

The University of Chicago

CHICAGO 37, ILLINOIS

Institute of Radiobiology and Biophysics

6200 Drexel Avenue

April 28, 1950

Dr. Frederick L. Stone, Chief
Office of Research Fellowships
Division of Research Grants and Fellowships
Public Health Service
National Institutes of Health
Washington, D. C.

Dear Dr. Stone:

I am writing to you in response to your inquiry of April 20 concerning Mr. Karl Gordon Lark who has applied for a Predoctoral Research Fellowship in Biochemistry under the sponsorship of Dr. Mark Adams. I wish to support the application of Mr. Lark since I believe that his work with Dr. Adams might turn out to be very fruitful. In particular I believe that:

- 1) Mr. Lark has definite research ability and shows as much promise as anyone in his age group whom I know.
- 2) Mr. Lark shows considerable originality of ideas.
- 3) His training and professional background are wholly adequate for the work which he proposes to do.
- 4) He has a very good personality and considerable ability to work in cooperation with others.
- 5) Mr. Lark had taken a course with Dr. Adams in bacterial viruses last summer and his present application and Dr. Adams' sponsorship are based on the fact that a satisfactory basis for collaboration had developed at that time.

Dr. Frederick L. Stone

- 2 -

April 28, 1950

6) I know of nothing that would reflect in the slightest on the character and loyalty to the United States of the applicant.

Sincerely yours,

Leo Szilard
Professor of Biophysics

LS/sds

1155 East 57th Street
Chicago 37, Illinois
December 19, 1950

Dr. David E. Price
Chief, Division of Research
Grants and Fellowships
National Institutes of Health
Bethesda 14, Maryland

Dear Dr. Price:

Re: RG 2814

I am writing to thank you for your very kind letter of October 24. I understand that the University of Chicago has already taken steps to activate this grant. I am enclosing copies of a manuscript which will appear in print in the December issue of the Proceedings of the National Academy and in which you might be interested.

Sincerely yours,

Leo Szilard

wv



FEDERAL SECURITY AGENCY • Public Health Service
NATIONAL INSTITUTES OF HEALTH • Bethesda 14, Md.

NATIONAL INSTITUTE OF ARTHRITIS AND METABOLIC DISEASES
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NATIONAL INSTITUTE OF NEUROLOGICAL DISEASES AND BLINDNESS
THE CLINICAL CENTER
DIVISION OF RESEARCH GRANTS

June 7, 1951

In reply refer
to: E-144

Dr. Leo Szilard
Professor of Biophysics
Institute of Radiobiology & Biophysics
The University of Chicago
Chicago 37, Illinois

Dear Doctor Szilard:

Recently, the National Microbiological Institute of the National Institutes of Health established an extramural program to be supported by grants-in-aid. One phase of this program is the granting of funds for research projects, similar to the research grant programs of the other institutes in the National Institutes of Health.

Concurrent with the establishment of this new program, active projects and pending applications in the fields of interest to the National Microbiological Institute were transferred to its jurisdiction. All such cases were renumbered, using the prefix letter "E". Accordingly, the designation of your project RG-2814 has been changed to E-144. This change in no way alters the status of the project.

It would be appreciated if you would make a corresponding change in your records and refer to this project hereafter by the new designation.

Sincerely yours,

G. Seger, Dr.P.H.
Project Review Officer

cc: Dr. L.T. Coggeshall
Mr. W.B. Harrell

5650 Ellis Avenue

April 15, 1952

Dr. Ronald E. Scantlebury, Chief
Research Fellowships Branch
Division of Research Grants
National Institutes of Health
Bethesda 14, Maryland

Dear Dr. Scantlebury:

Dr. Maurice S. Fox is applying for a U. S. Public Health Service research fellowship in biophysics and has given my name as a sponsor. I shall be very happy to act in this capacity.

I understand that I am supposed to give a confidential evaluation of his background, research ability, and research promise. Dr. Fox is a physical chemist by training. His thesis work was in the field of radiochemistry; it was published this year in the Journal of Chemical Physics. He received his Ph.D. about a year ago with Professor Willard F. Libby of the Institute for Nuclear Studies, The University of Chicago. Dr. Fox has had very thorough training both in physics and chemistry and ^{has} a broad knowledge in most of the related fields of natural sciences. During the war he served for two years as a weather forecaster with the U. S. Air Force where he holds a reserve commission. (He holds a B.S. degree in meteorology from the University of Chicago.)

Prior to receiving his Ph.D. degree, he expressed to me his desire to work in the biological field. In preparation for such work he took special courses in the fields of bacterial viruses and bacterial genetics (with Dr. Mark Adams and Dr. Evelyn Witkin respectively), which were offered last summer in the Carnegie

Institution of Genetics at Cold Spring Harbor. This coming summer he hopes to attend a two months course in microbial biochemistry given by Dr. van Niel at Pacific Grove.

For the last six months, Dr. Fox has worked with me studying mutations in bacteria in continually growing cultures by means of special techniques which he has developed. He is an extraordinarily capable research worker. He has a good sense of proportion which enables him to choose from among various research projects the one which deserves to be given preference, he is skillful in choosing methods with which to attack the problem chosen, he has both initiative and perseverance and the ability critically to evaluate the experimental results which he obtains. He is a man who is happy in the laboratory, very pleasant to work with, and generally liked by all his coworkers.

Because of these characteristics, I believe that he holds very great promise for the future as a mature and independent scientist.

Very truly yours,

Leo Szilard
Professor of Biophysics

LS/sds

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September 24, 1953

In re. E-4113

Mr. Ronald E. Scantlebury, Ph. D.
National Institutes of Health
Bethesda 14, Md.

Dear Dr. Scantlebury:

I am writing in response to your letter addressed to Dr. Maurice Fox, dated September 21, 1953, in re. E-4113, in which you asked for a letter from his sponsor evaluating his progress during the tenure of his fellowship ending September 30 of this year.

Dr. Fox studied the mutations of bacteria with a device which he developed in which bacteria are kept growing and in which the bacterial population is maintained in a steady state by controlling the feeding of fresh nutrient into the culture through a photo cell which is responsive to the turbidity of the culture.

By observing the number of mutants present in the culture over a period of several days, the mutation rate can be determined. Dr. Fox made over one hundred such determinations under different growth conditions and obtained new and interesting results which will be stated in the short report which he is going to submit.

I believe that this work represents a significant contribution to our knowledge of bacterial mutations and will in a number of respects considerably modify the views held at present on this subject.

Very truly yours,

Leo Szilard

LS:jda



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THE CLINICAL CENTER
DIVISION OF RESEARCH GRANTS

February 5, 1957

Professor Leo Szilard
Quadrangle Club
University of Chicago
Chicago, Illinois

Dear Dr. Szilard:

I was very happy to see you at the conference in New York City last month. As you may remember, we discussed the possibility of your visiting NIH so that you could give a lecture and have an opportunity to see the Institutes.

I mentioned this matter to Dr. Robert Livingston, who is the Research Director of my Institute. He was delighted at the prospect of your visiting NIH and had independently planned to invite you.

As we discussed the matter, he suggested the possibility of your paying us an extended visit, say of two or three weeks, more or less as a Scientist in Residence. It seemed to both of us that this would give you a better opportunity to see various people at NIH, and we felt sure that this would be mutually stimulating.

We would, of course, remunerate you for this stay at NIH.

I would appreciate it if you would let me know of your interest in a prolonged visit of this type, and what dates you might find convenient. We are certainly looking forward to your visit.

With best regards,

Sincerely yours,

Alexander Rich, M.D.
Chief, Section on Physical Chemistry
National Institute of Mental Health



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THE CLINICAL CENTER
DIVISION OF RESEARCH GRANTS

February 11, 1957

Dr. Leo Szilard
Department of Biophysics
University of Chicago
Chicago 37, Illinois

Dear Dr. Szilard:

There is a possibility that over the next few years a growing activity in basic radiation biology and biochemistry will be sponsored by the National Institute of Arthritis and Metabolic Diseases. This likelihood is favored by the fact that the National Bureau of Standards is planning to construct certain of the facilities of nuclear physics in the adjoining town of Gaithersburg and some collaboration between that Institute and ours is envisioned.

It would be my hope to find some person or persons, who could give inspired leadership to a group of investigators to study, as a general assignment, the effects of ionizing radiation upon biological systems or upon related chemical reactions. I firmly believe that the success or failure of such a project will depend very largely upon the leadership which is secured for it. I would, therefore, appreciate receiving from you any suggestions which you may have of people, who might be interested in heading or participating in such a program.

In view of the tenuous nature of the present suggestions, I would appreciate your keeping confidential the present inquiry insofar as it is convenient.

Very truly yours,

DeWitt Stetten, Jr., M.D., Ph. D.
Associate Director in Charge of
Research, NIAMD

DS:jom

February 20, 1957

Dr. Alexander Rich
Chief, Section on Physical Chemistry
National Institute of Mental Health
Bethesda 14, Maryland

Dear Dr. Rich:

Many thanks for your very kind letter of February 5th. I find your invitation very tempting, and I wonder whether I might come to Washington in response to it around March 23rd and stay for two weeks. If it seems desirable, I could prolong my stay for ^{another} ~~one~~ week. Please let me know whether this period of time would be convenient to you and Dr. Livingston.

In the meantime I had a letter from Dr. Livingston also to which I am going to reply very soon.

Assuming that this is a good time for my visit, I would like to raise two questions: First, would it be possible for me to have the use of a secretary (on a part-time basis - say three hours a day, in the morning or in the afternoon, whatever is best from your point of view), who can take shorthand and who has only moderate difficulties with scientific terms? Would it be possible for me to make some private arrangements for the use of a secretary occasionally in the evening, say from 7 to 10, if I cannot get through with my work during the day?

Is there any convenient place for me to stay near the Institutes in Bethesda or should I plan to stay at the Sheraton Park Hotel (my usual hang-out in Washington) and commute by taxi or bus?

I may or may not go to the Columbus meeting but if I do I should expect to see you there.

With kind personal regards,

Sincerely,

L.

Leo Szilard

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Embossed Paper of Febr 5/57

February 21, 1957

Dr. DeWitt Stetten, Jr.
National Institute of Arthritis and
Metabolic Diseases
National Institutes of Health
Bethesda 14, Maryland

Dear Dr. Stetten:

This letter is in answer to your query of February 11th. I remember with great pleasure my visit to your laboratory when you were still at the Public Health Institute of New York City.

Some time before the middle of April, beginning perhaps with March 23rd, I expect to spend two weeks in Bethesda, and I shall then call, if I may, on you and perhaps discuss, among other things, the subject matter of your letter.

I think I understand the problem with which you are faced. Good men are, of course, scarce and whether any one really good would accept the position about which you write will probably largely depend on whether he can hope to assemble a really outstanding group of young investigators. On the face of it, it would look as if working conditions in Bethesda were excellent, particularly for younger men. I should hope to learn more about this point, however, during the two or perhaps three weeks I may spend there in the near future, and will then know better who among those whom you may consider desirable might be expected seriously to consider such a position.

With kind personal regards,

Sincerely yours,

Leo Szilard



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DL 64000
Wm Ext 2142
Rich Ext 3397

March 13, 1957

Professor Leo Szilard
The Fermi Institute for Nuclear Studies
The University of Chicago
Chicago 37, Illinois

Dear Leo:

I'm very happy that you are able to accept our invitation to visit NIH. As Bob Livingston has told you, the two or three weeks after March 23 will be a fine time to visit.

