

UNIVERSITY OF PENNSYLVANIA  
PHILADELPHIA

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THE COLLEGE

Zoological Laboratory  
38th St. and Woodland Ave.

January 12, 1948

Dear Joshua:

I am sorry that I haven't had a chance to answer to your letter until now, but ending the semester and taking care of of bugs following the Chicago trip seems to have taken a good deal of time.

First of all, does kappa reproduce at the site of the gene K? As you pointed out, the only evidence on this point is provided by the kinetics of kappa increase. If kappa increases exponentially (in other words, if the amount of kappa produced is a function of the amount of kappa present) rather than by a certain quantity being produced in each cell per generation, then the implication is that kappa is self-reproductive. Whether this means that kappa does not reproduce at the site of the gene, however, depends exactly on what assumptions are made about how kappa increase occurs, how many macronuclear "genes" are present, etc. As you indicate, I do not think that the demonstration of exponential increase excludes the possibility of reproduction occurring at the site of the gene. (Although, personally, I don't believe it likely that kappa reproduction would be so restricted.)

It seems to me, however, that the evidence indicates very strongly that kappa does increase exponentially. Otter showed by the mathematical treatment which I mentioned that the average multiple by which the particles of kappa increase in each interfission interval is related to the slope of the line produced when the  $\log(-\log)$  of the proportion of animals with no particles is plotted against the number of fissions. Since straight lines are produced by plotting the experimental data in this manner, the slope, and the average multiple by which the particles increase in each interfission interval must be constant. Increase by a constant average multiple is, of course, just another way of saying exponential increase. The assumption, of course, must be made that the same exponential rate of increase must have occurred early in the experiments when the concentration of kappa was so great that the proportion of animals with no particles could not be measured. But this assumption is only necessary in order to calculate the starting number of kappa particles. The same thing can be shown in a less precise way using the Poisson series.

Another fact which bears on the exponential manner of kappa increase was pointed out by Dr. Sonneborn in the CSH Symposium. Killers growing six fissions per day retained a high

kappa concentration. Animals containing only a few particles of kappa also maintained a constant low concentration of kappa for many fissions at six fissions per day. The only explanation consistent with this fact is that kappa increases exponentially at a maximum rate of six doublings per day.

To tell you the truth, I am not a real expert on the mathematics of this business. I had difficulty in understanding the derivation of the equations which you sent. The derivation of Otter expresses the rate of particle increase in multiples of the number of particles occurring in each interfission interval. This, of course, would be constant for exponential increase; and for any case in which the particle concentration showed changes would be variable for non-exponential increase. In any case where the particle concentration were known, it should be possible to express the rate of increase in either way according to his equations. I wish I could send you the whole of his treatment now, but it is rather lengthy. However, a long discussion of it was sent to Stern to be published in Genetics (as a part of my thesis) about a month ago. So, assuming everything goes alright, it should appear before long. The <sup>complete</sup> derivation of the equations will be given by Otter in a separate publication in the Proceeding of the National Academy of Sciences--probably toward the end of this year. However, I have his derivation, and should you be interested after seeing the business in Genetics I'd be glad to make a copy of it for you.

It's rather hard to make this stuff intelligible without going into a good bit of detail, but I hope you'll be able to figure out what I have written.

Thanks very much for your letter, and let me know if you have any further ideas on the subject.

sincerely,

  
John R. Preer, Jr.