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Small polypeptide hormones in plant

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Abstract

Generally the cell-to-cell communications take place by classical phytohormones such as auxin, cytokinin, ethylene, gibberellin, and abscisic acid. Likewise the plant peptide hormones are also involved in various aspects of growth and development. The physicochemical interactions of peptide hormones with their receptors activate downstream signaling which modulates cellular functions. These peptide actively involved in plant defense system improvements against biotic and abiotic stress (es), growth and development over the past decade have heralded the beginning of a new and potential growing field of polypeptide signaling in plants. Here, we review the currently known major plant polypeptides, their receptor proteins, polypeptide/receptor-mediated signaling cascades and their functions in plant.

Keywords: peptide hormones, signal peptides, receptors, posttranslational modifications, cysteine-rich peptides, plant-insect interaction

Introduction

Cell-to-cell signaling mediated by hormones and membrane-localized receptors is one of the vital mechanisms by which the growth and development of multicellular organisms are regulated. The physicochemical interactions of such hormones with receptors activating downstream signaling, fates through conformational changes in the membrane-localized receptors, which modulates cellular functions. Thus membrane-localized receptors act as master switches of complex intracellular signaling processes in response to extracellular signals.

The first peptide hormone, insulin, was discovered in animals by Banting and Best in 1922 (Banting and Best, 1992) ^[1]. In plants, due to the early discovery of nonpeptidic hormones (like auxins, cytokinins, etc.), peptide hormones remained in the shadow for a long time. However, the first signal peptide, systemin, involved in defense reactions was detected in tomato 1991 (Pearce *et al.*, 1991) ^[2]. The discovery of this peptide inspired most plant biologists to search for other peptide signals. In 1996, phytosulfoalkines (PSK) were identified, which are involved in the regulation of cell division; PSKs were the first identified plant signal polypeptides with posttranslational modification (Matsubayashi *et al.*, 1996) ^[3].

The polypeptide give active signals for plant defense system improvements against biotic and abiotic stress(es), growth and development over the past decade have heralded the beginning of a new and potential growing field of polypeptide signaling in plants. Generally it is accepted that the peptides are substances whose molecules contain less than 50 amino acids. In such clause, it is completely incorrect to call some hormones as peptide, but it is necessary to call them proteinaceous (for example, in fact many CRPs are proteins). However, in the literature committed to peptide hormones, all peptide and protein hormones are called peptide hormones so as not to split up the family and not to create confusion in the definitions. We will follow this convention.

All signal peptides can be divided into three groups: two groups of secreted peptides (with their specific N-terminal signal sequence, which determines extracellular transportation) and one group of nonsecreted peptides without a signal sequence. The secreted groups include posttranslationally modified peptides (nine families identified) and cysteine-rich peptides (13 families identified). In a mature state, posttranslationally modified peptides (PTMP) are small (less than 20 AA) and, after translation, may undergo proteolytic processing and amino acid modifications that leads to the conformation changes in peptides.

Whereas the cysteine-rich peptides (CRP) includes larger (up to 160 AAs) proteins that are positively charged and, as a rule, contain from 4 to 16 cysteine residues, forming disulfide bridges, which are important for the formation of the three-dimensional structure of the peptide. The nonsecreted signal peptides (NSPs), lacking the N-terminal signal sequence, are also delivered to the extracellular space in some cases, where they act as an intercellular signal.

The number of groups of peptide phytohormones is constantly growing, since new families are discovered almost every year. For example, more than 30,000 ORF (open reading frames) have been found in *Arabidopsis thaliana*, encoding peptides ranging in length from 25 to 250 amino acids that have not yet been studied and characterized (Lease K.A. and Walker J.C., 2006) [4]. Here, we review the currently known major plant polypeptides, their receptor proteins, polypeptide/receptor-mediated signaling cascades and their functions in plant.

