INDIANA UNIVERSITY
BLOOMINGTON, INDIANA

DEPARTMENT OF ZOÖLOGY

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Dr. Sol Spiegelman
Long Island Biological Association
Cold Spring Harbor
Long Island, N.Y.

Dear Sol:

Miss Fisher sent me the material from Lindegren and I have sent my replies back to her. I should be glad if you would look over my manuscript as well as my discussion with Lindegren so that you might use this material as a basis for your discussion of the relation of the kappa problem to the theory of gene action you proposed at the conference. You will see that in my answer to Lindegren I concluded by calling upon you to answer this question.

I too have done some thinking about this problem and I may say, for your information, that I am inclined to believe your theory will prove to be much more general than the relations we have discovered in Paramecium, although I am still unconvinced that a satisfactory reconciliation between our findings and your studies could be made along the lines that you discussed with me. I should like to have you look back into my paper in the Annals of the Missouri Botanical Garden and think over the remarks I made concerning the significance of nuclear dualism in Paramecium for the problem under discussion. I am inclined to lay considerable emphasis on that point. As I pointed out in that paper, I think the fact that we have in the Ciliates a very special situation which makes it possible to have the genes disintegrate in the micronucleus in a way that they could not get away with in cells lacking this particular type of nuclear dimorphism. I should therefore be surprised to find cases like the killer case, in which the gene cannot produce the corresponding plasmagene, occurring in other kinds of material. The scheme that you have proposed seems to me much more likely to be the general rule from my point of view. The very fact that we have this extremely unique situation in the Ciliates provides special opportunities for studying the situation when the conditions are different from the ordinary, that is, when the gene does not produce plasmagene. And the interest is heightened by the fact that we have very closely related varieties of the same "species" in which very likely your scheme is the one that operates. I should be very glad to get your reactions to these suggestions because I think in our discussion we ought to put on record the results of our considered deliberations rather than our initial reactions that we ~~might have~~ had during the heat of the conference.

I think you are under a false impression as to the uncertainty of our knowledge of the self duplicating capacity of kappa. The situation which you had considered final, namely, what has already been published about kappa, is still the rule and it is important to keep that in mind.

What we have done in recent months is to make a deliberate search for really rare exceptional conditions, for I am a great believer in the validity of Bateson's old motto "Cherish your exceptions". It is certainly a fact that, in the overwhelming majority of cases, when K is replaced by k, kappa disappears very rapidly in the way I have described in my published accounts. We had to make a long and careful search before we found any apparent exceptions to this and it is these rare exceptions which we are now analysing. Since I wrote to you last we have begun to get our first and preliminary results on the genetic analysis of one exceptional case, and in this case it appears, contrary to my expectation, that the genotype of the clone under investigation is actually kk, in spite of the fact that a small proportion of the individuals of the clone remained killer for a remarkably long time before all turned to sensitives. These are only preliminary results and I do not want you to consider them final by any means or even typical of the exceptions. We are proceeding with the analysis of this material and I shall keep you informed of the results. There is clearly something very unusual in these cases and we do not yet have the clue as to what it may be. The main point to keep in mind, however, is this: cases of this sort are not typical, they are rare and they may well involve some exceptional conditions which will not only be satisfactorily explained in time but which may provide a means of gaining further fundamental information about kappa.

I do not know how familiar you are with the history of genetics, but it may be worth while to compare the case I have been discussing with the situation in Drosophila genetics about 1912,- to compare small things with great. At that time the chromosome theory was just getting on its feet. It had already proved its value by the many predictions that were made and fulfilled, when Bridges ~~discussed~~ discovered certain exceptional types of heredity which seemed at first to be practically a death blow to the general ideas. In his situation also the exceptional results were very rare. The whole matter, however, was eventually resolved when it was shown that he was dealing with a failure of the x chromosome to segregate at meiosis, yielding the condition which we now know as non-disjunction. The exception, therefore, turned out to be actually one of the strongest proofs for the general rule of chromosome determination. Of course, I cannot be sure that the exceptions I am dealing with now will turn out so happily, but it seems to me that this is entirely possible. I am inclined to believe that anything that occurs so rarely as as the type of thing I am now studying should not, for the present at least, be considered as weighty evidence in deciding whether the general rules that have been discussed concerning the self duplication of kappa should be held in abeyance. Of course, this is a matter which you will have to use your own judgement on, but I ~~would~~ want you to know the facts fully and also how they appear to me.

Even if others are led to minimize the importance of my early findings, I shall of course continue to seek out exceptions and analyse them because of my faith that this is good methodological procedure.

With very best regards and good wishes,

Cordially yours,

Tracy