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WASHINGTON UNIVERSITY
SCHOOL OF MEDICINE
SAINT LOUIS

DEPARTMENT OF MICROBIOLOGY
EUCLID AVENUE AND KINGSHIGHWAY

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Dr. Joshua Lederberg
University of Wisconsin
Madison, Wisconsin

Dear Josh:

As you probably know my visit to Stanford materialized into a decision to accept their offer. Aside from the obvious climatic and geographical attractions, I think there will be better opportunities for graduate student teaching and a degree of intimacy between the medical and university that will minimize trade school behavior. Troublesome administrative problems will inevitably arise, but I think the mechanisms for solution at Stanford will be easier to reach than at so large and complex a place as Berkeley. It's awful leaving Washington University; the traditions of scholarship are well established here and we have a number of good friends.

The whole group of us here will be moving and we will be able to appoint two additional people who I hope will better represent physical and organic chemistry than we do now. We've been able to plan the space we will occupy and should be moving late in the spring of 1959 when completion of the buildings is anticipated. With everybody helping, the move shouldn't cost us too much time or anguish.

I would have liked to write you sooner about the isolation of DNA but I had, and am afraid still have, very little to offer. The DNA we have used routinely in our work is prepared from calf thymus by the Kay and Dounce procedure. We have also used T2 phage DNA prepared by osmotic shock and centrifugal removal of the ghosts and Hemophilus DNA prepared by Zamenhof's method using the Sevag procedure. I have reservations about the application of detergent or Sevag procedures to getting out E. coli DNA since we know that a DNAase which degrades T2 phage DNA withstands these manipulations to a considerable extent. The use of RNAase destroys an inhibitor of DNAase which masks a considerable amount of the DNAase activity in crude fractions; Pardee and Kozloff have described this phenomena. The use of Mg^{++} binders, such as citrate or versene, is not a certain way of inhibiting DNAase, since we know of the existence of 4 distinct DNAases in coli and the metal requirements may vary widely. We would of course prefer to avoid the use of strong acid and alkali and heat. Up to recently we haven't needed E. coli DNA and weren't in a position to distinguish "good" from "bad"; as a result we haven't given this problem a lot of attention. For a few weeks this summer, Dale Kaiser and Dave Hogness were making some passes at coli transformation and spent most of their time trying to learn how to extract coli DNA.

Our own work has taken a hopeful turn. After several wearying months of trying to free our enzyme from its contaminating DNAases we seem to have a useful preparation. First we were able to show net synthesis that more than equals the DNA we use as "primer". The next finding was that more thymus DNA "primer" was necessary with high levels of the purified enzyme, than with comparable levels of the less purified preparations. However, preincubation of the DNA with one of the discarded fractions activated it about 3-fold; similar activations are possible with extremely minute

amounts of pancreatic DNAase. With the purified enzyme, samples of DNA eluted from a resin column (Ecteola) with increasing salt behave differently as "primers". All this becomes more and more suggestive of end groups as reactive components. There are some interesting kinetic results with pyrophosphorolysis which indicate that such reversal is rapid when the DNA chain is being formed but is very slow or slight once it has been formed. Before too long we'll have another look at the synthesis of the hemophilus transforming DNA.

Sylvy and I are going to spend October in Japan and then go around the world in November. The stimulus is an enzyme symposium in Tokyo. We're eager to have you and Esther come down here and when I know my commitments for next winter and spring more precisely, I hope we can persuade you to visit us.

Thanks a lot for sending me the data about your medical genetics course. I passed some of it on to key people here and will pushing for genetics instruction for medical students at Stanford.

As ever,

Arthur Kornberg

AK/b