Department of Genetics
University of Wisconsin
Madison, Wisconsin
March 17, 1952

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

Dear Dr. Szilard:

I spoke to Dr. Puck and the arrangements have been made for my visit to Denver. I intend to take the night train from Chicago to Denver on Sunday the 30th of March. If it would be convenient for you I could come to Chicago that Sunday morning (11;00 AM) and we might spend the day talking.

Sincerely,

Norton

Norton

5650 Ellis Avenue

March 24, 1952

Mr. Norton Zinder
Department of Genetics
University of Wisconsin
Madison, Wisconsin

Dear Zinder:

I have your letter of March 17th. I think it would be important for you to see Harrison Davies in Chicago, the Acting Director of this Institute, who has expressed a desire to talk to you. You could do this on Sunday, and I suggest that you call him over the telephone upon your arrival at 11:00 a.m. at Museum 4-1014. If for any reason this Sunday is not convenient for you, you could talk to Davies on your way back from Denver through Chicago, provided you come through here not later than Thursday, for Davies is leaving town Thursday night.

I am not quite sure that I will be in Chicago on Sunday, but try calling me at the Quadrangle Club, Hyde Park 3-8601, and if I am not in my room ask them to page me in the library. In any case, call also Novick at Midway 3-1959.

If Chicago or Denver has anything to offer, listen to both and take a week or two to make up your mind.

If I don't see you Sunday I shall expect to see you on your way through Chicago back from Denver. With kind regards,

Sincerely,

Leo Szilard

LS/sds

cc: Mr. Davies

NZD

Department of Genetics
University of Wisconsin
Madison, Wisconsin
April 12, 1952

Drs. L. Szilard and A. Novick
Institute of Radiobiology and Biophysics
University of Chicago
Chicago 37, Illinois

Dear Drs. Szilard and Novick:

I have written today to Dr. Davies rejecting the offer he made to me. Although I've not decided definately where I shall go I felt that unless I was extremely serious about Chicago I would not want to bother the many people needed for references for a U.S.P.H.S. fellowship.

Dr. Puck made a very nice offer which pre-empted Chicago, a research instructorship for two years at $ 5000. I shall decide between there and Rockefeller when I go East this month and can speak to the various people involved.

Well I think the issue of the relationship of phage and F' is settled for the time being anyway. The filtration endpoint of the two were identical, ninety-nine percent of both removed at A.P.D. 120 mu. This gives a size of about 90 mu for both. Also in a repeat of the adsorption experiment both phage and FA reach saturation at the same point and the ratio of phage to FA is constant throughout in the supernates, 10 * phage particles per FA unit for one character. The maximum adsorption of phage was low, as I had predicted, only 7 particles per bacterium. I used up all of the concentrate available in this experiment and if I get a chance I shall prepare another to send to Putnam.

Yours sincerely,

Norton

Norton

* This ratio is the same for all FA preps. I have had.

5650 Ellis Avenue

May 13, 1952

Dr. Norton Zinder
Department of Genetics
The University of Wisconsin
Madison, Wisconsin

Dear Zinder:

Many thanks for letting me know by your letter of April 12th that you have decided against Chicago. I understand that by now you have decided in favor of accepting the position in the Rockefeller Institute. This is precisely what I would have done in your place.

With kind regards,

Sincerely,

Leo Szilard

LS/sds

April 8, 1957

Dr. Norton Zinder
The Rockefeller Institute
66th Street and York Avenue
New York City, New York

Dear Zinder,

I wonder whether you were able to talk to Lederberg about the experiment which we had discussed. When I last saw you, you suggested that we use the het strain and induce it to segregation. I do not know how easy it is to use the het strain, but it seems to me that we could obtain equally good results by simply crossing an HFR strain with an F^- strain, provided we introduce the following improvement over the original plans:

We use an HFR strain which carries a Lac_4 gene and a Lac_1^+ gene, and which is resistant to T_6 (and if need be also resistant to T_1 -- see later). This strain can make permease but not "the enzyme", β-galactocidase.

