

ABSTRACT

GENOME-WIDE ANALYSIS OF TRANSCRIPTIONAL REPRESSION
MECHANISMS IN THE DROSOPHILA EMBRYO

By
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Transcriptional repressors control temporal and spatial patterns of gene expression in animal development through co-repressors, which interact with histone modifying enzymes and chromatin remodelers. In this work, I used genome-wide approaches to understand the mechanisms of repressors and corepressors by identifying biochemical changes on chromatin using the *Drosophila* Hairy long-range transcriptional repressor protein as a paradigm. I found that Hairy induces wide-spread and diverse changes in histone modifications. Intriguingly, many sites are targeted errantly by Hairy to modify chromatin landscape, even though gene expression is unaffected. I propose that many eukaryotic transcription factors may induce similar dynamic modifications on off-target sites, and speculate that this errant activity may provide a path for creation of new regulatory elements, facilitating the evolution of novel transcriptional circuits. In addition to these evolutionary insights, my studies on roles of corepressors showed that CtBP corepressor – also associated with short-range repressors - contributes to Hairy mediated repression in a quantitative and gene-specific fashion, suggesting that different classes of transcriptional repressors can utilize common corepressors to effect distinct histone modification patterns across the genome.