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News and Views

Battle for survival: the role of plant thioredoxin in the war against *Barley stripe mosaic virus*

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Battling against pathogenic microbes is a major challenge in agriculture. Destructive crop diseases cause nearly a 16% drop in global crop yield (Ficke et al., 2018). Because of global climate change and burgeoning human populations, there is an urgent need for plant scientists and breeders to develop novel antiviral strategies to defend against a variety of plant pathogens and support the drive to achieve sustainable food security by 2050.

Resolving the molecular mechanisms underlying host–virus interactions represents one of the most compelling questions in plant biology. During the co-evolutionary arms race between hosts and pathogens, plants have evolved a sophisticated immune system to recognize and defend themselves against pathogen attacks, while pathogens have developed countermeasures to evade host surveillance and achieve successful infection. Notably, virulent pathogens are able to defeat the host immune system through the action of secreted viral proteins referred to as "effectors" (Jones and Dangl, 2006). A growing body of evidence has substantiated the versatile roles of viral effectors in plant infection (Hou et al., 2019; Medina-Puche et al., 2020).

Barley stripe mosaic virus (BSMV), a canonical member of the genus *Hordeivirus*, is a positive-strand RNA virus that preferentially infects *Hordeum vulgare* (barley) and *Triticum aestivum* (wheat). The common symptoms of BSMV infection include yellow streak or mosaic leaves and retarded growth. The viral proteins of BSMV are encoded by three RNA segments designated RNAα, RNAβ, and RNAγ. In particular, the γb protein encoded by RNAγ is emerging as a virulent effector that activates BSMV pathogenesis and promotes viral cell-to-cell movement via suppression of the hosts' immune systems (Jiang et al., 2020). As such, deciphering the molecular functions of the γb effector protein during host–pathogen interactions is crucial for developing directed strategies aimed toward breeding BSMV-resistant plants.

The phytohormone salicylic acid (SA) plays a key role in perceiving pathogens and in protecting plants against a variety of viral infections in plants (Ding and Ding, 2020). The mechanisms by which pathogens perturb SA-dependent immune responses to achieve effective plant infections, however, remain largely unknown. In this issue of *Plant Physiology*, Jiang et al. (2022) address the multifaceted interaction between BSMV invasion and the SA defense pathway. The authors report that BSMV infection elicits SA-induced antiviral defense signaling, which is evident by the upregulated expression of SA-elicited downstream defense genes following infection (Jiang et al., 2022). In support of this finding, the exogenous addition of 0.5 mM SA substantially attenuates BSMV infection and dramatically decreases the accumulation of BMSV proteins in the host, *Nicotiana benthamiana* (Jiang et al., 2022). BSMV, however, has co-evolved mechanisms to partially overcome SA-mediated plant defense responses: specifically, the γb protein of BSMV exerts a negative effect on SA-mediated defenses by compromising the expression of SA responsive genes in BSMV-infected *N. benthamiana* leaves (Jiang et al., 2022). Therefore, this study provides insight into virus-induced suppression of SA immune responses, in this case, mediated by the BSMV γb protein.

To shed light on the regulatory function of γb protein in the SA defense signaling pathway, Jiang et al. (2022) searched for the interaction partners of γb protein in *N. benthamiana* using a large-scale yeast two-hybrid screen. Ultimately, they identified *N. benthamiana* h-type thioredoxin 1 (NbTRX h1), which belongs to a superfamily of small thiol-disulfide oxidoreductases (Geigenberger et al., 2017), as an interactive partner with the γb effector. The primary function of thioredoxin is to reduce oxidized cysteine residues and to cleave disulfide bonds in target proteins. TRX h isoforms in *Arabidopsis thaliana* (Arabidopsis), including AtTRX h3 and AtTRX h5, play essential roles in the SA-dependent defense signaling pathway. Upon

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pathogen infection, they catalyze the monomerization of NONEXPRESSOR OF PATHOGENESIS-RELATED GENES 1 (NPR1) by reducing the intermolecular disulfide bonds between two neighboring NPR1 proteins (Figure 1; Tada et al., 2008). Monomeric NPR1s are then translocated to the nucleus to activate expression of SA-induced defense genes. In this study, Jiang et al. (2022) show that NbTRX h1 is essential for plants to defend against BSMV invasion based on the BSMV-sensitive phenotype of *NbTRXh1-RNAi* lines compared with control lines (Jiang et al., 2022).

Intriguingly, apart from NtTRX h1, the γb protein has recently been found to interact with a plastid-localized thioredoxin, the so-called NADPH-dependent thioredoxin reductase C (Wang et al., 2021). Together with the results presented in this study (Jiang et al., 2022), this suggests that γb protein might play a common role in the perturbation of host cellular redox status by manipulating the functions of plant thioredoxins.

