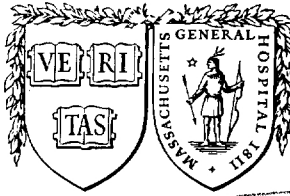


HARVARD MEDICAL SCHOOL

LABORATORY OF
CELLULAR NEUROPATHOLOGY



Warren Anatomical Museum
Harvard Medical School
Boston 15, Massachusetts

January 18, 1962

Dr. Joshua Lederberg
Department of Genetics
Stanford University Medical Center
Palo Alto, California

Dear Dr. Lederberg:

I am enclosing reprints of our papers on autoradiographic studies of neural development, as you requested.

You asked about evidence on DNA turnover in the absence of mitosis in neurons. No data are available. Causey and Stratmann (J. Anat. 1959 93:341-347) studied neurons of the rabbit superior cervical ganglion at time intervals after denervation, up to 28 days. They measured relative DNA content in neuron nuclei by Feulgen microspectrophotometry and recorded a progressive fall from 85 units to about 50 units in about two weeks time after nerve section. They suggested that neuronal DNA may be labile, at least in part, and suggested a few possible reasons why. They did not extend the measurements long enough to learn if the $2n$ value would have been restored. If their data are correct, a neuron either retains permanent evidence of injury (lowered DNA content) or resynthesizes DNA in the absence of cell division.

Our own published observations extend only to 30 days beyond birth and we did not recognize loss of tritium during that time. However, ~~we~~ I am sure you recognize that such a statement is not worth much unless one makes accurate and representative grain counts, measures nuclear sizes (which change postnatally) and corrects for variations in histological methods, autoradiographic emulsion, development time, etc.

I hope to have a reasonable answer to your question in about two to three months. We have a series of animals

R.L. Minkiewicz

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injected with thymidine- H^3 at various embryonic stages and killed at two years of age. These are being processed now. We also have littermates in the same series, but killed at earlier postnatal ages.

The neuroglia present another problem. The best data are those of Smart and Leblond (J. Comp. Neur. 1961 116: 349-367). Their tables, especially Table 2, suggest either DNA turnover or mitosis. Little evidence of mitosis was found, even with the aid of colchicine. There are several possible explanations for these data, including DNA turnover. You might also glance at another of Leblond's papers in Am. J. Anat. 1960 106:247-285, especially page 257.

Assuming DNA half-life of neurons is very long, it is possible that these specialized cells may depend on neuroglial cells to do things for them in a symbiotic sense, things which other cells do for themselves and which involve DNA turnover. However, even these crude speculations are best deferred for a few months until we have some decent numbers.

Thank you very much for your interest. I will write again when I have something to say. Please give my warmest regards to Cliff Grobstein.

Sincerely,



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RLS/jh
Encls.