cells (Kulasekara et al., 2013). The "high" versus "low" cdG state of the *P. aeruginosa* cell, marked by the presence versus absence of polar FimW, reflects the asymmetric partitioning of the cdG phosphodiesterase Pch to the daughter that inherits the unipolar flagellum (Kulasekara et al., 2013). Innovative use of microfluidics devices seeded with lung epithelial cells allows Laventie et al. (2019) to demonstrate that wild-type *P. aeruginosa*, whose heterogeneous progeny both stay at and detach from a surface after the initial "touch" and attachment, rapidly and uniformly colonize this biotic surface. In contrast, Δ*pch* mutants, whose progeny have uniformly elevated cdG levels, form small microcolonies that seed the surface near the point of inoculation but are less able to colonize—and damage—cells at a distance.

In the end, is surface sensing mediated by pili or flagella, cAMP or cdG? A wily opportunist, *P. aeruginosa* seems to answer "all of the above." Flagellar-associated components both facilitate the initial cdG pulse that sets off T4P assembly in one cell and maintain a low cdG state that allows another to swim away. At longer timescales, T4P-mediated mechanosensing increases intracellular cAMP and promotes expression of virulence traits in surface-attached cells (Persat et al., 2015; Siryaporn et al., 2014). And what happens to the many bacteria that only transiently sample a surface? Most interestingly, they might form a cAMP-based chemical "memory" that subsequently biases these swimming *P. aeruginosa* toward surface attachment and biofilm formation (Lee et al., 2018). Increasing use of innovative real-time cell tracking and analysis techniques will undoubtedly continue to illuminate the complex behaviors that underlie the bacterial sense of "touch" and adaptation to a surface.

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Second to None: Plant Secondary siRNAs as Defensive Agents against *Phytophthora*

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https://doi.org/10.1016/j.chom.2018.12.007

The eukaryotic plant pathogen *Phytophthora* encodes conserved effector proteins to eliminate host secondary siRNAs. In this issue of *Cell Host & Microbe*, Hou et al. (2019) report that reduction in secondary siRNA levels renders the host hypersusceptible to *Phytophthora* and plant secondary siRNAs likely serve as *trans*-species defensive molecules against pathogens.

Plants produce diverse small regulatory RNAs that play important roles in various biological processes. As a general rule, small RNAs act as specificity determinants that guide silencing complexes to target RNAs selected on the basis of complementarity (Axtell, 2013). Depending on the particular type of small RNA and associated silencing complex, this can lead to a combination of translational repression, RNA degradation, and/or reinforcement of repressive DNA and histone modifications at homologous DNA regions. Many plant small RNAs are homeostatic and control processes such as development, cell identity, nutrient acquisition, and suppression of transposons. Other plant small RNAs are induced

upon viral infections and play anti-viral roles. A new article from Wenbo Ma and colleagues in this issue of *Cell Host & Microbe* extends this defensive paradigm of plant small RNAs to an important oomycete plant pathogen (Hou et al., 2019).

Phytophthora spp. are oomycetes that cause serious diseases on a number of important crops. Perhaps most famously in the Western world, *P. infestans* was responsible for a devastating outbreak of potato blight in Ireland between 1845 and 1849 that contributed to a severe famine, social upheaval, and mass human migration. *Phytophthora* continues to plague agriculture around the world (Derevnina et al., 2016). Like most cellular pathogens, *Phytophthora* delivers virulence effector proteins into the host cell, which serve to target and manipulate key host processes to the pathogen's advantage. Previous work from Ma's group described two effectors from *Phytophthora sojae* that decrease plant small RNA accumulation (Qiao et al., 2013). The existence of these effectors, termed *Phytophthora* suppressors of RNA silencing (PSR1 and PSR2), implied that host small RNAs might negatively impact *Phytophthora*. Importantly, the PSR2 effector is conserved in multiple species of *Phytophthora*, including *P. infestans*, and promotes *Phytophthora* growth in host plants engineered to express PSR2 (Xiong et al., 2014).

In the new work, Hou et al. (2019) conclusively identify the types of plant small RNAs affected by PSR2 and provide tantalizing clues to how those small RNAs might work against *Phytophthora*. By examining small RNA profiles of *Arabidopsis* plants expressing a *PSR2* transgene, Hou et al. find that a specific type of small RNA, secondary small interfering RNAs (siRNAs), are reduced. Secondary siRNAs depend on an initial "trigger" small RNA to direct the cleavage of a target RNA (Fei et al., 2013). The severed target RNA fragment is used as a template by an RNA-dependent RNA polymerase for the synthesis of double-stranded RNA (dsRNA), which is subsequently processed to make secondary siRNAs. The production of secondary siRNAs can be thought of as an amplification loop, with an initial small RNA targeting event giving rise to numerous subsidiary small RNAs with homology to the original target.

