UNIVERSITY OF PITTSBURGH

PITTSBURGH 13, PENNSYLVANIA

DEPARTMENT OF BIOPHYSICS

December 15, 1958

Dr. Joshua Lederberg
Department of Medical Genetics
University of Wisconsin
Madison 6, Wisconsin

Dear Doctor Lederberg:

First of all, allow me to congratulate you on receiving the Nobel Prize in medicine for this year. This recognition of your work will stimulate interest not only in microbial genetics but also in all fundamental quantitative biology.

You have expressed an interest in the "filaments" or "pili" of bacteria. Enclosed is a summary of results of research I have done recently on these structures, and I should appreciate very much your comments on and criticisms of this work, all of which is unpublished as yet. I plan to submit an abbreviated version of this summary for publication in Nature. Three full-length papers are now in rough-draft form.

"The electrophoretically effective dimensions of biological surfaces and the mobilities of piliated and non-piliated bacteria."

"Identification of hemagglutinating, virus fixing, and colicine activities with pili and other surface structures of E. coli."

"Genetics of the change from piliation to non-piliation in a strain of E. coli."

If you are interested, I can also send you these manuscripts.

I am wondering if it would be possible for me to continue my research on pili with you in your laboratory. In my present situation, the time I can spend on this subject is limited and, in addition, there is no one else in this department interested in bacteria. I feel that the pili are a new and exciting field with many novel aspects which is at this moment ripe for further investigation. Some of the ideas I have on future lines of research are as follows:

1. Determine whether or not the potentiality for piliation or piliation itself is transferable by viral transduction or recombination. Maccacaro has attempted this by recombination but has not done a proper job since he ignored the spontaneous change $P^+ \rightleftarrows P^-$ within a given strain.

2. Determine some specific pilial antigens and see if they are transducable as are flagellar antigens.

3. Analyze genetically the $P^+ \rightleftharpoons P^-$ variation in other strains of E. coli and also in other species of bacteria in the same way as strain E. coli B-L(E) has been analyzed to determine the generality of occurrence of high mutation rate, growth rate difference, and temperature effect on mutation rate.

4. Rate of growth of pili can be measured by removing them mechanically and measuring the decrease of electrophoretic mobility with time. Determine the effect of various treatments such as chloramphenicol, phage infection, irradiation, etc., on the rate of growth of pili.

5. I have shown that anti-pili serum does not interfere with bacterial growth. A fluorescent anti-pili serum could be prepared and living piliate and non-piliate organisms could be distinguished in the fluorescence microscope. Hereditary cell lines could then be studied by micromanipulation in hanging drops.

6. There is a similarity between the "grandes" and the "petites" yeast mutants of Ephrussi and the P^+ and the P^- phases of bacteria. Perhaps the $P^+ \rightleftharpoons P^-$ mutation also reflects a difference in respiratory enzymes. I am now testing O_2 consumption by the two forms.

There are many other aspects of the problem which I would be delighted to discuss with you if you are interested. The effect of temperature and cultural conditions on the $P^+ \rightleftharpoons P^-$ variation and its high rate of mutation may be related to the general problem of cellular differentiation.

As far as the terms under which I could work in your department are concerned, I could apply for an NSF postdoctoral fellowship. However, I have had my Ph.D. for only four years and the senior postdoctoral fellowships require that it be held for five years. The junior postdoctoral fellowships carry a stipend of only $4500 which is rather meager to support myself and the wife I will soon acquire. Perhaps I could qualify for a position in the new department you are forming at Stanford. Or, you may know of some other fellowship. However, if no position or other fellowship is available, I would be willing to come as a junior postdoctoral fellow.

A brief resumé of my qualifications is listed below.

Age - 32
B.S. - Physics, Carnegie Institute of Technology, 1949
Ph.D. - Biophysics, University of Pittsburgh, 1955

Present position - Research associate, Department of Biophysics, University of Pittsburgh
Present salary - $5700/year
Experience -
1953-1955: Radiobiology at Institut du Radium, Paris;
1955-1956: Electron microscopy and genetics of piliated bacteria, Biophysics Department, University of Geneva;
1956-present: Physical chemistry of tobacco mosaic virus nucleic acid and protein, studies on bacterial pili, theory of electrophoresis.

Some recent publications -

"The electrophoresis of viruses, bacteria, and cells, and the microscope method of electrophoresis," by C. C. Brinton, Jr., and M. A. Lauffer, in Electrophoresis, Theory, Methods and Applications edited by Milan Bier, p. 427-492, Academic Press (1958).

"Polymerization-depolymerization of tobacco mosaic virus protein," by M. A. Lauffer, A. T. Ansevin, T. E. Cartwright, and C. C. Brinton, Jr., Nature 181:1338, 1958.

Qualified to teach - General biophysics, Biophysical methods (theory and practice), Effects of radiation on biological material (theory and practice).

I am looking forward to your reply.

Sincerely yours,

Charles C. Brinton, Jr.

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Enclosure 1
Manuscript