Large-Scale Heterochromatic Remodeling Facilitates DNA Repair

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Arabidopsis pericentromeric heterochromatin is condensed into structures called chromocenters that are enriched in histone H3 lysine 27 monomethylation (H3K27me1). Previously, we have shown that this mark is deposited by the homologous proteins ARABIDOPSIS TRITHORAX RELATED 5 (ATXR5) and ATXR6. We have used loss of function and gain of function mutants in these two proteins to investigate the role of H3K27 methylation in chromatin structure and gene regulation. *atxr5,6* double mutants show a loss in H3K27me1 that results in the over replication of heterochromatin. This over replication results in DNA damage and extensive chromocenter remodeling into unique structures we have named Over Replication-Associated Centers (RACs). Super-resolution microscopy shows that RACs have a highly ordered structure, with an outer layer of condensed heterochromatin, an inner layer enriched in the histone variant H2Ax, and a low-density core containing foci of phosphorylated H2Ax (a marker of double-strand breaks) and the DNA-repair enzyme RAD51. These results suggest a novel mechanism for heterochromatic DNA-damage repair that involves large-scale chromatin remodeling. Using gain-of-function mutants in ATXR5/6, we are able to replace heterochromatic H3K27me1 with H3K27me2 or H3K27me3. In this way, we have been begun to investigate the functional significance of H3K27 methylation level on chromatin structure, DNA replication, and gene regulation.

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