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Review

Plant phosphoinositides—complex networks controlling growth and adaptation☆

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ABSTRACT

Plants differ in many ways from mammals or yeast. However, plants employ phosphoinositides for the regulation of essential cellular functions as do all other eukaryotes. In recent years the plant phosphoinositide system has been linked to the control of cell polarity. Phosphoinositides are also implicated in plant adaptive responses to changing environmental conditions. The current understanding is that plant phosphoinositides control membrane trafficking, ion channels and the cytoskeleton in similar ways as in other eukaryotic systems, but adapted to meet plant cellular requirements and with some plant-specific features. In addition, the formation of soluble inositol polyphosphates from phosphoinositides is important for the perception of important phytohormones, as the relevant receptor proteins contain such molecules as structural cofactors. Overall, the essential nature of phosphoinositides in plants has been established. Still, the complexity of the phosphoinositide networks in plant cells is only emerging and invites further study of its molecular details. This article is part of a special issue entitled Phosphoinositides.

1. Plants—different yet similar to other eukaryotes

Plants are characterized by their sessile mode of life and their capacity to photosynthesize, making them the primary producers of most organic substance on earth. Also, plants are sources of diverse biochemical compounds (plant secondary metabolites) with nutritional and medicinal value that cannot be synthesized by other organisms. At the structural level, plants also differ in some ways from other eukaryotic cells types. For instance, plant cells are surrounded by cell walls, which preclude cell migration, and plant cell shape follows an intricate interplay of turgor pressure and cell wall-rigidity. However, despite numerous obvious differences to animal and fungal cells, plant cells share the basic cellular built with other eukaryotic cells. Basic similarities include the general subcellular organization and compartmentation of the cells, and the principal modes of membrane trafficking and some cytoskeletal structures that are involved [1]. In recent years it has emerged that phosphoinositides (PIs) are likely as important for the function of plant cells, as they are in other eukaryotic cells.

In all eukaryotes PIs can serve as lipid ligands for target proteins that possess specific PI-recognition domains, such as the Pleckstrin-homology (PH)-domain, the Fab1 YOTB Vac1 EEA1 (FYVE)-domain or the phagocytic oxidase (phox or PX)-domain, or others [2,3]. The binding to PIs can recruit proteins to membranes or modify the biochemical activity of various proteins, including enzymes, ion channels and ATPases [4–6]. The Arabidopsis genome encodes numerous proteins with putative PI-binding domains, which are candidates for regulation by PIs, but so far only little is known about the functional effects of such lipid-protein interactions. PIs can also be cleaved by phospholipase C (PLC), thus serving as the precursors of diacylglycerol (DAG) and inositol bis- or trisphosphates [4,5]. In animal cells signaling molecules such as DAG and inositol 1,4,5-trisphosphate ($Ins(1,4,5)P_3$) are important second messengers that activate protein kinase C [7] and effect Ca^{2+}-release from intracellular stores [8], respectively. It is an important distinction of plants that these downstream cascades appear to be absent. Generally, the links between PIs and Ca^{2+}-signaling have not so far been explored and remain largely unresolved. However, plant signaling networks are not necessarily less complex than those of animals. So far, the interconnections between PIs and other signaling pathways have just not been exhaustively studied in plants.

2. The biosynthesis of PIs in plants: enzymes and intermediates

As in other eukaryotes, plant PIs are derived from the membrane phospholipid, phosphatidylinositol (PtdIns), which can be phosphorylated by specific lipid kinases in different positions of the inositol head group [4–6]. Most PIs known from other eukaryotic organisms have been detected in plants, including phosphatidylinositol 3-phosphate (PtdIns3P), phosphatidylinositol 4-phosphate (PtdIns4P),

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phosphatidylinositol 5-phosphate (PtdIns5P), phosphatidylinositol 3,5-bisphosphte (PtdIns(3,5)P_2) and phosphatidylinositol 4,5-bisphosphate (PtdIns(4,5)P_2). The presence of phosphatidylinositol 3,4-bisphosphate (PtdIns(3,4)P_2) and phosphatidylinositol 3,4,5-trisphosphate (PtdIns(3,4,5)P_3) is still debated. Overall, the biosynthetic reactions leading to the formation of the known PI species are more limited than those reported for animal cells, due to the nature of the enzymes involved [9] (Fig. 1).

PtdIns is phosphorylated by PI-kinases to PtdIns-monophosphates, such as PtdIns3P and PtdIns4P. The genome of the model plant *Arabidopsis thaliana* encodes one PI 3-kinase (AtVPS34) [10,11] with similarity to the *Saccharomyces cerevisiae* Vps34 [12] (Fig. 1A). Both these enzymes are type III PI 3-kinases, and thus the 3-position of the inositol ring is phosphorylated only on PtdIns, but not on PtdIns-monophosphates or PtdIns-bisphosphates. PI 4-kinases are represented in Arabidopsis as four isoforms (PI4Kα1, PI4Kα2, PI4Kβ1 and PI4Kβ2) resembling mammalian PI 4-kinases (Fig. 1B). The α-isoforms contain a PH-domain that binds to PtdIns4P, the product of the reaction [13]. In contrast to yeast or mammals, there are two β-isoforms of PI 4-kinases in plants [9,14]. The eight members of an annotated type II subfamily of Arabidopsis PI 4-kinases γ contain ubiquitin-like domains and have not been demonstrated to harbor catalytic activity against PI-substrates [15]. These enzymes appear to be protein kinases rather than lipid kinases. PtdIns5P has been detected in plants [16], but based on the analysis of available plant genomes, there is no candidate for a PI 5-kinase. It appears that PtdIns5P is formed by an unknown phosphatase mediating the dephosphorylation of a PtdIns-bisphosphate precursor. The exact route of PtdIns5P-formation remains currently unclear.

