 12 Adenovirus."
H. Yamamoto and H. Shimojo, Institute of Medical Science, Tokyo: "Less Tumorigenic Mutants of Adenovirus 12 Defective in Induction of Cell Surface Change and Transplantation Immunity."

VIRUS AND CELLULAR DNA INTERACTIONS

M. Dieckmann, D. Brutlag, and P. Berg, Stanford Medical Center, Stanford, California: "Detection of Polyoma DNA Sequences in Abortive and Stable Transformants of BHK: An Improved Protocol for Measuring Annealing Kinetics."
K. Hirai and V. Defendi, Wistar Institute, Philadelphia: "Significance of SV40 DNA Integration in the SV40 Infected Chinese Hamster and SV40 Transformed Cells."
G. Sauer, W. Waldeck, and K. Kammer, Institut fur Virusforschung, Heidelberg, Germany: "Integration of SV40 DNA into Particular Sequences of the DNA of Productively Infected Cells."
H. Turler, University of Geneva, Switzerland: "Association of Parental Polyoma DNA with Mouse Chromosomal DNA Early During the Lytic Infection."
W. P. Cheevers and J. Kowalski, University of Western Ontario, London, Canada: "Studies on the Mechanism and Control of Cellular DNA Replication in Polyoma Virus Infection."
S. G. Baum, R. I. Fox, M. S. Horwitz, and J. V. Maizel, Einstein College of Medicine, Bronx, New York: "Studies of Enhancement of Human Adenovirus Replication by SV40."
M. A. Jerkofsky and F. Rapp, Pennsylvania State School of Medicine, Hershey: "Host Cell DNA Synthesis as a Possible Factor in the Enhancement of the Replication of Human Adenoviruses in Simian Cells by SV40."
G. Wadell, M. L. Hammarskjold, and T. Varsanyi, Karolinska Institutet, Stockholm, Sweden: "Characterization of Incomplete Adenovirus Particles."

SATURDAY, AUGUST 19

PROTEIN SYNTHESIS

C. Tibbetts and L. Philipson, Uppsala University, Uppsala, Sweden: "On the Separation of the Complementary Strands of Adenovirus DNA."
L. V. Prage and N. R. Morris, Rutgers Medical School, New Brunswick, New Jersey: "Methylation of Adenovirus DNA."
W. C. Russel and J. J. Skehel, National Institute for Medical Research, London, England: "Adenoviruses: Structural and Infected Cell Polypeptides."
M. Anderson, C. Anderson, U. Pettersson, C. Mulder, and B. Allet, Cold Spring Harbor Laboratory: "*in vitro* Synthesis of Adenovirus 2 Polypeptides."
F. Cuzin, D. Paulin, and P. Rouget, Institut Pasteur, Paris: "Search for Polyoma Specific Proteins."
M. S. Horwitz, C. Brayton, and S. G. Baum, Einstein College of Medicine, Bronx, New York: "Synthesis of Adenovirus Type 2 DNA in the Presence of Cycloheximide."
P. E. Branton and R. Sheinin, Massachusetts Institute of Technology, Cambridge: "Studies on the Protein Requirements for Polyoma DNA Replication."
P. P. McCann and R. G. Martin, NIH, Bethesda, Maryland: "Studies of the SV40 Core Complex."
B. Hirt, Swiss Institute for Experimental Cancer Research, Lausanne: "Cellular Origin of the Basic Proteins in SV40 and Polyoma Virus Particles."

POLYOMA, SV40, AND ADENOVIRUS TRANSFORMED CELLS

H. S. Smith, E. W. Kingsbury, A. J. Hiller, C. R. Dorey, and P. W. Wright, University of California, Berkeley; Bionetics Research Laboratory; NIH, Bethesda, Maryland: "Cell Surface Properties and the Expression of SV40 Virus Transformation."
H. C. Renger and C. Basilico, New York University Medical Center, New York City: "Temperature Sensitive SV40-transformed Cells."
R. Pollack, Cold Spring Harbor Laboratory: "FISV3T3 is Capable of Density-dependent Inhibition of DNA Synthesis."
A. Vogel, Cold Spring Harbor Laboratory: "Negative Selection of Serum and Density Revertants of SV40 Transformed 3T3."
P. H. Fishman, R. O. Brady, and P. T. Mora, NIH, Bethesda, Maryland: "Alteration of Ganglioside Biosynthesis in Mouse Cells Associated with DNA Virus Transformation."

BACTERIOPHAGE MEETINGS (LYTIC AND LYSOGENIC)

Attended by 226 participants

Lytic Section

SATURDAY, AUGUST 26

W. A. Clark and D.Geary, American Type Culture Collection, Rockville, Maryland: "ATCC Collection of Bacteriophage."
J. A. Sands, W. Snipes, and S. Person, Pennsylvania State University, University Park: "Temperature Sensitive Mutants of Phage PM2."
A. Jacquemin-Sablon and Y. Thery Lanni, Institut Gustave-Roussy, Villejuif, France: "Lambda-repressed Mutants of Phage T5."
L. A. Goscin and D. H. Hall, Duke Medical Center, Durham, North Carolina: "Further Studies on Hydroxyurea-sensitive Mutants of T4."
K. V. Chace and D. H. Hall, Duke Medical Center, Durham, North Carolina: "Isolation of T4 Mutants Unable to Induce Thymidine Kinase Activity."
J. R. Johnson and D. H. Hall, Duke Medical Center, Durham, North Carolina: "Isolation of T4 Mutants Resistant to Folate Analogs."
L. S. Ripley, University of Illinois, Urbana: "An Assay for Transversion Mutations Induced in UAA Codons in the *r*II Gene of T4."
T. Homyk and J. Weil, Vanderbilt University, Nashville, Tennesee: "Deletion Mutants in Phage T4."

SUNDAY, AUGUST 27

L. B. Rothman-Denes, R. Haselkorn, and G. C. Schito, University of Chicago, Chicago: "Selective Shut-off of Catabolite-sensitive Host Synthesis by Bacteriophage N4."
D. C. Morrison, P. Tomich, and G. R. Greenberg, University of Michigan, Ann Arbor: "Excretion of Cyclic Nucleoside 2',3'-monophosphates after T4 Phage Infection at 42°."
T. Mattson, J. Richardson, and D. Goodin, University of Geneva, Switzerland; Indiana University, Bloomington; Purdue University, Lafayette, Indiana: "A T4 Mutation which Affects the Expression of Several 'Early' Genes."
J. D. Karam, South Carolina Medical University, Charleston: "Mutations to Over-production of T4 'Early' Gene Products."
C. R. Stewart, Rice University, Houston: "Regulation of Late Protein Synthesis During SP82 Infection of *Bacillus subtilis*."
E. Goldman and H. F. Lodish, Massachusetts Institute of Technology, Cambridge: "T4 Phage and T4 Ghosts Inhibit f2 Phage Replication by Different Mechanisms."

AFTERNOON SESSION

M. Vallee and J. B. Cornett, CNRS, Ste. Croix de Quintillargues, France; College of Medicine, Tucson: "Immunity Function of Bacteriophage T4."
R. C. Condit, M. L. Goldberg, and J. A. Steitz, Yale University, New Haven, Connecticut: "DNA Directed FMET Dipeptide Synthesis."
T. Landers, T. Blumenthal, E. Lazarides, and K. Weber, Harvard University, Cambridge, Massachusetts: "Involvement of Protein Synthesis Elongation Factors Tu and Ts in Qβ Replicase."
M. P. Oeschger, X. Sauda, W. Wagner, and C. Tan, Yale University, New Haven, Connecticut: "Temperature Sensitive Mutants of the Phage Subunit of Qβ RNA Replicase."
R. B. Luftig and N. P. Lundh, Duke Medical Center, Durham, North Carolina: "Role of Tau-particles in T4D Head Morphogenesis."
N. Mykolajewycz and J. King, Massachusetts Institute of Technology, Cambridge: "Structural Intermediates in T4 Baseplate Assembly."
R. Fitten and J. King, Massachusetts Institute of Technology, Cambridge: "Assembly of the Baseplate of T4 *in vitro*."



J. Dawes and E. B. Goldberg, Tufts Medical School, Boston: "Roles of Baseplate Proteins in Bacteriophage T4 Infection."
M. Dewey, Pennsylvania Medical School, Philadelphia: "A) Extragenic Suppression of T4 Gene 40. B) Gene 49 Antigen."

