### INDIANA UNIVERSITY

BLOOMINGTON, INDIANA

Science 101
DEPARTMENT OF ZOOLOGY

May 10, 1949

Dr. Leo Szilard Institute of Radiobiology and Biophysics 6200 Drexel Avenue Chicago, Illinois

Dear Szilard:

This is to let you know that I finally decided not to come to Chicago. It was a very hard decision to make. However, you probably understand what the chief motivating factors were. I indicated some of my doubts during the conversation we had while you were in Bloomington. Financially, the two possibilities worked out about the same over the long run, but a more definite security could be offered here for a longer time, as Indiana University offered to extend my tenure until 73, and to underwrite my research, at as high a level as the University of Chicago did, until that age. I thought it best in view of all this to remain where I knew the situation more definitely rather than to risk insecurity and to face various unknown factors that were hard to estimate without prolonged trial. If I had been only a few years younger I should have probably decided the other way.

At the same time, I feel it a great loss to have missed. this opportunity to be more closely associated with you, and also with several of the others at your institute, notably Dr. Franck and Dr. Boche. I hope you will not be disgusted with me for having turned down this wonderful chance, and that I may continue at least to sit in on the conferences of the joint genetics group.

My wife joins me in sending our kindest personal regards, and the hope that you will visit us when you come to Bloomington again.

Sincerely yours,

H. J. Muller

H. J. Muller

HJM/dem

1155 East 57th Street Chicago 37, Illinois May 17, 1949

Professor H. J. Muller Department of Zoology Science 101 Indiana University Bloomington, Indiana

Dear Dr. Muller:

I wish to thank you for your very kind letter of May 10th informing me of your decision not to accept the appointment offered by the University of Chicago. As you can imagine, everyone here was very sorry that you decided not to come, but I believe that everyone also appreciated the validity of your reasons. As far as I myself am concerned, I would go even farther and say that were I faced with a similar choice, I would decide as you did.

Novick and I have been keeping very busy these last two months trying to finish up experiments on the light reactivation of ultraviolet inactivated bacteria before we go away on vacation during the first week of July. We found some rather striking, simple regularities, and if we should succeed in recording them in a short rather than a long paper, we were considering publishing it in the Proceedings of the National Academy. I wonder whether it would be convenient for you to read the manuscript and let us know whether you consider it suitable for publication in the Proceedings.

With best personal wishes,

Sincerely yours,

Leo Szilard

Date

Mr. C. T. Forster, Executive Secretary Loyalty Board United States Department of Agriculture Administration Building Washington, D. C.

Dear Mr. Forster:

It has come to the attention of the Executive Committee of the Genetics Society of America that an investigation is under way to determine the loyalty of Dr. L. J. Stadler of the U. S. Department of Agriculture and the University of Missouri. They have informed the members of the society of the nature of the investigation and of the gravity of the situation thus arising. As one of the members of the Genetics Society, the undersigned wishes to make the following statement.

Dr. Stadler has been a member of the Genetics Society since its inception in 1932, and, previously to that, was a member of its parent organization, the Joint Genetics Sections of the American Society of Zoologists and the Botanical Society of America. He has held various offices in these societies, among them that of Chairman of the Genetics Sections in 1931 and of President of the Genetics Society in 1938. As one of the most distinguished scientists of this country, he has actively participated in numerous scientific conferences. For these reasons I, as a member of the Genetics Society, am well acquainted with Dr. Stadler. Moreover, I have followed Stadler's scientific publications for many years, with growing admiration. In this regard, my personal judgment agrees with that of geneticists the world over who see in Stadler one of their outstanding leaders.

Every contact with Dr. Stadler has strengthened my admiration of him both as a scientist and as a person. It is important, in reaching a judgment concerning Dr. Stadler's attitude towards matters of ideology, to give particular weight to the fact that Dr. Stadler's activities in genetics would have been condemned in the Soviet Union. The science of genetics has been severely attacked by the administrative authorities within the Soviet Union and the countries under its influence and by the proponents of the Communist Party throughout the world. Certain geneticists outside of the Soviet Union and its dependencies have openly advocated a position towards genetics which can only be explained by their adherence to the Communist Party line. In contrast, Dr. Stadler has continued in those genetic activities which the Communists denounce.

In my acquaintance with Stadler he has shown himself to be a loyal American citizen and in no case has he ever made any remarks derogatory to our democratic system of government. I have full confidence in the veracity of his answers.

Yours truly,

Indiana University June 17, 1949 from H.J. Muller Indiana University
Bloomington, Indiana

Science Hall 101

June 17, 1949

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I have had additional occasion to know Stadler because of the relation of his line of work in genetics to my own. We have done parallel work on the problem of mutations and their artificial production, he with plant and I with animal material. For this reason I have paid particular attention to his publications for over twenty years and have had frequent conversations with him. I have throughout this time been struck by the integrity of his character, his lack of bias, lack of jealousy or envy, his candidness, and his humaneness in all his dealings and judgments. I was also entertained at his home and struck by the charm of his home life and the high principles held by him and his family.

My personal judgment concerning Dr. Stadler agrees with that of geneticists the world over, who see in him one of their most outstanding leaders. He is equally highly regarded both as a scientist and as a person. It is important, in reaching a judgment concerning Dr. Stadler's attitude towards matters of ideology, to give particular weight to the fact that Dr. Stadler's activities in genetics would have been condemned in the Soviet Union. The science of genetics has been severely attacked by the administrative authorities within the Soviet Union and the countries under its influence and by the proponents of the Communist Party throughout the world. Certain geneticists outside of the Soviet Union and its dependencies have openly advocated a position towards genetics which can only be explained by their adherence to the Communist Party line. In contrast, Dr. Stadler has continued in those genetic activities which the Communists denounce.

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Yours truly, H. J. Muller

HJM:mnv

Science Hall 101 June 20, 1949

Dear Member of the Genetics Society of America:

The undersigned has been delegated by the President of the Genctics Society of America to call your attention to a situation which we believe to be dangerous to all American science, and to solicit your help. It arises out of the fact that Dr. L. J. Stadler, on applying through the Department of Agriculture, by which he is employed, for a passport to attend the International Genetics Congress at Stockholm, was refused the Department's approval for a passport and thus at the last moment prevented from going, and that since that time he has been subjected to an investigation by the Department of Agriculture's F. B. I. Loyalty Board which threatens to deprive him of his position. His lawyer, Mr. Clifford J. Durr, who has had experience in such cases, informs him that the chances of his dismissal are about even and that there is no time to be lost.

We have seen the questionnaire which was presented to Dr. Stadler, and his answers. So have about eighteen other responsible geneticists who were present at a Gene Conference on Shelter Island, N. Y., early this month, and who took the matter under advisement. Among these were three of the five members of the Executive Committee of the Genetics Society of America, namely the President, Dr. Sonneborn, Dr. Curt Stern and myself. All of these geneticists were convinced that the stated grounds for suspicion of Dr. Stadler's loyalty were purely casual circumstances such as might be found in the case of any of them themselves, and that if such grounds could lead to dismissal the whole body of scientists in government employment was threatened. One of the points brought forward as major, and that which had been alleged to be the basis for the refusal of the passport, was the presence of his name, some years ago, on the list of sponsors of a committee called "The American Committee to Save Refugees," on which the names of other entirely unimpeachable and responsible scientists also appeared; this organization was not on the "subversive list." Other major points, representative of the points raised in general, were the fact that, among persons who had on occasion met at his house during the same period (that of the military alliance between the U.S.A. and the U.S.S.R.) were perhaps two supposed Communists, and that during some months of this period, while he was subscribing to a great many lay periodicals of the most varied kinds, The Daily Worker was included among these.

We have talked to Dr. Stadler and are convinced that he is very far from being a Communist and thoroughly disbelieves in the methods of deceit, underground action, force, minority rule and suppression of intellectual freedom which they practice. We found his answers candid, comprehensive and convincing. We believe that he was only practicing his right and duty as the citizen of a free democratic country to inquire into all questions of interest or importance, to consult whatever possible sources of information he chose, and to discuss matters of general concern with whomever he saw fit. These discussions and inquiries strengthened him more than ever in the conclusion that the Communists are on the wrong track. We believe that conclusions thus arrived at are far more valuable than those accepted merely on authority. It is necessary that people's right to arrive at conclusions in this way be upheld if we are not to fall into the very same errors as those of the Communists themselves.

If Dr. Stadler can be dismissed on such charges so large a proportion of the personnel of scientists in government employ could be dismissed likewise that the whole of science under government auspices would be very grievously damaged. Moreover, few new recruits of value would enter such work. It is certain that in addition many state universities and other public institutions would take their cue from this and would be likely to follow a similar procedure on a large scale.

It must be emphasized that there is no question of security in this case as Dr. Stadler is not working on Atomic Energy or other security projects. The case is therefore much more far reaching in its implications than the Condon case. And since there is also a move to apply to those receiving government funds of any kind for research, even though not themselves in government employ, the same sort of "security procedures" as to the government employees themselves, this would be likely to affect the great majority of scientists, particularly since it seems probable that the National Science Foundation will soon be established. It is therefore up to every scientist to do what he can to prevent Stadler's dismissal, which would form a precedent for such widespread action.

