THE RICE INSTITUTE

HOUSTON, TEXAS

DEPARTMENT OF BIOLOGY

5 November 1952

Dr. Joshua Lederberg
University of Wisconsin
Madison 6, Wisconsin

Dear Dr. Lederberg:

Thank you for your letter of October 31. I am sorry that I cannot agree with the last statement in your letter: "The classification of these elements is entirely debatable".

Nuclear genes of course would be distinguishable from cytoplasmic genes (or any other cytoplasmic bodies) by their segregation. Genes (no matter where found) would be distinguished from autocatalysts by the fact that (1) genes are capable of mutation; autocatalysts are not, (2) genes cannot arise <u>de novo</u>; autocatalysts can (under gene control).

The identification of an autocatalyst is sometimes possible (as I have shown in the case of mating type in Paramecium), and the existence of a plasmagene is therefore not demonstrated until a possible autocatalyst is ruled out.

Genes are distinguishable from viruses or viroids by the fact that (1) genes are units of inheritance (that is, they are not divisible by crossing over, or by any other known mechanism, into ~~a~~ smaller units that retain the properties of self-reproduction and mutation, (2) viruses and viroids are organisms, and contain genes (or units corresponding to genes) as parts of ~~their~~ organization). They have a regular life cycle, including sexual reproduction, essentially similar to that of other organisms (see Luria, C.S.Harbor Symposium, 1951). Their hereditary mechanism is probably essentially similar to that of other organisms (see Hershey, C.S.H. Symposium, 1951). Moreover, they are of exogenous origin, not endogenous.

I have never heard of the yellow fever virus or any other highly pathogenic virus in animals being referred to as a gene. It is only when the virus is parasitic or symbiotic ~~as~~ in a bacterial cell, or when it has previously been confused with a gene, that the problem of nomenclature arises. It is true that in some cases we may not yet have determined whether a virus, a viroid, or a gene is determining some phenotypic effect. But when we find that an agent has the properties characteristic of viruses (as the agent responsible for CO_2 sensitivity in Drosophila) then we should call it a virus.

Of course, if we call any self-reproducing body in the cytoplasm a plasmagene, then by definition viruses are genes. However, one of the problems that confronts geneticists today is whether the cytoplasm contains hereditary units similar to nuclear genes. I do not see that we help solve this problem by calling a virus a gene, simply because it has the capacity of reproduction. Nor do I see that we gain anything by continuing to call kappa~~s~~ a gene, if we admit that it is a symbiont related to a Zoochlorella. We might just as logically call the Zoochlorellae of the green hydra genes.

It is true that we sometimes cannot readily distinguish between the effects of genes, viruses, and other cytoplasmic elements. Such cases require further analysis before they can be said to have any bearing on the problem of cytoplasmic genes. At present, however, there is no conclusive evidence that I am aware of, ~~regarding~~ of cytoplasmic genes in the animal kingdom. As for the plant kingdom, the situation is different. Here we find plastids. But even in the plant kingdom, there is no clear-cut evidence of cytoplasmic genes apart from plastids. In my opinion, the cases of cytoplasmic inheritance found in Epilobium and Oenothera are without doubt tied up with the plastids.

Would you be good enough to furnish me with the references to Wollman (1925), and if convenient any other "similar speculations" that you refer to in your letter?

Yours sincerely,

Edgar Altenburg

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