MONDAY, AUGUST 28

J. Skare and W. C. Summers, Yale Medical School, New Haven, Connecticut: "Localization of a Late Promotor Site of Coli-phage T7."
S. G. Zimmer and R. L. Millette, Colorado Medical Center, Denver: "*in vitro* Transcription of Phage PM-2 DNA by RNA Polymerase from Pseudomonas Ba1-31."
K. Hercules and W. Sauerbier, Colorado Medical Center, Denver: "Transcription Units in Bacteriophage T4."
J. W. Morse and P. S. Cohen, University of Rhode Island, Kingston: "Properties of T4 Messenger RNA Synthesized in the Absence of Protein Synthesis."
L. Snyder, Michigan State University, East Lansing: "RNA Polymerase Mutants Defective in Shut-off of Host Transcription by T4."
R. Horvitz, Harvard University, Cambridge, Massachusetts: "Small T4-specific Polypeptides Bound to Host RNA Polymerase."
B. R. Zetter and P. S. Cohen, University of Rhode Island, Kingston: "Discontinuous Synthesis of T4 Lysozyme."
M. L. Walsh and P. S. Cohen, University of Rhode Island, Kingston: "Compartmentation of Polysomesin T4-infected *Escherichia coli.*"

AFTERNOON SESSION

R. W. Hyman, I. Brunovskis, and W. C. Summers, Yale Medical School, New Haven, Connecticut: "Evolution as Seen in the Femal-specific Coliphages T7, T3, ϕI, ϕII, W31, and H."
B. Gomez and D. Lang, Universidad Nacional Autonoma de Mexico; University of Texas, Dallas: "Denaturation Map and Direction of DNA Transcription."
S. Hattman, University of Rochester, New York: "Plasmid-controlled Variation in the Content of Methylated Bases in the DNA of Phages λ, fd, and M13."
N. Hartman and N. D. Zinder, Rockefeller University, New York City: "Effect of B Restriction on Linkage Relationships in f1 Bacteriophage."
K. Horiochi, G. F. Vovis, and N. D. Zinder, Rockefeller University, New York City: "Cleavage of Replication Form DNA of Bacteriophage f1 by B-restriction Endonuclease."
J. H. Middleton, M. H. Edgell, and C. A. Hutchison III, University of North Carolina, Chapel Hill: "Detection of Restriction Enzymes with Different Cleavage Site Specificities."
C. A. Hutchison III, J. H. Middleton, and M. H. Edgell, University of North Carolina, Chapel Hill: "DNA Fragment Map of Phage ϕX174."
M. Sclair, M. Edgell, and C. Hutchison III, University of North Carolina, Chapel Hill: "Mapping of ϕX174 K and 15 Restriction Sites Using Specific RF DNA Fragments."

TUESDAY, AUGUST 29

G. Mosig, D. Bowden, and S. Bock, Vanderbilt University, Nashville, Tennessee: "Participation of Host Functions in Phage T4 DNA Replication and Recombination."
A. Breschkin and G. Mosig, Vanderbilt University, Nashville, Tennessee: "Role of Host Proteins in T4 Gene 32 Independent DNA Synthesis."
L. A. Moran, J. E. Barry, H. Hama-Inaba, D. C. Mace, J. Wiberg, and B. Alberts, Princeton University, Princeton, New Jersey; Rochester Medical School, New York: "Proteins Required for DNA Replication in T4: Isolation of the Products of Genes 62, 44, 45, and 41."
P. V. O'Donnell and J. D. Karam, Sloan-Kettering Institute, New York City; South Carolina Medical College, Charleston: "On the Biological Function of T4 DNA Polymerase."
K. Carlson and A. W. Kozinski, University of Pennsylvania, Philadelphia: "Multiple Initiation of T4 DNA Replication: The Effect of BUdR-substitution in the DNA."
P. J. Buckley and A. W. Kozinski, University of Pennsylvania, Philadelphia: "Multiple and Specific Sites for the Initiation of Bacteriophage T4 DNA Synthesis."
J. Chao, L. Chao, and J. F. Speyer, University of Connecticut, Storrs: "T4 Contains Some RNA Linked to DNA."

AFTERNOON SESSION

P. J. Buckley, L. Kosturko, and A. W. Kozinski, University of Pennsylvania, Philadelphia: "An RNA-DNA Copolymer from Bacteriophage T4 Infected *Escherichia coli.*"
M. Wovcha, P. Tomich, C.-S. Chiu, and G. R. Greenberg, University of Michigan, Ann Arbor: "Studies on the Apparent Complex Function of T4 dCMP Hydroxymethylase."
A. S. Grandis and R. E. Webster, Duke Medical Center, Durham, North Carolina: "Inter-relationships between DNA Synthesis and Membrane Accumulation in f1-amber Mutant Infected Cells."
F. Bouvier and N. D. Zinder, Rockefeller University, New York City: "Growth of Bacteriophage f1 on Temperature-sensitive Mutants of *E. coli.*"
L. T. Dunham and A. R. Price, University of Michigan, Ann Arbor: "Deoxyribonucleotide Metabolism after ϕe Infection of *Bacillus subtilis.*"
A. R. Price, University of Michigan, Ann Arbor: "Infection of *Bacillus subtilis* by PBS2 Phage Whose DNA Contains Uracil."
M. Iwaya, McGill University, Montreal, Canada: "A New Class of Rep$^-$ Mutants of *E. coli.*"
A. J. Zuccarelli, R. M. Benbow, and R. L. Sinsheimer, California Institute of Technology, Pasadena: "Mapping of the ϕX174 Genome by Electron Microscopy."
F. D. Funk, Pennsylvania State University, Hershey: "Studies on the Function of Gene C of Bacteriophage ϕX174."

WEDNESDAY, AUGUST 30

W. Benz and H. Berger, Johns Hopkins University, Baltimore: "Repair of Unmatched Regions in T4 Heteroduplex DNA."
J. Levy, L. A. McNicol, and E. Goldberg, Tufts Medical School, Boston: "Effect of Glucosylation Patterns on Local Variation in Recombination Frequency in Bacteriophage T4D."
L. A. McNicol and A. W. Kozinski, Pennsylvania Medical School, Philadelphia: "Gradient of Transformation Efficiency of Sonicated T4 Phage DNA."
N. V. Hamlett and H. Berger, Johns Hopkins University, Baltimore: "Replication and Recombination in a DNA-delay Mutant of Bacteriophage T4."
R. Sandri and H. Berger, Johns Hopkins University, Baltimore: "Role of Polynucleotide Ligase in T4D Bacteriophage Genetic Recombination."
L. J. Heere and J. D. Karam, South Carolina Medical College, Charleston: "Relationships Between *Escherichia coli* and T4 DNA Ligase Functions."
B. Sheftall and H. Drexler, Bowman Gray School of Medicine, Winston-Salem, North Carolina: "Effect of UV Irradiation on the Ability to Transduce with Lysates of the Virulent Phage T1."
G. L. Williams and D. M. Green, University of New Hampshire, Durham: "Molecular Sharing in SP82G DNA Infection."

Lysogenic Section

THURSDAY, AUGUST 31

D. L. Wulff, University of California, Irvine: "Mutant of Lambda Suppressing the cII68 Mutation."
S. J. Hayes and B. K. Roe, University of Wisconsin, Madison: "Maintenance of λ Repressor Transcription in the Absence of Active Repressor and of tof, cII, or cIII Products."
H. Echols and L. Green, University of California, Berkeley; "Repression of the cII and cIII Genes of Phage λ by cro Product."
H. Inokuchi and W. F. Dove, University of Wisconsin, Madison: "Structure of the Lambda Operon P_L to *int*."
M. Lieb, Southern California Medical School, Los Angeles: "Prophage Substitution in Nsus Lysogens."
T. Takano, NIH-LMB, Bethesda, Maryland: "Bacterial Function Required for Plasmid Formation by P1 and λNNpGal8."

FRIDAY, SEPTEMBER 1

M. Shulman and M. Gottesman, NIH-NCI, Bethesda, Maryland: "ATT Mutants."
K. Shimada, R. A. Weisberg, and M. E. Gottesman, NIH-NCI, Bethesda, Maryland: "On the Mechanism of λ Phage-induced Mutations in *E. coli* K12."
H. Shizuya, D. M. Livingston, and C. C. Richardson, Harvard Medical School, Boston: "Transduction of the dnaE Locus of *E. coli* K12 by Bacteriophage λ."
R. K. Chan, B.-K. Tye, and D. Botstein, Massachusetts Institute of Technology, Cambridge: "Specialized Transduction of Tetracycline Resistance by Phage P22."
J. D. Wall and P. D. Harriman, Duke University, Durham, North Carolina: "Mutants of P1 with Altered Frequencies of Transduction."
J. L. Rosner, NIH-NIAMD, Bethesda, Maryland: "Non-lysogenizing, Modification-deficient Mutants of Bacteriophage P1."
M. Stodolsky, University of Chicago, Chicago: "General Method for the Selection of Specialized Transducing Derivatives of the Generalized Transducing Bacteriophage P1."

