DOI:

10.1038/nrm2149

URLs

Clr3
<http://ca.expasy.org/uniprot/P56523>

Clr2
<http://ca.expasy.org/uniprot/O13881>

Ccq1
<http://ca.expasy.org/uniprot/Q10432>

Swi6
<http://ca.expasy.org/uniprot/P40381>

CHROMATIN

Shaping the landscape

Heterochromatic gene silencing in *Schizosaccharomyces pombe* occurs at both transcriptional and post-transcriptional levels. Shiv Grewal and colleagues have now identified an effector complex — SHREC (Snf2/Hdac-containing repressor complex) — that mediates transcriptional gene silencing (TGS) and regulates nucleosome positioning to assemble higher-order heterochromatin structures that are involved in various cellular functions, such as recombination suppression, long-range chromatin interactions, and regulation of centromere and telomere function.

The histone deacetylase **Clr3** has been shown to contribute to heterochromatic transcriptional silencing. Grewal and his team affinity purified Clr3 and identified its interaction proteins as the silencing factors Clr1 and **Clr2**, a novel factor, Mit1, which bears homology to the SNF2 family of chromatin-remodelling factors, and **Ccq1**, which has been linked to telomeres. Chromatin immunoprecipitation (ChIP)-chip analysis showed that Mit1 and Clr1–3 are associated with all major heterochromatic regions, but also with certain euchromatic sites. Instead, the binding profile of Ccq1 indicates that it is mainly restricted to telomeres. The core SHREC complex that is ubiquitous across all heterochromatin domains therefore contains four components, Mit1 and Clr1–3, whereas Ccq1 might recruit SHREC to telomere ends. This seems to be the case, as SHREC is enriched at telomere-associated sequences, which are occupied by the telomere-binding protein Taz1. Taz1 might cooperate with Ccq1 to recruit SHREC to telomeric heterochromatin, although there might be an additional pathway involving the RNA interference machinery that contributes to telomeric silencing through SHREC.

But how are SHREC components recruited to heterochromatic regions? HP1 proteins are thought to function as recruitment platforms for factors that affect gene activity in heterochromatin regions. Levels of SHREC components were dramatically reduced at heterochromatin regions in strains that lacked the

HP1 protein **Swi6**, although some protein still bound. These findings are consistent with the idea that SHREC recruitment is independent of Swi6, but that stable binding and spreading requires Swi6. By contrast, recruitment of SHREC to euchromatic loci is independent of Swi6. These findings indicate that there are distinct mechanisms for recruiting SHREC to heterochromatin and euchromatin.

When the authors inserted reporter genes at major heterochromatic regions in strains that lacked individual SHREC components, heterochromatic transcriptional silencing was derepressed. In addition, increased levels of acetylated H3K14 — which results in ‘open’ chromatin structures — and greater RNA polymerase II (Pol II) occupancy were detected in these mutant strains. These findings indicate that SHREC functions as an effector complex for the transcriptional silencing of heterochromatic regions by limiting the occupancy of Pol II.

Next, Grewal and co-workers mutated the histone deacetylase domain of Clr3 and the ATP-binding domain of Mit1. Both mutants alleviated transcriptional silencing at heterochromatic loci, which coincided with increased Pol II occupancy and H3K14 acetylation. This implies that the activities of Clr3 and Mit1 are both important for heterochromatic TGS by SHREC. The authors argue that SHREC might effect TGS by regulating the higher-order chromatin organization — strains that lacked either Clr3 or Mit1 activity showed altered micrococcal nuclease digestion patterns across a broad heterochromatin domain. SHREC might therefore facilitate proper nucleosome positioning that is required to assemble repressive heterochromatin.

It will be interesting to see whether similar effector complexes mediate heterochromatic silencing in higher eukaryotes.

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ORIGINAL RESEARCH PAPER Sugiyama, T. et al. SHREC, an effector complex for heterochromatic transcriptional silencing. *Cell* **128**, 491–504 (2007)

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