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REFER TO:

Tuberculosis Research Laboratory,
411 East 69th St., New York 21, N. Y.

November 21, 1951.

Dr. Joshua Lederberg,
Department of Genetics,
The University of Wisconsin,
College of Agriculture,
Madison 6, Wisconsin.

Dear Joshua:

I thought you might like to know about the further follow-up on some of your mutants, though I don't suppose the details of their metabolic behavior are very important for your purposes.

W-1427 is a quadruple aromatic auxotroph blocked at the earliest known site: it responds well to shikimic acid or its precursor, 5-dehydroshikimic acid, and poorly to the next precursor, which we call Compound W. like our strains of that type

SW-38 accumulates a large amount of Compound Z1 and small amounts of shikimic and Z2, while W-1104, W-1426 and W-1150 accumulate Z2 and shikimic, without any Z1.

Z1 and Z2 are biologically inactive derivatives of shikimic acid that yield shikimic acid on autoclaving with acid. Z1 seems to arise at a later step since our several dozen mutants fall into the same groups as yours, namely, accumulators of Z1 plus a trace of Z2, or else of Z2 without Z1.

One exceptional property of your strains is that W-1426 is an almost pure Z2 accumulator with very little shikimic, and is uneffected by the presence or absence of citrate in the medium. This is the behavior of one of our Aerobacter mutants, whereas our E. coli strains of this group tend to accumulate a much higher ratio of shikimic, and the ratio is increased by the presence of citrate. I don't know what all this means metabolically, but it suggested that W-1426 might be an Aerobacter rather than a coli. On testing for this possibility, we find it to be an intermediate; in contrast to Aerobacter it does not utilize citrate as a whole carbon source, but in contrast to our W coli its response to glucose is accelerated by citrate.

PF-21 turns out to be no longer an unknown, since it responds well to B_{12} or methionine. We found it to be quite unstable and mixed, so if a pure culture derived from it would be useful to you I would be glad to send it back. The identification of this mutant proved difficult since it is inhibited by components of the usual mixtures that we are at present tracking down. I find this of more than casual interest since the existence of a B_{12}/methionine requirement in coli and B_{12}/desoxyribosides in lactobacilli has presented something of a mystery. The presence of the B_{12}/methionine requirement in a Pseudomonad might be worth a brief note somewhere. Since this is your mutant, how would you feel about it? I would rather mention it in the course of some other paper, but unfortunately have dropped B_{12} for the time being. Incidentally, you might be as amazed as I was to learn that at Merck they run 2,000 assays a day with our B_{12}/methionine strain. Just tell that to your dishwasher!

PF-11, which requires a pyrimidine plus citrulline, is interesting in utilizing orotic acid as a pyrimidine; our corresponding coli mutant does not. I got PF-11 and PF-21 confused in my letter of September 28th and hope you will make the correction. PF-21 is leucine plus B_{12}/methionine.

I wonder whether you could give me an answer to the question raised in my latter of October 10th as to whether the methionine plus lysine requirement of W-1069 arose from a single mutation. I would like to mention this fact in discussing POB function at an ACS symposium on B vitamins in Texas next month.

I hope the washed agar proved satisfactory; if you want a little more we would be glad to send it, and if you want a regular supply the recipe is easy to follow.

I thought you might be interested in the enclosed manuscript, which is being submitted as an editorial in Public Health Reports. It represents an effort to disseminate Truth among the Masses.

Have a nice Thanksgiving.

Sincerely yours,

Bernie

Bernard D. Davis

BDD/hl