

**ISWI regulates higher-order chromatin structure and histone H1 assembly in vivo.**

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**Authors:** Davide F V Corona, Giorgia Siriaco, Jennifer A Armstrong, Natalia Snarskaya, Stephanie A McClymont, Matthew P Scott, John W Tamkun

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**Public Summary:**

Imitation SWI (ISWI) and other ATP-dependent chromatin-remodeling factors play key roles in transcription and other processes by altering the structure and positioning of nucleosomes. Recent studies have also implicated ISWI in the regulation of higher-order chromatin structure, but its role in this process remains poorly understood. To clarify the role of ISWI in vivo, we examined defects in chromosome structure and gene expression resulting from the loss of *Iswi* function in *Drosophila*. Consistent with a broad role in transcriptional regulation, the expression of a large number of genes is altered in *Iswi* mutant larvae. The expression of a dominant-negative form of ISWI leads to dramatic alterations in higher-order chromatin structure, including the apparent decondensation of both mitotic and polytene chromosomes. The loss of ISWI function does not cause obvious defects in nucleosome assembly, but results in a significant reduction in the level of histone H1 associated with chromatin in vivo. These findings suggest that ISWI plays a global role in chromatin compaction in vivo by promoting the association of the linker histone H1 with chromatin.

**Scientific Abstract:**

Imitation SWI (ISWI) and other ATP-dependent chromatin-remodeling factors play key roles in transcription and other processes by altering the structure and positioning of nucleosomes. Recent studies have also implicated ISWI in the regulation of higher-order chromatin structure, but its role in this process remains poorly understood. To clarify the role of ISWI in vivo, we examined defects in chromosome structure and gene expression resulting from the loss of *Iswi* function in *Drosophila*. Consistent with a broad role in transcriptional regulation, the expression of a large number of genes is altered in *Iswi* mutant larvae. The expression of a dominant-negative form of ISWI leads to dramatic alterations in higher-order chromatin structure, including the apparent decondensation of both mitotic and polytene chromosomes. The loss of ISWI function does not cause obvious defects in nucleosome assembly, but results in a significant reduction in the level of histone H1 associated with chromatin in vivo. These findings suggest that ISWI plays a global role in chromatin compaction in vivo by promoting the association of the linker histone H1 with chromatin.

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