March 19, 1952

Dr. P. R. Edwards
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Chamblee, Ga.

Dear Dr. Edwards:

The O-variant S. typhimurium that you sent us a couple of weeks ago has been working quite nicely. In 27 out of 27 trials (sic!) it has given rise to diphasic H-forms after exposure to FA from a diphasic source. We are in the course of 1) preparing FA from the O-variant to be tested against S. typhi/anti-d, and 2) testing FA from monophasic (1,2) S. typhimurium against the O-variant. The FA was genetically marked, and there can be no question of bacterial contamination. In first tests with the o-variant as received, there were one or two "spontaneous" variations to motility (to give diphasic H); with colony reisolates, these have not been seen again. This raises the question, however, whether the FA is contributing the antigenic specificity itself, or, more likely restoring the capacity of the cells to produce flagella of a predetermined type. The paralallism of the flagellar type of the FA with that of the progenitor of the O-variant creates some difficulties in interpretation. We are looking, therefore, for as many O-variant types in groups B and D as we can find. Unfortunately, there seems to be no systematic way of finding them. For whatever your laboratory could provide by way of cultures or suggestions we should be most obliged. I note the listing of "S. typhi O 901W", #58 in your Kentucky "catalog". Is this reasonably stable under the selective conditions of the Wassen-Gard tests?

Your 1946paper in Proc. Soc. on non-motile flagellate cultures has been the the back of my mind for some time, but I just recovered a reference to it. It occurs to me that the paralyzed S. sandiego may represent an additional level of flagellar determination (antigen; structure; function) that could profitably be subjected to genetic study. Would this culturesstill be available? Have any further examples in groups B-D been discovered or described in print?

It finally dawned on us that the exceptions to the relationship between XII antigen and FA-absorption could be related to Form-Variation, the FA being related to the XII_2 component. We are checking this more closely with the variant and normal S. pullorum, but would like to nail it down with S. typhi T2vand T4(Almon & Stovall). Stovall, here at Madison, has long since forgotten about these cultures. Do you have them or know where they might be in the US?

In typhimurium X typhi, we have still found only the IX, XII, i-- form, and have been unable to obtain any progressive changes in the latter. It would appear to be a promising antigen for the production of anti-i, but our sera have not yet reached full titer. What this means for the genetics of phase variation is difficult to say, except perhaps that the potentiality for variation is inherent in the cell rather than the antigen itself— not a remarkable conclusion.

Our attempts at somatic antigen transduction have been completely inconclusive, the difficulty being with sufficiently blocking the present O-type with IX serum. I am a little uncertain about your experiments with meleagridis to cambridge. Do you use the somatic serum in sufficient quantity to completely block the migration of the homologous cells (as in the H-changes), or is it possible to get by with less stringent blocking?

I am still intrigued by the suggestion that Bruner and you raised as to the possibility of inductive effects in these changes. If FA were produced by the cells used for absorption, it would certainly be present in the adsorbed sera. I note that you comment that transductions to III, XV were obtained with several sera absorbed with III,XV types. Does this mean that III, X, XXVI serum absorbed, e.g., with senftenberg or other III, non-XV bacteria would not evoke the alteration of [X, XXVI] to XV?

Our remaining possibility for somatic transductions with the typhimurium system is, I think, to use the I antigen rather than the IX antigen as a "handle". We plan to set this up now (enteritidis cells + typhimurium FA in the presence of senftenberg serum: quite a menagerie).

I know little enough of your organizational set-up at Chamblee to wonder if requests of a more or less routine nature might not be routed differently so as to minimize their burden on yourself. This particular letter is not what I would call routine; may I summarize what I have hinted at in its body:

S. typhi O 901 W, and any other Salmonella B or D O-variants (or info. on them)
S. typhi T2 and T4 (Almon-Stovall; Kauffmann)
S. san diego (Edwards, Moran & Bruner 1946--nonmotile, flagellate)
if available for release

Again with my thanks,

Sincerely yours,

Joshua Lederberg