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# This Week's Citation Classic

**Messier B & Leblond C P.** Cell proliferation and migration as revealed by radioautography after injection of thymidine-$H^3$ into male rats and mice. *Amer. J. Anat.* **106**:247-85, 1960. [Department of Anatomy, McGill University, Montreal, Canada]

**Following a single injection of $H^3$ -thymidine into young rats and mice, the labeled nuclei were identified by radioautography at times varying from 20 minutes to three months thereafter. It was thus found that cell populations may be classified into three categories on the basis of HMhymidine uptake: static, expanding, and renewing. [The *SCI*® indicates that this paper has been cited over 430 times since 1961.]**

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"This article was published at the dawn of the $H^3$-thymidine era. Indeed, the recent commercial availability of tritiated thymidine in the late 1950s prompted investigators involved in DNA synthesis research to call on this DNA specific precursor for an answer to long-awaited questions. $C^{14}$-thymidine had timidly pointed in that direction a few years previously, but the prohibitive cost of this precursor curbed its wide use. The competition between $H^3$-thymidine and $C^{14}$-thymidine quickly favored the former, for two main reasons: first, the possibility of obtaining samples with high specific activities and, second, the soft beta rays emitted by the decomposition of the tritium atoms. Although the latter property constituted, at the time, a difficulty for the biochemical assessment of the radioactivity levels in biological specimens, this same property proved to be a major asset for a good radioautographic localization.

"Because of the shortcomings of mitotic counts for the study of cell proliferation, the availability of a specific DNA precursor providing an excellent radioautographic localization allowed a new approach to the problem of cell kinetics. Indeed, the use of a pulse injection of labeled thymidine introduces a radioactive marker in the DNA of proliferating cells. The retention of the label in nuclei of various tissues for periods as long as six months offered the possibility of following the fate of newly-formed cells.

"With less than a dozen papers published on the subject in 1959, C.P. Leblond and I engaged in a comprehensive radioautographic survey of $H^{3-}$ thymidine uptake in several tissues of rats and mice to assess their rates of cell proliferation and migration. This work constituted the core of my PhD program. Coincident with this survey were the technical improvements put forward in collaboration with Beatrix Kopriwa to the then recently developed dipping technique of radioautography.[1] Counts of many thousands of radioactive and nonradioactive nuclei helped in classifying the cell populations into three categories: *static,* in which no labeled nuclei appear; *expanding,* in which a small number of indefinitely persisting labeled nuclei appear in proportion to the rate of growth; and *renewing,* in which the occurrence of large numbers of labeled nuclei indicates active cell production, while the subsequent rapid decrease and disappearance of the labeled nuclei indicates a corresponding cell loss.

"The atmosphere of scientific dedication in our laboratory played a major role in the success of this research project, but the timely coincidence of favorable circumstances was also helpful. This timely coincidence of the commercial availability of $H^{3-}$ thymidine and technical improvements of the radioautographic method probably account for the frequent citation of the paper. More recent work in the field has been published by Kopriwa."[2]

1. **Kopriwa B M & Leblond C P.** Improvements in the coating technique of radioautography. *J. Histochem. Cytochem.* **10**:269-84,1962.
2. **Kopriwa B M.** A comparison of various procedures for fine grain development in electron microscopic radioautography. *Histochemistry* **44**:201-24,1975.