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Journal club

WHAT HOLDS EPIGENETIC MEMORY?

How epigenetic memory is stored and inherited is an on-going debate (Ptashne). In so-called '*cis* memory', epigenetic information is proposed to be physically stored in local chromatin states that are associated, for example, with DNA methylation or histone modifications. By contrast, in '*trans* memory', epigenetic information is stored in the concentration of a diffusible factor such as a transcriptional repressor.

> epigenetic memory of *FLC* repression is physically located in the local chromatin environment

An elegant natural system in which to study this issue is the cold-induced epigenetic silencing at *Arabidopsis thaliana FLOWERING LOCUS C* (*FLC*). *FLC* mRNA and protein decrease quantitatively with increasing cold exposure, as *FLC* becomes repressed in an increasing number of cells over time (Angel *et al.*).

PHD-Polycomb repressive complex 2 components are required for the induction and maintenance of the repressed *FLC* state. These factors promote cold-induced changes in the chromatin state at *FLC*, specifically a localized increase in trimethylated Lys27 of histone 3 (H3K27me3) covering nucleosomes +3, +4 and +5. This peak then 'spreads' upon return to warmth, and high levels of H3K27me3 accumulate to cover the whole *FLC* locus, which is associated with long-term epigenetic silencing. Taken together, these results suggested a *cis*-based epigenetic memory of cold, with inheritance of the silenced state occurring independently at each locus. However, as in other model epigenetic systems, until recently it was difficult to exclude the existence of *trans* factor-based memory in which the FLC protein (a MADS box transcriptional repressor) and/or non-coding RNA produced at *FLC* feed into a *trans*-regulatory network.

A study stimulated by theoretical considerations of epigenetic regulation provided the definitive proof for *cis* memory (Berry *et al.*). Two distinguishable fluorescent reporters of *FLC* expression present in the same cells were used to investigate the *cis* memory storage capability of *FLC* chromatin. After cold treatment, expression of the two reporters was independent; in other words, one of the *FLC* reporters could be repressed in the same cell in which the other reporter was active. Furthermore, this 'mixed' expression state was stably inherited through multiple cell divisions, indicating that the epigenetic memory of *FLC* repression is physically located in the local chromatin environment (Berry *et al.*). The debate is over for Polycomb-mediated silencing — local chromatin states can hold memory.

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ORIGINAL ARTICLES Ptashne, M. On the use of the word 'epigenetic'. *Curr. Biol.* **17**, R233–R236 (2007) | Angel, A. *et al.* A Polycomb-based switch underlying quantitative epigenetic memory. *Nature* **476**, 105–108 (2011) | Berry, S. *et al.* Local chromatin environment of a Polycomb target gene instructs its own epigenetic inheritance. *eLife* **4**, e07205 http://dx.doi.org/10.7554/eLife.07205 (2015)