Utilizing transcription factors for improving banded leaf and sheath blight disease resistance in maize: a review

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ABSTRACT

Banded leaf and sheath blight (BLSB) disease, incited by *Rhizoctonia solani*, is destructive, difficult to manage and greatly threatens maize (*Zea mays* L.) production across continents. Plant transcription factors (TFs) act as functional nodes that integrate defense signals to activate relevant immune outlets via large-scale transcriptional reprogramming of the expression of massive sets of defense-related genes (DRGs). Recent studies revealed complex changes in the maize transcriptome during BLSB infection. More than 30 TFs belonging to the WRKY, NAC, TCP, bHLH, and bZIP families, among others, have been putatively identified as core genes inducible in maize by the virulence factors of *R. solani*. Sadly, no progress has been made in characterizing these TFs in maize resistance to BLSB. Having reviewed the progress made so far, we propose future studies to prioritize functional characterization of the potential TFs and their manipulation through genome editing technology as well as the use of synthetic TFs to improve maize resistance to BLSB.

1. Introduction

Maize (*Zea mays* L.) has become an important agricultural crop that is used for food, feed, fuel, and primary products for a variety of food and non-food industries in temperate, tropical, and subtropical regions of the world (Mandal 2014). In 2020, global maize production amounted to 1.16 billion tons in a production area of 201.98 million hectares, resulting in 57,547 hectograms per hectare (FAOSTAT 2022). As a crop that is widely adapted to multiple environmental conditions and a wide range of agroecologies (Badu-Apraku et al. 2012; Ajayo et al. 2021), increases in maize production and productivity may offer better prospects for food security than any other crop worldwide. Despite its ecological suitability and yield potential, maize production is constantly menace by a plethora of fungal, bacterial, and viral plant diseases. In particular, fungal pathogen-incited foliar diseases, including banded leaf and sheath blight (*R. solani*) southern corn leaf blight, northern corn leaf blight, gray leaf spot, and common rust, are the main threats that limit maize production and productivity in various production regions of the world (Subedi 2015; Bruns 2017; Rahamawati et al. 2020; Badu-Apraku et al. 2021; Khokhar et al. 2021). These foliar diseases are destructive and ravaging and generally cause a significant yield loss annually (Yang et al. 2017; Khokhar et al. 2021). BLSB is not only destructive and devastating, its causal pathogen is ubiquitously distributed, can survive variable ecological conditions, and is difficult to manage and, therefore, has become a serious threat across continents (Ahuja and Payak 1982; Chaudhary et al. 2016; Hooda et al. 2017; Sagar and Bhusal 2019). Furthermore, ecological conditions are often favorable for the pathogen growth and infection in most maize germplasms (Ahuja and Payak 1982; Hooda et al. 2017).

Banded leaf and sheath blight disease of maize has been reported worldwide since Bertus first discovered it in Sri Lanka about a century ago (Sagar and Bhusal 2019). At the initial stage of BLSB development, the first and second leaf sheaths of maize are infected showing discolored bands and lesions. As the infection progresses, the symptoms progress to the leaves, stalks, and ears, resulting in a serious loss of grain yield (Ahuja and Payak 1982). Maize farmers may suffer a loss of grain yield of up to 100% if BLSB is left unmanaged (Chaudhary et al. 2016; Hooda et al. 2017). The causal pathogen of BLSB in maize is a ubiquitous soil-borne fungus, *Rhizoctonia solani* f. sp. sasaki (Ahuja and Payak 1982; Hooda et al. 2017). In *R. solani*, 14 anastomosis groups (AGs: AG1 – AG13 & AGBI) have been characterized, and AG1-IA within the AG1 group causes BLSB in maize and sheath blight in rice (Hooda et al. 2017; Singh et al. 2018). Important virulence factors, including secreted and effector proteins, carbohydrate-active enzymes (CAZymes), proteins associated with the production of primary and secondary metabolites, and virulence-associated (VA) miRNAs (small RNAs similar to miRNA), participate in the pathogenicity of *R. solani* AG1-IA and suppression of maize resistance (Lin et al. 2016; Xia et al. 2017; Shamim et al. 2020; Meng et al. 2021).

Most elite maize germplasm lines and varieties, such as B73, B104, Mo17, B84, EV1428, CML478, DHM121, EV5098, and DHM109, are susceptible to BLSB (Yang et al. 2005; Chen et al. 2013; Madhavi et al. 2018; Sagar et al. 2019). Crop protection experts advise an integrated disease management approach, including sanitation to reduce the risk of spreading contaminated seed or soil, and the use of biocontrol agents, fungicides, and resistant varieties. The most effective and economical protection method is the use of resistant varieties; however, when not available, the
application of fungicides is often the main strategy to manage the disease (Hooda et al. 2017; Singh et al. 2019). The application of some fungicides such as thifluazonam, azoxystrobin, trifloxystrobin, thiabendazole, carbendazim, and validamycin has been reported to be effective against BLSB (Malik et al. 2018; Basandrai et al. 2020; Yao et al. 2020). Although fungicides are effective in reducing the incidence of BLSB, their use has certain limitations. One of such drawbacks includes the build-up of fungicide-resistance, particularly, in an environment with prevalent resistant isolates of *R. solani* (Bennett 2012; Zhao et al. 2019; Cheng et al. 2020). Moreover, fungicide residues in soil and edible plant products arouse conceivable ecological and health risks (Thind 2017; Yao et al. 2020). Altogether, these disadvantages of fungicide application pose a serious challenge to the effective management of BLSB, especially, when resistant varieties are not commercially available.

Availability of BLSB-resistant maize varieties will contribute to the reduction of fungicide use and safeguard grain yield. Regrettably, a low level of resistance to *R. solani* has been reported in maize germplasm in different regions of the world (Chen et al. 2013; Asif and Mall 2017; Madhavi et al. 2018; Sagar et al. 2019; Meena et al. 2021). This has hampered the development of BLSB-resistant varieties via conventional breeding methods (Ahmar et al. 2020). Fortunately, advanced technologies such as genome editing (GE) tools (e.g. CRISPR–Cas systems) are now available for rapid, precise, and predictable genetic modifications of crops and have been applied to introduce heritable and enhanced-disease resistance (EDR) traits in various model crops (Wang et al. 2014; Wang et al. 2016; Zhang et al. 2016; Schmidt 2017; Nawaz et al. 2020). To exploit the potential of GE tools in plant-genome modification for EDR, the first step is to identify key targets that are important for mounting immune responses.

During the co-evolution of plant pathogens, plants recognize pathogen-associated molecular patterns (PAMPs) by pattern recognition receptors (PRRs) located on the plasma membrane (Bacete et al. 2018), and promptly transduce perceived signals by intracellular signaling components such as phytohormones, reactive oxygen species, and protein-kinases [e.g. mitogen-activated protein kinases (MAPK) and calcium-dependent protein kinases (CDPK)], to transcription factors (TFs), which then modulate the expressions of downstream defense-related genes (DRGs) (Figure 1) for immune system activation (Dangl et al. 2013; Erpen et al. 2018). Thus, TFs act as the final transducer and major immune regulator by activating or repressing the expressions of downstream DRGs. To promote susceptibility in host plants, adapted pathogens suppress host immune activators (positively regulating TFs) or activate host immune regulators (negatively regulating TFs) (Jones and Dangl 2006; Boyd et al. 2013; Dangl et al. 2013). Being a master regulator of gene expression, TFs are suitable targets and valuable resources for the EDR program.