We will be able to arrange the use of a secretary for you and will make arrangements to get someone to assist you during the evenings. I have looked into the matter of places to stay and, aside from the larger hotels which are in town, there is only the Kenwood Country Club nearby which might be suitable. It is about 2 miles from NIH in a direction away from the center of town. I am at the present time looking into the possibility of obtaining an apartment for you on the NIH grounds. If this can be done it would be very convenient.

I was interested in reading your note on the possibility of obtaining transformations in mammals. I must confess that as I read through the paper and the Medawar experiments, it sounded to me very much like a case of bacterial transformation. I hope you are arranging to get this experiment done.

Since the New York meeting, we have learned something very interesting. As you perhaps remember, when polyadenylic acid is exposed to polyuridylic acid, it spontaneously forms a two-stranded helical molecule which has a diffraction pattern very similar to DNA. Recently, we have investigated this interaction more carefully, and found that it was possible to coax this two stranded DNA-like molecule to take on still another third strand of polyuridylic acid to make a three stranded molecule, 2 U's and one A.

Professor Leo Szilard - 3/13/57

This is an interesting reaction because of the following possibility. As you know, DNA has four possible sites at each nucleotide level. One of the simplest ways to imagine that DNA could make RNA is that each of these sites would be specific for a given ribonucleotide and that the DNA molecule could act in the cell by synthesizing a single stranded RNA molecule which has a specific base sequence related to the base sequence in DNA. That is, the helical groove in DNA would be filled by this incoming strand.

The most intriguing aspect of the enclosed work is the specificity of the interaction. That is, while the (A + U) molecule will take on poly U, it will not take on polyadenylic, polycytidylic, or polyinosinic acids.

And so, there is a slight possibility that we may have a model reaction here which is similar to the important reaction which occurs when RNA is synthesized intracellularly.

It will be very pleasant to have you about here for an extended period and to be able to discuss these matters with you more fully. Let me know if I can be of further help.

With best regards,

Yours sincerely,



Alexander Rich

May 8, 1957

Dr. Alexander Rich
Chief, Section on Physical Chemistry
National Institute of Mental Health
Bethesda 14, Maryland

Dear Alex,

When I saw you in Urbana, I thought that by this time I should be in Washington. However, something unexpected came up. My work started to go exceedingly well and I do not want to interrupt this spell of productive thinking. I have written to Livingston, asking him if I may come later. My present plan would be to come either before June 15th and as early as I get through here with the job at hand. Please let me know if you plan to be away from Washington in June.

With kind regards,

Sincerely,

Leo Szilard

June 14, 1957

Dr. Alexander Rich
Section on Physical Chemistry
National Institute of Mental Health
Bethesda 14, Maryland

Dear Alex,

Enclosed you will find a copy of a paper which was sent to the Proceedings of the National Academy.

I wonder whether you have seen the May issue of the Proceedings of the National Academy? It has not reached our library yet but in a copy I just saw I found published a memorandum by Crick, Griffith and Orgel (to which I refer in my manuscript) with certain important amplifications added. I am adding a note and an Appendix to my paper referring to these amplifications.

These raise a number of questions. Apparently Brenner believes that trinucleotides may carry one amino acid each. As you will see from my manuscript, I have considered this possibility but was not happy about it and merely mention it for the sake of completeness. The only smoothly working model that I could think of is based on the assumption that different ribose trinucleotides (and probably also tetranucleotides) carry each a particular sequence of three (respectively four) amino acids. I postulate that each nucleotide within the tri- (or tetra) nucleotide carries on the (2) carbon atom of the ribose moiety a phosphate or pyrophosphate group which carries the amino acid as an acid anhydride.

I wonder whether you can see any difficulty with this model? If there is a really serious objection, I suppose I can still withdraw the paper without causing any serious inconvenience to anyone, provided I withdraw it soon.

Incidentally, has the idea of using trinucleotides carrying one amino acid been ever mentioned in any ^{earlier} publication to your knowledge? If that is the case, please let me know so that I may be able to give proper credit.

One of the purposes of my paper was to estimate the ^{maxi-}minimal rate of protein synthesis. This, I suppose, is of lesser interest to you, and you need not bother with this estimate if you do not feel like it.

With kind regards,

Sincerely,

Leo Szilard

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Encl.



DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

PUBLIC HEALTH SERVICE

BETHESDA 14, MD.

NATIONAL INSTITUTES OF HEALTH

Jun 18, 1957

Dear Dr. S. L. O. L. L. L.,

I shall very soon forward
a more readable edition of my article
about protein synthesis & heterozygosity.

I was very thankful for your
letter to Bhabha and most impressed
by your formulations. Wish I can
fulfill yours & his expectations (!)
Hope to see you soon.

Sincerely yours

Thomas M. Kalkman

P.S.

Add my warmest greetings to the little Ferni granddaughter
Alice Olivia Weiner

June 24, 1957

Dr. Alexander Rich
Section on Physical Chemistry
National Institute of Mental Health
Bethesda 14, Maryland

Dear Alex,

Since I wrote you about a week ago, I looked at known amino acid sequences in polypeptides in the hope that they would throw light on the mechanism of polypeptide synthesis. The attached memorandum gives the conclusion to which they lead. Since my manuscript was to be held until further notice, I can now withdraw it without any trouble, which I shall do without delay.

I am pursuing further the considerations relating to the rate of protein synthesis, and shall probably incorporate parts of the manuscript which relate to this problem into another paper that is in preparation.

With kindest regards,

Sincerely,

Leo Szilard



DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

PUBLIC HEALTH SERVICE

BETHESDA 14, MD.

NATIONAL INSTITUTES OF HEALTH

June 27, 1957

Professor Leo Szilard
The Enrico Fermi Institute
for Nuclear Studies
The University of Chicago
Chicago 37, Illinois

Dear Leo:

Yesterday, I wrote you a letter about your paper. In it, I pointed out why the scheme would not work for 20 sets of three amino acids, due to the large number of expected first and second neighbors. Fortunately, I have not mailed the letter, and your note of this morning makes it unnecessary.

As you know, Gamow, Ycas, and I wrote an article in Advances in Biophysics IV on the coding problem, in which we were concerned with the neighbor relations in proteins. As you can see from the large table in the article, we came to the conclusion that there is no preferred relationship for first or second neighbors. In this regard, a more complete and up to date compilation has been made by Sidney Brenner, more or less supporting the conclusions that we had come to when this article was written about two years ago.

You can also see that we were thinking at the time of various trinucleotide schemes with varying amounts of overlap. Thus, the two triangular codes represented different trinucleotide schemes, though each triplet coded for only one amino acid.

The reason for using twenty trinucleotides rather than any other number is, of course, because these may each code for an individual amino acid. If you attach more than one amino acid to this trinucleotide, then there is no reason to restrict yourself to ^{just} first twenty.


Of course, the entire difficulty in a scheme like the commaless code is one of geometry. One amino acid has along its peptide bond a translation of 3.6\AA . The repeating periodicity of polypeptides in an extended form is 7.2\AA , but this is a distance spanned by two amino acids rather than one. One essentially ends up with a following conundrum: if it appears that three nucleotides are required to carry the information content necessary to place one amino acid, how can these three nucleotides be disposed in space on a temperate mechanism such that they can be packed about 3.6\AA apart? This is a difficult problem and it is not at all apparent right now what the solution is or if there is a solution.

I think on the whole you are doing a wise thing by withdrawing your paper in view of the fact that the Commaless Code paper has now been published. However, it seems to me that your estimation of the rate at which protein synthesis can be carried out is quite an interesting one and should very well be published. In it, you need not restrict yourself to a definite target area such as represented by trinucleotide or dinucleotide. Instead, you could use those as approximations and end up with quite a reasonable order of magnitude estimate.

Next week, I am going to Cambridge, England for a three weeks' stay to attend a meeting there on the structure of collagen. During this time, Crick and I hope to finish two papers which we have left hanging over. When I get back, Leslie Orgel will be visiting here at NIH for a month or so. It would be very pleasant if you could arrive at the same time and we could speak at length about such matters as coding.

With best regards.

Yours sincerely,



Alexander Rich

July 1, 1957

Dr. Alexander Rich
Department of Health, Education, and Welfare
National Institutes of Health
Bethesda 14, Maryland

Dear Alex,

Many thanks for your letter of June 27th. In the meantime I had also heard from Crick, who pointed out the rather fatal error in my would-be paper concerning the distance between two adjacent amino acids -- to which your letter also refers: If in the extended polynucleotide the distance between adjacent nucleotides is about 7\AA , and if the distance between adjacent amino acids in a polypeptide is 3.6\AA , then even if each trinucleotide were to carry three amino acids, the amino acids would be twice as far from each other (when the trinucleotides are all lined up) as the required length.

I plan to be in Europe in September and early October, and as much of August as possible. If you had planned to be back in Washington during the last week of July, maybe we could overlap there for at least a week or perhaps two. Or is the date of your return to Washington not fixed as yet?

With kind regards,

Sincerely,

Leo Szilard



DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

PUBLIC HEALTH SERVICE

BETHESDA 14, MD.

Personal

NATIONAL INSTITUTES OF HEALTH

August 2, 1957

Professor Leo Szilard
The University of Chicago
Enrico Fermi Institute for Nuclear Studies
Chicago 37, Illinois

Dear Leo:

Unfortunately, your letter of July 1 was not forwarded to me in England. I have just returned now and would be delighted to have you visit me in Bethesda during the next week or two if that fits into your schedule. Leslie Orgel is now with me and we have been playing with some new coding schemes.

Crick and I put in a hard month's work during my stay in Cambridge. We settled many of the remaining issues in our collagen work and spent some time on polynucleotide structures. He is hard at work setting up a microsomal particle system for carrying out experiments on protein synthesis. I'm sure you will find this of great interest if you get to Cambridge.

With best regards,

Yours sincerely,

Alexander Rich

August 9, 1957

Dr. Alexander Rich
Department of Health, Education, and Welfare
National Institutes of Health
Bethesda 14, Maryland

Dear Alex,

Many thanks for your kind letter of August 2nd.
I still do not know when I can get away from here and whether
I can come to Washington before I go to Europe.

There is a rumor that you have accepted M.I.T. Do
you expect to remain in Washington in any case through October
and November or might you be gone by that time? I am asking
this because of the possibility of spending a few weeks in
Washington in the second half of October or in November.

With kind regards,

Sincerely,

Leo Szilard



Department of HEALTH, EDUCATION, AND WELFARE • Public Health Service

National Institutes of Health • Bethesda 14, Md.

See file

NATIONAL INSTITUTE OF ARTHRITIS AND METABOLIC DISEASES
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THE CLINICAL CENTER
DIVISION OF RESEARCH GRANTS

September 10, 1957

In reply refer
to: SF-180

Dr. Leo Szilard
University of Chicago
Chicago 37, Illinois

Dear Doctor Szilard:

In applying for a Senior Research Fellowship of the Public Health Service, Dr. L.S.Lerman has given your name as a reference. This program, which provides five years of support, has as its purpose the fostering of additional research in the preclinical sciences and the strengthening of the preclinical departments.

The Selection Committee for Senior Research Fellowships will need your opinion of this applicant's ability to get along with his co-workers, his character, personality, and general scholastic attainments, and his specific aptitude and motivation for scientific research in a preclinical science. The Committee will appreciate receiving from you information as to the applicant's potential as a teacher as well as a research investigator and administrator. Will you also be good enough to evaluate for us his scientific interests, and any of his publications with which you are familiar?

This information, as well as any other relevant data you may have, will be of assistance in selecting the limited number of applicants who can receive this highly competitive award. We assure you that your reply will be held in confidence.

