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A new take on organelle-mediated stress sensing in plants

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Summary

Plants are able to adjust phenotype in response to changes in the environment. This system depends on an internal capacity to sense environmental conditions and to process this information to plant response. Recent studies have pointed to mitochondria and plastids as important environmental sensors, capable of perceiving stressful conditions and triggering gene expression, epigenomic, metabolic and phytohormone changes in the plant. These processes involve integrated gene networks that ultimately modulate the energy balance between growth and plant defense. This review attempts to link several unusual recent findings into a comprehensive hypothesis for the regulation of plant phenotypic plasticity.

Keywords

chloroplast; epigenetics; mitochondria; phenotypic plasticity; retrograde regulation

I. Introduction

Phenotypic plasticity is a concept that encompasses diverse mechanisms to allow plants to adjust their growth behavior in response to environmental change (Schlichting, 1986). In general, plastic growth responses are adaptive and may be heritable, reflecting an accelerated evolution process that facilitates the acclimation of a plant species to new niches. Phenotypic plasticity does not necessarily manifest in morphological changes, and can reflect subtle physiological adjustments in growth rate, day-length response or behavior under stress. The underlying mechanisms that reprogram growth in response to environmental change are only just coming into focus, with a surprising interlinkage of metabolism, stress networks and organellar redox effects on the plant adaptation process (Margalha et al., 2019).

II. Energy-generating organelles as important environmental sensors in plants

Mitochondria and plastids function as signal integrators to link metabolic processes with environmental sensing and can lead to epigenetic changes in the plant. The vast majority of

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proteins required for mitochondrial and chloroplast function are nuclear-encoded, so nuclear communication with organelles, or anterograde regulation, is essential to adjust organellar properties during development. Retrograde, or organelle-to-nucleus signaling, is mediated by a variety of organelle-generated molecules that direct plant responses (Box 1), many involving environmental sensing (Wang et al., 2020). Not surprisingly, the numerous metabolic intermediates that participate in plastid retrograde signaling are regulated through their organellar export and/or import. For example, plastid signaling involves carotenoid-derived β-cyclocitral and dihydroactiniolide as a consequence of increased singlet oxygen (Ramel et al., 2012), derivatives of the isoprenoid precursor methylerythritol cyclodiphosphate (MEcPP) to influence salicylic acid (SA) and jasmonate pathways (Xiao et al., 2012), or 3′-phosphoadenosine 5′-phosphate, a metabolite affecting 5′–3′ exoribonuclease activity within the nucleus (Estavillo et al., 2011). The spectrum of intermediates identified as components of retrograde signaling point to a vital function of plastid envelope transport systems in the evolution of this intracellular communication (Unal et al., 2020). What remains unclear is how these transport systems partition to specialized plastid types.

Retrograde signaling links to nuclear RNA metabolism to broadly impact nuclear gene expression (Zhao et al., 2020). The resulting adaptive responses can be complex, such as repressing photosynthesis-associated nuclear genes while simultaneously inducing photoprotectant anthocyanin accumulation in response to light shifts (Richter et al., 2020) or supporting nuclear microRNA (miRNA) biogenesis under stress conditions to alter development and environmental stress responses (Fang et al., 2019). Similarly expansive nuclear influence on organellar gene expression is accomplished via nuclear-encoded RNA-binding proteins that include organellar ribosome maturation and splicing domain proteins, pentatricopeptide repeat proteins, DEAD-Box RNA helicases and S1-domain containing proteins (Lee & Kang, 2020). The multifarious nature of this coregulation system reflects a post-endosymbiotic evolution process that has equipped the plant system for broad-spectrum responsiveness through coordinated organelle-nuclear networks.

Components of plastid redox regulation, including plastoquinone and tocopherol pools, also influence nuclear gene expression (Havaux, 2020) and reactive oxygen is a vital component of organellar signaling. In plastids, the relationship of plastoquinone to reactive oxygen species (ROS) homeostasis is not yet entirely clear, but PQ-9 can influence photosynthetic acclimation by adjusting ROS signaling with SNT7, a kinase that alters redox homeostasis by phosphorylation of light-harvesting components (Tikkanen et al., 2012). This process of dictating ROS production generates cell-wide signals that alter hormonal networks within the cell (Tikkanen et al., 2012). Likewise, hydrogen peroxide accumulation within the PQ pool can participate directly in retrograde signaling to alter gene expression (Mubarakshina & Ivanov, 2010; Exposito-Rodriguez et al., 2017; Havaux, 2020). This plastid-nuclear ROS signaling can be surprisingly direct through physical interaction of clusters of perinuclear plastids via organellar stromule extensions or plastid-nuclear complexes (Mullineaux et al., 2020).