The PtdIns-monophosphates PtdIns3P and PtdIns4P can be further phosphorylated by PI3P 5-kinases and PI4P 5-kinases, respectively, yielding PtdIns(3,5)P_2 and PtdIns(4,5)P_2. There are four isoforms of PI3P 5-kinases in Arabidopsis that resemble *S. cerevisiae* Fab1 [9] (Fig. 1C), and one isoform has recently been shown experimentally to transform PtdIns3P to PtdIns(3,5)P_2 in vitro [17]. So far it remains open, whether plant Fab1-like enzymes exclusively form PtdIns(3,5)P_2 or whether conversions of other PIs are also catalyzed. PI4P 5-kinases are represented in Arabidopsis by eleven isoforms (PIP5K1-11), which are categorized into two subfamilies [9] (Fig. 1D). Isoforms PIP5K10 and PIP5K11 make up subfamily A with domain structures similar to those of mammalian PI4P 5-kinases. Isoforms PIP5K1-PIP5K9 represent subfamily B and are characterized by the presence of additional N-terminal protein domains (Fig. 1D). These additional domains include an N-terminal (NT)-domain, a region not conserved in sequence between isoforms that is substantially larger in the enzymes of subfamily B over those of subfamily A. Furthermore, enzymes of subfamily B contain a membrane occupation and recognition nexus (MORN)-repeat domain and a variable linker (Lin)-domain, the latter of which is plant-specific. Enzymes of both PI4P 5-kinase subfamilies A and B prefer PtdIns4P as a substrate in vitro, yielding PtdIns(4,5)P_2 as a product, but will also display detectable catalytic activity towards PtdIns3P, which is transformed to PtdIns(3,5)P_2 [18–20]. A type II PIP-kinase (PI5P 4-kinase) has not been found in plants.

The lipid kinases involved in PI biosynthesis are counteracted by lipid phosphatases, adding complexity to PI metabolism. Only limited information is available to date about such phosphatases. A well-studied example are the phosphatase and tensin homolog deleted on chromosome ten (PTEN) enzymes, which are represented

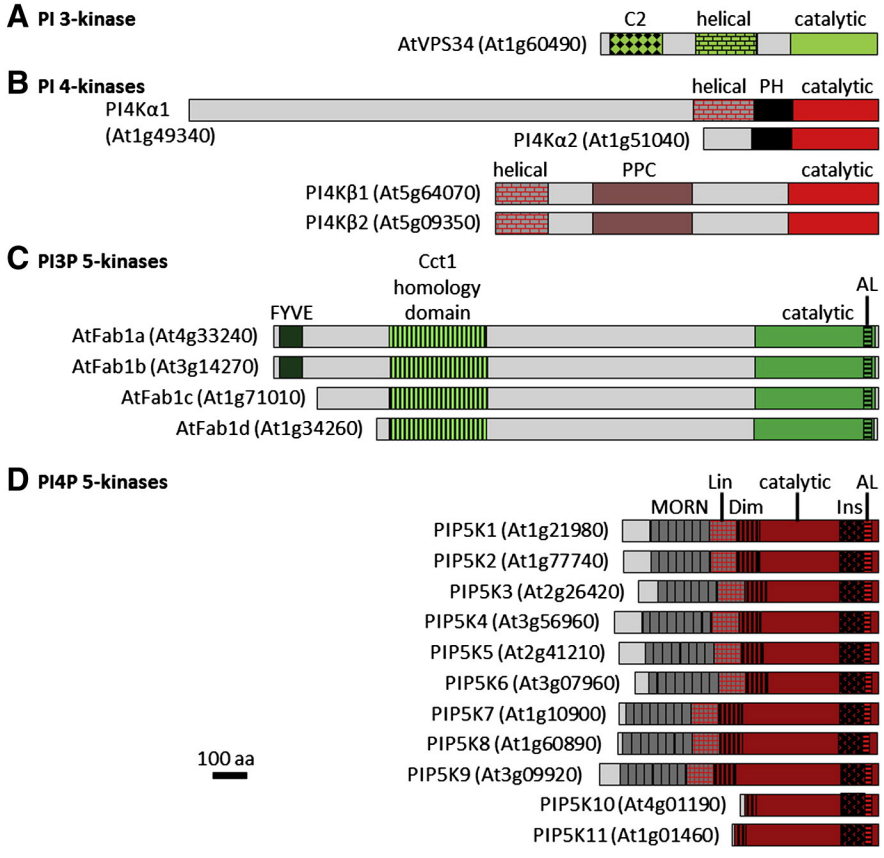

Fig. 1. Enzymes of PI biosynthesis in Arabidopsis. The Arabidopsis genome encodes various enzymes of PI biosynthesis, as indicated. The AGI locus identifiers for the corresponding Arabidopsis genes are listed in parentheses. A, PI 3-kinase; B, PI4-kinases. The putative γ-subfamily of PI 4-kinases is not depicted as no member has been shown to harbor PI 4-kinase activity. C, PI3P 5-kinases; D, PI4P 5-kinases. All enzymes and their domains are represented to scale. Grey domains indicate protein regions with unclear functional annotation. AL, activation loop; C2, Ca^{2+}-dependent lipid binding domain; catalytic, catalytic domain; Cct1 homology, chaperonine-containing t-complex protein1-homology-domain; Dim, dimerization domain; FYVE, Fab1 YOTB Vac1 EEA1-domain; helical, helical domain; Ins, variable insert domain; Lin, variable linker domain; MORN, membrane occupation and recognition nexus repeat domain; PH, Pleckstrin homology-domain; PPC, plant PI4K charged region-domain.

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