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Department of Microbiology
and Immunology

SAN FRANCISCO, CALIFORNIA 94143

November 10, 1982

Mr. Alan C. Davis
Vice President
American Cancer Society, Inc.
777 Third Avenue
New York, New York 10017

Dear Mr. Davis:

Thanks for your letter about the forthcoming AS ACS Science Writers' Seminar. I would be interested in attending if you feel I can be helpful, with the proviso that I am obligated to be in Denver on the 23rd of March; hence my participation in San Diego would have to be confined to the 21st or 22nd, preferably the former.

As you may know, work in this laboratory is now centered abou the issues of how two important classes of viruses - the retroviruses and hepatitis B viruses - replicate and induce tumors. From the viewpoint of your audience, the most pertinent aspect of our work concerns the oncogenic activity of these viruses. One theme we have been pursuing with particular emphasis in the past couple of years is the mechanism(s) by which viruses without their own oncogenes nevertheless manage to induce tumors. Two years ago, our laboratory and Hayward's showed that induction of B cell lymphomas in chickens was due not to viral gene products but (at least in part) to the activation of cellular genes adjacent to the place in a host chromosome at which viral DNA had been integrated during infection. After Hayward's group showed that the activated gene was c-myc, the cellular progenitor of a viral transforming gene, we demonstrated that there were multiple arrangements of viral DNA and c-myc that could lead to enhanced expression of the cellular gene. We have also explicitly identified a region of viral DNA that appears to be responsible for gene activation when the viral DNA is not positioned to donate its own transcription promoter to c-myc. This sort of phenomena may be important in understanding the effects of chromosomal translocations (e.g., of the sort recently defined in Burkitt's lymphoma) upon the activity of genes at or near the recombination sites.

We are using the model now provided by avian lymphomas to ask whether other oncogenic viruses without their own oncogenes also induce tumors by inserting their DNA adjacent to a putative cellular oncogene. We are addressing several situations in this manner, but the most provocative results have come from studies of mammary cancers induced in mice by the mouse mammary tumor virus.

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We have found that over two-thirds of breast tumors in C3H mice bear viral DNA in the same region of a host chromosome. This region does not contain any previously recognized gene, but it does include at least one gene that is unexpressed in normal mammary tissue and expressed at low levels in the mammary tumors. We are in the process of identifying the protein product of this gene, in the hopes that it will be important in the pathogenesis of mammary cancer in mice and perhaps other animals, regardless of the inducing factor.

I hope these brief comments will be helpful to you.

With best regards,

Harold E. Varmus, M.D.
Professor of Microbiology & Immunology

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