In mitochondria, potential damage from overactive electron flow is mitigated by alternative oxidase encoded by Alternative oxidase I (AOX1) (Millar, et al., 2011). Investigation of the

AOX1 system by forward genetic screens unveils a number of unexpected links between this electron bypass system to cellular growth and metabolism. *Regulator of Alternative Oxidase* (*rao*) mutants are identified by their inability to induce AOX1a expression in response to antimycin A, an inhibitor of mitochondrial cytochrome c reductase (Zarkovic, et al., 2005). A diverse set of AOX regulators have been identified through this screen, providing details of mitochondrial association with plant growth functions. *RAO1*, for example, encodes the *Cyclin-Dependent Kinase E1* (*CDKE1*) (Ng et al., 2013). This gene regulates both *AOX1a* and *Light Harvesting Complex B* (*LHCB*) to integrate mitochondrial and plastid retrograde signals during stress (Blanco et al., 2014). *RAO1* also interacts with *KIN10* (Ng et al., 2013), a subunit of the *Sucrose Nonfermenting-Related Kinase 1* (*SnRK1*), which balances energy signaling for growth with plant defense response (Baena-González et al., 2007).

Interestingly, RAO mutants also encode components of auxin transport in the plant. These include *rao3/big*, *rao4/pin1*, *rao5/mdr1/abcb19* and *rao6/asymmetric leaves 1* (*as1*) (Ivanova et al., 2014). Studies of these mutants, together with chemical inhibitors of auxin, reveal an antagonistic relationship between auxin and mitochondrial retrograde signaling, presumably part of the plant's ability to modulate growth during stress. Auxin can activate the TARGET of RAPAMYCIN (TOR) pathway (Schepetilnikov et al., 2013) and, in plants, the TOR pathway works antagonistically with SnRK1 in adjusting the balance in energy for growth with stress response (Margalha et al., 2019). Discovery of AOX1 in this network serves to interlink these cellular programming controls with mitochondrial status and further elaborates mitochondrial influence at the plant–environment intersection.

Plastid functions appear similarly intrinsic to establishing energy balance and stress perception by the plant. For example, instability of the plastid genome triggers a specific nuclear genome response. Enhanced nuclear endoreplication and altered cell cycle regulation occur in response to chemical and genetic disruption of the plastid genome (Duan et al., 2020). This phenomenon requires the gene *SOG1*, a putative nuclear transcription factor responsive to DNA damage (Duan, et al., 2020). Plastid genome disruption triggers increased ROS to effect this response and, remarkably, SOG1 interacts with *Sucrose Nonfermenting-Related Kinase 1* (*SnRK1*) (Hamasaki et al., 2019), reiterating the linkage of plastid status with energy homeostasis. Mitochondria maintain their cellular population through fission and fusion, so that functions they perform are relatively uniform in scope across cell types. However, plastids do not fuse and, thus, can undergo spatiotemporal differentiation to acquire specialized properties in various plant tissues (Wise, 2007). These properties include photosynthesis and light perception, cellular metabolism, carbohydrate and lipid storage, and environmental sensing, each requiring specialized plastid proteome components.

III. The potential role of sensory plastids in stress signaling

Sensory plastids reside within epidermal and vascular tissues and differ in size, thylakoid structure and proteome composition from the mesophyll chloroplast of neighboring cells (Beltrán et al., 2018). The sensory plastid, while presumably photosynthetic (Barton et al., 2016), contains a proteome enriched in components of shikimate pathway-associated metabolism and stress response. Estimating the extent to which sensory plastids participate

in retrograde signaling and environmental sensing is confounded by the fact that past and present studies of chloroplast functions are generally carried out in experiments that pool mesophyll and sensory plastids.

