SCIENCE CHINA
Life Sciences

The genetic arms race between plant andXanthomonas: lessons learned from TALE biology

Jiao Xue, Zhanhua Lu, Wei Liu, Shiguang Wang, Dongbai Lu, Xiaofei Wang and Xiuying He

Citation: SCIENCE CHINA Life Sciences **64**, 51 (2021); doi: 10.1007/s11427-020-1699-4

View online: https://engine.scichina.com/doi/10.1007/s11427-020-1699-4

View Table of Contents: https://engine.scichina.com/publisher/scp/journal/SCLS/64/1

Published by the Science China Press

Articles you may be interested in

Cell biology and immunology lessons taught by Legionellapneumophila
SCIENCE CHINA Life Sciences **59**, 3 (2016);

Eight lucky lessons learned
Science in China Series C-Life Sciences **52**, 111 (2009);

Identification of an avirulence gene, avrxa5, from the rice pathogen Xanthomonas oryzae pv. oryzae
SCIENCE CHINA Life Sciences **53**, 1440 (2010);

The pathogenic site of the C-toxin derived from Bipolaris maydis race C in maize (Zea mays)
Chinese Science Bulletin **45**, 1787 (2000);

Hybrid plant regeneration from interfamilial somatic hybridization between grapevine (Vitia vinifera L.) and Red Thorowax (Bupleurum scorzonerifolium Willd)
Chinese Science Bulletin **44**, 1878 (1999);

SCIENCE CHINA
Life Sciences

•REVIEW•

January 2021 Vol.64 No.1: 51–65
https://doi.org/10.1007/s11427-020-1699-4

The genetic arms race between plant and *Xanthomonas*: lessons learned from TALE biology

Jiao Xue, Zhanhua Lu, Wei Liu, Shiguang Wang, Dongbai Lu, Xiaofei Wang & Xiuying He*

Rice Research Institute, Guangdong Academy of Agricultural Sciences, Guangdong Provincial Key Laboratory of New Technology in Rice Breeding, Guangzhou 510640, China

Received February 6, 2020; accepted March 29, 2020; published online July 10, 2020

The pathogenic bacterial genus *Xanthomonas* infects a wide variety of host plants and causes devastating diseases in many crops. Transcription activator-like effectors (TALEs) are important virulence factors secreted by *Xanthomonas* with the ability to directly bind to the promoters of target genes in plant hosts and activate their expression, which often facilitates the proliferation of pathogens. Understanding how plants cope with TALEs will provide mechanistic insights into crop breeding for *Xanthomonas* defense. Over the past 30 years, numerous studies have revealed the modes of action of TALEs in plant cells and plant defense strategies to overcome TALE attack. Based on these findings, new technologies were adopted for disease management to optimize crop production. In this article, we will review the most recent advances in the evolutionary arms race between plant resistance and TALEs from *Xanthomonas*, with a specific focus on TALE applications in the development of novel breeding strategies for durable and broad-spectrum resistance.

transcription activator-like effectors, *Xanthomonas*, susceptibility genes, resistance genes, TALE application

Citation: Xue, J., Lu, Z., Liu, W., Wang, S., Lu, D., Wang, X., and He, X. (2021). The genetic arms race between plant and *Xanthomonas*: lessons learned from TALE biology. Sci China Life Sci 64, 51–65. https://doi.org/10.1007/s11427-020-1699-4

Introduction

Bacterial pathogens severely reduce the yield of many crops of global importance, including rice, tomato, pepper, wheat, cotton, and citrus. The pathogenicity of many bacteria depends on the injection of effector proteins via a conserved type III secretion system (T3SS) into host cells to manipulate cellular processes (Deng et al., 2017). Transcription activator-like effectors (TALEs or TAL effectors) represent a kind of T3SS effectors and exhibit contribution to virulence by specifically activating the expression of host susceptibility genes and consequently benefit TALE-carrying pathogens from a favorable environment for their growth (Boch et al., 2014; Ji et al., 2018). Although TALEs have been found in many bacteria such as *Xanthomonas* species, *Ralstonia solanacearum* and *Burkholderia rhizoxinica* (Perez-Quintero and Szurek, 2019; Li et al., 2013; de Lange et al., 2014), the feature of TALEs are more commonly characterized from *Xanthomonas*, a bacterial genus that attacks plants and causes destructive diseases in more than 300 plant species (Boch et al., 2014; Schornack et al., 2013).

Plants possess a highly sophisticated and multilayered innate immune system to defend against pathogen infection (Jones and Dangl, 2006). In response to the invasion of *Xanthomonas*, plants have developed strategies such as loss of susceptibility and the use of *R* genes to trigger resistance (Kourelis and van der Hoorn, 2018). To escape host immunity, *Xanthomonas* has evolved and deploys several different mechanisms to interfere with TALE-dependent plant defense responses (Ji et al., 2016; Read et al., 2016; Triplett et al., 2016; Zuluaga et al., 2017). In addition to natural selection, the role of human selection during crop domes-

*Corresponding author (email: hexiuying@gdaas.cn)

© Science China Press and Springer-Verlag GmbH Germany, part of Springer Nature 2020

https://engine.scichina.com/doi/10.1007/s11427-020-1699-4

tication and breeding makes the genetic coevolution between plants and *Xanthomonas* more complicated and competitive (Erkes et al., 2017; Quibod et al., 2020).

After decades of effort, the molecular bases and modes of action of TALEs are now largely understood. Knowledge of plant countermeasures has also expanded (as reflected in the references) (Yoshimura et al., 1998; Iyer and McCouch, 2004; Schornack et al., 2004; Kay et al., 2007; Zhang et al., 2015a; Xu et al., 2019; Eom et al., 2019). The intertwined coevolution between TALE proteins and plant resistance has taught us a valuable lesson about the genetic arms race during plant-microbe interactions. Based on the understanding of these mechanisms together with the integration of genome-editing and plant breeding technology, scientists have developed multiple strategies to engineer plants to increase defense, and promising applications of plant-mediated resistance to TALEs are emerging. In this article, we review the most recent progress in understanding the modes of TALE action and plant strategies for defending against TALEs. We further discuss the current applications of TALE biology in plant disease management and biotechnology. Improved methods for exploring the transcriptome shed light on a new mechanism by which TALE bidirectional transcription may target and control a broad range of genes. Ultimately, this overview facilitates a better understanding of the mechanisms involved in plant-microbe interactions, and provides comprehensive insights into the application of TALE biology in crop resistance breeding.

The TALE code

TALEs localize to the nucleus of host cells and directly activate gene expression by binding to effector-specific promoter sequences (effector binding elements, EBE). The correlation between TALEs and their target DNA specificity is known as the TALE code, which was decoded by two separate groups in 2009 (Boch et al., 2009; Moscou and Bogdanove, 2009). A typical TALE includes an N-terminal T3SS signal, a central region of polymorphic repeats (CRRs), a C-terminal with functional nuclear localization signals (NLSs) and an acidic transcription activation domain (AD) (Figure 1A and B). CRRs are the most distinctive feature of TALE proteins and are usually 33–35 amino acids in length; their sequences are nearly identical except for the 12th and 13th amino acid residues (referred to as repeat-variable di-residues, RVDs) (Moscou and Bogdanove, 2009). RVDs are responsible for base-specific DNA targeting and are the determinants of the TALE-DNA recognition code. The crystal structures of TALEs indicate that each repeat form two α-helices and one RVD loop, in which the 13th amino acid residue specifies the DNA-binding ability, while the 12th residue stabilizes the conformation of the RVD loop (Mak et al., 2012; Deng et al., 2012).

Evolutionary insights into TALE genes

Under the dual pressure from natural selection and human activity, pathogens have to rapidly mutate and evolve to survive in the changing environment. As CRRs confer DNA-binding specificity, variation in the number or order of repeats in TALEs results in distinct DNA-targeting specificity (Boch et al., 2009; Moscou and Bogdanove, 2009). The number of TALEs also varies greatly between different *Xanthomonas* species (Table 1). Some TALEs that have lost their functional domains during evolution (e.g., deletion of the transcription activation domain or RVD domains) and were previously considered pseudogenes have recently been demonstrated to play roles in interfering with the resistance of hosts. These studies provided important insights into protein sequence polymorphisms resulting in functional diversity in TALEs (Ji et al., 2016; Read et al., 2016; Triplett et al., 2016).

Variations in TALE repeats, such as recombination, duplication, InDels and SNPs in RVDs, have greatly contributed to the production of new toxicity and the escape of plant immunity by the pathogens (Erkes et al., 2017). Comparative analyses of TALEs from three African *Xoo* strains indicate that the TALEs within this group are highly conserved but that they are genetically distant from the TALEs of Asian *Xoo* strains. These TALEs are classified into nine clusters, three of which show higher levels of variation in their RVDs, possibly caused by recombination events (Tran et al., 2018). The genomic rearrangement of TALEs is another common strategy whereby the evolutionary fitness of *Xanthomonas* may be improved. A recent report analyzed the whole genomes of many *Xanthomonas* species and found that TALE genes were often accompanied by transposases, insertion elements or bacteriophage-related recombinant enzymes (Ferreira et al., 2015). The unique composition of TALEs and their neighboring genes highlights the occurrence of horizontal gene transfer during TALE evolution. The analysis of the genomes of 17 *Xanthomonas* strains causing bacterial blight in beans revealed two TALEs shared between phylogenetically distant strains, suggesting the recent horizontal transfer of these genes between these *Xanthomonas* strains (Ruh et al., 2017).

Tricks of TALEs in plant cells

Cytoplasm-nucleus TALE trafficking

TALEs are secreted into the cytoplasm of plant cells by *Xanthomonas* through the T3SS (Figure 1A). To fulfill their roles in transcription activation, TALEs must be transported

https://engine.scichina.com/doi/10.1007/s11427-020-1699-4

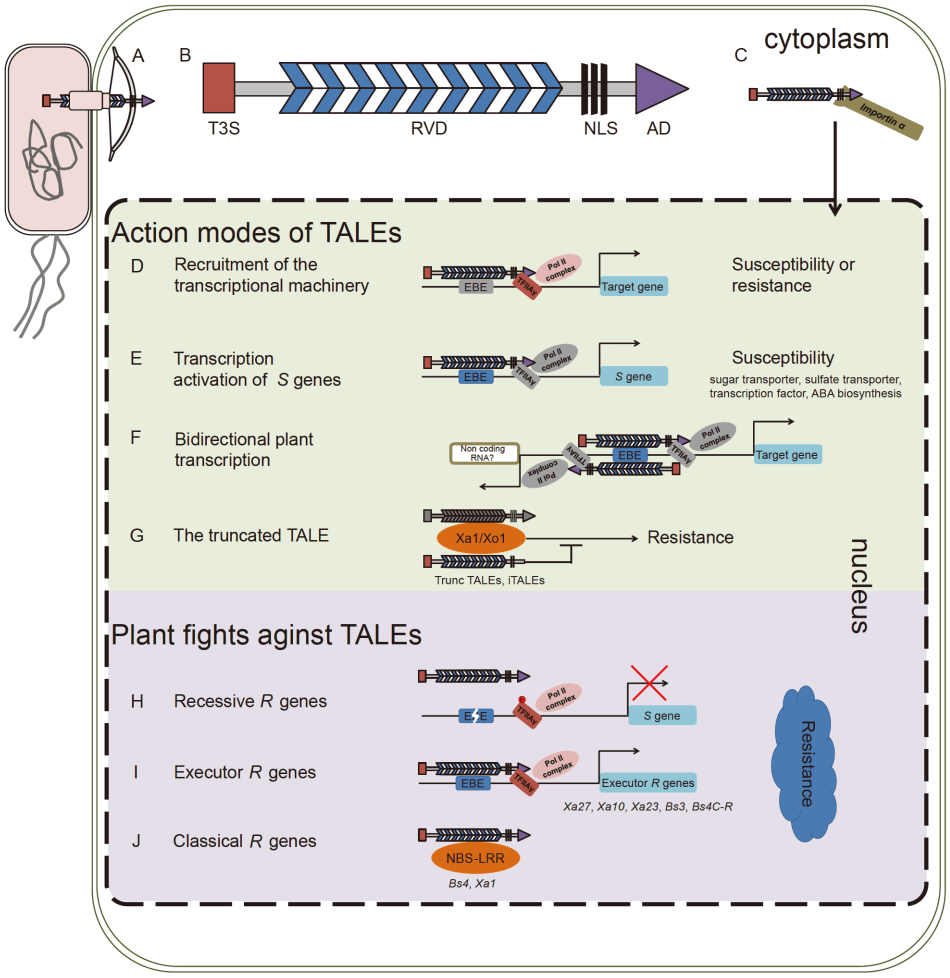

Figure 1 A model of TALE action modes and plant strategies for fighting against TALEs. A, TALEs are secreted by T3SS of *Xanthomonas*. B, A typical model of the TALE molecule. T3S, N-terminal T3SS signal; RVD, repeat-variable di-residues; NLSs, nuclear localization signals; AD, transcription activation domain. C, Importin proteins mediate transportation of TALEs from cytoplasm into nucleus. D–G, TALE action modes in plant cells. D, TALEs recruit TFIIAγ, a basal component of RNA polymerase II complexes, for initiation of the transcription of target genes. E, TALEs bind to the EBEs in susceptibility genes to activate their expression. F, TALEs drive plant transcription bidirectionally from either the forward or reverse strand of the targeted EBEs. G, The truncated TALEs repress plant immunity that is mediated by NBS-LRR. H–J, Plant strategies for fighting against TALEs. H, Loss-of-susceptibility of recessive resistance genes by mutating their EBEs or coding regions. I, TALEs bind to the EBEs of executor *R* genes and trigger defense responses. J, Plant classical NBS-LRR protein recognizes TALEs and triggers defense responses.