In maize, complex transcriptome changes and differential expressions of DRGs, including TFs and genes associated with cell-wall biosynthesis, pathogenesis-related responses, signal transduction, metabolic and oxidative stress pathways, have been reported during attack by *R. solani* (Zhang et al. 2012; Gao et al. 2014; Li et al. 2017; Yang et al. 2017; Li et al. 2019; Cao et al. 2021). More than 30 TFs belonging to the WRKY, NAC, TCP, bHLH, and bZIP families, among others, have been putatively identified as core genes inducible in maize by *R. solani* virulence factors, suggesting that TFs are critical for maize resistance to BLSB (Gao et al. 2014; Cao et al. 2021; Meng et al. 2021). Regrettably, little or no effort has been made in characterizing these TFs in resistance of maize to BLSB, and consequently, our knowledge of the transcriptional regulations of maize susceptibility/resistance reaction to infection by *R. solani* is greatly limited. In this review article, we provide an overview of recent progress in the biology of *R. solani*, the epidemiology and molecular basis of pathogenicity, the genetic control of resistance to BLSB, and changes in the maize transcriptome during attack by *R. solani*, and summarize the roles of TFs in plant immunity. Finally, we proposed frontier research priorities that focus on the functional characterization of potential TFs and their manipulation through genome editing technology, as well as the use of synthetic TFs to improve maize resistance to BLSB.

### 2. Brief review on the biology of *R. solani*, epidemiology, and pathogenicity

#### 2.1. Taxonomy, description, host range, and classification of *R. solani*

The taxonomic classification of *Rhizoctonia solani* is as follows: Domain: Eukaryota; Kingdom: Fungi; Phylum: Basidiomycota; Class: Agaricomycetes; Order: Cantharellales; Family: Ceratobasidiaceae; Genus: *Rhizoctonia*; Species: *solani* (National Center for Biotechnology Information 2022). *R. solani* is a ubiquitous soil-borne fungus that has important ecological roles as pathogen, saprotroph, and endophyte and is the most widely studied species within the genus *Rhizoctonia* (Hooda et al. 2017; Ajayi-Oyetunde and Bradley 2018). In general, *R. solani* thrives as a necrotrophic pathogen in economic plants, a saprophyte in the soil, and an endophytic symbiont in mosses and orchids (Warcup and Talbot 1966; Currah et al. 1987; Vilgalys and Cubeta 1994). *R. solani* has distinctive characteristics that distinguish it from other *Rhizoctonia*. Typically, *R. solani* exhibits uniform texture sclerotia and septate hyphae with central pores (dolipores) that allow free cell-to-cell movement of the cytoplasm, nuclei, and mitochondria. Furthermore, it shows undifferentiated hyphae (monilioid cells), multinucleated young colorless hyphae, and brown pigmented mature hyphae. The hyphae are often branched at a right angle (Duggar 1915; Parmeter and Whitney 1970).

The soil-borne fungus exists primarily as vegetative mycelium and/or sclerotia (propagules) and predominantly reproduces asexually. Although, it occasionally produces sexual spores (basidiospores) to initiate sexual reproduction by fusion of sexually compatible nuclei to produce double nuclei, and eventually, form a multinucleate cell through meiotic processes (Ajayi-Oyetunde and Bradley 2018). Under harsh ecological conditions, the sclerotia (diameter: about 1–3 mm) persist in soil and plant residues for a long period, but when favorable environmental conditions are restored, they germinate to produce infective hyphae that infect host plants (Ahuja and Payak 1982). As a necrotroph, *R. solani* is a destructive and versatile pathogen that infects a wide range of agricultural crops (more than 30 families of plants) including maize, rice, potatoes, soybeans, sugar beet, sorghum, wheat, barley, tobacco, peanut, cucumber,
coffee, lettuce, tomato, among others, at all stages of development, and causes lesions, black scurf, seedling blight, necrotic leaf spot, brown patch and canker, banded leaf and sheath blight, damping off and rot in the stem, ear, pod, root, seedling crown, and hypocotyl in the various host plants (Hooda et al. 2017; Ajayi-Oyetunde and Bradley 2018; Singh et al. 2019; Haque and Parvin 2021).

The isolates of *R. solani* display high morphological and genetic variabilities as well as varying virulence potential with host preference and selection fitness mechanisms (Wei et al. 2014; Xia et al. 2017). Based on high heterogeneity, varying levels of aggressiveness and other useful traits that exist among members of the *R. solani* population, several tools such as culture morphology, pathogenicity analysis, biochemical and genetic markers, have been employed to classify them into a widely accepted AG system of classification (Kuninaga et al. 2000; Hooda et al. 2017; Yamamoto et al. 2019; Rashed et al. 2021). To date, 14 genetically distinct AGs (AGs 1–13 and AG-BI) have been recognized in *R. solani* (Carling et al. 2002; Ajayi-Oyetunde and Bradley 2018). Some groups within the AGs have been further segregated into subsets. Notably, the application of advanced molecular methods such as analyses of rDNA and internal transcribed spacer sequences offered a useful and convenient system for discriminating the diverse population of *R. solani* into AGs and subsets within each group (Budge et al. 2009; Hooda et al. 2017; Rashed et al. 2021). Fast expansion in genomic sequencing technology offers valuable resources to better understand the evolutionary relationship and genetic variability among *R. solani* species. AG1-1A, a subset of AG1, predominantly causes BLSB in maize and sheath blight in rice (Singh et al. 2018; Singh et al. 2019). However, some researchers have isolated AG1-1B, AG1-1C, and AG4 from a field infected with BLSB in southwest China (Li et al. 1998; Shi et al. 2021). This shows that BLSB causal isolates are highly heterogenous and genetically diverse, and this may have serious implications for their management if resistant maize varieties are not available. Depending on the isolate, genetic variability may confer contrasting virulence potentials or probable fungicide-resistance risks. Therefore, making it difficult to manage the disease effectively through fungicide applications or cultural practices alone if resistant maize varieties cannot be developed.

### 2.2. Distribution and economic impact of *R. solani*

Since the first report of *R. solani* in Sri Lanka, about a century ago (Bertus 1929), the outbreak of BLSB in maize fields in various agroecologies has been continuously reported across continents (Sharma et al. 2002; Hooda et al. 2017; Sagar and Bhusal 2019). It has become a menace in different nations of the world, particularly countries in Asia (Thailand, Bhutan, China, Korea, Indonesia, Japan, Nepal, India, Myanmar, Bangladesh, Laos, Taiwan, Vietnam, Pakistan, Philippines, and Malaysia); Africa (Nigeria, Sierra Leone, South Africa, and Ivory Coast); Latin America (Venezuela, Brazil, Argentina, and Mexico); United States of America (Nebraska, Arkansas, and the central north United States); England in Europe and Australia (Sharma et al. 2002; Hooda et al. 2017; Ajayi-Oyetunde and Bradley 2018; Budiarti et al. 2020; Singh et al. 2020).

