Biochimica et Biophysica Acta xxx (2012) xxx–xxx

Contents lists available at SciVerse ScienceDirect

Biochimica et Biophysica Acta

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

Review

Plastid-to-nucleus communication, signals controlling the running of the plant cell ☆

Juan de Dios Barajas-López, Nicolás E. Blanco, Åsa Strand *

Umeå Plant Science Centre, Department of Plant Physiology, Umeå University, S-901 87 Umeå, Sweden

ARTICLE INFO

Article history:
Received 10 February 2012
Received in revised form 14 June 2012
Accepted 15 June 2012
Available online xxxx

Keywords:
Signaling
Retrograde
Plastids
Stress
Redox
Photosynthesis

ABSTRACT

The presence of genes encoding organellar proteins in both the nucleus and the organelle necessitates tight coordination of expression by the different genomes, and this has led to the evolution of sophisticated intracellular signaling networks. Organelle-to-nucleus signaling, or retrograde control, coordinates the expression of nuclear genes encoding organellar proteins with the metabolic and developmental state of the organelle. Complex networks of retrograde signals orchestrate major changes in nuclear gene expression and coordinate cellular activities and assist the cell during plant development and stress responses. It has become clear that, even though the chloroplast depends on the nucleus for its function, plastid signals play important roles in an array of different cellular processes vital to the plant. Hence, the chloroplast exerts significant control over the running of the cell. This article is part of a Special Issue entitled: Protein Import and Quality Control in Mitochondria and Plastids.

1. Introduction

Chloroplasts, like mitochondria, evolved from free-living prokaryotic organisms that entered the eukaryotic cell through endosymbiosis. The gradual conversion from endosymbiont to organelle during the course of evolution has been accompanied by a dramatic reduction in genome size as the chloroplasts lost most of their genes to the nucleus and the endosymbionts became dependent on their eukaryotic host. The plastid genomes of current land plants encode 75 to 80 proteins [1] whereas the number of proteins in the chloroplast is estimated to be between 3500 and 4000 proteins [2]. Thus, the majority of the plastid proteins are encoded in the nucleus. The presence of genes encoding plastid proteins in both the nuclear and the plastid genomes presents the complex problem to the plant cell to coordinate the activities of the these different genomes [3–5]. In the photosynthetic electron transport complexes of the thylakoid membrane, the core subunits are encoded by the chloroplast genome and the peripheral subunits are encoded by the nuclear genome. In the stroma, the large subunit of Rubisco is encoded in the plastids whereas the small subunit is nuclear encoded. To ensure that all these photosynthetic complexes are assembled stoichiometrically, and to enable their rapid reorganization in response to changes in the environment, the process of so called retrograde signaling has evolved where plastids emit signals that regulate nuclear gene expression to match the status of the plastids [6–9].

The first evidence of the existence of a "plastid signal" came from studies of mutants with morphologically aberrant plastids. These include mutants with defective plastid protein synthesis such as the plastid ribosome-deficient *albostrians* barley mutant and the *Brassica napus al* mutant [10–12]. These mutants demonstrated reduced expression of nuclear genes encoding plastid components suggesting that a plastid signal was emitted to repress the nuclear encoded photosynthesis genes [12]. These results opened the research field to investigate how different plastid processes trigger signals that modulate nuclear gene expression [6]. We now know that several different plastid processes produce signals that regulate specific sets of genes or regulons and several molecular candidates for plastid signals have been described. Plastid signals and communication between the plastids and nucleus is of particular importance during plant stress responses. For plants to respond optimally to environmental stresses it is necessary that the cytosolic and plastid signaling networks are integrated to produce a coordinated response in the different cellular compartments [13]. Plastid signals also coordinate cell cycle and coupling of DNA replication in the cell and play a major role during chloroplast development [14,15]. Furthermore, it was recently demonstrated that organelle-to-nucleus communication also plays a role in intercellular communication via plasmodesmata [16] and that plastid signals are key factors driving the transition from cell proliferation to cell expansion [17]. Thus, it is clear that plastid signals play important roles in an array of different cellular processes of the plant.

Plastid signals are essential to the plant both during the initial developmental stages (biogenic control) and in adult stage to face

☆ This article is part of a Special Issue entitled: Protein Import and Quality Control in Mitochondria and Plastids.

