

ID No.	K2001
Project Title	Regulation and Function of DNA methylation
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Report	<p><u>Project #1: Mechanism of maintenance DNA methylation</u></p> <p>Using a cell-free system derived from <i>Xenopus</i> egg extracts, and structural analyses, and mouse ES cells, we identified PAF15 as a novel DNMT1-interacting protein. PAF15 undergoes multiple mono-ubiquitylation in UHRF1-dependent manner and transiently binds to replicating chromatin in a complex with PCNA. Ubiquitylation of PAF15 promotes DNMT1 recruitment to DNA methylation sites and PAF15 deficient mouse ES cells shows decreased DNA methylation, particularly in early-replication domains. Collectively, these observations identify a novel pathway regulating maintenance DNA methylation.</p> <p><u>Project #2: Mechanism of DNA demethylation by DPPA3</u></p> <p>We uncovered that local and active DNA demethylation by TET1/2 is required for the expression of DPPA3. DPPA3 in turn inhibits maintenance DNA methylation by displacing UHRF1 from chromatin. We also show that DPPA3 alone is capable of inducing global DNA demethylation in non-mammalian species (<i>Xenopus</i> and medaka). Our findings suggest that the evolution of DPPA3 facilitated the emergence of global DNA demethylation in mammals.</p>