

Pollock, Martin

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Dr. Martin Pollock  
Medical Research Council  
The Lister Institute  
Chelsea Bridge Road  
London, S. W. 1, England

Dear Dr. Pollock:

I have received your letter of March 18th, as well as the enclosed copies of your paper, for which many thanks from myself and from my colleagues.

It is quite obvious from your letter that we have indeed many things to discuss in great detail. Your results with purines and pyrhalidines is very exciting indeed, as well as very gratifying, as you can well imagine. We have been obtaining a rather large amount of information on the phosphate metabolism of the yeast cell under various conditions, primarily using tracer phosphate to study these problems. At present we are concentrating on examining what happens when the cell is synthesizing new protein.

Most recently we have been successful in transforming a genetically negative (that is to say, completely unable to adapt to galactose under any conditions) yeast into one which has acquired this ability. This has been accomplished by incubating such cells with cell-free extracts from adapted genetic positives. We have been trying to accomplish this result for some time but have only recently succeeded in doing it in a marked strain, which insures that the transformed strain is the negative one with which we started out. I shall tell you more about this when I see you, and probably will report these results in Copenhagen if they are ready.

With reference to Sevag, it is difficult to say how seriously he is taken over here. He is certainly not taken seriously by anyone who is familiar with biochemistry because, not only in his reviews but even in his own papers, he commits horrible blunders. He has apparently a genius for getting himself involved in sophomoric semantic difficulties. It is impossible to answer in one article all the specious and illogical arguments raised by Sevag. The unfortunate thing about it is that it is certainly desirable to raise some of the questions he did with reference to the nature of enzymatic adaptation, but the valid objections are so buried in a mass of

Sevag's own personal misinformation, that it is difficult to discuss them seriously. We are, however, taking the opportunity, as we write up our own material, to discuss certain aspects of Sevagomania.

We have a paper coming out in the Archives of Biochemistry which offers rather conclusive evidence that the apoenzymatic or protein moiety of the enzyme system is the one that is modified in the process of galactose adaptation. In this paper we take Sevag to task on several points. We are also taking the opportunity to discuss other portions in another paper on the relation between metabolism and enzymatic adaptation. In a sense this is necessary because the problem of enzymatic adaptation is attracting the attention of more purely biologically-minded people whose biochemical training is relatively meager. Such people could only with difficulty evaluate the validity of Sevag's arguments.

One more point which I should like to answer briefly. You raised the question of why formate could not provide the energy for synthetic activity, although it apparently is sufficient to function in the reduction of nitrate. We know this about compounds, the oxidation of which leads to synthetically-useful energy; the energy of their oxidation is trapped by a simultaneous formation of an organic phosphate bond. This is one thing that it would be difficult to imagine formate doing, so that one would guess that although it could be oxidized, since there does not exist any way by means of which you could couple the phosphorylation to it, that such oxidation could not lead to the accumulation of energy-rich bonds which could then later be used for synthetic activity.

I shall leave it at that since undoubtedly we will get the opportunity to discuss this more fully and more leisurely.

Sincerely yours,

S. Spiegelman

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