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Dear Francesco:

Broadly, I can divide the work in three general areas.

First is the work on f1 histone. Although this work started with experiments directly related to SV40, it has taken a slightly different turn. Basically, the finding is that f1 histone binds preferentially with superhelical DNA, and in fact, the extent of complex formation by labeled DNA is a direct function of the extent of superhelicity...all other aspects of the circular DNA being identical. F1 histone is the largest of the five common histones, is the lysine rich histone, is less conserved from an evolutionary standpoint than are the other histones. Various recent proposals on the relation between DNA and histone in chromatin structure generally leave f1 out of consideration because the x-ray patterns of chromatin are unchanged when f1 is selectively removed. Also, it is present in about half the molar amount of the other histones. Our finding seems to be exciting because it offers the first new data in years suggesting what f1 might be doing. Tikva Vogel, who discovered the reaction, is busy studying basic chemical properties using SV40 DNA and calf thymus histone. We are anxious to initiate some physiological work along the following lines. There is good reason, though not firm data, to believe that histone synthesis is stimulated upon synthesis of viral DNA after infection of permissive monkey cells with SV40. We would like to know if f1 synthesis is stimulated, what the time course relation of the synthesis is in relation to SV40 synthesis, whether the f1 is phosphorylated or not and ultimately what role it plays in DNA metabolism. You might be interested in starting on such experiments. The methods are available and you could start right in.

Second general area is development of an in vitro system for SV40 DNA synthesis. We (Don LeBlanc) has good SV40 DNA synthesis in nuclei from infected cells but the DNA is primarily linear, that is, the circles

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are not completed. Adding cytoplasm seems to increase the extent of circles and we would like to find out what component of the cytoplasm is responsible. This should allow us to sort out the mechanism of circularization...presently unknown. There are also many other aspects of the DNA synthesis that could be studied...Okazaki mechanisms, RNA priming, enzymes, etc. You could easily choose something interesting here.

The third major area relates to defective SV40 that arises upon serial undiluted passage of the virus. These defectives are of many types, deletions, reiterations, and substitutions with host DNA. The latter class is the one we are interested in. This is a difficult but fascinating area. The major technical difficulty is that the structure of the defective DNA keeps changing. But we seem to have a preparation that is relatively stable, although probably a mixture of two different defectives. Restriction enzymes are used for analysis of structure. The defectives also interfere with replication of good virus and the mechanism of interference is an area we would like to do more work on, but have not had time. There are many other aspects of this, but it is complicated to explain in a letter.

What I suggest is that you spend the first week here reading and talking with all of us and then decide what you would most like to do.

Are there any things I could do to ease your arrangements here?

With best regards.

Sincerely,

Maxine Singer