FUNGAL BIOLOGY REVIEWS XXX (2017) 1–18

British Mycological Society promoting fungal science

journal homepage: www.elsevier.com/locate/fbr

Review

LOVe across kingdoms: Blue light perception vital for growth and development in plant–fungal interactions

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ARTICLE INFO

Article history:
Received 28 August 2017
Received in revised form
21 November 2017
Accepted 23 November 2017

Keywords:
Blue light
HIGS
Host-pathogen interaction
LOV domain
Photoreceptor
White Collar

ABSTRACT

Blue light plays an important role in the growth and development of fungi. Environmental cues enable plant pathogenic fungi to synchronise essential metabolic pathways to that of their hosts to gain a competitive advantage. Phylogenetic analysis of the LOV domain present in blue light receptors across all three kingdoms suggests that these receptors in fungal lineages have undergone convergent evolution to use the same domain for control and regulation of similar cellular and metabolic processes. In this review, the genetic basis of blue light photoperception in fungi, and the functions it regulates, will be discussed. Furthermore, the evolution of the light sensing domain and its role in pathogenesis is hypothesised concluding with how knowledge of conserved LOV domains may be exploited for fungal disease control in crop plants.

1. Circadian rhythms of fungal pathogens

The Earth's rotation on its axis creates daily fluctuations in temperature as well as in light. Living organisms have evolved in such a way to be able to adapt to these daily changes. Adaptations to light signals enables organisms to anticipate changes in their environment through biological clocks, which are responsible for creating a circadian rhythm in all the cells of the organism. The circadian clock allows the organism to entrain its biological clock to that of the external environmental time cues (Hunt *et al.*, 2010). In this way, organisms can ensure that certain developmental and behavioural

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https://doi.org/10.1016/j.fbr.2017.11.003
1749-4613/

Please cite this article in press as: Liversage, J., et al., LOVe across kingdoms: Blue light perception vital for growth and development in plant–fungal interactions, Fungal Biology Reviews (2017), https://doi.org/10.1016/j.fbr.2017.11.003

processes are executed at the optimal time of day to maximize survival advantage.

Circadian rhythms are under the control of positive and negative elements, which form the core of the physiological oscillator. These biological oscillators are controlled by positive elements that activate the transcription of the negative elements, which in turn suppress their own transcriptional activation (He et al., 2002). This forms a network, which activates downstream cellular events, and includes post-transcription and post-translational modifications, and the production and degradation of the circadian clock elements (Schafmeier et al., 2005). This review will focus on the role of blue light in circadian rhythms, characterised downstream functions regulated by blue light in fungi, and will address the evolutionary relationship of blue light perception between fungi and plants and how this possibly links to pathogenesis.

2. Blue light photoreception by fungi

A well described rhythm is one which is mediated by blue light (~410–520 nm) (Linden, 1997). Photoreceptors are proteins, which are able to harvest light and generate a signal that is then transported into the nucleus to activate the transcription of light-responsive genes. The co-factors for these photoreceptors are chromophores that are able to absorb the light and bind to the receptor thus activating the light dependent signalling pathway (Froehlich et al., 2005). This has been well studied in the bread mold *Neurospora crassa*, which is the model organism in eukaryotes used to study photoperiodism, and thus provides us with a basis to examine biological clocks in other fungi (Olmedo et al., 2013).

The main protein components activating the fungal circadian clock are the two GATA-type transcription factors: White Collar-1 (WC-1) and White Collar-2 (WC-2) (Ballario and Macino, 1997; Linden, 1997 and reviewed by Fuller et al., 2016). This was experimentally proven through mutation studies where an absence of either or both of the proteins in *N. crassa* resulted in the fungus unable to sense light (Linden and Macino, 1997). The White Collar proteins interact through their respective PAS domains to form a heterodimer known as the White Collar Complex (WCC), which acts as a transcription factor that drives the expression of light responsive genes, in particular the expression of the frequency gene (*frq*) (Froehlich et al., 2002; Malzahn et al., 2010). Accumulation of FRQ inhibits the function of WCC thus negatively regulating the circadian clock (Denault et al., 2001). Blue light is thus perceived by WC-1, which requires WC-2 in order to activate light responsive genes including FRQ, which regulates the circadian rhythm (Fig. 1).