AFTERNOON SESSION

W.-J. Schrenk, R. Weisberg, and K. Shimada, Harvard Medical School, Boston; NIH, Bethesda, Maryland: "General Method for Obtaining Specialized Transducing Phage Lines."
H. Inokuchi and W. F. Dove, University of Wisconsin, Madison: "Further Analysis of the Replication System of Lambda."
R. Weisberg and M. Gottesman, NIH, Bethesda, Maryland: "Gene Expression by a Phage Unable to Circularize its DNA."
D. Freifelder, A. Folkmanis, N. Baran, L. Chud, and E. Levine, Brandeis University, Waltham, Massachusetts: "Some Properties and Requirements of the Insertion, Excision, and Terminase Systems of λ."
W. Wackernagel, K. S. Sriprakash, and C. Radding, Yale University, New Haven, Connecticut: "Biological Activity of Inverted Molecules of λ DNA."
B. H. Lindqvist and E. W. Six, University of Iowa, Iowa City: "P4 Transcription and P4 Activated P2 Transcription."
R. Goldstein, M. Marsh, J. Levy, G. Pruss, W. Gibbs, and R. Calendar, University of California, Berkeley: "Head Size Direction and *in vitro* Morphogenesis of Satellite Phage P4 and Helper Phage P2."



SATURDAY, SEPTEMBER 2

L. H. Johnston and H. Echols, University of California, Berkeley: "*in vitro* Inactivation of λ c1 Protein by an Activity from Mitomycin Treated *E. coli.*"
T. Maniatis and M. Ptashne, Harvard University, Cambridge, Massachusetts: "Nature of Operators in Lambda."
J. E. Dahlberg, H. A. Lozeron, and W. Szybalski, University of Wisconsin, Madison: "Identity of *in vivo* and *in vitro* Initiation of Four Phage Lambda RNAs."
B. Allet, J. Katagiri, and P. Jeppesen, Cold Spring Harbor Laboratory: "*in vitro* Protein Synthesis Directed by λ DNA."
P. Botchan, J. Wang, and H. Echols, University of California, Berkeley; "*in vitro* Transcription of Closed Circular λ b2 DNA as a Function of Superhelicity."

AFTERNOON SESSION

R. Ehring, K. Staack, and W.Wetekam, Institut fuer Genetik der Universitaet zu Koeln, Germany: "Relief of Polarity in DNA-dependent Cell-free Enzyme Synthesis."
G. N. Gussin, V. Peterson, L. Katz, N. Loeb, and J. Dodds, University of Iowa, Iowa City: "Deletion Mapping of the Lambda rex Gene."
E. Daniell and J. Abelson, University of California, San Diego: "Hetero-duplex Structures of Bacteriophage Mu DNA."
A. I. Bukhari and M. Metlay, Cold Spring Harbor Laboratory: "Genetic Map of Prophage Mu."
J. B. Zeldis, A. I. Bukhari, and D. Zipser, Cold Spring Harbor Laboratory: "Orientation of Mu Prophages with Respect to the Genome of *E. coli.*"
E. G. Bade, Cold Spring Harbor Laboratory: "Transcription of Bacteriophage Mu-1."
J. Geisselsoder, M. Mandel, R. Calendar, and D. Chattoraj, Universities of Hawaii, Honolulu; California, Berkeley; Wisconsin, Madison: "*in vivo* Transcription Patterns of Temperate Phage P2."
P. N. Ray and M. Pearson, University of Toronto, Canada: "Transcription of λ Head Genes: Further Evidence for Late Translational Control."

SUNDAY, SEPTEMBER 3

Y. Sakakibara and J. Tomizawa, NIH-NIAMDD, Bethesda, Maryland: "Phage and Bacterial Mutations which Affect Replication of Lambda RNA."
D. I. Friedman, R. J. Mural, and C. T. Jolly, University of Michigan, Ann Arbor; "Inhibition of N Gene Expression by a Bacterial Mutation. II. What's Nus?"
L. W. Enquist and A. Skalka, Roche Institute of Molecular Biology, Nutley, New Jersey: "Replication of gam⁻ Mutants in rec A⁻ Bacteria."
D. Henderson and J. Weil, Vanderbilt University, Nashville, Tennessee: "New Bacterial Mutant that Prevents Growth of Lambda."
N. Sternberg, NIH-NICHD, Bethesda, Maryland: "A Mutant of *E. coli* Defective for the Synthesis of Stable RNA and for Phage λ Head Formation."
N. Sternberg, NIH-NICHD, Bethesda, Maryland: "A Mutant of *E. coli* Defective for the Synthesis of Stable RNA and Phage λ Head Formation (gorE). II. The Propagation of Phage λ."

AFTERNOON SESSION

F. W. Stahl, K. D. McMilin, M. M. Stahl, R. E. Malone, and Y. Nozu, University of Oregon, Corvallis: "Recombination in Lambda."
H. Drexler, Wake Forest University Bowman Gray Medical School, Winston-Salem, North Carolina: "Transcription-activated Recombination in Transduction by Coliphage T1."
R. L. Roehrdanz, University of Wisconsin, Madison: "Transcriptional Stimulation of Site-specific Recombination in Lytic Crosses."
G. Guarneros and H. Echols, University of California, Berkeley: "Effect of Temperature on Site Specific Recombination by Bacteriophage λ."

MONDAY, SEPTEMBER 4

D. Botstein, K. K. Lew, and V. McClain-Jarvik, Massachusetts Institute of Technology, Cambridge: "Repression and Immunity in Lysogenes of Phage P22."
D. Botstein and I. Herskowitz, Massachusetts Institute of Technology, Cambridge: "P22-λ Hybrid Phages."
B. Hoffman and M. Levine, University of Michigan, Ann Arbor: "Gene 25 Product of Phage P22."
S. L. Barclay and W. F. Dove, University of Wisconsin, Madison: "Studies on the Possibility of Immunity Regulation in P2."

HERPES VIRUSES MEETING

Attended by 71 participants

SUNDAY, AUGUST 20

BIOCHEMISTRY OF HERPESVIRUS STRUCTURE AND MULTIPLICATION
Chairman: P. Wildy, University of Birmingham, England

P. Wildy, G. R. B. Skinner, M. E. Thouless, and A. J. Gibbs*, University of Birmingham, England; *Australian National University, Canberra City: "Serological Properties of Herpes Virus."
B. Roizman, N. Frenkel, W. Gibson, and D. Furlong, University of Chicago, Chicago: "Structure of the Herpesvirion and its DNA."
P. Sheldrick, M. Laithier, D. Lando, and M. L. Ryhiner, Insitut de Recherches Scientifiques sur le Cancer, Villejuif, France; Institut Pasteur, Paris: "Characterization of Infectious DNA from Herpes Simplex Virus."

G. A. Gentry, D. Campbell, and S. Evans, Mississippi School of Medicine, Jackson: "Studies with Equine Abortion Virus. I. DNA."
J. S. Pagano and E.-S. Huang, North Carolina School of Medicine, Chapel Hill: "Purification of Cytomegalovirus and Viral DNA."
Y. Becker, M. Gordin, U. Olshevsky, and J. Feder, Hebrew University-Hadassah Medical School, Jerusalem, Israel: "Studies on Herpesvirus DNA, mRNA, and Transcriptase."
H. S. Rosenkranz, U. Olshevsky, and Y. Becker, Hebrew University-Hadassah Medical School, Jerusalem, Israel: "Transcription and Translation of Genetic Information from HSV Parental DNA Genomes."

MONDAY, AUGUST 21

BIOCHEMISTRY OF HERPESVIRUS STRUCTURE AND MULTIPLICATION

Chairman: B. Hampar, Emory University Medical School, Atlanta

N. Frenkel, B. Roizman, and E. Cassai, University of Chicago, Chicago: "Transcription of Unique and Common Sequences of HSV-1 and HSV-2."
S. Silverstein, S. L. Bachenheimer, N. Frenkel, and B. Roizman, University of Chicago, Chicago: "Structure of Herpesvirus RNA and Some Regulatory Features of Its Synthesis."
T. Ben-Porat, T. Rakusanova, and A. S. Kaplan, Vanderbilt School of Medicine, Nashville, Tennessee: "Effect of Herpesvirus Infection on the Synthesis of Cell-specific RNA."
K. R. Cameron, R. P. Eglin, L. J. N. Ross, and P. Wildy, University of Birmingham, England: "Studies with Ultraviolet Light."

ANTIGENIC COMPOSITION OF HERPESVIRUSES

Chairman: A. Nahmias, Emory University Medical School, Atlanta

S. Luff, R. W. Honess, and A. Buchan, University of Birmingham, England: "Antigens Synthesised in Cells Infected with Herpes Virus."
G. H. Cohen and M. Ponce de Leon, University of Pennyslvania, Philadelphia: "Soluble Antigens of Herpes Simplex Virus Infected Mammalian Cells."
D. H. Watson, C. Sim, R. W. Honess, and K. L. Powell, University of Birmingham, England: "Some Structural Antigens of Herpes Simplex Virus."
K. S. Kim and R. I. Carp, New York Institute for Research in Mental Retardation, Staten Island: "Restriction to Murine Cytomegalovirus (MCMV) Replication in Human Diploid Cells (W1-38)."

