A mechanism for switching from local to systemic signaling in innate immunity

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The appropriate transition from locally confined to systemic organismic responses to environmental cues is of fundamental importance for all multicellular organisms and especially crucial during pathogen responses. Early signaling events after pathogen perception include the formation of local and systemic Calcium (Ca^{2+}) signals as well as accumulation of ROS (reactive oxygen species). Ca^{2+} elevation and ROS accumulation appear to be interconnected by largely unknown mechanisms. Our recent work has established that Calcineurin-B-like (CBL) Ca^{2+} sensor proteins upon interaction with CBL-interacting protein kinases (CIPKs) can activate NADPH oxidases (NOX, designated as RBOH in Arabidopsis) to trigger Ca^{2+}-induced ROS production.

Here I will detail the regulation of the NOX RBOHD during innate immunity responses. In this context, the concerted activity of a specific Ca^{2+}-dependent kinase (CDPK) together with defined CBL-CIPK complexes allows for synergistic NOX activation. Alternative activation of this NOX can be triggered by the Ca^{2+}-independent cytoplasmic receptor-like kinase (RLcK) BIK1 in a process that can be modulated by direct Ca^{2+} binding to the NOX. Derived from our investigations that combined signal circuit reconstitution in human cell lines with mutant analyses and *in vivo* Ca^{2+} imaging, I will present a model that provides the mechanistic basis for switching from local to systemic signaling in innate immunity.