Table 1 Number of TAL effectors and repeat number of RVDs

Pathogen	Host plant	Disease name	RVD repeat number	Number of TAL effectors	Source or reference
X. oryzae pv. *oryzae*	Rice	Bacterial leaf blight	1.5–33.5	7–20	Gonzalez et al., 2007; Boch and Bonas, 2010; Mücke et al., 2019
X. oryzae pv. *oryzicola*	Rice	Bacterial leaf streak	5.5–26.5	12–28	Boch and Bonas, 2010; Wilkins et al., 2015
X. axonopodis pv. *manihotis*	Cassava	Cassava bacterial blight	13–22	1–5	Scholze and Boch, 2011; Bart et al., 2012; Cohn et al., 2014
X. citri pv. *citri*	Citrus	Citrus canker	6.5–22.5	1–4	Scholze and Boch, 2011; Gochez et al., 2018; Roeschlin et al., 2019
X. gardneri	Pepper	Bacterial spot	13.5	1	Boch and Bonas, 2010
X. campestris pv. *vesicatoria*	Pepper/tomato	Bacterial leaf spot	17.5	1	Boch and Bonas, 2010
X. translucens pv. *undulosa*	Wheat	Bacterial leaf streak	15.5–18.5	7–8	Falahi Charkhabi et al., 2017
X. campestris pv. *malvacearum*	Cotton	Bacterial blight	13.5	6–10	Cox et al., 2017; Boch and Bonas, 2010
X. campestris pv. *armoraciae*	Brassicaceae	Bacterial leaf spot	11.5–21.5	0–3	Boch and Bonas, 2010
X. axonopodis pv. *citri*	Citrus	Citrus canker	14.5–18.5	1–4	Boch and Bonas, 2010

https://engine.scichina.com/doi/10.1007/s11427-020-1699-4

into the nucleus of plants efficiently and precisely. This process has been elucidated in reports describing TALE trafficking via nuclear import receptor proteins. In pepper, importin α is part of the nuclear import machinery and interacts with *Xcv* AvrBs3 through an NLS in the C-terminus of the protein.Two genes encoding importin α proteins were isolated by using the yeast two-hybrid system, which was used to search for AvrBs3-interacting pepper proteins (Szurek et al., 2001). Rice genomes possess at least three nucleus importin α proteins, OsImpα1a, OsImpα1b and OsImpα2 (Jiang et al., 1998, 2001; Hui et al., 2019b), while only OsImpα1a and OsImpα1b interact with TALEs (Hui et al., 2019b). Interestingly, there are three NLSs in a typical TALE, but only the second NLS, which is highly conserved between *Xoo* and *Xoc* strains with different geographical distributions, has been specifically selected to trap host cytoplasm-nucleus shuttle proteins (Figure 1C) (Hui et al., 2019b).

Recruitment of the transcriptional machinery

Upon arriving at the nucleus, TALE proteins specifically bind to the promoters of host susceptibility (*S*) genes or resistance (*R*) genes following the principles of the TALE code. The assembly of the RNA polymerase II transcriptional machinery is essential for the initiation of transcription. TFIIA is a basal component of RNA polymerase II complexes in eukaryotes (Hoiby et al., 2007). Rice TFIIA consists of the large subunit TFIIAαβ and the small subunit TFIIAγ5 (*Xa5*) (Yuan et al., 2016). TFIIAαβ, encoded by a single gene is presumably post-translationally processed by threonine aspartase1 (taspase1) into two subunits, TFIIAα and TFIIAβ to form a TFIIA ternary complex with TFIIAγ (Ma et al., 2018b). Only TFIIAγ5, and not TFIIAαβ, directly interacts with TALEs for pathogen invasion (Yuan et al., 2016). TALEs directly interact with the N-terminal of the small subunit of TFIIAγ5 together with TFIIAα. TFIIAβ specifically associates with the C-terminal of TFIIAγ5. TFIIAα acts in coordination with TALEs to bind TFIIAγ5 to upregulate *S* genes (Figure 1D) (Hui et al., 2019a).

TFIIAγs not only benefit TALE functions, but also act as TALE-targeted host genes. *TFIIAγ1*, which is activated by PthXo7, can compensate for the absence of *TFIIAγ5* (Sugio et al., 2007). A recent study showed that the induction of *TFIIAγ1* facilitates the transcription of host genes targeted by TALEs (Ma et al., 2018a). However, it is still unknown whether *TFIIAγ1* is involved in the transcriptional machinery.

Transcription activation of S genes

As an important virulence factor for *Xanthomonas*, the main biological function of TALEs is to exploit *S* genes to facilitate the proliferation of pathogens. Although *S* genes play important roles in supplying nutrients, assisting in host recognition and suppressing plant immunity (Table 2), most of the identified TALE-activated *S* genes encode transporters and transcriptional factors.

Typically, the SWEET family members of sugar transporter, *OsSWEET11* (*Xa13*, *Os8N3*) (Yang et al., 2006), *OsSWEET13* (*Xa25*, *Os12N3*) (Liu et al., 2011) and *OsSWEET14* (*Xa41(t)*, *Os11N3*) (Hutin et al., 2015) are cloned as three *S* genes in rice. *OsSWEET11* encodes an indispensable plasma membrane protein whose expression is specifically induced by strains of *Xoo* carrying the PthXo1 effector (Yang et al., 2006). *OsSWEET11* was found to act as a sugar transporter that benefits the growth of pathogens and their interaction with rice copper transporters to remove copper from xylem vessels via the rice-*Xoo* interaction (Chu et al., 2006; Yang et al., 2006; Chen et al., 2010; Yuan et al., 2010). *OsSWEET13* and *OsSWEET14* have also been identified as TALE targets in several *Xoo* strains (Antony et al., 2010; Yu et al., 2011; Streubel et al., 2013; Zhou et al., 2015). The SWEET family genes of other plants are TALE targets as well. *GhSWEET10* encodes a sugar transporter that is induced by Avrb6, a TALE that determines the pathogenicity of *Xcm* causing bacterial blight in cotton. Activation of *GhSWEET10* by designer TAL effectors (dTALEs) restores the virulence of *Xcm* avrb6 deletion strains, whereas the silencing of *GhSWEET10* compromises the susceptibility of cotton to infections (Cox et al., 2017). In addition to the SWEET family genes, the sulfate transporter gene *OsSULTR3;6* was shown to be a major *S* gene for bacterial leaf streak and is targeted by Tal2g from *Xoc* (Cernadas et al., 2014).

Another major class of TALE-dependent *S* genes are the transcription factors. In addition to the above-mentioned *TFIIAγ1*, several other transcription factors are characterized as TALE targets that assist in transcription. *CsLOB1* is a member of the Lateral Organ Boundaries (LOB) family of transcription factors and is associated with cell expansion. TALEs from *Xcc* strains are reported to induce the expression of *CsLOB1* (Hu et al., 2014). In rice, it was shown that a leucine zipper domain (bZIP) transcription factor *OsTFX1* is induced by PthXo6 from *Xoo* (Sugio et al., 2007). The AvrBs3-targeted *upa20* gene encodes a basic helix-loop-helix (bHLH) transcription factor, and upregulation of this gene by *Xcv* causes hypertrophy in pepper (Kay et al., 2007). Two tomato bHLH transcription factor genes (*Solyc03g097820* and *Solyc06g072520*) are highly upregulated in the presence of AvrHah1 (Schwartz et al., 2017).

Notably, a new susceptibility gene was revealed in a recent study. Wheat 9-*cis*-epoxycarotenoid dioxygenase (*TaNCED*) is the rate-limiting enzyme in the biosynthesis of abscisic acid, the classic hormone involved in the response to water-stress. Tal8 from *Xtu* induces the expression of *TaNCED-*

https://engine.scichina.com/doi/10.1007/s11427-020-1699-4

Table 2 Reported TALEs and target genes[a)]

TALE avirulence effectors	*Xanthomonas* strain	Origin	Plant species	Target gene	Encoded protein	Reference
Tal3a, Tal3b	*Xoo* PXO99A	Philippines	Rice	*Xa1*	NBS-LRR	Ji et al., 2016
PthXo1,	*Xoo* PXO99A,	Philippines	Rice	*Xa5*	TFIIA Transcription factor small subunit	Yuan et al., 2016;
AvrXa10	*Xoo* PXO86, PXO112, PXO145	Philippines	Rice	*Xa10*	Transmembrane protein	Yoshimura et al., 1995; Tian et al., 2014
PthXo1	*Xoo* PXO99A	Philippines	Rice	*Xa13 (SWEET11)*	MtN3/saliva family	Yang et al., 2006; Römer et al., 2010; Antony et al., 2010; Oliva et al., 2019
AvrXa23	All the natural *Xoo* strains tested so far	China, Philippines, Japan, Korea, Bangladesh, Africa	Rice	*Xa23*	Transmembrane protein	Wang et al., 2014a; Wang et al., 2015
PthXo2	*Xoo* JXO1 and MAFF 311018	Japan	Rice	*Xa25 (SWEET13)*	MtN3/saliva family	Ochiai et al., 2005; Yang and White, 2004; Zhou et al., 2015; Oliva et al., 2019
AvrXa27	*Xoo* PXO99A	Philippines	Rice	*Xa27*	N-terminal signal-anchor-like sequence	Wu et al., 2008
AvrXa7, PthXo3, TalC, Tal5	*Xoo* PXO86, JXO1A, BAI3, MAI1	Philippines, Burkina Faso, Mali	Rice	*Xa41 (SWEER14)*	MtN3/saliva family	Römer et al., 2010; Chu et al., 2006; Antony et al., 2010; Yu et al., 2011; Streubel et al., 2013; Oliva et al., 2019
PthXo6, PthXo7, TalB	*Xoo* PXO99A, MAI1	Philippines, Mali	Rice	*OsTFX1*	Transcription factor genes	Sugio et al., 2007; Römer et al., 2010; Tran et al., 2018
TalB	*Xoo* MAI1	Mali	Rice	*OsERF#123*	Transcription factor genes	Tran et al., 2018
PthXo6, PthXo7, AvrXa27	*Xoo* PXO99A	Philippines	Rice	*OsTFIIAγ1*	Transcription factor genes	Sugio et al., 2007; Ma et al., 2018a
diverse TAL effectors transformed in X11-5A	X11-5A	USA	Rice	*Xo1*	Unknown	Triplett et al., 2016
Tal9a	*Xoo* PXO99A	Philippines	Rice	*OsHen1*	Methyltransferase	Moscou and Bogdanove, 2009
Tal1c	*Xoc* BLS256	Philippines	Rice	*OsHen1*	Methyltransferase	Moscou and Bogdanove, 2009
Tal2h	*Xoc* BLS256	Philippines	Rice	*Xo1*	Unknown	Read et al., 2016
Tal2g	*Xoc* BLS256	Philippines	Rice	*OsSULTR3;6*	Sulfate transporter	Cernadas et al., 2014
Tal7	*Xoc* YNB0-17	China	Rice	*Os09g29100*	Cyclin-D4-1 zinc finger family protein	Cai et al., 2017
TAL20	*Xam*668	Indonesia	Cassava	*MeSWEET10a*	Sugar transporter	Cohn et al., 2014
PthA4, pthAw	*Xcc*306, *Xcc*Aw	Brazil	Citrus	*CsSWEET1*	Sugar transporter	Hu et al., 2014
PthA4, pthAw	*Xcc*306, *Xcc*Aw	Brazil	Citrus	*CsLOB1*	Transcription factor	Hu et al., 2014; Li et al., 2014
AvrBs3	*Xcv* 85-10	USA	Pepper	*Bs3*	Flavin monooxygenases	Römer et al., 2007
AvrHah1	*X. gardneri* XV444	Costa Rica	Pepper	*Bs3*	Flavin monooxygenases	Schornack et al., 2008
AvrBs4	*Xcv* 85-10	USA	Pepper	*Bs4C-R*	Transmembrane protein	Strauss et al., 2012
AvrBs3	*Xcv* 82-2	USA	Pepper, Tobacco	*upa20*	Transcription factor	Kay et al., 2007
AvrHah1	*X. gardneri* 153	Ohio and Michigan	Tomato	*bHLH3, bHLH6*	Transcription factor	Schwartz et al., 2017
AvrBs4	*Xcv*75-3	Brazil	Tomato	*Bs4*	NBS-LRR	Ballvora et al., 2001; Schornack et al., 2004
Tal2, Tal4b	*Xtu* ICMP11055	Iran	Wheat	Unknown	Unknown	Falahi Charkhabi et al., 2017
Tal8	*Xtu* XT4699	KS, USA	Wheat	*TaNCED*	9-*cis*-epoxycarotenoid dioxygenase	Peng et al., 2019
Avrb6	*Xcm*H1005, N1003	Upper Volta, Africa, Oklahoma	Cotton	*GhSWEET10*	Sugar transporter	Cox et al., 2017