Sincerely yours,

Ronald E. Scantlebury

Ronald E. Scantlebury, Ph.D.
Chief, Research Fellowships Branch
Division of Research Grants

Enclosure
(1 envelope)

Gen. file

September 18, 1957

Dr. Ronald E. Scantlebury
Chief, Research Fellowships Branch
Division of Research Grants
Department of Health, Education, and Welfare
National Institutes of Health
Bethesda 14, Maryland

Reference: SF-180
Your letter Sept. 10, 1957

Dear Dr. Scantlebury:

I am writing to you with reference to your inquiry of September 10th, relating to Dr. L. S. Lerman's application for a Senior Research Fellowship of the Public Health Service.

Dr. Lerman is interested in important problems of molecular biology and has shown exceptional ability to formulate questions to which the answers can be obtained by experiments that may be expected to lead to important results. He is thoroughly trained in physics, chemistry, and biology, and his training makes him ideally fit for a career with the main emphasis in research on molecular biology. His published papers give evidence of his ability to perceive significant problems and to attack them in an imaginative way. He is particularly distinguished in his work by his great ability to evaluate his own experiments as well as the experiments of others.

He is a man of both personal and scientific integrity, very cooperative and generally liked. Given an opportunity to establish himself at a medical school, he will make a very valuable member of the faculty, both in regard to the development of research and the stimulation and guidance which he can give to the students.

I regard it as almost certain that such a fellowship would enable Dr. Lerman to obtain a tenure position in one of the leading medical schools and thus would enable him to pursue his research and teaching activities to the best advantage.

I am basing the above statements not only the published work of Dr. Lerman and my personal contact with him at the Medical School of the University of Colorado, but also on my observations of his perfor-

mance at the Institute of Radiobiology and Biophysics of the University of Chicago, where Dr. Lerman spent the first years of his post-doctoral career.

If there is any further information that I may be able to give you about Dr. Lerman's fitness for the fellowship for which he has applied, please do not hesitate to let me know.

Very sincerely yours,

Leo Szilard

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cc: Dr. Theodore T. Puck

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Dr. Seibold

Am. Helms

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JAN. 1957

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SUNDAY



DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

PUBLIC HEALTH SERVICE

BETHESDA 14, MD.

NATIONAL INSTITUTES OF HEALTH

August 19, 1958

Dr. Leo Szilard
Professor of Biophysics
University of Chicago
5640 Ellis Avenue
Chicago 37, Illinois

Dear Dr. Szilard:

We are forwarding to you the enclosed set of research grant applications for your possible use in making application for a grant to support a planning conference concerning research needs in some of the basic biological areas. Please give special attention to the permissible expenditures and allowances governing such conferences; these are included as a special mimeographed sheet.

We recognize that the amount of instructional material may seem to be rather extensive, but you will realize, I am sure, that this packet is made up on a multi-use basis in order to satisfy the thousands of requests for this material that we receive every year.

I will be only too glad to review any proposal you might like to submit before you actually formally submit it on the forms provided. Your proposal can be sent me informally as a letter in which it is structured in accordance with your general plan. If you do this, direct the letter to me personally.

In the meantime, I trust you had a very rewarding experience at the Boulder Conference and I hope to see you again soon. You may recall that we met in 1949 or 1950 during the time that the Public Health Service Research Fellowship program was providing rather extensive support at the predoctoral level to graduate students who were endeavoring to get their "double major" Ph. D. degree through the Committee on Biophysics of the University of Chicago.

Sincerely yours,

Frederick L. Stone

Frederick L. Stone, Ph. D.
Assistant Chief

Division of General Medical Sciences

Encl.

1951

2496
BUREAU OF BACTERIOLOGY
WASHINGTON, D. C.

Handwritten:
L. M. Muehring
at Albany, N.Y.
Paris
Oct 19-26

Dear Sirs:
I am writing to you regarding the matter of the
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I am writing to you regarding the matter of the
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I am writing to you regarding the matter of the
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I am writing to you regarding the matter of the
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Very truly yours,

Director
Bureau of Bacteriology
Washington, D. C.

August 18, 1951





DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

PUBLIC HEALTH SERVICE

BETHESDA 14, MD.

NATIONAL INSTITUTES OF HEALTH

October 8, 1958

Dear Dr. Szilard:

I am sorry that we did not have an opportunity to discuss the possibility of your joining the NIH staff before the current misunderstanding arose.

Let me say first that all of us are gratified by your interest and would be happy to have you locate here; however, the terms of our offer cannot be as they were first presented to you, and I feel it important that they be clarified.

Since we are an Agency of the Federal Government, it is not possible for us to arrange for our scientists to spend part of their time here at Bethesda and part at another research institution. Government employment is predicated on the assumption of full-time duties and responsibilities for which there is adequate compensation. Thus, we could not agree to a plan for you to divide your time between the Rockefeller Institute and the NIH, however advantageous that might be for both institutions and for you personally.

Although the facilities available to us in Bethesda increased substantially after World War II, there have been no new laboratories constructed since 1952, and the shortage of research and office space has become very acute. If you should accept our offer, we could make available to you at the outset only a single laboratory, with the possibility of another unit in a year or so, and with a corresponding limitation on the immediate staff of technicians or junior scientists at your disposal. While this space deficit would not affect your immediate contributions as consultant and advisor to the NIH scientific staff in your field of special competence, you may feel it would limit your ultimate contributions because it might not permit you to initiate and develop a sound series of research projects of your own.

In terms of salary levels, we have only recently acquired authorization to establish a limited number of senior positions paying up to \$19,000, as contrasted with the \$16,000 which was heretofore our ceiling. These so-called supergrade or 208(g) positions are used for the most part either to recognize outstanding research

competence, to attract a specialized and scarce professional skill into our environment, or to compensate those who have singularly responsible positions in research administration. Clearly your unique talents and your unusual ability to contribute to research at NIH justify your inclusion in the 208(g) series. But, in the absence of responsibility for a major area of research program administration, and with opportunities for your own research limited by space, we could not, within the policies governing use of these positions, offer you the very top of the 208(g) pay scale.

There are of course many factors to be considered, including some which have even more direct bearing on the NIH environment and the opportunity it could provide for you to contribute to scientific knowledge during the coming years. The sum of these factors is that we can offer you a 208(g) position in the basic laboratories of the Neurology and Mental Health Institutes, at a salary level of \$17,000, and subject to the space and supporting staff limitations indicated earlier.

Either Dr. Smadel or I will be glad to discuss this offer with you further if you should wish. We are holding a 208(g) vacancy for you until November 1, hoping to have a definitive answer from you by then.

It could be, alternatively, that you would wish to consider some less permanent arrangement with us, such as Visiting Scientist or Consultant. Although we would welcome you as a productive investigator in your own right, we would place equal or perhaps even greater importance on the contributions you would make to others in research here by bringing your scientific knowledge and your point of view to bear on biological investigations here across the board. We would feel you could contribute in this latter sense almost as well whether yours was a permanent or a part-time relationship.

I am very sorry that there have been misunderstandings in this negotiation. I hope this note will clarify our position and that we can move forward from this point to a speedy and satisfactory resolution.

Let me reiterate our recognition of your significant contributions to science as a whole and your unique accomplishments in your specialized field. All of us hope that you will find it possible to bring these attributes into our environment.

Sincerely yours,

A handwritten signature in dark ink, appearing to read "James A. Shannon". The signature is fluid and cursive, with a long horizontal stroke at the end.

James A. Shannon, M. D.
Director

Dr. Leo Szilard
Dupont Plaza Hotel
Dupont Circle
Washington, D. C.



DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

PUBLIC HEALTH SERVICE

BETHESDA 14, MD.

NATIONAL INSTITUTES OF HEALTH

October 22, 1958

Dr. Ieo Szilard
National Institutes of Health
Bethesda 14, Maryland

Dear Dr. Szilard:

As I recall our conversation of last week concerning the Civil Service Retirement System you asked the following two specific questions:

1. Is it necessary that service be continuous? The answer to this question is, No, however, periods of inactive or non-pay status in excess of 6 months per calendar year are not creditable for retirement purposes.
2. Assuming you now accept employment at the NIH and work for a period of time (say two years), then resigned, and assuming you were re-employed at NIH after an interval of a few years (say at age 65), you could then work past age 70 (in this case age 78) until you would have completed a total of 15 years of service (13 years between 65 and 78 and 2 previously). The number of days actually on duty as a consultant is also counted toward the 15 years of service. In any event, it would be necessary for you to be re-employed prior to the age of 70 in order to participate in the Civil Service Retirement System.

Attached is a pamphlet of questions and answers on the Federal Retirement System which may be helpful to you. If I can be of further assistance please call.

Sincerely yours,

Gordon Klovdahl

Enclosure (1)

hmv

October 24, 1958

Dr. James A. Shannon
Director
National Institutes of Health
Bethesda 14, Maryland

Dear Dr. Shannon:

I am writing in order to acknowledge your letter of October 8 in which you extended to me a formal offer for a senior staff position. I am grateful for your offering me an opportunity to discuss the points raised by your letter with you or Dr. Smadel. Should you or Dr. Smadel wish to see me, I shall hold myself available at your convenience and Dr. Livingston's office will know how to reach me. I might have to go, however, to New York for a few days next week and also the week thereafter.

I would very much want to discuss with you or Dr. Smadel, at some time, points raised by your letter, but I should be just as happy to defer the discussion until later, because I believe that our discussion might be more productive at a later time. Previously, at the time when I had accepted the offer extended to me by the National Institutes of Health through Dr. Livingston, I had a clear picture of how I might solve the problem of laboratory space and the problem of finding capable collaborators. When I received your letter, I was in the grips of a working spell and right now I find it rather difficult to divert my attention from my work and think through clearly the full implications of some of the points raised by you. X

In your letter you have set a deadline for November 1st for the staff position which you are offering me, and in order to meet that deadline, I am now writing to say that I am accepting that position. Accordingly, I have also amended my application which I filed with Dr. Livingston's office in July so as to bring it into line with the lower salary that you have set in your letter.

While my acceptance of your offer is not qualified in any way, I know that you would probably want to have some response from me to points which you have raised and, therefore, I should like to say a few things on this occasion. I shall send a more detailed statement to Dr. Livingston in which I shall try to cover all the circumstances which have a bearing on my attitude towards the National Institutes of Health in general, and in particular with reference to the situation in which I find myself at the present time.

Because you seem to think that a relationship as a consultant to the National Institutes of Health might perhaps be more satisfactory, I have given some thought to this possibility. From a personal point of view, this might be a workable solution, provided that I were attached to the Rockefeller Institute in New York. No staff appointment could be offered me there, however, prior to the meeting of their Board of Trustees in the third week of January. I have seen Dr. Bronk since the receipt of your letter and he told me if I were on the staff of the Rockefeller Institute, there would be no objection on his part to my serving

as a consultant to the National Institutes of Health.

Concerning the question of what I might be able to accomplish if I were to enter into a firm relationship as consultant with the National Institutes of Health, there has recently emerged a rather exciting possibility in connection with the work which I am doing at present. Attached to this letter you will find a memorandum on what I have in mind in this respect. As you will see, it is as yet too early to try to appraise objectively the merits of the particular approach outlined in my memorandum and it is difficult to say how much time will elapse until such an appraisal can be made. This uncertainty is one of the reasons which induce me to accept your offer for a staff position now, rather than to ask for an extension of the November 1st deadline you have set. Nevertheless, I should appreciate learning about your general reaction to the "project" outlined in the memorandum which envisages the possibility of my serving as a consultant to the National Institutes of Health rather than as a member of the staff.