Perhaps the most well-detailed plastid retrograde signaling pathway, mediated by SAL1 and 3′-phosphoadenosine 5′-phosphate (PAP), appears to be sensory plastid-associated. The redox-regulated phosphatase SAL1 localizes to both mitochondria and plastids, with predominant expression in vascular tissues, and regulates the concentration of PAP by dephosphorylation to adenosine monophosphate (Estavillo et al., 2011). A by-product of sulfur metabolism, PAP is transferred to the nucleus where it influences gene expression by inhibiting XRN type exoribonucleases (Estavillo et al., 2011; Litthauer & Jones, 2018). These exoribonucleases target miRNAs that can broadly influence plant response. Tocopherols, derived from tyrosine in the sensory plastid, serve to upregulate PAP and, consequently, nuclear miRNA biogenesis (Fang et al., 2019). What links this process to the sensory plastid is its dependence on CUE1 (Fang et al., 2019), a phosphoenolpyruvate import protein that resides on the inner membrane of the sensory plastid (Lundquist, et al., 2014; Beltrán et al., 2018). Disruption of *CUE1* (also named *PPT1*) results in a *reticulata* green venation phenotype because of its association with vascular plastids, while its counterpart, *PPT2*, serves to import PEP within mesophyll chloroplasts (Hilgers et al., 2018). Genetic evidence of *CUE1* dependence for the tocopherol-influenced XRN activity locates SAL1-PAP signaling to the sensory plastid and to vascular tissues of the plant, but parallel association of this pathway to mesophyll chloroplasts remains unclear.

One means of rescuing the *cue1* mutant, and other sensory plastid-associated *reticulata* mutants, is by supplementing with aromatic amino acids (Streatfield et al., 1999). This observation is consistent with proteome studies showing sensory plastid enrichment for components of the shikimate pathway (Beltrán et al., 2018). Aromatic amino acid metabolism plays a significant role in plant defense, and effector-triggered immunity is characterized by significant increases in phenylalanine pools, and phenylpropanoid metabolism more generally (Yoo et al., 2020). Thus, specialized plastids may also play a previously undetailed role in biotic stress response.

ICS2, a gene encoding isochorismate synthase, converts chorismate to isochorismate during the biosynthesis of phylloquinone, a component of electron transport. This enzyme is also encoded by *ICS1*, and both participate in SA biosynthesis, an important component of plant defense (Garcion et al., 2008). The genes are differentially regulated by environmental factors (Macaulay et al., 2017), but *ICS2* predominantly localizes to vascular tissue. Consistent with this localization, sensory plastid perturbation induces upregulation of the SA pathway (Shao et al., 2017; Yang et al., 2020).

Fluctuating light is an important environmental factor that elicits plastid retrograde signaling in plants. In response, epidermal plastids display dynamic stress-response morphological behaviors that are distinct from neighboring mesophyll chloroplasts. These visible changes involve abundant stromule production, perinuclear association and H_2O_2 plastid-nuclear transfer (Brunkard et al., 2015; Exposito-Rodriguez et al., 2017). Studies of this signal, using an elegant fluorescent sensor, show H_2O_2 within plastids of epidermal cells that align

in physical association with the nucleus (Exposito-Rodriguez et al., 2017). While aspects of this light response, as well as plastid stromule production, can also occur in mesophyll chloroplasts, epidermal and mesophyll plastids are distinct systems as evidenced in their response to sucrose and photosynthesis inhibitors (Brunkard et al., 2015; Virdi et al., 2016; Exposito-Rodriguez et al., 2017).

Unique to the sensory plastid proteome are components that contribute to phenotypic plasticity by triggering epigenetic changes in the plant (Mackenzie & Kundariya, 2020). The plant-specific gene *MSH1* encodes a dual-targeted mitochondrial and plastid protein that resides within the sensory plastid but not the mesophyll chloroplast (Xu et al., 2011). Downregulation or disruption of *MSH1* causes sensory plastid perturbation, a reduced plastoquinone pool, and enhanced expression of abiotic and biotic stress response pathways (Xu et al., 2011, 2012; Virdi et al., 2016; Shao et al., 2017). Progeny from *MSH1*-suppressed plants, when restored for *MSH1* expression, can display heritable *msh1* stress memory (Xu et al., 2012; Virdi et al., 2015) that depends on RNA-directed DNA methylation (RdDM) pathway components (Yang et al., 2020), The *msh1* memory phenomenon alters gene expression and DNA methylation in auxin response, phytohormone signaling, circadian rhythm and alternative RNA splicing pathways (Yang et al., 2020). Recapitulation of these memory effects in other plant species (Xu et al., 2012; Yang et al., 2015; Raju et al., 2018) suggests this to be a conserved process in plants.