TUESDAY, AUGUST 22

HERPESVIRUS GENETICS AND EXPRESSION OF VIRAL GENES IN NON-PRODUCTIVELY INFECTED CELLS

Chairman: A. Granoff, St. Jude's Children's Hospital, Memphis

J. H. Subak-Sharpe, M. C. Timbury, M. Brown, and D. A. Ritchie, University of Glasgow, Scotland: "ts Mutants of Herpes Simplex Viruses."
P. A. Schaffer and M. Benyesh-Melnick, Baylor College of Medicine, Houston: "Temperature-sensitive Mutants of Herpes Simplex Virus Type 1."
M. Terni and R. Manservigi, University of Ferrara, Italy: "ts Mutants of Herpes Simplex Virus."
R. L. Davidson, Children's Hospital Medical Center, Boston: "Expression of Herpes Thymidine Kinase in TK Deficient Mouse Cells."

LATENCY AND CELL TRANSFORMATION BY HERPES SIMPLEX VIRUS

Chairman: J. S. Pagano, University of North Carolina Medical School, Chapel Hill

J. G. Stevens and M. L. Cook, University of California, Los Angeles: "Further Characterization of Latent Herpes Simplex Virus Infection of Murine Spinal Ganglia."
L. Aurelian, Johns Hopkins School of Medicine, Baltimore: "Herpesvirus Hominis: From Latency to Carcinogenesis?"
R. Duff and F. Rapp, Pennsylvania State Medical Center, Hershey: "Characteristics of Hamster Embryo Fibroblasts Transformed *in vitro* by Herpes Simplex Virus Type 2."
W. E. Rawls, Baylor College of Medicine, Houston: "Seroepidemiological Studies of Herpesvirus Type 2 in Cervical Cancer."
A. Nahmias, M. Fritz, G. Chang, R. Duff, and F. Rapp, Emory Medical and Dental School, Atlanta; Hershey Medical Center, Hershey, Pennsylvania: "Reversed Transmembrane Potential and Membrane Fluorescence in Herpesvirus Infected and Transformed Cells."



ONCOGENIC HERPESVIRUSES OF FROGS, FOWL, AND MONKEYS

Chairman: G. Klein, Karolinska Institutet, Stockholm, Sweden

F. Deinhardt, L. Falk, and L. Wolfe, Rush Medical College, Chicago: "Herpesvirus Saimiri: A Simian Counterpart of Epstein-Barr Virus of Man."

M. A. Epstein, Bristol Medical School, England: "Observations on the Development and Maturation of Herpesvirus Saimiri in Monkey Kidney Lines by Immunofluorescence and Electron Microscopy."

R. Laufs and L. V. Melendez, Harvard Medical School, Boston: "Purification and DNA Characteristics of a New Oncogenic Agent: Herpes Ateles."

K. Nazerian, U. S. Department of Agriculture, East Lansing, Michigan: "Marek's Disease Virus–Current Advances."

R. R. Naegele and A. Granoff, St. Jude's Children's Hospital, Memphis: "Attempts to Culture the Lucke Tumor Virus."

M. Mizell, Tulane University, New Orleans: "Pathology of Tumorigenesis in Developing Embryos."

HERPESVIRUSES ASSOCIATED WITH LYMPHORETICULOPROLIFERATIVE INFECTIONS OF MAN

Chairman: K. Nazerian, U.S. Department of Agriculture, East Lansing, Michigan

G. Klein, Karolinska Institutet, Stockholm, Sweden: "Sensitivity to EBV-superinfection and EBV-antigen Induction with BUDR and IUDR in Established Lymphoblastoid Lines of Human Origin."

B. Hampar and J. Derge: "Activation of the Epstein-Barr Virus Genome in Human Lymphoblastoid Cells."

G. Miller and M. Lipman, Yale Medical School, New Haven, Connecticut: "Epstein-Barr Virus Permissiveness of Transformed Marmoset Leukocytes."

H. Zur Hausen and H. Wolf, Institute fur Klinische Virologie, Erlangen, Germany: "Studies on Biological Activities of EBV."

THURSDAY, AUGUST 24

HERPESVIRUSES ASSOCIATED WITH LYMPHORETICULOPROLIFERATIVE DISEASES OF MAN

Chairman: F. Deinhardt, Rush Medical College, Chicago

G. de The, International Agency for Research on Cancer, Lyon, France: "Behavior of EB Type Herpesvirus in Population at Different Risk of BL, NPC, IM."

G. Giraldo, E. Beth, F. Haguenau, and C. L. Vogel, Laboratoire d'Immunologie des Tumeurs, Centre Hayme, Hopital St. Louis, Paris: "Presence of Herpes-type Virus Particles in Tissue Culture of 5 Cases of Kaposi's Sarcoma from Different Geographical Regions."

G. Miller and J. Niederman, Yale Medical School, New Haven, Connecticut: "Prolonged Oropharyngeal Excretion of Epstein-Barr Virus Following Infectious Mononucleosis."

T. Shope and G. Miller, Yale Medical School, New Haven, Connecticut: "Heterophile Responses in Squirrel Monkeys Inoculated with EBV-transformed Autologous Leukocytes."

PROTEIN SYNTHESIS MEETING

Attended by 152 participants

TUESDAY, SEPTEMBER 5

S. Bhaduri, G. Shanmugam, G. Vecchio, and M. Green, St. Louis Medical School, St. Louis: "*in vitro* Synthesis of RNA Tumor Virus Porteins by Cells Transformed by Murine Sarcoma Virus."

R. B. Arlinghaus, R. B. Naso, and C. S. Wang, University of Texas, Houston; Anderson Hospital and Tumor Institute, Houston: "*in vitro* Polypeptide Synthesis Programmed with Rauscher Leukemia Virus RNA."

M. Revel, E. Falcoff*, B. Lebleu, U. Nudel, and R. Falcoff*, Weizmann Institute of Science, Rehovoth, Israel: *Institut de Radium, Paris: "Interferon Treatment inhibits Mengo RNA and Hemoglobin mRNA Translation in Extracts of L Cells."

S. D. Adamson, W. R. Woodward, P. Yau, and E. Herbert, University of Oregon, Eugene: "Control of Globin Synthesis by Hemin."

A. J. M. Berns and H. Bloemendal, University of Nijmegen, The Netherlands: "Translation of Calf Lens Messengers in Heterologous Systems."

W. D. Grazidaei III, D. Roy, W. Konigsberg, and P. Lengyel, Yale University, New Haven, Connecticut: "Translation of *in vitro* Synthesized Reovirus Messenger RNAs into Reovirus Capsid Protein-like Proteins in a Mouse L Cell Extract."

M. B. Mathews, C. Milstein, G. G. Brownlee, and T. M. Harrison, M.R.C. Laboratory of Molecular Biology, Cambridge, England: "Immunoglobulin Light Chain Synthesis *in vitro*."

P. Leder, H. Aviv, S. Packman, D. Swan, NIH-NICHHD, Bethesda, Maryland: "Translation, Purification and Reverse Transcription of mRNA Isolated from Immunoglobin Light Chain-producing Tumor Cells."

T. Morrison and H. Lodish, Massachusetts Institute of Technology, Cambridge: "Translation of QB mRNA in an Ascites Cell-free System."

WEDNESDAY, SEPTEMBER 6

D. S. Shih and P. Kaesberg, University of Wisconsin, Madison: "Cell-free Synthesis of Brome Mosaic Virus Coat Protein in a System Derived From Wheat Embryo."

A. H. Scragg and D. Y. Thomas, National Institute for Medical Research, London, England: "Production of Mitochondrial Membrane Proteins in an *E. coli* Cell-free System Primed with Mitochondrial DNA."

W. Siegert, R. Konings, H. Bauer, and P. H. Hofschneider, Max-Planck-Institut fur Biochemie, Martinsried bei Munchen, Germany: "Translation of Avian Myeloblastosis Virus RNA in a Cell-free System of *E. coli*."

B. Oberg and A. J. Shatkin, Roche Institute of Molecular Biology, Nutley, New Jersey: "Initiation and Synthesis of EMC Virus Proteins *in vitro*."

R. Kamen, M. Kondo, W. Romer, and C. Weissmann, Institut fur Molekularbiologie der Universitat Zurich, Switzerland: "Protein Synthesis Interference Factor i is a Functional Subunit of QB RNA Replicase."

M. Schweiger, P. Herrlich, E. Scherzinger, and H. J. Rahmsdorf, Max-Planck-Institut fur Molekulare Genetik, Berlin-Dahlem: "Repression of Gene Expression After T7 Infection."

A. Travers, MRC Laboratory of Molecular Biology, Cambridge, England: "Response of RNA Polymerase Activities in *E. coli* to Changes in Growth Conditions."