It is hoped to carry the principle of the matter eventually to authorities higher than the Department of Agriculture and the F. B. I. That would however take time and money. In the meantime the case of Stadler himself confronts us. We believe, on the basis of the experience of others, that the best way to help in this individual case will be for each member of the Genetics Society who in a general way agrees with us to write a supporting letter for Stadler. The geneticists at the Shelter Island meeting unanimously agreed, after consulting with Dr. Stadler, that all members of the Genetics Society of America be invited to participate in this way. For your help and guidance in this matter a sample letter is enclosed. You may use exactly this letter if you wish or make any modification in it which you deem fitting or write entirely your own letter. Of course individualized letters would probably be more effective. The letter should be addressed to Mr. C. T. Forster, as the model one is, and should be sent in triplicate, but instead of mailing the letter to Mr. Forster it should be mailed to Dr. Stadler's lawyer, Mr. Clifford J. Durr, at the following address: 1625 K Street, N. W., Washington, D. C. Mr. Durr will collect the letters and will use them at the appropriate time. If sent directly to Mr. Forster they would be of much less help to the defense and might even be used in a way opposite to that intended by the writers of them.

In phrasing such a letter it should be remembered that negative statements are not merely of no value but may even be harmful to the case. Unless you make all statements at least as positive as those in the model letter it is best not to write any letter at all. On the other hand, some of the members may have had contacts with Stadler that allow the introduction of material not present in the general letter. Some of the members of the Executive Committee are introducing additional material of this kind, and to give an example of it I am also enclosing a copy of the letter which I myself am sending.

We believe that in your letter general arguments against the mode of procedure used, such as the arguments given in this letter, should be avoided, as should any statements that might be viewed antagonistically by the Loyalty Board. The place for such material will be in the discussion of principles raised in the case which we hope will later be presented to authorities higher than this board.

It should be emphasized, finally, that there is no time to be lost since action on the case may be taken any day now. Please remember, if you send a letter, to send it in triplicate to Mr. Durr. We hope that we will be able to give you a more favorable report on this case, at the time of the annual meeting next December.

Yours truly,

H. J. Muller

H. J. Muller

Member, Executive Committee Genetics Society of America

HJM:mnv Enc.

### INDIANA UNIVERSITY

BLOOMINGTON, INDIANA

Science Hall 101
DEPARTMENT OF ZOOLOGY

June 21, 1949

Dr. Leo Szilard The University of Chicago 1155 East 57th Street Chicago 37, Illinois

Dear Dr. Szilard:

I should be very glad to have a chance to read your short paper when it is ready. As to sending it in to the Proceedings of the National Academy, I would of course do that, but I should consider it absurd for me to try to pass upon the suitability of a paper you had written.

Enclosed are some communications that I am sending to members of the Genetics Society and in which I am sure you will be interested. I had been meaning to take this matter up with you sooner but had no time. Perhaps you would talk about it to some of those at Chicago, such as Urey, Rabinowitch et cetera who are strong for keeping politics out of science. Sonneborn (who unfortunately for the case has now left for Europe) suggested that the matter be taken directly to Truman and I think the idea is a good one. The question is through what intermediaries could such an approach be arranged. Perhaps with the experience of the Condon case some of your associates would be able to give suggestions for help. I may say that D. A. MacInnes, the man who works on electrophoresis at the Rockefeller Institute in New York, who was active in the Condon case, is also interested in this, although he has not carried out his promise to write me since I saw him at the Gene Conference on May 31. Sonneborn says that Weaver of the Rockefeller Foundation, has been interested in the case by MacInnes.

Yours sincerely,

H. J. Miller

HJM; mnv Enc.

P.S. Hollaender who has just seen Weaver writes me that Weaver is afraid the proposed letters might antagonize the Board, as they might feel they were being subjected to the action of a "pressure group." However, these tactics have been known to work elsewhere and Stadler's lawyer need use the letters only if and when he finds it advisable. I think that the important thing is to have the letters available in his hands and not wait, as Weaver would do, until an adverse decision has already been reached by the Board. Weaver does agree that an adverse decision is not unlikely and that it would be an outrage. Fosdick, who has also read the material, is more optimistic however. I would like to send you a copy of the documents in the case and will do so as soon as I can get hold of them.

BLOOMINGTON, INDIANA

Science Hall 101 DEPARTMENT OF ZOOLOGY

June 26, 1949

Dr. Leo Szilard The University of Chicago Institute of Radiobiology and Biophysics 1155 East 57th Street Chicago 37, Illinois

Dear Szilard:

Stadler called me up from Missouri last night and told me that his lawyer, Durr, thought it best for me to hold up sending out the proposed letters to the members of the Genetics Society as an avalanche (as he put it) of very similar letters might not be helpful at the present time. On the other hand, the letters already received from some of the people who were at the Shelter Island Conference will be very helpful he thinks and, in general, he is now considerably more optimistic about the situation than he was. He thinks it may still be desirable to send out the letters and I should hold them, but that it will be best to decide about this later, probably after the hearing has been held.

Perhaps you saw the remark made by President Truman in a recent speech, deprecating the witch hunts that are going on. I hope this means that he will institute a real change in policy. Unless we get good evidence that this has been done however I think that this case shows that the principle of the thing should be called to the attention of some very high authority, preferably Truman, since it threatens science and intellectual freedom in general. However, I do not wish to make a move that might jeopardize the Stadler case and, since finding out that I had been wrong in trying to push the matter as I was doing, I do not feel like taking any more initiative on my own. I do think though that the group of people you know who are interested in such matters should be informed and should consider what sort of action could and should be taken to bring the principle of the matter to the attention of higher authorities.

With regards,

Sincerely yours,

H. J. Muller

H. J. Muller

H. J. Muller

H. J. Muller

How P. S. I am evelosing copy of a letter from Paconner, received since I dictated the above.

H. J. M. J.

The University of Chicago

CHICAGO 37, ILLINOIS

Institute of Radiobiology and Biophysics

1185 East 57th Street Chicago 37, Illinois Jume 29, 1949

Professor H. J. Millor Science Hall 101 Department of Zoology Indiana University Bloomington, Indiana

Dear Dr. Muller:

a hour

I just got your kind letter of June 21st yesterday when I returned from the East.

As to the problem of Stadler, I think it is for his lawyer to say whether letters addressed to Mr. Poster will help or hinder the case of his client, but sime the public interest is involved, I wonder what further action we ought to take.

devoted a whole issue to the harassment of geneticists in Russia, it might well wish to devote a few pages to the harassment of a distinguished geneticist in America, and reprint in full the questions and answers contained in the interrogatory which you sent me. I am having a copy made which I should have by temorrow, and I will send it to E. Rabinowitch, whose present address is: Wardsboro, Vermont. I shall write to Rabinowitch urging him to adopt this course of action and to comment editorially on the issue. I wonder whether you could not find out in the meantime from Mr. Stadler and his lawyer whether they would welcome publication of the full text of the Interrogatory by the Bulletin of the Atomic Scientists. I expect to be in Washington in about a week's time, and might then discuss the case with a friend

1155 East 57th Street Chicago 37, Illinois June 29, 1949

Professor H. J. Muller Science Hall 101 Department of Zoology Indiana University Bloomington, Indiana

Dear Dr. Muller:

I just got your kind letter of June 21st yesterday when I returned from the East.

As to the problem of Stadler, I think it is for his lawyer to say whether letters addressed to Mr. Foster will help or hinder the case of his client, but since the public interest is involved, I wonder what further action we ought to take.

Ly own feeling is that since the Bulletin of the Atomic Scientists devoted a whole issue to the harassment of geneticists in Russia, it might well wish to devote a few pages to the harassment of a distinguished geneticist in America, and reprint in full the questions and answers contained in the interrogatory which you sent me. I am having a copy made which I should have by tomorrow, and I will send it to E. Rabinowitch, whose present address is: Wardsboro, Vermont. I shall write to Rabinowitch urging him to adopt this course of action and to comment editorially on the issue. I wender whether you could not find out in the meantime from Mr. Stadler and his lawyer whether they would welcome publication of the full text of the Interrogatory by the Bulletin of the Atomic Scientists. I expect to be in Washington in about a week's time, and might then discuss the case with a friend

Professor H. J. Muller June 29, 1949 of mine, Joseph Rauh, who has successfully handled the case of Mr. Remington which you may have seen reported in the New Yorker. With kind regards, Sincerely yours, m

THIS SIDE OF CARD IS FOR ADDRESS

BUY U S SAVIOS BONDS ASK YOUR POSTM SIER

PM. H. J. Muller Science Hall 101 university Bloomington

## PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES

Harvard School Public Health, Boston, 22 1949
Dear Sir:  I beg to acknowledge your article entitled Exts. on Light-  reactive time to be Novicle to System
It is my understanding that you desire to order.
reprints and
desire to see proof. If for any reason the article cannot be accepted
for publication in the Proceedings, you will be notified promptly.
Will go to press for October isse B. WILSON, Managing Editor
Will set over 6 hopes and authors will be billed for overset &

1155 East 57th Street Chicago 37, Illinois June 30, 1949

Professor H. J. Muller Science Hall 101 Department of Zoology Indiana University Bloomington, Indiana

Dear Dr. Muller:

I just received your letter of June 26th. Because of the information contained in it, I shall not communicate with Rabinowitch at this time. Since I will be away from Chicago in July, August, and part of September, I shall send you the copies of the Interrogatory that are being typed in the Bulletin office, and leave it to you to communicate with Rabinowitch when, in your opinion, the time shall be ripe for that. Enclosed you will find an extra copy of my last letter to you which you might then wish to send on to Rabinowitch also, together with an explanation of why I did not communicate with him.

