



FEDERAL SECURITY AGENCY
PUBLIC HEALTH SERVICE

IN REPLYING, ADDRESS THE

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

December 7, 1950.

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

Dear Joshua:

To answer one question raised in your letter of October 11th, we reported carbon source mutants of *E. coli* in the first issue of *Microbial Genetics Bulletin*. To answer another, I don't think any of our experiments would have revealed a mutant with the sort of instability that you describe for the Mal⁺. Finally, did I ever get around to sending you the W strain you requested, as well as the stack of mutants? I have an uneasy feeling that I put your letter away and may not have answered this request.

After a very dull period for a couple of months several interesting things have turned up recently. You may recall that one of the weaker points in the shikimic story has been the postulated interference by compound X with the subsequent conversion of shikimic acid to tyrosine and phenylalanine. Enclosed are two pictures that give the answer. The addition of X, in the low concentrations available some time ago, failed to inhibit the growth of the quintuple mutant on shikimic. From the quadruple, however, which accumulates X, we isolated some spontaneous secondary mutants appearing in the presence of shikimic, and found that these would now grow in the presence of shikimic alone, and had simultaneously lost the ability to accumulate X. These are labelled QdM₂. Since they differ from the parent Qd as just described, and also differ from the earlier blocked Qt mutant in being unable to respond to X, it therefore seemed possible that they might have a double block both before and after X. This interpretation is verified by the appearance of a third sub-strain in the presence of excreted X, noted in the photograph as QdM₃. This strain on isolation proves to be indistinguishable from the Qt strain, responding well to either X or shikimic. With the QdM₂ strain, which neither makes nor utilizes X, one of the enclosed pictures shows negative syntrophism, the X excreted by Qd inhibiting the adjacent growth of QdM₂ on shikimic. The other photo shows inhibition of response of QdM₂ to added crystalline X, which has recently been isolated by Dr. Salamon. The inhibitory ratio is about 1:1.

Dr. Joshua Lederberg

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The other interesting thing to turn up recently is the explanation of the mode of action of PABA, which is a useful chemotherapeutic agent against rickettsiae in relatively high concentrations. It acts as a competitor of POB in a ratio of 100:1. We have here an interesting situation in which PABA is a metabolite at a very low concentration; a source of POB for the quintuple mutant at a slightly higher concentration; and an antagonist of POB with wild type or mutants at much higher concentrations.

One other odd thing: Some of the mutants picked up by the class this past summer turn out to accumulate a biologically practically inactive factor which becomes shikimic acid after autoclaving. Strange things grow in California!

Incidentally, in the hope of keeping the literature clean, I got Plough's remarkable set of alternative responding mutants for verification. The only one of the alternative 17 responses that he lists which we can repeat is the well-known one of cystine or cystine/methionine. Half the rest had "reverted" in his lab, several of the mutants ^{he sent} were mixed cultures, and the remainder showed only a single response. I hate to pester such a gentle appearing fellow; however, I sent this information to him and do hope he will retract some of the nonsense in print.

Werner and I send the Season's greetings to you and Esther.

Cordially,



Bernard D. Davis

BDD/h1

CRYSTALLINE COMPOUND X
Stimulates Quintuple (Qt)
Inhibits Response Of Qd secondary (Qd M₂) to Shikimic



Shikimic 30 %/ml.



X 30 %/ml.



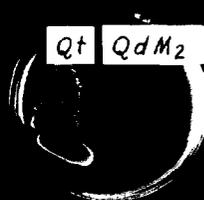
Shikimic 30 %/ml.
X 30 %/ml.



Shikimic 10 %/ml.

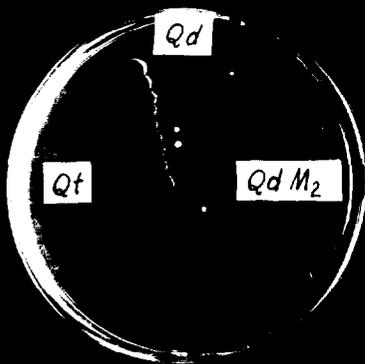


X 10 %/ml.

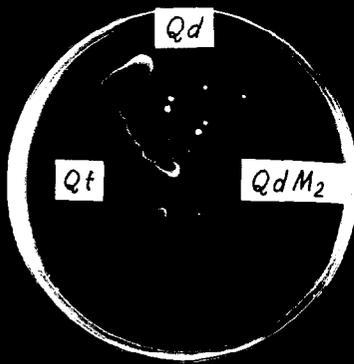


Shikimic 10 %/ml.
X 30 %/ml.

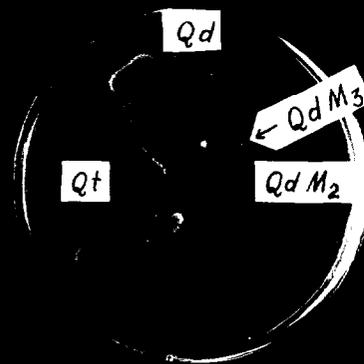
COMPOUND X EXCRETED BY QUADRUPLE (Qd)
Stimulates quintuple (Qt)
Inhibits response of Qd secondary (Qd M₂) to shikimic
Stimulates Qd tertiary (Qd M₃)



Tyr 1 %/ml. Trypt 0.5 %/ml.
Φ 2 %/ml. PABA 0.01 %/ml.



Same +
Shikimic 1 %/ml.



Same +
Shikimic 10 %/ml.