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OFFICE OF THE PRESIDENT

February 14, 1990

I'm sorry, this was put on a shelf while I was traveling.
J. L.

Dr. Robert E. Kohler
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Dear Dr. Kohler:

Thank you for letting me have your manuscript on George Beadle and Biochemical Genetics. I very much enjoyed the approach that you took. (The copy you gave me was lacking page 1 and I hope you can replace that.)

I was especially gratified to learn of Jack Schultz's involvements which, as you say, were mainly unpublished. He was quite a man!

You have a point about Drosophila nutrition having been a precursor of the idea of moving to Neurospora. But I think you may be highlighting it a bit more than the evidence would demand. There is no indication that they had any expectation of finding, and therefore of looking, for mutants with altered nutritional status in Drosophila. They had to think about synthetic media if they were going to use feeding as a much more convenient method of introducing intermediates than by transfusion. But you do have a point and certainly they began their work on fly nutrition a couple of years before Neurospora was introduced.

To this day I just don't know whether anyone has gotten a nutritional mutant in Drosophila. You might want to check the Drosophila catalogs on that point! It's rather difficult to do, since one has to maintain strictly sterile conditions; and that would have been multiply difficult before the advent of antibiotics. I don't know whether Drosophila, as would be the case for many other insects also have symbiotic bacteria (as part of their "extended genome") and that would further complicate nutritional studies.

A few little nitpicks: don't you want to say 1940s or at least from 1946 when you refer to K12? Also while neurospora sitophila was used for the first one or two experiments, it was very promptly replaced by Neurospora crassa.

X... cf.
✓ 3/26/90 cm

Page 4: this is partly obliterated on my copy but do you have "cystinuria" in Dalmatian hounds connected with the name of Irwin Brand? I am just not acquainted with that connection. Brand was of course a protein biochemist -- Francis Ryan collaborated with him on amino acid analyses -- but I usually connect Dalmatian hounds with the excretion of uric acid; and I am just not aware of Brand coming into that. (The dalmatian uric acid excretion story was advertised for years as a likely example of a genetic defect in uricase: it has turned out to be much more complex and has to do with thresholds of renal resorption of uric acid from the blood and is still not thoroughly understood.)

Page 39: "inspiration struck Beadle" that was probably in January 1941; which is an astonishly short time before they actually consummated their experiments. The course was given between January and March 1941. According to Carleton Schwerdt's notes the references to fungal nutrition and in particular: "biotin -- required by certain fungi" was on February 18, 1941. (On February 27th he gives an account of the phenylketonuria and alcaptinuria and the notes say "above reactions may be blocked with incomplete metabolism due to presence of recessive genes". There is an account, beginning March 6th, or the Drosophila pigment story; it then goes on to the plant pigments. But there is no mention of Drosophila nutrition in Schwerdt's notes for this particular course.

I rechecked the 1939 nutrition paper and of course he really did not succeed in developing a defined medium, although he had evidence that additional riboflavin, above what was in yeast extract, was needed for rapid growth.

Page 46: the early methods of bioassay with Neurospora, before the growth tube, simply involved filtering out the mycelium either on glass filters or even on filter paper, washing them, rolling them up and wringing them between your fingers, drying them out and weighing them. The method of growth tubes was really Ryan's contribution, of course in Tatum's laboratory.

Where did you get #1090 as the strain number of the thiamine mutant? (I don't have the strain catalogs handy. If I don't remember, it may be that it was a sitophila mutant and the stocks that I worked with were all a little later, and in N. crassa. Or it may have been unstable to a troublesome degree and was then superceded by mutants with later numbers.)

Again thank you, I very much enjoyed the article.

Yours sincerely,

Joshua Lederberg

Refs: S 303
P 268