B. Hall, B. Harada, and J. Gallant, University of Washington, Seattle: "Role of the RC Gene Product in Translation."

R. Block and W. A. Haseltine, Harvard University, Cambridge, Massachusetts: "*in vitro* Synthesis of MS I and MS II."

AFTERNOON SESSION

A. A. Infante and M. A. Hall, Wesleyan University, Middletown, Connecticut: "Ribosome-subunit Equilibrium of Sea Urchins: Effects of Centrifugation, Pressure, Mg^{++} and K^{+}."

K. Cremer, D. Schlessinger, and L. Silengo, Washington University Medical School, St. Louis: "Polyribosomes in Antibiotic-treated *E. coli*."

M. Nomura, University of Wisconsin, Madison: "Bacterial Ribosomes."

J. Vournakis, V. Leick, and A. Rich, Massachusetts Institute of Technology, Cambridge: "Size, Shape and Functional Changes in Ribosomes."

N. D. Zinder and K. Jakes, Rockefeller University, New York City: "Structural Requirements for *in vitro* Inactivation of *E. coli* Ribosomes by Colicin E3."

A. Bollen, J. Petre, and H. Grosjean, University of Brussels, Belgium: "Direct Biochemical Evidence for the Structural Heterogeneity of the *E. coli* 30S-ribosomal Subunits."

R. T. Garvin, R. Rosset, and L. Gorini, Harvard Medical School, Boston: "Functional Modification of *Escherichia Coli* Ribosomes Upon Growth in Streptomycin."

I. G. Wool, C. Eil, and F. Ventimiglia, University of Chicago, Chicago: "Phosphorylation of Ribosomal Proteins."

E. Kuechler and A. P. Czernilofsky, University of Vienna, Austria: "Proteins of the tRNA Binding Site on the *Escherichia Coli* Ribosome."

THURSDAY, SEPTEMBER 7

E. A. Linney, M. N. Hayashi, and M. Hayashi, University of California, San Diego: "Two Natural Initiators of Protein Synthesis in the Cistron A of X174."

H. D. Robertson, B. G. Barrell, H. L. Weith, and J. Donelson, M.R.C. Laboratory of Molecular Biology, Cambridge, England: "Ribosome-binding Sites from Bacteriophage DNA."

J. A. Steitz, Yale University, New Haven, Connecticut: "Recognition of RNA Phage RNAs by Ribosomes of *B. stearothermophilus*."

K. K. Bose and N. K. Gupta, University of Nebraska, Lincoln: "Characteristics of Terminal and Internal Methionine Codon Recignition by *E. coli* Met-$tRNA_f^{Met}$."

R. E. Thach and F. Golini, Washington University Medical School, St. Louis: "Studies on the Specificity of Protein Synthesis Initiation."

N. K. Gupta, C. L. Woodley, Y. C. Chen, C. P. Cheung, S. C. Chen, and Y. N. Chen, University of Nebraska, Lincoln: "Protein Synthesis Initiation in Rabbit Reticulocytes."

H. P. Ghosh and K. Ghosh, McMaster University, Hamilton, Canada: "Specificity of Initiator tRNAs in Protein Synthesis."

D. H. Levin, D. Kyner, and G. Acs, Institute for Muscle Disease, Inc., New York City: "Stepwise Formation of Protein Initiation Complexes in a Eukaryotic System."

AFTERNOON SESSION

R. G. Crystal, A. W. Nienhuis, N. A. Elson, P. M. Prichard, W. C. Merrick, D. Picciano, D. G. Laycock, H. Graf, J. Barker, and W. F. Anderson, NIH-NHLI, Bethesda, Maryland: "Model Systems for the Study of Mammalian Protein Synthesis."

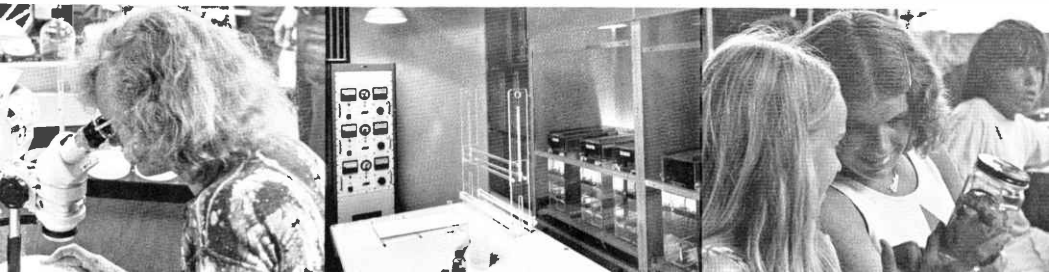
M. H. Schreier and T. Staehelin, Basel Institute for Immunology, Basel, Switzerland: "Mammalian Initiation Factors: Purification, Characterization and Specificity of mRNA Binding Factor From Various Sources."

H. O. Voorma, R. Benne, N. Naaktgeboren, C. Vermeer, and L. Bosch, University of Lieden, The Netherlands: "Binding and Recycling of the Initiation Factors IF1 IF2 and IF3."

J. C. LeLong, R. Stoffler, A. Bollen, D. Lazar, and F. Gros, University of Paris; Max-Planck-Institute, Berlin: "Study of Ribosomal Sites Involved in Initiation."

A. H. Lockwood, P. Sarkar, and U. Maitra, Einstein College of Medicine, Bronx, New York: "Interaction of IF2 and GTP with Ribosomes."

R. Kaempfer, Harvard University, Cambridge, Massachusetts: "Initiation Factor IF3: A Specific Inhibitor of Ribosomal Subunit Association."



A. J. Wahba, M. J. Miller, and R. Annett, Sherbrooke Medical Center, Sherbrooke, Canada: "Further Studies on Chain Initiation Factors from *E. coli* MRE 600."
S. Lee-Huang, S. Sabol, and S. Ochoa, New York University School of Medicine, New York City: "Messenger-selecting Species of Initiation Factor IF3."
M. Revel, Y. Groner, Y. Pollack, and R. Scheps, Weizmann Institute of Science, Rehovot, Israel: "Cistron Specific Initiation Factors in *E. coli*."

FRIDAY, SEPTEMBER 8

R. D. Goldman, Case Western Reserve University, Cleveland, Ohio: "The Structure and Possible Functions of Cytoplasmic Microtubules, Filaments and Microfilaments."
M. Cashel, NIH-NICHD, Bethesda, Maryland: "The Metabolic Lability of Phosphate Labeling of Purine Nucleotides in *Escherichia coli*."
N. Brot, E. Yamaski, M. Boublik, and H. Weissbach, Roche Institute, Nutley, New Jersey: "Studies on Ribosomal Proteins L-7 and L-12."
D. Richter, Rockefeller University, New York City: "Overlap of Ribosomal Binding Sites for Elongation Factors EF1 and EF2 and Phenylalanyl-tRNA in a Cell-free System From Hypothalamic Tissue."
A. Parmeggiani, G. Chinali, R. C. Marsh, and G. Sander, Gesselschaft fur Molekularbiologische Forschung, Stockheim, Germany: "Interaction of EF G and EF T with Ribosomes."
J. H. Highland*, J. W. Bodley†, R. Hasenback‡, G. Stoffler, and J. Gordon*, *Friedrich Miescher-Institut, Basel, Switzerland; †University of Minnesota, Minneapolis; ‡Max-Planck-Institut, Berlin: "Identification of the Ribosomal Proteins Involved in Interaction with Elongation Factor G and GTP."
J. Modolell, B. Cabrer, and D. Vazquez, Instituto de Biologia Celular, Madrid, Spain: "Elongation Factor EF G and Aminoacyl-tRNA Bind to the Ribosome on Mutually Exclusive Sites."
T. Blumenthal, T. Landers, E. Lazarides, and K. Weber, Harvard University, Cambridge, Massachusetts: "Involvement of Protein Synthesis Elongation Factors EF-Tu and EF-Ts in QB Replicase."

AFTERNOON SESSION

J. W. Bodley and N. Richman, University of Minnesota, Minneapolis: "Irreversible Inhibition of the Interaction Between Elongation Factor Tu and Phenylalanyl-tRNA by N-tosyl-L-phenylalanyl-chloromethyl Ketone."
S. Pestka, R. Harris, and H. Rosenfeld, Roche Institute of Molecular Biology, Nutley, New Jersey: "Transpeptidation on Polyribosomes and a Model of Ribosome Function."
B. D. Davis, B. J. Wallace, and P.-C. Tai, Harvard Medical School, Boston: "Mechanism of Action of Streptomycin and Other Ribosome Inhibitors."
C. F. Heredia, A. Sandoval, C. San Jose, and A. Torano, Universidad Autonoma, Madrid, Spain: "Interactions of Phe-tRNA and N-Ac-Phe-tRNA with Yeast Soluble Protein Factors, Ribosomes, and Ribosomal Subunits."
J. Ravel, University of Texas, Austin: "Interaction of Rabbit Reticulocyte EF1 with GDP, GTP, and Aminoacyl-tRNA."
J. E. Allende, A. Tarrago, and S. Litvak, University of Chile, Santiago: "Studies of Elongation Factor 1 from Wheat Embryos."
O. Henriksen and M. Smulson, Georgetown Medical School, Washington, D.C.: "Subribosomal Particulate Forms of Elongation Factors and Aminoacyl-tRNA Synthetases in HeLa Cells."
E. S. Maxwell and E. A. Robinson, NIH-NIAMDD, Bethesda, Maryland: "Chemical Properties of Elongation Factor 2: Amino Acid Composition, NH_2-terminal Residue and Sulfhydryl Reactivity."