* Corresponding author. Tel.: +46 90 786 9314; fax: +46 90 786 6676.
E-mail address: Asa.Strand@plantphys.umu.se (Å. Strand).

0167-4889/$ – see front matter © 2012 Elsevier B.V. All rights reserved.
doi:10.1016/j.bbamcr.2012.06.020

changes in the environment (operational control) [18]. However, the tentative plastid signals identified to date can be linked primarily to specific stress conditions. The photosynthetic reactions housed in the chloroplasts are extremely sensitive to stress and the chloroplasts could therefore play a critical role as sensors of changes in the growth environment [13,19]. This review will focus on two different types of plastid signals influencing nuclear gene expression during different stress conditions; 1) metabolites as plastid signaling molecules, tetrapyrroles and the recently discovered phosphonucleotide 3′-phosphoadenosine 5′-phosphate (PAP) and 2) signals related to photosynthetic electron transport such as changes of the redox state of the chloroplast and accumulation of the reactive oxygen species, singlet O_2 and H_2O_2. Plastid signaling has also been associated with the organellar transcriptional and translational activity (PGE) involving GUN1 in particular [14,20,21] and to the carotenoid biosynthesis [22]. Due to space limitations these aspects will not be covered in this review.

2. Metabolites as plastid signaling molecules

2.1. The putative role of tetrapyrroles in plastid signaling

Higher plants synthesize four major tetrapyrrole molecules via a common branched pathway in the plastids: chlorophyll, heme, siroheme and phytochromobilin. Many tetrapyrroles are excited by light and if left unquenched they can form highly toxic radicals. Tetrapyrrole synthesis is therefore tightly regulated to prevent the accumulation of intermediates that may endanger the plant cell. Perturbations in the tetrapyrrole pathway have been shown to affect expression of photosynthesis-associated nuclear genes (*PhANGs*) in both green algae and higher plants [23–31]. Mutants with impaired communication between the chloroplast and the nucleus referred to as the genome *un*coupled, or *gun* mutants were isolated from genetic screens [7,32]. The *gun1–6* mutants express *PhANGs* when exposed to oxidative stress whereas wild type demonstrates strong suppression of photosynthetic gene expression under the same conditions [7,32]. Five of the six GUN genes, *GUN2–6*, encode components closely associated with tetrapyrrole biosynthesis and the respective mutants have impaired flux through the tetrapyrrole biosynthesis pathway. GUN1 on the other hand, is a chloroplast localized pentatricopeptide-repeat (PPR) containing protein with unknown function. Thus, the *gun* mutants provided strong evidence for the involvement of tetrapyrroles in communication between the chloroplast and the nucleus in plants.

Environmental changes affect flux through the tetrapyrrole biosynthesis causing perturbations and the accumulation of specific metabolites. Thus, flux through tetrapyrrole biosynthesis could act as an indicator of changes in the environment and the signals triggered by flux perturbations are therefore important during stress responses but they also play roles during seedling and chloroplast development [25,32,33]. Heme and Mg-ProtoIX affect expression of *PhANGs* and in the *gun5* mutant expression of genes encoding proteins involved in the light harvesting and electron transport reactions of photosynthesis, enzymes in metabolic pathways such as the Calvin cycle and tetrapyrrole biosynthesis, and proteins involved in translation of chloroplastic-encoded genes is mis-regulated following exposure to oxidative stress [25]. In addition, Mg-ProtoIX has been shown to coordinate cell cycle and coupling of organellar and nuclear DNA replication in red alga and tobacco BY-2 cells [15]. In red algae Mg-ProtoIX was shown to mediate a proteasome-dependent protein degradation by binding to and inhibiting a SCF-type E3 ubiquitin ligase (FBX3). Inhibition of FBX3 results in release of Cyclin 1 and activation of CDKA, stimulating nuclear DNA replication [34]. Furthermore, in non-photosynthetic plastids of BTY2 tobacco cells, tetrapyrroles were shown to play a role in amyloplast differentiation and regulation of the nuclear encoded starch biosynthesis genes ADP-Glucose Pyrophophorylase (AGpS) and the Granule-Bound Starch Synthase (GBSS) [35]. Thus, the collected data suggests that tetrapyrroles play important regulatory roles in diverse cellular processes in plants and algae.

