

MS08-P09 | STRUCTURAL STUDY FOR RECOGNITION OF UBIQUITYLATED HISTONE H3 BY DNA METHYLTRANSFERASE

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Cytosine methylation in CpG dinucleotide plays an important role in gene silencing, genome imprinting, X-chromosome inactivation and carcinogenesis. After DNA replication, DNA methylation patterns in somatic cells are faithfully maintained to uphold the cell identity. Two proteins are essential for the maintenance of DNA methylation; DNA methyltransferase DNMT1 and its recruiter UHRF1. After genome replication, UHRF1 SRA domain specifically recognize hemi-methylated DNA and subsequently catalyzes the multi-monoubiquitylation on histone H3 at K14, K18 and K23. DNMT1 RFTS domain recognizes the ubiquitylated histone H3, which recruits the DNMT1 on the DNA methylation sites.

Here, we present the structural basis for recognition of dual-monoubiquitylated histone H3 (ubiquitylated at K18 and K23) by DNMT1 RFTS domain. We show the sample preparation of ubiquitylated histone H3 analogs, detail of recognition of ubiquitylated histone H3, and activation of DNMT1 methyltransferase activity upon binding of the ubiquitylated histone H3. These data suggest that activation of DNMT1 at proper timing and location ensures the DNA methylation maintenance. Finally, we will discuss the recognition of triple monoubiquitylated histone H3 by DNMT1 RFTS.