


 CHROMATIN

## Colour-coded classification

The traditional classification of chromatin into transcriptionally active euchromatin and repressed heterochromatin has been a useful model but is due for an upgrade to accommodate our increasing knowledge of chromatin functional domains. A massive integrative genome-wide analysis of 53 chromatin-associated proteins in *Drosophila melanogaster* has revealed that chromatin comes in five principal types; these could form a new framework for describing the epigenome.

Filion and colleagues selected a broad panel of proteins from the chromatin proteome and mapped their genomic locations in an embryonic *D. melanogaster* cell line using the DamID method. In this technique, each protein of interest is fused to DNA adenine methyltransferase (Dam), which marks protein–DNA interaction sites with a methyladenine footprint. The authors then used a data-driven computational classification strategy to identify recurrent, distinct combinations of protein association across the genome. Genomic regions — varying in length from 1 kb to more than 100 kb — fell into five clear classes as defined by their protein signature, and the authors gave each a colour name.

The GREEN and BLUE chromatin classes are consistent with two previously defined types of repressive chromatin: ‘classic’ heterochromatin that includes

heterochromatin protein 1 (HP1) (GREEN chromatin) and polycomb group (PcG)-associated chromatin (BLUE chromatin). Using chromatin immunoprecipitation, Filion *et al.* also found that the histone modifications in GREEN and BLUE regions matched previous knowledge of these heterochromatin subtypes.

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Strikingly, the authors found that the most abundant form of repressive chromatin, which covers ~48% of the genome and can form large (>100 kb) domains, was a new type (designated BLACK). Although BLACK chromatin domains are relatively gene poor, they contain >4,000 genes that Filion *et al.* showed to have no or very little transcriptional activity. Reporter transgenes inserted into BLACK regions are often repressed, which suggests that BLACK chromatin actively represses transcription. Genes that are in silent BLACK chromatin in embryonic cells are expressed in some other tissues, so the authors suggest this form of chromatin might be linked, at least in part, to developmental regulation.

The classification of the DamID data also showed that euchromatin consists of two distinct types. YELLOW and RED chromatin both contain proteins and histone modifications that are typical of transcriptionally active regions and produce substantial amounts of mRNA, but RED chromatin carries several regulatory proteins that are unique to this chromatin, including the nucleosome remodeller Brahma. Also, histone H3 trimethylated at lysine 36, which has previously been described as a universal marker of transcriptional elongation, was highly enriched at genes in YELLOW but not in RED chromatin, despite similar levels of transcription. Interestingly, these two types of active chromatin might reflect distinct regulatory mechanisms for different types of genes: genes in YELLOW chromatin are predominantly widely expressed and have housekeeping cellular functions, whereas genes in RED chromatin are more specialized.

Chromatin-associated proteins are broadly conserved among species, so it is likely that this classification will be widely applicable. Further investigation of the new domain types should provide a more nuanced view of how chromatin helps to control gene expression.

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**ORIGINAL RESEARCH PAPER** Filion, G. J. *et al.* Systematic protein location mapping reveals five principal chromatin types in *Drosophila* cells. *Cell* 30 Sep 2010 (doi:10.1016/j.cell.2010.09.009)