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Research review paper

Recent advances in genes involved in secondary metabolite synthesis, hyphal development, energy metabolism and pathogenicity in *Fusarium graminearum* (teleomorph *Gibberella zeae*)

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ABSTRACT

The ascomycete fungus, *Fusarium graminearum* (teleomorph *Gibberella zeae*), is the most common causal agent of *Fusarium* head blight (FHB), a devastating disease for cereal crops worldwide. *F. graminearum* produces ascospores (sexual spores) and conidia (asexual spores), which can serve as disease inocula of FHB. Meanwhile, *Fusarium*-infected grains are often contaminated with mycotoxins such as trichothecenes (TRIs), fumonisins, and zearalenones, among which TRIs are related to the pathogenicity of *F. graminearum*, and these toxins are hazardous to humans and livestock. In recent years, with the complete genome sequencing of *F. graminearum*, an increasing number of functional genes involved in the production of secondary metabolites, hyphal differentiation, sexual and asexual reproduction, virulence and pathogenicity have been identified from *F. graminearum*. In this review, the secondary metabolite synthesis, hyphal development and pathogenicity related genes in *F. graminearum* were thoroughly summarized, and the genes associated with secondary metabolites, sexual reproduction, energy metabolism, and pathogenicity were highlighted.

Contents

1. Introduction

Fusarium graminearum (teleomorph *Gibberella zeae*) is an ascomyceteous fungus that causes *Fusarium* head blight (FHB) in cereal crops, including wheat, barley, rice, and oats, as well as ear rot and stalk rot in maize (Fernando et al., 1997; Goswami and Kistler, 2004; Munkvold, 2003; Parry et al., 1995; Sutton, 1982). As a major global pathogen of cereals, the threat caused by this fungus is multifaceted. It leads not only to yield and quality losses but also contaminate grains by producing mycotoxins that are hazardous to livestock and humans (Glenn, 2007; Hussein and Brasel, 2001; Placinta et al., 1999). The losses can happen at two stages. In the first, research has shown that the

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Table 1
Gene involved in the secondary metabolites production in *F. graminearum*. AUR, aurofusarin; DON, deoxynivalenol; NRPS, nonribosomal peptide synthetase; PKS, polyketide synthase; TRI, trichothecene; WT, wild-type strain; ZEA, zearalenone; β-ZOL, β-zearalenonol; ROS, reactive oxygen species.

