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Mechanism of MAPK-targeted gene expression unraveled in plants

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Mitogen-activated protein kinase (MAPK) cascades—phosphorelay modules minimally composed of a MAPK kinase kinase, a MAPK kinase and a MAPK—are key players in eukaryotic cell signaling, linking developmental or environmental stimulus perception to alteration/adaptation of gene expression. Their prominent role in mammalian cancer development, but also in regulating plant development and stress adaptation are well-documented (reviewed in refs. 1–4). Through their kinase activity, MAPK cascades translate incoming environmental signals into post-translational modification of target proteins, e.g., transcription factors, to ultimately reorganize gene expression and stress adaptation.

Our recent study (PNAS, 2009, in press) delineates the signaling pathway downstream of *Arabodopsis thaliana* MPK3, a major MAPK in early stress responses, and closes the hitherto unknown gap between MPK3 activation and transcriptional reprogramming. An earlier report by the same group had identified VirE2-interacting protein 1 (VIP1) as a substrate of MPK3.[5] VIP1 undergoes cytoplasmic-nuclear translocation upon phosphorylation by MPK3, which can be activated by a number of biotic and abiotic stresses. The plant pathogen *Agrobacterium tumefaciens*, whose pathogenicity is based on manipulating the host through integration of its transfer DNA (T-DNA), has "learnt" to benefit from being recognized as an enemy. Like other pathogens, Agrobacterium triggers MPK3 activation but at the same time hijacks VIP1 for delivering its T-DNA into the plant nucleus.[5]

Starting with the assumption that the only purpose of a plant protein and its tightly controlled stress-dependent cytoplasmic-nuclear trafficking cannot be to support enemy invasion, we now provide evidence for a role of VIP1 as a functional bZIP transcription factor which binds to a novel DNA hexamer motif termed VIP1 response element (VRE). We show that VIP1 strongly enhances expression from a synthetic promoter harboring multiple VRE copies and that VIP1 can directly interact with VREs in vitro and in vivo. VREs are overrepresented in promoters responding to activation of the MPK3 pathway such as *Trxh8* and *MYB44,* whose expression is activated in a VRE-dependent manner. Accordingly, plants overexpressing VIP1 accumulate high levels of *Trxh8* and *MYB44* transcripts, whereas stress-induced expression of these genes is impaired in *mpk3* mutants. Chromatin immunoprecipitation assays of the *MYB44* promoter confirm that VIP1 binding to VREs is enhanced under conditions of MPK3 pathway stimulation. By directly activating expression of a number of stress-responsive transcription factors, VIP1 translates the incoming stress signal into an appropriately choreographed stress response.

How can Agrobacterium take advantage of the stress-triggered nuclear translocation of VIP1 if nuclear VIP1 activates the defense response? In fact, numerous defense genes are induced in the early response to Agrobacterium infection,[6] but expression of defense genes is subsequently suppressed during infection by strains that can transfer virulence (Vir) proteins along with their T-DNA into plant cells.[6] Intriguingly, once VIP1 has fulfilled its function as T-DNA transporter, VIP1 undergoes proteasomal degradation that is triggered by *the* agrobacterial factor VirF.[7] Thus, Agrobacterium uses virulence factors not only to interact with host factors for efficient T-DNA transformation of plant cells, but other virulence factors of these bacteria seem to have evolved efficient mechanisms to inhibit defense gene expression at the transcriptional level. Taken together, although Agrobacterium transformation has revolutionized plant science twenty years ago, much can still be learnt from studying the interaction of Agrobacterium with plants.

