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1. Etienne-Manneville, S. & Hall, A. *Nature* **420**, 629–635 (2002).
2. Sander, E. E. *et al. J. Cell Biol.* **147**, 1009–1022 (1999).
3. Nimnual, A. S., Taylor, L. J. & Bar-Sagi, D. *Nature Cell Biol.* **5**, 236–241 (2003).
4. van Leeuwen, F. N. *et al. J. Cell Biol.* **139**, 797–807 (1997).
5. Rottner, K., Hall, A. & Small, J. V. *Curr. Biol.* **9**, 640–648 (1999).
6. Arthur, W. T. & Burridge, K. *Mol. Biol. Cell* **12**, 2711–2720 (2001).
7. Noren, N. K., Niessen, C. M., Gumbiner, B. M. & Burridge K. *J. Biol. Chem.* **276**, 33305–33308 (2001).
8. Arthur, W. T., Petch, L. A. & Burridge, K. *Curr. Biol.* **10**, 719–722 (2000).
9. van Leeuwen, F. N. *et al. Nature Cell Biol.* **1**, 242–248 (1999).
10. Sanders, L. C., Matsumura, F., Bokoch, G. M. & de Lanerolle, P. *Science* **283**, 2083–2085 (1999).
11. Bokoch, G. M. & Diebold, B. A. *Blood* **100**, 2692–2696 (2002).
12. Joneson, T. & Bar-Sagi, D. *J. Biol. Chem.* **273**, 17991–17994 (1998).
13. Tsuji, T. *et al. J. Cell Biol.* **157**, 819–830 (2002).
14. Suh, Y. A. *et al. Nature* **401**, 79–82 (1999).
15. Kheradmand, F. *et al. Science* **280**, 898–902 (1998).
16. van Wetering, S. *et al. J. Cell Sci.* **115**, 1837–1846 (2002).

RNA repaired

The genome is continuously bombarded by ionizing radiation, bathed in a cocktail of nucleic acid modifying compounds and subjected to errors during its replication. To ensure faithful maintenance of genetic information, all organisms have evolved intricate and highly specialized means to repair this unavoidable damage. Defects in a number of these pathways result in cancer, premature ageing, developmental defects or even death.

One of the modifications nucleotides are subjected to is alkylation. Currently, three independent ways to deal with mutagenic alkylation have been elucidated: methylpurine DNA glycosylase and the base excision repair pathway removes 3-methyladenine, whereas methylguanine DNA methyltransferase specifically modifies O^6-methylguanine and 1-methyladenine or 3-methylcytosine are subject to oxidative demethylation by AlkB. The latter two base modifications are formed in much higher yields in single- versus double-stranded DNA, and abundantly also in RNA. In fact, RNA is subject to over 60 other forms of post-transcriptional modification, some of which have been shown to affect RNA folding and RNA protein interactions, and hence transcription and translation. Although some of these modifications are clearly of regulatory importance, others are not and would be expected to render messenger- and other RNA non-functional at best or to generate potentially detrimental proteins at worst. Until now, it had been unclear how the cell deals with chemically aberrant RNA: is it selectively degraded, left alone or repaired?

Now, Hans Krokan, Erling Seeberg and colleagues (*Nature* 10.1038/01363) report comparative functional analysis of three members of the AlkB demethylase family; *E.coli* AlkB, and the human homologues hABH2 and hABH3. Biochemical analysis with recombinant enzymes demonstrated that all three demethylated 1-methyladenine and 3-methylcytosine in DNA. However, the three enzymes showed markedly divergent substrate preferences: whereas hABH2 was most active on double-stranded DNA, AlkB exhibited a moderate preference for single-stranded substrates and hABH3 showed a strong preference for single strands. Strikingly, both types of methylated bases were also repaired in the context of RNA by AlkB and hABH3. Krokan and colleagues then went on to show that the three demethylases will also function to re-activate methylated bacteriophages when expressed in *AlkB*-deficient *E. coli.* AlkB and hABH2 re-activated the single-stranded DNA phage M13, as well as the double-stranded λ phage. In contrast, and consistent with the *in vitro* substrate preferences, methylated forms of the single-stranded RNA bacteriophage MS2 were re-activated only by AlkB and hABH3, resulting in significantly increased phage survival.

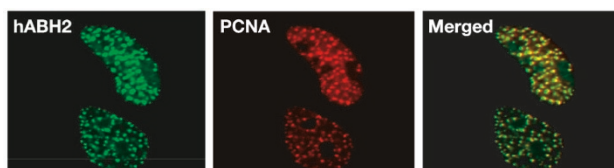

Figure 1 **Subcellular localization of hABH2. Transient expression of hABH2–EYFP and ECFP–PCNA in HeLa cells.**

Although it remains unclear if hABH3 can also function in RNA repair in eukaryotic cells, data is presented on the initial characterization of their subcellular localization in cultured cells. The enzymes are nuclear, but localize differentially, with hABH2 showing some preference for nucleoli and relocating to replication foci during S phase (see figure).

Altogether, these data may hint at a role for hABH2 during DNA replication, whereas hABH3 and AlkB may be involved in maintaining mRNA in a demethylated functional state. It is notable that certain plant RNA viruses also seem to employ AlkB homologues, lending credence for an involvement of enzymes of this family in RNA repair. Although direct support for the occurrence and functional importance of RNA repair in eukaryotic cells will have to await future studies, this study opens a new chapter in the intricate book of nucleic acid repair.

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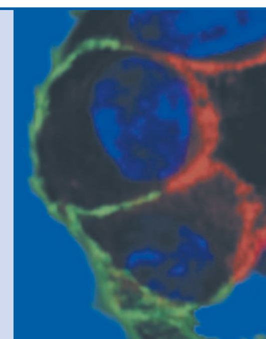

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