Naturally, it is for Stadler and his lawyer to say whether they want the Interrogatory to be made public. There is little doubt in my mind that from the standpoint of public policy publication would be desirable, though it might be argued that publication should take place after rather than before the loyalty investigation of Mr. Stadler is closed.

I am taking this view because it seems to me more important to create the proper climate of public opinion in the United States with respect to such matters than to get the Administration to take this or that kind of specific remedial action.

Approaching Truman can, of course, do no harm and this might very properly be done by the Genetics Society of America. If you wish to take such action, I would suggest though that you get some advice in Washington from people who know the local scene. If you talk to Mr. Joseph Rauh (1631 K Street, Washington; telephone: RE 7795) and mention my name, I am certain you will find him helpful.

Sincerely yours,

Leo Szilard

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Science Hall 101
DEPARTMENT OF ZOOLOGY

August 12, 1949

Dr. Leo Szilard University of Chicago 1155 East 57th Street Chicago, Illinois

Dear Szilard:

Your letter reached me two days ago on my return from a trip to Washington. I sent in your manuscript to Wilson, for the Proceedings of the National Academy of Sciences, today. So far as I know, this Journal publishes more promptly than any other which takes articles in the biological field. I am, however, asking Wilson to give me an estimate of when it will appear.

I felt it a great privilege to act as transmitter for such a fine piece of work and I am grieved and ashamed to have held it up so long. It is a great satisfaction to see how well the results fit together — one seldom gets such good fits in biological work. I do not see what reasonable interpretation there could be other than the one you give. Moreover, it fits in very well with Stone's results in inducing bacterial mutations by # treatment of the medium.

Hollaender tells me that Stone has recently found that only rather short ultraviolet will work in the way he found, i. e., via the medium, even though somewhat longer ultraviolet (provided it is shorter than 3100 Å) is still mutagenic. I do not know, however, what wave length Stone was using when he got his effect. I wonder whether this difference in the form of the result bears any relation to reactivability by visible light, in other words, to the magnitude of your factor q. It might be of interest for you to make a determination of q at different wave length. I realize though that this is only one of many lines of attack that are opened up by your new finding.

Thank you for letting me see your proposed statement about the employment of Communists in universities. I am inclined to agree with the adoption of such a policy but must confess that I am not 100% convinced because adherence to the Communist line is becoming an even clearer demonstration of lack of intellectual integrity. It is hard to see what better proof could be obtained and, furthermore, whether the attempt to attain it might not do excessive damage to persons whose integrity was erroneously questioned. The same question arises in connection with Nazis, Fascists and Kau Kluxes, for I think it is arguable that proof of a person's adherence to such an organization might be taken as sufficient evidence of his lack of intellectual integrity or else of his lack of sufficient social-mindedness to allow him to hold a position of cultural influence. There must be a line drawn somewhere, and the question of just where, is one about which I have not been able completely to make up my mind. I think that the position of this

line has to be allowed to vary somewhat with the amount of danger in each direction, so that if the group in question became a goodt deal stronger than at present, or had a strong chance of doing so, the measures against them would have to be increasingly stronger. In other words, we cannot expect to have complete freedom of communication and association so long as there are groups which may misuse these to abolish them. But let us keep them as long as these groups do not constitute a real threat to us. Deciding when this is the case is, however, a matter in which judgments might vary very much. I should be inclined to lean over backwards, in the direction of allowing freedom, while taking steps to counteract the influence of groups against freedom by active exposition of what their policies really amount to.

In the hope that you are having an exhiliarating vacation,

Yours sincerely,

H. J. Muller

HJM:hs

Enclosure: (1) Statement

August 16, 1949

Professor H. J. Muller Department of Zoology Science Hall 101 Indiana University Bloomington, Indiana

Dear Professor Muller:

Your letter of the 12th was forwarded to Dr. Szilard only today because it arrived at the weekend, which in this case happened to include Monday as well. I mention this so you will know approximately when your letter will reach Dr. Szilard in Colorado.

Sincerely yours,

Norene Mann (Mrs.) Secretary to Dr. Szilard

# INDIANA UNIVERSITY

BLOOMINGTON, INDIANA

Science Hall 101

August 25, 1950

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

Dear Dr. Szilard:

Owing to the fact that I had to meet a deadline on a manuscript of mine I have only just now had a chance to read the one that you sent me. To say that it "may interest" me is a ridiculous understatement. For me to transmit it to the National Academy for publication would make me feel like a coolie carrying the rajah's diamond. It would make me feel tiny but I should glitter in its reflection.

I suppose you know about the work of Zamenhof, reported in a little abstract in 1945 in Genetics, volume 30, page 28. I wonder why his results were different in regard to the relation between mutation and bacterial multiplication. Can it be that there are different ways of slowing or halting bacterial multiplications, even at the same temperature and water-content, some of which reduce the mutation rate markedly and others of which do not? Perhaps what you call "lag" is a kind of surfeit state in which metabolism is mainly dormant and in which there are few mutations, whereas in the state you useatype of metabolism in which multiplication goes on when it has a chance is continuously being carried on. At any rate, now that you have your chemostat you can easily find out the effect on the mutation frequency of using different methods of cutting down the rate of multiplication.

I marvel at your new method of picking up mutations of comparative indifference—what a clever way of fencing out a lot of natural selection! Perhaps as you get to extremely slow rates of multiplication you will again find more mutations that hinder survival. For it may be pretty difficult to get along for a long period of time without any multiplication at all.

The method of using dips in the frequency of indifferent mutants to find otherwise invisible change-overs also seems to me of the greatest promise. I imagine you'll get change-overs with a good deal greater frequency after more time has elapsed to allow those to make themselves evident which are due to mutants whose degree of advantage is less. How long a time will it take to reach a new optimum, and what will the relative frequency of advantageous mutations, as compared with the total, turn out to be?

To use this method of "dips" to find "change-overs" one has of course to be sure that there is no sexual process, i.e. no genetic recombination like that studied by Lederberg. On the other hand the method is itself a test for this-and perhaps this too could be regulated by cultural conditions.

I'm greatly looking forward to a chance to talk to you about it all. Will you be at Columbus? At present I must meet several more deadlines—no vacation this year either.

Yours cordially.

HJM:00 P.S. I'm not too surprised at the low Q10, despite the Drosoflike results, which I've recently come to think probably represent a coincidence.

August 25, 1950

Dear Dr. Szilard:

The University of Chicago Chicago 37. Illinois

Dr. Leo Szilard

COPY

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Yours cordially,

/s/ H. J. Muller

HJM:eo

H. J. Muller

P.S. I'm not too surprised at the low Q10, despite the Drosophila results, which I've recently come to think probably represent a coincidence.

October 16. 1950

Dr. H. J. Muller Department of Zoology University of Indiana Bloomington, Indiana

Dear Dr. Muller:

This summer I read with great pleasure your Harvey Lecture, "Evidence of the Precision of Genetic Adaptation." I wonder what you would think of the following interpretation of your results:

If A substance is produced at some rate through the action of gene A, then and in meneral there is present in the cell also a gene B which produces an enzyme that destroys the substance at a rate proportionate to the concentration c of the substance. The number of enzyme molecules present in the cell are postulated to be proportionate to the number of genes B present in the cell, and the rate at which the substance is produced by the genes A is assumed to be proportionate to the number of genes A in the cell.

Assuming that there is only one gene A and B in the cell, we may express the result of the function of gene A by writing

and we may express the result of the action of the gene complex B by writing

The concentration of the substance which establishes itself is then given by

1+ = a-6c =0 or e= a .\*

I am assuming that this is quite generally true whether gene A is located in the X chromosome or in one of the autosomes. However, if gene A is located

2 - H. J. Muller, October 16, 1950

in one of the autosomes, there is no reason why the corresponding general B should be located in the same autosome. Whereas if gene A is located in the X chromosome, it is a necessary and sufficient condition for dosage compensation that the corresponding gene be also located in the X chromosome.

Sincerely,

Leo Szilard

WV

1155 E. 57th Street Chicago 37, Illinois November 7, 1950

Dr. H. J. Muller Department of Zoology University of Indiana Bloomington, Indiana

Dear Dr. Muller:

Enclosed you will find a copy of the manuscript which you sent to the <u>Proceedings of the National Academy of Science</u> for your files. It will appear in the December issue. Enclosed with it is another manuscript for your files which describes the apparatus we used and which will appear in <u>Science</u>. This seems like a good opportunity to thank you for having submitted our paper to the National Academy. We are very happy to have this paper appear there.

Sincerely yours,

Leo Szilard

### INDIANA UNIVERSITY

BLOOMINGTON, INDIANA

DEPARTMENT OF ZOOLOGY

December 13, 1950

Dr. Leo Szilard Institute of Radiobiology and Biophysics University of Chicago Chicago 37, Illinois

Dear Szilard:

I should have answered your interesting letter about dosage compensation a long time ago, but didn't have as much time to think about the matter before answering it as I wanted to. It is a most intriguing suggestion as to how the effect is produced and it is amusing to see that it applies the mechanism of your chemostat, with destruction substituted for overflow and origination of gene-products substituted for inflow. I imagine it must be an essentially true explanation in some form or other but I am not very happy about the form of it.

