Basal crosstalk

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Trimethylation of histone H3 at Lys4 (H3K4me3) is typically associated with active gene promoters, but it has been unclear how this histone modification is linked to transcriptional activity. Vermeulen *et al.* now report that H3K4me3 provides a binding site for the basal transcription factor TFIID, thereby supporting transcriptional activation.

Using SILAC (stable isotope labelling by amino acids in cell culture) technology to screen for H3K4me3-peptide-protein interactions, Vermeulen *et al.* identified TFIID. A decrease in the H3K4me3 mark *in vivo* led to reduced transcription from a subset of gene promoters, which was linked to the reduced association of TFIID to these promoters.

The plant homeodomain (PHD) finger is a known interactor of methylated H3K4. The TFIID subunit TAF3 contains a PHD finger, which, when deleted, resulted in defective H3K4me3 binding. *In vitro* binding assays revealed a specific, high-affinity preference of the PHD finger for H3K4me3. Native yeast nucleosomes that had been affinity purified using the TAF3 PHD finger were enriched for H3K4me3. By contrast, binding

of the TAF3 PHD finger was lost in H3K4me3-defective yeast strains.

Interestingly, asymmetric dimethylation of H3R2 reduced the binding of the TAF3 PHD finger to H3K4me3, whereas acetylation of H3K9 and H3K14 increased the binding of TFIID subunits to H3K4me3. So, agonistic and antagonistic crosstalk exists between histone H3 modifications and TFIID, resulting in increased or decreased binding, respectively, of TFIID to the histone tail.

Finally, the authors showed that TAF3 functions as a bona fide transcriptional coactivator that relies on its PHD finger for coactivation. They propose that H3K4me3 "...provides a binding site for TFIID, resulting in enhanced recruitment or stability of the RNA polymerase II preinitiation complex." These results make a compelling case that epigenetic changes are linked directly and mechanistically to the basal transcriptional apparatus.

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ORIGINAL RESEARCH PAPER Vermeulen, M. *et al.* Selective anchoring of TFIID to nucleosomes by trimethylation of histone H3 lysine 4. *Cell* **131**, 58–69 (2007)

“...H3K4me3 provides a binding site for the basal transcription factor TFIID...”

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