Posttranslational Modified Peptides (PTMPs)

A common feature of posttranslationally modified peptides is that their molecules, about 05–20 AAs, are formed from a larger precursor. In addition to proteolytic processing, posttranslational modifications of AAs, such as sulfation of tyrosine and hydroxylation of proline, followed by hydroxyproline arabinosylation, are important for the maturation of PTMP. Such modifications are essential to maintain the stability of the peptides as well as for their interaction with receptors (Okamoto *et al.*, 2016) [5]. The functions of PTMPs in plant development are extremely diverse. PTMPs include the following families of peptides: Clavata3/Embryo Surrounding Region-Related (CLE), Root Growth Factor/Golven/Cle-Like (RGF/GLV/CLEL), Plant Peptides Containing Sulfated Tyrosine (PSY), Phytosulfokine (PSK), Hydroxyproline-Rich Glycopeptide Systemins (HypSys), C-Terminally Encoded Peptides (CEP), Casparian Strip Integrity Factors (CIF), Inflorescence Deficient in Abscission (IDA), Pamp Induced Secreted Peptides (PIP). Proteolytic processing is of paramount importance for the maturation of PTMP. Little is known about the mechanisms of proteolytic processing, however, the families of enzymes that play a primary role in the processing and maturation of different PTMP groups have been identified: for example, the formation of functionally active IDA peptides requires enzymes of the subtilisin like proteinases (SBT) (Schardon *et al.*, 2016) [6], while carboxypeptidase SOL1 (SUPPRESSOR OF LLP1) for the processing of peptide CLE19 from the CLE family (Tamaki *et al.*, 2013) [7]. The hydroxylation of proline in PTMP is catalyzed by the enzyme prolyl-4-hydroxylase (P4H), a membrane protein localized in the ER and the Golgi apparatus (Gorres *et al.*, 2010) [8]. Tyrosine sulfation is mediated by tyrosyl protein sulfotransferase (TPST)-an enzyme in the Golgi apparatus that catalyzes the transfer of sulfate to the phenolic group of tyrosine. Tyrosine sulfation takes place during the maturation of the peptides PSK, PSY1, and RGF and is further important for their interaction with receptors (Song *et al.*, 2016) [9]. The *tpst-1* mutant is characterized by serious defects in development: it has reduced root meristem and lacks coordination between cell division and enlargement. Treatment of PTMP with PSK, PSY1, and RGF1 results in the complete restoration of the normal phenotype in the *tpst-1* mutant, which indicates the role of tyrosine sulfation in their maturation (Matsuzaki *et al.*, 2010) [10]. PTMP receptors are serine-threonine receptor protein kinases with an extracellular domain containing leucine-rich repeats having receptor-like kinase (LRR-RLK).

the CLE, IDA, RGF, PIP, PEP, and CIF receptors belong to LRR-RLK subclass XI, receptor PSK–PSKR to LRR-RLK subclass X, and the receptor for HypSys peptides is unknown (Hirakawa *et al.*, 2017) [11].

The extracellular domains of the LRR-RLK contain leucine-rich repeats (LRR), which form the helix necessary to form the surface for interaction with the peptide ligand. The “defective” LRR-RLK, lacking a ligand-binding or kinase domain, often act as receptors and coreceptors for PTMP binding (Yamaguchi *et al.*, 2016) [12].

Clavata3/Embryo Surrounding Region-Related (CLE)

The most studied peptide phytohormones are CLE peptides. The Genes encoding CLE peptides and along with their receptors have been discovered in various plants, including monocots, dicots, algae and mosses (Kucukoglu, M. and Nilsson, O., 2015) [13]. The functional part of this peptide is the CLE-domain located near the C-terminus of the full-length precursor peptides. Instantaneously after the translation, CLE precursor peptides undergo proteolytic processing, consequently of which only the CLE domain remains from the precursor peptide. Thus, the mature CLE peptide consists of 12–13 AAs and contains from 1 to 3 highly conserved proline residues. The first identified member of the CLE family was CLAVATA3 (CLV3), which was identified as a key regulator of the activity of the shoot apical meristem; its function was well known to suppress the expression of the *WUSCHEL* (*WUS*) gene that encoding a homeodomain-containing TF, which is a regulator of the organizing center of the meristem (Schoof *et al.*, 2000) [14]. The CLE peptides is expressed in the peripheral layers apical meristem of the shoot and binds to three receptors: CLV1 (CLAVATA1), CLV2 (CLAVATA2) (which forms a complex with the receptor kinase SUPPRESSOR OF LLP1-2 (SOL2)/CORYNE (CRN) to bind CLV3) and RECEPTOR-LIKE PROTEIN KINASE 2 (RPK2)/TOADSTOOL2 (TOAD2). The receptors, by linking the CLE peptides, trigger an almost unexplored signaling pathway, leading to repression of the *WUS* gene transcription. The small GTPase ROP, the MAP kinase cascade, as well as protein phosphatases of the 2C POLTERGEIST (POL) and POLTERGEIST-LIKE1 (PLL1) families are among the identified components of this pathway (Hirakawa *et al.*, 2017) [11].