a) Xcm: *Xanthomonas citri* subsp. *Malvacearum*; Xtu: *Xanthomonas translucens* pv. *undulosa*; Xcv: *Xanthomonas campestris* pv. *vesicatoria*; Xam: *Xanthomonas axonopodis* pv. *manihotis*; Xoo: *Xanthomonas oryzae* pv. *oryzae*; Xoc: *Xanthomonas oryzae* pv. *oryzicola*; X.gardneri: *Xanthomonas gardneri*.

https://engine.scichina.com/doi/10.1007/s11427-020-1699-4

5BS, leading to elevated abscisic acid levels, reduced host transpiration and increased spreading of the bacteria in infected leaves (Peng et al., 2019). As phytohormones such as abscisic acid, jasmonates and salicylic acid are known to act as regulators in the manipulation of plant defense, it remains to be seen whether other TALE-targeted *S* genes participate in hormone biosynthesis or signaling pathways (Figure 1E).

Bidirectional plant transcription

The binding sites of TALE proteins usually occur on the forward strand of target promoters. However, recent studies suggested that TALEs could drive plant transcription bidirectionally from either the forward or the reverse strand of the targeted EBEs. Tal3c, a native TALE of the *Xoc* strain, was proven to activate its target gene from both the forward and reverse strands (Wang et al., 2017b). TALEs can initiate transcription from various positions in the *OsSWEET14* promoter even by binding in a reverse orientation (Figure 1F) (Streubel et al., 2017). These observations of the bidirectional transcription of TALEs in plant importantly suggested that a large portion of the TALE targets on reverse strands may be ignored throughout plant genomes. Another factor indicated by this mechanism that should not be ignored is noncoding DNA regions that transcribe noncoding RNAs such as microRNAs, phasiRNAs and lncRNAs. Noncoding RNAs have been reported to function in diverse biological processes, including plant defense against *Xanthomonas* (Deng et al., 2018; Yu et al., 2018; Yu et al., 2019; Yu et al., 2020). We noticed that in the human pathogen field, HSV-1 (Herpes simplex virus type 1) is prevalent worldwide and could induce the expression of approximately 1,000 antisense transcripts from the human host cell genome. These transcripts show different susceptibilities (Wyler et al., 2017). These observations implied that TALE bidirectional transcription is not incidental. Considering these emerging roles, abundance and wide variety of noncoding RNAs in plants, it is necessary to reevaluate as-yet unrecognized protein coding or noncoding targets on both the forward and reverse strands of EBEs.

The truncated TALE: a decoy

In nature, some truncated TALEs, referred to as truncTALEs or iTALEs (interfering TALEs), tend to mimic virulent TALEs to neutralize *R*-gene mediated plant disease resistance (Zuluaga et al., 2017). Compared with typical TALEs, both truncTALEs and iTALEs represent a type of truncated TALEs with deletions in a functional domain, such as the N-terminus or activation domain (Ji et al., 2016; Read et al., 2016). These TALEs act as decoys to repress plant innate immunity mediated by nucleotide binding site and leucine-rich repeat (NBS-LRR) genes. The recognition of *Xa1* (NBS-LRR) and *Xo1* (candidate NBS-LRR) has been found to be suppressed by truncated TALEs (Figure 1G) (Ji et al., 2016; Read et al., 2016; Triplett et al., 2016; Zuluaga et al., 2017). Given the frequent occurrence of truncated TALEs in *Xanthomonas*, these decoys may explain why only a few NBS-LRR genes have been characterized as TALE-dependent resistance (*R*) genes in plants.

Plant fights back against TALEs

Plants are sessile but are not silent in response to the action of TALEs. They have evolved various effective strategies to overcome TALE attack, including loss of susceptibility through natural variations, TALE awakening of executor genes and non-transcriptional based resistance.

Recessive R genes: loss of susceptibility through polymorphisms

Natural variations may occur in either the promoter or the coding region of *S* genes and result in off-target or target silencing of TALEs in the host. The natural alleles of SWEET family genes in which EBEs are mutated to block the binding of TALEs are typical examples of loss of susceptibility in plants (Chu et al., 2006; Zhou et al., 2015; Liu et al., 2011). The recessive rice bacterial blight resistance gene *xa13* encodes an identical protein of *OsSWEET11* but exhibits crucial sequence differences in its promoter region compared with the dominant gene, *Xa13* (Chu et al., 2006). The recently reported recessive bacterial blight resistance gene *xa-45(t)* co-localizes with the *xa13* locus on chromosome 8. Plants carrying *xa-45(t)* show specific resistance to pathotype PbXo-8 compared with plants carrying *xa13*. However, whether *xa-45(t)* interacts with a TALE remains to be studied (Neelam et al., 2020). Polymorphisms in the *OsSWEET14* promoter were screened in 169 rice accessions in a proof-of-principle experiment, and the investigators identified a single allele with a deletion of 18 bp overlapping with the EBEs of several TALEs. This allele, which is referred to as *xa41(t)*, confers resistance against half of the tested *Xoo* strains, indicating that the deletion in the promoter of *OsSWEET14* prevents TALE-mediated gene activation and leads to resistance (Zhou et al., 2015).

Another recessive *R* gene, *xa25*, is allelic to the susceptibility gene *OsSWEET13*, which shows sucrose transport activity (Zhou et al., 2015). The *Xoo* strain PXO339 can induce the expression of dominant *Xa25* but not recessive *xa25*. Because of nucleotide polymorphisms, the *Xa25* promoter from susceptible varieties is different from that of resistant varieties. Additionally, the proteins encoded by *xa25* and *Xa25* show an eight amino acids difference. The difference in the expression pattern of *xa25* and its dominant

https://engine.scichina.com/doi/10.1007/s11427-020-1699-4

allele, *Xa25*, suggests that *Xa25* may be a race-specific susceptiblity gene, whereas *xa25* has evolved as a mutant that cannot be induced by rice-*Xoo* interaction (Liu et al., 2011). It is worth studying whether the difference in amino acids affects sucrose transport activity because the *xa25*-encoding protein is different from that encoded by its dominant allele, *Xa25*. The recessive *xa5* allele is a natural allele of *TFIIAγ5*, resulting in a valine to glutamine change (TFIIAγ5^{V39E}), which plays a critical role in TALEs-dependent gene expression in rice (Iyer and McCouch, 2004; Jiang et al., 2006). A missense mutation in *xa5* attenuates the transcription of downstream TALE-targeted *S* genes, thus improving rice resistance by abolishing the interaction between virulence factor TALEs and the preinitiation complex (Figure 1H) (Iyer and McCouch, 2004; Schornack et al., 2006; Gu et al., 2009; Schornack et al., 2013).

Executor R genes: giving TALEs a taste of their own medicine

Molecular mimicry is widely deployed in the evolutionary arms race between pathogens and hosts. TALEs from pathogens are mimics of plant transcription factors, and plants also employ a TALE-bound promoter mimic to trigger defense responses. Executor *R* genes (E genes) employ this kind of TALE-bound promoter mimic to trap cognate TALEs and to restrict pathogen growth and diffusion. Thus far, only five E genes have been cloned, including *Xa27*, *Xa10* and *Xa23* from rice and *Bs3* and *Bs4C-R* from Solanaceae.

Xa27 was the first cloned *E* gene in rice; the specificity of the resistance of *Xa27* to various Chinese and Philippine *Xoo* races is determined by its promoter rather than by its gene product (Gu et al., 2005). It encodes a predicted protein of 113 amino acid residues with a signal anchor-like sequence at the N-terminal region directing this protein to the destination of the apoplast (Wu et al., 2008). The expression of *Xa27* in rice resulted in thickened vascular elements, suggesting that *Xa27* is critical for the resistance reaction (Gu et al., 2005).

Xa10 and *Xa23* share many characteristics, such as adjacent genomic loci on chromosome 11, similar protein sequences, potential transmembrane helices and endoplasmic reticulum localization (Wang et al., 2014b; Wang et al., 2015). Nevertheless, the resistance spectra of *Xa10* and *Xa23* in rice are considerably different. Since avrXa10 is only present in a few *Xoo* races, the resistance of *Xa10* is very limited, while *Xa23* confers a much broader spectrum corresponding to the wide distribution of avrXa23 in most of the existing *Xoo* strains (Wang et al., 2014a; Wang et al., 2015).

The pepper *Bs4C-R* gene also encodes an executor protein localized to the endoplasmic reticulum membrane (Wang et al., 2018). The immune response induced by *Bs4C-R* is dependent on EBE in the *Bs4C-R* promoter and the transcriptional activation domain of AvrBs4. An allele of *Bs4C-S* with a two-nucleotide polymorphism in the EBE could not be activated by AvrBs4 and resulted in susceptibility to bacteria carrying AvrBs4 (Strauss et al., 2012).

Unlike the above four proteins, which harbor potential transmembrane domains, pepper *Bs3* is the only executor protein known to exhibit the conserved domain of the flavin monooxygenases (Römer et al., 2007). *Bs3* is transcriptionally activated by the first characterized TALE, AvrBs3. The YUCCA (YUC) family proteins, which catalyze the final step in auxin biosynthesis, are the most closely related flavin monooxygenases to *Bs3*. However, *Bs3* leads to the accumulation of salicylic acid and pipecolic acid, two defense-related metabolites that are involved in systemic acquired resistance (Figure 1I) (Kronauer et al., 2019).

Classical R genes: non-transcriptional based resistance

Independent of TALE transcriptional activity, classical *R* genes trigger plant resistance via TALE-R protein interactions. A large number of NBS-LRR genes have been proven to mediate plant resistance against pathogens, but only two of them have been identified as *R* genes corresponding to TALEs, including *Bs4* from tomato and *Xa1* from rice.