It seems wasteful to have such a continuous production and destruction going on, or could the rate of these processes be yery slow? Of course, you may say that the "destruction" may simply be a conversion to something else that can be used, but even so a significant amount of energy might be lost when all gene-controlled processes are taken into consideration. Moreover, one might think that if the converted product were itself useful a great change in the rate of its own production might, in turn, significantly affect further processes of importance for the organism. It would have corresponded more with my own expectations if the limitation imposed by the compensating genes in the amount of effect of the "primary" gene could be caused by some sort of inhibition or containment of the primary gene or gene-product, yet I don't see how this would work so as readily to get the result which, as you show, would be produced by destruction: namely, half as much activity by means of twice as much compensator.

I tried to the it by supposing that one dose of compensator reduces the primary gene effectiveness to a halfowhat it would otherwise be, and two doses to a quarter. But this requires a more special set of conditions than your hypothesis does. Moreover, it would only work for one dose and two doses of primary and compensator. I am going to test it out as soon as I can by observations on so-called "superfemales", which have three X-chromosomes and two sets of autosomes, but I am expecting that in general they will give results substantially like ordinary males and females rather than consistently different in the direction predicted by my hypothesis, and that they will therefore support your hypothesis.

Would it new, however, be possible for the form of your hypothesis to be modified in such a way as not to require the gene-products to be destroyed by the compensator? An analogy to this would be given by Boyle's law, in which doubling the pressure on a gas halves the volume, without any molecules being destroyed. If then the number of molecules of gas were doubled too, the original volume would be restored. However, it seems hard to think of a physic chemical situation which would work analogously to this. Can you think of one?

As you stated the matter, there was only one compensator or destroyer for the product of each primary gene, whereas there are probably several or many which, in combination, have the given effect. This, however, is no objection to the essentials of your hypothesis. One could also admit that, in the case of sex-linked genes, there could be very weakly acting destroyers located in autosomes also, but that the action was too weak to come into the picture practically, unless of course the compensators in the X-chromosomes should be removed. The same could, for that matter, be postulated concerning inhibitors that act in other ways.

On the destruction mechanism, it would, as you say, be natural to suppose that this worked in the case of genes in general but that in the case of autosomal genes the destroyers were not localized in any given chromosomes. The establishment of this general method of regulating the amount of effect of a gene would, of course, be of great interest: so far as I know it has not been proposed as a general method for this. This increases the desirability of finding tests for deciding whether or not it is true in the case of the sex-linked genes, and it also becomes desirable to find out whether the form of the hypothesis could be changed so as to have some other kind of interaction take the place of destruction or permanent conversion.

Thank you very much for your comments. You ought to publish them. I shall let you know what, if any, results I get from my tests, although I am not too optimistic about the decisiveness of tests that I can readily perform in the near future because there are not many genes I can readily use in the manner mentioned, and because the phenotype of the super-females is pretty much disturbed anyway, by reason of the abnormal ratio of X's to autosomes. One might also that other abnormal X:autosome types, such as intersexes and "super males", but these are harder to get and require one to work through triploids. I do not at present have triploids and even if I got them I should have to introduce the genes to be studied into these flies, which are very difficult to breed. Personally, I have never yet gotten an adult super-male, since they are so inviable. As for the intersexes, the difference to be expected between the results on the two hypotheses would be less in them than in super-females, anyway.

With kindest personal regards, and best wishes for the holidays,

Yours sincerely.

H. J. Muller

hjm/bjb

\* This of course must be due to incompletoness of dorage compensation, including probably the action of sex-determining genes.

1155 East 57th Street Chicago 37, Illinois February 13, 1951

Dr. H. J. Muller Department of Zoology University of Indiana Bloomington, Indiana

Dear Dr. Muller:

Just a few lines in a hurry to thank you for the comment made in your letter of December 13 in which I was very much interested. I hope that our paths shall cross soon so that we can talk about this and other things.

Sincerely,

Leo Szilard

WV

DEPARTMENT OF ZOOLOGY

January 25, 1957

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

Dear Dr. Szilard:

Yes, of course! But I didn't think I'd live to see it! I'd be most happy to be an Affiliate Member of the Research Institute. I do hope not too many of those on your list have turned you down. But I hope that even if they have you won't give up because I believe the possibilities of personnel for Affiliate Membership aren't exhausted yet. For instance, some of those you have thought of as Staff Members might not wish to give up their present positions but might be suitable and available for Affiliate Membership.

Please pardon my long delay in replying. I was having to meet several unavoidable deadlines for things that were very time-consuming and because of the very importance of your project I did not want to answer you on the basis of an inadequate consideration of it. Not that I have yet considered it as much as I should have but at least I feel sure that it would be a privilege for me to be associated with it if it materializes.

Naturally there are various features regarding which I do not see eye to eye with you. My major criticism is that I think it is planned or hoped to attack too many largely disconnected fields. I have in mind especially the fields of coronary disability and of cigarette smoking as dubious for the Institute. I am willing to be convinced but it is not clear to me that an attack of only a few years would be likely to get decisive results in either field, more especially in the coronary field. So far as reaching a decision on the basis of human statistics is concerned the number of variables usually present provides a discouragingly high possibility of spurious correlation to to be found. Of course animal work may help in this even though different species of animals are likely to present major differences in regard to systems that appear to be so delicately balanced as in this case. But perhaps you have certain specific, critical tests in mind and I am probably pre-judging the situation.

A feature of the administration that seems to me to be impracticable is the ten-year time limit on Research Associates. I agree that such a limit would be highly desirable in itself but I am afraid that it would make the obtaining of good Research Associates extremely difficult and would work undue hardship on many of those who were obtained. The reason is that our Research Associates would face a high probability of being left high and dry when their ten-year period was up. One of the banes of the research grants of today is that they cannot or do not offer tenure to the Research Associates and it is therefore seldom possible to get people to occupy these positions unless they have some disability (such as belonging to a minority group that is strongly discriminated against) that makes it impossible for them to get an appointment with tenure or one that is likely to lead to one with tenure. Moreover, the longer they stay in such a position the more nearly impossible does it become for them to get a suitable offer from elsewhere. I have seen this situation develop again and again with really good Research Associates. Even when they

had very high recommendations universities shied off from taking them merely on the ground that they did not have a university position or in fact a permanent position and that there must ipso facto be something the matter with them. Nevertheless many of them were better than the average person having a corresponding position in a university, with tenure. At the same time, they might not be good enough for us to want to continue them. What then? I should be glad to have your suggestions as to how this difficulty may be met.

Before things get too crystallized I should very much like to have a talk with you. It happens that I have to give a lecture at Northwestern University, Evanston, Illinois, on the evening of Tuesday, February 19. I have to take the night train back in order to be able to meet my class here Wednesday morning but I could come to Chicago late in the afternoon on Monday. If the weather is good enough to allow the Lake Central Airlines plane to fly I could arrive at the Midway Airport, Chicago, at a little before 6:00 P.M., otherwise I could take an Eastern Airlines plane that would get me to Chicago at 7:37 P.M.) We could then have a talk that evening (but don't make it late) and/or Tuesday morning. I should like to talk about several of the projects and also about some matters of personnel.

Even in this case I think it is better to hit a few things hard, if they are likely to prove crucial things, than to get nowhere slowly by spreading out too much. To me it seems that the proposed funds are inadequate to do anything like what the project envisages. But if the Institute by concentrating really makes a good go at something recognized later as important that might put it into a strategic position to make additions later or to establish metastases.

It happens that until some time in March I shall be more busy than usual having to meet a number of further deadlines. I may therefore continue to be a little remiss in my correspondence about this matter but please do not take it as an indication of my lack of interest. But I do hope you willfind it feasible to have a conference with me on the 19th.

Yours cordially

NE & BORTON

HJM:sh cc: Dr. Doering, Mr. Canfield enc: (MS-EControlled fertilization

H. J. Muller

and its larger implications

Second from "Out of the Night." Sound about Confield

P.S. You may be interested to look through the enclosed manuscript, because of its connection with some of the points which you made. I had promised to send it to Mr. Canfield so I would ask you to forward it to him after you are finished with it. Perhaps Dr. Doering would care to see it also. I have no present plans for publishing it.

I should favor your proposal of leaving the way open for some such activities in the investigation of social or political possibilities as you mention in cases in which the agreed upon heavy majority decides in favor of such an activity.

In regard to personnel on active status, do you think the following might also be considered: Spiegelman , Levinthal? As for Affiliates, what

Hollander is having a big symposium on the medium plenomenon & related to fiew beginning app. I at Gatherburg near Dals Ridge, & would don't less be glad to hove you come. Michigan will then come here to speak on it I will be estudied interview at Dake Ridge.

January 30, 1957

Professor H. J. Muller Department of Zoology Indiana University Bloomington, Indiana

Dear Dr. Muller:

Many thanks for your very kind letter of January 25th. I am grateful for the various suggestions which you make in your letter and would, of course, very much like to talk with you about some of them. Whether I shall be in Chicago on February 19th, I do not yet know but I shall keep in touch with you about this possibility.

The suggestions which I made in the appendix concerning possible projects that the Institute for Problem Studies might take up were put forward only to start the discussion of this topic by the "Affiliate Members." The only point I really wanted to establish was that there would be no shortage of tasks for an organization of the right sort. Fritz Lipmann has suggested that we arrange for a meeting of the potential affiliate members in which every topic can be discussed in a "relaxed and comfortable atmosphere," and I believe Mr. Canfield will probably want to arrange such a conference when we have the responses to the initial inquiry that was sent out.

Apart from Lipmann, I have been so far in contact only with Harrison Brown and Jonas Salk, whom I met more or less accidentally and with whom subsequently I had a prearranged discussion.