2.1.1. Chlorophyll intermediates putative plastid signals during oxidative stress

Over 20 years ago Mg-ProtoIX and its methyl ester Mg-ProtoIX-ME were suggested to act as plastid signals regulating nuclear encoded genes associated with photosynthesis. This proposal was based upon studies demonstrating that accumulation of these chlorophyll intermediates coincided with changes in nuclear gene expression [29,30,36,37]. This model was later supported by the characterization of the *gun5* mutant. The *gun5* mutant has a lesion in the H-subunit of Mg-chelatase that catalyzes the first reaction in the "chlorophyll branch" of tetrapyrrole biosynthesis and has impaired flux through the tetrapyrrole biosynthetic pathway [38]. The *gun5* mutant demonstrates a mis-regulation of a large number of *PhANGs* when exposed to oxidative stress [25] and in contrast to wild type, *gun5* did not demonstrate significant accumulation of Mg-ProtoIX following exposure to oxidative stress [25]. To induce oxidative stress and to trigger the GUN5 signal, seedlings are commonly grown on norflurazon. Norflurazon inhibits phytoene desaturase (PDS) in the carotenoid biosynthetic pathway. The photooxidation caused by norflurazon treatment is limited to the plastid and results in complete destruction of the thylakoid membrane [39,40]. However, norflurazon treatment generates an artificial condition of severe stress where specific responses of the plant may be difficult to reproduce due to pleiotropic effects caused by the treatment [41–43]. The role of Mg-ProtoIX/Mg-ProtoIX-ME as a plastid signal was subsequently questioned when reported accumulation of Mg-ProtoIX following norflurazon treatment was not observed in two different studies [42,43]. Consequently, no correlation between *LHCB* expression and Mg-ProtoIX amounts could be reported in those studies. While the source of the GUN5 dependent plastid signal induced by oxidative stress was still believed to be linked to tetrapyrrole biosynthesis, the exact nature of the signal was challenged. It was suggested that either rapid changes in the flux through the tetrapyrrole pathway, ROS accumulation, activity of Mg-chelatase or accumulation of Mg-ProtoIX in a specific cellular compartment could be the origin of the plastid signal [42,43].

The contradictory results and the controversy regarding the signaling role for Mg-ProtoIX have stimulated the field to make efforts to elucidate the mechanisms involved in the tetrapyrrole-mediated signal. Arabidopsis mutants affected in the I-subunit of the Mg-chelatase, *cs* and *chl42* mutants did not demonstrate a gun phenotype following exposure to oxidative stress [38] . This was an unexpected result and provided support for a specific function for the H-subunit (GUN5) of the Mg-chelatase complex in plastid signaling. It was previously suggested that CHLH monitors porphyrin levels by binding excess ProtoIX and/or Mg-ProtoIX, sending a negative signal or inhibiting a positive signal to the nucleus via a hypothetical downstream factor(s) [38]. However, it was subsequently shown in Arabidopsis that there are two genes encoding I-subunits of Mg-chelatase, CHLI1 and CHLI2 [44]. When the double mutant, *chli1chli2,* was generated, the double mutant did indeed demonstrate a gun phenotype [45], suggesting that the signal is not dependent on CHLH but is linked to the tetrapyrroles.

It was also suggested that ROS accumulation was the origin of the GUN5/tetrapyrrole mediated plastid signal instead of the specific accumulation of Mg-ProtoIX/Mg-ProtoIX-ME [42,43]. The conditions used to trigger the GUN5 mediated plastid signal results in oxidative stress and accumulation of ROS. The different ROS species activate distinct signaling pathways [13] and the release of ROS could be an alternative explanation for the role of tetrapyrrole intermediates in retrograde signaling because many porphyrins are photoreactive and generate $^1O_2$ in the presence of light [46]. However, specific ROS eliminators were shown to only partly reverse the norflurazon-triggered repression of *LHCB*

Please cite this article as: J.D. Barajas-López, et al., Plastid-to-nucleus communication, signals controlling the running of the plant cell, Biochim. Biophys. Acta (2012), doi:10.1016/j.bbamcr.2012.06.020