Peptide CLE40 is synthesized in columella cells and then bind to receptor kinases CLV1 and ACR4 (ARABIDOPSIS CRINKLY 4), forming homodimer and heterodimers. The *CLE41* and *CLE44* genes, expressing in phloem, encode TDIF proteins that stimulate cambium cell proliferation and inhibit xylem differentiation (Ito *et al.*, 2006) [15]. The peptides CLE41 and CLE44 enter in to the apoplast from the phloem and then they bind to the TDIF receptors RECEPTOR/PHLOEM INTERCALATED WITH XYLEM (TDR/PXY) on the plasma membrane of procambium and cambium cells; the signaling induced by them leads to the activation of the expression of another member of the *WOX* gene family, *WOX4*, which functions as a positive regulator of cambium cell proliferation (Kondo Y. and Fukuda H., 2015) [16].

The peptide CLE10 is well known in regulating the development of the plant conducting system. It negatively regulates vascular development by inhibiting the expression of the *ARR* genes of type A, *ARR5* and *ARR6*, encoding cytokinin signaling repressors (Kondo *et al.*, 2011) [17]. We know the cytokinins stimulate the proliferation of cambium cells and

inhibit xylem cell differentiation; it is believed that CLE10, enhancing cytokinin signaling, negatively regulates the formation of vessels. The CLE45 peptide is involved in the development of phloem, which negatively regulates the formation of protoxylem in *A. thaliana* root meristem. The LRR-RLK BAM3 and STERILITY REGULATING KINASE MEMBER1 (SKM1) take part in the CLE45 reception.

In addition to the regulation of histogenesis in the postembryonic period, some CLE peptides are also involved in the regulation of embryogenesis; for example, the CLE8 peptide is a regulator of the early stages of embryogenesis and seed development (Yamaguchi *et al.*, 2016) [12]. The target of CLE8 is the *WOX8* gene, which regulates the identity of the basal domain of the embryo; the CLE8 receptor is unknown, but the synthetic peptide CLE8 may bind to the receptor kinase BAM1 (Osipova *et al.*, 2012) [18].

In legumes, some CLE peptides, such as MtCLE13 in *Medicago truncatula* and PsCLE13 in *Pisum sativum*, are the components of nodule autoregulation system and inhibit formation of excessive nodules (Yamaguchi *et al.*, 2016) [12]. The CLE peptides of this group is formed in the leaves via the xylem, where they interact with receptor-CLV1-like receptor kinase, MtSUNN of *M. truncatula*/PsSYM29 of *P. sativum* and trigger an unknown secondary signal, which is supposedly going to be part of the root and overwhelms development of nodules. In addition to this, some CLE peptides can also regulate the number of lateral roots formation. The expression of the *CLE1*, *CLE 3*, *CLE 4*, and *CLE 7* genes in *A. thaliana* is induced by a lack of nitrogen in the roots, and their overexpression inhibits the growth of the lateral root primordia, which prevents growth of the root system in adverse conditions. So in some adverse conditions like drought stress, salinity stress, water logging stress etc, CLV1 might be the target to increase number of lateral root formation under such stressed conditions.

More importantly some CLE peptides are regulating interactions with pathogens. For example, during the development of tumors induced by *Agrobacterium tumefaciens* some CLE genes were expressed. Surprisingly, some parasitic nematodes also secrete CLE-like peptides, which are necessary for successful plant infection. Thus, in the genome of the nematode *Heterodera glycines*, which induces the development of galls on plant roots, there are genes *HgCLE1/2B10/Hg-SYV46* and *HgCLE2/4G12*, encoding CLE peptides and expressing in cells of the pharyngeal glands. On the surface of plant cells, CLE peptides secreted by nematodes bind to the receptor complex CLV2/CRN (Replogle *et al.*, 2013) [19].