Urey has been traveling about and should be by now back in Oxford, England, and Teller will not be back to his office in Berkeley for another two weeks. Where Pauling is hanging out at the moment, I do not know. In any case no negative responses have been received so far.

I am looking forward to reading the material that you sent along with your letter.

With kind regards,

Sincerely,

Leo Szilard

m cc: Mr. Cass Canfield Mr. Cass Canfield, Chairman Editorial Board Harper & Brothers 49 E. 33rd St. New York 16, N.Y.

Dear Mr. Canfield:

I am glad to know that enough people are interested in the project of the research institutes to make a meeting advisable. However, as you will see in my letter of January 25 to Dr. Szilard, I have too many commitments in February for any conference except the one I proposed to him for the evening of February 18 and/or the morning of the 19th, and that would have to be in Chicago since I have another engagement there on the evening of the 19th. As for March, I should have any week-end free except the first one but since I have classes every Monday, Wednesday and Friday at about noon, I should have to make a special arrangement if I were to be away during the week. Moreover, I have, in addition to my class, another fixed engagement on Friday, March 15. Anything in the last week of March, beginning March 25, would also be impossible for me.

In general, it seems to me that it would be far more practicable for us all to meet in Chicago or in the East than in California because the less# traveling would be required even though a few people would have to travel more. Moreover, those of us who could get away only for a week-end would thereby be spared losing two nights' sleep in plane travel -- an experience that affects me adversely.

Dr. Szilard has not yet indicated to me whether he wishes to talk with me next Monday or Tuesday, February 18-19, but of course if we all are to meet together there would be no point in this separate meeting. If I do not hear further about the matter I will rearrange my travel reservations for Chicago so as only to meet my lecture engagement there on the evening of the 19th.

I am writing in haste because I am leaving today for an engagement in Massachusetts, from which I shall have returned by Monday. Many thanks for your letter. With best wishes,

Yours sincerely.

HJM:sh ce: Dr. Szilard

Greetings from H. J. Mulle

April 3, 1957

Dr. H. J. Maller Department of Zeology University of Indiana Bloomington, Indiana

Dear Dr. Muller:

Cass Canfield has left for Europe where he will be for about six weeks, and I assume that he had no time to write you before his departure. Therefore, I am writing to you in his place.

Commonwealth Fund in our project. The attitude of the Ford Foundation is, as far as we can ascertain, not negative. That the Ford Foundation will move into the area of science is likely and, if they do so, the new division will be under Vice President William McPeak. They have so far not appointed a program director though they appear to be looking for one and estimate that it will take another three months before this is done. Until then no further progress can be made with the Ford Foundation.

In this situation, Canfield, Doering and I thought it best to turn our attention to private individuals rather than other foundations. Accordingly during the past two weeks we made certain initial contacts which now will be pursued in Canfield's absence by Doering. Arrangements have been made for a trip for Doering that will take him to Texas, and I shall try to keep you informed of any substantial progress that may be made.

In the meantime it does not seem necessary to bother any of the potential Affiliate Members; i.e. those who have been approached and who have expressed an interest. Also it would not seem advisable to enlarge in the meantime the circle of potential Affiliate Nembers.

There is, however, no reason why the general idea should not be discussed with others who might be interested and helpful.

I sent copies of the memorandum and appendix to Cy Levinthal and to Hillary Koprowski and received rather favorable reactions from both. Koprowski will be Director of the Wistar Institute which is located on the campus of the University of Pennsylvania, where he has much space and a reasonable budget, but considerably more space than budget. I shall keep in touch with him and we shall see whether and to what extent the operation he is setting up might be integrated with our larger plans.

Are you going to the Oak Ridge meeting? I have so far not made a reservation but I might wire to Oak Ridge today.

With kind personal regards,

Sincerely,

Leo Szilard

DEPARTMENT OF ZOOLOGY

Sept. 9, 1957

Dr. Leo Szilard
The Enrico Fermi Institute
for Nuclear Studies
University of Chicago
Chicago 37, Ill.

Dear Dr. Szilard:

Only today, on my return from the West, have I had an opportunity to read your letter of August 15 and the memorandum and appendix enclosed with it. I find myself in remarkable agreement with the memorandum, and more especially with your major thesis that we must learn to live with the bomb for a considerable time to come (or at least until there are major political changes behind the Iron Curtain). I told the Humanists this at their International Congress in London in July. I am inclined to agree that a series of conferences of the kind you propose would be helpful in getting this and related ideas clarified and disseminated.

It is pretty obvious that the Soviet group of countries wishes to use the agitation against nuclear tests simply as a steppingstone toward the official banning of nuclear weapons, a measure that would be not merely unstabilizing but unstabilizing in their favor. Not only would they be likely to have the advantage in conventional arms and armies but they might be able to turn their nuclear "plowshares into swords" faster than we could. At any rate, if the banning were not a farce the present deterrents based on the power of mutual destruction would be considerably reduced. The sooner everyone's cards get laid on the table, regarding this matter, the less opportunity would be given for a build-up of opinion against us in countries at present not committed and even among the large sections of our own peoples.

Because only world-wide amity based on a partial relinquishment of national sovereignties can give a final answer to the problem of living with the bomb, even though not in the presently foreseeable future, it is important at the same time to work toward that end, Utopian though it may at present seem. Among ways of doing so might be conferences of realistically minded persons in the social sciences, perhaps participated in also by a few persons from the natural sciences and from public affairs, to discuss the bases of the political, economic, and, in general, ideological differences between the two major opposing groups, and means of diminishing them without the sacrifice of what we might agree upon as essential. At least we on the one hand (including the Western European countries) and the Poles and Jugoslavs on the other hand, might be able to come somewhat closer together in the opinions on such matters. This would tend to exert a pull on those with more recalcitrant ideology. It would also exert a pull in the opposite direction on our own more reactionary elements.

Overlapping with the above (the second) group of topics would be a discussion of policies to be pursued by the West in regard to the uncommitted and underdeveloped peoples. If what has been called the "salami" policy like that pursued by the Russians in Syria recently is to be prevented from winning them the world or from bringing the situation to the brink of nuclear war it is important for us to offer more effective

Muller to Szilard, Sept. 9, 1957, p. 2

aid to the more progressive and democratic elements in noncommitted and underdeveloped countries as well as to their peoples in general and it is also important for us to set a better example of the human relations that our type of organization results in in our own country in our relations to one another as well as to other countries. But of course we cannot mix this up much with the discussion of military and international matters that you have proposed for the meetings organized by your Chicago departments.

I bring up these other matters now only because I think that they are related to the matters you have brought up and because I think that ultimately they will all have to be seen in relation to one another. Eaton, at the suggestion of the letter I would favor a follow-up meeting, presumably at Pugwash. I enclose a copy of the letter to Eaton. The Humanists, at their London meeting in July, were also in favor of some such meeting, to be participated in mainly (so far as I could gather) by persons not in the natural sciences. I neither proposed nor advacted opposed this project but I did get them to include some natural scientists (not specified) in case it were to be carried through. If they do try to carry it through they are likely to appeal to Eaton to help them in it.

I think that additional conferences of these kinds are to be welcomed so long as they do not mess things up. This makes it the more desirable to have the scientists' conferences come first, to clarify the most acute difficulties. This clarification could well be carried over to the other conferences, especially if there were some overlapping of membership. All this would help in dissemination and coordination. I should be glad to know your own opinion on these matters.

Yours sincerely,

H.J. Whaller

H. J. Muller

HJM:sh enc.

September 23, 1957

Professor H. J. Muller Department of Zoology Indiana University Bloomington, Indiana

Dear Dr. Muller:

I am about to leave for Europe, and I am just writing you in a hurry to thank you for your letter of September 9th. Gradually the answers to my inquiry are coming in, and they will be received in my absence by Dr. Grodzins, Chairman of the Department of Political Science. You may hear from him or from me again upon my return from Europe.

With kindest regards,

Sincerely,

Confdeld

## INDIANA UNIVERSITY

BLOOMINGTON, INDIANA

DEPARTMENT OF ZOOLOGY

Oct. 4, 1957

Dr, Leo Szilard
The Enrico Fermi Institute
for Nuclear Studies
The University of Chicago
Chicago 37, Ill.

Dear Dr. Szilard:

In my opinion the communist countries would not for a moment tolerate the idea of giving money for the support of an institute of the kind proposed that was located outside of their own borders, nor would they support it if the main personnel were non-Soviet. Moreover, so far as Russia is concerned, it is still, as a result of Stalin's influence, considerably more backward than the major western powers (including the United States) in its approach to matters of reproduction, genetics, and the fundamental structure and processes of living matter. Moreover, they are not yet willing to admit this and would resent any attempt to push them in such respects. As for Nehru, I have an entertaining and pretty book on evolution for children written by him which is completely Lamarkian in its outlook. Of course Haldane, who would be consulted if India were in question, has a very progressive outlook, but he has developed such an antipathy for both westerners (especially Americans) and Russians that he would be likely to resent and try to block their "intrusion".

Far more likely to be free enough from prejudice and far-seeing enough to support the Institute would be persons or circles in the Scandinavian countries, England, France, Japan, or Isreal, although of course the money would be harder to come by than it would in Russia if Russia really wanted to do the thing. But I believe that there are still certain possibilities in the United States which should be explored in the search for funds. One of these perhaps would be Rockefeller Prentiss and another Cyrus Eaton. Possibly Charles Collier (a dairy farmer who is the son of the famous John Collier and whose address is Indian Spring Farm, Darlington, Maryland) might have some suggestions concerning possible donors. A further point to be considered is that it would be very difficult to get competent American scientists to take up work on a permanent or near-permanent basis outside of North America.

