



SCHOOL OF MEDICINE
Department of Microbiology
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Dear Bob:

I enjoyed your recent visit here and think our symposium was a great hit. Since your departure I've had many conversations about the recent work on complementation assays in your lab, and we have given some serious thought to the kinds of things we should send to you. Part of the difficulty in coming to a firm decision about some of these reagents may reflect a misguided ambition on the part of some of us here to consider setting up the complementation assay to exploit some of the more specialized reagents we have on hand. Furthermore, some of these reagents were made at some considerable effort and represent unique materials yet to be fully reported. Let me run down the list and perhaps we can talk on the telephone about your feelings about each of these items.

(1) I have talked to Roel in Amsterdam and he intends to attempt to try transformation assays with new clones of the int-1 locus linked to proviruses more appropriately positioned in the int-1 locus than in the clones currently available. I believe appropriate clones could be made from the available materials simply by adding retroviral or SV40 regulatory regions to clones that contain what we believe to be the entire int-1 transcriptional unit. I would be willing to consider making these here. Alternatively, we would be happy to send the int-1 lambda clones from the normal mouse library. These would probably not be expressed unless a promoter or enhancer were introduced.

(2) We have, as I mentioned, plasmids in which the v-src gene is under the control of the MMTV LTR. These plasmids contain enhancer sequences and the constitutive level is sufficiently high in most of our transformed cells to cause morphological transformation without anchorage independence. These clones undergo 4- to 5-fold induction of src in the presence of dexamethasone resulting in anchorage independence. We have also made similar plasmids that lack enhancer sequences of src and are likely to have lower constitutive levels of expression, but these have not yet been tested directly. As you know, we have yet to describe the construction of the dexamethasone-regulated viral src gene, but we would certainly be willing to discuss further the possibility of sending you either of the two described plasmids.

(3) As you know, Richard Parker has c-src under the control of SV40, resulting in efficient expression. He is mulling over the question of whether he would like to consider setting up this kind of assay when he arrives at Columbia, or whether he should offer you that reagent.

(4) We have a potentially interesting c-myc clone that you might want to consider for further testing. Dave Westaway has sequenced part of the c-myc gene in a locus containing a provirus positioned backwards and upstream, and has found that somatic mutations must have occurred in the coding sequence because a Sac I site has been altered in an allele which contains the Sac I site in the germ line of the same animal. It might be worthwhile to consider testing the locus cloned from this tumor with and without the substitution of an unaltered c-myc coding domain.

(5) Lastly, I gather from conversations with Manfred that he is preparing to send you a clone of the N-myc gene, the myc-related gene that is amplified in neuroblastomas.

I hope this isn't all too complicated, and that we can soon have some useful materials flowing in your direction. I'll be out of town next week, but perhaps you can give me a call the week of the 27th to discuss these things further.

I note, by the way, that you will be coincident with me in Paris. Let me recommend Hotel Saint-Simon, 14, rue de Saint-Simon. I'll be staying there from the 7th to the 10th of September and, as you know, my taste in hotels is indisputable.

Look forward to seeing you soon,

Harold E. Varmus, M.D.
Professor

HEV/jm