Root Growth Factor/Golven/Cle-Like (RGF/GLV/CLEL)

Generally these types of peptides are 13-18 AAs long and contain hydroxylated proline and sulfated tyrosine by the TPST enzyme (Amano *et al.*, 2007) [20]. These peptides were first identified in *A. thaliana* and subsequently detected in other plants too (Matsuzaki *et al.*, 2010) [10]. The mature RGF peptides are formed from a precursor peptide 86–163 AA long by proteolytic processing and correspond to the conserved sequence of a GLV domain.

It is well known that the RGF1 peptide is implicated in maintaining the undifferentiated status of cells of apical meristem of the root and the coordination of divisions of the columella stem cells (Matsuzaki *et al.*, 2010) [10]. Another function of RGF peptides is related to the control of polar auxin and root gravitropism: the *GLV3*, *GLV6* and *GLV9* genes overexpression leads to the growth of wavy roots

(therefore, the family got its name “GOLVEN,” which means “waves” in Dutch) (Whitford *et al.*, 2012) [21]. Treatment of roots with RGF3 peptide causes a rapid accumulation of PIN2 protein, which is one of the important regulators of polar auxin transport, in the plasma membrane and vesicles of epidermal cells of the root tip (Whitford *et al.*, 2012) [21]. Thus by regulating the polar transport of auxin, RGF/GLV/CLEL peptides can participate in the control of other auxin-dependent processes, such as the growth of root hairs and the development of lateral roots. Recently, RGF peptide receptors called RGF RECEPTORS - RGFR1, RGFR2, and RGFR3 have been found in *A. thaliana*.

Phytosulfokines (PSK)

Phytosulfokines were known by searching for a cell proliferation factors in a suspension culture of plant cells. In 1996, two very short peptides (a total of 4-5 AAs), consisting of a disulfated pentapeptide named PSK α (YIYTH) and disulfated tetrapeptide PSK β formed from PSK α precursor by removing the C-terminal glutamine residue, were isolated from the *Asparagus officinalis* mesophyll culture [Pearce *et al.*, 1991] [2], (Yang *et al.*, 1999) [22].

Adding PSK to the medium causes cell division even in low density cultures. However, PSK cannot stimulate cell division without auxin and cytokinin (Matsubayashi *et al.*, 1999) [23], thus PSK is a quorum signal that allows cells in a culture to divide when there is, firstly, a certain cell density and, secondly, stimulators of cells division - auxins and cytokinins. In planta PSK are formed from protein precursors consisting of 80–120 AAs and containing the N-terminal signal sequence, which directs the protein to the secretory pathway (Yang *et al.*, 1999) [22]. In *A. thaliana*, five genes encode the precursors of PSK α (*AtPSK1-5*) (Matsubayashi *et al.*, 2006) [24]. The precursor peptide undergoes sulfation at conservative tyrosine residues; this reaction is catalyzed by the TPST enzyme; the sulfated precursor of PSK is then subjected to proteolytic processing in the apoplast using the subtilase (serine protease) AtSBT1.1 (Srivastava *et al.*, 2008) [25]. PSK receptors are Phytosulfokine Receptors (PSKR) of protein kinases, which were first found in carrots (DcPSKR1) (Matsubayashi *et al.*, 1999) [23]. Interestingly, PSK receptors are unique LRR-RLKs that possess guanylate cyclase activity along with protein kinase activity as well as the properties of calmodulin-binding proteins: the kinase domain of AtPSKR1 contains a guanylate-cyclase catalytic center and a binding site for calmodulin that are important for the PSK signal transmission (Sauter M., 2015) [26].