Genes	Proteins	Phenotype of mutants	Functions	References
Clm1	Longiborneol synthase	*Clm1* gene disruptants produced no culmorin but were able to convert exogenously added longiborneol to culmorin	Clm1 encodes a longiborneol synthase and is required for culmorin biosynthesis in *F. graminearum*	Gardiner et al. (2009a)
Fgl1	A secreted lipase	Δ*Fgl1* mutants showed reduced extracellular lipolytic activity and to reduced virulence to both wheat and maize, and it exhibited up-regulated DON production during wheat head infection and revealed a dramatically enhanced ZEA production on kernels	Fgl1 may be involved in hyphal growth during infection of the spikelet and activation and expression of other enzymes responsible for fast growth of fungal hyphae. Fgl1 may also involve in regulation of eight PKS genes and ZEA production	Voigt et al. (2005, 2007)
FgLaeA	Global regulator	Deletion of *FgLaeA* led to earlier induction of perithecia formation as well as drastically reduced disease symptoms in wheat. Overexpression of *FgLaeA* caused the increased production of TRIs and additional metabolites	FgLaeA may be a member of putative FgVeA complex and controls secondary metabolism, sexual development, and virulence	Kim et al. (2013)
Fgos1	Osmosensor histidine kinase	Δ*Fgos1* mutants produced a reduced amount of AUR. The transcript levels of *Pks12* and *Gip2* were reduced in the Δ*Fgos1* mutants	FgOs1 is a putative component of the osmotic stress signal transduction pathway. FgOs1 plays role in AUR biosynthesis and regulates Pks12 and Gip2	Ochiai et al. (2007)
Fgos4, *Fgos5* and *Fgos2*	MAPK kinase pathway	Mutants of *Fgos4*, *Fgos5*, and *Fgos2* showed markedly enhanced AUR production and failed to produce TRIs in aerial hyphae. Also, the transcript levels of *Pks12* and *Gip2* were enhanced. Expression of *Tri4* and *Tri6* were markedly reduced.	This osmoregulatory MAPK pathway regulates secondary metabolism associated with AUR and TRIs. It's very likely that this MAPK pathway affects AUR by regulating Pks12 and Gip2	Ochiai et al. (2007)
Fgp1	Wor1-like Protein	Deletion of the *Fgp1* results in greatly reduced pathogenicity and loss of TRI toxin accumulation in infected wheat plants and in vitro. Δ*fgp1* mutants show defects in asexual and sexual spore development	Fgp1 is essential for TRI production. It affects asexual and sexual reproduction. Fgp1 may also regulates expression of gene clusters and other genes encoding PKS or NRPS proteins	Jonkers et al. (2012)
FgVe1	Velvet	Disruption of *FgVe1* caused phenotypes include hyperbranching of the mycelium, suppression of aerial hyphae formation, reduced hydrophobicity of the mycelium and highly reduced sporulation	FgVe1 modulates the production of the AUR pigment and is essential for the expression of Tri genes and the production of TRIs. It is a positive regulator of virulence. It may also affect hyphal development and reproduction	Merhej et al. (2012)
FgVelB	Velvet	Δ*FgVelB* strains produced fewer aerial mycelia with less pigmentation;Production of TRI and ZEA was dramatically reduced compared with the WT strain. The Δ*FgVelB* strains were incapable of colonizing host plant tissues;The Δ*FgVelB* strains produced no fruiting bodies but retained male fertility under sexual development conditions	FgVelB regulates mycotoxin production, sexual reproduction and pathogenicity, probably by acting as a member of a possible velvet protein complex	Lee et al. (2012)
Gip1	A putative laccase	Δ*Gip1* mutants produced no AUR on PDA and showed yellowish color	Gip1 are required for AUR production in *F. graminearum*, and it is downstream of Pks12 in the AUR biosynthetic pathway	Y.T. Kim et al. (2005)
Gip2	A putative transcription factor	Δ*Gip2* mutants could not produce AUR on PDA. Overexpression of *Gip2* increases AUR production and reduces mycelial growth	Gip2 is required for AUR biosynthesis, and it was required for transcription of the genes in the AUR biosynthetic cluster	Kim et al. (2006)
GzGpa1	Gα subunit	Deletion of *GzGpa1* resulted in female sterility and enhanced DON and ZEA production	GzGpa1 is required for normal sexual reproduction and repression of toxin biosynthesis	Yu et al. (2008)
GzGpb1	Gβ subunit	Production of DON and ZEA was enhanced in the Δ*GzGpb1* mutants. Deletion of *GzGpb1* resulted in 75% of the hyphal growth and mutants were much less virulent than the WT	GzGpb1 negatively control mycotoxin production like *GzGpa1*. *GzGpb1* are essential for the virulence of *F. graminearum*	Yu et al. (2008)
Hep1	Heterochromatin protein	AUR genes are highly up-regulated and AUR production is greatly enhanced, while gene expression and metabolites are lower for the TRI cluster in the *Hep1* deleted strains	Hep1 has a repressive role on AUR gene cluster and a positive function for DON biosynthesis	Reyes-Dominguez et al. (2012)
Lh1 (*Tri1*)	P450 oxygenase	Δ*Lh1* mutants no longer produced 15-acetyl DON, but rather accumulated calonectrin and 3-deacetylcalonectrin	*Lh1* gene encodes a P450 responsible for oxygenation at one or both of these positions (C-7 and C-8) in the TRIs biosythesis pathway	McCormick et al. (2004)
Map1	MAPK	DON and 3-acetyl DON production were reduced in Δ*Map1* mutants. Δ*Map1* mutants lost pathogenicity, and also lost their ability to form perithecia in vitro	The Map1 signaling protein controls multiple events in disease establishment and propagation, including root colonization, wheat ear colonization, DON synthesis and perithecia formation	Urban et al. (2003)
Mgv1	MAP kinase	DON production and virulence were reduced in mutants. Mutants had weak cell walls and were hypersensitive to cell wall degrading enzymes. They were self-incompatible when tested for heterokaryon formation and were female-sterile	Mgv1 in *F. graminearum* is involved in multiple developmental processes related to sexual reproduction (essential for female fertility), plant infection, and cell wall integrity	Hou et al. (2002)
Nrps2	NRPS	Δ*Nrps2* mutants did not produce ferricrocin, which differed from the WT strain	Nrps2 is responsible for the biosynthesis of ferricrocin that is an intracellular siderophore	Tobiasen et al. (2007)
Nrps6	A putative NRPS	Deletion of *Nrps6* resulted in reduced virulence and hypersensitivity to H_2O_2 as well as increased sensitivity to iron depletion	Nrps6 may be responsible for the biosynthesis of siderophores, whose role is to supply an essential nutrient, iron, to the pathogenic fungi in planta	Oide et al. (2006)

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