DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

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Dr. Joshua Lederberg
Stanford University Medical School
Stanford, California

Dear Doctor Lederberg:

In the process of preparing a manuscript which describes the results of some experiments on anti sheep erythrocyte hemolysin formation in C3H mice bearing transmissible plasma cell tumors (X5563) I would like to ask your opinion upon applicability to these results of the elective theory of antibody formation which you recently published in Science (129: 1649, 1959).

Following a single immunizing injection of sheep erythrocytes to mice bearing these tumors one observes significantly reduced circulating hemolysin titers in some mice or the complete lack of demonstrable amounts of the antibody. A second injection of the antigen after an interval of 7 to 21 days results in a secondary response which agrees very favorably with the response seen in the non tumor bearing mice serving as controls.

It would seem possible to explain this result within the framework presented in your discussion referred to above. If one assumes that the actively growing neoplasm invades and perhaps destroys some of the relatively small number of antibody producing cells participating in the primary response then the observed reduction in titer would follow. To explain the absence of demonstrable circulating hemolysin in about 40% of the tumor mice (singly immunized) it is necessary to conclude that the circulating antibody was present in amounts below the sensitivity of the titration procedure. Since none of the mice stimulated with a second antigen injection failed to produce circulating hemolysin in very satisfactory amounts it would seem that at least a few clones "genotypically adapted" must have been produced by the first antigen stimulation.

Since this tumor (X5568) resembles human multiple myeloma in some respects it is possible that some metabolic disturbance might explain the observed results. I would appreciate any comment you would care to make relative to the attempt to explain the observations briefly described above.

Sincerely yours,

Falconer Smith

Falconer Smith, Head
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