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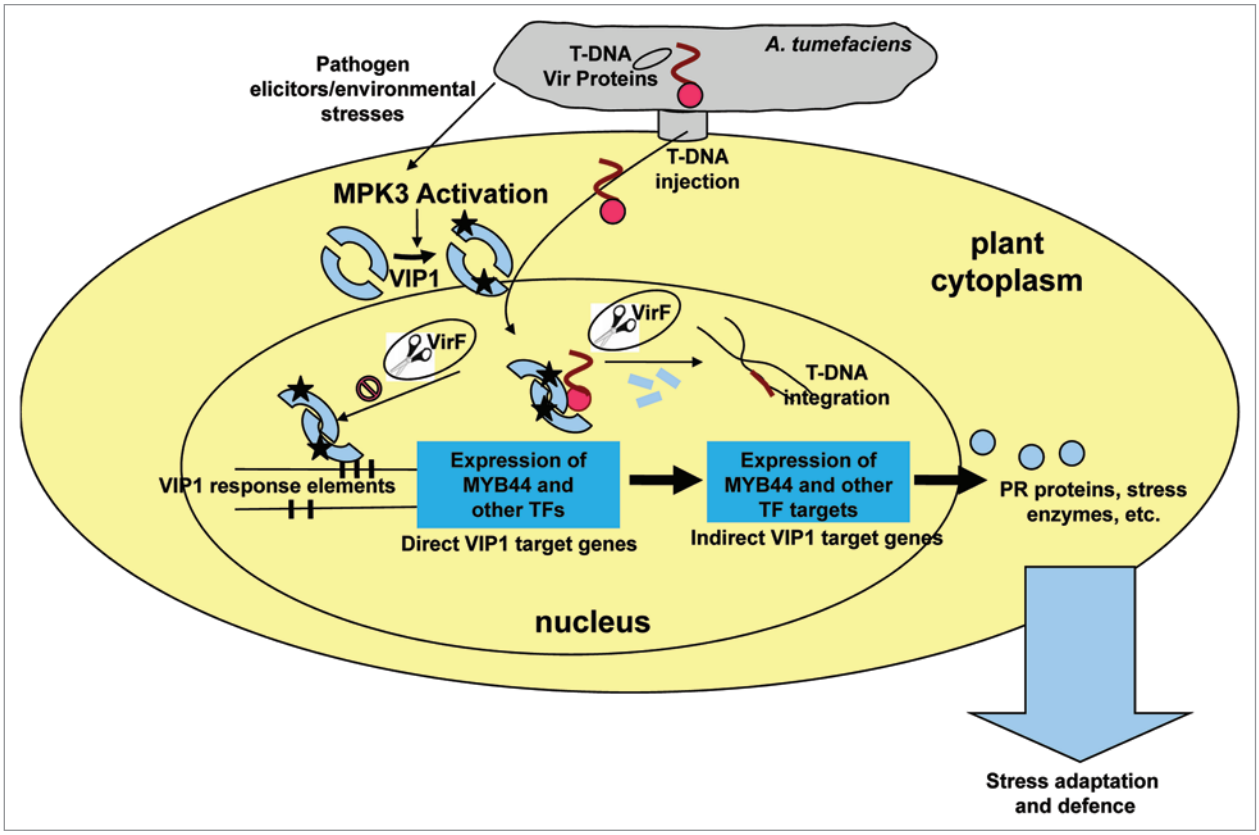

Figure 1. How agrobacteria circumvent the plant defence system. A number of abiotic and biotic stresses lead to a rapid activation of the MAPK MPK3. This in turn phosphorylates (*) the bZIP transcription factor VIP1, resulting in cytoplasmic-nuclear translocation. VIP1 binds to VIP1 response elements adaptation and defence cytoplasmic (VREs) in promoters of stress-responsive genes, thereby contributing to re-programming of gene expression. *Agrobacterium tumefaciens* also triggers MPK3 activation. In addition, it hijacks VIP1 as nuclear transporter for its Transfer-DNA, which ultimately is integrated into the plant genome resulting in manipulation of the host metabolism. The agrobacterial factor VirF (ellipse) assists proteasomal degradation of VIP1 in the nucleus. This degradation allows release of the T-DNA for chromosomal integration on the one hand and suppression of VIP1-mediated defense gene activation on the other hand.