January 10, 1956.

Dr. H. Gobind Khorana
British Columbia Research Council
University of British Columbia
Vancouver 8, Canada

Dear Dr. Khorana:

I have been terribly slow in answering your last letter because we have had unexpected trouble in making PRPP. To begin with the barium salt of PRPP which I promised to send had deteriorated to a level of about one-half the activity it had a year ago, with a corresponding increase in inorganic pyrophosphate. I, therefore, asked one of the newly arrived Fellows to prepare some PRPP. After a number of delays occasioned by his learning how to prepare the necessary enzymes, he has finally obtained a product which I put in the mail yesterday. It differs from the previous materials in that it was precipitated from eluate (from a Dowex chromatogram) as a lithium salt by acetone. I am most disappointed in the analysis and quantity of the product, but rather than put you off any longer I thought I would send it along any way.

I sent about 50 mgms. 1 mg. contains in μmole about 0.40 PRPP, .17 P_i, .60 pentose, .19 inorganic pyro, 1.0 acid-labeled P, and 1.85 total P. Another fraction which gives a considerably better analysis and is more pure is, unfortunately, very tacky and we have kept it in solution. I am rather embarrassed with the poor quality of this material and I hope you will excuse it on the basis that it is not the focus of any genuine research interest for the moment. The person who prepared this material may carry out an experiment of trying to see how the ATP is transferred to ribose-5-phosphate. If he does, I will let you know the results.

I would like to tell you about a problem with which we are preoccupied at the moment. It is an enzyme system which carried out reactions which are consistent with the following sequence: thymidine $\xrightarrow{ATP}$ thymidine-5-phosphate $\xrightarrow{ATP}$ thymidine triphosphate $\xrightarrow{ATP}$ [thymidylic X] $\xrightarrow{ATP}$ polydeoxyribonucleotide. At the moment we are working on the conversion of thymidine triphosphate to polynucleotide. The requirement for at least two discrete heat-labile fractions, as well as the need for ATP, suggests that more than one step is involved. We have used your method as described for uridine polyphosphate synthesis by thymidylic acid. On chromatography we obtained a nymber of thymidine polyphosphates, as indicated by chromatography behavior and analysis. Some strange discrepancies between chromatography behavior and analysis were oberved which may be due to the formation of N substituted thymidylic derivatives, such as described by you and Dekker for adenylic acid. We have also found that fractions which

analyze like thymidine di- and triphosphate produce the incorporation of enzymatically prepared, isotopically labeled thymidine, and a thymidine triphosphate. Such inhibition is comparable to a dilution effect but, of course, have another basis too. I am eager to know whether you have any personal experience with the discoxynucleotide polyphosphate synthesis and, if so, we would be grateful for your suggestions. As you can gather from this letter, and the one that Dr. Berg wrote you yesterday, we are becoming very much enamoured with this problem.

I have wondered whether there might be some possibility of having you come to St. Louis for a visit and a seminar, if you can possibly arrange for some time between now and next June. Unfortunately, Dr. Lipkin is leaving this week to spend the next eight months in England and Sweden, but there are other chemists and biochemists who are eager to hear about your work. We can take care of your expenses, or if you are coming near or through St. Louis we can provide a modest honorarium.

With best wishes,

Sincerely yours,

AK/McK

Arthur Kornberg.