November 7, 1952

Dr. Edgar Altenburg
Department of Biology
Rice Institute
Houston, Texas

Dear Dr. Altenburg:

I certainly do agree that one can make an unambiguous definition for a gene, namely that it is a unit according to the best analytical techniques that one chooses to apply. As you say, we can locate genes in the nucleus by their segregation in parallel with the chromosomes. I do not believe that there is strong evidence for the location of single genes in isolation anywhere in the cell, and by this strict definition, viruses are by no means genes. You will admit that they do have genetic components, and that it many cases they have at least quasi-genetic functions. Whether a given viroid is of exogenous origin is, on the one hand, not easily proven, and on the other not much more pertinent than the exogenous origin of chromosomes in the establishment of hybrid complexes such as Nicotiana, Gossypium, or Triticum. The important thing is whether the imported genetic material constitutes an adaptive or potentially adaptive accretion to the genotype; i.e., whether the new complex can now constitute a unit for adaptive evolution. I do not believe that we are in serious disagreement, although we may prefer different modes of expression. My only objection to calling sigma a virus, for example, is that it may tend to discourage geneticists' interest in it, just as its designation as a "genoid" has probably hindered the fullest application of microbiological techniques to it. I have expounded this kind of treatment in greater detail in my review, which should be in print momentarily, and I will send you a reprint as soon as possible. you will find that I have gone to the logical conclusion of treating the symbiotic chlorellae not as genes (i.e. units), but as genetically interesting.

The one point on which I do not fully understand your views is the distinction of autocatalysts and genetic factors. The criterion of mutation may be no more than a reflection of the complexity of organization [the argument is in the review]; Genes have arisen de novo (in the strictest sense of the term, from non-living material) at least once. I am willing to concede that the chromogenes have an unusually well developed organization and technique of self-perpetuation if provided with the particular environment of the intact cell, but the elementary reactions of this perpetuation can hardly fail to be built up from autocatalysts. I do not think that it will be possible to draw a definitive line between progressive organizational hierarchies, which will identify the gene. In practice it may be sufficient to characterize the extremes, but it would be unfortunate to exclude the pertinence of one for the other.

Yours sincerely

Joshua Lederberg

I may have been too vague in referring to "similar speculations"— you may have had different aspects of your discussion in mind. I had in mind largely a reversal of Darlington's evolutionary sequence of Johnson's "viraplasm" and Darlington's plasmagene-"provirus"-virus hypotheses. More particularly, the following references may be of immediate interest to you:

Johnson	J. Agr. Res. 64:443 1942 (and prev.)
Green	Biodynamica II (39):1-8 1938
Meyer-Abich	Bibliotheca Biotheoretica 5:1-206 1950
Wallin	Symbionticism and the Origin of Species. Williams&Wilkins 1927
Burnet	Austr. J. Exp. Biol. Med. Sc. 6:276; 14:27 1929, '36 also, Biol. Rev. 9:332 '34
Wollman~~xxxx~~	Ann, Inst. Pasteur 39:789 1925

There are probably others in the review.