

November 28, 1961

Dr. Francis H. C. Crick
Cavendish Laboratory
Free School Lane
Cambridge, England

Dear Francis:

This is just a brief note to express my deep admiration for the paper on the genetic code which I recently received and found of greatest interest. You and your colleagues are to be congratulated on a very pretty piece of reasoning and a magnificent experimental contribution.

A few thoughts occur to me, which undoubtedly you have also thought of. One, is the obvious prediction from your mechanism that, if leaky phenotypes can occur, as a result of either deletion or addition mutations, none should be found at the beginning of a cistron. They should rather tend to cluster near the end. This, of course, assumes that it is not true, in general, that the last several residues in a polypeptide are essential for its function. But, in any event, the correlation should hold with respect to the formation of CRM material. Also, I found it a little surprising that you didn't cite the paper by Dientzis (PNAS, 47, 247-261) which supports the idea very strongly that the transcribed code is indeed read sequentially and always from the same end. While not perhaps necessary for your arguments, it supports them by implication.

One of the questions we have been trying to get at is whether the genome is read at random or in some sequential order. We have been using hybridizability of RNA made during different periods of infection and examining competitive interaction. Our data are sufficiently clear, at present, to state that some RNA molecules synthesized late in infection do not compete with hybridization of molecules made early. We are trying to push this further in an attempt to see whether we can define the stage of infection with the type of RNA molecule which is synthesized.

I understand from John Kendrew, whom I saw in Rome, that you have some plans to come to the States in the not too distant future. I sincerely hope that if you do, you may find it possible to arrange for a visit here. I can assure you of a very warm welcome and a profitable stay.

With kindest regards,

Sincerely yours,

S. Spiegelman
Professor of Microbiology

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