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FACULTY OF MEDICINE

DEPARTMENT OF BACTERIOLOGY AND IMMUNOLOGY
THE HAMILTON KING MEEK MEMORIAL LABORATORY

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November 24, 1953

Dr. Joshua Lederberg,
Department of Genetics,
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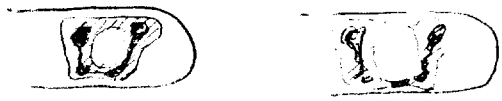
MADISON 6, Wis., U.S.A.

Dear Lederberg:

I was delighted to get your detailed letter and to know the problem that besets you. We have to learn a lot about the structure of the normal nucleus before any really useful understanding can result. In the end there will have to be an evaluation of cytological observations together with the genetic observations, but it seems too early to go as far as Werner Braun has gone in his recent book.

It is most interesting that you have real doubts, even when approaching the problem from the genetic angle. We have not been able to find a spindle, but we can find the constellations of granules that DeLamater figures as metaphase plates and spindle poles. However, all the parts that should be achromatic prove to be chromatic - as we had suspected from his pictures and his methods. If you take selected chromatin patterns you could make up a series to fit a concept of mitosis; but you could make other series to fit almost any hypothesis. So it would seem to be worth restricting ourselves to the observational plane.

I have done few experiments on the nuclear structure of young coliforms and the general impression was something like this:-



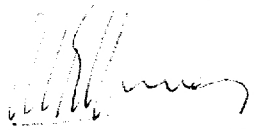
This is remarkably similar to the pictures drawn by Hollande in the 30's, although his nucleosome is an uncertain quantity! We have been trying to follow the fate of these components

during some phage infections and they seem to behave as if they were distinct components.

A difficulty, at the moment, is that "direct" staining (fixed films stained for 20-30 minutes in Giemsa and differentiated in water acidified with a drop of acetic acid) provides information about the chromatin alone. Looked at with a suitable filter they look very good and the elements appear to be less fragmented than the same group hydrolyzed in the usual way. This means that all the ideas concerning "core" and "matrix" are really dependent upon indirect methods. I wonder if the chromatin that is partitioned into each daughter "nucleus" is all in one complex but connected piece. The complexities of individual nuclei may represent various stages in the synthesis of a new chunk rather than stages in a mitotic cycle. Fitz-James, working on both the chemical and cytological aspects of spore germination in B. megaterium, feels that there is continuous production of DNA and that the number of chromatin granules does not increase $3 \rightarrow 6$ but rather $3 \rightarrow 4 \rightarrow 5 \rightarrow 6$. There may be some chance of a quantitative approach in that situation.

We have always used Giemsa diluted with a phosphate buffer of pH 7.0. Actually, we use the buffer tablets supplied for the purpose by Gurr and have had no cause for complaint. I tried buffering to pH 5 the other day and did not find any great difference. I would like to know what the troubles were that prompted the change of pH.

Yours sincerely,



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R. G. E. Murray, M.D.
Professor