

May 7, 1945

Dr. Van R. Potter
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Madison, Wisconsin

Dear Dr. Potter

Permit me to express our appreciation for the interest expressed in your letter about the adaptive enzyme work. Mr. Lindgren suggested that I undertake to answer your letter since the enzyme duplication aspect was initiated and is still being prosecuted in my laboratory.

Unfortunately the particular reprint you requested is not as yet available. However, you will receive under separate cover several reprints which are at hand which deal with various aspects of this problem. The one entitled "The Physiology and Genetic Significance of Enzymatic Adaptation" will perhaps be of particular interest to you since it summarizes the earlier work and discusses in some detail the evidence for, and significance of enzyme duplication. This represents the paper I read before the conference on gene action in microorganisms which was held here in St. Louis early in February.

It was some time ago that I studied your extremely interesting article on the cancer problem which appeared in the last volume of *Advances in Enzymology*. At the time I was already well into the experiments which led to the enzyme self-duplication hypothesis. I was therefore struck particularly by one aspect of the theory of cancer you presented viz; that enzyme X which was assumed to be almost identical with the "cancer virus" itself possessed autosynthetic capacities. Since enzyme X was presumed to be a normal constituent of cells this meant that you were willing to assume that there do exist units (enzymatic in nature) other than genes and viruses which are autosynthetic. Needless to say, I regarded this assumption with great sympathy and admiration.

The relation between the work on enzyme duplication and the cancer problem was noted by several people who attended the gene-action conference at which I read the paper. Unfortunately time limitations prevented a full discussion and furthermore only one person (Jess Greenstein) at the conference was working directly on the cancer problem. You will note by the way from the discussion at the end of the paper that the classical geneticists present were approaching the self-duplication hypothesis with great caution, sort of poking it with a mental 10 foot pole to see if it would bite. To get them to come that close, I was told, was a great achievement.

With reference to the question you raised of whether it would be feasible to explore the cancer angle of the work let me state that I am eager to expand my experiments in any direction which it is thought would give promise of throwing any light on this problem. To give you some idea as to the direction being taken by the research at present I have enclosed a copy of a research program I drew up several

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months ago and which is being followed along with several other things which have since cropped up.

I may be mistaken but it is my feeling that the general nature of the program is fixed by the nature of the phenomenon rather than its ultimate use. In other words, even were the cause of cancer the primary question being considered, the initial stages of the investigation of enzyme duplication would remain pretty much as outlined. I am however open to other ideas on this point and would appreciate hearing from you concerning it.

At present I have one full-time assistant with me. If I could receive further support the work would undoubtedly go faster since we could then do our investigations in parallel rather than in series and we could undertake certain experiments which have been laid aside as too prohibitively time consuming. If you think the work as outlined would receive the support of any of the cancer foundations I would be grateful for any information you could give me.

I wish it were possible to get together with you in the near future for a talk. I have wanted to do so for some time and was almost successful about four months ago. I will try again and hope for better luck. Again, let me thank you for your kind letter and assure you that I will greatly appreciate any advice you can give me on the matter.

Sincerely yours,

S. Spiegelman

SS/McK