Incorporation of *msh1* mutants as rootstocks in graft experiments to wild-type scions produces progeny that are also altered heritably. Whereas the parental rootstock displays stress effects, the graft progeny plants are enhanced in growth vigor and resilience relative to the wild-type (Virdi et al., 2015; Kundariya et al., 2020). This unexpected acquired vigor is similarly small interfering RNA- and RdDM-dependent (Kundariya et al., 2020).

DNA methylation and gene expression in *msh1* graft progeny reveal a pronounced auxin response signal that is phenotypically evident in vigorous lateral root growth (Kundariya et al., 2020). Network-based analysis of DNA methylation repatterning for the *msh1*-derived vigor phenotype identifies *TOR*, *SnRK1* and *PP2C* as putative network hubs integrating growth with stress response (Kundariya et al., 2020). Extending upon previous reports of mitochondrial *AOX1*-directed stress behaviors, these observations support mito-plastid coordination in environmental sensing and reveal a capacity to influence key integrators of growth and stress response towards reprogramming of plant phenotype (Fig. 1).

IV. Alternative RNA splicing as a nuclear response to organellar signaling

One means of broad and rapid influence on nuclear gene expression, following organellar perturbation, occurs through alternative RNA splicing (Staiger, 2015). The light environment of a plant appears to be a strong determinant of alternative splicing behavior as a likely means of enhancing growth plasticity (Tognacca et al., 2020). Changing light conditions leads to reduction of the plastoquinone pool in plastids, which alters particular splicing factors for light-responsive nuclear genes (Petrillo et al., 2014). Auxin response factor regulation by alternative splicing is likewise an important component of phenotypic resilience during environmental change (Lanctot & Nemhauser, 2020). DNA methylation

repatterning following *MSH1* suppression shows changes in numerous components of the RNA spliceosome pathway (Yang et al., 2020).

During abiotic stress, alternative splicing occurs predominantly in regulatory loci, with outcomes that range from nonsense mediated decay to activation of otherwise nonfunctional transcripts (Mastrangelo et al., 2012). This association of environment-induced alternative splicing activity with regulators offers an elegant means of rapidly deploying phenotypic plasticity to a system under stress. It is perhaps not surprising, then, that gene-associated DNA methylation repatterning occurs within gene networks that align with stress response pathways and phenotype changes (Yang et al., 2020; Kundariya et al., 2020); subtle methylation changes may be sufficient to adjust or respond to local splicing changes that relax phenotypic constraints (Zhang et al., 2020).

V. Conclusions

Mitochondria and plastids, as energy-generating, light-sensing, phytohormone-producing and metabolic regulators of the cell, function as central integrators of environmental information for the plant (Fig. 1). Thus, organellar signaling is multifaceted and broadly targeted. Yet, cell- and tissue-level resolution of plant processes make it feasible to localize organellar sensing and signaling functions, with epidermal and vascular tissues appearing particularly important.

Implementation of forward genetic mutant, transcriptomic, epigenomic and physiological studies by numerous groups reveal striking intersection of organellar signaling with central gene networks to regulate bioenergetics for growth and plant defense. This emerging research provides the most comprehensive view yet of the components underpinning phenotypic plasticity in plants and offers a preliminary road map for understanding the genotype-to-phenotype relationship under dynamic change.

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Box 1.

Signaling metabolites that participate in retrograde regulation.

Metabolite	References
Tetrapyrrole derivatives	
Heme	Woodson et al. (2011)
GUN4/5	Mochizuki et al. (2001), Larkin et al. (2003)
Mg-ProtoIX	Strand et al. (2003)
Carotenoid derivatives	
β′ cyclocitral (β-cyc)	Ramel et al. (2012)
Dihydroactinidiolide	Shumbe et al. (2014)
3′-Phosphoadenosine 5′-phosphate (PAP)	Estavillo et al. (2011)
2-C-methyl-D-erythritol 2,4-cyclodiphosphate (MEcPP)	Xiao et al. (2012)
Ca^{2+}	Guo et al. (2016)
Fatty acids (FAs)	
Oxylipin	Muñoz & Munné-Bosch (2020)
NO_2-FAs	Mandal et al. (2012)
Free fatty acid (FFAs)	Walley et al. (2013)
Dihydroxyacetone phosphate (DHAP)	Alsharafa et al. (2014)

