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This Week's Citation Classic

Scherrer K & Darneil J E. Sedimentation characteristics of rapidly labelled RNA from HeLa cells. *Biochem. Biophys. Res. Commun.* **7**:486-90, 1962.
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The techniques developed for extraction of infectious viral nucleic acid were used to extract cell RNA, resulting in the recognition, for the first time, of high molecular weight nuclear RNA from mammalian cells. The dominant rapidly labeled peaks, '45S' and '35S,'were subsequently found to be ribosomal precursor RNA, and the polydisperse material was characterized as the so-called 'heterogeneous nuclear RNA,' the hnRNA. [The *SCI*® indicates that this paper has been cited over 900 times since 1962.]

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"My earliest experience with poliovirus RNA synthesis, and my postdoctoral time with Francois Jacob during the year of the prediction and demonstration of messenger RNA in bacteria, had convinced me that the time (1961) was ripe to begin a study of mammalian cell RNA.[1-7] It is obvious from the flood of talented people who soon also came to work on animal cell RNA synthesis that many others agreed. Thus, more or less by accident, our work was an early forerunner in a subsequently popular field. Klaus Scherrer, my first postdoctoral fellow at MIT, and I first began by trying to extract labeled RNA from HeLa cells labeled for 20 to 30 seconds. The available nucleosides were insufficiently radioactive for us to obtain a labeled preparation in this manner, so we lengthened our label times to minutes. With this length of label we were able to reproducibly obtain the high molecular weight RNA. Only recently have we returned to the extremely short label times.[8]

"Two aspects of the 1962 paper probably account for its frequent use as a reference by the large group that has become interested in RNA synthesis. First, the method described allows extraction of the majority of the total cell RNA without (or with minimal) degradation. We were pointed toward this goal by the earliest work of John Colter[9] and E. Wecker[10] who had with similar techniques obtained infectious viral RNA of over 2 x 10^6 daltons from animal tissue. The method in outline involved: (1) pulse labeling of cultured cells to observe kinetics of labeling of various RNA components; (2) cell lysis with SDS and RNA extraction with phenol at elevated temperature (60°); (3) zonal sedimentation of RNA to separate discrete species of RNA; (4) radioassay of labeled RNA (newly made) and optical assay of UV absorbance for preexisting RNA. Second, the paper showed that RNA extracted from human cells was different from that of bacteria and this meant there was something to study in the field of animal cell RNA metabolism. Because a major fraction of the RNA from cells labeled for short times was discrete in size but larger than the RNA from cells labeled for long times, the possibility of a precursor to ribosomal RNA was first suggested by this work, although it took another six months or so to suggest that point more strongly. Finally, at the end of an additional 15 years, the probable role of the non-ribosomal polydisperse nuclear RNA, the so called heterogeneous nuclear RNA, as an mRNA precursor appears likely as well."

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