ID No.	K2015	
Project Title	Regulation and Function of DNA methylation	
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Report

UHRF1-dependent maintenance of DNA methylation plays an essential role in maintaining cell fates during cell proliferation, and DPPA3 is an intrinsically disordered protein that specifically interacts with UHRF1 and promotes DNA demethylation by inhibiting UHRF1 chromatin localization. However, the molecular basis of how DPPA3 interacts with and inhibits UHRF1 remains poorly understood. We determined the solution NMR structure of mouse UHRF1 PHD domain in complex with DPPA3. Induced α-helices in DPPA3 upon binding of the UHRF1 PHD contribute to stable complex formation with multifaceted interaction unlike canonical ligand proteins of a PHD domain. Mutations on the binding interface and unfolding of helical structure of DPPA3 inhibited binding to UHRF1 and the chromatin localization of UHRF1. Our results provide structural insight into the mechanism underlying the inhibition of nucleocytoplasmic translocation of UHRF1 by DPPA3.