Grain yield losses of 42% and above have been reported due to the incidence of BLSB in maize (Summer 1989). The severe incidence of BLSB could result in a complete loss of grain yield, if the infected maize field is not managed and, consequently, may become a threat to life if food shortage occurs (Sharma et al. 2002; Chaudhary et al. 2016; Hooda et al. 2017). The severity level of BLSB in the maize field could be as high as 90% (Pascual et al. 2000), and a direct relationship between the severity of BLSB and the loss of grain yield has been reported (Sharma et al. 2002; Sagar and Bhusal 2019).

### 2.3. Infection process and symptoms of BLSB in maize

Primarily, the development of BLSB in maize is greatly favored by high humidity (80–100%), warm temperature
(27–37°C and 30°C as optimal level), and higher application of nitrogenous fertilizer (Ahuja and Payak 1982). Infection can occur in the sheath, leaves, and stalk and can advance to the ear (Ahuja and Payak 1982; The CIMMYT Maize Program. 2004). Seedlings of about 30–50 days are more vulnerable to the pathogen, particularly, when the inoculum is present in the soil and ecological conditions are favorable (Ahuja and Payak 1982). Sclerotia in the soil or plant residues from previous cropping seasons are the initial sources of inoculum, but the subsequent spread of infection is by active inoculums which are already present on the tissues of infected plants. Active sclerotia which are buried deep in the soil are exposed to the soil surface during land preparation and germinate to infective hyphae, which come in contact with and infect maize seedlings’ drooping leaf blade and leaf sheath adjacent to the soil surface (Ahuja and Payak 1982; Sagar and Bhusal 2019).

Under favorable conditions, the fungal inoculum germinates, grows, and spreads rapidly within 12 h (Ahuja and Payak 1981, p. 1982). The infection progresses upward from the lower to upper sheaths and then to the leaves and becomes conspicuous in the basal part of the leaf lamina. Uneven globular to elongated lesions (1–3 mm in diameter) formed on the sheaths and leaf as water-soaked areas, and the affected parts appear bleached or chlorotic and blighted, turning into straw-colored necrotic patches (Figure 2). The blighted spots (1.5–2.5 cm) are interspersed with dark green to brown bands (1–2 cm wide), and the lesions spread rapidly in the leaf areas resulting in a characteristic symptom of banded blight (Ahuja and Payak 1981, 1982).

Lesions or spots are also formed on the rind of the stalk beneath the infected sheaths and may extend to the internodes. The lesions then coalesce and appear as dark-brown to black and sometimes turn into canker. At the advanced stage of infection, symptoms progress to the ear and all aerial parts except the tassel, resulting in severe loss of grain yield and quality (Ahuja and Payak 1981, 1982; The CIMMYT Maize Program. 2004). The sclerotia in the plant debris after harvest persist in the soil and serve as primary inoculum for the subsequent cropping season.

### 2.4. Molecular basis of pathogenicity

Infective hyphae that grow from *R. solani* inoculum or sclerotia extend and attach to the layer intersecting the epidermal cell walls of tissues of compatible host to initiate pathogenic relationship (Dodman and Flentje 1970; Keijer 1996). The growing hyphae aggregate and develop into infection structures (lobate appressoria or dome-shaped infection cushions) and penetrate the cuticle via the stomata or wound to colonize the cellular hub of the host plant (Dodman and Flentje 1970; Keijer 1996; Weinhold and Sinclair 1996). The formation of infection structures is induced by topographic or surface plant signals, such as epicuticular waxes, plant chemical signals, and stomata pores perceived by the fungal pathogen (Lo Presti et al. 2015). Hyphae growing within host epidermal cells result in necrotic cell death incited by spontaneously secreted toxins such as phenylacetic acid, *m*-hydroxyphenylacetic acid, *p*-hydroxyphenylacetic acid, β-furonic acid, among others, and cell wall degrading enzymes including polygalacturonase, polymethyl-galacturonase, cellulases, β-glucosidase, pectin methyl-galacturonic acid trans-eliminase, and polygalacturonic acid trans-eliminase (Aoki et al. 1963; Bateman 1970; Weinhold and Sinclair 1996; Chen et al. 2006; Xue et al. 2018).

The publicly available genome sequences for *R. solani* AG1-1A and AG1-1B (Wibberg et al. 2013; Chen et al. 2016), and maize (Schnable et al. 2009), offer invaluable resources to determine key factors that underline the molecular mechanisms of BLSB infection. Recent genomic and transcriptomic studies revealed a wide range of pathogenicity-associated genes, secreted and effector proteins, proteins associated with the synthesis of primary and secondary metabolites, redox-associated proteins, transporter proteins, CAZymes, protein degradation-related genes, and miRNAs associated with virulence as important virulence factors recruited by *R. solani* AG1-1A for penetration and colonization of maize tissues and successful establishment of BLSB infection (Anderson et al. 2016; Anderson et al. 2017; Xia et al. 2017; Ghosh et al. 2018; Hu et al. 2018; Li et al. 2019; Shamim et al. 2020; Meng et al. 2021). These reports suggest that *R. solani* AG1-1A employs various active biomolecules to penetrate and colonize the host’s cellular hub for suppressing host resistance.

Several putative CAZymes that mediate chitin, lignin, celluloses, and hemicelluloses (cell-wall components) were reported to be absolutely necessary for penetration and proliferation of hyphae and the successful development of BLSB infection in maize (Xia et al. 2017; Li et al. 2019). Furthermore, ATP-binding cassette transporters have been shown to be responsible for the efflux of secreted toxins into the maize cellular environment (Xia et al. 2017). A recent study shows that maize leaf sheaths are more susceptible than leaves and stalks to phytotoxins secreted by *R. solani* AG1-1A (Hu et al. 2018).

To subvert host plant surveillance and defense systems, fungal pathogens, including *R. solani*, deploy a repertoire of effector proteins to promote host colonization and susceptibility (Lo Presti et al. 2015). Vast number of potential effector proteins including peroxidase, peptidases 24-like domain-containing protein, HSP70 domain-containing protein, hypoxia induced-protein conserved region domain-containing protein, histone deacetylase inhibitor, polygalacturonase, oxalate, peptidase inhibitor 19 domain, inter alia, have all been identified to play key roles in pathologic processes by *R. solani* isolates (Zheng et al. 2013; Xia et al. 2017; Ghosh et al. 2018; Ghosh et al. 2019). The amount of secreted effector protein is directly linked to the virulence level of *R. solani* isolates (Xia et al. 2017). Polygalacturonases have been shown to play important role in *R. solani* AG1-1A pathogenesis by inducing necrosis in host tissues once the infection is established (Chen et al. 2018; Rao et al. 2019). Specialized isolates of *R. solani* employ α-1, 3-glucan to conceal PAMP recognition by pattern recognition receptors to invade host tissue and promote infection (Fujikawa et al. 2012).