Plant Peptides Containing Sulfated Tyrosine1 (PSY1)

The PSY1 is about 18 AAs long glycopeptide containing one sulfated tyrosine residue and two hydroxylated pralines functionally similar to PSK. There are two genes in *A. thaliana* encoding the PSY1 precursor peptides. They are expressed in the whole plant but with maxima of expression in shoot apical meristem and root elongation zone. The receptor of PSY1 is PSY1R (PSY1 RECEPTOR) receptor kinase, which forms a heterodimer with the SERK1 coreceptor (SOMATIC EMBRYOGENESIS RECEPTOR KINASE1) upon ligand binding. The target of its action is membrane H⁺-ATPase AHA2. PSY1R kinase promotes acidification of the intercellular space and increases cell wall lability, which promotes cell enlargement (Oehlenschlaeger *et al.*, 2017) [27].

Functionally like PSK the PSY1 peptides are also involved in regulation of the plants and pathogens. Thus, it was shown that the expression of *PSKR1*, *PSK1*, *2*, *4*, and *PSY1* genes

was induced upon infection of *Pseudomonas syringae* pv. *Tomato*. Activation of the PSY1R receptors leads to inhibition of salicylic acid signaling (in response to biotrophic pathogens) and increases jasmonic acid signaling and, therefore, PSY1 peptide receptors enhances protection against necrotrophic pathogens and response to injury.

Inflorescence Deficient in Abscission (IDA)

The plants unlike animals constantly forms new organs, such as leaves, flowers, and lateral roots. With aging leaves and flowers, as well as fruit ripening, the expression of the genes encoding the Inflorescence Deficient in Abscission (IDA) peptides begins in response to a reducing in auxin level and a rising ethylene level in the cells of the separation layer. In *A. thaliana* genome eight *IDA-LIKE (IDL)* genes have been identified. Their products are peptides of 70–80 AAs long that undergo proteolytic processing (Vie *et al.*, 2015) [28]. The functional part of such peptide is the C-terminal 20 AAs domain which is called EPIP (Extended PIP). It was revealed that exogenous EPIP restores the phenotype of *ida* mutant (Stenvik *et al.*, 2008) [29].

The IDA peptides bind to HAE (HAESA) and HSL2 (HAESA-Like2) receptor kinases on the extracellular cell surface of the separation layer. Once it binds to receptors, the MAP kinase cascade (Mitogen-Activated Protein Kinase) is launched. Activation of this MAP kinase signaling cascade stimulates the expression of genes encoding enzymes, which be used as “disintegrating agents” of the cell wall (Cho *et al.*, 2008) [30]. An additional function of IDA peptides is the regulation of lateral root growth (Kumpf *et al.*, 2013) [31]. Further IDA peptides activate the expression of genes that play a role in the reorganization of the cell wall.

The physiochemical changes in the properties of the cell wall can impinge on the resistance of plants to phytopathogens. Therefore, IDA peptides may be involved in plant-microbial interactions. It has been shown that IDL6 activates expression of *ADPG2* gene encoding polygalacturonase, which reduces pectin content and leaf strength, making it less resistant to bacterial infection (Wang *et al.*, 2017) [32].

Hydroxyproline-Rich Glycopeptide Systemins (HypSys)

The Hydroxyproline systemins are plant protective signal peptides. They are not like to systemins but have similar biological activity and the same size of the molecule for which they got their name. Yet, various HypSys peptides are isolated from tobacco, tomatoes, petunias, nightshade, and sweet potatoes. The most studied HypSys peptides are NtHypSysI and NtHypSysII, which are originate in tobacco. The NtHypSysI and NtHypSysII sequences are located at different ends of the precursor peptide: NtHypSysI near the N-terminal end and NtHypSysII near the C-terminal end [Pearce, G 2011 59]. Nothing is currently known about the HypSys peptide receptors. The expression of the many genes encoding HypSys is augmented in *Nicotiana tabacum* when it is eaten by the larvae of *Manduca sexta* and the imago of *Bemisia tabaci* (Pearce, G., 2011) [33]. Additionally, it has been shown that the *HypSys* transcripts are accumulated in tomato, tobacco, petunia, nightshade, and sweet potatoes under mechanical damage or treatment with methyl jasmonate (Pearce, G., 2011) [33]. Such transcripts accumulation in response to eating or wounding indicates functions of HypSys as a contributor in plant defense reactions. Undeniably, the overexpression of *NtHypSys* in transgenic *N. tabacum* plants increases the number of protease inhibitors and polyphenol oxidases, consequential in improved protection from the

larvae. Recently, it has been exposed that tomato systemin and HypSys act in a coordinated manner in response to herbivores eating, stimulating the synthesis of jasmonic acid (Pearce, G., 2011) [33].