SATURDAY, SEPTEMBER 9

D. L. Engelhardt, University of Connecticut, Storrs: "Mode of Action of a Protein Synthesis Inhibitor Produced by Density-inhibited Animal Cells."
E. C. Henshaw and C. A. Hirsch, Beth Israel Hospital; Harvard Medical School, Boston: "Polyribosome Cycle in Mammalian Protein Synthesis."
W. P. Tate, A. L. Beaudet, and C. T. Caskey, Baylor College of Medicine, Houston: "Characterization of Rabbit Reticulocyte Release Factor."
J. Morrisey and B. Hardesty, University of Texas, Austin: "A Met-tRNA Hydrolase From Reticulocytes Specific for Met-$tRNA_f^{Met}$ on 40S Ribosomal Subunits."
J. R. Menninger, C. Walker, P. F. Tan, and J. Strathern, University of Oregon, Eugene; Iowa State University, Ames: "Metabolic Role of Peptidyl-tRNA Hydrolase."
G. Blobel, Rockefeller University, New York City: "Some Properties of the mRNA-protein Complexes Released from Eukaryotic Polysomes."
A. R. Subramanian and B. D. Davis, Harvard Medical School, Boston: "Release of Intact 70S Ribosomes from Polysomes in *E. coli*."
O. A. Scornik, Dartmouth Medical School, Hanover, New Hampshire: "*in vivo* Synthesis, Export, and Degradation of Proteins in the Regenerating Mouse Liver."
K. Ogawa, A. Hirashima, and A. Kaji, Pennsylvania Medical School, Philadelphia: "Factor Dependent Release of Ribosomes at the Termination Signal."

AFTERNOON SESSION

M. C. Ganoza, University of Toronto, Canada: "Characterization of a Mutant Defective in Termination and Initiation of Protein Synthesis."
M. P. Oeschger, Yale University, New Haven, Connecticut: "Temperature Sensitive SU1 Suppression Mutants of *E. coli*."
B. Littlewood and J. Davies, University of Wisconsin, Madison: "Mutants Affecting Macromolecular Synthesis in *Saccharomyces Cerevisiae*."
M. R. Capecchi, J. D. Sharp, and N. E. Capecchi, Harvard Medical School, Boston: "Analysis of 8Azaguanine Resistant Mutants Isolated in Mouse Fibroblast Tissue Culture Cell Lines."
H. Kleinkauf, Technische Universitat, Berlin: "Amino Acid Activation Mechanism of Nucleic Acid-free Polypeptide Biosynthesis."
S. G. Lee, Rockefeller University, New York City: "Separation of Subunits from Polyenzymes Involved in Tyrocidine Synthesis."
K. Bauer, Rockefeller University, New York City: "Studies on the Biosynthesis of Linear Gramicidin (LG)."

IN-HOUSE SEMINARS

Cold Spring Harbor in-house seminars were initiated to be a semi-formal avenue for communication between the various research groups at the laboratory. They are particularly useful for research personnel who had joined the laboratory during the summer. Every person involved in research at the laboratory gave at least one seminar in the series. The seminars also provided a necessary opportunity for the graduate students and post-graduate staff members to develop their skills in defending, organizing, and presenting their research.

October

12th. John J. Dunn, Molekulare Genetik, Universitat Heidelberg, Germany. "Transcription of T3 by *E. coli* and T3 Polymerase."

22nd. Donald Brown, Carnegie Institute of Washington, Baltimore. "Isolation and Structure of Ribosomal and 5S Genes from Xenopus."

November

5th. Tom Wegmann, Harvard University, Cambridge, Massachusetts. "Immunological Tolerance: 'Forbidden Clones' Allowed in Tetraparental Mice."

12th. Vincent Marchesi, National Institute of Arthritis and Metabolic Diseases, Bethesda, Maryland. "The Role of Glycoproteins in Membrane Structure."

19th. Richard Hollberg, Cornell University, Ithaca, New York. "DNA Base Sequence Homology among Mitochondrial DNA from Man, Mouse, and Xenopus Lavies."

December

3rd. Victor Ling, Ontario Cancer Institute, Toronto, Canada. "An Approach to DNA Sequencing."

6th. James A. Kirkland, Queen Elizabeth Hospital, Woodville, Australia. "Human Cancer Cervix: Relationship of Chromosome Number to Malignant Potential."

10th. William Folk, Imperial Cancer Research Fund Laboratories, London, England. "Simian Virus 40 Specific RNA in SV40 Transformed Cells."

17th. Roland Rueckert, University of Wisconsin, Madison. "Structure and Morphogenesis of Picornaviruses."

20th. Richard Russell, California Institute of Technology, Pasadena. "Behavioral Properties of Nematodes."

21st. Richard Roberts, Harvard University, Cambridge, Massachusetts. "A Novel Species of Transfer RNA."

January

5th. Lennart Philipson, Columbia University, New York City. "Lytic Adenovirus Infection as a Model for Transcription and Processing of Eukaryotic Cells."

14th. Eugene Katz, State University of New York, Stony Brook. "Slime Mold."

21st. Pat Spears, Rockefeller University, New York City. "Membrane-bound Proteins Specified by Herpes Simplex Virus."

28th. Richard Goldsby, Yale University, New Haven, Connecticut. "Interferon."

February

3rd. Nancy Hopkins and Rex Risser, Harvard University, Cambridge, Massachusetts. "Action of P1 Restriction Endonuclease on SV40 DNA."

4th. Hayden Coon, National Institutes of Health, Bethesda, Maryland. "Somatic Cell Hybrids."

11th. Stephen Roth, The Johns Hopkins University, Baltimore. "Growth Control and Cell Membranes."

18th. Harmut Renger, New York University School of Medicine, New York City. "Mutation Causing Temperature-sensitive Expression of Cell Transformation by a Tumor Virus."

23rd. R. Zimmerman, Universite de Geneve, Switzerland. "Location of Ribosomal Protein Binding Sites on the 16s RNA Molecule."

29th. Rudolf Werner, University of Miami School of Medicine, Florida. "DNA Replication in vivo."

March

3rd. Tom Benjamin, New York City Public Health Laboratory. "Polyoma Mutants."

10th. Sondra Schlesinger, Washington University, St. Louis. "Sindbis Virus: Formation of Viral Proteins and Defective Particles."

17th. Stanley Crain, Albert Einstein School of Medicine, Bronx, New York. "Tissue Culture Models of Developing CNS Functions."

22nd. Edwin S. Minkley, Jr., Harvard University, Cambridge, Massachusetts. "RNA Synthesis."

24th. Stuart Heywood, University of Connecticut, Storrs. "in vitro Synthesis of Myosin."

27th. Marcus Noll, Northwestern University, Evanston, Illinois. "Ribosome Cycle Sequence of Events in a Purified System Consisting of amB_2R17 RNA Defined Ribosomes Initiation, Translation, and Relief Factors."

31st. Howard M. Temin, University of Wisconsin, Madison. "RNA Directed DNA Synthesis in Cells."

April

12th. Lee Hood, California Institute of Technology, Pasadena. "The Immune System: A Model for Differentiation in Higher Organisms."

21st. Helen Smith, Naval Biomedical Research Laboratory, Oakland, California. "Characterization of Simian Virus 40 Transformed 3T3 Cells."

25th. Georgi P. Georgiev, Institute of Molecular Biology, Moscow, USSR. "On the Structural Organization of Transcriptional Units in Eukaryotic Cells."

28th. Leslie Weiner, The Johns Hopkins University School of Medicine, Baltimore. "SV40-like Virus in Human Brain."

May

5th. Sherman Weissman, Yale University, New Haven, Connecticut. "Approaches to the Sequencing of SV40."

10th. Robert D. Goldman, Case Western Reserve University, Cleveland, Ohio. "The Possible Functions of Cytoplasmic Fibers in Cell Motility."

12th. Karl Erik Helstrom, University of Washington School of Medicine, Seattle. "Cellular Immunity to Tumor Antigens."

19th. Norman Salzman, National Institute of Allergy and Infectious Diseases, Bethesda, Maryland. "SV40 DNA Initiation and Replication."