Concerning the issue of laboratory space, upon which you touch in your letter, Dr. Livingston had told me in June that I could not count on any substantial laboratory space for about five years. He thought, however, that there was a reasonable hope that within about a five-year period some new construction might be authorized.

Concerning the salary of \$17,000 which you have specified, I wish to say that I regard a salary of \$17,000 per year as a high salary -- as academic salaries for biologists go. When

Dr. Bronk discussed with me in June the possibility of a position at the Rockefeller Institute, he talked in terms of a salary of \$16,000 per year and I told Dr. Bronk at that time that I regarded this salary as satisfactory. There is no reason why I should expect actually to draw more from the National Institutes of Health. There is, however, a major difference in this respect between my working for the National Institutes of Health and for an institution like the Rockefeller Institute. This difference came to my attention when I visited the National Institutes of Health in June and July.

It was brought home to me forcefully -- at that time -- that scientists on the staff of the National Institutes of Health, who are capable of being creative, may do a disservice to the Institutes if they keep their noses too much to the grindstone, spending all of their working time in Bethesda and doing nothing but what may be regarded as their "job" -- in the narrow sense of the term. On the other hand, were such men to ask, again and again, for "permission" to pursue -- in or out of Bethesda -- interests which are not manifestly an integral part of their work at the Institutes, they would obviously soon be looked upon as a "nuisance". Clearly, it would be far better for all concerned if such men were to go on leave of absence without pay, whenever there is any question on whether their projected activity falls within the scope of their work at the Institutes.

I was so impressed with the importance of this point that I raised it with Dr. Livingston before I had any thought that I myself might hold a position at the National Institutes

of Health. It seemed to me, at that time, that the solution to this problem may well lie in setting the salary of the clearly creative scientists so high that they may be able to go on leave of absence without pay, and in encouraging them to do so whenever desirable, for periods totalling two months, or so, per year.

Accordingly, when I received the first offer from the National Institutes of Health which specified a salary of \$19,000 per year, the high salary meant to me above all that I could count on being on leave without salary for two months each year. Thus I could pursue interests that may not be manifestly connected with my work at the National Institutes of Health, without discussing on each occasion the merits of the case at issue. This would then mean that I would actually receive not quite \$16,000 per year and this is slightly less than I would receive at the Rockefeller Institute where I could pursue all of my interests while still drawing my salary.

Let me then say on this occasion, for future reference, that I am prepared to enter into a formal commitment actually not to draw, on the average, more than \$16,000 per year -- in case I should receive an appointment at the National Institutes of Health providing for a salary of \$19,000 per year, at a future date.

A discussion of this question, as well as of the more difficult question of my possible cooperation with other laboratories, may well be deferred until such time as I may have an interview with you or Dr. Smadel. Since all of us are interested

in the same thing, i.e. how to make the National Institutes of Health scientifically more productive, I believe there is reasonable hope that we shall be able to work out a "modus vivendi."

By saying this, I do not want to imply that men who are agreed on aims can with certainty be counted upon also to agree on the means. And, because this is manifestly not so, it is conceivable that you or Dr. Smadel might, for reasons of administrative expediency, find some of the ways in which I may propose to operate unacceptable. If this should happen and if, perchance, I should in the meantime be offered elsewhere working arrangements which would permit me to perform at, or near, to my maximal capacity, then, I trust, you would not hold it against me if I were to resign from the National Institutes of Health.

Sincerely yours,

Leo Szilard

cc: Dr. Robert B. Livingston
Dr. Joseph A. Smadel

Shannon

MEMORANDUM

October 24, 1958

FROM: Leo Szilard
TO: James A. Shannon

In this memorandum I propose to explore whether I might be of service to the N.I.H. if I were attached to it, perhaps for the next three to six years, as a consultant and subsequently joined its staff. X

I have during the months of August and September apparently hit upon a basic idea concerning the nature of the aging process and I am in the process of completing a manuscript on this subject. Mimeographed copies of this manuscript should be available within two weeks' time.

Apparently, this paper leads to a new approach to the problem of the life shortening effect of ionizing radiation. Such an effect has been found to exist, both in a population exposed to radiation and in the offspring of that population.

As you might know, this field of research is at present rather in a mess. This is, to some extent, due to the experimental difficulties of the field, but it seems likely that something more may be involved: if one has no inkling as to what the right answers to a problem might be, then it is sometimes difficult to ask the right questions.

If my views prove to be correct, then I shall be in a position to state what experiments need to be done in order to clear up the present mess.

Whether or not my views are in fact correct, I am not in a position to say at this time. I am rather enthusiastic about the paper which I have written but it is well known - and quite natural - that while the creative process is operating it generates a considerable amount of enthusiasm - in the author. Therefore, I would not want to commit myself to any long term plan of action on the basis of the paper - at least not until my views have been subjected to the criticism of men like, for instance, H. J. Muller, Tracy Sonneborn and Joshua Lederberg.

If my own evaluation of my work remains unchanged - after the dust has settled - then I shall be inclined to explore the possibility of entering into an enduring relationship with the N.I.H. as consultant, with the following in mind:

The problem of radiation damage might in time become the most important Public Health problem in the United States. So far, most of the work on this problem has been carried out at the various establishments of the A.E.C. There is nothing wrong with this but, nevertheless, it remains true that the first concern of the A.E.C. must be the development of the applications of atomic energy and they cannot devote too much of their attention to the Public Health problems involved.

Such "philosophical" considerations are of little avail, however, unless one is able to say concretely what steps the N.I.H. could take in order to be not only active, but also productive, in this field. Up to recently - even though I was generally aware of the problem - I was not able to see what the N.I.H. ought to do and even less what I myself might want to do

to clean up the present "mess" in the field of radiation damage.

When I started to think in August of the problem of aging, I did so without any thought of the possible applications to the problems of radiation damage. But the theory of aging with which I have come up, turns out to lead to quantitative predictions concerning the effects of ionizing radiation on the life expectancy of adults who have been exposed to a given dose of ionizing radiation. Further, it leads to predictions concerning the life expectancy of the offspring of irradiated parents.

In these circumstances, it might perhaps make sense for me to become a consultant to the N.I.H., in order to operate somewhat as follows:

I could try to find capable young men who wish to work in this field. Since there are no suitable facilities at the N.I.H. at present, quite apart from the shortage of laboratory space, one would have to arrange for these men to work at establishments of the A.E.C. at laboratories in Oak Ridge, Brookhaven, Los Alamos, or Chicago. I would probably be prepared to assume the responsibility for guiding their work. Even though many of the experiments must, of necessity, be slow in producing results, some results might be forthcoming within three or four years.

It was my understanding when Dr. Livingston discussed with me the laboratory situation at the N.I.H. in June, that there is a reasonable chance that new construction might be authorized, though perhaps not earlier than in about five years' time. X
X

Let me suppose now, for the sake of argument, that I may take charge of a research program carried out by men located

at various establishments of the A.E.C. The research team carrying out this work would then be expected to move to Washington at the time when new laboratory space is available and it could form the nucleus of a laboratory which might be attached to one of the existing institutes. Naturally, if Robert Livingston is at that time Director of Basic Research of the NIMH, my preference would be that this laboratory be attached to that Institute.

The mode of operation described above would require close collaboration with some of the establishments of the A.E.C. for the next five or six years. I have some reason to believe that no insurmountable difficulties would stand in the way of my working out such an arrangement with one or several of these establishments.



DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

PUBLIC HEALTH SERVICE

BETHESDA 14, MD.

NATIONAL INSTITUTES OF HEALTH

November 4, 1958

Dear Dr. Szilard:

Thank you for your letter of October 24, 1958, in which you accept the position offered by me in my letter of October 8, 1958, the salary agreed upon being \$17,000 per annum. We will accordingly proceed to process your papers.

Since you have accepted the offer of full-time employment here, we need not go into a consideration of the proposition of your working as a consultant to the National Institutes of Health as outlined in your memorandum or as a part-time worker with an upper limit on remuneration to be expected. Either Dr. Smadel or I will be willing to discuss your research plans with you when they have matured further. You will need to work closely with Dr. Livingston in order to make the best use of the severely constricted space limitations of the Basic Research Program.

With all good wishes.

Yours sincerely,

James A. Shannon, M. D.
Director

Dr. Leo Szilard
Dupont Plaza Hotel
Dupont Circle
Washington, D. C.

Office Memorandum • UNITED STATES GOVERNMENT

TO : Dr. Leo Szilard

DATE: Oct. 1959

FROM : Marie Davies

SUBJECT: Messages

1. Mr. Garwood would like to talk with you - EX 3-3430
(call - Oct. 2)
2. Gertrude Landey - OL 4-7201 - re working at NIH.
(call - Oct. 7)
3. Dr. Karl Hausser of Heidelberg called fr. airport.
Going this week to Princeton; probably New ^ZYork on
Saturday; and next week at Brookhaven Labs.
H. K. Baer, OL-6-4000, Ext. 671 will know his where-
abouts. (call - Oct. 5)



DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

PUBLIC HEALTH SERVICE

BETHESDA 14, MD.

April 22, 1960

NATIONAL INSTITUTES OF HEALTH
O Liver 6-4000

Professor Leo Szilard
Memorial Hospital
New York 66, New York

Dear Dr. Szilard:

When Dr. Heinrich Klüver escorted us around the Chicago Campus a week ago, he showed us the plaque commemorating man's first mastery of nuclear fission. This forcefully reminded me of my intention previously to write you to congratulate you upon receiving the recent peace prize.

Most of all I want you to know that we frequently think of you and hope you will soon be sufficiently recovered to be a familiar figure again here at the NIH.

With best regards,

Sincerely yours,

Paul MacLean

Paul D. MacLean, M.D.
Chief, Section on Limbic Integration
and Behavior
National Institute of Mental Health

June 7th. 1960.

Dr. Alex Rich,
Department of Biology,
Massachusetts Institute of Technology,
Cambridge, Mass.

Dear Alex,

I understand that Howard Dintzis is working in your laboratory. Attached to this letter is a memorandum which might interest you and which you might pass on to Dintzis. I think he ought to publish something about this method and after he has done so I might write something, along the lines of the attached memorandum, for publication.

I wonder whether Dintzis might want to do the experiment outlined in my memorandum. I talked to Alen Garen about this experiment and he thought that it would fit in well with the general program at M.I.T., provided that phosphatase were picked as the enzyme. I am sending to him a copy of this letter with a request that he pass it on to Cy also. Let me know the final outcome so that I know who is going to do what.

With kindest regards,

Sincerely,

Leo Szilard.

Enclosures:

Comments.

The calculated values in the data sheets agree quite well with the experimental values. However, I would prefer the following modification of the gamma globulin template assumptions:

(The combining groups in an antigen are designated: haptenic sites; the complementary combining groups in an antibody are designated: combining sites.)

An antigen has a number of haptenic sites (in egg albumin about 16), which are of the order of 24 amino acids residues or equivalent to units of 3000 M.W. They would be distributed at random over the surface of a globular molecule. An antibody which has an elongated shape has at least 2 combining sites, one at each end. According to Porter (5) a gamma globulin molecule consists of 3 parts: a central part, identical for all gamma-globulins with M.W. ca. 50000 and 2 end parts, containing the combining sites with M.W. ca. 55000. If the combining sites are also equivalent to units of 3000 M.W. as in the antigen, then each gamma globulin may carry 20 sites per end part, and thus may act as antibody to 20 different haptenic sites.

