Structures of a DYW domain shed first light on a unique plant RNA editing regulation principle

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As part of RNA editosomal protein complexes, pentatricopeptide repeat (PPR) proteins with a C-terminal DYW domain have been characterized as site-specific factors for C to U RNA editing in plant mitochondria and plastids [1-2]. While substrate recognition is conferred by their repetitive PPR tract, the exact role of the DYW domain has not been clarified. The DYW domain shares a low sequence conservation with known cytidine deaminase structures (from 5 to 19% residue identities). Lastly, missing structural information has left the exact function and catalytic properties of DYW domains within the RNA editosome open [3]. We present structures and functional data of a DYW domain in an inactive ground state and a catalytically activated conformation. DYW domains harbour a cytidine deaminase fold and a C-terminal DYW motif, with catalytic and structural Zn atoms, respectively. The deaminase fold is interrupted by a conserved domain, which regulates the active site sterically via a large-scale conformational change and mechanistically via the Zn coordination geometry. Thus, we coined this novel domain 'gating domain' and the accompanying unusual metalloprotein regulation principle 'gated Zn-shutter'. An autoinhibited ground state and its activation by the presence of either ATP, GTP or the inhibitor tetrahydro uridine is consolidated by differential scanning fluorimetry as well as in vivo / vitro RNA editing assays. In vivo, the framework of an active plant RNA editosome triggers the release of DYW autoinhibition to ensure a controlled, coordinated deamination likely playing a key role in mitochondrial and chloroplast homeostasis [4, 5].

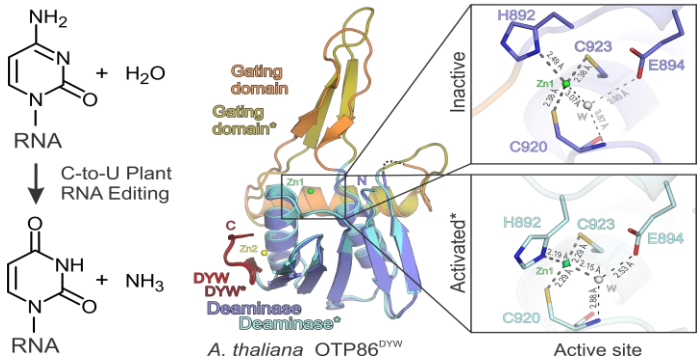

Fig. 1 An unusual regulation mechanism in plant RNA

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