

## UNIVERSITY OF CAMBRIDGE

PROFESSOR R. A. FISHER, Sc.D., F.R.S.

DEPARTMENT OF GENETICS

WHITTINGHAM LODE

MISS M. F. I. SPEYER, B.Sc.  
Research Assistant and Secretary

44 STOREY'S WAY

CAMBRIDGE

Tel. 55822

11/1/1950

My dear Lederberg,

Thank you very much for your letters. I am glad to know that 123 has worked; you will see that it gives better results (larger and nicer prototrophs) with B-M strains. I had a record of lysogenicity in a cross K 12 x 123 but never carried it further; your remark as well as Mrs. Lederberg's letter are very illuminating, and how interesting too. It is possible that lysogenicity may be a widespread barrier against hybridization (by the way, is the offspring resistant? if so, isolation of a resistant strain might increase yields considerably, and I am looking forward to the resistant strain you are looking for). Perhaps with organisms of great reproductivity as bacteria the task of Nature is that of preventing outbreeding rather than favouring it as with higher organisms.

As to growth requirements of 123, all I knew about it some time ago was that it could grow on a (hoped to be vitamin-free) casein hydrolysate. In December I spent a week in Glasgow at Pontecorvo's Department, where I also courageously gave a public demonstration of crossing bacteria at the presence of sceptical bacteriologists. One of them was Lominski, to whom I am sending the cultures now. After the show, they seemed to be convinced that there may be something in it, which is a great achievement, I think. We then made with Ponte some experiments to establish growth requirements of 123 and could see that a really vitamin free, acid hydrolysed casein supported growth, but hydrolysed ~~casein~~<sup>insulin</sup> did not. Later Ponte could see that addition of proline and methionine to insulin gave growth. He is interested to the strain because he hopes that there may be a polypeptide requirement in view. I am now trying single omissions from an artificially reproduced insulin, but lack some of the amino acids. Anyhow, the growth requirements should be pretty complex, but ~~with~~<sup>with</sup> proline and methionine I could not get any better back mutants. It is therefore likely that two or more other amino acids are involved. Perhaps you have already a clue to the problem, and your results will be highly welcomed.

Coming to the second part of your letter, I wish to thank you very much for your attention to my person. My present position here is an appointment as assistant of research for three years, renewable, with a not too bad salary for a junior post. One of my most ardent wishes is of course that of spending a year or much more in The State but unfortunately a fellowship of a year is little compatible with a family of two children, of which one expected. Therefore I never tried so far to seek a fellowship or similar. The best compromise between family needs and scientific interest would be that of spending as soon as possible two or three months, preferably in the summer if the people I am interested to meet (you are the first of course) are not away on holiday. I made a first unsuccessful trial for a summer teaching post for statistical genetics; it may be successful some other year, but perhaps Cold Spring Harbor may be a better excuse. I don't know however what will be on/in summer 1950. A couple of months in your laboratory will not allow me to start on a serious work, but would be of tremendous help for solving shorter problems of which there is always plenty, seeing techniques, and above all have the leisure of discussing problems with you at length. But unfortunately I have no immediate solutions available for this.

For the far future I have no exact plans, except a strong inclination towards the U.S., due both to the attraction of working in the U.S. atmosphere, and that of avoiding

the distressing possibility of an even temporary domination of Lysenian Genetics in Europe. Moving to the U.S., even for a good appointment might be too difficult for me now on the basis of private grounds with which I should not like to bother you, but I have this plan in mind for a not too far future, and it is very gratifying to hear from you that you are willing to help me, and may be in a position to do so in the future.

To complete the picture, anyhow, I shall have to tell you that I shall be 28 before the end of this month, and as to my qualifications I hold an Italian M.D. (Pavia), and the usual Cambridge M.A. granted to University officers. By the way, did I tell you that I am giving since last year a course in Microbial Genetics at this University? I may be able to get a Cambridge Ph.D. in genetics if there will be no bureaucratic difficulties against it. All this information may be useful, if not now, in a, I hope, not too distant future.

Thank you very much for letting me know of the development of diploid analysis. Do you think that the possibility of aneuploids, with duplications for certain chromosome segments, arising through a translocation or similar in the original strains, is to be discarded? It certainly would not explain ~~crossing~~ the rare crossing-overs in "diploids", but it may be after all that "somatic" crossing-over (outside independent of meiosis) ~~is~~ not impossible in bacteria. My UV killing curves in the comparison of Nfr and Hfr are multi-hit; I fancy what X-ray curves will be, but, with analogy to B/r ~~they~~ might well be single-hit curves. Are your statements about multinucleation entirely morphological, or <sup>grounded on base on radiation curves</sup> also <sup>in mice</sup> genetical? Perhaps an analysis of recessive mutations might help, and I have been thinking for some time of doing it for the comparison of Nfr and Hfr, should the Hfr behaviour have any connection with it. The identity of UV killing curves in both strains suggests, however, that average number of nuclei per cell might be the same.

My work is delayed, or I could better say, desperately lagging, for lack of adequate technical help and for very irritating difficulties like a marked decrease of all recombinations since a longish time; elimination of possible causes is not yet finished, but I am left to the hopeless ones like influence of copper in distilled water and analogous ones.

I am enclosing a copy of a list of symbols I am planning to send to <sup>for which you may have a number of suggestions to make.</sup> MGB. I thought to send a list of strains available, especially because it may be of help to European research workers to know which of the K-12 strains (I am excluding Het) they might be able to find on their continent. But it occurred to me that, unless one standardises symbols for the most ~~six~~ frequent mutants, description of your strains will take pages. So a standard list of symbols for the most frequent types of growth requirements may be of use for this and similar purposes.

Yours sincerely

*Luigi Cavalli*

P.S. Pontecorvo gave me <sup>were</sup> his dried cultures of his mutants of <sup>adaptables</sup> Aerobacter aerogenes. He told me you <sup>were</sup> interested to have them some time ago. There is about a dozen of adaptable and a dozen of non-adaptable mutants. ~~Are~~ you still interested in them? If so, please let me know. I have not checked the adaptable cultures but for viability.

Symbols for growth-Factor deficiencies.

Aminoacids.

Al	alpha-alanine.	L	Leucine
Am	aminobutyric acid	Ly	Lysine
Ar	arginine	M	Methionine
As	aspartic acid	Nl	Norleucine
Ci	citrulline	Nv	Norvaline
C	cystine	O	Ornithine
Ce	cysteine	Ph	Phenylalanine
Dp	dihydroxyphenylalanine	P	Proline
Ga	glutamic acid	Se	Serine
G	glycine	T	Threonine
H	histidine	Tr	Tryptophane
Hp	hydroxyproline	Ty	Tyrosine
I	isoleucine	V	Valine

Vitamins.

A	Anæurin (B <sub>1</sub> )	Pb	Paraaminobenzoic (PAB) acid
R	Riboflavin (B <sub>2</sub> )	Ch	Choline
Py	Pyridoxine (B <sub>6</sub> )	In	Inositol
F	Folic acid (B <sub>c</sub> )	B	Biotin
Pa	Pantothenic acid	K	Methylnaphtoquinone
Na	Nicotinic acid/amide	Co	Cobione (B <sub>12</sub> )

Purines and Pyrimidines ,

Ad	Adenine	Hx	Hypoxanthine
Cy	Cytosine	Th	Thymine
Gu	Guanine	U	Uracil
	X	Xanthine	