

January 13, 1956

Dr. W. E. Knott
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Dear Gene:

It was very thoughtful of you to send me an advance copy of your review, which I received a few minutes ago. It came at an opportune time, for Cavalli and I have been writing amonograph on "Genetics and Chemotherapy" and had planned a chapter on "adaptations in individual organisms" for which your review will be a wonderful supplementary source. I not, however, that you did not spend much time on pharmacological accomodation or "tachyphylaxis", but perhaps you have accumulated literature references on adaptive responses a) of isolated organ preparations or b) of whole animals, without the demonstration of clearcut biochemical changes, which were not appropriate for the review. If you can advise me on any material of this kind, I would be very grateful to you, as I have been able to find almost no scientific work on these topics beyond what is mentioned (e.g., the addiction problem). I have not yet made th close study of your article that I intend.

There was one philosophical point I did not grasp clearly. At p. 124 you seem to approve of the idea that inducing substrates act as models or components of the adaptive enzymes; elsewhere you take pains to emphasize the role of the physiological background. Perhaps you may understand my question more clearly if you read the enclosed commentary, which was offered at the "International Symposium on Enzymes" at Detroit in November. Unfortunately, I will have to trouble you to return the ms. copy, but I would be interested in your point of view. I was actually quite startled that Monod seemed to favor the idea of substrate as template, as he has contributed much of the evidence against it. Elsewhere I had expressed my dissatisfaction with the concept of enzymatic adaptation, but to call this induction, as is now the fad [and with the implied connotation of the word] is jumping from the pan into the fire,

Sincerely,

Joshua Lederberg