Keep Sugar Away to Stay Active: Glycosylation of Methyl Salicylate Shuts Down Systemic Signaling

Plant hormones are frequently modified by glycosylation, hydroxylation, methylolation, and other conjugations, and these modifications can alter the hormone’s activity and stability (Wang et al., 2019). The phytohormone salicylic acid orchestrates effective defense and mediates local and systemic acquired resistance (SAR) against biotrophic pathogens such as the bacterium *Pseudomonas syringae*. Reversible Glc conjugation of salicylic acid aids its storage, and the formation of methyl ester salicylic acid (MeSA) facilitates long-distance transport and systemic communication (Park et al., 2007). Mounting a competent defense response is, therefore, critically dependent on the homeostasis between active salicylic acid molecules and inactive conjugated forms as well as the movement of mobile signals. Many factors are thought to influence this homeostasis (Liu et al., 2011).

In this issue of *Plant Physiology*, Chen et al. (2019) studied the impact of glycosylation of MeSA on the homeostasis of salicylic acid, and hence, on plant immunity. The authors identified the occurrence of Glc conjugates of MeSA and presented evidence for a key role of one particular uridine diphosphate-glycosyltransferase (UGT) in modulating SAR in Arabidopsis (*Arabidopsis thaliana*). Upon infection with *Pseudomonas syringae*, UGT71C3 is induced at the transcriptional level mainly in leaves, pointing to a potential role in immunity. In vivo and in vitro biochemical analyses showed that UGT71C3 acts specifically on methyl salicylate but not salicylic acid itself or other structurally close benzoic acids.

SAR occurs with the onset of salicylic acid signaling in the local infected tissue and the activation of defense in the distal tissues that have not been exposed to the pathogen. Chen et al. (2019) show that UGT71C3 overexpression leads to more severe disease symptoms and SAR deficiency. Conversely, the loss-of-function mutants showed substantially reduced symptoms and accumulated more salicylic acid and MeSA compared with wild-type plants. These phenotypes are associated

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**Figure 1.** Glycosylation of MeSA negatively regulates plant systemic defense. At the site of primary infection (local tissue), the salicylic acid (SA) pathway is activated and SA (blue spheres) and MeSA (red spheres) levels increase. As a mobile signal, MeSA reaches the systemic tissue, where it is converted to salicylic acid. UGT71C3 is up-regulated in response to the pathogen and MeSA accumulation, and in turn accelerates the glycosylation of MeSA. The Glc conjugates of MeSA glucoside (MeSA-glc; dark purple spheres) are not active or mobile and affect the steady-state levels of free SA. Any MeSA that reaches the systemic tissue is further glycosylated by UGT71C3, thus preventing the accumulation of MeSA and competing with methyl esterase (MSE), which ensures its subsequent demethylation to form SA. The homeostasis of MeSA and SA is thus disrupted and the SA-dependent gene expression is attenuated, leading to defective defense. The reactions in the systemic tissue simulate a scenario where UGT71C3 acts as a defense switch-off strategy. The chemical structures and bioactive status are given for all three metabolites. BSMT1, Benzoic acid/salicylic acid carboxyl methyltransferase1. Adapted from Chen et al. (2019), figure 9.
with differential expression of SAR-related genes. The activation of SAR requires optimal communication between the local and the systemic leaves and the accumulation of both MeSA and salicylic acid to adequate levels. The authors demonstrate that glycosylation of MeSA alters the homeostasis of MeSA and salicylic acid and prevents further conversion of MeSA to salicylic acid, which is required for proper development of SAR. Collectively, the data presented by Chen et al. (2019) establish UGT71C3 as a key and novel component of plant immunity negatively modulating the MeSA-dependent SAR (Fig. 1).

Mobile signals other than MeSA have been described as SAR signals, including chemically diverse molecules like the lipid transfer protein DEFECTIVE IN INDUCED RESISTANCE1, azelaic acid, and the Lys derivative pipolic acid (Dempsey and Klessig, 2012; Hartmann and Zeier, 2019). Chen et al. (2019) showed that an additional layer of regulation can be added to this sophisticated and complex network. So, one could ask, how do plants manage that many SAR signals, and how are these connected and perceived in the systemic tissue to further activate gene expression and de novo salicylic acid biosynthesis? On the other hand, how do plants fine-tune SAR and switch it off to avoid excessive costs, once a dynamic and efficient response is in place? Addressing these questions will enhance our understanding of the mechanisms to achieve SAR. For the time being, this new report shows that glycosylation of immune-related compounds is an important factor.

Analysis of plant UGTs continues to attract interest, and the role of previously uncharacterized members of this big family is emerging (Song et al., 2016; Thompson et al., 2017; Huang et al., 2018; Irmisch et al., 2019). Investigating UGT functions is enabled and facilitated by the availability of plant genome sequences and the development of large-scale methods for data gathering and analysis. A key question is how many glycosyltransferases remain to be characterized. The answer is, too many to handle if we continue with the strategy of analyzing single genes. Scientific breakthroughs in this field can be achieved by using approaches that couple functional and structural analyses to data-driven machine learning for the prediction of enzyme activity (Yang et al., 2018).

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LITERATURE CITED

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www.plantphysiol.org/cgi/doi/10.1104/pp.19.00747