Under these circumstances one template of 1200 nucleotides would be required for the central part of all the different gamma globulins and a template of 1400 nucleotides for each set of end parts, if for the purpose of this discussion it is assumed that the end parts of a given gamma globulin molecule are identical. 1400 Nucleotides are equivalent to a M.W. of 440,000 and this to about $3.5 \cdot 10^6$ templates per cell. If each end part carries 20 sites, a total of $7 \cdot 10^7$ antibody sites would be available from $3.5 \cdot 10^6$ templates.

However, it must also be assumed, that the haptenic sites of a given antigen are all different. Then in an antigen-antibody conglomerate, as many different antibodies as there are haptenic sites on the antigen would be involved and thus reduce the number of antigens to which specific antibodies could be available to about $5 \cdot 10^6$. Incidentally, the notion of different antibodies for a given antigen might explain both cross reactions and variations in avidity.

(5) R. R. Porter, Nature, 182, 670 (1958).

Experimental Data:

(on the average: \pm 50% error)

Rabbit weight: 2500 g

Gamma globulin concentration: 20 g/liter

Intra + extra vascular volume: 0.5 liters

Total gamma globulin per rabbit: 10 g

Turnover rate: 0.1 per day (1)

Gamma globulin produced daily: 1 g

Molecular weight of gamma globulin: 160,000

Reticulo-endothelial (lymphatic) system: 2% of body weight = 50 g.

Plasma cells: 10^{-3} cm diameter = $5 \cdot 10^{-10}$ cm³ = $5 \cdot 10^{-10}$ g.

Number of cells in reticulo-endothelial system: $\frac{50}{5 \cdot 10^{-10}} = 10^{11}$

RNA content: 0.5% = $2.5 \cdot 10^{-12}$ g/cell (2)

Protein content: 15% = $7.5 \cdot 10^{-11}$ g/cell (2)

Antibody synthesized in vitro: 5 - 25% of total cell protein. (3)

(1) A. S. McFarlane, Biochem. J., 62, 135 (1956).

(2) Spector: Handbook of Biological Data; Saunders, 1956.

(3) D. F. Steiner and H. S. Anker, Proc. Natl. Acad. Sci., U. S., 42, 580 (1956)

Derived Data:

Gamma globulin: 1300 amino acid residues

For 3 nucleotides per amino acid, nucleotides required per gamma
globulin molecule: 4000

Molecular weight of 4000 nucleotides: 1250,000

Number of units of 4000 nucleotides (templates) per cell:

$$\frac{2.5 \cdot 10^{-12} \times 6 \cdot 10^{23}}{1.25 \cdot 10^6} = 1.2 \cdot 10^6 \text{ templates/cell}$$

Time required for synthesis of a protein molecule per template: 2 minutes (4)

$$\text{Number of protein molecules per cell: } \frac{7.5 \cdot 10^{-11}}{1.5 \cdot 10^5} \cdot 6 \cdot 10^{23} = 3 \cdot 10^8$$

Time required for $1.2 \cdot 10^6$ templates to synthesize $3 \cdot 10^8$ protein molecules:

$$2 \cdot \frac{3 \cdot 10^8}{1.2 \cdot 10^6} = 500 \text{ minutes} = 8.5 \text{ hours.}$$

$$\text{Antibody produced per cell per day: } \frac{1}{10^{11}} = 10^{-11} \text{ g.}$$

$$\text{Ratio of antibody per cell to total protein per cell: } \frac{10^{-11}}{7.5 \cdot 10^{-11}} = 0.13$$

(4) T. Peters Jr., J. Biol. Chem., 229, 659 (1957)

Remarks:

I have not been able to arrive at a satisfactory theory of antibody production myself, but I believe that you might give consideration to the following assumptions:

1.) In sterily raised animals and in the absence of all antigenic stimuli, the stem cells (immature cells) of the reticuloendothelial system are few in number and divide at a slow rate. This may not be achievable in experiments due to the generation of internal antigens (B-polysaccharides in A individuals etc.).

2.) In the presence of antigenic stimuli, stem cells divide and yield, in part, maturing cells. The maturing cells divide very rapidly, differentiate in an irreversible fashion, and are eventually destroyed.

If the rate of division is of the order of twice per day, the number of cells destroyed in a day is identical with the number of cells present at any one time. A good model for cell destruction is given by Howard Green's experiments on action of complement. As the cells are destroyed their cytoplasm is released as antibody (Nucleic with little cytoplasm may persist longer).

3.) Every stem cell contains not just one or several gamma globulin templates, but all of them. I don't see how any other assumption is tenable.

4.) In the absence of antigen every template in a stem cell is replicated once per division. Their activity is inhibited by being blocked with ^a gamma globulin molecule (or end part of).

5.) After administration of antigen, the stem cells take up at random a few molecules to about small amounts, from [^] 10^7 to 10^8 each. The presence of antigen may unblock the template (as in adaptive enzyme formation) (6) and lead both to gamma globulin synthesis and to template replication (extra

replication over and above that associated with cell division). Assuming a time of 10 days for a primary response and a division time of 12 hours, 20 cell generations will have been produced in this time. If one extra replication of a single template occurs every 12 hours in addition to that at cell division, the final complement of each cell will be $1.2 \cdot 10^6$ templates, identical to those in the stem cell, plus 10^6 templates, all alike, and of the type having been the object of the extra replication. Each cell will therefore have doubled its RNA content. The quantity of antigen necessary to keep the templates unblocked through 20 generations depends on the rate of protein synthesis. Assuming a rate of 2 minutes the quantity of antigen required is much too large to fit inside a cell. The effect of the extra RNA on the matured cells is unclear to me, as is the reason, why in the last generation before destruction the templates remain unblocked and produce free antibody. A few molecules of antigen per stem cell could unblock for a short time only, resulting in a slight increase of the template undergoing extra replications. Such cells, not containing perceptible amounts of extra RNA, might be involved in the secondary response.

6.) In a normal rabbit with 10^{11} reticuloendothelial ^{cells} _^ enough antigen may be available to keep the system operating, presumably in the secondary response phase, so that 10^{11} ^{cells} _^ are generated and destroyed every day. Normal gamma globulin would be antibody to unknown antigens (7).

7.) In artificial immunization, the amount of antigen used far exceeds that available under natural conditions, such as infections. The response in immunological experiments may exceed the capacity of the reticuloendothelial system and therefore be atypical.

(6) H. J. Vogel, Proc. Natl. Acad. Sci., U.S., 43, 491 (1957).

(7) G. J. Thorbecke and F. J. Kenning, J. Infectious Diseases, 98, 157 (1956).

MASSACHUSETTS INSTITUTE OF TECHNOLOGY
DEPARTMENT OF BIOLOGY
CAMBRIDGE 39, MASSACHUSETTS

June 22, 1960

Dr. Leo Szilard
c/o Dr. Fox
Rockefeller Institute
York Avenue at 66th Street
New York 21, New York

Dear Leo:

For some time I have been meaning to visit you, but for a variety of reasons I have been unable to. However I hope to come to New York sometime in July and call on you.

I was pleased to read your memorandum on enzyme repression and have spoken with Howard Dintzis about it. His experiments, as you know, are directed more towards an understanding of the protein assembly mechanism and only incidentally is he interested in carrying out experiments on enzyme repression. He has found that it takes the order of a minute to assemble fully a hemoglobin molecule. It is quite likely that a good part of this time is used up by the mechanism for attaching the heme groups rather than the simple assembly of the polyamino acid chain. He now has a complete time sequence for all of the ^{tryptic}~~trypsin~~ digest peptides. His next step is to prove that the time sequence is identical with spatial sequence in the molecule. He may possibly have this information by the end of the summer.

I believe that a student of Cy's is trying to work on enzyme repression using the phosphatase system and the method developed by Dintzis. However, I don't believe he has made much progress so far.

Sometime ago I was attracted to the possibility of having the three-stranded polynucleotide complexes serve as a model for the formation of a single-stranded RNA in the deep groove of the double-stranded DNA molecule. However, despite a fair amount of effort on my part, I have never been able to make a model which was stereochemically satisfactory; and recently I have come to the conclusion that this is probably not the mechanism for producing the genetic form of RNA. In fact, I began to think that it was likely that the RNA is produced by forming a strand which is complementary to a single strand of DNA in a manner similar to the mechanism for producing a complementary DNA strand. Once I had this

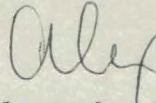
idea firmly in mind I decided to try and carry out an experiment to determine the feasibility of such a mechanism--that is, to see whether it is possible to make a two-stranded complementary helix in which one strand has a RNA backbone and the other strand a DNA backbone.

This experiment was successful, and I am enclosing a manuscript describing this work. Included in the manuscript are other aspects of the problem relating DNA to RNA. Perhaps we can discuss this more fully when I visit you in New York.

I hope things are going well. I enjoyed watching you on TV and felt the program had a useful role.

Jane sends her best wishes.

Cheers,



Alexander Rich

AR:jrv



DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

PUBLIC HEALTH SERVICE

BETHESDA 14, MD.

NATIONAL INSTITUTES OF HEALTH
O Liver 6-4000

December 16, 1960

Prof. Leo Szilard
Enrico Fermi Institute for Nuclear Studies
University of Chicago
Chicago 37, Illinois

Dear Prof. Szilard:

I recently have seen your article, "Dependence of the Sex Ratio at Birth on the Age of the Father" that appeared in the May 21, 1960 issue of Nature. I thought that you might be interested in the following references discussing the relationship between the sex ratio at birth and age of father.

There is an analysis of such data in an article, "Birth order, parental age, and sex of offspring", by E. Novitski and A. W. Kimball in the American Journal of Human Genetics 10, 268-275, 1958. The conclusion of these authors was that the sex ratio is independent of age of mother but depends on birth order and parental age.

A brief reference to this subject also appears in an article, "Age of father and survival of offspring", by J. Yerushalmy published in Human Biology 11, 342-356, 1939. Dr. Yerushalmy reported a decrease in the sex ratio with increasing age of each parent when the age of the other parent is held constant.

This result with respect to the relationship between the sex ratio at birth and age of mother is in conflict not only with the report by Novitski and Kimball but also by that reported by Robert J. Myers in an article published in the Milbank Memorial Quarterly 32, 275-281, 1954 entitled "The effect of age of mother and birth order on sex ratio at birth". Myers showed that the observed decrease in the sex ratio at birth with increasing age of mother is due to the positive association of birth order with age of mother. In other words, birth order has a definite effect upon the sex ratio at birth regardless of age of mother, whereas age of mother has almost no effect on the sex ratio at birth for a fixed birth order.

Sincerely yours,

Harold F. Dorn
Biometrics Research Branch
National Heart Institute

*Ext. 5827
Apr. 10*



DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

PUBLIC HEALTH SERVICE

BETHESDA 14, MD.

NATIONAL INSTITUTES OF HEALTH
O Liver 6-4000

May 16, 1961

Dr. Leo Szilard
Hotel Dupont Plaza
1500 New Hampshire Avenue, N.W.
Washington 6, D.C.

Dear Doctor Szilard:

Your petition reached this office after Dr. Huebner left on an extended European visit. He is in Russia at present as a member of a delegation of virologists to that country, after which he will visit other laboratories in Eastern and Western Europe.

Under the circumstances, It doesn't appear feasible to send the petition on to him. The mail we have sent to date either reached him after a prolonged period or not at all.

Dr. Huebner will return to the laboratory some time after July 1, 1961, at which time your letter will be brought to his immediate attention. If there is something else you would rather this office do to expedite the matter, please let us hear from you.

