

Madison, Wis.  
March 12, 1950.

Dear Cavalli:

I trust that the lambda-positive culture of your 123 strain arrived safely; they were sent some time ago. I must admit however that there does not seem to be any improvement in crosses.

I feel I owe you a letter concerning the radiation expts. The predominant effect of UV seems to be a haploidization, which is detectable even during the threshold dosage level. I think that haploidization can account for all of the first decade or two of killing, but the fraction of diploids among the survivors does not continue to drop off rapidly, but levels off at 15% or so. In absolute terms, the rate of ~~the transition from diploid to haploid~~ disappearance of diploids (i.e. to haploids or killed) also falls off with higher doses. This may be due to some heterogeneity in the diploid cells, but this is not reflected in the overall survival curves. On the other hand, some chemicals (particularly Acetic anhydride) have given complete haploidization. The survival curves for UV of ~~the~~ haploid and diploid cultures are superimposable.

Our X-ray facilities are limited, and I have been able to do only one extensive experiment (at the University of Chicago)-- up to 40,000 r. The log survival curves are essentially linear, but may show a concave-downward trend, which will have to be verified with higher doses. (Also Hollaender has found the O<sub>2</sub> effect for X-ray killing of bacteria....) The Results are exactly comparable to UV: haploidization; very few or no lethals.

Radiation effects are also duplicated by a number of chemicals: nitrogen mustard; formaldehyde; acetic anhydride; dimethyl sulfate, and some other alkylating agents of which I am less certain. Other chemicals and heat kill without any obvious change among the survivors -- methyl green; Ethyl carbamate; iodoacetamide. I think it quite reasonable to suggest that radiation effects are mediated either by short-lived free radicals, or by unstable compounds (viz. peroxides) which have a comparable reactivity by releasing such radicals or ions.

Some little progress on the segregation mechanism. A Lacv Malv diploid has been isolated. Segregation is usually complete in one step, but some partial segregants (i.e., Lacv Mal-) have been found. These may help to clarify the apparent hemizyosity for Mal which is usually found among the persistent diploids. At the moment, I am troubled by the possibility that the spontaneous segregation is not necessarily always meiotic, but may be the same sort of thing as is induced at a higher rate by UV. This would account for the apparent low frequency of crossing-over, and for the absence of complementary segregants in Zelle's single-cell pedigrees (one exception found recently).

Sincerely,

Joshua Lederberg