Dept. Genetics
University of Wis.
Madison 6.

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Dear Dr. Huxley:

It would take longer than your patience would endure to answer your questions fully, which only means, of course, that the field of virus genetics is still somewhat fluid. The best general source reference that I can give you (and I recommend it highly) is Luria's book, General Virology, published in England by Chapman and Hall. His views are close to yours and mine. Dr. Rhoads has told me that he gave you a reprint of my article on "Cell Genetics..." which, by now, is only slightly out of date.

On some specific points: I am rather suspicious of Rose's experiments on the site-specific viruses of amphibia, partly because he has been rather quiet about them himself. His data so far were startling, but not statistically impressive.

Luria's older idea that phage broke up into "subunits" (how does that term differ from units?) has been largely abandoned by its early proponents. The virus-infected bacterium may be considered as a growing population of virus nuclei, more or less panmictic. There is no evidence that the unit of replication and of mating is anything less than the whole genome of the virus. There is no better (or worse) evidence for partial recombination in phage than in higher organisms, except perhaps for the transient "partial heterozygotes" which Levinthal has studied, and reported on in Genetics. This is very close to Belling's older ideas on crossing-over in plants.

As to lysogenicity, there is growing (but admittedly not yet decisive) evidence which relates it to the transduction of other markers: i.e., we have a fragment of the bacterial chromosome which first synapses, and then exchanges with the homologous chromosome. I notice that Goldschmidt, in his recent book, also found this last step hard to believe, as I did too when it first came up. The hypothesis of copy-choice, i.e., that this exchange is not a physical displacement, but an incorporation of the specificity of the fragment at the next replication of the chromosome, may make the idea more plausible. There are, in a sense then three modes of transduction: 1) of "bacterial" genes, via DNA; 2) of the same, as incidental passengers in a virus particle, 3) of the virus nucleus itself, viewing this as a special segment of the bacterial genome.

I will send you some reprints, under separate cover, which develop these ideas; they are more fully stated elsewhere, in press. The favor of a regular exchange would be appreciated, if you are interested. We will be delighted to see you if you can visit us again next summer.

With best wishes for the New Year,

Yours sincerely,

Joshua Lederberg
Professor of Genetics

P.S. It is almost a truism that a cancer virus, or any other plasmid, is part of the cancer cell. How it originated, whether by "mutation" or by "hybridization" would be hard to decide.