Bs4 encodes a TIR-NBS-LRR (Toll-interleukin 1-nucleotide binding site leucine-rich repeat) protein that localizes to the plant cytoplasm and interacts with multiple TALEs such as AvrBs4, Hax3 and Hax4 (Schornack et al., 2004; Kay et al., 2007). The severely truncated version of AvrBs4 including only parts of the N-terminal and 3.5 repeats domain is sufficient to induce *Bs4*-mediated resistance, indicating that the recognition of Bs4 to TALEs is independent of TALE nucleus localization and transcriptional activity (Schornack et al., 2004). *Xa1* was the first NBS-LRR type bacterial blight resistance gene identified in rice. It is not expressed in intact leaves but can be induced by the stimulus of wounding or pathogen infection. *Xa1* confers specific resistance to Japanese *Xoo* strain race 1 (T7174) by initiating a hypersensitive response (Yoshimura et al., 1998). Moreover, rice *Xo1*-mediated resistance can be suppressed by truncTALE without DNA-binding specificity, implying a direct interaction of truncTALE and the Xo1 protein. Although it has not yet been cloned, the genome locus of *Xo1* was mapped and has now been narrowed to an interval of 1.01 Mb that harbors six full-length NBS-LRR genes (Figure 1J) (Triplett et al., 2016). Taking rice as an example, the position of TALE target genes on the rice chromosomes is shown in Figure 2.

Notably, two other NBS-LRR genes, *Xa39* and Weaker Defense (*WED*), were revealed to mediate the rice response to bacterial blight according to recent reports, but whether they are triggered by TALEs is unknown (Zhang et al., 2015b; Tang et al., 2019). *Xa39* mediates broad-spectrum

https://engine.scichina.com/doi/10.1007/s11427-020-1699-4

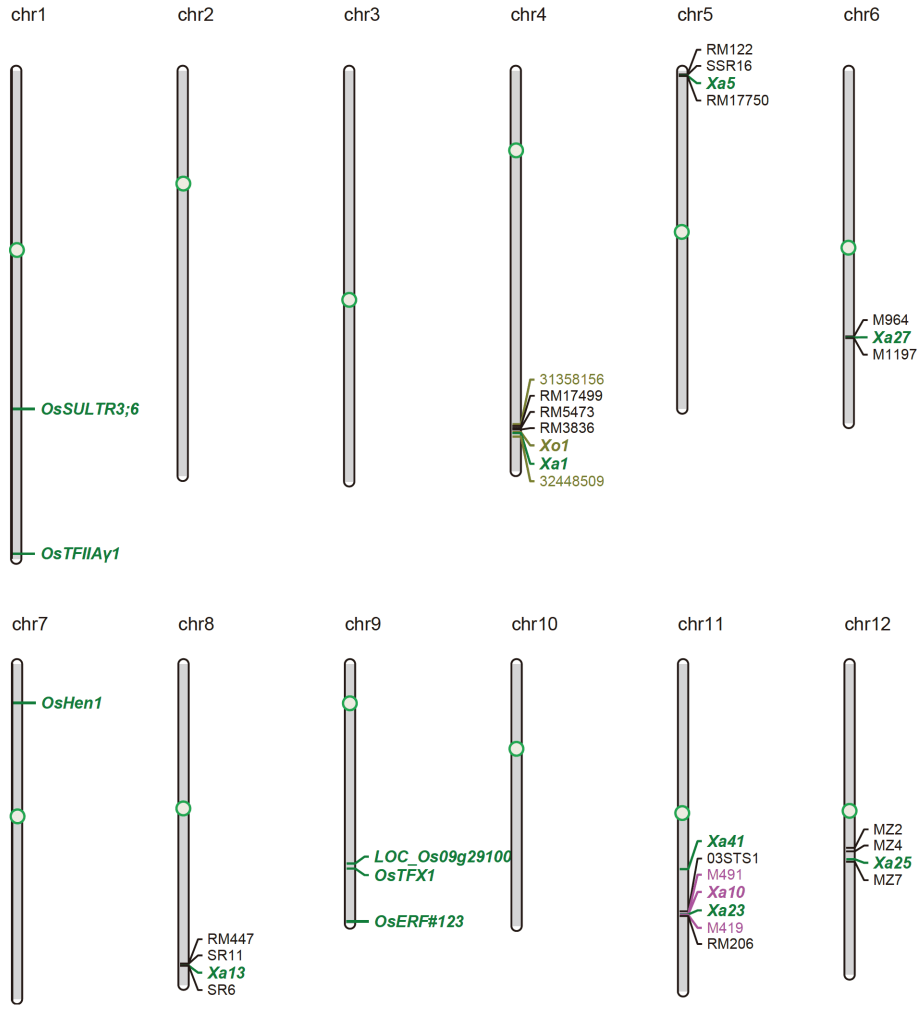

Figure 2 Distribution of TALE target genes on rice chromosomes. The genomic loci of the TALE target genes on rice chromosomes are derived from the *Oryza sativa*-Nipponbare-Reference-IRGSP-1.0 (https://rapdb.dna.affrc.go.jp/). All the cloned TALE targets or fine mapped target have been characterized by gene names (cloned gene are labeled in green; *Xo1* labeled in brown is fine mapped). *Xa10* is marked between M491 and M419 for it is identifed from rice cultivar Cas 209 and cannot be accurately marked on Nipponbare chromosome.

resistance to *Xoo*. Fine mapping of *Xa39* showed that a CC-NBS-LRR (coiled-coil-nucleotide binding site-leucine-rich repeat) protein coding gene is the most likely candidate (Zhang et al., 2015b). *WED* also encodes a CC-NBS-LRR protein. One amino acid substitution in the NBS domain of the WED protein generates a gain-of-function mutant *wed* with compromised immunity and increased susceptibility to *Xoo* (Tang et al., 2019). As NBS-LRR genes usually induce autoimmunity in plants, it is intriguing that gain-of-function of *wed* presents a distinct function of the NBS-LRR gene in plant susceptibility.

Strategies and applications of TALE biology in plant disease control and biotechnology

Identifying novel targets of TALEs

The discovery of the TALE code provided a key to understanding how TALEs bind to their targets in host cells. Accordingly, TALE-related data, including bacterial TALE sequences and TALE binding sites, could be used to predict new TALE targets (Perez-Quintero et al., 2018; Erkes et al., 2019). The genomes of two *Xoo* strains from the Philippines and India were sequenced in a recent report. Integrating computational target predictions and rice transcriptomics data, 12 specifically induced target rice genes were identified, five of which are hypothesized to be targets and four of which are new targets (Mücke et al., 2019). Databases have been established to store the genome data of *Xanthomonas* species, and several algorithms have also been developed to predict TALE targets in plants (Table 3, Figure 3A).

As described for the bidirectional transcription of TALEs above, noncoding RNAs that are expressed close to predicted EBEs from either the forward or reverse strand should be included if they have the potential to act as novel targets of TALEs. Although effective bioinformatics tools have not yet

https://engine.scichina.com/doi/10.1007/s11427-020-1699-4

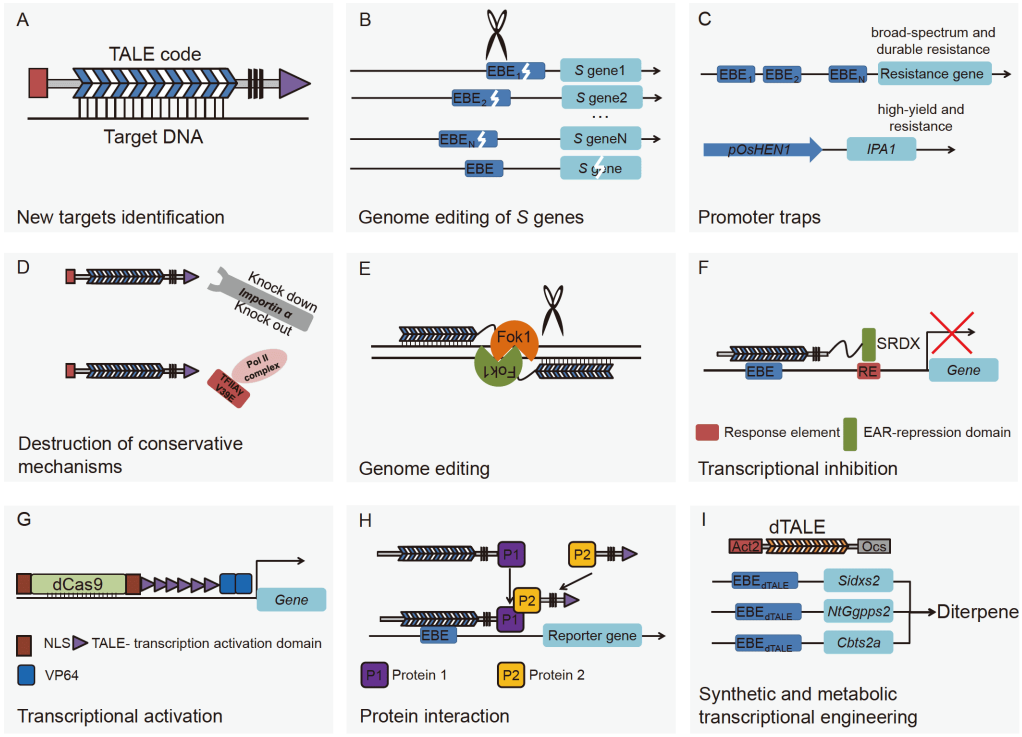

Figure 3 Summary of strategies and applications of TALE biology. A, Identification of new targets according to TALE code. B, Genome editing in promoters of different susceptibility genes or coding regions of susceptibility genes. C, Introducing multiple EBEs in resistance gene promoter or using TALE-dependent promoter traps to drive expression of *IPA1*. D, Suppressing the expression of Importin α to attenuate the shuttling of TALEs from the cytoplasm to the nucleus or using TFIIAγ^{V39E}-type mutation to destroy its interaction with TALEs. E–I, Applications of TALEs in biotechnology. E, TALEN used in genome editing. F, TALE RVD coupled with the EAR-repression domain (SRDX) to inhibit gene expression. G, dCas9 coupled with the activation domain of TALE and two copies of VP64 to activate gene expression. H, DNA-binding domain and activation domain of TALEs are separately fused to protein interacting domains for analyzing protein-protein interactions. I, Using dTALE-activated promoters for metabolic engineering of the plant diterpene pathway, *SlDXS2*, tomato 1-deoxyxylulose 5-phosphate synthase. *NtGGPPS2*, tobacco GGPP synthase; *CBTS2a*, tobacco cembratrienol synthase.

Table 3 TALE target prediction databases

Database	Website	Reference
Target Finder	http://tale-nt.cac.cornell.edu/	Doyle et al., 2012
Talvez	http://bioinfo.mpl.ird.fr/cgi-bin/talvez/talvez.cgi	Perez-Quintero et al., 2013
TALgetter	http://jstacs.de/index.php/TALgetter	Grau et al., 2013
SIFTED	http://thebrain.bwh.harvard.edu/sifted.html.	Rogers et al., 2015
daTALbase	http://bioinfo-web.mpl.ird.fr/cgi-bin2/datalbase/home.cgi	Perez-Quintero et al., 2018
PrediTALE	http://jstacs.de/index.php/PrediTALE	Erkes et al., 2019
Storyteller	http://bioinfo-web.mpl.ird.fr/xantho/tales/#vntrs	Perez-Quintero et al., 2013

been developed for predicting TALE-targeted noncoding regions, we believe that this will be an in-depth trend of future research on the TALE biology.

Genome editing in promoters or coding regions of S genes

Previous studies have reported that constitutive interference with TALE-dependent *S* genes by mutating their protein coding sequences or RNA interference may improve the resistance of host plants. For example, compromised expression of either *OsSWEET11* or *OsSWEET14* in rice can confer resistance to *Xoo* strains (Chu et al., 2006). However, this strategy also caused defects in reproductive development as an undesirable side effect. Therefore, it is usually not suitable to use traditional loss-of-function methods to modulate crop resistance in breeding.

