

**TUBERCULOSIS IMMUNIZATION  
RESEARCH CENTRE**

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Telephone: Asta 2817

Telegrams: Statsserum

c/o STATENS SERUMINSTITUT  
AMAGER BOULEVARD 80  
COPENHAGEN S.

ES/GS

June 10th 1960

Professor J. Lederberg  
Department of Genetics  
School of Medicine  
Stanford University  
Stanford, California  
U.S.A.

Dear Joshua,

Quite apart from the accompanying letter I like to ask for a little favour. Can you spare me a reprint of your inspiring Nobel-lecture and the antibody theory paper, both from "Science".

Boyden and I have recently conducted a few experiments on animals with neonatally induced tolerance to human serum albumin (HSA), which might have some bearing on yours and Nossal's experiments, since they might disprove (?) indirectly the one cell-one antibody hypothesis. Rabbits on the day of birth were injected with 100 mg. antigen (HSA). After a few more small doses of antigen these unresponsive animals were after reaching immunological maturity, injected with antigen-azo-hapten (HSA - N = N -  -SO<sub>2</sub>H) or rabbit albumin (RSA)-azo-hapten. The rabbits, unresponsive to HSA, did not react to HSA-bound-hapten, while parallel groups reacted nicely to this hapten when bound to RSA. Our present interpretation is that the same cells which produce anti-HSA antibodies are also making antibodies to the hapten when attached to or carried by HSA. Needless nearly to say that normal animals made anti-HSA and anti-hapten antibodies.

Further control experiments have meanwhile shown that if one takes serum protein from adult rabbits, couples them with hapten and puts coupling product back into the same animals (A-serum-azo-hapten in A, B-serum-azo-hapten into B, etc.) or also into other normal animals, then antibodies to hapten can easily be discovered in all groups. Of course the 'self-proteins' might have conceivably been altered to 'not-self' by coupling, though some other results seem to make this doubtful. Yet the results showed clearly ~~the~~ responsiveness to hapten. Naturally, it is difficult to measure anti-self protein antibodies as they would be all absorbed by the self-proteins. Tests with RSA as test antigen were correspondingly all negative. All tested in tannic acid haemagglutination test.

Although Boyden is now in Canberra, we are actively continuing the collaboration on this aspect and we keep you informed if you wish so.

Best wishes,

Sincerely,



Ernst Sorkin