WASHINGTON UNIVERSITY
SCHOOL OF MEDICINE
SAINT LOUIS

THE EDWARD MALLINCKRODT
DEPARTMENT OF PHARMACOLOGY
EUCLID AVENUE AND KINGSHIGHWAY

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Dr. Joshua Lederberg
Department of Medical Genetics
Genetics Building
University of Wisconsin
Madison 6, Wisconsin

Dear Josh,

Here are the extracts and a sample of novobiocin. I am embarrassed about the time that has crept by since I was in Madison. I made the first extract right after Christmas but worked it up in a relaxed fashion. When it turned out to be a dud, I did the next one more hastily. I am enclosing four tubes, each dried from 5 ml. of solution. The source and content of acetylamino sugar nucleotide is marked on each tube. Each tube represents the extract from cells obtained from 500 ml. of culture (about 1.3 Gm packed wet weight). For future reference, I have previously removed a duplicate 5 ml. from each tube I am sending to you. However, you can have these samples whenever you need them, or I can make more.

I thoroughly enjoyed the afternoon with you. The possibility of getting at the compounds in the "other" sequence(s) through the mutant approach intrigues me. Two things we didn't discuss occurred to me later: It is possible that the small amount of residual dye from the crystal violet extracts will be bacteriostatic. This dye separates well from some of the interesting compounds on electrophoresis. I could easily prepare from the extracts whenever desirable electrophoretic strips (1/2" wide?, 1"?, 2"?) which could be overlaid with agar. This latter technique might be interesting in any case. Similarly, these extracts have all been through a cold TCA precipitation which might destroy labile compounds. The extracts can also be prepared with boiling water at neutral pH, which might be less harmful.

Thanks very much for the cultures. They all arrived safely. I assume the TLB auxotroph is a theonine, leucine, biotin auxtroph. Neither I nor Dave Hogness understand the terminology DAP-prototroph. Does this refer to a primary isolate as contrasted to a DAP-auxotroph obtained in the laboratory? So far I have done nothing except transfer the cultures. I think I can get to them next week, so I may have some more news shortly. Guy Barry sent me a culture of K235L+O, the colimínic acid producing strain, so I don't need to trouble you for it any more.

TLB,
DAP⁻

Thanks also for Kandler's paper. It does not change my feelings about *S. aureus*. Two major criticisms are: 1. The method of preparation of walls in NaOH would undoubtedly destroy walls of cells like *S. aureus* (cf. Mitchell and Moyle). I can't be sure without seeing the paper in press that these are walls. 2. The occurrence of a normal amount of DAP in hydrolysates of whole cells might only indicate the presence of DAP precursors, such as we might find in the organisms you sent us. In a more general way, however, possibly the point of interruption of cell wall synthesis is not exactly the same in *B. proteus* and *S. aureus*. In fact the data do indicate that the "walls" of the "instable" form have lost some accessory structure, as contrasted to the basic structure. They may be very incomplete "walls", and again inhibition of some wall "polymerase" might be implicated. However, as I said, the idea that a uridine nucleotide transglycosidase is specifically inhibited is only one interesting hypothesis, and possibly some general property of the membrane is interfered with by penicillin having a slightly different effect in the two organisms.

Novobiocin inhibits at a point different from penicillin. It seems to be closer to crystal violet, and we should know exactly in about a week.

I'm delighted to hear you'll be coming in May.

Sincerely,

Jack

Jack L. Strominger

JLS:ab

The extracts marked (A) are better than those marked (B).

Best regards to Esther. How about a float trip on the Current River if it can be arranged? It should be warm enough by mid-May.