I shall be interested to know whether you turned up any ipromising prospects for the project during your trip in Europe. With personal regards,

Yours sincerely,

H.J. Thuller

H J My Man

HJM:sh

cc: Mr. Cass Canfield

Dr. William Doering

Dr. Harrison Brown

Dr. Fritz Lipmann

Dr. Linus Pauling

Denver, Colorado December 31, 1958

Professor H. J. Muller Department of Zoology The University of Indiana Eloomington, Indiana

Dear Dr. Muller:

Enclosed you will find an excerpt of my paper. The paper itself will appear in the January issue of the Proceedings of the National Academy of Science. It seems to me that in order to test this theory, one might have to proceed as follows: We take two inbred strains of mice and irradiate both, for a number of generations, avoiding consanguinous matings while doing so. Subsequently we would obtain the F<sub>1</sub> hybrid for a number of different pairs of mice.

We then determine for each pair of mice the number of faults by making brother-sister matings in the F<sub>1</sub> and observing how often the zygote is homozygous for a fault. (I presume this could be done by comparing early in pregnancy the number of embryos with the number of corpus lutes.) Similarly we would determine the number of the recessive lethals, which are not faults. (This I presume could be done by determining the number of embryonal deaths and still births.)

On this basis one might sort out two groups of pairs. One group would contain those pairs who contain few faults but contain many recessive lethals which are not faults. The other group would contain those pairs who contain many recessive lethals which are not faults but contain few faults. The experiment consists in comparing the life expectancy of the adult F<sub>1</sub> offspring for the two groups of pairs, with each other and the control.

It is my prediction that the life expectancy of the adult offspring will be appreciably shortened in comparison with the (unirradiated) control for one group and that it will not be shortened for the other group.

I still hope to be able to visit Bloomington on my way back East during the second half of January.

With kindest regards,

Sincerely,

Leo Szilard

YR,

Denver, Colorado February 20, p1959

Dr. H. J. Muller Department of Zoology University of Indiana Bloomington, Indiana

Dear Dr. Muller:

When I saw you at Ames, I told you that I was puzzled about the fact that the haploid set of genes of mammals represents about 10<sup>6</sup> DNA molecules if the DNA molecule is assumed to have a molecular weight of 2 million.

I was inclined to interpret this by saying that only a small fraction of the DNA molecules, perhaps 1/100 or 1/50, in the mammalian cell represents genes which are genetically relevant from the point of view of the survival of the fittest, and that the rest of the DNA molecules are genetically unimportant.

You told me that you were puzzled about the large amount of DNA in the mammalian cell also, and that you were inclined to interpret this by saying that the DNA molecules which represent the mammalian genes might be 10 or 15 times larger than those of a fruit fly. This, you thought, would fit in well with the fact that the sensitivity of the mammalian genes with respect to the production of mutations by X-rays is about 10 to 15 times higher than that of the fruit fly. If I remember correctly, you were thinking of writing something on the subject.

In the memorandum which you will find attached you will find an argument which seems to speak in favor of my view rather than yours, and I should appreciate any comment that you might care to make.

Dr. H. J. Muller February 20, 1959 Page 2

I find that I am being kept busy in various places out West, and I do not know for the present when I will penetrate as far east as Bloomington. I do hope, however, that somehow we will be able to have another discussion in the non-too-distant future.

With kindest regards,

Sincerely,

LS:er



NO. 352-V

#### KODAK EASEL CHRISTMAS FOLDERS

MADE IN U.S.A.

of your illness. But do not worry about your unfinished business. It will make men of us For that we have you to than

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7

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If all or most of the Y chromosome represents heterochromatin that is paralleled by a similar bulk of heterochromatin in the X and other chromosomes then the above effect may be upped by about 50% of its previous value since the euchromatin of the X (the "differential" chromatin, X minus Y) would then form 6% instead of 1% of the total chromatin that gage rise to mutations that should be counted. In addition, I consider it not impossible that our estimate of the total mutation rate may be as low as one half of the actual rate, although I do not think that very likely.

I hope that you stood the trip and meetings in Moscow well, and that you feel it was worth while. Since it seems that the Russians have decided that they do now want a rapprochement I imagine that they did make it worth while. Of course it is another question whether or not they intend to try to use such a rapprochement by taking advantage of us after our guards have been let down. I feel that they would be better than we at conducting a rapprochement without really letting their guards down, and that they would be counting on that. How can one duly combine trust and mistrust? Do you think there is any possibility of the so-called "instead" program getting adopted and working? I enclose a copy, in case you have not seen it.

With all best wishes,

Yours sincerely,

H. J. Muller

HJM:slh enc.

Dr. H. J. Muller Department of Zoology Indiana University Bloomington, Indiana

Dear Dr. Muller:

Many thanks for your letters, which I found in my mail when I recently returned from Europe. At present I am in Washington, where I expect to remain for the next few weeks, at the Hotel Dupont Plaza. Should you be in Washington in the near future, I would appreciate your contacting me there.

Enclosed you will find a memorandum proposing a method for studying the mutagenic effect of ionizing radiation in mice. I am in the process of discussing with Dr. Zelle whether experiments along these lines might be set up in one of the A. E. C. laboratories. Any comments which you might care to make would be most welcome.

With kindest regards,

Sincerely,

February 24, 1962

Professor H. J. Muller Department of Zoology University of Indiana Bloomington, Indiana

Dear Doctor Muller:

Would you be good enough to read the attached "speech" and let me know whether you are sufficiently interested to be willing to be part of this operation.

I am emclosing some indication of the responses, and if you are interested I shall mail you a set of press clippings and photocopies of a sample of my mail.

Please let me know as soon as you can what you think about all this by writing to me at my Washington address given below.

Sincerely,

Leo Szilard

Hotel Dupont Plaza
Washington 6, D. C.
Telephone: HUdson 3-6000

Enclosures

Washington, D. C. March 3, 1962

Professor H. J. Muller Department of Zoology University of Indiana Bloomington, Indiana

Dear Dr. Muller:

The attached letter is meant for you and those others whose names are listed in the memo "The Next Step". I should be very grateful to you for reading the attached letter and the enclosures, and for advising me as soon as possible whether you are willing to serve as an Associate.

Sincerely,

Leo Szilard

Hotel Dupont Plaza
Washington 6, D. C.
Telephone: HUdson 3-6000

# Enclosures

P.S. I am enclosing the revised and final version of my speech, which will be printed in the April issue of the Bulletin of the Atomic Scientists.

forte: Curent 16 March 1962 H. J. Muller Department of Zoology Indiana University Bloomington, Indiana Dear Dr. Muller: I am very happy to have your letter of 13 March and to see that you are willing to serve as an Associate. The Associates will be regarded as members of the committee called The Committee for a Liveable World but they will not be burdened with any extra trips to Washington. If they do come to Washington, if the time permits the Council will probably want to arrange for them to see some of the key people in Congress or the Administration. The structure of the organization is sufficiently undemocratic to preclude the possibility that it may be taken over by any extreme group. Since the Fellows elect the Board of Directors, all power is vested in the Fellows and they will be all distinguished as well as level-headed scientists even though some of them may be so young that only those who work in the same field may realize why they have been picked. With kindest regards. Sincerely,

DUPONT PLAZA file:6

DUPONT CIRCLE AND NEW HAMPSHIRE AVENUE N. W., WASHINGTON 6, D.C.

HUdson 3-6000

September 19, 1962

Professor H. J. Muller Department of Zoology University of Indiana Bloomington, Indiana

Dear Dr. Muller:

Enclosed I am returning the reprint which you were kind enough to lend me. Enclosed you will also find a preprint which gives the conclusions which I have reached on "dosage compensation". I wonder whether it might be worthwhile publishing this manuscript, perhaps in Perspectives of Biology, and any comment that you might care to make in this regard would be appreciated.

I have recently returned from the Pugwash Meeting in Cambridge, England, and had upon my return a number of very interesting conversations in high places. I now know what would need to be done and I shall try to do it, but of course I don't know if I can bring it off.

With kindest regards.

Sincerely,

Me: 6 INDIANA UNIVERSITY BLOOMINGTON, INDIANA DEPARTMENT OF ZOOLOGY Oct. 4, 1962 204 Jordan Hall Dr. Leo Szilard Hotel Dupont Plaza Dupont Circle and New Hampshire Ave., N.W. Washington 6. D.C. Dear Dr. Szilard: Information has reached me that the meeting of the Committee on Radiation Protection that I will attend in Washington will be held Friday and Saturday, October 26 and 27. I am arranging my schedule so as to arrive in Washington (immediately after a visit to the Worcester Foundation for Experimental Biology) at 5:29 P.M. on Thursday, October 25. If you would have a little while to see me at any time during the evening after 6:00 P.M. on October 25 I should be glad to come to your hotel. I would bring along your manuscript on dosage compensation to discuss. Perhaps there would also be matters concerning the Council for Abolishing War to be taken up -- among other things, whether the Council would indicate its moral support of Bayh and would count contributions for his campaign as contributions for the Council. With best wishes. Yours sincerely, HJM:slh cc: Dr. Robert G. Risk

October 5, 1962

Dr. H. J. Muller Department of Zoology 204 Jordan Hall Indiana University Bloomington, Indiana

Dear Dr. Muller:

Many thanks for your letter of October 4. Unfortunately, there is a meeting of the Salk Institute scheduled in New York on October 25, and I plan to leave for New York on October 24. It is conceivable but by no means certain that I shall be back in Washington by 6:00 p.m. on October 25th.

