

# Characterization of the Dual Function of ATXR5 PIP motif in PCNA and Nucleosome Binding

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ATXR5 (*Arabidopsis* trithorax-related protein 5) is a SET domain lysine methyltransferase (KMTase) playing an important role in genomic stability and DNA replication (Jacob *et al.* 2009). Previous studies established that the plant homeodomain (PHD), the proliferating cell nuclear antigen (PCNA) interacting peptide (PIP) and the SET domain of ATXR5 contribute to its biological roles (Bergamin *et al.* 2017). While our previous findings established that ATXR5 SET domain preferentially methylate histone H3.1 on lysine 27 (H3K27) when incorporated in a nucleosome core particle (NCP) (Jacob *et al.* 2014) and that its PHD domain is important for ATXR5 activity (Bergamin *et al.* 2017), the role of its PIP motif has remained poorly explored. In this study, we show that two molecules of ATXR5 binds to a PCNA trimer and the crystal structure of PCNA bound to ATXR5 PIP demonstrates that a di-phenylalanine motif is important for high affinity binding of the methyltransferase to PCNA. Surprisingly, increasing concentration of PCNA blocks ATXR5 KMTase activity on the NCP suggesting that the NCP and PCNA have overlapping binding sites on ATXR5. Accordingly, ATXR5 PIP mutants show lower methyltransferase activity demonstrating that this region of the enzyme is important for high affinity binding to the NCP. Our studies collectively demonstrate that the PIP motif of ATXR5 interacts with PCNA and performs a secondary function by regulating the interaction of the enzyme with the NCP.

## References

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