UNDERGRADUATE RESEARCH PARTICIPATION PROGRAM

Summer 1972

Another aspect of the summer program at the Laboratory is the participation of college undergraduate students in active research projects under the supervision of full-time Laboratory staff members. The program was initiated in 1959 and since that year, 139 students have completed the course.

The objectives of the program are 1) greater understanding of the fundamental principles of biology; 2) increased appreciation of major problem areas under investigation; 3) increased awareness of physical and intellectual tools for modern research and the pertinence of this information to future training, and 4) personal acquaintance with research, research workers, and centers for study.

The following students, listed with topics of research and Laboratory sponsors, were enrolled in the program sponsored by the National Science Foundation:

Janice Blustein, The Johns Hopkins University *Supervisor:* Walter Keller	Separation of the subunits of RNA-dependent DNA polymerase from avian myeloblastosis virus
David Burstein, Columbia University *Supervisor:* Ernesto Bade	Transcription of Mu-1 prophage
Hugh Cairns, Brown University *Supervisor:* Robert Pollack	Cell volume alterations in synchronized populations
Terrell Gibbs, Massachusetts Institute of Technology *Supervisor:* David Zipser	Computer simulation of nucleic acid
Helen Hollingsworth, Brown University *Supervisor:* Jeremy Bruenn	Isolation of mRNA degradation-deficient mutants of *Escherichia coli*

Ben Kim, Harvard College *Supervisor:* Peter Greenaway	Purine trace analysis of SV40 DNA
Mary Martin, Reed College *Supervisor:* Peter Greenaway	Pyrimidine tract analysis of SV40 DNA
T. Kevin Sweeney, Cornell University *Supervisor:* Hajo Delius	Partial denaturation map of T5 DNA
Janis Townsend, Princeton University *Supervisor:* Carl Anderson	Characterization of tryptic peptides of actin
Jerome Zeldis, Brown University *Supervisor:* Robert Pollack	Fluctuation analysis of mutagen-induced reversion of transformed cells

NATURE STUDY COURSES

Children 6-18

The Children's Nature Study program, attended by 381 participants, was designed to create an interest in Nature and to teach young people how to help themselves learn the answers to questions from everyday observation of Nature.

Otto Heck, program director, completed his 15th consecutive year on the staff.

The Laboratory provided a headquarters building (Jones Laboratory) and much of the laboratory and field equipment. The course members explored the Laboratory grounds and waterfronts, the reserves at St. John's Church, Fox Hollow and Uplands Farms, and the Church Sanctuary.

The Huntington Federal Savings and Loan Association donated the tuition for five children. The Laboratory gratefully acknowledges the Association's 13th annual contribution to the Nature Study program.

STAFF

Otto Heck, Assistant Professor of Biology, Trenton State College, New Jersey
Beth Blauman, Student, University of Colorado, Boulder
Robert Budliger, Instructor, Bay Shore Middle School
Leslee Cattrall, Student, University of Chicago
Fred Maasch, Instructor, Islip High School
Alex Pepe, Instructor, East Side School, Cold Spring Harbor
Richard Roseman, Instructor, Cold Spring Harbor High School
Thomas Stock, Instructor, Selden Junior High School, Centereach
Debby Taylor, Student, Cedar Crest College, Allentown, Pennsylvania

COURSES

General Nature Study
Advanced Nature Study
Seashore Life
Bird Study
Advanced Bird Study
Geology
Geology of Long Island
Animals with Backbones
Plant-Insect Relationships
Plant Ecology
Animal Ecology
Ecology of the Estuary
Freshwater Life
Ichthyology-Herpetology
Marine Biology

NATURE STUDY WORKSHOP FOR TEACHERS

The 17th annual Workshop in Nature Study was offered during the summer of 1972 and was attended by 33 elementary and secondary school teachers. The program was designed to familiarize the teachers with the natural environment of the Long Island area, including the animals and plants living there. There were field trips to ponds, streams, seashore, woodlands, fields, and other natural habitats to collect and study first-hand the flora and fauna of the locale.

Upon satisfactory completion of the course requirements, four in-service credits are awarded to participants by the New York State Department of Education.

Instructors were Otto Heck and Robert Budliger.

LABORATORY STAFF

November 1972

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James D. Watson

Administrative Director
William R. Udry

Research Scientists
Ahmad Bukhari
John Cairns
Hajo Delius
Francoise Falcoz-Kelly
Raymond Gesteland
Terri Grodzicker
Walter Keller
Carel Mulder
Ulf Pettersson
Robert Pollack
Richard Roberts
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Phillip Sharp
Klaus Weber
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David Zipser

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Martha Howe
Peter Jeppesen
Jan Oey
James Shineberg

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Bradford Ozanne
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Walter Schroder
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Arthur Vogel

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Peter Baum
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The Board of Trustees
Cold Spring Harbor Laboratory
Cold Spring Harbor, New York:

We have examined the balance sheet of Cold Spring Harbor Laboratory as of October 31, 1972 and the related statements of current revenues, expenditures and transfers and of changes in fund balances for the year then ended. Our examination was made in accordance with generally accepted auditing standards, and accordingly included such tests of the accounting records and such other auditing procedures as we considered necessary in the circumstances.

In our opinion, except for the absence of recording certain equipment as explained in note 2 to the financial statements, such financial statements present fairly the financial position of Cold Spring Harbor Laboratory as of October 31, 1972 and the results of its operations for the year then ended, in conformity with generally accepted accounting principles applied on a basis consistent with that of the preceding year.

Peat, Marwick, Mitchell & Co.

December 20, 1972

FINANCIAL REPORT

Year Ended October 31, 1972 with comparative figures for 1971

Exhibit A

ASSETS

	1972	1971
Current funds:		
Unrestricted:		
Cash	$ 144,220	$ 124,576
Accounts receivable (less allowance for doubtful accounts, 1972–$8,000; 1971–$6,000)	44,059	49,782
Inventory of books at cost (less allowance for obsolescence, 1972–$59,954; 1971–$40,679)	71,984	72,152
Prepaid and deferred expenses	16,253	13,197
Total unrestricted	276,516	259,707
Restricted:		
Cash	116,781	55,249
Grants receivable (note 1)	878,033	1,025,028
Total restricted	994,814	1,080,277
Total current funds	$1,271,330	$1,339,984
Plant funds:		
Unexpended – cash	294,998	100,677
Invested in plant (note 2):		
Land and improvements	138,297	138,297
Buildings	1,100,203	1,017,447
Furniture, fixtures and equipment	23,869	–
Laboratory equipment	141,330	100,841
	1,403,699	1,256,585
Less allowance for depreciation	273,124	195,379
	1,130,575	1,061,206
Construction in progress	72,814	–
Total invested in plant	1,203,389	1,061,206
Total plant funds	$1,498,387	$1,161,883

LIABILITIES AND FUND BALANCES

Current funds:		
Unrestricted:		
Accounts payable	$ 59,928	$ 68,702
Accrued expenses	34,679	33,680
Deferred income on future publications	6,472	5,650
Fund balance (Exhibit C)	175,437	151,675
Total unrestricted	276,516	259,707
Restricted:		
Fund balance (Exhibit C)	994,814	1,080,277
Total restricted	994,814	1,080,277
Total current funds	$1,271,330	$1,339,984
Plant funds:		
Unexpended – fund balance (Exhibit D)	294,998	100,677
Invested in plant:		
Investment in plant (Exhibit D)	1,203,389	1,061,206
Total invested in plant	1,203,389	1,061,206
Total plant funds	$1,498,387	$1,161,883

See accompanying notes to financial statements.

STATEMENT OF CURRENT REVENUES, EXPENDITURES AND TRANSFERS

Year ended October 31, 1972
with comparative figures for 1971

Exhibit B

	1972	1971
Revenues:		
Expendable grants (Exhibit C)	$1,463,526	$ 846,484
Indirect cost allowance on grants	470,874	226,235
Contributions	125,287	79,958
Summer programs	113,876	104,150
Laboratory rental	21,272	27,095
Investment income	15,913	10,503
Book sales	175,850	182,156
Dining hall	75,625	64,373
Rooms and apartments	79,615	67,970
Other sources	2,625	674
Total revenues	2,544,463	1,609,598
Expenditures:		
Research	1,334,052	711,230
Summer programs	146,205	154,290
Library	39,730	14,621
Operation and maintenance of physical plant	259,853	216,980
General and administrative	210,708	240,732
Scholarships	1,452	1,400
Book sales*	129,933	158,090
Dining hall*	77,598	63,714
Rooms and apartments (excludes depreciation of $15,699 recorded in plant funds)*	14,216	19,823
	2,213,747	1,580,880
Transfers:		
To unexpended plant funds	318,573	143,326
To investment in plant	13,420	11,930
	331,993	155,256
Total expenditures and transfers	2,545,740	1,736,136
Excess of expenditures and transfers over revenues	$ 1,277	$ 126,538

Reported exclusive of an allocation for operation and maintenance of physical plant and general and administrative expenses.

ee accompanying notes to financial statements.