Cystein-Rich Peptides (CRP)

Cysteine-rich peptides (CRP) are a wide-ranging group of plant polypeptides. Its distinctive features are the size (up to 160 AAs residues) and they contain a C-terminal domain containing 2-16 cysteine residues. The CRP peptides like PTMP undergo the posttranslational proteolytic processing during their maturation and they have only the C-terminal domain, containing conserved cysteine residues.

The CRPs perform various functions, such as cell growth by enlargement, differentiation of specific cell types, and interaction with symbiotic and pathogenic microorganisms (Higashiyama T., 2010) [34]; (Qu *et al.*, 2015) [35]. In some plant species the CRP encoding genes accounts for up to 2% of the total protein-coding genes. This group includes Rapid Alkalinization Factor (RALF), *S*-Locus Cys-Rich/*S*-Locus Protein 11 (SCR/SP11), Lycopersicon Anther-Specific Protein 52 (LAT52) and Stigma-Specific Protein 1 (STIG1), Small Cystein Adhesion/Lipid Transfer Protein (SCA/LTP), Tapetum Determinant1 (TPD1).

The CRP is secreted into the apoplast, where they are bound on LRR RLK family's receptor kinases. Additionally, the SERK receptor kinases often act as co-receptor for the CRP receptors. Besides to signal peptides, they include defensins, antimicrobial peptides found in plants and animals (Stotz *et al.*, 2009) [36], therefore CRP are frequently called defensin-like peptides.

Rapid Alkalinization Factor (RALF)

The Rapid Alkalinization Factor (RALF) peptides were first isolated from tobacco leaf cells as factors that significantly increase the pH of medium when they were added to a tobacco cells culture (Olsen *et al.*, 2002) [37]. Such peptides suppress cell enlargement during plant development. About 34 genes encoding RALF peptides were detected in *A. thaliana* (Olsen *et al.*, 2002) [37]. These peptides are matured by proteolytic processing from 115 AAs precursor. Matured RALF peptides bind to the FERONIA receptor kinase (FER). Newly, RIPK receptor-like kinase has been shown to interact with FER to bind RALF. Its components of signaling include the Ca²⁺ signaling and the MAP kinase cascade (Murphy E. and de Smet I. 2014) [38].

The RALF raises the pH of the medium thus suppresses AHA activity and negative regulators of cell enlargement. It is antagonists of auxin and PSY peptides. The auxin and PSY increase cell wall lability by acidifying the intercellular space consequentially activating membrane H⁺-ATPases while RALF peptides operate in the opposite manner.

Tapetum Determinant1 (TPD1)

The TPD1 peptides (about 100 AAs) are essential for the specialization of tapetum cells, which necessary for the normal maturation of pollen. In the anthers of the *tpd1* mutant, there is no layer of tapetum cells, which leads to male sterility of plants. In contrast, *TPD1* overexpression increases the proliferation of the anther tapetum cells and slow down the destruction of tapetum in the process of pollen maturation (Yang *et al.*, 2005) [39]. The *TPD1* gene encodes 176 AAs long precursor protein is expressed in microsporocyte progenitor cells. This precursor protein has an N-terminal signal sequence and a C-terminal functional domain. only the

100 AAs C-terminal functional domain containing six conserved cysteine residues remains from the precursor peptide (Huang *et al.*, 2016) ^[40]. The Lrr-Rk Excess MicrosporocyteS1 (EMS1)/Extra Sporogenous Cells (EXS) are the known receptor for TPD1 peptide. Binding of TPD1 to their receptor activate the expression of *A9*, a marker gene of tapetum cells and periclinal division of tapetum cells (Huang *et al.*, 2016) ^[40].