Fungal reproduction and activation of effectors and virulence molecules were putatively reported to be mediated through signaling by G proteins and other proteins associated with mitogen-activated protein kinase cascades (Charnosopharat et al. 2008; Xia et al. 2017). It is important to clarify here that the signal transduction mechanism during infection of *R. solani* AG1-1A is not yet exemplified. Therefore, more studies are required to characterize major key...
players that are involved in the molecular signaling of pathogenesis in *R. solani* AG1-1A.

### 3. Progress in genetic control, transcriptome changes, and the molecular basis of resistance to BLSB in maize

#### 3.1. Genetic control and breeding for resistance to BLSB in maize

In resistance breeding, evaluation of germplasm resistance levels, analysis of the genetic basis of resistance, and identification of resistance sources or genes/quantitative trait loci (QTL) are critical for the development of resistant varieties (Kumar and Singh 2004; Yang et al. 2005; Narayanasamy 2008). Studies on screening of maize germplasm for resistance to BLSB revealed a low level of resistance diversity among maize inbred lines or accessions (Kumar and Singh 2004; Chen et al. 2013; Asif and Mall 2017; Sagar et al. 2019; Meena et al. 2021). In southwest China, maize researchers evaluated 282 inbred lines under artificial inoculation of *R. solani* and found that approximately 99% of the germplasm screened were susceptible, with only four lines (1%) showing a low level of resistance to BLSB (Chen et al. 2013). Notably, Chen et al. (2013) clearly showed that the elite inbred lines such as B73, B104, B84, EV1428, and Mo17, which are commonly used as parents in commercial hybrids were all susceptible to BLSB. Similar levels of maize resistance to BLSB have also been reported in other countries in Asia, including India, Korea, and Nepal (Kumar and Singh 2004; Tagele et al. 2018; Sagar et al. 2019; Meena et al. 2021).

The low level of resistance to BLSB or the lack of a complete resistant donor among maize germplasm is a major impediment to the conventional breeding of BLSB-resistant cultivars. The problem of maize susceptibility to BLSB is not limited to Asia, but extends to other continents, although the level of sensitivity varies by region. A recent study on the phenotypic analysis of the natural maize population consisting of 318 inbred lines of diverse genetic backgrounds revealed that genotypes of tropical/subtropical (subpopulation) origin showed a relatively higher resistance level to BLSB compared to the inbred line of subpopulations of temperate or mixed origin (Li et al. 2019). There are currently no maize varieties with high resistance to BLSB; however, germplasms that exhibit low resistance including CML270, CML323, EV1417, PFSR18, R18, Qi318, PA31, MH117, Shen3336, and KH-94 have been reported in several articles (Yang et al. 2005; Chen et al. 2013; Asif and Mall 2017; Madhavi et al. 2018; Sagar et al. 2019; Meena et al. 2021).

Evidence from genetic studies revealed both qualitative and quantitative inheritance of BLSB resistance (Kumar and Singh 2004; Izhar and Chakraborty 2013), and that additive form of gene action was preponderant over the dominance gene action for modulation of BLSB resistance in maize (Izhar and Chakraborty 2013). Although quantitative resistance is more durable, it is difficult to assay (Yang et al. 2017). However, identification of BLSB-resistant genes or QTLs can facilitate rapid improvement of elite maize varieties (Yang et al. 2005; Zhao et al. 2006). Yang et al. (2005) performed QTL mapping with 125 SSR markers using BC1: 2 population comprising 322 lines generated from (CML270 × 478) × CML270 and identified 12 QTLs linked to resistance to BLSB. In subsequent studies (Zhao et al. 2006; Garg et al. 2010; Lin et al. 2013), which involved mapping of F2 populations with SSR linkage markers, more than 50 QTLs were identified to be associated with BLSB resistance in maize. Most of these mapped QTLs are documented in Hooda et al. (2017), and they may be exploited in marker-assisted selection (MAS) breeding for the development of BLSB-resistant maize. Unfortunately, little or no progress has been made in the exploitation of these QTLs for the improvement of maize germplasms through MAS. One reason for such drawback could be related to the reliability of these QTLs, as most of the identified QTLs were undetected across multi-environments (Yang et al. 2005; Zhao et al. 2006; Lin et al. 2013).

#### 3.2. Maize transcriptome changes and molecular mechanisms of resistance during the BLSB infection process

Wide-scale genomic studies reveal complex changes in the transcriptome in maize; showing enrichment of several core genes associated with transcription, pathogenesis-related responses, cell wall-related proteins, signal transduction, metabolic and oxidative stress pathways, due to the challenge of *R. solani* (Zhang et al. 2012; Gao et al. 2014; Cao et al. 2021). A recent bioinformatic study identifies 56 putative maize target genes, including TFs that are targeted by 16 VA-miRNAs from *R. solani* (Meng et al. 2021). Most of the *R. solani* VA-miRNAs target maize genes that are strongly linked with plant immunity (Meng et al. 2021). Moreover, the stress induced by *R. solani* in maize causes significant changes in the expressions of certain novel miRNAs, which target TFs and proteins associated.

![Figure 2. Symptoms of banded leaf and sheath blight disease incited by *R. solani* in maize.](image-url)
with metabolic pathways and oxidative stresses (Gao et al. 2015; Luo et al. 2015). Target genes and their related miRNAs are found to reveal an inverse association, indicating negative transcriptional or posttranscriptional regulations of target genes by miRNAs (Gao et al. 2015; Luo et al. 2015).

In a recent study by Meng et al. (2021), a protein member of the Kelch motif family (GRMZM2G412674) targeted by a VA-miRNA (Rhi-miR9829-5p) of *R. solanii* functions as a positive regulator of resistance to BLSB in maize mutants. In another study, an F-box-like protein, ZmFBL41 (GRMZM2G109140), is found to act as a negative regulator of maize resistance to *BLSB* in maize mutants. The interaction of ZmFBL41 with the ZmCAD protein results in the breakdown of the enzyme [cinnamyl alcohol dehydrogenase (CAD)] (Li et al. 2019). The interaction of ZmFBL41 with ZmCAD results in a substantial decrease in cell wall-lignin content, and BLSB resistance (Li et al. 2019), indicating that ZmCAD functions as a negative regulator of maize resistance to *R. solanii* by targeting a lignin metabolic-associated enzyme.

In recent transcriptome studies, binding sites for several TF families such as TCP, bZIP, NAC, bHLH, WRKY, MYB, AP2/EREBP, HSF, and ZF are identified to be enriched in the promoter regions of differentially expressed maize genes during infection by *R. solanii* (Cao et al. 2021; Meng et al. 2021). Understanding the molecular regulation of the expression of these pathogenesis-related genes in maize, which are inducible by virulence factors derived from *R. solanii*, will benefit the improvement of maize resistance against *R. solanii*. However, more studies are required to elucidate the transcriptional control or regulation of expressions of these genes by TFs during attack by *R. solanii*.

