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Journal club

A HISTONE CODE FOR DNA REPAIR

In 1998, Rogakou, Bonner and colleagues reported that irradiation of mammalian cells causes a subtle but immediate alteration in the mobility of a small fraction of histones, as revealed by the analysis of samples using two-dimensional (2D) gel electrophoresis. The novel mobility histone species were attributable to radiation-induced phosphorylation of the histone H2A variant, H2AX, on Ser139 of its carboxy-terminal tail. The same authors later showed, in 1999, that antibodies specific for γH2AX (H2AX phosphorylated on Ser139) decorate the chromatin flanking mammalian DNA double-strand breaks. They calculated that megabase tracts of chromatin might be modified at Ser139 of H2AX in the vicinity of a chromosome break — a new idea that immediately caught the attention of the field. Although relationships between chromatin structure and DNA repair had been suggested by previous studies, the discovery of a single, simple, locally break-responsive histone mark seemed to provide the 'ocular proof' of this concept.

> "one of the cornerstones of this emergent field was a tiny spot on a 2D gel"

Today we have an increasingly sophisticated understanding of the biochemical events of the γH2AX response and its importance in preventing genome instability. We appreciate that γH2AX, together with the adaptor protein mediator of DNA damage checkpoint protein 1 (MDC1), forms part of a 'histone code' of DNA repair, which recruits DNA damage response proteins to regions of damaged chromatin.

It is instructive to recall that there was a time when the chromatin response to chromosome breaks was considered of marginal interest. I take pleasure in the thought that one of the cornerstones of this emergent field was a tiny spot on a 2D gel (shown in Figure 1 of the 1998 paper by Rogakou *et al.*), which Rogakou, Bonner and colleagues had the confidence not to ignore.

Ralph Scully

Department of Medicine, Harvard Medical School, Beth Israel Deaconess Medical Center, CLS 438, 330 Brookline Avenue, Boston, Massachusetts 02215, USA.
e-mail: rscully@bidmc.harvard.edu

ORIGINAL RESEARCH PAPERS Rogakou, E. P. *et al.* DNA double-stranded breaks induce histone H2AX phosphorylation on serine 139. *J. Biol. Chem.* **273**, 5858–5868 (1998) | Rogakou, E. P. *et al.* Megabase chromatin domains involved in DNA double-strand breaks *in vivo*. *J. Cell Biol.* **146**, 905–916 (1999)