3D Domain Swapping Dimerization of the Receiver Domain of Cytokinin Receptor CRE1 From Arabidopsis thaliana and Medicago truncatula

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Cytokinins are phytohormones regulating many biological processes that are vital to plants. CYTOKININ RESPONSE1 (CRE1), the main cytokinin receptor, has a modular architecture composed of a cytokinin-binding CHASE (Cyclases/Histidine kinases Associated Sensory Extracellular) domain, followed by a transmembrane fragment, an intracellular histidine kinase (HK) domain, and a receiver domain (REC). Perception of cytokinin signaling involves (i) a hormone molecule binding to the CHASE domain, (ii) CRE1 autophosphorylation at a conserved His residue in the HK domain, followed by a phosphorelay to (iii) a conserved Asp residue in the REC domain, (iv) a histidine-containing phosphotransfer protein (HPt), and (v) a response regulator (RR). This work focuses on the crystal structures of the REC domain of CRE1 from the model plant *Arabidopsis thaliana* and from the model legume *Medicago truncatula*. Both REC domains form tight 3D-domain-swapped dimers. Dimerization of the REC domain agrees with the quaternary assembly of the entire CRE1 but is incompatible with a model of its complex with HPt, suggesting that a considerable conformational change should occur to enable the signal transduction. Indeed, phosphorylation of the REC domain can change the HPt-binding properties of CRE1, as shown by functional studies.

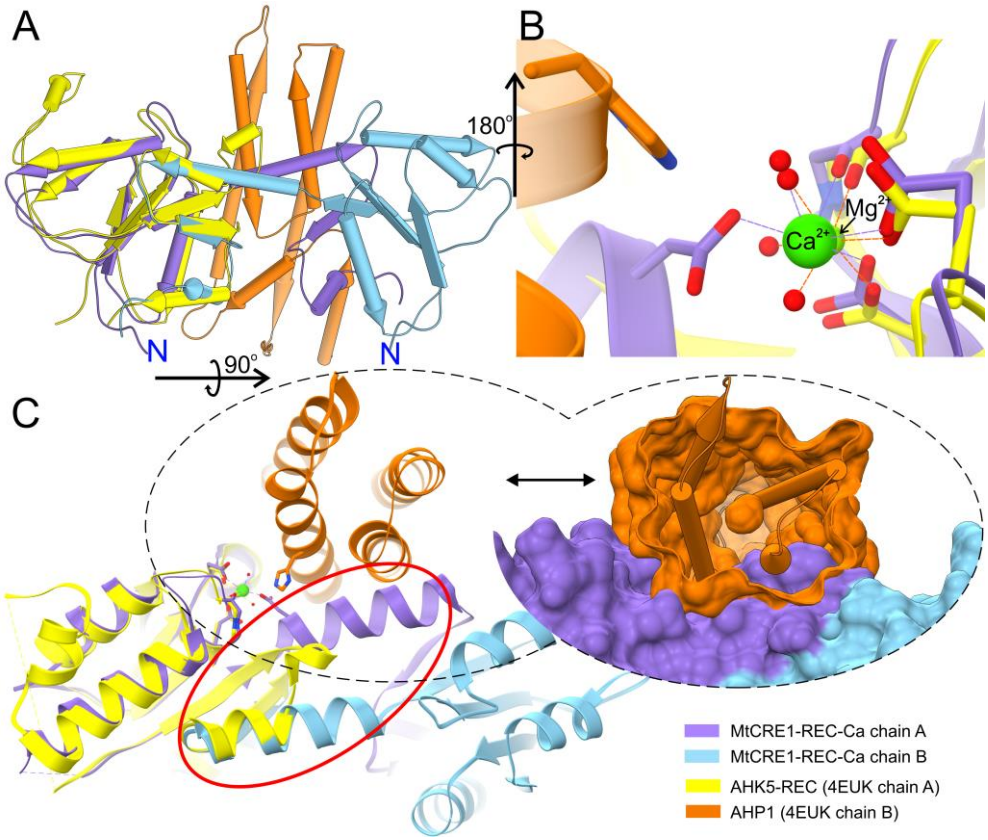

Figure 1. Superposition of the MtCRE1-REC dimer (purple/blue) onto the AHK5-REC (yellow) complex with AHP1 (orange) (A). MtCRE1-REC and AHK5-REC share a similar flavodoxin-like core structure. They also have a similar metal-binding site, shown in stick representation (B). While MtCRE1-REC binds Ca^{2+}, AHK5-REC binds Mg^{2+}. An attempt to superpose the two structures leads to severe clashes between AHP1 (orange surface) and MtCRE1-REC (purple surface), as shown in (C). The clashes occur because of the presence of the swapping domain (circled in red). In MtCRE1-REC, the purple α helix juts toward the second subunit (blue), while in AHK5-REC it flips back in the opposite direction (yellow).