Some specific TFs have been identified to be inducible or targeted by virulence factors of *R. solanii*. Molecular phylogenetic analysis reveals two maize WRKY genes (ZmWRKY4: GRMZM2G083717; ZmWRKY39: GRMZM2G148561) with a putative function in *R. solanii* sensitivity (Gao et al. 2014). Interestingly, more than 30 TFs belonging to TCP, MAD, WRKY, bHLH, bZIP, AP2/EREBP, MYB, NAC, inter alia (Table 1), have been putatively identified in two independent transcriptome studies as core genes considerably inducible by virulence factors of *R. solanii* (Cao et al. 2021; Meng et al. 2021). Hence, TFs are critical in the resistance of maize to BLSB. However, no studies have experimentally characterized the roles of these TFs in the response of maize to *R. solanii*. Hence, future studies should be geared towards characterizing and utilizing these major immune regulators in maize for the development of resistant varieties.

### 4. Role of transcription factors in plant immune system

Upon recognition of phyto-pathogen, plants rapidly reprogram their transcriptome for rapid immune responses, and TFs play a major role in the transcriptional regulation of the expression of DRGs (Birkenbihl et al. 2017). Plants have developed complex biochemical and molecular surveillance systems, which are integrated by different components, and are highly regulated by TFs in a dynamic and temporal manner within plants’ cellular hub (Mengiste 2012; Birkenbihl et al. 2017; Miller et al. 2017; Bacete et al. 2018). Upstream of TFs are major intracellular signaling transducers, which promptly transmit PAMP or pathogen-derived effector signals to TFs for defense activation (Figure 1).

In general, two immune systems including PAMP-triggered-immunity (PTI) and effector-triggered-immunity (ETI) are activated to constrain pathogenic proliferation and infection progress in plant. The PTI is the first-level of immunity but can easily be suppressed or compromised by intracellular effector-proteins or toxins produced by specialized pathogens (Jones and Dangl 2006; Mengiste 2012; Miller et al. 2017; Thulasi Devendrakumar et al. 2018). Unlike PTI, ETI leads to hypersensitivity with greater and superior immune responses. Nonetheless, ETI shares several components with PTI, and complex interactions exist between the two immune responses via signaling pathways (Jones and Dangl 2006; Dangl et al. 2013; Weßling et al. 2014; Gao et al. 2014).

### Table 1. List of TFs inducible in maize transcriptome studies following infection by *R. solanii*.

| S/N | Gene ID       | Transcription factor | References         |
|-----|---------------|----------------------|--------------------|
| 1   | GRMZM2G353548 | ZmTCP18              | Meng et al. (2021) |
| 2   | GRMZM2G089290 | ZmNAC0               | Meng et al. (2021) |
| 3   | GRMZM2G058451 | ZmbHLH164            |                    |
| 4   | GRMZM5G887276 | ZmGLK48              |                    |
| 5   | AC207043_F.G002 | ZmVQ29              | Cao et al. (2021)  |
| 6   | AC23853.1_F.G002 | ZmbZIP17            |                    |
| 7   | AC23416.1_F.G004 | ZmGRAS42            |                    |
| 8   | AC198725.4_F.G004 | ZmOPF19            |                    |
| 9   | GRMZM2G080834 | ZmEREB114            |                    |
| 10  | GRMZM2G333356 | ZmbHLH130            |                    |
| 11  | GRMZM2G132550 | ZmNAC0               | Meng et al. (2021) |
| 12  | GRMZM2G176141 | ZmNAC40              | Meng et al. (2021) |
| 13  | GRMZM2G176173 | ZmOrphan319          |                    |
| 14  | GRMZM2G417164 | ZmbHLH82             |                    |
| 15  | GRMZM2G154533 | ZmWRKY119            |                    |
| 16  | GRMZM2G172658 | ZmMYB26              |                    |
| 17  | GRMZM2G15256 | ZmMYB40              |                    |
| 18  | GRMZM2G73427 | ZmbZIP11             |                    |
| 19  | GRMZM2G105348 | ZmHSF18              |                    |
| 20  | GRMZM2G125653 | ZmWRKY40             |                    |
| 21  | GRMZM2G169966 | ZmWRKY57             |                    |
| 22  | GRMZM2G421256 | ZmWRKY80             |                    |
| 23  | GRMZM2G439903 | ZmNAC41              |                    |
| 24  | GRMZM2G89470 | ZmTCP3               |                    |
| 25  | GRMZM2G901003 | ZmbHLH13             |                    |
| 26  | GRMZM2G802901 | ZmbHLH27             |                    |
| 27  | GRMZM2G117497 | ZmMYB847             |                    |
| 28  | GRMZM2G37510 | ZmMADS34             |                    |
| 29  | GRMZM2G159547 | ZmMYB48              |                    |
| 30  | GRMZM2G390050 | ZmbHLH13             |                    |
| 31  | GRMZM2G015251 | ZmWRKY100            |                    |
| 32  | GRMZM2G417229 | ZmZF-HD12            |                    |
| 33  | GRMZM2G17089 | ZmMJJ22              |                    |
| 34  | GRMZM2G083717 | ZmWRKY4              | Gao et al. (2014)  |
| 35  | GRMZM2G148561 | ZmWRKY39             |
Thulasi Devendrakumar et al. 2018). The integration of efficient defense signaling and its transmission to relevant immune outlets are highly regulated by multiple TFs (Dangl et al. 2013; Zhang et al. 2020).

Rapid activation of the expression of DRGs is essential for the molecular activation of plant defense systems (PTI and ETI) upon attack of the plant by pathogens. The product of a rapid and tremendous transcriptional output response in an appropriately timed manner is a significant event of both ETI and PTI signaling (Buscaill and Rivas 2014; Miller et al. 2017). Once immune signals are perceived, TFs rapidly translate the signals to appropriate immune responses by activating or repressing the expression of downstream DRGs. Generally, immune responses are triggered by up- or down-regulation of downstream DRGs by binding of TFs to the cis-elements in the promoter regions of DRGs, leading to immune activation or suppression (Garner et al. 2016; Birkenbihl et al. 2017). Thus, plant TFs act as functional nodes for regulating and mounting the different plant defense pathways, and therefore, may be targeted for EDR in plant. Targeting TFs for EDR may offer the advantage of resistance to multiple diseases against several fungal pathogens (Chattopadhyay et al. 2019). For example, overexpression of wheat TF, TaWRKY45, confers enhanced resistance to multiple fungal pathogens including Fusarium graminearum, Puccinia triticina, and Blumeria graminis (Bahmani et al. 2011).

Adapting and mounting efficient immune responses to pathogenic attacks by plants results in a large-scale transcriptional reprogramming of a massive set of gene expressions in a temporal and dynamic manner. While maintaining the trade-off for growth, various types of TFs cooperatively function to reprogram plant transcriptome for survival during the infection process (Buscaill and Rivas 2014; Tsuda and Somsich 2015; Birkenbihl et al. 2017; Ng et al. 2018; Peng et al. 2018). Plant TFs can act alone or with other regulatory proteins to reprogram the transcriptome of plant cells in favor of immunity to survival (Buscaill and Rivas 2014; Birkenbihl et al. 2017; Miller et al. 2017; Chattopadhyay et al. 2019).