STATEMENT OF CHANGES IN CURRENT FUND BALANCES

Year ended October 31, 1972 — **Exhibit C**

UNRESTRICTED FUNDS

Balance at beginning of year	$ 151,675
Add adjustment for 1971 expenditure transferred to restricted funds (note 3)	25,039
Balance at beginning of year as adjusted	176,714
Deduct excess of expenditures and transfers over revenues	1,277
Balance at end of year	$ 175,437

RESTRICTED FUNDS

Balance at beginning of year		$1,080,277
Deduct adjustment for 1971 expenditures transferred from unrestricted funds (note 3)		25,039
Balance at beginning of year as adjusted		1,055,238
Add:		
Grants	$1,986,619	
Other	4,227	1,990,846
		3,046,084
Deduct:		
Current expenditures	1,463,526	
Indirect cost allowance	470,518	
Plant expenditures	42,084	
Unexpended funds returned to grantor	75,142	
		2,051,270
Balance at end of year		$ 994,814

See accompanying notes to financial statements.

STATEMENT OF CHANGES IN PLANT FUND BALANCES

Year ended October 31, 1972 — Exhibit D

UNEXPENDED PLANT FUNDS

Balance at beginning of year		$ 100,677
Add:		
Gifts		40,400
Transfer from current unrestricted funds		318,573
		459,650
Deduct expenditures for plant		164,652
Balance at end of year		$ 294,998

INVESTMENT IN PLANT

Balance at beginning of year		$1,061,206
Add:		
Capital expenditures financed by unrestricted funds	$ 13,420	
Capital expenditures financed by unexpended plant funds	164,652	
Capital expenditures financed by grant awards	42,084	
		220,156
		1,281,362
Deduct depreciation of buildings and equipment (note 2)		77,973
Balance at end of year		$1,203,389

See accompanying notes to financial statements.

NOTES TO FINANCIAL STATEMENTS

October 31, 1972

(1) Grants Receivable

Grants receivable of the current restricted funds represent amounts pledged to the Laboratory for certain operations and for the completion of designated projects. The grants will be collected as expenditures are made by the Laboratory for the designated projects.

(2) Plant Assets and Depreciation

Plant assets are stated on the following bases:

Land, improvements thereon, and buildings are stated at cost or at the May 1, 1963 values as carried on the books of Long Island Biological Association prior to their transfer to Cold Spring Harbor Laboratory.

Equipment acquired prior to the year ended October 31, 1971 is not recorded on the financial statements since the cost of the equipment is now known. In addition, certain Government owned equipment is utilized by the Laboratory in connection with its performance under agreements with the Government. The Laboratory is, however, accountable to the Government for such equipment.

Construction in progress represents accumulated costs for renovations and new facilities under several projects. Costs to complete these projects will aggregate approximately $210,000.

Depreciation is provided on the straight-line method over the estimated useful lives of all buildings and recorded equipment acquired with non-federal funds in order to more accurately reflect the indirect operating expenses of the Laboratory for cost recovery purposes under certain Federal grants.

(3) Current Fund Balances

During fiscal 1971, the Laboratory charged current unrestricted funds for certain expenditures, totaling $25,039, which were subsequently determined to be chargeable directly to current restricted funds. An adjustment in the aforementioned amount has been reflected in each of the current fund balances.

(4) Retirement Plan

The Laboratory employees are covered by Teachers Insurance and Annuity Association of America – College Retirement Equities Fund plan. Total expenditures under the plan for the year ended October 31, 1972, and 1971 amounted to $59,635 and $43,573, respectively. There are no unfunded past service costs.

(5) Claims Under Completed Grants

The Laboratory has submitted claims approximating $165,000 to the National Institutes of Health for reimbursement of allowable costs incurred during fiscal years 1969 to 1971. Recovery of the claims is dependent upon the granting agency's availability of funds and, therefore, will be recorded as payments are received.

(6) Donated Books and Periodicals

The contents of a library, consisting principally of scientific books and periodicals, have been donated to the Laboratory. In the event the Laboratory elects, at any time, not to retain these publications, the conveyance requires that they be offered to certain educational institutions. The donation has not been recognized in the accompanying financial statements pending determination of an appropriate valuation basis.

FINANCIAL SUPPORT OF THE LABORATORY

The Laboratory is completely dependent upon the generous contributions of its sponsors, participating institutions, and friends for new programs, central institutional needs, and capital improvements.

Methods of Contributing to Cold Spring Harbor Laboratory

- *Gifts of Money*
- *Appreciated Securities and Real Estate*
- *Charitable Remainder Unitrust*
- *Gifts of Life Insurance*
- *Charitable Remainder Annuity Trust*
- *Appreciated Art Works and Other Tangible Personal Property*
- *Conversion of Private Foundation to Public Foundation Status*

  This may be done by creating a separate fund within Cold Spring Harbor Laboratory whereby the assets of the private foundation could be accounted for as a separate fund and used for the purposes specified by the donor. Alternatively, the private foundation can be established as a "supporting organization of the Cold Spring Harbor Laboratory." Conversion of a private foundation has obvious advantages and includes the following:

  All income is tax exempt.
  Deduction for full market value of long term appreciated property.
  Deduct contributions up to 50% of adjusted gross income with carry-over privilege.
  No limit on percentage of stock of family corporations which can be held.
  Accumulate income and maintain corpus.
  Record keeping and reporting simplified.

The Cold Spring Harbor Laboratory is a publicly supported educational institution chartered by the University of the State of New York and may receive contributions which are tax exempt under the provisions of the Internal Revenue Code, particularly Section 501C.

For additional information please contact the Administrative Director, Cold Spring Harbor Laboratory, P.O. Box 100, Cold Spring Harbor, New York 11724 or call area code 516-692-6660.

GRANTS

October 31, 1972

Grantor	*Investigator or Program*	*Total Award*	*Duration of Grant*
NEW GRANTS			
National Science Foundation	Dr. Zipser	$ 83,200	1/1/72-12/31/73
National Institutes of Health	Dr. Watson	7,500,000	1/1/72-12/31/76
	General Research Support	96,706	1/1/72-12/31/72
	Nematode Workshop	5,400	8/20/72-8/22/72
American Cancer Society	Herpesvirus Meeting	4,000	8/20/72-8/24/72
CONTINUING GRANTS			
National Science Foundation	Dr. Cairns	75,000	9/15/70-3/15/73
	Symposium Support	5,000	5/1/72-4/30/73
	Dr. Gesteland	121,000	9/1/71-8/31/74
	Undergraduate Research	18,148	6/1/72-5/31/73
National Institutes of Health	Dr. Zipser	190,000	1/1/70-12/31/73
	Dr. Zipser	92,000	5/1/70-4/30/75
	Dr. Gesteland	80,000	1/1/69-12/31/73
	Dr. Pollack	423,275	1/1/70-12/31/74
	Symposium Support	69,300	4/1/69-3/31/74
American Cancer Society	Dr. Cairns	581,352	1/1/69-6/30/89
	Dr. Pollack	30,311	5/1/71-12/31/72
	Dr. Sambrook	100,000	12/1/70-11/30/75
Jane Coffin Childs Memorial Fund for Cancer Research	Dr. Jeppesen	17,688	9/1/71-8/31/73
Alfred P. Sloan Foundation	Dr. Watson	450,000	10/1/70-9/30/75
Volkswagen Foundation	Dr. Watson	60,000	1/1/71-12/31/75
Atomic Energy Commission	Symposium Support	8,000	6/6/72-6/13/72

PARTICIPATING INSTITUTIONS

Albert Einstein College of Medicine
The City University of New York
Columbia University
Duke University Medical Center
Harvard Medical School
Long Island Biological Association
Massachusetts Institute of Technology
New York University Medical Center
Princeton University
The Rockefeller University
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LONG ISLAND BIOLOGICAL ASSOCIATION

The Laboratory was founded in 1890 by several local philanthropists and the Brooklyn Institute of Arts and Sciences. The first chairman of the Board of Managers of the Laboratory was Eugene G. Blackford, who served from 1890 until his death in 1904. William J. Matheson succeeded him, serving until 1923.

In that year, when the Brooklyn Institute of Arts and Sciences withdrew from Cold Spring Harbor, the local supporters of the research formalized their efforts by incorporating as the Long Island Biological Association. Colonel T. S. Williams became the first Chairman of the new group. Jointly with the Carnegie Institution of Washington, LIBA continued to support and direct the research at Cold Spring Harbor Laboratory.

In 1962 the Laboratory was reorganized as an operating organization and LIBA relinquished its management responsibilities to concentrate its efforts on obtaining financial support from the community for the Laboratory's work.

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View of Cold Spring Harbor from the sandspit. Photo by Hajo Delius.