3RD WORLD PLANT GENOMICS AND PLANT SCIENCE CONGRESS
&
4TH WORLD MYCOLOGY AND MUSHROOM CONGRESS

July 15-16, 2019
Osaka, Japan

Targeting mechanism of H3K27me3 demethylase REF6 and its role in transgenerational thermomemory in *Arabidopsis*

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Relative of Early Flowering 6 (Ref6/Jmj12), a Jumonji C (JmjC)-domain-containing H3K27me3 histone demethylase, finds its target loci in Arabidopsis genome by directly recognizing the CTCTGYTY motif via its zinc-finger (ZnF) domains (1, 2). REF6 tends to bind motifs located in active chromatin states and depleted for heterochromatic modifications. However, the underlying mechanism remains unknown. Here, using biochemistry, structural biology, and high-throughput sequencing, we showed that REF6 binding affinity to specific regions is repelled by DNA methylation within CTCTGYTY motif. In addition, we also found that heat-induced Heat Shock Transcription Factor A2 (HSFA2) directly activates REF6, which in turn derepresses HSFA2. REF6 and HSFA2 establish a heritable feedback loop which is involved in transgene rational thermo memory and stress adaptation.

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