Several numbers of TFs belonging to the families of WRKY, NAC, AP2/ERF, inter alia, have been characterized as activators or repressors of plant immunity (Seo et al. 2015; Garner et al. 2016). Recent studies in maize reveal that overexpression of ZmWRKY65 and ZmERF105 positively activate resistance to Botrytis cinera (Huo et al. 2021) and Exserohilum turcicum (Zang et al. 2020), respectively. In rice, the OsWRKY53 (Peng et al. 2020) and the OsWRKY4-OsWRKY80 module (Peng et al. 2016) are found, respectively, as negative and positive regulators of sheath blight caused by R. solani. Moreover, constitutive expression of OsWRKY30 promotes the expression of resistance genes and immunity against fungal pathogens in rice (Peng et al. 2012). Additionally, TaNAC30 has been reported to act as a negative regulator of wheat resistance against the stripe rust pathogen (Puccinia striiformis) (Wang et al. 2018). In another study, ZmNAC41 and ZmNAC100 are reported to be directly linked with maize sensitivity to Coleotrichum graminicola (Voitsik et al. 2013). In rice, OsNAC4 is reported to be directly involved in disease resistance and hypersensitive responses (Kaneda et al. 2009). The significant roles of plant TFs in plant immunity have been extensively covered in several reviews (Seo et al. 2015; Garner et al. 2016; Erpen et al. 2018; Yuan et al. 2019) and will not be reviewed here in great detail.

5. Prospect to improve resistance to BLSB in maize through manipulation of transcription factors

5.1. Functional characterization of specific TFs that respond to Rhizoctonia solani invasion

One of the counter-defense strategies employ by adapted pathogens is to manipulate host immune responses, by producing virulence factors that target and promote the expression of host transcriptional repressors, which activate the expressions of downstream susceptible genes leading to attenuation of host resistance (Weßling et al. 2014; Seo et al. 2015; Birkenbihl et al. 2017). Functional studies to investigate the roles of defense-related TFs, which have been putatively identified from previous transcriptome analyses of maize response to infection by R. solani (Gao et al. 2014; Cao et al. 2021; Meng et al. 2021), will offer invaluable resources for the improvement of BLSB resistance. Such studies will reveal which of the candidate TFs function as activator or repressor of maize defense against BLSB, and provide useful information on the molecular and transcriptional regulatory mechanisms that underscore maize sensitivity to R. solani during its coevolution. Moreover, important downstream genes that are regulated by these TFs can be identified. Identification of downstream defense-related genes targeted by TFs will further provide valuable information on the transcriptional regulatory networks of the maize defense pathway against R. solani and other fungal pathogens.

An effective strategy to investigate the functions of TFs is through their manipulation, as their modification often induces phenotypic changes in plants (Mitsuda and Ohme-Takagi 2009; Viola and Gonzalez 2016; Birkenbihl et al. 2017). A direct method to explore the regulatory role of functional TFs is through their inactivation or mutation in a normal plant by a mutational approach, to create a loss-of-function phenotype or mutant plant that lacks the encoding gene or expresses an altered version of the TF (Figure 3) (Alberts et al. 2002). This conveniently disabled the function of the TF in the mutant, which can be investigated by studying the mutant plant. Mutational tools such as RNAi, T-DNA insertion, and site-directed nucleases such as the CRISPR/Cas9 system, transcription activator-like effector nucleases (TALEN), and zinc finger nucleases (ZFN) have been successfully used to study gene functions in model crops including maize, rice, wheat, grape, tomato and Arabidopsis (Bouchez and Höfte 1998; Kodama and Komamine 2011; Wang et al. 2013; Gentzel et al. 2020).

Alternatively, candidate TF can be expressed in a considerably higher amount than normal using the plant transformation system. This can be achieved by fusing the TF coding sequence with a powerful promoter and inserting it into a multicopy vector, and then integrating the construct into the normal plant genome by biolistic or Agrobacterium-mediated transformation methods (Alberts et al. 2002; Viola and Gonzalez 2016). Such overexpression produces a unique phenotype with novel gain-of-function activity (Figure 3) (Alberts et al. 2002). The gain-of-function assay is, particularly, useful for genes that are important for plant growth and development (Tan et al. 2020). For example, independent overexpression of OsWRKY4 and OsWRKY30 in transgenic lines uncovered the functional
role of each TF in rice resistance to sheath blight incited by *R. solani* (Peng et al. 2012; Wang et al. 2015).

Furthermore, most TFs form functional interactions with other proteins, and such interactions may play crucial roles in the activation and repression of immune responses in plants (Alves et al. 2014). Therefore, functional analysis of proteins that are complex with defense-related TFs will be of valuable significance in characterizing transcriptional regulatory networks that modulate maize defense signaling pathways. Notably, the TF-protein interactions can be predicted via relevant bioinformatic tools (Mitsuda and Ohme-Takagi 2009; Ding and Kihara 2019; Dong et al. 2019), and the prediction can be validated by protein interaction assays such as bimolecular fluorescence complementation (BiFC) or yeast-two hybrid (Y2H). Moreover, coexpression network analysis can be used to identify novel proteins that functionally relate to and/or putatively interact with TFs of interest.

In this current review, we have compiled a complete list of several maize TFs (Table 2), which have been putatively identified as core genes inducible by *R. solani* virulence factors after BLSB infection from different studies (Gao et al. 2018).

**Table 2.** Application of CRISPR technology for the improvement of fungal disease resistance in different crops.

| Disease       | Pathogen name            | Plant species       | Target gene | System          | Transgene-free | Outcome                                  | References             |
|---------------|---------------------------|---------------------|-------------|-----------------|----------------|------------------------------------------|------------------------|
| Rice blast    | *Magnaporthe oryza*      | Rice (*Oryza sativa*) | Pi21/cds region | CRISPR/Cas9     | Yes            | Improved resistance to disease           | Nawaz et al. (2020)    |
| Rice blast    | *Magnaporthe oryza*      | Rice (*Oryza sativa*) | OsERF922/cds region | CRISPR/Cas9     | Yes            | Improved resistance to disease           | Wang et al. (2016)     |
| Northern leaf | *Exserohilum turcicum*   | Maize (*Zea mays*)  | ZnNL818 (WAK) | CRISPR/Cas9     | Yes            | Improved resistance to disease           | Schmidt (2017)         |
| Powder mildew | *Blumeria graminis* f. sp. tritici | Wheat (*Triticum aestivum*) | TaMLO/cds region | CRISPR/Cas9 &TALEN | Yes            | Improved resistance to disease           | Wang et al. (2014)     |
| Powder mildew | *Blumeria graminis* f. sp. tritici | Wheat (*Triticum aestivum*) | TaEDR1/cds region | CRISPR/Cas9     | No             | Improved resistance to disease           | Zhang et al. (2017)    |
| Gray mold     | *Botrytis cinera*        | Tomato (*Solanum lycopersicum*) | SlMAPK3/cds region | CRISPR/Cas9     | No             | Improved resistance to disease           | Yu et al. (2019)       |
| Powder mildew | *Oidium neolycopersici*  | Tomato (*Solanum lycopersicum*) | SiMo1/cds region | CRISPR/Cas9     | Yes            | Improved resistance to disease           | Nekrasov et al. (2017) |
| Powder mildew | *Oidium neolycopersici*  | Tomato (*Solanum lycopersicum*) | SiPMR4/cds region | CRISPR/Cas9     | No             | Improved resistance to disease           | Santillán Martínez et al. (2020) |
| Gray mold     | *Botrytis cinera*        | Grape (*Vitis vinifera*) | VvWRKY52/cds region | CRISPR/Cas9     | No             | Improved resistance to disease           | Wang et al. (2018)     |
The information provided in this report will serve as valuable resources for maize researchers, and research efforts to better understand how these core TFs function in maize reaction to infection by *R. solani* will be doubled. Such research efforts will benefit the development of BLSB-resistant maize.