The authors further addressed how γb protein and NbTRX h1 counteract each other's effects to gain advantage in the battle between plants and BSMV. By using immunoblotting analyses and a BSMV duplex fluorescence reporter system (Jiang et al., 2020), the authors revealed a negative effect of NbTRX h1 on the viral cell-to-cell movement (Jiang et al., 2022). Notably, this regulation relies specifically on the reducing activity of NbTRX h1 since the redox-active NbTRX h1 inhibits BSMV infection but the cysteine-mutated NbTRX h1 does not (Jiang et al., 2022). Furthermore, an *in vitro* insulin reduction assay revealed that γb protein suppresses the reductase activity of NbTRX h1, which further dampens the expression of SA-downstream defense genes in planta (Jiang et al., 2022).

In addition, the authors also tested whether NbTRX h1 plays a conserved function in resisting a wide spectrum of plant viruses. Strikingly, they found NbTRXh1-mediated common antiviral defenses against *Lychnis ringspot virus*,

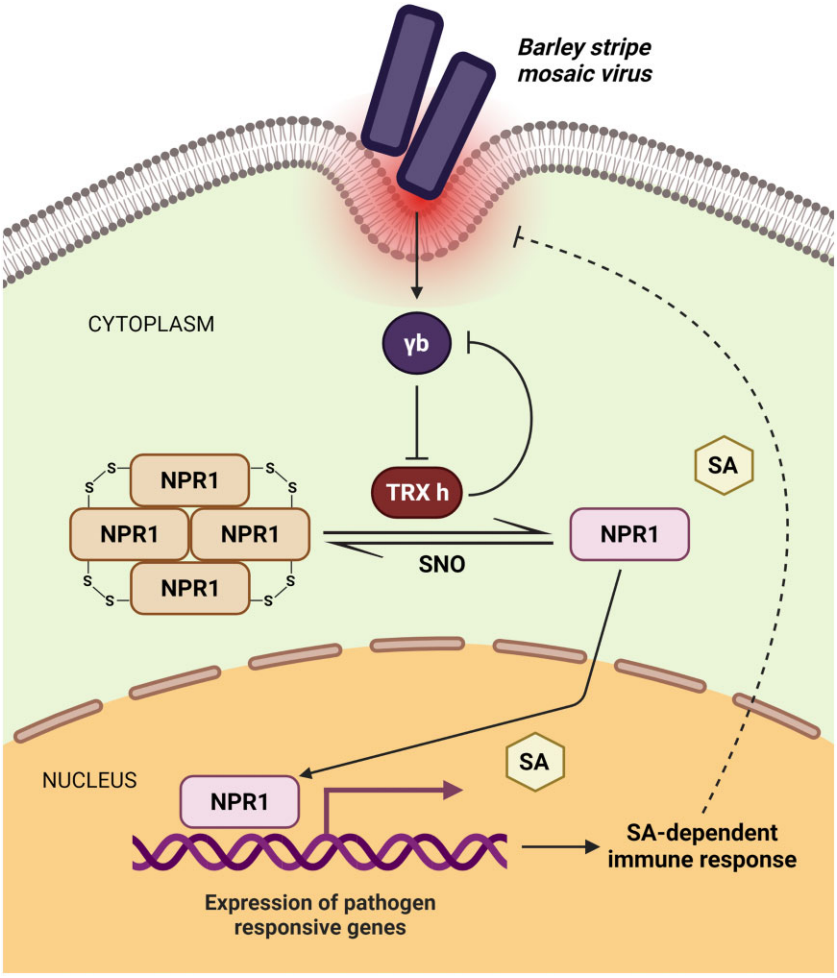

Figure 1 Model for the action of γb protein in the SA signaling pathway. In uninfected cells with a low level of SA, most NPR1 forms inactive oligomers via intramolecular disulfide bonds, a process promoted by *S*-nitrosothiol (SNO). Upon infection with BSMV, the h-type thioredoxin (TRX h) triggers monomerization of NPR1 by reducing disulfide bonds. NPR1 monomers then move to the nucleus and induce the expression of pathogen-responsive genes in a SA-dependent manner, thereby enhancing plant defense. The γb proteins of the BSMV interact with TRX h (*N. benthamiana* TRX h1 in this study) and inactivate its reducing activity, which ultimately compromises SA-mediated immune responses. Adapted from Tada et al. (2008) and Jiang et al. (2022).

Beet black scorch virus, and *Beet necrotic yellow vein virus*. Therefore, the acquisition of TRX h during plant–virus co-evolution confers broad-spectrum viral resistance in plants, thereby providing an excellent candidate for bioengineering viral-resistant plants.

Overall, this study unravels a versatile role of the SA-triggered defense pathway in defending against BSMV infection and elegantly depicts a molecular mechanism underlying the battle between BSMV and the SA-dependent defense pathway (Figure 1). In this model, γb protein directly impedes the reducing activity of NbTRX h1 to impede SA signaling and, in turn, promotes viral movement through *N. benthamiana*. As a counterstrategy, the SA defense pathway negatively controls BSMV cell-to-cell movement through some form of interaction between NbTRX h1 and γb protein.

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Conflict of interest statement. None declared.

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