

January 13, 1953

Dear Dr. Anderson:

I have given very serious consideration to your letter of the 7th. I appreciate that it may not be convenient for you to alter your plans at this date, but regret that I must express some reservations to your travel plans.

A month's visit seems entirely too short to settle down to any serious work, and rather too long for any purely intellectual exercises. I should, I think, enjoy having you visit us but for long enough that we might practise an effective collaboration. Might I persuade you, if you are still free to do so, to extend your visit to three months (let us say 10 weeks at the least)? In view of the meetings this summer at Cold Spring Harbor and in Europe, this could best be accomplished by your starting here in April. If such an arrangement is impossible, I will, of course be happy to attend you for a visit of three or four days at your convenience. I do hope you can manage the longer visit, somehow, which would be, I am sure, to our mutual benefit.

Your recent note on the mechanism of ϕ 6 phage adaptation was of the deepest interest. While preparing the review "Cell Genetics and Hereditary Symbiosis", I searched the literature for clues on the mechanism of this adaptation, and found none. My brief comment on page 420, paragraph 3 was written in ignorance of your most recently published studies. The possibility that host-induced phenotypic modification may be closely tied in with the blending of phenotypes in phages issuing from mixedly infected bacteria seems still open, and quite intriguing.

We have recently been obliged to pay closer attention to such modifications in our own work. Mrs. Lederberg has been studying the genetic basis of these differences between hosts, e.g., *E. coli* strains K-12 and lines similar to 122. There seems to be a single factor, distinct from the λ locus itself to which lambda is closely connected, which determines both the sensitivity pattern of the bacterium, and the host range patterns of the phages grown on the different hosts. But this does not exclude a second phage as the underlying factor in host-induced-modification, though we have not yet found it.

Our PLT-22 phage also has an interesting adaptation to *S. paratyphi* B. The relative e.o.p. (plaque count on typhimurium/count on para.B) is about 10^6 for the original phage, 0.05 for the phage adapted to para.B, and 10^4 for this readapted to typhimurium. As the adaptation is not completely reversible, one suspects the superposition of two mechanisms, as in your own material. I would be delighted to see some further quantitative statements which might help to reconcile the two mechanisms. I have not yet done the single-step growth experiments which are, I think, necessary to verify the hypothesis of host-induced phenotypic modifications, as against the possibilities of selection of spontaneous host-variants even during the growth of a single plaque. The paraB strain is certainly, and the typhimurium very likely, carrying other phages and it will be amusing to test the bearing of these phages on the adaptation.

Yours sincerely,

Joshua Lederberg
Associate Professor of Genetics