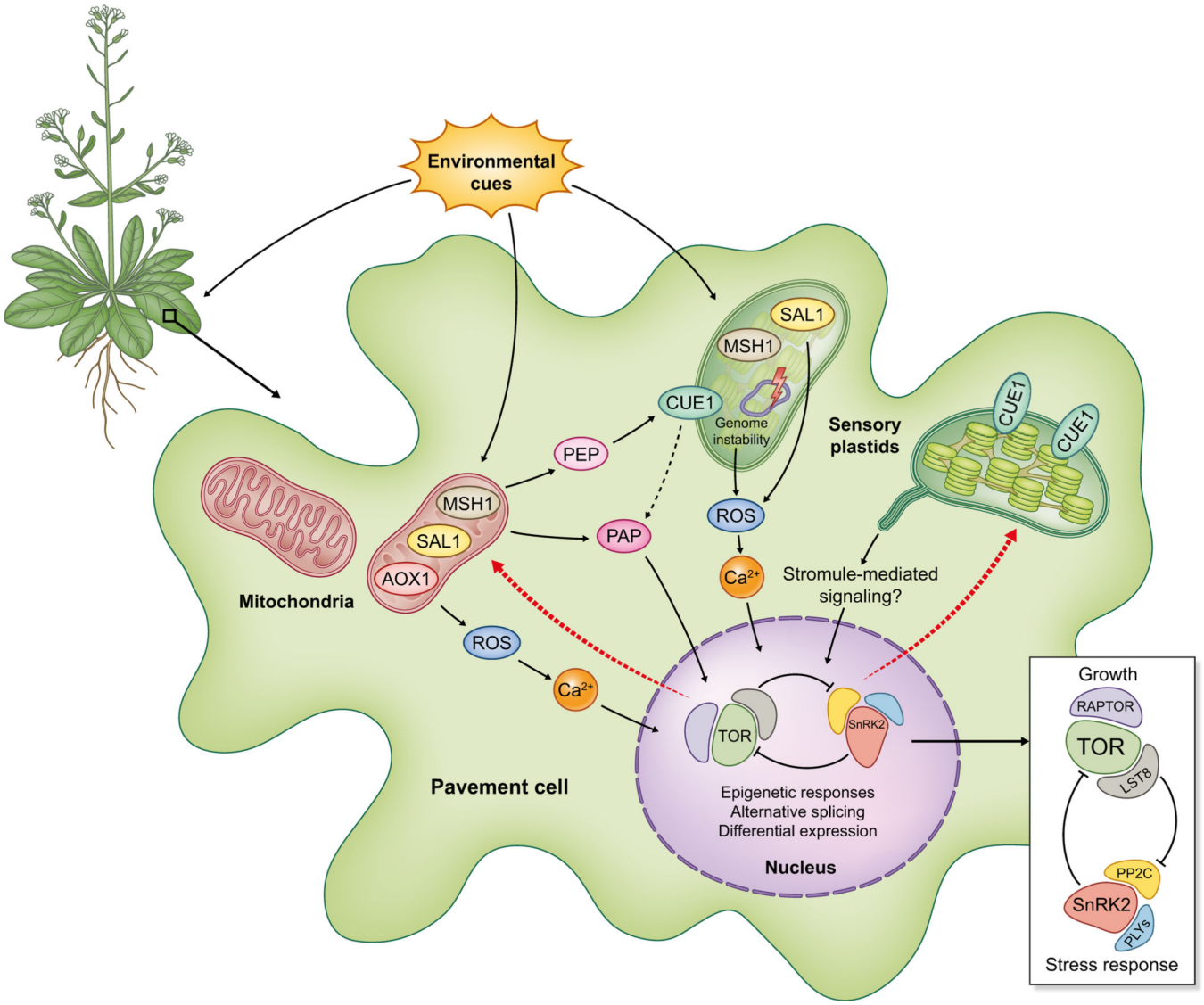

Fig. 1.

Highly simplified diagram of nuclear-organellar communication in an epidermal pavement cell in plants. An example of retrograde regulation involving epidermal sensory plastids and mitochondria is shown in the SAL1–3′-phosphoadenisine-5′-phosphate (SAL1-PAP) pathway. Anterograde signaling is depicted by red dashed arrows, emanating from components linked to the growth-stress network represented by TARGET of RAPAMYCIN (TOR), SnRK1/2 and associated components. MSH1, shown within the sensory plastid, is suppressed by environmental stress and its depletion can induce organellar genome changes that are postulated to trigger plastid-nuclear signaling. ROS, reactive oxygen species; PEP, phosphoenolpyruvate.