

 CHROMATIN

A haul of new histone modifications

“ histone Kcr is present in eukaryotic cells from yeast to human ”

In recent years there has been great progress in uncovering the roles of histone post-translational modifications (PTMs) in regulating chromatin-based processes, such as transcription. But, as a new paper reveals, there is still a lot to learn even about the basic repertoire of PTMs. This work by Tan *et al.* has increased the number of known PTM sites in eukaryotes by ~70% and includes sites for two previously uncharacterized marks, lysine crotonylation (Kcr) and tyrosine hydroxylation.

The authors used a mass spectrometry-based approach that combined analysis of histone peptides generated by four different methods; this enabled higher sequence coverage (87–100%) of histones than previous approaches. They identified 130 unique PTM sites, 67 of which were novel, including sites for lysine methylation and lysine acetylation (Kac), as well as 28 Kcr sites and six for another new mark, tyrosine hydroxylation.

Crotonyl groups (C_4H_5O) have two more carbon atoms than acetyl groups (C_2H_3O), and Tan *et al.* characterized Kcr in more detail. They demonstrated that histone Kcr is present in eukaryotic cells from yeast to human and, by several lines of evidence, that Kcr is distinct from Kac. For example, altering expression of histone acetyltransferases and deacetylases did not have a substantial effect on Kcr. By chromatin immunoprecipitation followed by sequencing (ChIP-seq), the authors

found that histone Kcr is enriched at the promoters and enhancers of active genes in human somatic cells. They then explored Kcr patterns during spermatogenesis in mice, as an example of developmental process with dynamic gene expression. Among their findings, they showed that after meiosis Kcr is enriched on sex chromosomes and marks testis-specific genes; the authors suggest that one of its roles may be to mark genes that escape sex chromosome inactivation.

These findings offer the tantalizing prospect that crotonylation, like methylation and acetylation, may be a modification with important roles in gene regulation, and this improved catalogue of PTMs will be a valuable resource for future studies.

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ORIGINAL RESEARCH PAPER Tan, M. *et al.* Identification of 67 histone marks and histone lysine crotonylation as a new type of histone modification. *Cell* **146**, 1016–1028 (2011)



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