ASCITES TUMOR-VIRUS SYSTEM AS A BIOLOGICAL TOOL

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At present we have little knowledge of the actual mechanism of infection of living cells by the so-called neurotropic viruses. Progress in this field has been impeded by the complexity of the tissues of the central nervous system which has been mainly used as the medium for viral growth.

During the past three years we have studied the effect of 13 "neurotropic" viruses upon the ascites tumors of mice.[1, 2] In the course of these investigations we have succeeded in demonstrating differences in the behavior of these viruses in relation to the same ascites tumor. Four viruses failed to propagate in the tumor cells; six were found to multiply without damage to the neoplastic cells; and three (the West Nile encephalomyelitis, Mengo encephalomyelitis, and Bunyamwera) multiplied in the ascites tumor and displayed powerful oncolytic effect, ultimately destroying its cells.

Our findings suggest that the ascites tumor-virus system offers an ideal tool for the study of the multiplication of animal viruses in cells and may throw new light on the interrelationship between different viruses based on their "growth requirements." There are, for example, no detectable differences between the invasive power of eastern equine encephalomyelitis and Mengo viruses for the central nervous system of Swiss albino mice and between the multiplication rates of these viruses in murine nervous tissue; and yet cells of the Ehrlich ascites tumor failed to support the growth of eastern equine encephalomyelitis, whereas the Mengo virus multiplied in this malignant neoplasm at a higher rate than it did in the nervous tissue.[2]

The study of the specificity of "growth requirement" is being further extended by the inclusion of ascites tumors other than the Ehrlich carcinoma,[3] which, among other properties, is characterized by tetraploid modality of chromosome number[4] and increased values in DNA content of the malignant cells as compared with normal cells.[5] The use of other ascites tumors, now available[5] and characterized by a diploid modality and lower values for DNA content, may throw additional light upon the growth requirements of different viruses. Furthermore, the availability of several types of sarcomas growing in the ascitic form renders it feasible to plan experiments on the effect of viral infection, not only upon tumors of epithelial, but also of connective tissue, origin.

The ascites tumor-virus system seems also to be well suited to the study

of the interference phenomenon between viruses. Although recent work has seemed to indicate the importance of the interference phenomenon in our understanding of the mechanism of the intracellular process of multiplication of viruses,[6, 7] such studies in the field of the so-called neurotropic viruses were limited by the complexity of tissues used as the medium of viral growth. The ascites tumor offers still another opportunity for conducting experiments on the interference phenomenon in an attempt to follow the results of "dual" viral invasion of the same homogenous cellular system through daily morphological and biological observations, since samples of ascitic fluid may be readily obtained from the experimental animal by aspiration from the peritoneal cavity. On the same score, the ascites tumor-virus system might also prove to be an effective tool in evaluating the action of chemical substances which may cause inhibition of viral multiplication through interruption of the intracellular process.

Finally, it is possible that the affinity of viruses for actively growing ascites tumor cells may permit the use of this system for a quantitative study of viral multiplication, similar to that conducted so successfully with the bacteria and bacterial viruses[8] and recently applied to the living cell-influenza virus system.[9] Ascites tumor cells grown either in vivo or in vitro may be used for this purpose, and in the latter case the study may involve not only quantitative determination of the viral population, but also observations on their qualitative composition, as determined by mutants.

Since the relationship between the ascites tumor and the virus embraces not only phenomena directly related to viral multiplication but also to the oncotic process, it should be noted that the specific cellular vulnerability of the ascites tumor to infection with Bunyamwera,[10] Mengo,[2] and West Nile[2] viruses may pose interesting problems. If the multiplication of the above infectious agents in the ascites tumor induces interference with the metabolic process of the malignant cell, resulting in its ultimate destruction, a careful study of enzymatic reaction accompanying this phenomenon might be indicated. Studies on the specificity of such a reaction for a given virus in relation to a given ascites tumor may facilitate an understanding of the mechanism of selective cell destruction.

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