Several recent studies have reported that the deletion of EBEs in the promoters of *S* genes represents an alternative strategy for effectively manipulating plant resistance to *Xanthomonas*. In the *OsSWEET11* gene promoter, a two gRNA-directed 149 bp deletion that includes the 31 bp pathogen-induced element resulted in failure of the induction

https://engine.scichina.com/doi/10.1007/s11427-020-1699-4

of the *OsSWEET11* gene by pathogens and conferred resistance in rice without leading to compromised performance of important agronomic traits (Li et al., 2020). As the resistance conferred by a single gene tends to drive the emergence of newly evolved pathogens with new toxicity, it is preferable to engineer resistance based on the combined mutation of multiple susceptible genes (Hutin et al., 2015; Carpenter et al., 2018). The most fascinating recent application of the TALE-OsSWEET interaction was the simultaneous mutation of the EBEs of *OsSWEET11*, *OsSWEET13* and *OsSWEET14* by CRISPR-Cas9-mediated genome editing in two independent research groups (Oliva et al., 2019; Xu et al., 2019). These applications provide exciting examples to advance our knowledge of the engineering of crops with broad-spectrum and durable resistance (Figure 3B).

Introducing promoter traps to R genes

Executor *R* genes are natural activation traps in plants. Learning from this mechanism, scientists designed and introduced TALE target sites into the promoters of *R* genes. One example is the deployment of the *Xa10* promoter in rice. Nipponbare carries two *Xa10*-like genes, *Xa10-Ni* and *Xa23-Ni*. Transgenic rice plants containing *Xa10* promoter-derived *Xa10-Ni* or *Xa23-Ni* exhibit AvrXa10-specific disease resistance to *Xoo* strains (Wang et al., 2017a). Transgenic rice plants carrying *Bs4C* under the control of *Xa10* promoter also show specific disease resistance to *Xoo* that delivers avrXa10 (Wang et al., 2018). A modified *Xa10* gene with five tandemly arranged EBEs of PthXo1, PthXo6, PthXo7, AvrXa10 and AvrXa27 was constructed in which the AvrXa10-binding site and adjacent flanking sequences in the native promoter of *Xa10* were replaced. The resulting stable transgenic rice plants showed broad-spectrum disease resistance to almost all the subjective *Xoo* strains (Zeng et al., 2015). As *Xa10* is a TALE- dependent executor *R* gene that only confers narrow-spectrum resistance to a few *Xoo* races (Gu et al., 2008), this research reveals an exciting fundamental strategy and sheds new light on plant disease management aimed at the generation of broad-spectrum, durable resistance to *Xoo*. Thus far, no executor R protein has been identified in citrus, and the *X. citri* effector gene *avrGf1* can trigger HR in citrus. Fourteen EBEs matching distinct *X. citri* TALEs were introduced into the promoter of the pepper *Bs3* gene. This engineered promoter was fused with AvrGf1. Bacterial growth was reduced by the expression of AvrGf1 (Shantharaj et al., 2017).

IPA1 (Ideal Plant Architecture1) is a crucial regulator of the crosstalk between plant growth and disease resistance. An appropriate increase in *IPA1* transcripts in rice results in an ideal plant architecture with a decreased number of unproductive tillers and increased panicle branch number and, thus, an increased yield (Jiao et al., 2010; Miura et al., 2010; Zhang et al., 2017). However, the constitutive expression of *IPA1* significantly reduces rice grain yield but enhances the broad-spectrum resistance against *Xoo* (Liu et al., 2019). A major problem in *IPA1* application is the question of how to engineer this gene to simultaneously increase grain yield and disease resistance against *Xoo*. The use of the TALE-dependent *OsHEN1* promoter trap provides a perfect solution to achieve this goal. *OsHEN1* encodes a TALE-induced methyltransferase that is involved in the stabilization of small RNAs (Moscou and Bogdanove, 2009; Cernadas et al., 2014). Transgenic rice expressing *IPA1* under the control of the *OsHEN1* promoter exhibited a high yield potential and increased disease resistance (Figure 3C) (Liu et al., 2019).

Targeting conserved mechanisms for TALEs

Since repeat domains are usually highly unstable during evolution, most of the applications of TALEs in plant resistance breeding based on the engineering of TALE repeat-dependent target genes still face very serious challenges in relation to the newly evolved toxicity of *Xanthomonas*. One approach that shows promising prospects is to target the highly conserved domains of TALEs, such as their NLSs and transcription factor-binding regions. The suppression of the expression of the NLS-binding proteins OsImpα1a and OsImpα1b attenuates the shuttling of TALEs from the cytoplasm into the nucleus, resulting in failure to induce the expression of susceptibility genes and consequently improving the broad-spectrum disease resistance of rice to *Xoo* and *Xoc* (Figure 3D) (Hui et al., 2019b).

In rice, TALEs interact with TFIIA by hijacking TFIIAα and TFIIAγ, but not TFIIAβ, to activate the expression of host genes (Ma et al., 2018b). Additionally, TFIIAγs are employed by TALE-carrying *Xanthomonas* to cause disease in other plants. The TALEs of *Xcc* causing canker in citrus and *Xcv* causing bacterial spot in pepper and tomato interact with the corresponding host TFIIAγs, as observed in rice. Transcriptionally suppressing TFIIAγs leads to resistance to *Xcc* in citrus and *Xcv* in pepper and tomato. Mutations in rice OsTFIIAγ5^{V39E}, citrus CsTFIIAγ^{V39E}, pepper CaTFIIAγ^{V39E}, and tomato SlTFIIAγ^{V39E} also lead to failed interactions with TALEs and prevent diseases in these plants. These results suggest that TALE-carrying bacteria share a common mechanism for infecting plants. Using the TFIIAγ^{V39E}-type mutation could be a general strategy for improving resistance to TALE-carrying pathogens in crops (Figure 3D) (Huang et al., 2017).

Applications of TALEs in biotechnology

In view of the highly modular nature of TALE units, the designed modules and the implications of these proteins present bright prospects in synthetic biology and bio-

https://engine.scichina.com/doi/10.1007/s11427-020-1699-4

technology. Several useful tools have been established for genome or epigenome editing and the transcriptional regulation of gene expression and protein interaction. One of the best-known applications of TALEs is the TALEN (transcription activator-like effector nuclease) technology used in genome editing. To increase the specificity of double-strand break events, TALEs are fused with monomers of the Fok1 nuclease domain and targeted to adjacent regions of DNA. TALENs are useful for generating knockout strains and for studying the biological function of genes or miRNAs in a variety of organisms, including plants (Figure 3E) (Morbitzer et al., 2010; Mahfouz et al., 2011; Shan et al., 2013; Blanvillain-Baufume et al., 2017; Cai et al., 2017; Bi et al., 2020; Malzahn et al., 2017; Xia et al., 2019).

TALEs can also be used to repress or activate the transcription of genes of interest by fusion with portable domains. The dHax3 TALE has been employed as a scaffold for the coupling of the EAR-repression domain (SRDX). This chimeric repressor targets the promoter of *Arabidopsis* RD29A and strongly inhibits the expression of the subjective genes (Mahfouz et al., 2012). Conversely, several dTALEs that bind to the promoters of targets have been shown to successfully activate genes (Figure 3F) (Gao et al., 2013; Gao et al., 2014; Wang et al., 2017a). On the other hand, the activation domains of TALEs can be used in association with nuclease-dead Cas9 (dCas9) to implement gene activation. Researchers have developed a new potent dCas9-TV gene activator containing six tandem repeats of the activation domain from TALE and two copies of VP64 through plant cell-based screens and shown that it exhibits stronger transcriptional activation of target genes than the dCas9-VP64 activator (Figure 3G) (Li et al., 2017).

The split-TALE (sTALE) system, which is mechanically similar to the widely used yeast two-hybrid assays is also deployed to analyze protein-protein interactions. In this system, the DNA-binding domain and activation domain from TALE are separated, and each domain is fused to protein-interacting domains (Schreiber et al., 2019). This method has been proven to be efficient in a recent report (Figure 3H) (Schubert et al., 2019).

The combined expression of multiple genes presents an immense scope for possible application in synthetic and metabolic transcriptional engineering. A series of synthetic promoters with a constant sequence of dTALE binding sites were constructed, and 43 of them were proven to be useful in driving the expression of the GUS reporter gene, with a strength of expression ranging from approximately 5% to almost 100% of 35S promoter activity. Using these promoters, three genes were transiently expressed in tobacco for the production of plant diterpenoids. This example showed the promising application of TALEs in the simultaneous expression of genetic circuits (Figure 3I) (Bruckner et al., 2015).

Future prospects

Facilitated by the recent development of genomics, gene editing technology and bioinformatics, great progress has been made in studies on the mechanism of plant-*Xanthomonas* interactions over the past 30 years. Research progress on crop disease resistance breeding has been accelerated accordingly. However, there is still a long way to go. For example, compared with the 45 bacterial blight resistance genes found in rice, only eight of the eleven cloned resistance genes interact with TALEs. A large number of disease-resistance genes need to be cloned (Neelam et al., 2020). Research on disease resistance genes and the pace of precision breeding will be accelerated. To achieve this progress, genome sequencing technology, gene editing technology and target gene prediction methods will be integrated. At present, the research on disease resistance genes mainly focuses on protein-coding genes. The discovery of bidirectional transcription of TALEs prompted us to re-examine TALE targets from the forward strand to the reverse strand, and non-protein-coding genes should not be ignored.

Ancient breeders seem to have been overly focused on reproductive traits such as grain yield, quality, shattering, seed size and shape, while placing too little weight on plant resistance. The domestication of crop wild relatives is usually accompanied by a fitness cost and compromised resistance. Therefore, the breeding of modern resistant agricultural varieties still largely relies on the identification of new resistance genes and the exploration of new mechanisms of TALE-target interactions. From a modern breeding perspective, the engineering of EBEs from recessive or dominant *R* promoters represents an effective approach for increasing plant disease resistance. As TALEs are genetically unstable because of their repeat domains, it is suggested that research should focus on the promoter engineering of multiple *R* genes. Another possibility is to interfere with the conserved domains and common mechanisms of TALEs to acquire broad-spectrum resistance, such as interfering with TALE transportation to the nucleus or the recruitment of the transcriptional machinery by TALEs. SA and JA are two important phytohormones related to plant immune responses. Accordingly, introducing promoter traps into the promoter regions of the core genes of plant hormone pathways to produce plants with broad-spectrum resistance is worth considering. We believe that further efforts aimed at crop breeding to resist *Xanthomonas* should adopt a combined strategy to avoid rapid loss of resistance.

Compliance and ethics *The author(s) declare that they have no conflict of interest.*

Acknowledgements *This research was supported by grants from the*

https://engine.scichina.com/doi/10.1007/s11427-020-1699-4

National Key R&D Program of China (2017YFD0100102), the National Natural Science Foundation of China (31471175), Natural Science Foundation of Guangdong Province, China (2017A030313183), Science and Technology Program of Guangdong Province, China (2017A070702006, 2017B020201003), Modern Agricultural Industry Technology System of Guangdong Province, China (2019KJ105), Joint Research on High Quality Rice Varieties (Yuecainong [2019]73), Special Fund for Science and Technology Innovation Strategy (Construction of High-level Academy of Agricultural Sciences) (Foundation of President of Guangdong Academy of Agricultural Sciences in China, BZ201909).

References

Antony, G., Zhou, J., Huang, S., Li, T., Liu, B., White, F., and Yang, B. (2010). Rice *xa13* recessive resistance to bacterial blight is defeated by induction of the disease susceptibility gene *Os-11N3*. Plant Cell 22, 3864–3876.

Ballvora, A., Pierre, M., van den Ackerveken, G., Schornack, S., Rossier, O., Ganal, M., Lahaye, T., and Bonas, U. (2001). Genetic mapping and functional analysis of the tomato *Bs4* locus governing recognition of the *Xanthomonas campestris* pv. *vesicatoria* AvrBs4 protein. Mol Plant Microbe Interact 14, 629–638.

Bart, R., Cohn, M., Kassen, A., McCallum, E.J., Shybut, M., Petriello, A., Krasileva, K., Dahlbeck, D., Medina, C., Alicai, T., et al. (2012). High-throughput genomic sequencing of cassava bacterial blight strains identifies conserved effectors to target for durable resistance. Proc Natl Acad Sci USA 109, E1972–E1979.