The WC-1 protein contains three PAS (**P**er-**A**rnt-**S**im) domains, named after the three proteins in which these elements were originally discovered, viz. the period circadian protein, aryl hydrocarbon receptor nuclear translocator protein and the single-minded protein (Ballario et al., 1996). WC-1 is the first fungal photoreceptor to be cloned and characterised (Ballario et al., 1996). The N-terminal PAS domains is a Light, Oxygen or Voltage (LOV) domain which is a specialised PAS domain that are able to bind the FAD (Flavin-adenine dinucleotide) chromophore, and are differentiated from other PAS domains by the presence of the GXN**CR**FLQG motif with a conserved photoreactive cysteine residue (He et al., 2002; Krauss et al., 2009). In addition, WC-1 also has a GATA-zinc-finger DNA binding domain, which allows it to bind to DNA and act as a transcription factor.

WC-2 does not contain a LOV domain and is not considered a photoreceptor (Linden and Macino, 1997). Gene disruption of *wc-2* resulted in mutants with a similar phenotype as *wc-1* loss of function mutants, which emphasises the essential role WC-2 plays in relaying the light energy to downstream pathways in WCC (Linden and Macino, 1997). The Zn-domain of WC-2 enables the WCC to interact with the promoter elements of light responsive genes (Collett et al., 2002; Wang et al., 2015). The fact that *wc-1* is present in the genomes of all fungal species also containing *wc-2* attests to the importance of the interplay between WC-1 and WC-2 (Dunlap and Loros, 2006; Idnurm et al., 2010).

FRQ is the central regulatory component of the circadian clock and forms the core of the physiological oscillator (Querfurth et al., 2011 and reviewed by Fuller et al., 2014; Hurley et al., 2015). The WCC heterodimer drives the rhythmic expression of *frq* (Froehlich et al., 2002). The FRQ protein dimerises and interacts with the RNA helicase FRH (He and Liu, 2005; Schafmeier et al., 2005). The FRQ-FRH complex enters the nucleus, where it inhibits WCC by either indirectly altering the phosphorylation status of WCC, or directly reducing its affinity for the *frq* promoter region, thus decreasing transcription of *frq* (Castro-Longoria et al., 2010; Cheng et al., 2005; Conrad et al., 2016; Denault et al., 2001; Guo et al., 2010; Hurley et al., 2013; Shi et al., 2010). During the course of the day FRQ is increasingly phosphorylated as part of clock-signalling phosphorylation (CSP) that ultimately determines the length of the clock (Larrondo et al., 2015). Hyperphosphorylated FRQ is a weak inhibitor of WCC, which over time is dephosphorylated and the cycle is restarted with synthesis of active WC-1 and WC-2. An independent termination-signalling phosphorylation (TSP) event, which does not affect the timing of the clock, is responsible for the turnover rate of FRQ. TSP phosphorylates FRQ, increasing its affinity for the SCE (Skp1-Cull-F-box) type ubiquitin ligase FWD-1 protein, which tags FRQ for degradation in the proteosome (Baker et al., 2009; Cheng et al., 2003b; Larrondo et al., 2015; Liu et al., 2000).

The importance of the five clock proteins, WC-1, WC-2, FRQ, FRH and FWD-1, has been functionally shown in the FRQ/WC-based circadian oscillator (FWO) of *N. crassa* (Loros and Dunlap, 2001). However, rhythmic events in *Δfrq* knockouts have suggested the presence of another oscillator that is dependent on the WC proteins only, termed the FRQ-less oscillator (WC-FLO) (Liu and Bell-Pedersen, 2006). A third oscillator was identified in *N. crassa* that does not require a functional WC-1 or WC-2 protein nor the FRQ protein, termed FRQ/WC-independent FLO (Liu and Bell-Pedersen, 2006). All three of these oscillators are present in the *N. crassa* system, but little is known about the molecular components of the FRQ-less and FLO. Only the FWO oscillator has been characterised in other fungal species thus far (Salichos and Rokas, 2009).

In *N. crassa* WC-1 is the limiting factor in WCC, and overexpression of WC-1 activates most, but not all, light responsive

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