Sincerely yours,

Harriet L. Streicher, Sec'y
Robert J. Huebner, M.D., Chief
Laboratory of Infectious Diseases
National Institute of Allergy and
Infectious Diseases

DEPARTMENT OF
HEALTH, EDUCATION, AND WELFARE

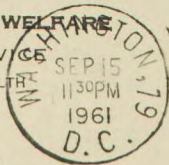
PUBLIC HEALTH SERVICE

NATIONAL INSTITUTES OF HEALTH

BETHESDA 14, MD.

OFFICIAL BUSINESS

RETURN AFTER FIVE DAYS



POSTAGE AND FEES PAID
U.S. DEPARTMENT OF H.E.W.

Prof. Leo Szilard
% W. B. Harrell
The University of Chicago
5801 S. Ellis Avenue
Chicago 37, Illinois

(To Applicant: Enter your name, institution and project title below and address card to yourself on the reverse side)

Receipt is acknowledged of an application for a research grant entitled:

"Quantitative Studies of General Biological Phenomena"

submitted by Prof. Leo Szilard

(Name of Investigator)

The University of Chicago

(Institution)

Received by Division of Research Grants

SEP 15 1961
(Date)

Encl. 6



DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

PUBLIC HEALTH SERVICE

BETHESDA 14, MD.

NATIONAL INSTITUTES OF HEALTH
O Liver 6-4000

March 2, 1962

Dr. Gertrude Weiss Szilard
Hotel Dupont Plaza
Washington 6, D. C.

Dear Dr. Szilard:

I am returning information on the urine specimen of February 28. The colony count was $>10^5$ org/ml, Proteus species (predominant organism) and Group D strep. A yeast, as yet unidentified, was also isolated. The sensitivity pattern of the Proteus organism is as follows:

Streptomycin	- Resistant
Chloramphenicol	- Sensitive
Tetracycline	- Resistant
Albamycin	- Moderately Sensitive
Gantrisin	- Resistant
Mandelamine	- Sensitive
Furadantin	- Sensitive

Sincerely yours,

Vernon Knight, M. D.
Clinical Director
National Institute of
Allergy and Infectious Diseases

file 6
Office Memorandum • UNITED STATES GOVERNMENT**TO : Dr. Leo Szilard****DATE: August 1, 1962****FROM : Marie Davies****SUBJECT: Information from Gordon Klovdahl obtained by phone call.**

Upon checking regarding your appointment as consultant to the Basic Research Program, I learned the following:

1. NINDB funds used for payment of fees and expenses of consultancy from appointment through June 30, 1962.
2. As of July 1, 1962, NIMH funds will absorb fees and expenses of consultancy.

md

P.S. You were Consultant to the Basic Research Program of both NIMH-NINDB through 6/30/62; currently Consultant to Laboratory of Neurobiology, NIMH (our Lab).

CONFIDENTIAL - PERSONNEL

HEW-397
March 1962

DEPARTMENT OF
HEALTH, EDUCATION, AND WELFARE

STATEMENT OF EMPLOYMENT AND FINANCIAL INTERESTS

PART I - TO BE COMPLETED BY THE PERSONNEL OFFICE

1. Dr. Leo Szilard
Name of Consultant
2. DHEW, PHS, NIH, NIMH
Operating Agency and Bureau or
Division by which employed
3. May be called upon to serve during the period 7/1/62 to 6/30/63.

PART II - TO BE COMPLETED BY THE CONSULTANT

By direction of the President, all Federal agencies must obtain from each consultant or adviser employed a statement of his private employment and financial interests. See the back of this form for detailed information concerning each question. Use a separate sheet of paper if necessary.

4. List all other Federal agencies to which you expect to render services during the period specified in item 3, and show the estimated number of days during this period you will work for each.

AGENCY

ESTIMATED NUMBER OF DAYS

none

5. List all the firms, institutions, etc., which are currently employing you in any capacity, and show the title or nature of your position with each, and whether you will draw a salary or other payment covering days for which you are working for the Government.

NAME OF FIRM, ETC.

TITLE OR KIND OF POSITION

SALARY (YES OR NO)

<i>University of Chicago</i>	<i>Professor of Biophysics</i>	<i>Yes</i>
<i>Salk Institute for Biological Studies</i>	<i>Non resident fellow</i>	<i>Yes</i>

6. List all the companies in which you or your spouse or minor children have any other financial interest, such as the ownership of securities, partnership, etc., having significant financial value.

none

I CERTIFY that the statements made by me on this form are true, complete, and correct to the best of my knowledge and belief, and are made in good faith.

SIGNATURE

DATE

Reviewed by General Counsel

Initials

Date

Detailed Instructions for Completing Form HEW-397

PART I - TO BE COMPLETED BY THE PERSONNEL OFFICE

1. First name, initial, and last name.
2. Enter the major unit of the Department (operating agency) and the name of the subdivision of that agency by which the consultant will be employed, e.g., "Public Health Service - National Institutes of Health," or "Food and Drug Administration - Bureau of Medicine."
3. Enter the period of the current appointment during which the consultant will be called upon to render advisory services.

PART II - TO BE COMPLETED BY THE CONSULTANT

- 4.- List all of the Federal agencies which you will serve in any advisory or consulting capacity, including other units of HEW, during the period of your current appointment with HEW which is shown in item 3. Enter an estimate of the number of days in this period on which you will actually be rendering services to each agency based on the advice received from the agency or your own best estimate.
5. List all of the companies, firms, research organizations, and educational institutions which you are currently serving as an employee, officer, member, director, consultant, etc.

Indicate in each case the title or kind of position you hold with the company, etc. Also indicate by answering yes or no in the right hand column whether you will be paid by any of these organizations for days when you are rendering service to the Government.

6. List all the companies in which you have any financial interest not covered in your answer to question 5, such as ownership of securities or other interests which have a significant financial value. You need not enter the amount of your investment or other interest, but you must list by name all of the companies in which you have such interest. "Significant financial value" means any interest of such size that change in its value could have an appreciable effect upon your personal financial situation.

Please be sure to sign and date the form.

IMPORTANT - This form should reflect your employment and other financial interests as of the date it is completed. The regulations also require that it be kept current during the period you are serving the Department as a consultant or adviser. Therefore, if during your service you should undertake any new position which would be shown under questions 4 or 5, or obtain any new financial interest which would be shown under question 6, you must file an amended statement.



DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

PUBLIC HEALTH SERVICE

WASHINGTON 25, D.C.

June 11, 1962

Refer to: OP-DCS

Dr. Leo Szilard
Dupont Plaza Hotel
Dupont Circle
Washington, D. C.

Dear Dr. Szilard:

In February of this year, the President issued a memorandum in which he established guidelines and requirements to help advisers and consultants to the Federal Government avoid potential conflicts of interest in connection with their Federal service. The intent of that memorandum is to assist the many individuals who serve in a consulting or advisory capacity to be alert to situations which might inadvertently cause embarrassment to themselves or to the Government.

A copy of the President's Memorandum is enclosed for your use. You will note that it provides for appointments of all consultants and advisers to be made for a period of time not to exceed the end of the fiscal year. For this reason, it is necessary for the Public Health Service to renew your consultancy appointment at the beginning of each fiscal year for the duration of your service with us. The first such renewal will be effective July 1, 1962.

The President's Memorandum requires that we ask you to provide us with certain general information about your private employment and financial interests. Having this information will enable us to assist you in identifying and avoiding situations in which there might be possible conflicts of interest. We are enclosing three copies of a special form which has been developed for your use in providing this information. Two copies of the form should be completed and returned in the enclosed envelope, and the third copy kept for your records. The information requested on this form will be handled confidentially and access to it will be limited to persons involved in necessary processing.

Sincerely yours,

Deputy Surgeon General

Enclosures

C

THE WHITE HOUSE

O

WASHINGTON

P

Y

MEMORANDUM TO THE HEADS OF EXECUTIVE DEPARTMENTS AND AGENCIES

Preventing Conflicts of Interest on the Part of Advisers and Consultants to the Government

Over the past twenty or more years departments and agencies of the Government have made increasing use of part-time consultants and advisers and of advisory groups. The services of highly skilled persons on a part-time and intermittent basis is in the interest of the Government and provides the Government with an indispensable source of expert advice and knowledge. Since, however, such persons have their principal employment outside the Government, and frequently with business entities which are doing business with the Government or with universities which receive Government grants, a number of conflict of interest problems arise from time to time. It is important that departments and agencies of the Government oversee the activities of such consultants in order to insure that the public interest is protected from improper conduct and that consultants will not, through ignorance or inadvertance, embarrass the Government or themselves in their activities.

Many intermittent personnel serving the Government today are individuals with specialized scientific knowledge and skills who are regularly employed in industry, research institutes or education. Their employers in many cases have contracts with or research grants from the Government. The areas in which the skills and talents of these individuals are put to use by the Government on a part-time basis may be the same as the areas with which the contracts or grants received by their employers from the Government are concerned. An individual employed by a university may act as an intermittent consultant not only for the Government but for a private firm and either his university or the firm or both may be engaged in work for or supported by the Government. A consultant to the Government may have other financial connections with firms doing business with the Government in the general area of his expertise and, therefore, his consultancy. The many possible interrelationships between a consultant's service to the Government and his own and his employer's financial interests demonstrate that conflicts problems may frequently arise.

Both the part-time adviser and the department or agency which makes use of his services must be alert to the possibility of conflicts. It is, of course, incumbent upon the consultant to familiarize himself

I have received an opinion from the Attorney General concluding that 18 U.S.C. 281 applies to all intermittent consultants and advisers on those days on which they are actually employed by the Government but that it applies only to certain consultants and advisers on the days during the period of their availability for Government service when they are not so employed. Those to whom section 281 applies on their days away from the Government service are: intermittent consultants and advisers who Government employment during the period of their availability occupies a substantial portion of that period, or affords their principal means of livelihood.

In order to clarify the application of section 281 and promote its policies, each department and agency should take steps to insure that at the time a consultant or adviser is appointed, an accurate estimate is made of the extent to which it will make use of his services. The following rules should be employed:

- (a) No appointment should extend beyond the end of the current fiscal year.
- (b) The period of appointment to be made for a part, or all, of the fiscal year, or of the remaining part of the fiscal year, should reflect the agency's best estimate of its employment of the individual.
- (c) Whether the estimate is that the consultant or adviser will be employed intermittently throughout the entire fiscal year or that part of the year which remains at the time of appointment, or throughout a shorter interval, the appointment should be made as follows:
 - (1) If the agency estimates that the consultant or adviser will be employed 40% or more of the time within the period designated, the individual should be carried on the rolls as a Government employee for the entire period and should be informed that he is administratively regarded as subject to section 281 for the entire period.
 - (2) If the agency estimates the consultant or adviser will be employed less than 40% of the period designated, the individual may be carried on the rolls as an intermittent consultant or adviser pursuant to an arrangement by which he would receive implementing appointments from time to time within the period, rather than an appointment for the entire period, and the individual should be informed that he will be treated as a Government employee for purposes of section 281 only on the day or days within the pertinent period covered by implementing appointments.

- (3) If the consultant or adviser is serving more than one department or agency, he shall inform each of his arrangements with the others so that appropriate administrative measures may be effected by the departments or agencies involved.
- (4) For consultative or advisory boards, individual appointments should be made for the entire fiscal year, or such other period as may be prescribed by law, and the appointee informed that insofar as his board membership is concerned, he will be regarded as a Government officer or employee only on the days when the board meets.

