Dear Albert:

Our two major virus programs in LID should be fairly clear to you, but I will try to put them in a couple of nutshells. They are mission-oriented, focused (1) on the development of meaningful reproducible laboratory tools for detecting virus infections (either past or present); and (2) using them to determine their importance in causing acute, chronic and neoplastic disease in humans. We have isolated over 30,000 strains of virus from children in the last 12 years, all of which have been identified; in LID we have discovered, described and classified perhaps half of the prevalent viruses known to infect man.

As a consequence of these studies, NIAID has been able to make two considerable steps forward. (1) We have defined the roles of many different viruses in human disease, including adenoviruses, Coxsackie, ECHO, respiratory syncytial and parainfluenza viruses which, with PPLO's, account for 70% of all respiratory disease in childhood. A concentrated effort is also being brought to bear on studying the natural history of rhinoviruses. This group appears to account for 20% to 30% of adult minor respiratory disease. (2) We have been enabled by Congress to mount a nation-wide preventive attack on the respiratory disease problem, by many magnitudes man's largest morbidity problem and also a significant cause of mortality in infants.
2.

Effective preventive vaccines are available for some of the adenoviruses and other vaccines which appear to be reasonably near to useful application, namely, for the prevention of Eaton PPLO pneumonia, and the illnesses caused by the three parainfluenza viruses. A vaccine for respiratory syncytial virus, which is the major single cause of pneumonia in infants and infant deaths, is still elusive, but this too can be expected to yield to intensive research. However, much more investment is required to bring these promising preventive vaccines to early fruition and we estimate that we will need at least $3 to $5 million additional each year for the next few years.

We have additional problems. We are stymied in moving forward on the vaccine front by two entirely new developments: (1) The fact that certain vaccine strains cause cancer in laboratory animals; and (2) by the fact that we have absolutely no funds available which are specified for rapidly clearing our candidate vaccine strains of the taint of "oncogenic sin."

Currently NIAID is spending approximately $3 million on the virus vaccine program each year. Because of the newly discovered oncogenic problems, we now must use nearly 30% of this amount for safety tests and for studies of the oncogenic effects which occur in order to assure that the experimental vaccine materials to be used in man are free of such oncogenic effects. This cost can be expected to increase exponentially, since we are only in the early stages on the necessary testing. This sudden side-tracking of funds has put a virtual halt to our plans for further development of the vaccines themselves. This situation is particularly serious, because it could
easily destroy the vaccine program, a program which has just begun to achieve some notable objectives. For instance, LID recently developed a new method of immunizing against adenovirus type 4 infection, shown over a ten-year period to be the most common etiological agent responsible for epidemic febrile respiratory disease among military recruits. This vaccine has proved 100% effective in recently conducted field trials. One can appreciate the significance of this achievement in light of the following statistics: Although military recruits account for approximately 5% of the total military population, they contribute 45% of the total number of hospital admissions for respiratory disease seen in the military service. Adeno 4 accounts for from 50% to 90% of these admissions. In addition to the very high morbidity, approximately 10% of the infected individuals develop pneumonia.

Finally, from another point of view, NIAID must become involved in the studies of human adenoviruses and other viruses that are known to cause cancers in animals. Five of the 31 human adenoviruses, several of which are quite prevalent, are known to be oncogenic in newborn animals. The importance of these viruses as possible causes of human cancer must be determined as soon as possible. This will not be easy, since these viruses do not persist in the animal tumors they cause. It will require very sophisticated laboratory skills and extensive epidemiological competence and experience in the study of viral infections of man to finally settle this problem - aye or nay.
Which of the national **XX** institutes is obviously best qualified to pursue this kind of research most effectively? Of course, we feel that NIAID **XXXX** has the laboratory and epidemiological talent available to seek answers to the questions now being posed about the oncogenic adenoviruses. To do this job properly, however, we estimate that we need at least $2 million appropriated directly to NIAID each year. This would include funds for intramural, collaborative and grant programs.

Albert, I think we **XX** have the capabilities and desire to accomplish what needs to be done in this area. Why should other institutes and divisions unprepared to work in this particular area be given the responsibility and funds for doing precisely what **XX** we are prepared and anxious to do?

Kindest regards,

Sincerely,

Bob.

Robert J. Huebner, M.D., Chief Laboratory of Infectious Diseases National Institute of Allergy and Infectious Diseases

cc: Drs. Jacobs and Bloom