

June 1, 1956

Dr. Philip E. Hartman
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Dear Dr. Hartman:

Thank you for your letter of May 23. I will be very happy to have an opportunity to discuss these matters with you at Baltimore. However I hope you will not take it amiss if I offer a comment about the writing of review articles. I know from my own experience that it is very tempting to try to keep up with the very latest work at the time of writing. However I have had enough sad experiences of my own to want to warn you against overdoing this. Material in published form is on the record for everyone to see and for you to make your own interpretations and there can be no later question about it. The responsibility is clear. Quite the opposite is true of attributions based on hitherto unpublished work, personal communications, etc. It would be difficult, for example, for me to give you at this time a sufficiently complete account of the work on abortive transduction of motility for it to be possible to write a completely responsible account of it. I would therefore urge that you not consider my remarks as being on the record and that you confine any attributions in your own account to work that has been published. There are, as you know, a few minor references to these studies in the Oak Ridge Symposium article and in an abstract in Genetics and perhaps a few other places. Right now both Stocker and I are busily engaged in writing up this material in definitive form but it is somewhat more complicated than your summary in the letter and it has been a rather difficult job to collect this material for proper publication. Off the record, Stocker's view would postulate two levels of unilinear inheritance. At the first level a particle is transmitted passively from generation to generation which confers motility on the cell which bears it. We call this simply a motility-conferring particle and the most plausible interpretation of it is that it is a single flagellum or flagellar Anlage. However a single act of transduction can apparently result in the formation of a large number of motility-conferring particles and the complexity arises from attempts to define the source of these many single particles. Dr. Stocker suggests that at transduction a particle which may be considered a non-reproducing gene is transmitted, we call this an E particle, that the E particle is also inherited in unilinear fashion and that the E particle has the property of manufacturing motility-conferring particles. Then at cell-division a sib to the cell which carries the E particle will contain a number of motility-conferring particles. The latter are then sorted out until there is one per cell and we then find unilinear inheritance of motility. Stocker and I differ only in our view in the intensity of the proof for the unilinear inheritance of an E particle. In my own experiments I have had some results which suggest that the property of producing many motility-conferring particles is not inherited in quite so straightforward a fashion as would be postulated on Dr. Stocker's interpretation. However neither of ~~the~~ is supported by entirely critical evidence and Dr. Stocker's picture must be considered as a rather plausible if not critically proven hypothesis. The question that I would raise is (a) whether unilinear inheritance really must imply the transmission of a single particle inasmuch as we know so little about the basic morphology of cell-division and the rules governing the transmission of

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cellular components. After all, "particle" simply means a rule of cell-division and the fact that in certain countries the inheritance of land is entailed does not mean that an acre is a particle. My second question is whether, given that E and MCP are particles, we have critical evidence to identify them respectively with a transduced gene and with the flagellum respectively. As I said before these are plausible viewpoints but they have not yet been subjected to really critical analysis. Rather than being a gene for example the E particle might simply be some organized product of the gene action. In that case we do not have to postulate the occurrence of "sterogenes" but merely that once a gene has been in a cell it may leave behind residues of its action even if it itself should fail to be incorporated into the chromosome. It would be difficult to design experiments that would distinguish between the inheritance of the transduced gene and that of some of its residual products. As I indicated before, these remarks are for your own information and I hope you will not quote them as communications for your review although of course you may make whatever use of them you wish in constructing your own interpretations. Another point on which Dr. Stocker and I differ is the notion that only cells carrying several MCP's are capable of swimming in semi-solid medium. The fraction of cells in a clone which form trails in agar depends so much on the precise concentration of the agar that I doubt if any qualitative distinctions can be made on this basis. The non-branching of trails is probably a consequence of the use of rather hard agar in which only a small fraction of cells can swim and also to the fact that there are chemotactic orientations in the agar away from the site of inoculation. When the experiments are done differently highly branched trails can be found. As to your question whether non-motile strains have been subjected to recombination, I think that there is an explicit answer on this point in the paper by Stocker, Zinder and myself in the Jour. of Gen. Microbiology. Trails have been found in every combination where one also found the occurrence of stable transductions of motility. As you probably know there has been only one example of recurrence of identical Fla⁻ mutations and this pair of seemingly allelic mutants, which were recovered from natural sources, may in fact have had a common origin. The Fla⁻ mutants appear to occur in two groups. One of them is a cluster closely linked to the H of one locus but we have been unable to get definite evidence of their linkage to one another by any direct paths. The other Fla⁻ mutants may or may not be linked to one another but are ~~absolutely~~ not linked to any common marker as far as we know.

With best regards,

Yours sincerely,

Joshua Lederberg
Professor of Genetics

JL/mv

P.S. I don't want to start a terminological squabble either here or at Baltimore nor do I intend to prescribe your own choice of definitions. However if you intend to use the term transduction in its narrower sense of phage mediated transduction I hope you will not make the error which has appeared in the literature of attributing that definition to me. As I think should be perfectly clear from the occasion of the first use of the term in this context, which was in a review article in Physiological Reviews, transduction was intended to name a hypothesis, namely the possibility of transmission of

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hereditary fragments from one cell to another. At the time the word was first used in this laboratory we had no notion that phage played a material role in the Salmonella example of transduction and it seems to me rather important to emphasize the genetic unity which has been demonstrated many times between transduction as we see it in Salmonella where phage is the vector and transduction by DNA which is exemplified in the pneumococcus transformation. I would also object to an error that I have made myself in referring to "a transduced cell". This may seem like grammatical purism but I think that one would be likely to lose sight of the process that we are trying to follow if we are careless in the use of these terms and I am very sorry that I was not more careful myself in this particular regard. I think that one must confine transduced to that which is transduced, namely the fragment, and refer if you like to transformed cells or transduction clones for what have you.

J. L.