

March 7, 1972

Dr. Robert J. Huebner  
Chief, Viral Carcinogenesis Branch  
National Cancer Institute  
Bethesda, Maryland 20014

RE: Your letter of 2-17-72, and  
Proc. Nat. Acad. Sci. 69:20-24 (1972)

Dear Dr. Huebner,

The last paragraph of our paper was intended to refer only to the provirus hypothesis. The point is that we have to date been unable to perform a definitive test of that hypothesis because of the presence of virus-specific nucleotide sequences in DNA of the various normal cells we have been using. Because of the limitations in sensitivity of the Gelb-Kohne-Martin technique, the presence of virus-specific DNA in normal cells could obscure a small but sufficient increase in such sequences as a consequence of transformation. What we need is a system in which the normal cell is completely devoid of RSV-specific DNA. Examination of such cells following transformation by RSV would provide a good test of the provirus hypothesis. We now seem to have our hands on such a system - normal and RSV-transformed 3T3 cells. We should have definitive data shortly. We recognize that all of the foregoing has little or nothing to do with the oncogene hypothesis. We also recognize that although we have yet to obtain data which can refute or confirm the provirus hypothesis, our present data provide a physico-chemical correlate to the biological data from which the oncogene hypothesis derives.

We were certainly remiss in omitting a reference to the work of yourself and S, Sarma, and apologize for this oversight.

Thank you for your comments, We appreciate your continuing interest in our work.

Sincerely,

J. Michael Bishop, M.D.  
Associate Professor  
Department of Microbiology

Harold E. Varmus, M.D.  
Department of Microbiology

JMB/HEV:js