The University of Chicago
CHICAGO 37, ILLINOIS
Institute of Radiobiology and Biophysics

6200 Drexel Avenue

October 27, 1949

Dr. A. R. Todd
Department of Chemistry
Cambridge University
Cambridge, England

Dear Dr. Todd:

Enclosed is a manuscript of a paper which will appear in the next issue of the proceedings of the National Academy and which will perhaps interest you.

Sincerely yours,

Leo Szilard

LS/sds
Enclosure

Chicago, January 6, 1953

Professor A. R. Todd
University Chemical Laboratories
Downing Street
Cambridge, England

Dear Professor Todd,

It has been some time since we had the pleasure of having you in Chicago. Today I am writing to find out if you can help us secure certain compounds which Novick and I have not been able to obtain in the U.S.A. Waldo Cohn, who is an old friend of ours, suggested that we write you.

As you will see from the enclosed reprint, Novick and I found that certain purine ribosides have a strong anti-mutagenic effect. They counteract at small concentrations the mutagenic action of caffeine and a number of other purine mutagens which we have investigated. They, in addition, reduce the "spontaneous rate" to 1/2 or 1/3. Adenosine, which is the most potent, has its full effect at concentrations above 5 mgm per liter. The purine nucleotides have only a slight effect but this might be due to low permeability. The pyrimidine nucleosides have no effect other than that which would result from 1% contamination with purine.

We would like, of course, to investigate the purine desoxyribosides. It is these compounds that we would hope to get from you. If preliminary tests indicate that they have anti-mutagenic effect, we would then try to set up to make them ourselves. We anticipate using between 1 and 5 mgm per experiment and should therefore much appreciate getting between 10 and 50 mgm samples, if it is possible for you to let us have such quantities.

Novick and I have no real understanding as yet of what the mechanism of this anti-mutagenic action is.

Yours sincerely,

Enclosure

Leo Szilard

LS/llt

February 13, 1953

Dr. J. Bodor
Secretary to Professor Todd
University Chemical Laboratory
Pembroke Street,
Cambridge, England

Dear Dr. Bodor,

I wish to thank you for your very kind letter of January 24. In the meantime the samples have arrived and we have begun using them.

Please convey my sincere appreciation of your help to Prof. Todd on his return.

Sincerely yours,

Leo Szilard

LS/llt

FROM
PROFESSOR A. R. TODD, F.R.S.

UNIVERSITY CHEMICAL LABORATORY,
PEMBROKE STREET,
CAMBRIDGE.
TELEPHONE: 5075.

24th January, 1953.

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

Dear Dr. Szilard,

Professor Todd is away from Cambridge on a visit to India, and I am therefore replying to your letter of 6th January. As requested I am sending you samples of the purine deoxyribosides.

Yours sincerely,

J. Brown.

Secretary to Professor Todd.

file

March 5, 1953

Prof. A. R. Todd
University Chemical Laboratory
Pembroke Street
Cambridge, England

Dear Professor Todd,

Dr. Aaron Novick has performed some preliminary experiments with the samples of deoxynucleosides that your secretary so kindly supplied to us.

As I wrote you earlier we had found that the ribonucleosides counteract very strongly the mutagenic effect of caffeine and several other purines and also cause a reduction in the spontaneous mutation rate.

Dr. Novick finds that the deoxynucleosides which you sent us are not nearly so effective. For example the reduction in mutation rate obtained with deoxyadenosine is equivalent to the reduction obtained with a 20 times lower concentration of adenosine.

Perhaps the deoxy-compounds really have no activity and the activity we observe is due to conversion of the deoxy- to the ribonucleoside by the bacteria. On the other hand, if there were 5% of ribonucleoside in the material you sent us, this too would explain the results. I wonder if you can tell us what is the maximum concentration of ribonucleoside that we might expect in the samples we have obtained from your laboratory.

With best wishes,

Yours sincerely,

Leo Szilard

LS/llt

BY AIR MAIL

AIR LETTER

IF ANYTHING IS ENCLOSED THIS LETTER WILL BE SENT BY ORDINARY MAIL.

CAMBRIDGE 7 SEPT 10 MCH 1953

6 POSTAGE 6

Dr. Leo Szilard,

Institute of Radiobiology and Biophysics,
The University of Chicago,

Chicago 37,

Illinois, U.S.A.

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Sender's name and address:-

Professor A. R. Todd, F.R.S.,

University Chemical Laboratory,

Pembroke Street, Cambridge.

From Professor A. R. Todd, F.R.S. University Chemical Laboratory,

Pembroke Street,

Cambridge.

10th March, 1953.

Dear Dr. Szilard,

I was most interested in the results you report in your letter of March 5th. It certainly is odd that there should be such a small amount of activity in the deoxynucleosides, but it may be a real effect. Obviously I could not guarantee that the nucleosides I sent you contained no trace of impurity, although they were considered by us to be pure in the ordinary chemical sense. In any case I find it hard to believe that there could be 5% of impurity in them, and even harder to believe that it could be ribonucleoside. The samples which you have were prepared from herring sperm deoxyribonucleic acid and I think it extremely unlikely that there could have been any noticeable amount of a ribonucleic acid in it. From your letter I gather that you were particularly interested in the deoxyadenosine; of all the samples which you had I should have thought that this was the least likely to contain any impurities. Obviously the point is am important one and it ought to be checked. Probably the easiest way would be to cross-check on a sample of deoxyadenosine obtained from some other source. I think you could probably get a sample of it from a University laboratory in the United States, or possibly from a commercial house like Schwarz. I should be very interested to hear if the effect shown by another sample is similar to that shown by ours, and if the two do not match up we might look into the matter further.

With best regards,

Yours sincerely,

Alex. R. Todd.

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

March 17, 1953

Prof. A. R. Todd, F.R.S.
University Chemical Laboratory
Pembroke Street
Cambridge, England

Dear Dr. Todd,

Many thanks for your very kind letter of March 10, which I discussed with Dr. Novick.

It seems to us very unlikely that we could obtain in the United States samples of deoxynucleosides which are anywhere near as pure as those which you sent us but if we are able to get any usable samples at all in the U.S. we shall run them just to see what we get.

We are still at a loss to explain why the ribonucleosides are effective and have not much hope to understand in the near future what is going on, in spite of the fact that we have many clear cut experimental results.

We are grateful to you indeed for the help you have given us.

With best regards,

Yours sincerely,

LS/llt

Leo Szilard