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Review

Mitochondrial retrograde regulation in plants

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Abstract

Plant cells must react to a variety of adverse environmental conditions that they may experience on a regular basis. Part of this response centers around (1) ROS as damaging molecules and signaling molecules; (2) redox status, which can be influenced by ROS production; and (3) availability of metabolites. All of these are also likely to interface with changes in hormone levels [Desikan, R., Hancock, J., Neill, S., 2005. Reactive oxygen species as signalling molecules. In: Smirnoff, N. (ed.), Antioxidants and reactive oxygen species in plants. Blackwell Pub. Ltd., Oxford, pp. 169–196; Kwak, J.M., Nguyen, V., Schroeder, J.I., 2006. The role of reactive oxygen species in hormonal responses. Plant Physiol. 141, 323–329]. Each of these areas can be strongly influenced by changes in mitochondrial function. Such changes trigger altered nuclear gene expression by a poorly understood process of mitochondrial retrograde regulation (MRR), which is likely composed of several distinct signaling pathways. Much of what is known about plant MRR centers around the response to a dysfunctional mtETC and subsequent induction of genes encoding proteins involved in recovery of mitochondrial functions, such as AOX and alternative NAD(P)H dehydrogenases, and genes encoding enzymes aimed at regaining ROS level/redox homeostasis, such as glutathione transferases, catalases, ascorbate peroxidases and superoxide dismutases. However, as evidence of new and interesting targets of MRR emerge, this picture is likely to change and the complexity and importance of MRR in plant responses to stresses and the decision for cells to either recover or switch into programmed cell death mode is likely to become more apparent.

Keywords: Mitochondria; Retrograde regulation; Retrograde signaling; Inter-organellar communication; Mitochondria-to-nucleus signaling

1. Introduction

Abiotic stresses, biotic stresses, or mutations can alter the functioning of organelles. In response, organelles can direct changes in nuclear gene expression. The alteration of nuclear gene expression directed by organelles through organelle-to-nucleus signaling is referred to as retrograde communication, retrograde signaling, retrograde stress signaling or retrograde regulation (Butow and Avadhani, 2004; Liao and Butow, 1993; Patil and Walter, 2001; Rhoads and Vanlerberghe, 2004; Rodermel, 2001; Surpin et al., 2002). In the case of plant mitochondria-to-nucleus signaling, we refer to it as mitochondrial retrograde regulation (MRR). Signaling due to changes in mitochondrial function could link to metabolic signaling pathways or general reactive oxygen species (ROS) signaling pathways and trigger gene expression responses, but these would still be mitochondria-directed responses. Mounting evidence indicates that retrograde regulation is an important regulatory/response mechanism for plants, animals and fungi.

Abbreviations: AA, antimycin A; ADH, alcohol dehydrogenase; AOX, mitochondrial alternative oxidase; CMS, cytoplasmic male sterility; COX, cytochrome *c* oxidase; CDPKs, calcium-dependent protein kinases; GAPDH, glycerol-3-phosphate dehydrogenase; HAE, hydroxyalkenal; HR, hypersensitive response; HSP, heat shock/stress protein; MAPKs, mitogen-activated protein kinases; MFA, monofluoroacetate; MRR, mitochondrial retrograde regulation; mt, mitochondrial; mtETC, mitochondrial electron transport chain; mtROS, mitochondrial reactive oxygen species; mrrd, mitochondrial retrograde regulation deficient; NCS, non-chromosomal stripe; PCD, programmed cell death; RNS, reactive nitrogen species; ROS, reactive oxygen species; RR, ruthenium red; SA, salicylic acid; sHSP, small heat shock/stress protein; TMV, tobacco mosaic virus; VDAC, voltage-dependent anion channel.

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This is a new but rapidly expanding area of biology. Relatively little attention has been given to retrograde regulation in plants especially to MRR.

In animals, mitochondrial dysfunction, and the MRR that likely results, is now thought to be an important factor in many human diseases (Butow and Avadhani, 2004; Lane, 2006; Weissig et al., 2004). Mitochondrial dysfunction, and in some cases MRR, has been connected to Alzheimer's disease (Moreira et al., 2006; Parihar and Brewer, 2007), Parkinson's disease (Beal, 2005; Kwong et al., 2006), Huntington's disease (Beal, 2005; Kwong et al., 2006; Marx, 2005), bipolar disorder (Iwamoto et al., 2005; Kato, 2005), schizophrenia (Ben-Shachar and Laifenfeld, 2004; Iwamoto et al., 2005), type 2 diabetes (Guo et al., 2005; Lowell and Shulman, 2005), cancer (Butow and Avadhani, 2004; Singh et al., 2005), and aging (Beal, 2005; Butow and Avadhani, 2004). MRR is a relatively new angle on the importance of mitochondria in diseases (Biswas et al., 2005; Butow and Avadhani, 2004; Singh et al., 2005).

