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Plant cytokine or phytocytokine

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Peptide hormones play an important role in plant growth and development. Some of them are secreted by stem cells and also regulate plant immunity through cell-cell communication and reprogramming the expression of immune related genes, such as CLAVATA3p (CLV3p) and phytosulfokine (PSK). These peptides play similar roles as cytokines in plant innate immunity. As explosive progress of plant omics, more and more such functional peptides will be discovered. I recommend that they should be named as plant cytokines or phytocytokines. This nomenclature will be convenient for study of plant secretory peptides and plant innate immunity.

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Cytokine is a group of peptides secreted by immune or neuron cells, working as signals of intercellular communication and immunity in mammals. On the earth, higher plants encounter the similar environment full of microbes as mammals, so the similar module of innate immunity has been evolved in all these organisms.[1] For example, T3SS effectors injected by bacteria into host cells can be recognized by NB-LRR proteins from both higher plants and mammals. Lipopolysaccharide can be bound by the conserved LPS binding protein in animals and plants. A great progress has been made in this field where many peptide hormones have been found to regulate plant growth and development. However, whether some peptide hormones involved in plant innate immunity acting as mammalian cytokines was still unknown.

In 2011, Lee et al. reported that stem-cell triggered immunity through CLV3p-FLS2 signaling.[2] They found that the CLV3 peptide (CLV3p) not only regulated division and differentiation of shoot apical meristem (SAM) cells through CLV1/2, a couple of Leucine Rich Repeat receptor kinases, but also enhanced the innate immunity via FLS2, a bacterial flagellin receptor kinase independently. CLV3p is a glycopeptide of 13 amino acid residues secreted by SAM cells, and regulates the expression of the transcriptional factor, WUS.[3] Its precursor consists of 96 amino acid residues, including an N-terminal sigal sequence and a C-terminal active peptide. It belongs to CLV/CLE peptide gene family. Some members of this gene family participate in development of plant memristem mediated by CLV1/CLV2 heterogonous kinases. The flg22-FLS2 signaling is one of important PTI (pathogen associated molecular pattern triggered immunity) regulatory pathways in higher plants to recognize environmental bacteria. The peptide of bacterial flagellin (flg22) binds to FLS2, and then this receptor kinase is autophosphorylated, followed by interacting with BIK1 and BAK1. Subsequently, the MAPK cascade is activated, and phosphorylates transcriptional factors of WRKYs that reprogram the expression of defense related genes (such as FRK1 and PR1). Lee's work revealed that FLS2 can recognize CLV3p to active flg22-FLS2 immune pathway, though the interacting sites on the receptor are not yet identified. In all, CLV3p is the first secretory peptide positively regulating plant immunity through intercellular communications.

Most recently, Igarashi et al. reported that PSK attenuates PTI in *Arabidopsis thaliana*.[4] PSK is a sulfated pentapeptide ($Y_{SO3H}IY_{SO3H}TQ$),[5] deprived from a group of prepropeptides with length of ~80 amino acid residues. These precursor peptides contain an N-terminal signal sequence and a conserved C-terminal active peptide, and are encoded by a multiple-gene family in higher plants. In *A. thaliana*, PSK precursors are encoded by 6 genes (*AtPSK1–6*). PSK is perceived by PSKR (PSK receptor), a LRR-receptor kinase to control cell proliferation, differentiation, growth and longevity in *A. thaliana*, though its signaling pathway has not been completely elucidated. Interestingly, the expression of some *AtPSK* genes is induced by fungal or bacterial pathogens. Igarashi' genetic data revealed that PSK suppresses PTI mediated by AtPSKR, which is also required for plant development. It is still not clear whether PSK interacts with other immune-related receptor kinase like FLS2. In fact, PSK is the first secretory peptide suppressing plant immunity.

Both CLV3p/CLEp and PSK regulate plant PTI, including plant growth and development. They share common features as cytokines as following. First, they are secreted by stem cells through N-terminal signal sequences, and active peptides are located at C-terminal. Second, they harbor post-translational modifications and act as signals of cell-cell communication. Third, they are perceived by LRR-receptor kinases and reprogram the expression of downstream genes. Lastly, they both regulate plant development and immune. Therefore, these peptides act similarly as cytokines in plant innate immune. I recommend that these peptides are called as plant cytokine or phytocytokine. The questions whether these plant peptides share the same ancestor with cytokines in evolution and these peptides are older than cytokines in evolutionary history still need be further answered. With the development of plant genomics, transcriptomics, proteomics and metabolomics, more and more "phytocytokines" will be discovered in plants. They will play an essential role in signaling of plant innate immunity.

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