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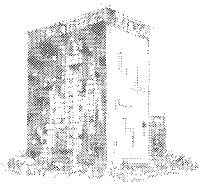

McARDLE LABORATORY
FOR CANCER RESEARCH
MEDICAL CENTER UNIVERSITY OF WISCONSIN • MADISON, WISCONSIN 53706

September 30, 1971

Prof. Arthur Kornberg
Department of Biochemistry
Stanford University Medical Center
Palo Alto, California 94304

Dear Arthur:

Bob wells has shown me a preprint of a paper by Brutlag, Shekman, and Kornberg on the involvement of RNA polymerase in the replication of M13 DNA. In addition, Doug Brutlag told me about this work at Cold Spring Harbor, and has now sent me his manuscript.

I find this paper very exciting because it defines the involvement of RNA synthesis in DNA replication (initiation?) in a very clean way; I expect that the study of the molecular basis of the coupling will proceed well in this case. Also, I find the explicit statement of the possibility of an RNA primer to be very constructive (i.e. testable). I am writing because I think that the manuscript may not communicate information on the generality of the phenomenon being described.

In the introduction and discussion you present good reasons for studying the possibility of an RNA primer; however, the average reader may not be aware that the involvement of RNA synthesis in the initiation of DNA replication has been studied extensively in λ (mainly by us) and has been suggested for E. coli by Lark (1969 review). In the case of λ, the evidence extends to the point implicating initiation rather than the movement of replication forks. Further, it is found that the transcription necessary for initiation must lie near the origin of replication. Finally (as is now implicit in the classical experiment of Rene Thomas and Elizabeth Bertani), the transcription which activates initiation of λ replication is subject to repression -- a fact which you can see has broad biological import.

I enclose our published work on the λ case so that you can evaluate this point. As I stated at the outset, I find your manuscript to be a valuable breakthrough in these studies, and in raising this point I do not intend to detract from its value.

Sincerely,

Bill.

William F. Dove

WFD/cw