To a considerable extent the prohibitions of section 281 are aimed at the sale of influence to gain special favors for private business and at the misuse of governmental position or information. In accordance with these aims, it is desirable that even a consultant or adviser who is subject to the section only on the days he serves the Government should make every effort to avoid any personal contact with respect to negotiations for contracts or grants with the department or agency which he is advising if the subject matter is related to the subject matter of his consultancy. I recognize that this will not always be possible to achieve since there are instances where the consultant or adviser may have an executive position and responsibility with his regular employer which will require him to participate personally in contract negotiations with the department or agency he is advising. Whenever this is the case the consultant or adviser should participate in the negotiations for his employer only with the knowledge and approval of a responsible government official, who should note his approval in appropriate form. In other instances an occasional consultant or adviser may have technical knowledge which is indispensable to his regular employer in his efforts to formulate a research and development contract or a research grant and, for the same reason, it is in the governmental interest that he should take part in negotiations for his private employer. Again he should participate only with the knowledge and approval of a responsible government official, who should note his approval in appropriate form.

The aim of preventing the sale of influence and the misuse of governmental position or information that is reflected by section 281 should be furthered in yet another way with respect to a consultant or adviser who under the foregoing rules is subject to section 281 only on the days he serves the Government. He should be barred, not only on those days but at all times during the designated period of his availability for service, from activities before a Government department or agency in relation to a matter in which the

Government is interested if he is to receive compensation for such activities from a non-Governmental source in addition to or in lieu of a normal salary or fee arrangement.

It should be noted that the prohibition of section 281 against certain compensated activities "before" a department or agency may go beyond an individual's personal appearance at the department or agency. A consultant or adviser should not, at times when he is subject to the prohibition of the section, prepare or assist in preparing proposals for contracts or grants to be presented to a department or agency by or on behalf of a non-Governmental firm or organization from which he receives compensation.

18 U.S.C. 283, 18 U.S.C. 284 and 5 U.S.C. 99. Section 283 in general prohibits an officer or employee of the Government from acting as agent or attorney for prosecuting any other person's claim against the Government, or assisting in the prosecution of any such claim other than in the discharge of his official duties. This statute, which extends to both compensated and uncompensated activities, overlaps 18 U.S.C. 281 insofar as the latter section pertains to claims activities. Therefore a consultant or adviser who is not subject to section 281 at times when not actually employed by the Government may nevertheless be subject at those times to the interdiction of section 283. Even if not interdicted by that section, however, he would be subject to the two post-employment statutes, 18 U.S.C. 284 and 5 U.S.C. 99. The first of these prohibits a former Government employee, for a period of two years after his employment has closed, from prosecuting in a representative capacity any claim against the United States involving any subject matter directly connected with which he was employed. 5 U.S.C. 99 prohibits a former officer or employee of an executive department, for a period of two years after his employment with the department has ceased, from prosecuting in a representative capacity, or aiding in the prosecution of, any claim pending in any department during his employment. It is apparent that a consultant or adviser would be subject to the prohibition of 18 U.S.C. 283 or one or both of 18 U.S.C. 284 and 5 U.S.C. 99 at all times until the termination of his last period of service to the Government. In addition he would be bound by the provisions of 18 U.S.C. 284 and 5 U.S.C. 99 for two years thereafter.

18 U.S.C. 434. This section sets forth a prohibition against certain actions on the part of a Government employee in his capacity as such. More particularly, the section, which applies to all consultants and advisers at all times during their span of service, prohibits a Government employee who is interested in the profits of any business entity from acting for the Government in the transaction of business with such entity.

It is in the best interests of the Government that the policy of this section be extended to consultants and advisers beyond its literal language. Accordingly, an adviser or consultant should be disqualified from the performance of duties involving the transaction of business with, or the rendering of advice which will have a direct and predictable effect upon the interests of, a business entity by which he is employed, or to which he renders consultant service, or in which he has a financial interest. In particular, he should be excluded from participation in the evaluation of contract or grant proposals which will directly affect the interests of such business entity. However, he need not be precluded from rendering general advice in situations where no preference or advantage might be gained therefrom by any particular business entity. A non-profit organization or educational institution shall be deemed a "business entity" for the purposes of this paragraph.

18 U.S.C. 1914. Section 1914 forbids a Government employee to receive compensation "in connection with" his Government service from a source other than the Government or State, county or municipality. The statute applies to an uncompensated as well as a compensated consultant or adviser. In cases where a consultant or adviser serves occasionally and for short periods, he may continue to receive his usual compensation from an outside private employer. And the continuation of the consultant or adviser's outside private compensation during a period of as much as 30 days a year of Government service would ordinarily be permissible on the assumption that it is not paid "in connection with" his Government services but rather as part of his normal salary arrangements with his private employer. However, if the length of his service exceeds these limits, it will be necessary to determine specifically whether the continued outside compensation is related to the consultant or adviser's services to the Government, and thus, improper, or whether it is permissible because made with respect to present, past, or future services for the outside employer. Cases of this nature should be referred to the chief legal officer of the department or agency for examination and recommendation as to the proper action to be taken.

Special Exemptions

Some consultants or advisers are appointed pursuant to a statute which exempts them from one or more of the conflict-of-interest laws. Nevertheless, a consultant or adviser so appointed should not participate in any matter where that participation, except for such exemption, would be within any of the statutes unless he receives permission to participate therein from the head of the department or agency he serves. The latter shall not consent to the participation of such consultant or adviser in the matter unless he finds that such participation is, on the particular facts, consistent with the interests of the Government. Nothing in this paragraph shall be deemed to relieve any department or agency head, or appointee of such department or agency head, of the obligation

to file a statement for publication in the Federal Register pursuant to the requirements of section 710(b) of the Defense Production Act of 1950 (50 U.S.C. App. 2160(b)) or of Executive Order No. 10647 of November 28, 1955 (20 F.R. 8769).

Ethical Standards of Conduct

Aside from the conflict-of-interest laws, there are elementary rules of ethics in the conduct of the public business by which all those who serve the Government are bound. That an individual may serve the Government only occasionally and for brief periods does not relieve him from the obligation to abide by those rules. That he may be needed to bring rare or specialized talents and skills to the Government does not mean that he should be considered for a waiver. The people of the nation are entitled to ethical behavior of the highest order in the conduct of their Government's affairs from the sometime worker to no lesser degree than from the career worker.

Inside Information. The first principle of ethical behavior for the intermittent consultant or adviser is that he must refrain from any use of his public office which is motivated by, or gives the appearance of being motivated by, the desire for private gain for himself or persons with whom he has family, business or financial ties. The fact that the desired gain, if it materializes, will not take place at the expense of the Government makes his action no less improper.

An adviser or consultant must conduct himself in a manner devoid of the slightest suggestion of the extraction of private advantage from his Government employment. Thus, a consultant or adviser must not, on the basis of any inside information, enter into speculation, or recommend speculation to members of his family or business associates, in the securities of any private company engaged in work for the Government in the field of his Government duties. He must obey this injunction even though those duties have no connection whatever with the financial and other arrangements between the Company and the Government. And he should be careful in his personal financial activities to avoid any appearance of acting on the basis of information obtained in the course of those duties.

It is important for consultants and advisers to have access to Government data pertinent to their duties and to maintain familiarity with the Government's plans and programs and the requirements thereof, within the area of their competence. Since it is frequently in the Government's interest that information of this nature be made generally available to an affected industry, there is generally no impropriety in a consultant or adviser's utilizing

such information in the course of his non-Government employment. However, a consultant or adviser may, in addition, acquire information which is not generally available to those outside the Government. In that event, he may not use such information for the special benefit of a business or other entity by which he is employed or retained or in which he has a financial interest.

In order to avoid any actual or potential abuse of information by a consultant or adviser, departments and agencies should, through information programs, make every effort to insure to the maximum extent possible that all firms within an industry have access to the same information that is available to a consultant or adviser who is employed by any of them. In addition, regular Government employees should avoid divulging confidential information to him unnecessary to the performance of his governmental responsibility, or information which directly involves the financial interests of his employer. Consultants and advisers should be instructed that information not generally available to private industry must remain confidential in their hands, and must not be divulged to their private employers or clients. In cases of doubt they should be encouraged to confer with the chief legal officer or other designated agency official who can assist in the identification of information not generally available and in the resolution of any actual or potential conflict between duties to the Government and to private employers.

Occasionally an individual who becomes a Government consultant or adviser is, subsequent to his designation as such, requested by a private enterprise to act in a similar capacity. In some cases the request may give the appearance of being motivated by the desire of the private employer to secure inside information. Where the consultant or adviser has reason to believe that the request for his services is so motivated, he should make a choice between acceptance of the tendered private employment and continuation of his Government consultancy. In such circumstances he may not engage in both. Furthermore, he should discuss any such offer of private employment with the chief legal officer of his Government agency whether or not he accepts it.

At times a private enterprise or other organization urges the appointment of one of its employees or members to a particular Government consultancy. The departments and agencies should discourage this practice. Any initiative in connection with the appointment of consultants, or in securing the names of qualified persons, should come from the Government.

Abuse of Office. An adviser or consultant shall not use his position in any way to coerce, or give the appearance of coercing, another person to provide any financial benefit to him or persons with whom he has family, business or financial ties.

Gifts. An adviser or consultant shall not receive or solicit anything of value as a gift, gratuity or favor for himself or persons with whom he has family, business or financial ties if he has reason to believe that it would not be made but for his position with the Government, or if the acceptance thereof would result in, or give the appearance of resulting in, his loss of complete independence or impartiality in serving the Government.

Industry, Labor or Agricultural Representatives

It is occasionally necessary to distinguish consultants and advisers from persons speaking for a firm or an industry, or for labor or agriculture, or in some other representative capacity. A consultant or adviser is a person whose advice is obtained by a department or agency because of his particular qualifications and who serves as an employee in an individual and independent capacity. A representative of a firm or industry or organization who is invited to appear before a Government department or agency presents his views in a representative capacity and is not an employee. The representative is not, therefore, within the scope of the conflict-of-interest laws. Departments and agencies should be careful to make and clarify the distinction noted here and should not compensate an industry or similar representative for his advice, though they may pay travel expenses and per diem allowances where appropriate.

Administrative Steps

All departments and agencies of the Government shall:

(1) bring this memorandum to the attention of all consultants and advisers employed by them and of all regular employees dealing with such consultants and advisers;

(2) review their existing rules and regulations and where appropriate, revise them or issue new rules and regulations to promote the policies set forth in this memorandum; and

(3) take such other measures as may be appropriate to impress upon consultants and advisers and upon Government officials with whom they consult that they have a responsibility to avoid situations in which a potential conflict-of-interest may exist. These individuals should also be cautioned to avoid situations in which the consultant or adviser might be thought to be influencing Government action in matters with regard to which he has a financial or other personal interest, or to be using inside information for private gain.

While it would be most advisable for a department or agency of

the Government, in order to minimize the occurrence of conflicts of interest, to avoid appointing individuals to advisory positions who are employed or consulted by contractors or others having a substantial amount of business with that department or agency, I recognize that the Government has, of necessity, become increasingly concerned with highly technical areas of specialization, and that the number of individuals expert in those areas is frequently very small. Therefore, in many instances, it will not be possible for a department or agency to obtain the services of a competent adviser or consultant who is not in fact employed or consulted by such contractors. In addition, an advisory group may of necessity be composed largely or wholly of persons of a common class or group whose employers may benefit from the advice given. An example would be a group of university scientists advising on research grants to universities. Only in such a group can the necessary expertise be found. In all these circumstances, particular care should be exercised to exclude his employer's or clients' contracts or other transactions with the Government from the range of the consultant's or adviser's duties.

