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Review

Involvement of thiol-based mechanisms in plant development ☆

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ABSTRACT

Background: Increasing knowledge has been recently gained regarding the redox regulation of plant developmental stages.
Scope of view: The current state of knowledge concerning the involvement of glutathione, glutaredoxins and thioredoxins in plant development is reviewed.
Major conclusions: The control of the thiol redox status is mainly ensured by glutathione (GSH), a cysteine-containing tripeptide and by reductases sharing redox-active cysteines, glutaredoxins (GRXs) and thioredoxins (TRXs). Indeed, thiol groups present in many regulatory proteins and metabolic enzymes are prone to oxidation, ultimately leading to post-translational modifications such as disulfide bond formation or glutathionylation. This review focuses on the involvement of GSH, GRXs and TRXs in plant development. Recent studies showed that the proper functioning of root and shoot apical meristems depends on glutathione content and redox status, which regulate, among others, cell cycle and hormone-related processes. A critical role of GRXs in the formation of floral organs has been uncovered, likely through the redox regulation of TGA transcription factor activity. TRXs fulfill many functions in plant development via the regulation of embryo formation, the control of cell-to-cell communication, the mobilization of seed reserves, the biogenesis of chloroplastic structures, the metabolism of carbon and the maintenance of cell redox homeostasis. This review also highlights the tight relationships between thiols, hormones and carbon metabolism, allowing a proper development of plants in relation with the varying environment and the energy availability.
General significance: GSH, GRXs and TRXs play key roles during the whole plant developmental cycle via their antioxidant functions and the redox-regulation of signaling pathways. This article is part of a Special Issue entitled: Redox regulation.

1. Introduction

Thiols, the sulfur analogues of alcohols, are organo-sulfur compounds that contain a carbon-bonded sulfhydryl group (R–SH). Thiols are readily prone to oxidation especially in a basic environment since thiol deprotonation leads to the formation of thiolate ($R\text{-}S^-$), a nucleophilic form sensitive to oxidation. In the presence of reactive oxygen species (ROS), such as hydrogen peroxide, oxidation leads to the formation of a sulfenic acid form (R-SOH) that can be further oxidized to sulfinic and sulfonic forms ($R\text{-}SO_2H$ and $R\text{-}SO_3H$, respectively) [1]. Of note, thiol groups can also be oxidized by reactive nitrogen species resulting for instance in S-nitrosylation (R-SNO) [2]. In other respects, when an oxidized cysteine residue is brought near a reduced cysteine residue, it generates a cystine unit with a disulfide bond (R-S-S-R′) that can alter protein folding, contributing to tertiary structure if the cysteines belong to the same polypeptide or to quaternary structure if they belong to different polypeptides. Owing to the physico-chemical properties of thiol groups and to their capacity to bind metals, proteins having these reactive cysteines play key roles in biology. They contribute for instance to ROS detoxification, to the control of cell redox homeostasis or to signaling transduction pathways in particular via redox post-translational modifications.

In most living organisms, thiol groups are mainly present in the sulfur-containing amino acid, cysteine, which is present in most proteins and is also a component of glutathione, a γ-Glu-Cys-Gly tripeptide existing either in a reduced form (GSH) or in oxidized forms, such as glutathione disulfide (GSSG) or nitrosoglutathione

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(GSNO). In plants, glutathione is present in most tissues with subcellular concentrations in the millimolar range [3,4] and is considered together with ascorbate as a major redox buffer [3,5]. Two enzymes: γ-glutamyl-cysteine ligase or γ-glutamyl-cysteine synthase (γ-GCS or GSH1) and glutathione synthetase (GS or GSH2) ensure the production of glutathione at the expense of ATP. The reduction of GSSG is catalyzed by glutathione reductase (GR), a NADPH-dependent flavoprotein [5]. The redox status of protein cysteinyl residues is controlled by two main types of enzymes termed thioredoxins (TRXs) and glutaredoxins (GRXs). Many of them, particularly TRXs, display disulfide reductase activity, and some are able to reduce sulfenic acid forms. GRXs are more specifically involved in the deglutathionylation of proteins reversibly modified by the formation of a mixed disulfide bond between glutathione and a cysteine. However, whereas it is firmly established that all GRXs from class I possess deglutathionylation activities, it is less clear whether GRXs belonging to classes II and III possess such activity [6]. Both TRXs and GRXs function via a catalytic site formed at least by a redox active cysteine which is generally separated in the primary sequence by two variable residues from another cysteine (often referred to as resolving cysteine) in most TRXs and in about half of GRXs or from a serine in the half remaining GRXs [6,7]. A WCGPC amino acid signature is generally quite well conserved among TRXs whereas a greater variability is found among GRXs being often of the CPYC, CPFC, CGFS or CCxC/S type. To obtain a complete view of the active site sequences and current classification of GRXs and TRXs, we invite the reader to refer to the following papers [8,9]. At the structural level, TRXs and GRXs adopt a specific TRX-fold that is usually characterized by a 4-stranded parallel beta-sheet core enclosed by 4 to 5 alpha-helices, and that is shared by several other protein families. In plant cells, the regeneration of oxidized TRXs and GRXs is generally achieved via distinct pathways (Fig. 1). For the large majority, GRXs use reduced glutathione as an electron donor but for example, a chloroplastic class II Grx from *Chlamydomonas reinhardtii* was shown to be recycled by the ferredoxin-Trx reductase [7,10]. The reduction of TRXs is more complex and further depends on their subcellular localization. Nuclear, cytosolic and mitochondrial TRXs are usually reduced by NADPH-thioredoxin reductases (NTR), enzymes with FAD cofactors [11] whereas chloroplastic TRXs are reduced in a light-dependent manner by a ferredoxin-dependent thioredoxin reductase (FTR), an iron-sulfur (Fe–S) enzyme composed of two different subunits and which converts the electron signal coming from photosystem I and relayed by ferredoxins into a thiol-reducing cascade [12]. Atypical reduction modes exist for some TRXs. A poplar TRX h4 and its plant orthologs are regenerated by the GSH/GRX system owing to the presence of an additional cysteine in the N-terminal region [13–15]. Some Trx-like and Trx-lilium can be recycled by GSH in a manner analogous to GRXs [16].