Although some target genes are in common among MRR pathways, there seem to be several distinct MRR signaling pathways in animals (Butow and Avadhani, 2004).

MRR in yeast has been well studied. The yeast *Saccharomyces cerevisiae* responds to mitochondrial dysfunction by altering nitrogen and carbon metabolism (Butow and Avadhani, 2004). Respiratory deficient cells shift metabolism in an attempt to maintain glutamate levels by restoring levels of TCA cycle intermediates. Gene induction involves regulation by RTG transcription factors in many of the best studied cases (Butow and Avadhani, 2004; Poyton and McEwen, 1996; Sekito et al., 2000), but at least two other MRR signaling pathways are present in *S. cerevisiae* (Devaux et al., 2002; Guaragnella and Butow, 2003).

Plants contain two energy-producing organelles: chloroplasts, which convert sunlight to chemical energy in the form of ATP and stored energy in the form of carbon compounds such as sugars and lipids, and mitochondria, which convert stored energy to ATP. Both organelles are able to communicate with the nucleus. Chloroplastic retrograde regulation pathways are, to date, the best studied retrograde signaling pathways in plants. Potential pathways have been identified for signaling in response to photomorphogenesis (Surpin et al., 2002), altered function during chloroplast biogenesis (Barr et al., 2004), and redox poise (Rodermel, 2001). In this review, we focus on our current understanding of MRR in plants, which has been revealed primarily in instances of mitochondrial dysfunction. Mitochondrial dysfunction caused by mutations in plants often results in male sterility, in an embryo lethal phenotype, or in chlorotic plants that do not survive to maturity (Newton et al., 2004). In addition, mitochondrial dysfunction in plants can be caused by abiotic and biotic stresses. Although relatively little is known about the specific cellular consequences of mitochondrial dysfunction in plants, there is growing evidence that the responses of mitochondria to biotic and abiotic stresses contribute significantly to overall plant stress responses. The molecular mechanisms used by retrograde signaling pathways have just begun to be defined; a few components have been identified in some cases. Mitochondria likely play vital roles in stress responses by contributing to altered nuclear gene expression. A great deal of flexibility in responses to stres-

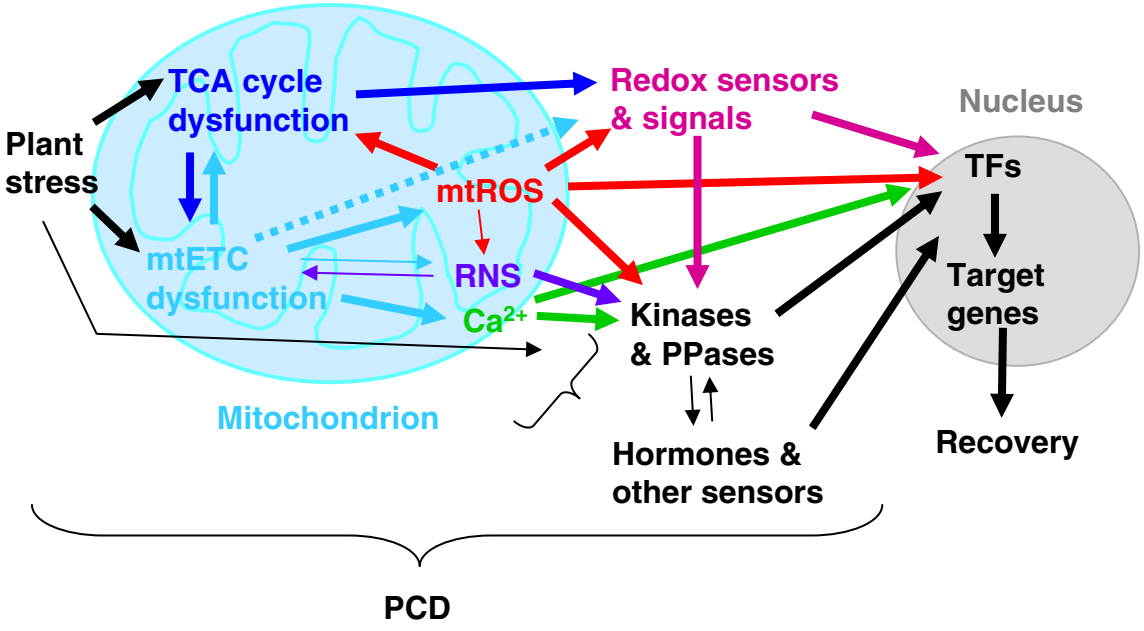

Fig. 1. Potential signaling pathways for plant MRR. For clarity, some potential signaling mechanisms have been omitted. These include signals such as lipid peroxidation products, calmodulin, cyclic nucleotides, and phospholipases. mtETC, mitochondrial electron transport chain, mtROS, mitochondrial reactive oxygen species; PPases, protein phosphatases; RNS, reactive nitrogen species; TFs, transcription factors.