### 5.2. Manipulation of TFs through genome editing for improved resistance to BLSB in maize

To promote desirable resistance levels in the host, the immune-suppressive action of adapted-pathogen within the host cellular hub must be interrupted. This can be achieved by precisely targeting and interfering with host immune transcriptional repressors' activities using advanced technology. Such high-precision modification of host plant that will adapt TFs functionality to the desired host resistance level can be achieved via the application of GE tools.

Genome-editing tools such as TALENs, ZFNs, and CRISPR–Cas system can be used for site-specific and predictable modification of plant genome for EDR (Borrelli et al. 2018; Zaidi et al. 2018; Yin and Qiu 2019; Ahmad et al. 2020; Gao 2021). Among these GE tools, the CRISPR–Cas system has attracted the greatest attention from researchers across the world and its application in plant GE has rapidly overtaken others due to its simplicity, low cost, high efficiency, ease of use, use in the production of transgene-free mutants, and multiplex compatibility (simultaneous editing of multiple target sites) (Ma et al. 2015; Malzahn et al. 2017; Yin et al. 2017).

The multiplex advantage of the CRISPR–Cas system makes this tool more suitable for the mutation of TF-encoding genes because TFs usually function in a complex network. Moreover, some members of TF family genes may have overlapping functions due to their similar structures. Therefore, mutation in a single TF gene may not be sufficient to repress phenotypic expression. Multiplex editing using the CRISPR–Cas system can be used effectively to mutate all target alleles of TF-encoding genes at once to produce a phenotype (Ma et al. 2015; Wilson et al. 2019; Zhang et al. 2019; Ahmad et al. 2020; Gao 2021). For more details on the application and procedures of CRISPR–Cas systems, the readers are referred to the following recent reviews (Ma et al. 2015; Malzahn et al. 2017; Chen et al. 2019; Zhang et al. 2019; Schenke and Cai 2020; Zhu et al. 2020; Gao 2021).

Another strategy is to modify the interacting or binding sites of *R. solani*-derived effectors at the promoter region of the DNA sequence of the potential host TF(s). This can be achieved by introducing specific bases or mutations of choice at the position of the effector's binding sites to avert host manipulation by the pathogen (Schenke and Cai 2020; Gao 2021). Such genome rewriting can be used to alter or interrupt the specificity or compatibility of host TFs with pathogen-derived effectors. Recently, a group of researchers applied a multiplex CRISPR–Cas system to disrupt the binding sites of *Xanthomonas oryzae*-derived effectors on the promoters of three rice genes: OsSWEET11, OsSWEET13 and OsSWEET14, and obtained mutants with improved broad-spectrum resistance to bacterial blight (Oliva et al. 2019). This approach is preferable if the TF(s) play an important role in plant growth and development or participate in resistance to other phytopathogens. Thus, the strategy eliminates the tradeoff risks associated with the inactivation of the TF(s).

In general, plant resources are diverted from growth to defense following pathogenic attacks due to transcriptional reprogramming of plant transcriptome to ensure plant survival. Such changes in plant transcriptome result in the down-regulation of genes involved in growth and photosynthesis, fine adjustment in normal plant metabolic flux, build-up of secreted proteins associated with plant defense, and nitrogen and carbon prioritization in the direction of biosynthesis of defense-related compounds (He et al. 2022). Although defense mechanisms are important for plant survival, their activation often creates a significant demand for resources and generally leads to active suppression of plant growth and development, a phenomenon that is generally known as growth-defense tradeoffs (Huot et al. 2014; He et al. 2022). The tradeoff also applies in the contrasting way, with active growth and development suppressing defense mechanisms (van Betselaar and Van den Ackerveken 2020; He et al. 2022). Plants with rapid growth tend to be more susceptible to phytopathogens during infection, possibly because growth takes precedence over defense (He et al. 2022). Thus, the stimulation of resistance in crops via inactivation or knockout of susceptible factors or genes often compromises growth, leading to reduced growth and development (Schenke and Cai 2020; van Betselaar and Van den Ackerveken 2020). Growing and defending can negatively be correlated as plant defense is closely intertwined with pathways that govern growth and development, so mutations in genes that are central to defense networks often have multiple pleiotropic effects (Huot et al. 2014; Karasov et al. 2017; He et al. 2022). For example, enhanced JA defense signaling and stunted growth phenotypes are observed in *Arabidopsis jaz* polymutants with multiple mutations in JAZ transcriptional repressor genes (He et al. 2022). Therefore, an alternative resistance type attainable via editing of pathogen binding sites in the crop genome that results in a balance of resistance with growth and yield is necessary and appreciable (Schenke and Cai 2020).

### 5.3. Using synthetic TFs to improve maize resistance to BLSB infection

Plant responses to infection by phytopathogens are modified by transcriptional adjustments of defense-related genes
during disease development (Birkenbihl and Somssich 2011; Birkenbihl et al. 2017). It would be much easier to improve resistance traits to phytopathogens if crop endogenous defense-related genes could be controlled and selectively activated or inhibited at the transcriptional level by incorporating novel TFs into the crop genome using an advanced biotechnological approach. Synthetic TF is an efficient biotechnological tool that provides an alternative method of targeting genome modifications in crops to improve resistance traits by specifically and selectively controlling the expression of downstream defense-associated genes in plants (Liu and Stewart 2016; Chattopadhyay et al. 2019; Soujanya 2019). By using synthetic TFs, resistance traits can be introduced into plants to enable them to process pathogen-derived factors from their environment and respond appropriately. The use of synthetic TFs offers incredibly higher expression strength and specificity than native TFs, allowing precise control of the expression of the gene of interest and reducing the tradeoff risks or metabolic burdens associated with inactivation or transgene overexpression of an endogenous TF (Liu and Stewart 2016).

