BRC Science Highlight
May 2020

Structural Basis for Ca^{2+}-Dependent Activation of a Plant Metacaspase

Background/objective

Plant metacaspases mediate programmed cell death in development, biotic and abiotic stresses, damage-induced immune response, and resistance to pathogen attack. Most metacaspases require Ca^{2+} for their activation and substrate processing, but, the Ca^{2+}-dependent activation mechanism remains elusive. Damage-induced intracellular Ca^{2+} flux activates Metacaspase 4 (*At*MC4), which modulates plant immune defense. This study determined crystal structures for *At*MC4 and characterized its Ca^{2+}-dependent activation, laying the basis for future engineering for stress response to enable biodesign of more sustainable crops.

Approach

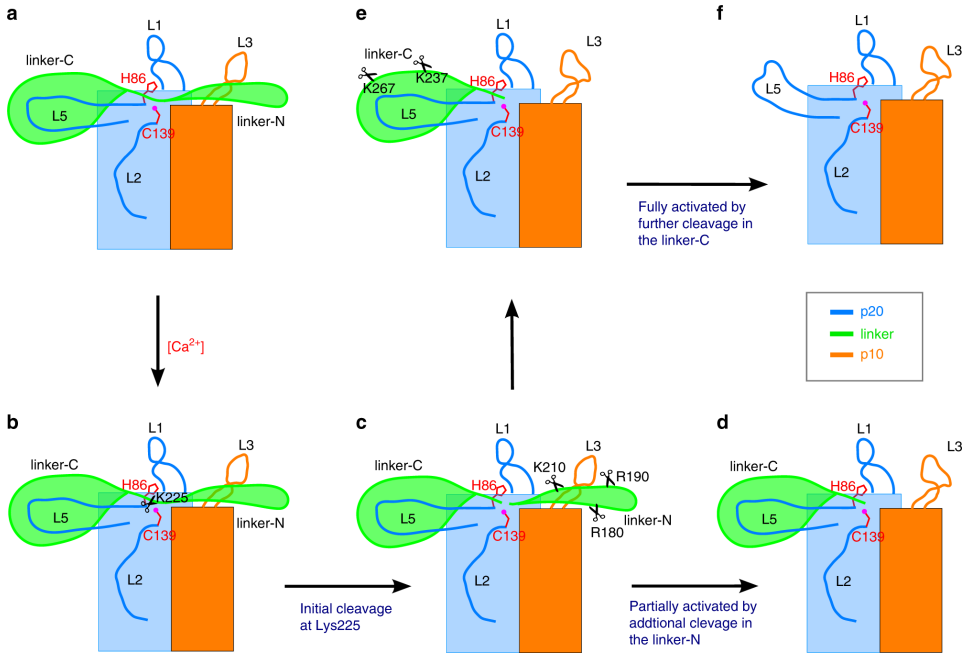
- Structure determination of inactive and Ca^{2+}-activated *At*MC4 structures by the QPSI and NSLS-II CBMS teams
- *In vivo* activity analyzed through tobacco (*Nicotiana benthamiana)* plants that were infiltrated with different gene combinations of amplified *At*MC4 and its mutants, and GST-Propep1 protein by the CABBI team

Results

- Determined crystal structures for *At*MC4 and characterized its Ca^{2+}-dependent activation and cleavage of substrate Propep1 from *Arabidopsis*
- Identified a linker domain that blocks the metacaspase activation
- Multiple cleavages in the linker domain induce conformational changes and processing of substrate Propep1 upon activation by Ca^{2+}

Significance

- Metacaspases may function as a Ca^{2+}-signature decoder to transduce Ca^{2+} signals to activate distinct response pathways.
- This lays the foundation for tuning *At*MC4 activity in response to abiotic and biotic stresses for engineering of more sustainable crops for biofuels.



Proposed mechanism of Ca2+-dependent AtMC4 activation
a. Inactive form b., c. Initial cleavage at Lys225 d. Additional cleavage in the linker-N for partial activation e. Further cleavage in the linker-C for full activation f. Fully activated form.

Zhu, P., et al. 2020. "Structural basis for Ca2+-dependent activation of a plant metacaspase". ***Nature Communications****. 11:2249.*
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