We shall cross this HFR strain with an F^- strain which is sensitive to T_6 and to T_1 and which carries a Lac_1^- gene and a Lac_4^+ gene. This strain is a cryptic; i.e. permease cannot be induced with TMG, but the strain can produce "the enzyme." (It would be very much preferable to use a Lac_1^- strain which cannot be induced by either TMG or <u>melibiose</u>; <u>a perfect cryptic</u>. I understand that the K_{12} strain, W_{677}, fulfills all of the requirements here listed, except that it happens to be resistant to T_1, and this might prove to be acceptable.)

Now if we assume that this F^- strain carries in the cytoplasm para-genes (which are produced by the Lac_4^+ gene which is carried by this strain) which will make "the enzyme" (in the presence of the TMG) but which are not self-duplicating, we should expect the following:

After the mating and segregation of the nuclei, the bulk of the population consists of two kinds of cells:

a) Cells which carry the Lac_1^- gene and the Lac_4^+ gene.

These cells cannot make the para-gene which produces the permease. They may have inherited some para-genes that can make permease if such para-genes appear in the cytoplasm in the short-lived heterozygotic condition subsequent to the mating.

All the parental type Lac_4^+ cells are sensitive to T_6 and can be destroyed by adding this virus a few generations after recombination has taken place, and most of the recombinants which carry the Lac_4^+ gene also will be sensitive to T_6 and can be similarly destroyed.

b) Cells which carry the Lac_1^+ gene and the Lac_4^- gene.

These cells will make permease. They cannot make the para-gene that makes "the enzyme" but they presumably have inherited para-genes that make the enzymes which were contained in the cytoplasm of the F^- strain. Most of the cells of this type (those which originate from a heterozygote in which there was one cross-over) will have inherited, together with the Lac_4^- gene, the gene which makes them resistant to T_6. Therefore, most of these cells will survive when T_6 is added to the culture a few generations after mating.

c) There will be a few recombinants of the Lac_1^+, Lac_4^+ type but these will be very few in number. These recombinants are dangerous for our experiment but I am assuming that they are very few in number, say 1 in 10^5 bacteria among the progeny. If this assumption should be wrong, then it might be necessary to get rid of these recombinants. This we could easily do if we could obtain an F^- strain similar to W_{677}, but in contrast to W_{677} sensitive to virus T_1 rather than resistant to it. We would then use an HFR strain which is resistant to virus T_1 (carrying the Lac_4^- gene and the Lac_1^+ gene). Practically all the "dangerous" recombinants would then be sensitive to T_1 and could be destroyed with T_1. Practically all of the progeny carrying the Lac_1^+ and Lac_4^- genes would be resistant to T_1 and would survive.

If we add TMG in a concentration of 10^{-5} M to the culture a few generations after mating, enzyme will appear mainly due to the cells of class b). At this concentration of TMG the wild type is induced to the ceiling, whereas the F^- strain here chosen is induced

only about 1/1000ths of the ceiling because it is a perfect cryptic. A less perfect cryptic K_{12} strain, like 2241, would go up at this concentration of TMG to about 1/100ths of a ceiling (even this might be tolerable). All this assumes that the cells are grown in succinate.

We should expect that when we add TMG at a concentration of about 10^{-5} M to the culture after mating emzyme will appear in the culture at a measurable rate. This rate should not depend on the number of generations that have elapsed since the mating. We would not go, and perhaps could not go, much beyond a thousandfold increase in population. I have not worked out the exact limit to which we could go, however.

Also I am not sure that we must use virus in this experiment, and we might get by without it.

The immediate question is: Is it possible for us to get an HFR Lac_1^+, Lac_4^- strain. If there is no such strain available, we would have to make it, and it would probably be better to make it from a known HFR by selecting for the Lac_4^- rather than use a known Lac_4^- and pick an HFR about which nothing is known.

Do you still think that it would be preferable to use a het? And do you think that we can get a het with one chromosome carrying the Lac_1^- (perfect cryptic) and the other chromosome carrying a Lac_4^- ?

I expect to be in New York for a few days after April 20th and it would be nice if we could reach at that time some decision about how, when, and where the experiment should be done.

With kind regards,

Sincerely,

Leo Szilard

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cc: Dr. Joshua Lederberg