Hou et al. (2019) find that PSR2 specifically reduces accumulation of secondary siRNAs triggered by the microRNAs miR161 and miR173. miR173 targets long non-coding RNAs in the *TAS1/TAS2* family, leading to *TAS1/TAS2*-derived secondary siRNAs. Both *TAS1/TAS2* secondary siRNAs and miR161 target protein-coding mRNAs from the *PPR* family, spawning *PPR*-derived secondary siRNAs. Upon infection with a strain of *P. capsici* that lacks PSR2, levels of miR161 and its resultant *PPR*-derived secondary siRNAs increase; this increase is dependent upon known immune signal transduction cascades. Importantly, plants with reduced levels of miR161/miR173-dependent secondary siRNAs are hypersusceptible to *P. capsici*, while plants with increased levels of these secondary siRNAs show enhanced resistance.

Hou et al. (2019) hypothesize that *PPR*-derived secondary siRNAs are exported from host plants, enter *Phytophthora*, and silence *Phytophthora* mRNAs. Consistent with this hypothesis, a *PPR*-derived siRNA is found in extracellular vesicles (EVs). EVs are small, membrane-bound vesicles secreted by plant cells that contain anti-pathogen molecules (Rutter and Innes, 2017). Additionally, Hou et al. find that mRNA levels of a putative *P. capsici* mRNA target and a reporter gene respond to manipulation of secondary siRNA levels in the host. Thus, it is likely that host secondary siRNAs are exported to *P. capsici* in a *trans*-species manner to reduce pathogen fitness. Hou et al. also show that the mechanism of PSR2 action is to interfere with the host DRB4 protein, a known co-factor in secondary siRNA biogenesis.

This work by Hou et al. (2019) is an exciting step forward in understanding host responses to *Phytophthora*. It is crystal clear that the *Phytophthora* PSR2 effector interferes with secondary siRNA biogenesis, which would otherwise impact pathogen growth. The data for *trans*-species delivery of host secondary siRNAs to *Phytophthora* are compelling and are part of a growing theme of *trans*-species small RNA activity during plant-pathogen interactions. Intriguingly, related miR173-dependent secondary siRNAs from *TAS1/TAS2* loci also appear to be delivered to the fungal plant pathogen *Botrytis cinerea* via EVs (Cai et al., 2018). Secondary siRNAs from other protein-coding mRNAs are also induced as a result of *trans*-species delivery of microRNA from the parasitic plant *Cuscuta campestris* to its hosts (Shahid et al., 2018). Thus, the *trans*-species small RNAs associated with diverse plant pathogens seem to consistently involve secondary siRNAs.

The involvement of miR161- and miR173-dependent secondary siRNAs in *Phytophthora* resistance raises interesting evolutionary questions. In contrast to many miRNAs that are well conserved among diverse plants, neither miR161 nor miR173 is present outside of the Brassicaceae plant family, although *PPR*-derived secondary siRNAs are present in a wider range of plant species. The fact that PSR2 enhances virulence of *P. sojae* growth on soybean roots (Xiong et al., 2014) shows that suppression of secondary siRNAs pays dividends for *Phytophthora* even when the host is not a member of the Brassicaceae and thus lacks miR161 and miR173. The fact that secondary siRNAs spawned by the *Arabidopsis* miR161/miR173/*TAS1/TAS2/PPR* network also affect the distantly related fungal pathogen *Botrytis* (Cai et al., 2018) further increases the mystery: how can the same set of secondary siRNAs affect gene expression in multiple, highly diverse pathogen transcriptomes? One intriguing idea discussed by Hou et al. (2019) is that the host is employing a "shotgun" approach to *trans*-species secondary siRNA delivery. In this scenario, it is the production and delivery of a sequence-diverse set of small RNAs that matters. Perhaps, unlike classic microRNA-target relationships, there is no purifying selection on the sequence of these secondary siRNAs in order to maintain complementarity to any particular pathogen mRNA. When delivered to the pathogen, many siRNAs will fail to interact with any target mRNAs, but by chance some will hit important targets in the pathogen. Detailed study of the molecular evolution of these secondary siRNAs, and their potential targets within diverse pathogen transcriptomes, will illuminate this very interesting problem. In the meantime, it is clear that *trans*-species delivery of small RNAs between plant hosts and their pathogens is a widespread phenomenon.

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