Disclosure of Financial Interests

In order to carry out its responsibility to avoid the use of the services of consultants or advisers in situations in which violation of the conflict-of-interest laws or of these regulations may occur, each department or agency of the Government shall, at the time of employment of a consultant or adviser, require him to supply it with a statement of his private employment and financial interests. The statement should indicate the names of all the companies, firms, research organizations and educational institutions which he is serving as employee, officer, member, director, or consultant, and the companies in which he has any other financial interest, such as the ownership of securities or other interests which have a significant financial value. He need not reveal precise amounts of investments. Each statement of financial interests should be forwarded to the chief legal officer of the department or agency concerned, for information and for advice as to possible conflict of interest. In addition, each statement should be reviewed by those persons responsible for the employment of consultants and advisers to assist them in applying the criteria for disqualification discussed in this memorandum as set forth above. Such statements should be kept current during the period the consultant is on the Government rolls.

Legal Interpretation

Whenever the chief legal officer of a department or agency believes that a substantial legal question is raised by the employment of a particular consultant or adviser he should advise the

the Department of Justice, through the Office of Legal Counsel, in order to insure a consistent and authoritative interpretation of the law.

This memorandum shall be published in the Federal Register.

/S/ John F. Kennedy

THE WHITE HOUSE

February 9, 1962

Appendix

18 U.S.C. 281

Whoever, being a Member of or Delegate to Congress, or a Resident Commissioner, either before or after he has qualified, or the head of a department, or other officer or employee of the United States or any department or agency thereof, directly or indirectly receives or agrees to receive, any compensation for any services rendered or to be rendered, either by himself or another, in relation to any proceeding, contract, claim, controversy, charge, accusation, arrest, or other matter in which the United States is a party or directly or indirectly interested, before any department, agency, court martial, officer, or any civil, military, or naval commission, shall be fined not more than \$10,000 or imprisoned not more than two years, or both; and shall be incapable of holding any office of honor, trust, or profit under the United States.

Retired officers of the armed forces of the United States, while not on active duty, shall not by reason of their status as such be subject to the provisions of this section. Nothing herein shall be construed to allow any retired officer to represent any person in the sale of anything to the Government through the department in whose service he holds a retired status.

This section shall not apply to any person because of his membership in the National Guard of the District of Columbia nor to any person specially excepted by Act of Congress.

18 U.S.C. 283

Whoever, being an officer or employee of the United States or any department or agency thereof, or of the Senate or House of Representatives, acts as an agent or attorney for prosecuting any claim against the United States, or aids or assists in the prosecution or support of any such claim otherwise than in the proper discharge of his official duties, or receives any gratuity, or any share of or interest in any such claim in consideration of assistance in the prosecution of such claim, shall be fined not more than \$10,000 or imprisoned not more than one year, or both.

Retired officers of the armed forces of the United States, while not on active duty, shall not by reason of their status as such be subject to the provisions of this section. Nothing herein shall be construed to allow any such retired officer within two years next after his retirement to act as agent or attorney for prosecuting or assisting in the prosecution of any claim against the United States involving the department in whose service he holds

a retired status, or to allow any such retired officer to act as agent or attorney for prosecuting or assisting in the prosecution of any claim against the United States involving any subject matter with which he was directly connected while he was in an active-duty status.

This section shall not apply to any person because of his membership in the National Guard of the District of Columbia nor to any person specially excepted by enactment of Congress.

18 U.S.C. 434

Whoever, being an officer, agent or member of, or directly or indirectly interested in the pecuniary profits or contracts of any corporation, joint-stock company, or association, or of any firm or partnership, or other business entity, is employed or acts as an officer or agent of the United States for the transaction of business with such business entity, shall be fined not more than \$2,000 or imprisoned not more than two years, or both.

18 U.S.C. 1914

Whoever, being a Government official or employee, receives any salary in connection with his services as such an official or employee from any source other than the Government of the United States, except as may be contributed out of the treasury of any State, county, or municipality; or

Whoever, whether a person, association, or corporation, makes any contribution to, or in any way supplements the salary of, any Government official or employee for the services performed by him for the Government of the United States --

Shall be fined not more than \$1,000 or imprisoned not more than six months, or both.

18 U.S.C. 284

Whoever, having been employed in any agency of the United States, including commissioned officers assigned to duty in such agency, within two years after the time when such employment or service has ceased, prosecutes or acts as counsel, attorney or agent for prosecuting, any claims against the United States involving any subject matter directly connected with which such person was so employed or performed duty, shall be fined not more than \$10,000 or imprisoned not more than one year, or both.

5 U.S.C. 99

It shall not be lawful for any person appointed as an officer, clerk, or employee in any of the departments, to act as counsel, attorney, or agent for prosecuting any claim against the United States which was pending in either of said departments while he was such officer, clerk, or employee, nor in any manner, nor by any means, to aid in the prosecution of any such claim, within two years next after he shall have ceased to be such officer, clerk, or employee.

file this copy

June 6, 1963

Dr. Carl Brewer
The National Institutes of Health
Bethesda 14, Maryland

Dear Dr. Brewer:

I am working at the University of Chicago under a research grant from NIH and I understand that if any of the expenses of a trip abroad are to be charged to my research grant I have to apply for approval prior to going on the trip.

I have an invitation to visit several laboratories in Europe and to attend meetings in Geneva and Marseilles. Photo-copies of these invitations are enclosed. As you see, my travel expenses between Washington and Geneva will be reimbursed either by WHO or CERN.

The issue I wish to raise here is whether I may charge to my grant such additional expenses as may arise up to \$1,000.

In explanation of this query, I may say the following:

When I visited Geneva last October, I suggested to a number of colleagues in Europe that they might set up a European Laboratory for molecular biology in close cooperation with CERN. This suggestion met with favorable response and John Kendrew (Nobel Prize, 1962) expressed his willingness to head up such a laboratory. Since my return to Washington last year a meeting was held at CERN by a number of my colleagues to discuss this matter further and the second such meeting is now scheduled to take place on June 28th. This is the meeting to which the letter of Professor Weisskopf, Director General of CERN, refers.

While I am in Europe, I would like to visit a number of laboratories where work on immuno-biology is in process or where such work could be initiated. These laboratories include the International Laboratory of Genetics and Biophysics in Naples, Dr. Pernis' laboratory in Milan, Monod's laboratory at the Institute Pasteur in Paris, the Mill Hill's laboratory of the Medical Research Council in London, headed by Dr. Medawar and Francis Crick's laboratory in Cambridge. I also would like to go to Hanover, if necessary, in order to discuss with the president of the Volkswagenstiftung the possibility of their collaboration in setting up and maintaining

Dr. Carl Brewer
Page two
June 6, 1963

laboratories working in the field of molecular biology.

I do not expect to have time to visit all these places, but I would like to visit as many of them as time permits.

Sincerely yours,

Leo Szilard

cc: The University of Chicago



DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

PUBLIC HEALTH SERVICE

BETHESDA 14, MD.

NATIONAL INSTITUTES OF HEALTH
Tel: 656-4000

June 18, 1963

GM 06876-04

Dr. Leo Szilard
Hotel Dupont Plaza
Dupont Circle and New
Hampshire Avenue, N.W.
Washington 6, D.C.

Dear Dr. Szilard:

Your letter of June 6, 1963, requesting permission to use up to \$1,000 from funds presently available under research grant GM 06876-04 for additional travel expenses to visit a number of foreign laboratories, has been carefully considered.

In reviewing our files, we find that \$7,500 has been approved for "travel to major research centers in the United States and Institute Pasteur" under the above grant. In view of this, no further prior Public Health Service approval is required insofar as such foreign travel is performed within the boundary limits of France, where the Institute Pasteur is located. The Public Health Service approved this travel on the premise that it meets the criteria under Part V 541D 3.

In view of the above limitation, and in the light of current United States Public Health Service policy relating to foreign travel, we must have an endorsement to your letter signed by the dean of your school, or similar operating official, for the travel to the other foreign laboratories mentioned in your request. The endorsement should indicate that such travel is to the interest of and within the operating policies of the University of Chicago and considered essential to the progress of the research being supported. Consideration will be given to your request upon receipt of the endorsement.

I trust that the information requested will cause no inconvenience, and hope you will understand our position in this matter.

Sincerely,

Carl R. Brewer, Ph.D.
Chief, Research Grants Branch
National Institute of General
Medical Sciences

cc:

Dr. Harrell
Mr. Cotton

June 21, 1963

Dr. Carl R. Brewer, Chief
Research Grants Branch
National Institute of General
Medical Sciences
Public Health Service
Bethesda 14, Maryland

RE: GM 06876-04

Dear Dr. Brewer:

Many thanks for your very kind letter of June 18th.
Because I am not certain how much time I will have to visit
the laboratories in Italy and England, I decided against
asking for an authorization to spend NIH funds in these two
countries and if necessary I shall just cover the additional
travel expenses out of my own pocket.

Sincerely,

Leo Szilard

cc: Mr. J. R. Johnson, Grants Administrator
The University of Chicago

file

Dr. Frederick Stone
The National Institutes of Health
Bethesda 14, Maryland
United States of America.

Geneva, 16th August, 1963

Dear Dr. Stone,

Sorry to bother you with this matter, but I do not have my files here with me in Geneva, and I do not know the proper office of the N.I.H. to write to.

I need to file an application for the renewal of my research grant at the University of Chicago and the deadline for filing this application is September 30th. I have left instructions with the University to send me the application forms airmail to Geneva, as soon as they are received by my secretary, but something went wrong somewhere. Since September is vacation time at the University and since after filling in these forms, I must mail them to the University for transmittal, time is getting very short.

For this reason I should be very grateful to you to have sent a duplicate of these forms, as an airmail letter, to me at the following address:

c/o Dr. Martin Kaplan
World Health Organization
Palais des Nations
Geneva, Switzerland.

Also, would you please have your office acknowledge the receipt of this letter to me at the above address.

Sorry to bother you with this.

With best wishes,

Yours sincerely,

Leo Szilard



file C.N.S.,
DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

PUBLIC HEALTH SERVICE

BETHESDA, MD. 20014

NATIONAL INSTITUTES OF HEALTH
Area Code 301 Tel: 656-4000

May 15, 1964

Dr. Leo Szilard
The Salk Institute for Biological
Studies
Post Office Box 9499
San Diego, California

Dear Dr. Szilard:

Dr. Livingston requested that I forward you the following addresses:

Dr. Jose P. Segundo
Department of Anatomy
School of Medicine
University of California
Los Angeles, California 90024

Professor Jerzy Konorski
Head, Department of Physiology
Nencki Institute of Experimental Biology
Pasteura 3
Warsaw 22, Poland

I have requested catalogues or listings of current Russian biomedical journals (English translations) from Pergamon Press and Consultants Bureau. When these are received, I will pass them along to you.

It is my understanding that the National Library of Medicine discontinued support for the cover-to-cover translation of the following: Sechenov Physiological Journal of the USSR; Pavlov Journal of Higher Nervous Activity; Biophysics; Problems of Oncology; Journal of Microbiology, Epidemiology, and Immunobiology; Problems of Hematology and Blood Transfusion; Problems of Virology; Biochemistry; and Bulletin of Experimental Biology and Medicine. This action was taken during the period December 1960 - December 1963. However, Pergamon and Consultants Bureau have continued publishing some of the journals.

With best wishes to you and Mrs. Szilard,

Sincerely,

Marie N. Davies