WATSON

September 15, 1952

Dear Jim:

Esther and I were delighted to hear from you. Just what are you up to these days?

The reprint you asked for, and some you didn't, are in the mail.

Your letter raises the question of the F+ agent = a temperate virus. This seems purely a matter of definition, of which one can make an arbitrary decision. Curiously, I wrote a review called Cell Genetics and Hereditary Symbiosis (in press in Physiol. Revs.) which belabors this point, before we started running seriously into the question in our experiments. The main points that seem to be established are 1) that F+ is not lambda and 2) that the F+ agent is not the actual carrier of hereditary material, as Hayes originally suggested. This is important because we do have systems of genetic exchange, viz. transduction in Salmonella in which phage particles do act as gene vehicles for the host bacteria. In the transduction system, however, we have no difficulty securing the phage in cell-free filtrates, and apparently only single factors (i.e. very small chromosome fragments) are carried over on any occasion. In the K-12 crosses, the occasional complete diploids show that the entire genotype of each parent may participate, although I am still somewhat embarrassed by the rather regular elimination of two factors, Mal, S, out of the many that have been tested.

Unless great care is taken to avoid premature generalizations, there is going to be an unholy mess. Larry Morse here has picked up what seems to be a bon afide transduction in E. coli K-12, via lambda. This is quite different from the "sexual" system because 1) the agent is filtrable, i.e. lambda; 2) the transduced changes are usually unstable, and 3) so far only one marker gene has been able to work, which is the main reason it was not picked up before this. Obviously we are quite pleased to have this system, for we can apply the more powerful techniques of genetic analysis provided by "sexual" recombination for this special problem.

I am going to be very much interested in whether genetic transductions turn out to be a fairly general attribute of viruses, in situations where the latter can infect without destroying the new host. It will certainly raise some thorny questions in the delineation of the host genotype from that of the virus. The story is not too unexpected except for the last stage, how does the transduced fragment reenter the genotype of the new host? For a possible answer to this, I am looking to the examples of apparent crossing-over in pseudo-alleles which in some instances (A locus in corn; Q in Neurospora; Lac_1 in K-12) involves a genetic exchange between chromosomes by either exceptional double-crossovers or some new mechanism altogether.

Sincerely,

Joshua Lederberg