Synthetic TFs are usually generated by combining tailored DNA binding domains (DBDs) with transcriptional activator or repressor domains (effectors) and nuclear localization signals to promote or inhibit the expression of a targeted gene(s) of interest (Liu et al. 2013; Liu and Stewart 2016; Soujanya 2019). Synthetic plant TFs for gene expression regulation have been created using engineered zinc finger proteins (ZFPs) and transcriptional activator-like effector (TALE) proteins fused with an activator or a repressor domain (Liu et al. 2013; Liu and Stewart 2016; Chattopadhyay et al. 2019; Soujanya 2019). ZFPs typically bind to DNA by forming a tandem array of 3–6 C2H2 fingers as monomers, each of which binds to a specific DNA binding site of 9–18 bp (Guan et al. 2002; Liu et al. 2013; Chattopadhyay et al. 2019). In contrast, the DBD of TALEs consists of tandem arrays of 30–42 (34 on average) amino acid repeats, each of which binds to every single nucleotide within the targeted DNA binding site (Boch and Bonas 2010; Liu et al. 2013; Chattopadhyay et al. 2019). Each amino acid repeat, apart from two hypervariable amino acids at the 12th and 13th positions named the repeat variable diresidues that are crucial for specific DNA binding of each repeat, is highly conserved (Boch and Bonas 2010). Compared to ZFPs, the design of synthetic TALEs might be simpler, as they do not require screening against expression libraries, which is necessary when designing synthetic ZFPs (Liu et al. 2013).

Synthetic ZF-TFs and TALE-TFs have been engineered by integrating customized DBDs into the activator domain such as VP16 and VP64, which facilitates the recruitment of multiple components, including histone acetyltransferases, TFIID, and TFIH, to the promoter region for the formation of a preinitiation complex (Triezenberg et al. 1988; Stringer et al. 1990; Xiao et al. 1994; Tumbar et al. 1999; Hirai et al. 2010), or a repressor domain such as EAR, SRDX, KRAB, and SID, which recruit chromatin remodeling factors to suppress gene expression (Hiratsu et al. 2003; Mahfouz et al. 2012; Liu et al. 2013; Liu and Stewart 2016; Chattopadhyay et al. 2019). Generally, the DNA binding specificity of synthetic transcriptional activators or repressors can be tailored to target specific promoter elements to regulate the expression of desirable endogenous genes or transgenes in plant genomes (Li et al. 2013; Liu et al. 2013; Petolino and Davies 2013; Kassaw et al. 2018; Chattopadhyay et al. 2019).

Since a wide array of genes associated with biosynthesis pathways of secondary metabolites such as phytoalexins and phytoanticipins (antimicrobials), cell wall strengthening molecules, and lignin are differentially induced in maize during BLSB infection by *R. solani* (Zhang et al. 2012; Li et al. 2019; Cao et al. 2021), engineering secondary metabolites of maize against *R. solani* can be facilitated through the development of domain-specific synthetic TFs, which can be used to target and regulate these defense-related genes in maize (Liu and Stewart 2016; Chattopadhyay et al. 2019). Several synthetic ZF-TFs and TALE-TFs have been developed and applied in *Arabidopsis thaliana, Brassica napus*, rice, maize, and tobacco for specific activation or suppression of transgenes and endogenous genes (Liu and Stewart 2016). ZF-TFs and TALE-TFs are evidently promising tools for improving agronomically desirable traits in crops by modulating endogenous gene expression in their native contexts. Using these synthetic TFs, it is possible to activate key regulatory proteins that are master switches for defense, metabolic, and various development pathways in crops (Gupta et al. 2012; Liu et al. 2013).

Alternatively, synthetic transcriptional activators and suppressors have been successfully developed using a deactivated/inactivated version of the Cas9 protein (the catalytic protein of a CRISPR–Cas9 system; dCas9) in recent years (Kassaw et al. 2018; Chattopadhyay et al. 2019; Soujanya 2019). As a result, dCas9 loses its ability to function as an endonuclease (that is, it no longer cuts DNA) but is still capable of binding to target DNA sites using programmable gRNA sequences (Kassaw et al. 2018). Therefore, the gRNA sequences determine the specificity of the binding of dCas9 to specific DNA sites to build a synthetic TF (dCas9-TF) by combining it with the effectors (activator or repressor domains, for example, VP64 or EAR) to modulate the targeted gene of interest (Kassaw et al. 2018; Chattopadhyay et al. 2019). Thus, dCas9-TFs can be developed for transcriptional activation or inactivation of specific defense-related gene promoters to modulate their activities for EDR traits in maize. Compared to synthetic ZF-TFs and TALE-TFs, transcriptional regulation mediated by CRISPR–Cas9 system (dCas9-TFs) has much more specificity and greater versatility since it relies on RNA–DNA interactions rather than DNA–protein interactions as in the case of ZF-TFs and TALE-TFs (Liu and Stewart 2016; Chattopadhyay et al. 2019). Therefore, by using gRNAs with sequence homology to the target DNA sites, dCas9-TF can be adapted to target any genomic DNA sequence in the plant genome for a desirable trait of interest (Liu and Stewart 2016). Furthermore, multiple genes can be simultaneously regulated by dCas9-based systems using multiple gRNAs in one module due to the multiplex advantage of the CRISPR–Cas9 system (Ma et al. 2015; Liu and Stewart 2016; Gao 2021). In tobacco and *Escherichia coli*, dCas9-TFs have been used to provide coordinated transcriptional activation and suppression of specific genes (Liu and Stewart 2016; Soujanya 2019). Therefore, synthetic TFs including dCas9-TFs, TALE-TFs, and ZF-TFs are novel tools that can be applied to manipulate the maize genome to improve resistance to *R. solani* and other major phytopathogens.
6. Conclusions

*Rhizoctonia solani* is destructive, difficult to manage, and potentially threatens maize productivity worldwide. Development and use of durable BLSB-resistant varieties will effectively safeguard maize productivity. Complex transcriptome changes occur in both maize and *R. solani* during their coevolution. *Rhizoctonia solani* employs vast arrays of virulence factors including active secreted and effector proteins, CAZymes, redox-associated proteins, transporters, as well as signaling and pathogenesis-related proteins, to suppress maize resistance during pathogenesis. Proteins associated with cell-wall metabolisms, DRGs and TFs, are the major targets in maize by *R. solani* virulence factors during their coevolution. The roles of TFs are central to the mounting, activation, and fine-tuning of appropriate defense responses by regulating the expressions of downstream DRGs during the infection process. Thus, TFs are the important targets and invaluable resources for GE technology and the development of resistant varieties. Several maize TFs belonging to families of WRKY, NAC, TCP, bHLH, MYB, MADs, bZIP, AP2/EREBP, inter alia, had been putatively identified to be targeted by *R. solani* virulence factors during infection. However, the transcriptional regulatory functions of these TFs in resistance of maize to BLSB have not yet been elucidated. Exhaustive studies are required to characterize the functions of these TFs in maize immunity against *R. solani* attack, as well as, in the utilization of these TFs in GE technology to modify and adapt their functions for enhanced BLSB resistance in maize. The advent of synthetic TFs offers a more robust opportunity and wider applications in the engineering of resistant varieties over the use of natural TFs. Therefore, the use of synthetic TFs such as dCas9-TFs, TALE-TFs, and ZF-TFs would be an effective alternative method to coordinatively and selectively controlling multiple endogenous defense-related genes for the enhancement of BLSB resistance and the engineering of improved maize varieties.

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