Bi, H., Fei, Q., Li, R., Liu, B., Xia, R., Char, S.N., Meyers, B.C., and Yang, B. (2020). Disruption of miRNA sequences by TALENs and CRISPR/Cas9 induces varied lengths of miRNA production. Plant Biotechnol J 18, 1526–1536.

Blanvillain-Baufume, S., Reschke, M., Solé, M., Auguy, F., Doucoure, H., Szurek, B., Meynard, D., Portefaix, M., Cunnac, S., Guiderdoni, E., et al. (2017). Targeted promoter editing for rice resistance to *Xanthomonas oryzae* pv. *oryzae* reveals differential activities for *SWEET14*-inducing TAL effectors. Plant Biotechnol J 15, 306–317.

Boch, J., and Bonas, U. (2010). *Xanthomonas* AvrBs3 family-type III effectors: discovery and function. Annu Rev Phytopathol 48, 419–436.

Boch, J., Bonas, U., and Lahaye, T. (2014). TAL effectors—pathogen strategies and plant resistance engineering. New Phytol 204, 823–832.

Boch, J., Scholze, H., Schornack, S., Landgraf, A., Hahn, S., Kay, S., Lahaye, T., Nickstadt, A., and Bonas, U. (2009). Breaking the code of DNA binding specificity of TAL-type III effectors. Science 326, 1509–1512.

Bruckner, K., Schäfer, P., Weber, E., Grützner, R., Marillonnet, S., and Tissier, A. (2015). A library of synthetic transcription activator-like effector-activated promoters for coordinated orthogonal gene expression in plants. Plant J 82, 707–716.

Cai, L., Cao, Y., Xu, Z., Ma, W., Zakria, M., Zou, L., Cheng, Z., and Chen, G. (2017). A transcription activator-like effector Tal7 of *Xanthomonas oryzae* pv. *oryzicola* activates rice gene *Os09g29100* to suppress rice immunity. Sci Rep 7, 5089.

Carpenter, S.C.D., Mishra, P., Ghoshal, C., Dash, P.K., Wang, L., Midha, S., Laha, G.S., Lore, J.S., Kositratana, W., Singh, N.K., et al. (2018). A strain of an emerging Indian *Xanthomonas oryzae* pv. *oryzae* pathotype defeats the rice bacterial blight resistance gene *xa13* without inducing a clade III SWEET gene and is nearly identical to a recent Thai isolate. Front Microbiol 9, 2703.

Cernadas, R.A., Doyle, E.L., Niño-Liu, D.O., Wilkins, K.E., Bancroft, T., Wang, L., Schmidt, C.L., Caldo, R., Yang, B., White, F.F., et al. (2014). Code-assisted discovery of TAL effector targets in bacterial leaf streak of rice reveals contrast with bacterial blight and a novel susceptibility gene. PLoS Pathog 10, e1003972.

Chen, L.Q., Hou, B.H., Lalonde, S., Takanaga, H., Hartung, M.L., Qu, X. Q., Guo, W.J., Kim, J.G., Underwood, W., Chaudhuri, B., et al. (2010). Sugar transporters for intercellular exchange and nutrition of pathogens. Nature 468, 527–532.

Chu, Z., Yuan, M., Yao, J., Ge, X., Yuan, B., Xu, C., Li, X., Fu, B., Li, Z., Bennetzen, J.L., et al. (2006). Promoter mutations of an essential gene for pollen development result in disease resistance in rice. Genes Dev 20, 1250–1255.

Cohn, M., Bart, R.S., Shybut, M., Dahlbeck, D., Gomez, M., Morbitzer, R., Hou, B.H., Frommer, W.B., Lahaye, T., and Staskawicz, B.J. (2014). *Xanthomonas axonopodis* virulence is promoted by a transcription activator-like effector–mediated induction of a SWEET sugar transporter in cassava. Mol Plant Microbe Interact 27, 1186–1198.

Cox, K.L., Meng, F., Wilkins, K.E., Li, F., Wang, P., Booher, N.J., Carpenter, S.C.D., Chen, L.Q., Zheng, H., Gao, X., et al. (2017). TAL effector driven induction of a SWEET gene confers susceptibility to bacterial blight of cotton. Nat Commun 8, 15588.

de Lange, O., Wolf, C., Dietze, J., Elsaesser, J., Morbitzer, R., and Lahaye, T. (2014). Programmable DNA-binding proteins from Burkholderia provide a fresh perspective on the TALE-like repeat domain. Nucleic Acids Res 42, 7436–7449.

Deng, D., Yan, C., Pan, X., Mahfouz, M., Wang, J., Zhu, J.K., Shi, Y., and Yan, N. (2012). Structural basis for sequence-specific recognition of DNA by TAL effectors. Science 335, 720–723.

Deng, W., Marshall, N.C., Rowland, J.L., McCoy, J.M., Worrall, L.J., Santos, A.S., Strynadka, N.C.J., and Finlay, B.B. (2017). Assembly, structure, function and regulation of type III secretion systems. Nat Rev Microbiol 15, 323–337.

Deng, Y., Liu, M., Li, X., and Li, F. (2018). MicroRNA-mediated R gene regulation: molecular scabbards for double-edged swords. Sci China Life Sci 61, 138–147.

Doyle, E.L., Booher, N.J., Standage, D.S., Voytas, D.F., Brendel, V.P., Vandyk, J.K., and Bogdanove, A.J. (2012). TAL Effector-Nucleotide Targeter (TALE-NT) 2.0: tools for TAL effector design and target prediction. Nucleic Acids Res 40, W117–W122.

Eom, J.S., Luo, D., Atienza-Grande, G., Yang, J., Ji, C., Thi Luu, V., Huguet-Tapia, J.C., Char, S.N., Liu, B., Nguyen, H., et al. (2019). Diagnostic kit for rice blight resistance. Nat Biotechnol 37, 1372–1379.

Erkes, A., Mücke, S., Reschke, M., Boch, J., and Grau, J. (2019). PrediTALE: A novel model learned from quantitative data allows for new perspectives on TALE targeting. PLoS Comput Biol 15, e1007206.

Erkes, A., Reschke, M., Boch, J., and Grau, J. (2017). Evolution of transcription activator-like effectors in *Xanthomonas oryzae*. Genome Biol Evol 9, 1599–1615.

Falahi Charkhabi, N., Booher, N.J., Peng, Z., Wang, L., Rahimian, H., Shams-Bakhsh, M., Liu, Z., Liu, S., White, F.F., and Bogdanove, A.J. (2017). Complete genome sequencing and targeted mutagenesis reveal virulence contributions of Tal2 and Tal4b of *Xanthomonas translucens* pv. *undulosa* ICMP11055 in bacterial leaf streak of wheat. Front Microbiol 8, 1488.

Ferreira, R.M., de Oliveira, A.C.P., Moreira, L.M., Belasque, J., Gourbeyre, E., Siguier, P., Ferro, M.I.T., Ferro, J.A., Chandler, M., and Varani, A. M. (2015). A TALE of transposition: Tn3-like transposons play a major role in the spread of pathogenicity determinants of Xanthomonas citri and other xanthomonads. mBio 6, e02505-02514.

Gao, X., Tsang, J.C.H., Gaba, F., Wu, D., Lu, L., and Liu, P. (2014). Comparison of TALE designer transcription factors and the CRISPR/dCas9 in regulation of gene expression by targeting enhancers. Nucleic Acids Res 42, e155.

Gao, X., Yang, J., Tsang, J.C.H., Ooi, J., Wu, D., and Liu, P. (2013). Reprogramming to pluripotency using designer TALE transcription factors targeting enhancers. Stem Cell Rep 1, 183–197.

Gochez, A.M., Huguet-Tapia, J.C., Minsavage, G.V., Shantaraj, D., Jalan, N., Strauß, A., Lahaye, T., Wang, N., Canteros, B.I., Jones, J.B., et al. (2018). Pacbio sequencing of copper-tolerant *Xanthomonas citri* reveals presence of a chimeric plasmid structure and provides insights into reassortment and shuffling of transcription activator-like effectors among *X. citri* strains. BMC Genomics 19, 16.

Gonzalez, C., Szurek, B., Manceau, C., Mathieu, T., Séré, Y., and Verdier, V. (2007). Molecular and pathotypic characterization of new

