WALTER REED ARMY INSTITUTE OF RESEARCH
WALTER REED ARMY MEDICAL CENTER
WASHINGTON 12, D. C.

IN REPLY REFER TO:

4 October 1956

Germfree Research Unit

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

Dear Dr. Lederberg:

Thank you for your letter of September 27th and the copy of your note on protoplasts. I was very interested in the observations on the formation of protoplasts in the presence of penicillin and your interpretation of these results with respect to the action of penicillin. I agree with you that they tie in very nicely with my observations --- especially in view of our findings of last fall and winter. Jack Strominger and I arrived at the same conclusions you have last January (quite independently) and at that time decided to publish jointly. Because Jack was just setting up shop in St. Louis and I have had a hectic year working with germ-free animals, we are only now writing up this work. Of course, both Strominger and I presented this work at the 130th ACS meeting and Strominger is discussing it again this month for the Pharmacology Society.

In essence, we found that cell walls contained the same amino acids and the same new amino sugar (and in the same proportions) as were present in the uridine derivative. On the basis of this and the published work on cell wall composition, it was proposed that penicillin interfered with cell wall formation and that one result of this was the interruption of a transferase reaction in which ordinarily the amino sugar-peptide was incorporated as a unit into cell wall. It was also pointed out that this interference with a synthesis which is essential to bacteria but not to animals could explain the selective toxicity of penicillin.

I am sending Jack a draft of our manuscript and after he works it over, I will send you a copy. This should be in less than two weeks. I think it would be worthwhile to refer to each others publication in press as each strengthens and complements the other so beautifully.

You ask about a UDP-- diaminopimelic acid complex. Relatively few organisms accumulate UDP-derivatives, and I have not studied appropriate organism with this in mind. You realize the UDP-derivative that has been studied contains three residues which may be unique to bacterial cell walls and for this reason one more unique compound does not add greatly to the argument.

I'm afraid I have no suggestions for quick tests of UDP enzymes beyond those Kalckar would suggest. I consider your interpretation of L-forms as protoplasts as correct and that this simple but remarkable observation has far-reaching implications not only in your genetic work but in many other fields as well.

Sincerely,

Jed

JAMES T. PARK