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DEPARTMENT OF BIOCHEMISTRY
UNIVERSITY OF LEICESTER

FROM
PROFESSOR H. L. KORNBERG F.R.S.

UNIVERSITY ROAD
LEICESTER LE1 7RH
TELEPHONE: 50000

also reprints on pyruvate; letter on chloroacetate

22nd April, 1974

Dear Dr. Lederberg,

Your very kind letter of 18th April gave me great pleasure, not only because of your friendly interest but because it convinced me that there are other and better people whose performance in the writing field does not quite match up to their intentions! I do not regret at all having pursued your early publications virtuously because, in the spirit of the three Princes of Serendip, I found many gems on the way.

My interest in the chloroacetate resistance phenomenon stems primarily from two sources. As you may remember from the seminar that I gave in your School (or, more likely, that you will not remember), I have for long been interested in the regulation and identity of the reactions that replenish the tricarboxylic acid cycle. It was thus of considerable interest to determine the fate of halogenated acetate and it is for that reason that we have, for some years, played about with fluoroacetate. The mutants that are resistant to fluoroacetate that we have obtained so far fall into two main classes. The first type lacks acetatekinase; the second phosphotransacetylase. However, the first class of mutants still grows slowly on acetate whereas the second does not: I suspect that this latter class also lacks malatesynthase which is known to be able to use FAcetyl-CoA as a substrate.

My second reason for being interested is that I have now been engaged for some years in the study of uptake systems for carbohydrates. Although such uptake systems are clearly defined for hexoses, pentoses, and sugar acids derived from them, there is only scanty evidence that molecules smaller than 3-carbon acids require a "permease". As you may note from the reprint enclosed, we have found an uptake system for pyruvate. We had hoped to see whether fluoroacetate-resistant mutants were resistant because they refused to admit fluoroacetate into the cell. Our data so far suggest that this is not so: there seems to be no unique, saturable, genetically-specified, "permease" for acetate. However, I am still continuing to look, in a desultory sort of way, and had hoped that the use of something other than fluoroacetate might have shed light on this.

I was most interested to learn from you that the class of mutants that you studied were deficient in formic hydrogenlyase. So far as I am aware, this enzyme is not formed to any significant extent during

Dr. Joshua Lederberg,
Stanford University Medical Center

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aerobic growth and thus plays no role in other than anaerobic conditions. Am I incorrect in this? If this were correct, it would be difficult to detect the lesion in aerobic conditions.

I am in the process of writing up some of our work (I really am!) and shall send you a copy of my paper if/when it is ready for submission.

With many thanks and best regards,

Sincerely yours,

Hans L. Kornberg

Dr. Joshua Lederberg,
Department of Genetics,
Stanford University School of Medicine,
STANFORD,
California 94305, U.S.A.