https://engine.scichina.com/doi/10.1007/s11427-020-1699-4

Xanthomonas oryzae strains from West Africa. Mol Plant Microbe Interact 20, 534–546.
Grau, J., Wolf, A., Reschke, M., Bonas, U., Posch, S., and Boch, J. (2013). Computational predictions provide insights into the biology of TAL effector target sites. PLoS Comput Biol 9, e1002962.
Gu, K., Sangha, J.S., Li, Y., and Yin, Z. (2008). High-resolution genetic mapping of bacterial blight resistance gene *Xa10*. Theor Appl Genet 116, 155–163.
Gu, K., Tian, D., Qiu, C., and Yin, Z. (2009). Transcription activator-like type III effector AvrXa27 depends on OsTFIIAγ5 for the activation of *Xa27* transcription in rice that triggers disease resistance to *Xanthomonas oryzae* pv. *oryzae*. Mol Plant Pathol 10, 829–835.
Gu, K., Yang, B., Tian, D., Wu, L., Wang, D., Sreekala, C., Yang, F., Chu, Z., Wang, G.L., White, F.F., et al. (2005). *R* gene expression induced by a type-III effector triggers disease resistance in rice. Nature 435, 1122–1125.
Hoiby, T., Zhou, H., Mitsiou, D.J., and Stunnenberg, H.G. (2007). A facelift for the general transcription factor TFIIA. Biochim Biophys Acta Gene Struct Exp 1769, 429–436.
Hu, Y., Zhang, J., Jia, H., Sosso, D., Li, T., Frommer, W.B., Yang, B., White, F.F., Wang, N., and Jones, J.B. (2014). Lateral organ boundaries 1 is a disease susceptibility gene for citrus bacterial canker disease. Proc Natl Acad Sci USA 111, E521–E529.
Huang, R., Hui, S., Zhang, M., Li, P., Xiao, J., Li, X., Yuan, M., and Wang, S. (2017). A conserved basal transcription factor is required for the function of diverse TAL effectors in multiple plant hosts. Front Plant Sci 8, 1919.
Hui, S., Liu, H., Zhang, M., Chen, D., Li, Q., Tian, J., Xiao, J., Li, X., Wang, S., and Yuan, M. (2019a). The host basal transcription factor IIA subunits coordinate for facilitating infection of TALEs-carrying bacterial pathogens in rice. Plant Sci 284, 48–56.
Hui, S., Shi, Y., Tian, J., Wang, L., Li, Y., Wang, S., and Yuan, M. (2019b). TALE-carrying bacterial pathogens trap host nuclear import receptors for facilitation of infection of rice. Mol Plant Pathol 20, 519–532.
Hutin, M., Sabot, F., Ghesquière, A., Koebnik, R., and Szurek, B. (2015). A knowledge-based molecular screen uncovers a broad-spectrum *OsSWEET14* resistance allele to bacterial blight from wild rice. Plant J 84, 694–703.
Iyer, A.S., and McCouch, S.R. (2004). The rice bacterial blight resistance gene *xa5* encodes a novel form of disease resistance. Mol Plant Microbe Interact 17, 1348–1354.
Ji, Z., Ji, C., Liu, B., Zou, L., Chen, G., and Yang, B. (2016). Interfering TAL effectors of *Xanthomonas oryzae* neutralize *R*-gene-mediated plant disease resistance. Nat Commun 7, 13435.
Ji, Z., Wang, C., and Zhao, K. (2018). Rice routes of countering *Xanthomonas oryzae*. Int J Mol Sci 19, 3008.
Jiang, C.J., Imamoto, N., Matsuki, R., Yoneda, Y., and Yamamoto, N. (1998). Functional characterization of a plant importin α homologue. J Biol Chem 273, 24083–24087.
Jiang, C.J., Shoji, K., Matsuki, R., Baba, A., Inagaki, N., Ban, H., Iwasaki, T., Imamoto, N., Yoneda, Y., Deng, X.W., et al. (2001). Molecular cloning of a novel Importin α homologue from rice, by which constitutive photomorphogenic 1 (COP1) nuclear localization signal (NLS)-protein is preferentially nuclear imported. J Biol Chem 276, 9322–9329.
Jiang, G.H., Xia, Z.H., Zhou, Y.L., Wan, J., Li, D.Y., Chen, R.S., Zhai, W. X., and Zhu, L.H. (2006). Testifying the rice bacterial blight resistance gene xa5 by genetic complementation and further analyzing xa5 (Xa5) in comparison with its homolog TFIIAγ1. Mol Genet Genomics 275, 354–366.
Jiao, Y., Wang, Y., Xue, D., Wang, J., Yan, M., Liu, G., Dong, G., Zeng, D., Lu, Z., Zhu, X., et al. (2010). Regulation of OsSPL14 by OsmiR156 defines ideal plant architecture in rice. Nat Genet 42, 541–544.
Jones, J.D.G., and Dangl, J.L. (2006). The plant immune system. Nature 444, 323–329.
Kay, S., Hahn, S., Marois, E., Hause, G., and Bonas, U. (2007). A bacterial effector acts as a plant transcription factor and induces a cell size regulator. Science 318, 648–651.
Kourelis, J., and van der Hoorn, R.A.L. (2018). Defended to the nines: 25 years of resistance gene cloning identifies nine mechanisms for R protein function. Plant Cell 30, 285–299.
Kronauer, C., Kilian, J., Strauß, T., Stahl, M., and Lahaye, T. (2019). Cell death triggered by the YUCCA-like Bs3 protein coincides with accumulation of salicylic acid and pipecolic acid but not of Indole-3-Acetic acid. Plant Physiol 180, 1647–1659.
Li, C., Li, W., Zhou, Z., Chen, H., Xie, C., and Lin, Y. (2020). A new rice breeding method: CRISPR/Cas9 system editing of the *Xa13* promoter to cultivate transgene-free bacterial blight-resistant rice. Plant Biotechnol J 18, 313–315.
Li, L., Atef, A., Piatek, A., Ali, Z., Piatek, M., Aouida, M., Sharakuu, A., Mahjoub, A., Wang, G., Khan, S., et al. (2013). Characterization and DNA-binding specificities of Ralstonia TAL-like effectors. Mol Plant 6, 1318–1330.
Li, Z., Zhang, D., Xiong, X., Yan, B., Xie, W., Sheen, J., and Li, J.F. (2017). A potent Cas9-derived gene activator for plant and mammalian cells. Nat Plants 3, 930–936.
Li, Z., Zou, L., Ye, G., Xiong, L., Ji, Z., Zakria, M., Hong, N., Wang, G., and Chen, G. (2014). A potential disease susceptibility gene CsLOB of citrus is targeted by a major virulence effector PthA of *Xanthomonas citri* subsp. *citri*. Mol Plant 7, 912–915.
Liu, M., Shi, Z., Zhang, X., Wang, M., Zhang, L., Zheng, K., Liu, J., Hu, X., Di, C., Qian, Q., et al. (2019). Inducible overexpression of Ideal Plant Architecture1 improves both yield and disease resistance in rice. Nat Plants 5, 389–400.
Liu, Q., Yuan, M., Zhou, Y., Li, X., Xiao, J., and Wang, S. (2011). A paralog of the MtN3/saliva family recessively confers race-specific resistance to *Xanthomonas oryzae* in rice. Plant Cell Environ 34, 1958–1969.
Ma, W., Zou, L., Zhiyuan, J.I., Xiameng, X.U., Zhengyin, X.U., Yang, Y., Alfano, J.R., and Chen, G. (2018a). *Xanthomonas oryzae* pv. *oryzae* TALE proteins recruit OsTFIIAγ1 to compensate for the absence of OsTFIIAγ5 in bacterial blight in rice. Mol Plant Pathol 19, 2248–2262.
Ma, L., Wang, Q., Yuan, M., Zou, T., Yin, P., and Wang, S. (2018b). *Xanthomonas* TAL effectors hijack host basal transcription factor IIA α and γ subunits for invasion. Biochem Biophys Res Commun 496, 608–613.
Mahfouz, M.M., Li, L., Piatek, M., Fang, X., Mansour, H., Bangarusamy, D.K., and Zhu, J.K. (2012). Targeted transcriptional repression using a chimeric TALE-SRDX repressor protein. Plant Mol Biol 78, 311–321.
Mahfouz, M.M., Li, L., Shamimuzzaman, M., Wibowo, A., Fang, X., and Zhu, J.K. (2011). *De novo*-engineered transcription activator-like effector (TALE) hybrid nuclease with novel DNA binding specificity creates double-strand breaks. Proc Natl Acad Sci USA 108, 2623–2628.
Mak, A.N.S., Bradley, P., Cernadas, R.A., Bogdanove, A.J., and Stoddard, B.L. (2012). The crystal structure of TAL effector PthXo1 bound to its DNA target. Science 335, 716–719.
Malzahn, A., Lowder, L., and Qi, Y. (2017). Plant genome editing with TALEN and CRISPR. Cell Biosci 7, 21.
Miura, K., Ikeda, M., Matsubara, A., Song, X.J., Ito, M., Asano, K., Matsuoka, M., Kitano, H., and Ashikari, M. (2010). OsSPL14 promotes panicle branching and higher grain productivity in rice. Nat Genet 42, 545–549.
Morbitzer, R., Römer, P., Boch, J., and Lahaye, T. (2010). Regulation of selected genome loci using *de novo*-engineered transcription activator-like effector (TALE)-type transcription factors. Proc Natl Acad Sci USA 107, 21617–21622.
Moscou, M.J., and Bogdanove, A.J. (2009). A simple cipher governs DNA recognition by TAL effectors. Science 326, 1501.
Mücke, S., Reschke, M., Erkes, A., Schwietzer, C.A., Becker, S., Streubel, J., Morgan, R.D., Wilson, G.G., Grau, J., and Boch, J. (2019). Transcriptional reprogramming of rice cells by *Xanthomonas oryzae* TALEs. Front Plant Sci 10, 162.
Neelam, K., Mahajan, R., Gupta, V., Bhatia, D., Gill, B.K., Komal, R., Lore, J.S., Mangat, G.S., and Singh, K. (2020). High-resolution genetic

https://engine.scichina.com/doi/10.1007/s11427-020-1699-4

mapping of a novel bacterial blight resistance gene xa-45(t) identified from *Oryza glaberrima* and transferred to *Oryza sativa*. Theor Appl Genet 133, 689–705.
Ochiai, H., Inoue, Y., Takeya, M., Sasaki, A., and Kaku, H. (2005). Genome sequence of *Xanthomonas oryzae* pv. *oryzae* suggests contribution of large numbers of effector genes and insertion sequences to its race diversity. Jpn Agr Res Q 39, 275–287.
Oliva, R., Ji, C., Atienza-Grande, G., Huguet-Tapia, J.C., Perez-Quintero, A., Li, T., Eom, J.S., Li, C., Nguyen, H., Liu, B., et al. (2019). Broad-spectrum resistance to bacterial blight in rice using genome editing. Nat Biotechnol 37, 1344–1350.
Peng, Z., Hu, Y., Zhang, J., Huguet-Tapia, J.C., Block, A.K., Park, S., Sapkota, S., Liu, Z., Liu, S., and White, F.F. (2019). *Xanthomonas translucens* commandeers the host rate-limiting step in ABA biosynthesis for disease susceptibility. Proc Natl Acad Sci USA 116, 20938–20946.
Perez-Quintero, A.L., Lamy, L., Zarate, C.A., Cunnac, S., Doyle, E., Bogdanove, A., Szurek, B., and Dereeper, A. (2018). daTALbase: a database for genomic and transcriptomic data related to TAL effectors. Mol Plant Microbe Interact 31, 471–480.
Perez-Quintero, A.L., Rodriguez-R, L.M., Dereeper, A., López, C., Koebnik, R., Szurek, B., and Cunnac, S. (2013). An improved method for TAL effectors DNA-binding sites prediction reveals functional convergence in TAL repertoires of *Xanthomonas oryzae* strains. PLoS ONE 8, e68464.
Perez-Quintero, A.L., and Szurek, B. (2019). A decade decoded: spies and hackers in the history of TAL effectors research. Annu Rev Phytopathol 57, 459–481.
Quibod, I.L., Atieza-Grande, G., Oreiro, E.G., Palmos, D., Nguyen, M.H., Coronejo, S.T., Aung, E.E., Nugroho, C., Roman-Reyna, V., Burgos, M. R., et al. (2020). The Green Revolution shaped the population structure of the rice pathogen *Xanthomonas oryzae* pv. *oryzae*. ISME J 14, 492–505.
Read, A.C., Rinaldi, F.C., Hutin, M., He, Y.Q., Triplett, L.R., and Bogdanove, A.J. (2016). Suppression of Xo1-mediated disease resistance in rice by a truncated, non-DNA-binding TAL effector of *Xanthomonas oryzae*. Front Plant Sci 7, 1516.
Roeschlin, R.A., Uviedo, F., García, L., Molina, M.C., Favaro, M.A., Chiesa, M.A., Tasselli, S., Franco-Zorrilla, J.M., Forment, J., Gadea, J., et al. (2019). PthA4^{AT}, a 7.5-repeats transcription activator-like (TAL) effector from *Xanthomonas citri* ssp. *citri*, triggers citrus canker resistance. Mol Plant Pathol 20, 1394–1407.
Rogers, J.M., Barrera, L.A., Reyon, D., Sander, J.D., Kellis, M., Keith Joung, J., and Bulyk, M.L. (2015). Context influences on TALE–DNA binding revealed by quantitative profiling. Nat Commun 6, 7440.
Römer, P., Hahn, S., Jordan, T., Strauss, T., Bonas, U., and Lahaye, T. (2007). Plant pathogen recognition mediated by promoter activation of the pepper *Bs3* resistance gene. Science 318, 645–648.
Römer, P., Recht, S., Strauss, T., Elsaesser, J., Schornack, S., Boch, J., Wang, S., and Lahaye, T. (2010). Promoter elements of rice susceptibility genes are bound and activated by specific TAL effectors from the bacterial blight pathogen, *Xanthomonas oryzae* pv. *oryzae*. New Phytol 187, 1048–1057.
Ruh, M., Briand, M., Bonneau, S., Jacques, M.A., and Chen, N.W.G. (2017). *Xanthomonas* adaptation to common bean is associated with horizontal transfers of genes encoding TAL effectors. BMC Genomics 18, 670.
Scholze, H., and Boch, J. (2011). TAL effectors are remote controls for gene activation. Curr Opin Microbiol 14, 47–53.
Schornack, S., Ballvora, A., Gürlebeck, D., Peart, J., Baulcombe, D., Ganal, M., Baker, B., Bonas, U., and Lahaye, T. (2004). The tomato resistance protein Bs4 is a predicted non-nuclear TIR-NB-LRR protein that mediates defense responses to severely truncated derivatives of AvrBs4 and overexpressed AvrBs3. Plant J 37, 46–60.
Schornack, S., Meyer, A., Römer, P., Jordan, T., and Lahaye, T. (2006). Gene-for-gene-mediated recognition of nuclear-targeted AvrBs3-like bacterial effector proteins. J Plant Physiol 163, 256–272.
Schornack, S., Minsavage, G.V., Stall, R.E., Jones, J.B., and Lahaye, T. (2008). Characterization of AvrHah1, a novel AvrBs3-like effector from *Xanthomonas gardneri* with virulence and avirulence activity. New Phytol 179, 546–556.
Schornack, S., Moscou, M.J., Ward, E.R., and Horvath, D.M. (2013). Engineering plant disease resistance based on TAL effectors. Annu Rev Phytopathol 51, 383–406.
Schreiber, T., Prange, A., Hoppe, T., and Tissier, A. (2019). Split-TALE: a TALE-based two-component system for synthetic biology applications in planta. Plant Physiol 179, 1001–1012.
Schubert, R., Dobritzsch, S., Gruber, C., Hause, G., Athmer, B., Schreiber, T., Marillonnet, S., Okabe, Y., Ezura, H., Acosta, I.F., et al. (2019). Tomato MYB21 acts in ovules to mediate jasmonate-regulated fertility. Plant Cell 31, 1043–1062.
Schwartz, A.R., Morbitzer, R., Lahaye, T., and Staskawicz, B.J. (2017). TALE-induced bHLH transcription factors that activate a pectate lyase contribute to water soaking in bacterial spot of tomato. Proc Natl Acad Sci USA 114, E897–E903.
Shan, Q., Wang, Y., Chen, K., Liang, Z., Li, J., Zhang, Y., Zhang, K., Liu, J., Voytas, D.F., Zheng, X., et al. (2013). Rapid and efficient gene modification in rice and *Brachypodium* using TALENs. Mol Plant 6, 1365–1368.
Shantharaj, D., Römer, P., Figueiredo, J.F.L., Minsavage, G.V., Krönauer, C., Stall, R.E., Moore, G.A., Fisher, L.C., Hu, Y., Horvath, D.M., et al. (2017). An engineered promoter driving expression of a microbial avirulence gene confers recognition of TAL effectors and reduces growth of diverse *Xanthomonas* strains in citrus. Mol Plant Pathol 18, 976–989.
Strauss, T., van Poecke, R.M.P., Strauss, A., Römer, P., Minsavage, G.V., Singh, S., Wolf, C., Strauss, A., Kim, S., Lee, H.A., et al. (2012). RNA-seq pinpoints a *Xanthomonas* TAL-effector activated resistance gene in a large-crop genome. Proc Natl Acad Sci USA 109, 19480–19485.
Streubel, J., Baum, H., Grau, J., Stuttman, J., and Boch, J. (2017). Dissection of TALE-dependent gene activation reveals that they induce transcription cooperatively and in both orientations. PLoS ONE 12, e0173580.
Streubel, J., Pesce, C., Hutin, M., Koebnik, R., Boch, J., and Szurek, B. (2013). Five phylogenetically close rice *SWEET* genes confer TAL effector-mediated susceptibility to *Xanthomonas oryzae* pv. *oryzae*. New Phytol 200, 808–819.
Sugio, A., Yang, B., Zhu, T., and White, F.F. (2007). Two type III effector genes of Xanthomonas oryzae pv. oryzae control the induction of the host genes OsTFIIA1 and OsTFX1 during bacterial blight of rice. Proc Natl Acad Sci USA 104, 10720–10725.
Szurek, B., Marois, E., Bonas, U., and Van den Ackerveken, G. (2001). Eukaryotic features of the Xanthomonas type III effector AvrBs3: protein domains involved in transcriptional activation and the interaction with nuclear import receptors from pepper. Plant J 26, 523–534.
Tang, J., Wang, Y., Yin, W., Dong, G., Sun, K., Teng, Z., Wu, X., Wang, S., Qian, Y., Pan, X., et al. (2019). Mutation of a nucleotide-binding leucine-rich repeat immune receptor-type protein disrupts immunity to bacterial blight. Plant Physiol 181, 1295–1313.
Tian, D., Wang, J., Zeng, X., Gu, K., Qiu, C., Yang, X., Zhou, Z., Goh, M., Luo, Y., Murata-Hori, M., et al. (2014). The rice TAL effector-dependent resistance protein XA10 triggers cell death and calcium depletion in the endoplasmic reticulum. Plant Cell 26, 497–515.
Tran, T.T., Pérez-Quintero, A.L., Wonni, I., Carpenter, S.C.D., Yu, Y., Wang, L., Leach, J.E., Verdier, V., Cunnac, S., Bogdanove, A.J., et al. (2018). Functional analysis of African *Xanthomonas oryzae* pv. *oryzae* TALomes reveals a new susceptibility gene in bacterial leaf blight of rice. PLoS Pathog 14, e1007092.
Triplett, L.R., Cohen, S.P., Heffelfinger, C., Schmidt, C.L., Huerta, A.I., Tekete, C., Verdier, V., Bogdanove, A.J., and Leach, J.E. (2016). A resistance locus in the American heirloom rice variety Carolina Gold Select is triggered by TAL effectors with diverse predicted targets and is effective against African strains of *Xanthomonas oryzae* pv. *oryzicola*.

