June 2, 1954

Doctor Seymour S. Cohen
Department of Pediatrics
University of Pennsylvania
The School of Medicine
1740 Bainbridge Street
Philadelphia 46, Pa.

Dear Seymour:

This is in answer to your very kind letter of May 26. The "bug" arrived. I hope you will forgive my repaying your kindness with further requests.

We had actually already done some work with your 15_T- strain and it was in part my own stupidity for being without it. Instead of making a copy form Luria's slant, I depended upon his, to provide me with starting material. We had performed enough experiments to convince ourselves that the system which you had uncovered really has great promise. We were able to obtain the synthesis of beta-galacosidase in these cells in the absence of thymine. Over the past year we have used a variety of other methods to inhibit DNA synthesis and have achieved similar results.

The caution which you urge with respect to such mutants as the uracilless is well taken. We also come across peculiar and profound effects of uracil depletion with both bacteria and yeast, which make definitive experiments difficult. But, by playing around with the kind of deficient growth, one can obtain cells which have their respiratory mechanism left intact. We have observed such modifications both with adenineless, as well as, uracilless.

Actually some of our most exciting results have come from yeast which possesses a free nucleotide pool which we have learned to play around with much as we have succeeded in the case of the free amino acid pool. The results we have obtained are extremely suggestive.

What I would like to ask you for is a copy of your paper on the thymineless mutant which is to come out in the June or July issue. We will send it back promptly. I have a postdoctorate-fellow, Ruth Ben-Ishai, working on this end of the story. Her time is short as she is supposed to return to Israel in a matter of two or three months. The time we would gain by having your paper on hand before it comes out in the Journal would be extremely important to her.

There is one other request I would like to make.....I understand that you have a constitutive mutant for the arabinokinase. I would very greatly appreciate receiving this and the parental strain. We have been examining the difference between constitutive and inducible mutants in the case of the beta-galacosidase system in E. coli, and have come up with the rather surprising findings that the inducible strain possesses an inhibitor which can stop enzyme formation in the constitutive counterpart. We have succeeded in purifying the inhibitor considerably and there is little doubt but that it is a protein. We would like to examine the generality of this situation with respect to other constitutive mutants, and yours is one of the few which I know of. I would also like to know where I could find a description of the methods which you employ for assaying for the arabinokinase. Finally, do you know of anybody who has any guanine or cytosine mutants?

I hope you will pardon these numerous requests, perhaps someday I can return your kindness and send you some yeast mutants.....what you would do with them, I don't know.....we still haven't found a virus for them.

With many thanks and kindest personal regards.

Sincerely yours,

S. Spiegelman
Professor of Bacteriology

SS:t