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Summary: Experimental Tumor Immunology; and Search for Tumor-specific Antigens in Human Tumors of Possible Viral Origin

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In discussion of Dr. Boyse's paper, there was considerable interest in the phenomenon of modulation of the TL antigen and the concomitant reciprocal increase in H-2D. Dr. Klein commented on the fact that TL and H-2D are closely linked genetically, yet the reciprocal relationship between these antigens occurs whether the genes are in the *cis* or *trans* position. Dr. Boyse summarized the evidence which indicates that the effect is an extrachromosomal one. Dr. Klein then asked whether the TL and H-2D antigens are on the same molecule. Dr. Boyse indicated that presently available data suggest that TL and H-2D determinants are on separate molecules: although the separations achieved by Davies have not been complete, column fractionation has given two peaks, one showing H-2 activity and the other showing TL activity. Dr. Frankel asked for details of preparation of TL antiserum and, in particular, for information on the number of immunizing injections, and Dr. Boyse responded that the usual procedure is to give one subcutaneous injection followed by two or more "booster" injections at intervals of approximately 3 weeks. Dr. Frankel asked whether antibody to TL is found during the passage of TL-positive leukemias, and Dr. Boyse replied that antibody is not in fact found under those conditions, presumably because the leukemia grows too rapidly. Dr. Boyse also indicated, in response to other questions about the mechanism of antigen modulation, that Fab fragments from other systems do not cause TL modulation, and that preliminary data from experiments with metabolic inhibitors suggest that protein synthesis is required for the phenomenon of modulation to occur.

The discussion next turned to a consideration of the results of immunodiffusion studies of tumor viruses and of tumor antigens. Dr. Fink reported some observations indicating a relatively high frequency of reaction between the sera of patients with Burkitt's lymphoma and virus-containing fractions derived from several tissue culture lines of this and other tumors. Large amounts of virus are apparently needed to give a positive reaction in this system. Dr. Old presented additional considerations bearing on this point, suggesting that, while it is possible that the difference between these results and those reported by himself are attributable simply to differences in the quantity amount of antigen used, it is more likely that two different systems are involved. Dr. Fink appears to be studying an infection-related viral antigen, while the antigen used in Dr. Old's laboratory is more likely a disease-related neoantigen, formed in cells that have actually been transformed by the herpes-like virus. An exchange of antigens and sera between these laboratories seems likely to clear up this matter.

Dr. Fahey commented on the theoretical and practical problems involved in the use of immunodiffusion technics for the detection of antiviral antibodies. In cases in which the antigen has a molecular weight of one million or many million, it would be expected to migrate only very slowly through the agar and to form a curved line of precipitate with antibody quite near the antigen well. Yet there are many reports in such systems showing the development of lines having a location and shape consistent with a molecular weight for the antigen of approximately 2.5×10^5. Dr. Fahey suggested that antigenic material of this sort can hardly be whole virus, but might in fact be a viral component or a cellular component revealed by this technic. Dr. Old responded that in one case studied in his laboratory, highly purified virus gave no reaction in immunodiffusion tests, but after ether treatment of these preparations, a band of precipitate was formed. In this and similar work, it would appear that it is soluble components that are being detected.

Dr. Fink next described the broad cooperative program, sponsored by the National Cancer Institute, in which large numbers of sera from patients with Burkitt lymphoma, American adults with leukemia, and American children with leukemia (and appropriate controls) are being tested against several standard lymphoma- or leukemia-derived antigens by various procedures. When the information resulting from this study is available, it should be possible to do future epidemiologic and analytic work with more assurance.

Dr. Fahey raised the difficult question as to whether the various cell lines that have been derived in tissue culture from human tumors are in fact representative of the actual neoplastic component of the original tumor. Some, but by no means all, of these lines give rise to tumors when transplanted into animals. Since the cells of many of these lines closely resemble each other, regardless of their origin, it was suggested by Dr. Fahey that extreme caution be used in applying the designation of "malignancy" to these cells. Some may actually be derived from normal cells contaminating the original tumors. Drs. Southam and Rauscher concurred in this view.

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