https://engine.scichina.com/doi/10.1007/s11427-020-1699-4

Plant J 87, 472–483.
Van den Ackerveken, G., Marois, E., and Bonas, U. (1996). Recognition of the bacterial avirulence protein AvrBs3 occurs inside the host plant cell. Cell 87, 1307–1316.
Wang, C.L., Qin, T.F., Yu, H.M., Zhang, X.P., Che, J.Y., Gao, Y., Zheng, C. K., Yang, B., and Zhao, K.J. (2014a). The broad bacterial blight resistance of rice line CBB23 is triggered by a novel transcription activator-like (TAL) effector of *Xanthomonas oryzae* pv. *oryzae*. Mol Plant Pathol 15, 333–341.
Wang, C., Fan, Y., Zheng, C., Qin, T., Zhang, X., and Zhao, K. (2014b). High-resolution genetic mapping of rice bacterial blight resistance gene Xa23. Mol Genet Genomics 289, 745–753.
Wang, C., Zhang, X., Fan, Y., Gao, Y., Zhu, Q., Zheng, C., Qin, T., Li, Y., Che, J., Zhang, M., et al. (2015). XA23 is an executor R protein and confers broad-spectrum disease resistance in rice. Mol Plant 8, 290–302.
Wang, J., Tian, D., Gu, K., Yang, X., Wang, L., Zeng, X., and Yin, Z. (2017a). Induction of *Xa10*-like genes in rice cultivar nipponbare confers disease resistance to rice bacterial blight. Mol Plant Microbe Interact 30, 466–477.
Wang, J., Zeng, X., Tian, D., Yang, X., Wang, L., and Yin, Z. (2018). The pepper Bs4C proteins are localized to the endoplasmic reticulum (ER) membrane and confer disease resistance to bacterial blight in transgenic rice. Mol Plant Pathol 19, 2025–2035.
Wang, L., Rinaldi, F.C., Singh, P., Doyle, E.L., Dubrow, Z.E., Tran, T.T., Pérez-Quintero, A.L., Szurek, B., and Bogdanove, A.J. (2017b). TAL effectors drive transcription bidirectionally in plants. Mol Plant 10, 285–296.
Wilkins, K.E., Booher, N.J., Wang, L., and Bogdanove, A.J. (2015). TAL effectors and activation of predicted host targets distinguish Asian from African strains of the rice pathogen *Xanthomonas oryzae* pv. *oryzicola* while strict conservation suggests universal importance of five TAL effectors. Front Plant Sci 6, 536.
Wu, L., Goh, M.L., Sreekala, C., and Yin, Z. (2008). XA27 depends on an amino-terminal signal-anchor-like sequence to localize to the apoplast for resistance to *Xanthomonas oryzae* pv *oryzae*. Plant Physiol 148, 1497–1509.
Wyler, E., Menegatti, J., Franke, V., Kocks, C., Boltengagen, A., Hennig, T., Theil, K., Rutkowski, A., Ferrai, C., Baer, L., et al. (2017). Widespread activation of antisense transcription of the host genome during herpes simplex virus 1 infection. Genome Biol 18, 209.
Xia, Y., Huang, G., and Zhu, Y. (2019). Sustainable plant disease control: biotic information flow and behavior manipulation. Sci China Life Sci 62, 1710–1713.
Xu, Z., Xu, X., Gong, Q., Li, Z., Li, Y., Wang, S., Yang, Y., Ma, W., Liu, L., Zhu, B., et al. (2019). Engineering broad-spectrum bacterial blight resistance by simultaneously disrupting variable TALE-binding elements of multiple susceptibility genes in rice. Mol Plant 12, 1434–1446.
Yang, B., Sugio, A., and White, F.F. (2006). Os8N3 is a host disease-susceptibility gene for bacterial blight of rice. Proc Natl Acad Sci USA 103, 10503–10508.
Yang, B., and White, F.F. (2004). Diverse members of the AvrBs3/PthA family of type III effectors are major virulence determinants in bacterial blight disease of rice. Mol Plant Microbe Interact 17, 1192–1200.
Yoshimura, S., Yamanouchi, U., Katayose, Y., Toki, S., Wang, Z.X., Kono, I., Kurata, N., Yano, M., Iwata, N., and Sasaki, T. (1998). Expression of Xa1, a bacterial blight-resistance gene in rice, is induced by bacterial inoculation. Proc Natl Acad Sci USA 95, 1663–1668.
Yoshimura, S., Yoshimura, A., Iwata, N., McCouch, S.R., Abenes, M.L., Baraoidan, M.R., Mew, T.W., and Nelson, R.J. (1995). Tagging and combining bacterial blight resistance genes in rice using rapd and rflp markers. Mol Breeding 1, 375–387.
Yu, Y., Streubel, J., Balzergue, S., Champion, A., Boch, J., Koebnik, R., Feng, J., Verdier, V., and Szurek, B. (2011). Colonization of rice leaf blades by an African strain of *Xanthomonas oryzae* pv. *oryzae* depends on a new TAL effector that induces the rice nodulin-3 *Os11N3* gene. Mol Plant Microbe Interact 24, 1102–1113.
Yu, Y., Zhang, Y., Chen, X., and Chen, Y. (2019). Plant noncoding RNAs: hidden players in development and stress responses. Annu Rev Cell Dev Biol 35, 407–431.
Yu, Y., Zhou, Y.F., Feng, Y.Z., He, H., Lian, J.P., Yang, Y.W., Lei, M.Q., Zhang, Y.C., and Chen, Y.Q. (2020). Transcriptional landscape of pathogen-responsive lnc^{RNA}s in rice unveils the role of ^{ALEX} 1 in jasmonate pathway and disease resistance. Plant Biotechnol J 18, 679–690.
Yu, Y., Zhou, Y., Zhang, Y., and Chen, Y. (2018). Grass phasiRNAs and male fertility. Sci China Life Sci 61, 148–154.
Yuan, M., Chu, Z., Li, X., Xu, C., and Wang, S. (2010). The bacterial pathogen *Xanthomonas oryzae* overcomes rice defenses by regulating host copper redistribution. Plant Cell 22, 3164–3176.
Yuan, M., Ke, Y., Huang, R., Ma, L., Yang, Z., Chu, Z., Xiao, J., Li, X., and Wang, S. (2016). A host basal transcription factor is a key component for infection of rice by TALE-carrying bacteria. eLife 5, e19605.
Zeng, X., Tian, D., Gu, K., Zhou, Z., Yang, X., Luo, Y., White, F.F., and Yin, Z. (2015). Genetic engineering of the *Xa10* promoter for broad-spectrum and durable resistance to *Xanthomonas oryzae* pv. *oryzae*. Plant Biotechnol J 13, 993–1001.
Zhang, J., Yin, Z., and White, F. (2015a). TAL effectors and the executor R genes. Front Plant Sci 6, 641.
Zhang, F., Huang, L., Zhang, F., Hu, D., Wu, W., Wang, W., Ali, J., Vera Cruz, C., Zhou, Y., and Li, Z. (2015b). Interacting transcriptomes revealing molecular mechanisms underlying *Xa39* mediated broad spectrum resistance of rice to bacterial blight. Plant Genome 8, plantgenome2014.12.0094.
Zhang, L., Yu, H., Ma, B., Liu, G., Wang, J., Wang, J., Gao, R., Li, J., Liu, J., Xu, J., et al. (2017). A natural tandem array alleviates epigenetic repression of IPA1 and leads to superior yielding rice. Nat Commun 8, 14789.
Zhou, J., Peng, Z., Long, J., Sosso, D., Liu, B., Eom, J.S., Huang, S., Liu, S., Vera Cruz, C., Frommer, W.B., et al. (2015). Gene targeting by the TAL effector PthXo2 reveals cryptic resistance gene for bacterial blight of rice. Plant J 82, 632–643.
Zuluaga, P., Szurek, B., Koebnik, R., Kroj, T., and Morel, J.B. (2017). Effector mimics and integrated decoys, the never-ending arms race between rice and *Xanthomonas oryzae*. Front Plant Sci 8, 431.

https://engine.scichina.com/doi/10.1007/s11427-020-1699-4