Until the last years, glutathione was mainly thought to act as a redox buffer in various processes like responses to environmental stress, plant–pathogen interactions and detoxification of xenobiotics and heavy metals [5]. Plant TRXs have been long presumed to mainly regulate photosynthesis and carbon metabolism enzymes [17] or to participate in the mobilization of seed reserves [18]. They have been also characterized as important actors in the responses of plants to oxidative stress [19]. The information concerning the sequence characteristics, the biochemical functions or the expression patterns of GRXs lag behind, since they have been identified later in plants compared with TRXs [7]. Although some have been reported quite early to play roles in flower development [20,21] and later in stress responses [22,23], the physiological roles of many GRXs remain elusive.

A role for TRXs and GRXs as key determinants in plant growth and development has only been recently uncovered together with the involvement of several ROS like NO or H_2O_2. This is in fact not surprising considering the capacity of the latter molecules to modify protein thiol groups. The cellular redox homeostasis is varying during specific developmental stages or in response to changing environmental conditions. It has thus to be tightly regulated and among the various types of effectors, thiol-containing components form an important signaling network. An additional layer of new information concerning the involvement of redox regulated circuits into developmental processes is the complex interplays that have been unveiled between glutathione in particular and several hormones. In this review, we describe the current knowledge and recent advances concerning the roles of glutathione and of disulfide reductases, GRXs and TRXs, in the control of development in relation to ROS and hormones.

2. Glutathione is essential for plant development

2.1. Direct involvement of glutathione in developmental stages of plants

Glutathione is synthesized in two steps catalyzed by the gamma-glutamyl cysteine synthase (GSH1) and the glutathione synthase (GSH2). In higher plants, GSH1 is exclusively located in plastids whereas GSH2 is dual-targeted to plastids and cytosol [24,25]. The crucial role of glutathione for plant development was first demonstrated by the characterization of different mutants in the biosynthesis pathway (Table 1). Unless GSH is added to the growth medium, Arabidopsis

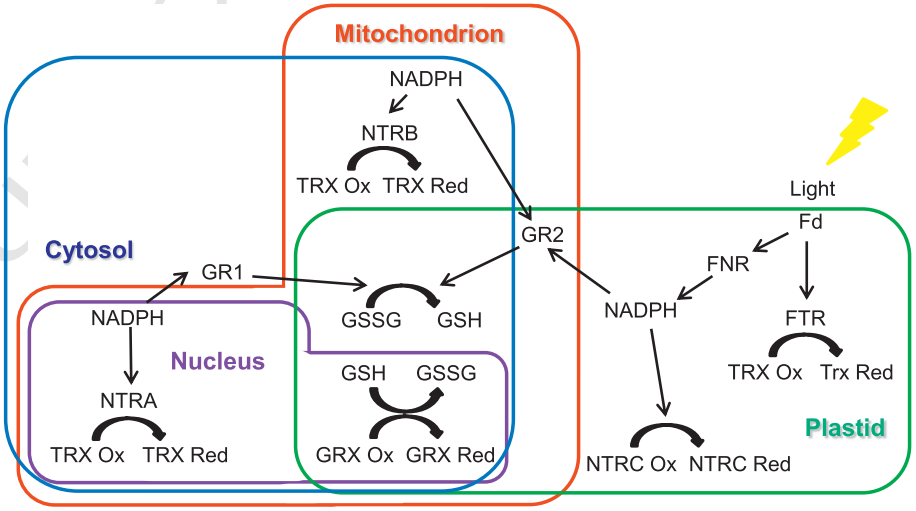

Fig. 1. Reduction pathways of the thiol-containing compounds, glutathione, glutaredoxins and thioredoxins in the main subcellular compartments of plant cells. GSH and GSSG, reduced and oxidized glutathione, respectively; GR, glutathione reductase (2 types, 1 and 2); GRX Ox and Red, oxidized and reduced glutaredoxin, respectively; TRX Ox and Red, oxidized and reduced thioredoxin, respectively; NTR: NADPH thioredoxin reductase (3 types: A, B and C); Fd, ferredoxin; FNR, ferredoxin $NADP^+$ reductase; FTR, ferredoxin thioredoxin reductase.

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