Since you plan to attend a meeting on October 26 and 27, perhaps it would be possible for us to arrange to meet afterwards, on the evening of the 27th.

By that time I should be back in Washington.

Concerning Bayh, I should say that it is the policy of the

Council that any campaign contribution which a supporter of the Council may

make to a Congressional candidate whom he considers to be deserving may be

regarded as a contribution in support of the movement, and may come out of

his two percent.

With kind regards,

Sincerely,

## Leo Szilard

P.S. I have just had a phone call from Chicago asking me whether I could fly to Chicago on October 26 to attend a meeting of about 350 of our supporters. I have not accepted yet, and Allan Forbes will have to go in any case, but if I do go to Chicago then, to my regret, I will miss you in Washington. I shall let you know about my going to Chicago as soon as it has been decided.

to face OINIVERSITY
GTON, INDIANA
Oct. 24, 1962

Me, N.W.

Oct. 24, 1962 INDIANA UNIVERSITY BLOOMINGTON, INDIAN DEPARTMENT OF ZOOLOGY 204 Jordan Hall Dr. Leo Szilard Room 745 Hotel Dupont Plaza Dupont Circle and New Hampshire Avenue, N.W. Washington 6. D.C. Dear Dr. Szilard: Unfortunately, by the time I was able to get around to telephoning you resterday (about 4:30 P.M. our time or 5:30 P.M. your time) telephone service to Washington had been interrupted. We were told that a telephone cable had been cut (that may have been only a way of saying that service for other than national purposes had been purposely interrupted because of the national emergency). At any rate, it is perhaps just as well that I now put down my thoughts about your manuscript on paper. I am sorry that, thinking that I would probably see you in person, I did do it sooner. It seems to me that it would be a good thing to have the manuscript published, at least in some revised form, so as to call people's attention to the known alternative ways in which the effects of the double doses of genes in the X-chromosome of the female may be equalized with the effects of the single dose of the same genes in the male. Certainly the mechanism is different in Drosophila from that of the Seroression of the action of all thx-chromosomes but one known to exist in the somatic cells of mammals, even though, as you point out, the same kind of mechanism as exists in Drosophila may be at work in mammals at an earlier stage (before the suppression of the additional X's begins, as well as in germ cells). A careful reading of my Harvey Lecture of 1948 will show that the genes which I called "compensators" were given the attributes of what you call "repressors". As I state in the paragraph beginning on page 209: "The relations must be so fixed that the compensators, when themselves in double dose, reduce the effect of a given dose of the primary gene to half of that which would obtain in the presence of a single dose of the compensators. For only thus can the effect of the female's double dose be reduced to that of the male's single dose. Such a result would be brought about most simply in a case in which the compensators, when themselves in single dose, reduced the primary effect to half what it otherwise would be, and in which, when their dose was raised, their own effectiveness rose in the usual geometrical manner.... Whether this simple scheme is usually true can probably be determined definitely through quantitative studies involving several different doses of compensators." It seems to me that it would be inadvisable, at the present time, to change the name of these genes from compensators to repressors, for several reasons. In the first place, we have no knowledge that the compensators cause repression by the same kind of mechanism, whatever that may be, as the repressor genes of bacteria work. Let me emphasize that there is nothing unusual in the fact that the products of genes interact so that the amount of expression of a given character is altered in a quantitative way assording to what genes are present, that have long been variously called modifiers, intensifiers, inhibitors, polygenes, multiple factors, plus and minus modifiers, etc. As I indicated in my diagram on interaction of genes effects on page 201 of the paper we are discussing, such interaction can take place on any level in the often long pathway between gene and character. As I understand it, the so-called

repressors of bacteria thus far studied are supposed to do their work at a level very near to the gene. But there is no reason to assume or infer that what I have called compensators do so, although they sometimes may. But the idea of "repression" in general, or "suppression", or "modifiers" in either direction, is nothing new and may be found, for example, in "The Mechanism of Mendelian Heredity", by Morgan, Sturtevant, myself, and Bridges, published in 1915, in a paper of mine in 1914 criticizing the interpretation of Castle and Phillips of their hooded rats' findings, and undoubtedly goes still further back. Again, compensators, unlike just any repressors, must be so quantitated in their action as to approximately equalize the expression in the two sexes.

It is necessary to be careful in saying (as you did on pages 4-5) that the development of the character is dependent on the "determining ratio". I discussed this matter on page 208 of my paper, saying, "it is easy to make the mistake of thinking that each dose of the compensator or compensators effects a given total amount of reduction of the activity of the primary gene (or rather, gene-product). If this were true however then the female with her two doses of both primary and compensators would show an effect equivalent to twice that produced by the one dose of primary and one of compensators in the male. In other words, there would be no equalization of the sexes. Moreover, in that case compensators acting strongly with hypomorphs would not work properly for genes at higher levels. We must therefore infer that the compensators, when present in any given dose, work in such a way as to effect the same proportionate amount of reduction in primary gene activity, regardless (within wide limits) of what the dose or activity of the primary gene is. This would ordinarily be the case if the inhibiting action of the compensator were itself little influenced, in return, by the amount of primary gene-product it had to affect. An example of this would be a situation in which the compensator's "product," determined indirectly by its gene, consisted in some such pervasive condition as a relatively high pH, which the primary gene's product, no matter how concentrated, had little effect on. In such cases, then, the compensators, at a given dose, would tend to reduce the primary action by a given proportion, rather than by a given absolute amount." A fourth reason why the compensators should not be equated with the known repressors of bacteria is that, as was pointed out in my paper, there is evidence that the different compensated genes commonly have several compensators, at different loci, working in concert. In other words, there is not just one compensator. (Still less is it true, of course, that different compensated genes usually have the same compensators.)

That the compensation depended upon not just one gene but several or a complex of genes was shown in the work that Margaret Lieb did with me for her M.A. thesis (written but not published in 1946), cited on my pages 206 and 207. It can send you a copy of this thesis ifyou wish. Not only the effects on the gene apricot were studied but also on scute, forked bristles, and Bar-eyet. The different pieces of the X-chromosome, obtained as fragments attached to parts of the little fourth chromosome, were found, when present in extra dose, to have different amounts of influence in the case of different ones of these mutant genes. Moreover, some chromosome regions even had an action the opposite of reduction, that is, of augmentation, on the character, but the entire X-chromosome, having these parts acting in concert, gave the compensating effect, just as we would expect if the system had been established, ultimately, by natural selection but with randomly fixed plus and minus deviations that were used to balance one another.

It is the above series of results, not the supposed 4:3 ratio of eye colors of males with an extra dose to females with an extra dose (of which you speak on pages 3 to 4), that shows the correctness of the compensator interpretation in Drosophila, rather than the kind of suppression of whole chromosomes seen in mammals. The results given in my own paper as well as in Lieb's show clearly that, with a given dosage of the "primary" gene (that under investigation), the addition of an extra

piece of the X-chromosome, not containing that primary gene, causes in many cases a reduction of the effect of the primary gene, although the reduction may not be as much as when all of the X-chromosome except the primary gene's locus is present.

I did not mention the 4:3 ratio in my paper -- at least, not in any prominent way. I would therefore suggest that the paragraph beginning near the bottom of your page 3 be changed to read as follows: "It would seem, however, that this postulate must not be extended to the fruit fly, because the behavior of the eye color in "apricot" fruit flies, and of the other sex-linked characters studied, cannot be explained by postulating that only one X-chromosome is functional in the somatic cells of the female fly. If this were the explanation, then we would not expect that changing the number of parts of the X-chromosome not containing the gene being studied would alter the expression of that gene. More specifically, the presence of an extra X-chromosome containing nearly all parts except a small region that includes the given locus (in other words, the presence of an X-chromosome deficient for that locus) would not cause the expression of the given gene, present in the other X-chromosome, to be reduced, as it was found to be. It would either be present in full strength, or not present at all, and different somatic cells would differ in this respect, as has been found, for instance, in the case of the error in glucose metabolism above referred to.(2) In Drosophila, the different elements of the eye, called ommatidia, and the different hairs and bristles, are developments of single cells, yet they show no mosaicism in such cases, unlike what is true in corresponding cases in mammals."

We have however to reckon with a possibility, that I did not consider specifically in my paper, which arises from an observation made by Bridges in an offhand manner in the course of a paper published in the 30's, to the effect that in the salivary glands the "single" (actually about 512-stranded, in well developed cells) X-chromosome seems about as wide (it is of course as long) as the "double" (actually, about 1024-stranded) X-chromosome of females. A long time after that, in a paper that I have at the moment lost track of, Dobzhansky rediscovered and called attention to the same point, and suggested that it might explain dosage compensation. This called my attention to the point and I tried to get several people to repeat the observation, using this time not only normal material but also material that I offered them which had various translocations between the X-chromosome and autosomes, but their work always fell through for one technical reason or another. I spoke to another cytologist, a Brazilian, Frota-Pessoa, about the matter when I was at a meeting in Vevey, Switzerland last September, and he promised to make some examinations along these lines after he returned to Brazil since, having been a student of Dobzhansky's, he was acutely aware of the problem. So far, however, I have not heard from him.

