



SECTION OF BIOCHEMISTRY, MOLECULAR AND CELL BIOLOGY

CORNELL UNIVERSITY

BIOTECHNOLOGY BUILDING, ITHACA, NEW YORK 14853

N.Y.S. College of Agriculture and Life Sciences  
A Division of the State University  
COLLEGE OF ARTS and SCIENCES

DIVISION OF BIOLOGICAL SCIENCES

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Dr. Harold Varmus  
Dept. Microbiol. and Immunol.  
University of California, HSE 401  
San Francisco, CA 94143

Dear Harold:

First of all my warmest congratulations to you and Mike for receiving the Nobel Prize. Many times have I compared your collaboration with Mike to that of the Cori's, Stein and Moore, or Brown and Goldstein. It requires a special psychological setting to work well. When it does, it's not just additive but cooperative. To my mind your work on src (which I call the E. coli for oncology) has been revolutionary, well deserving the prize. I hope that the many invitations and distractions you will be exposed to will not seriously interfere with your future work. C-src is still a growing baby that needs Mike's and your attention. I still remember my last visit with Goldstein and Brown which happened on the third day following the announcement. They had disconnected their phone communications and went back to work, finding time to spend over one hour to discuss science with me.

Are you still interested in the work you did with Dr. Verderame? On your suggestion he wrote to me. I think that his observation that the mutant src from chicken cells, but not from rat cells, phosphorylates GAT (6:3:1) is an interesting clue. I suggested that he look for a different post-translational modification in the two src kinases, but perhaps a more likely explanation is that there are different contaminants in the immune complexes obtained from the two cell lines. I believe I told you that BSA and some intracellular proteins stimulate GAT phosphorylation by src. The immune complex prepared with Baculo virus src appears to contain such an activator of GAT phosphorylation. I recommended to Dr. Verderame the use of your method of purifying src with an antibody affinity column (if it is feasible on a small scale). This brings me to a request. Could you spare some purified c-src or enough monoclonal antibody for making an affinity column? After obtaining a mg of antibody from Joan, I did not want to impose on her further and she sent me her hybridoma clone. For some reason we are getting very poor yields of antibody in the hybridoma supernatant as well as in nude mice. Cornell does not have a special nude mice facility, so we only injected 5 mice. Three had solid tumors and the other 2 gave us less than 2 mg antibody after protein A column purification.

Should you not be able to help us with c-src or the antibody or both, do you have some suggestions as to what our problem is? Would you recommend switching to another hybridoma (e.g. SR 2-17, suggested by Sarah Courtneidge)? I strongly feel that before publishing we should repeat some of our experiments at least with pure c-src because of the above mentioned contaminants in our immune complexes.

Please convey my warmest congratulations to Mike and remind him to send me the manuscript he promised me in Vienna.

With best wishes for a successful future career.

Sincerely yours,

Efraim Racker