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UNIVERSITY of PENNSYLVANIA

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The School of Medicine

DEPARTMENT OF PEDIATRICS
1740 Bainbridge Street
Philadelphia 46, Pa.

November 7, 1958

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

Dear Josh:

I have been delaying my reply to your last letter so that I would also be able to congratulate you on the well-deserved recognition which you have just received.

I have no additional a priori arguments against the view that antibodies are differentiated on the basis of amino acid sequence. However the full implication of my argument may not have been clear. The starting point of our analysis is the recognition that immunologic specificity is based on unique constellations of the side chains (R groups) of amino acid residues. This means that if the antigen is to play a determinative role in sequence, there must not only be a mechanism for the instruction of sequence by the antigen. The antigen must also be able to select a sequence which on subsequent folding of the polypeptide chain will give rise to the appropriate R group constellation.

Any theory which assigns an elective role to the antigen avoids the above difficulty, of course. But it seems to me that the present theories of this kind raise more conceptual problems than they clarify. Furthermore I believe that the cell transfer experiments, particularly those involving in vitro incubation of lymph node cells and antigen, provide evidence against the clonal theory.

With best regards and congratulations also to your wife since she probably did most of the work.

Sincerely yours,

Fred

Fred Karush

FK:ms

KARUSH, F.