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Role of the PCNA-interacting protein box of Dnmt1 in the maintenance of DNA methylation

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Abstracts

Rigorous inheritance of DNA methylation patterns is essential for maintaining cellular phenotypes of individual differentiated cells in vertebrates. Cell type-specific DNA methylation patterns are established and maintained by the collaboration of three DNA methyltransferases: Dnmt1, Dnmt3a, and Dnmt3b. The maintenance of DNA methylation is mainly mediated by Dnmt1, which converts hemi-methylated DNA to its fully methylated form, although the mechanism of how this conversion is coupled with DNA replication is largely unknown. We demonstrate here that DNA replication-dependent chromatin loading of Dnmt1 requires the protein's PCNA-interacting protein box (PIP box) and its ubiquitin interacting motif (UIM). Hence, substitutions of conserved amino acids within each of these domains to alanine abolish DNA replication-dependent chromatin loading of Dnmt1. Thus, our present results suggest that collaboration of multiple domains in Dnmt1 ensures maintenance of DNA methylation during DNA replication.