S-Locus Cys-Rich/S-Locus Protein 11 (SCR/SP11)

The SCR/SP11 peptides are involved in controlling the self-incompatibility reaction. The self-incompatibility reaction take place when there are identical alleles of *S*-locus. Sporophytic incompatibility depends on the genotype of male sporophyte tissue in which pollen was formed while gametophytic self-incompatibility depends on the genotype of pollen grain. The mature form of the SCR/SP11 peptide has 6 kD mass and contains approximately 50 AAs a length including eight cysteine residues forming four disulfide bridges (Qu *et al.*, 2015) ^[35]. The gene is expressed in tapetum and ripening pollen grain. The *SCR/SP11* gene product accumulates in the pollen shell and acts as a ligand for SRK kinase homodimers exposed on pistil stigma cell membranes (Qu *et al.*, 2015) ^[35].

Lycopersicon Anther-Specific Protein 52 (LAT52) and Stigma-Specific Protein 1 (STIG1)

The rate at which the pollen tube growth, which is stimulated by both the autocrine signals of the pollen grain itself and the signals secreted by the pistil tissues, is one of the determining factor in the productivity of flowering plants. In tomato (*Solanum lycopersicum*) plant, the CRP LAT52 and the CRP STIG1 is the stimulating signal of the pollen grain and of the pistil tissue respectively (Tang *et al.*, 2004) ^[41]. The matured STIG1 has 7 kD mass and contains 14 cysteine residues.

The PRK2 (Pollen Receptor Kinase 2) is the receptor for LAT52. The PRK2 is one of the LRR-RLK present on the pollen grains surface (Huang *et al.*, 2016) ^[40]. The binding of LAT52 to its receptor PRK2 leads to the activation of pollen tube growth. Unlike LAT52 peptide, STIG1 binds to PRK2 receptor at the stage of its elongation. The STIG1 peptide is present in the exudates of stigma and accumulates on surface of germinating pollen tube.

Stigma/Style Cystein-Rich Adhesin/ Lipid Transfer Proteins (SCA/LTP)

This type of peptides stimulating the adhesion of the tube to the tissues of the maternal sporophyte and consequentially regulate the growth of pollen tube by. The Stigma/Style Cystein-Rich Adhesin (SCA) is the first identified peptide of this group in pistil cells of a lily plant (Chae K. and Lord E.M. 2011) ^[42]. It has a mass of 9-10 kD and includes eight cysteine residues. The SCA interact with the pectins of the cell walls. Similar functions are achieved by Lipid Transfer Protein 5 (LTP5), ortholog of SCA in *A. thaliana* (Chae K. and Lord E.M. 2011) ^[42]. The mature LTP peptide consists of four helices stabilizes by four disulfide bonds. Until the functions of most LTPs are not fully understood, but their role presently includes the regulation of plant-microbial interactions, resistance to abiotic stresses, regulation of pollen tube growth, cutin synthesis and participation in somatic embryogenesis. Currently the receptors and signaling pathways of SCA/LTP peptides are unknown.

Nonsecreted Signal Peptides

The nonsecreted signal peptides (NSP) do not contain an N-terminal secretory sequence, and, therefore, these peptides perform their important functions by either remaining inside the cell or by entering into the apoplast during cell destruction. Like other secretory plant signal peptides, NSPs are translated as long precursors, whose proteolytic processing at specific sequence is main key to the formation of functionally active mature peptides. The NSP group includes systemin, Plant Elicitor Peptides (PEP) and Early Nodulin 40 (ENOD40) peptides.

Systemin

The first detected and isolated plant peptide is Systemin in tomato leaves in 1992 (Banting and Best, 1992)^[1]. It consists of 18 AAs residues and is involved in the activation and enhancement of plant defense response against phytophages. The systemine is formed from its precursor called Prosystemin, which consists of 200 AAs. systemine does not have an N-terminal signal sequence. Expression of the prosystemin gene is induced by any mechanical damage or/and insect phytophagous damage. An extremely low concentration (40 fmoles) of exogenous systemin induces the expression of genes encoding serine protease inhibitors in tomatoes. When wounding, systemin can enters in to the conduction system and transferred to other parts of the plant to induce a defensive reaction. Additionally systemin also stimulates the release of plant volatile substances that attract parasitize insects of phytophages attacking insect of the plant (Corrado *et al.*, 2007) ^[43]. Thus, systemin is implicated not only in the direct but also in the indirect mechanism of regulation of the plant's protective response to external stimuli by biotic stress (ess). The SR-160 (Systemin Cell Surface Receptor) protein (160 kD) acting as receptor for specifically binding to systemin, After binding of systemin to receptor, membrane bound phospholipase is activated, which releases linolenic acid from the phospholipids of the cell membrane. linolenic acid is a precursor of biosynthesis of jasmonic acid which is one of the main "protective" plant hormones (Li *et al.*, 2003) ^[44].