However, I consider it unlikely that such a difference, affecting the degree of activation of the X-chromosomes as wholes, in a manner corresponding to their size, could serve as the chief or whole interpretation of the dosage compensation in Drosophila. One reason for this judgment consists in the line of evidence to which I called attention on page 191 of my dosage-compensation paper, which runs as follows: "Further evidence that the chromosome configuration in itself has nothing to do with the matter is seen in the cases in which a piece of the Xchromosome has become broken off and attached to another chromosome and/or, conversely, in which a part of another chromosome has become translocated onto the X. Whether the pieces are large or small, or derived from one or another chromosome region, the result is the same: the genes, both those originally of the X and those of other chromosomes, still have the same dosage effects as they did in their old positions. Compensation is a chemical mechanism, or rather, system of mechanisms, stably established in the distant past, with reference only to those particular genes which regularly existed in different doses in the two sexes, and so it continues to operate now even when we change the very conditions that must once have called it forth."

Muller to Szilard, Oct. 24, 1962, p. 4

Another line of argument, that works in the same direction lies in the demonstrated influence of other parts of the X-chromosome than the one containing the "primary" gene under consideration, in any case, in modifying the effects of that gene. Nevertheless, this matter of chromosome size and activity should certainly be looked into further as it might play some role in dosage compensation. Moreover, the relatively undeveloped stage of dosage compensation in the newly acquired parts of the X-chromosome of species like Drosophila pseudo-obscura, mentioned on pages 210 to 212 of my paper, should be considered in connection with the same cytological studies.

There is still another phenomenon which deserves consideration in connection with this group of problems. That is, the long-known mosaicism in the expression of genes in a chromosome region, originally euchromatic, which has by an inversion or translocation or shift been placed near a heterochromatic region and which has come to be partly heterochromatized itself by the influence of the nearby heterochromatin proper -- what I have termed "variegated position effects". But although this effect was first found in the case of genes of the X-chromosome of Drosophila I found it to be true of genes in other chromosomes also, when they were subjected to such a change in position. Moreover, one would not expect the effects to extend throughout an entire X-chromosome. But there may well be something in common between this mechanism and that of the X-chromosome suppression found in mammals, even though the former does not have the feature of applying to extra chromosomes but appears even in the case of genes in the single X-chromosome of the male.

I am sorry to have made this letter so long but perhaps you will see why I felt such length to be necessary, and also why I had preferred to talk it over with you in person rather than to go to this length on paper. I do feel that the people who have been considering X-chromosome suppression in mammals have not had their attention called sufficiently to the difference between this and the dosage compensation in Drosophila. There are a lot of other things in my paper that have not been realized either, because it was published in a publication so little seen by geneticists. I tried to get it published in Evolution also, for that very reason, but the editor of Evolution, Ernst Mayr, refused it publication there on the ground that they do not reprint articles. He would have printed a greatly shortened version, but I did not have time for that. Many statements made in recent years by Dobzhansky, in which a whole school of geneticists followed him, would not have been said if he had had an adequate relization of my paper.

I am returning the manuscript you sent me (though keeping a duplication of it), because it has various minor corrections of typographical errors, etc., that there is no use in putting down in a letter. Where your paper should be published is somewhat of a problem. I imagine that not very many people get to see Perspectives in Biology and Medicine. I don't know whether more of the people whom you would want to have see it would see it if you published it in the American Naturalist, but that is another possibility to be considered. I do not think it is too long (in its present length, at any rate) to appear in the Naturalist as a letter rather than a major article, and letters get pretty quick publication there. Other possibilities would be Science or Nature or Genetics. Of these, I think Science would be best if it agreed to publish the article quickly as a letter.

I am sorry I did not find out about the ideas which you brought back from the Pugwash Conference concerning what needs to be done in a national way to try to meet the international crisis. I wonder if your ideas on this matter have been changed by the events of the past few days. At any rate, I should like to see you for a little while, if possible, provided that the meeting of the NCRP, that was cancelled for Friday and Saturday of this week, is held at a later date, that permits my attendance at it.

Muller to Szilard, Oct. 2h, 1962, p. 5

Dr. Risk continues to hope that the Council for Abolishing War will allow Bayh to say that he has its moral support. It seems to me that this would help both him and the Council in these parts and in general.

With kindest personal regards,

Yours sincerely,

HJM:slh
enc.: MS

P.S. Allen Forbes has (since my writing the above) telephoned and gotten my name in endorsement of the telegram in which you and three others suggest that a bilateral 10-day moratorium be established. As I mentioned to Forbes, I hope that a request also be made to have some means set up of verifying to some extent that the moratorium, if accepted, is adhered to by both sides, but some stop-gap measure is certainly imperative now.

March 22, 1963

Dr. H. J. Muller Department of Zoology University of Indiana Bloomington, Indiana

Dear Dr. Muller:

I have been just re-reading the detailed discussion contained in your letter of October 24th of last year. I was in Geneva, Switzerland, when your letter arrived in Washington but it was forwarded to me there. I seem to recall that I may have written you upon my return from Switzerland in December, to thank you for the great trouble to which you went in discussing my very imperfect manuscript, but I see no notation on the letter indicating that I have in fact answered. Let me then say again, if I didn't do so before, that I very much appreciate your having gone to the trouble to make these detailed comments.

I expect to stay in Washington a while longer and I trust that you will let me know if you should visit Washington.

With kindest regards,

Sincerely,

June 19, 1963

H. J. Muller Department of Zoology University of Indiana Bloomington, Indiana

Dear Dr. Muller:

I meant to write you because I was told that you are retiring from the University of Indiana and that you will go to the City of Hope. I was wondering whether this is the City of Hope in Los Angeles and whether your going there represents a satisfactory solution of your problem.

I am inclined to think that I will move to La Jolla to be a Resident Fellow of the Salk Institute, and if you were in Los Angeles, then I might have an opportunity to visit with you on frequent occasions, which would give me great pleasure.

Sometime ago, you sent me a reprint of a major article which deals with the possibility of avoiding the degeneration of the human race (that might result from continued mutations, in the absence of adequate selection) through a change in social custom that would permit women to make the choice of the father of theirhichildren independent from the choice of their husbands. I would be very grateful if you could send me another reprint, Air Mail, care of Professor Victor Weisskopf, Director General, CERN, Geneva, Switzerland. I am flying to Geneva on June 24th and your reprint would probably not catch me in Washington before that date, particularly since June 22nd and June 23rd fall on a weekend.

Incidentally, do you happen to know what percentage of married couples are incapable of having children and in what fraction of these cases infertility is due to the seterility of the male?

Do you happen to know what fraction of the American population is congenitally normal mentally and what fraction is congenitally mentally defective or on the borderline of being mentally defective?

With kind regards,

Sincerely.

## INDIANA UNIVERSITY

BLOOMINGTON, INDIANA

JORDAN HALL XX 201

June 21, 1963

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

Dear Dr. Szilard:

By separate airmail I am sending articles of mine of the type that you requested to your address in Switzerland. I have written a number of articles along these lines, whose contents overlap considerably, and I am not sure which one you received from me earlier. It may have been an article that I had in Science, vol. 13h, p. 6h3-6h9, in 1961, but I omitted it since Science would probably be available in Switzerland.

Since I am answering your letter at once, and do not have access to my sources of information here, I cannot give you exact figures concerning infertility and mental defect. According to my recollection it is estimated that approximately one-tenth of American couples are incapable of having children, at least by each other, and the fraction of these cases in which the male is sterile has been variously estimated from one-third to two-thirds.

As for the proportion that are congenitally mentally defective, the figure depends of course upon the place at which you draw the line below which you classify the person as a mental defective or "feeble minded" person. Often this line is set at 70 I.Q. In that case the data show approximately 5% of the population to be mentally defective. The curve is, roughly speaking, a Gaussian one, but with a larger task below normal than above to the might of the

Unfortunately, news has gotten about that I am to go to the City of Hope, near Los Angeles, this year. Actually, I will be on active service at Indiana University until June, 1964, and for the year after that will have a position, that will give me a great deal of freedom, at The Institute for Advanced Learning in the Medical Sciences, of the City of Hope, Duarte, California (about twice as far as Pasadena from Los Angeles and in the same direction). If you are to be at La Jolla I will very much look forward to conferring with you sometimes. I am glad to know that you are continuing to be well e nough to move about so much as you seem to be doing.

With kind personal regards,

Yours sincerely.

HJM:slh cc sent to address in Switzerland

H. J. Muller

HOTEL DUPONT PLAZA WASHINGTON, D.C.

December 6, 1963

Dr. Steven Muller, Director Center for International Studies Cornell University Ithaca, New York

Dear Dr. Muller:

At last I have brought to paper the thoughts which I had expressed in the conversations which I had in London about six weeks ago. I am enclosing an unedited rough draft of the manuscript for your information.

Please let me know what you think of it, if you have an opportunity to do so.

As soon as I get to it, I shall write to Germany and send you a copy of my letter.

Sincerely,

May 20, 1964

Professor H.J. Muller Department of Zoology University of Indiana Bloomington, Indiana

Dear Dr. Muller:

Enclosed is a preprint which might interest you. Any comment which you might care to make would be appreciated.

On April 1st I joined The Salk Institute (see address given above).

When you move to Los Angeles I hope we shall have an opportunity of seeing you on frequent occasions.

With kindest regards,

Sincerely,

Leo Szilard

LS:jm

Enclosure