

STANFORD UNIVERSITY
MEDICAL CENTER
PALO ALTO, CALIFORNIA

DEPARTMENT OF BIOCHEMISTRY
School of Medicine

February 8, 1961

DAvenport 1-1200

Dr. Joshua Lederberg
Department of Genetics
Stanford University
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Palo Alto, California

Dear Josh:

The following are comments on Herman Eisen's manuscript:

1. The title is confusing. Since microsomal antibody activity exists before the experiment begins, and the authors are showing a solubilization of this activity, I would suggest as title, "The Solubilization of Microsomal Antibody Activity by the Specific Interaction Between Lymph Node Microsomes and a Crystallizable Fraction of Gamma Globulin".

2. I don't think the word "subunit" should be used since there is no evidence that gamma globulin is actually composed of the three Porter fractions as real biologically relevant units. Suppose, for example, as has been suggested by Edelman, γ -globulin is made up of 3 chains and the papain cleaves these chains vertically into 3 units, each containing portions of the 3 chains. The word "subunit" has a special sense and will be essential later on when a clear understanding of synthesis is accomplished. I therefore would suggest "fraction" which is more precise.

3. The experiments on "Passive cutaneous anaphylaxis reaction of microsomal antibody", page 8, don't seem to lead to any conclusion. If there is one, it would well be stated. It is not clear whether the position is that the animal's normal γ -globulin liberates microsomal antibody to give a cutaneous reaction, or if microsomes per se are capable of entering into the reaction. This should be clarified.

The major change that I would suggest is in the discussion. The experiments with ribosomes are suddenly introduced. These experiments are critical to understanding of the phenomena. Antibody is shown to be linked to ribosomes.

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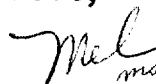
If it were true that fraction III liberates antibody activity by virtue of an exchange reaction and then one should expect the same reaction for the ribosomes to which γ -globulin is linked. Unless, of course, some other hypotheses are introduced. It is not clear why this very simple experiment wasn't performed or mentioned.

One other interpretation might be mentioned. Suppose that we picture microsomes as a bag in which (a) antibody floats free, and (b) antibody is linked to ribosomes. The free antibody is that antibody which is on the way towards being secreted. The mechanism of γ -globulin - fraction III liberation would be part of the mechanism of secretion. The raising of this point is because of the findings of Brambell et al. that γ -globulin will pass the egg sac membranes as will fraction III, whereas fractions I and II do not.

Lastly, some statement concerning the possibility of a chemical interaction between fraction III and the material involved in microsomal antibody activity should be brought up.

Please put this into English.

Best,

A handwritten signature in cursive script, appearing to read "Mel" with "ms" written below it.

Mel Cohn

MC:ms
enc.