Plant Elicitor Peptides (Pep)

The PEP1 protein was detected as an extracellular peptide with protective functions. The matured PEP1 protein is 23 AAs long formed from the processing of 92 AAs peptide precursors. In view of the fact that the PEP1 precursor peptide lacks a specific N-terminal signal sequence, it is assumed that the mature PEP1 enters in to the extracellular space when a cell is destroyed as a result of injury or attack by pathogens, that means PEP1 peptide do functions as DAMP.

The PEPR1 and PEPR2, belongs to LRR-RK, are receptors for PEP1 (Yamaguchi *et al.*, 2010) ^[45] and BAK1/SERK3 kinase is the co-receptor interacting with PEPR1 and PEPR2 since BAK1/SERK3 kinase lacks a ligand-binding domain. When PEP interacts with PEPR1 and PEPR2 receptors, systemic immunity is activated and increases the plant's resistance to various pathogens. In addition, PEP1 in *A. thaliana* activates the defensin *PDF1.2* gene expression and increases the production level of hydrogen peroxide, which is necessary for the improvement of the immune response (Hou *et al.*, 2014) ^[46].

Early Nodulin 40 (ENOD40)

The nodules formation in legumes is associated with dedifferentiation of the root cortex cells caused by rhizobial nodule factors (Nod-factors). Subsequently expression of

nodulin genes, one of which is *ENOD40*, induced in plant tissues. The *ENOD40* gene is the target of the Nodule Number Control1 (NNC1) Transcription Factor, which negatively regulates nodule formation (Wang *et al.*, 2014)^[47]. However, due to its small size, the ENOD40 peptides may possibly be able to move from cell to cell through a symplast. The main principle function of ENOD40 is to initiate cell division in root bark cells during the initial nodule formation stage. The interaction of ENOD40 with sucrose synthase was also shown, therefore it is assumed that they promote the entry of sucrose into the root cortex cells and contribute to their division.

Conclusions

The peptide phytohormones regulate the development of plants and they participate in growth responses to various external and internal environmental factors, acting both locally and systemically. In this review, we tried to take into account of all the functionally well characterized classes of peptide phytohormones. Despite the great diversity, peptide hormones have a number of common properties such as the production of functionally active peptides is characterized by the “maturation” by proteolytic cleavage of the precursor protein. All peptide phytohormones function outside the cell by binding to the receptors on the plasma membrane, while all identified receptors and co-receptors of these peptides belong to the receptor kinases with leucine-rich repeats, LRR-RLK. In addition to studying the mechanisms of interaction between peptide phytohormones with their receptors, research in the field of peptide plant growth regulators is aimed at finding the underlying components of signaling cascades activated in a plant cell during the interaction of signal peptides with LRR-RLK. A promising line of research is to the study how the peptide phytohormones interact with other plant hormones. A number of data indicating the presence of such interactions has been obtained. The RGF peptides regulate the polar transport of auxin in the root (Whitford *et al.*, 2012)^[21]; PSK peptides stimulate cell division only in the presence of auxin and cytokinin (Matsubayashi *et al.*, 1999)^[23]; expression levels of some *CLE* genes can be regulated by cytokinin and auxin, whereas the *CLE* peptides themselves (*CLE10*) can inhibit the expression of the *ARR5* and *ARR6* genes, activating cytokinin signaling (Kondo *et al.*, 2011)^[17].

Another direction in the study of peptide phytohormones is related to their implication for the development of plant pathogen, insect and pest tolerance in plants. Seed priming with such peptide hormones/ externally applying peptides hormones might be develop earlier tolerance in plant that may helps to reduce losses and increase productivity of agricultural crops.

Thus, the keen study of peptide phytohormones is an actively developing area of modern biochemistry, physiology and genetics of plant development, very promising in terms of obtaining fundamental knowledge and practical application in agriculture.

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