Srivastava have contributed equally to this work.

**INTRODUCTION**

Plants are deprived of mechanical articulation in parts of their bodies. Unlike animals, which defend themselves from enemies through fight and flight, plants are comparatively more vulnerable to damages caused by biotic and abiotic stresses due to their sessile life style. Also, by default, they are programmed to replace lost body organs such as leaves and flowers on regular basis. The pluripotent stem cells, which are the sustainer of their lifelong activities, provide a constant supply of precursor cells to form differentiated tissues and body organs (Aichinger et al., 2012). In plants, the shoot apical meristem (SAM), the root apical meristem (RAM), and the vascular meristem are the custodians of stem cells. These stem cell niches maintain a specific signaling environment to stop them from entering into differentiation all at once yet keep a required number of undifferentiated stem cells through a process of self-renewal (Aichinger et al., 2012; Hwang et al., 2012). Being a custodian of the next generation of plants through seeds and flowers, the SAM constantly supplies cells to meet the programming and contingency requirements and is expected to safeguard its integrity from agents that can derail its genetic preprogramming (Aichinger et al., 2012; Hwang et al., 2012).

It is noteworthy to mention that phytoplasmal infection reprograms the meristem determination. Thus it changes tomato plant apex architecture through pathogen induced meristem derailment (Wei et al., 2013). Likewise, by deploying 2b-suppressor protein, Cucumber Mosaic Virus (CMV) inhibits anti-viral RNA silencing surveillance system and causes infection in the SAM (Sunpapao et al., 2009). Despite the pathogen guided interventions in the SAM stem cell niches, disease free plants can be generated from the SAM and this underscores the sterile nature of the shoot apex.

The exact mechanisms how the SAM stem cell niches are naturally immune was not known until recently. In this perspective article, we focus on recent reports delineating the mechanism of stem-cell-triggered immunity in the SAM (Lee et al., 2011, 2012a). We also highlight skepticism voiced (Mueller et al., 2012; Segonzac et al., 2012) and discuss future prospects regarding peptide-mediated stem cell signaling in plant immunity.

**OVERVIEW ON ROBUST SAM SIGNALING NETWORKS**

The SAM is a dynamic structure of a hemispherical collection of identical appearing cells with a stable organization that maintain a balance between the self-renewal of stem cell population and conversion of meristematic cells into aerial organs such as shoot, leaves, and flowers (Perales and Reddy, 2012; Song et al., 2012). In Arabidopsis the SAM is comprised of three regions (Figures 1A,B), the central zone (CZ) is at the tip of the SAM and comprises the pluripotent stem cells. A collection of multipotent stem cells derived from the CZ constitutes the peripheral zone (PZ), from which the primordia of leaves and flowers come into existence (Aichinger et al., 2012). The rib meristem lies beneath the central and PZs, it turns into cells of the stem, as well as its vasculature. Plant hormone cytokinins (CKs) are believed to be the key signaling mediators in maintaining the integrity of the SAM stem cell niche (Hwang et al., 2012). In Arabidopsis enhanced plant CK responses stimulate meristem activities, whereas decreased CK signaling reduces meristem size (Nishimura et al., 2004; Bartrina et al., 2011). The expression of SHOOT MERISTEMLESS (STM) directly activates...
the transcription of the CK biosynthetic enzyme ISOPEN-TENYLTRANSFÉRASE (IPT7). Also, stm-1 mutants are unable to initiate the SAM formation, suggesting that STM-mediated CK activation is important for the sustenance of the SAM (Aichinger et al., 2012). Besides the activation of CKs, STM also prevents the expression of the ASYMMETRIC LEAVES1 (AS1) gene in the leaf primordium. Auxin represses the meristem promoting activities of CKs in the leaf primordium, while STM represses AS1 in the meristem (Hwang et al., 2012; Perales and Reddy, 2012; Figure 1A).

In the CZ (Figure 1A), a pool of pluripotent stem cells is maintained by WUSHEL (WUS)/CLV3 mediated negative-feedback loop via CLAVATA1, 2 (CLV1/2) receptor signaling pathways (reviewed in: Matsubayashi, 2011; Aichinger et al., 2012; Figure 1C). CLV3p belongs to a family of 32 peptides called CLV3/EMBRYO SURROUNDING REGION peptide (CLEp), which is endogenously modified into mature (signaling) CLEp (Kondo et al., 2006; Gish and Clark, 2011) CKs induce the expression of WUS through their receptors ARA-BIDOPSIS HISTIDINE KINASE 2 and 4 (AHK2 and AHK4), but represses CLV1 to avoid CLV3p-mediated WUS inhibition in the SAM (Hwang et al., 2012). In addition, members of CK type-A response regulators, ARABIDOPSIS RESPONSE REGULATORS 7 and 15 (ARR7 and ARR15), which activate CLV3p, are inhibited by AUXIN RESPONSE FACTOR 5 (ARF5), which in turn increases CK signaling and hence the induction of WUS (Aichinger et al., 2012; Perales and Reddy, 2012). These findings demonstrate that key nodes of stem cell signaling networks are under the regulatory control of auxin and CK signaling in the SAM.

THE STEM CELL SIGNALING IMMUNITY MODEL AND CKs CROSSTALK

The importance of the CVL3/WUS-mediated module in the SAM, and the fact that mature 12-aa amino acid (aa) CLV3(peptide) p controls the maintenance of the SAM through CLV1 and CLV2 receptor complex (Hwang et al., 2012; Song et al., 2012) have already been well established. Besides these and similar receptors important for the development of SAM, CLV3p has been shown to interact with the well-known innate immune receptor FLS2. Analogous to flg22 (minimal 22-aa amino acid flagellin peptide, pathogen associated molecular pattern (PAMP); detailed in Sun et al., 2013), CLV3p binds to FLS2 and activates MITOGEN-ACTIVATING PROTEIN KINASE (MAPK) activities and induces the expression of PAMP-Triggered-Immunity (PTI) marker genes in Arabidopsis (Jones and Dangl, 2006; Lee et al., 2011). Unlike the flg22-FLS2 mediated immunity, which is coupled with growth inhibition of seedlings, the CLV3p-FLS2 activation results only in an immune response without growth inhibition (Lee et al., 2012a). Premature and precursor CLV3 peptides can be modified endogenously into various forms, such as 13aa-CLV3p and 12aa-CLV3p. However, FLS2 is shown to be specifically sensitive to 12-aa CLV3p (Lee et al., 2011, 2012b). These results suggest that there is a selective specificity for 12aa-CLV3p and that the FLS2 receptor seems to be blind to other variants of the same peptide.

These findings on stem-cell-triggered immunity were further complemented by genetic approaches (Lee et al., 2011). Accordingly, fls2 mutant plants failed to show immune gene expression as well as MAPK activation by both CLV3p and flg22. However, the elongation factor EF-Tu (EFR) receptor mutant cfr-1 showed normal immune response both to flg22 and CLV3p.
AN OUTLOOK ON STEM-CELL-TRIGGERED IMMUNITY

An extraordinary mechanism of bacterial cleansing with immune defense is deployed by stem cells in the SAM (Lee et al., 2012b). This type of immunity has great similarities to that of flg22-FLS2-triggered innate immune response in plants, such as the dimerization of co-receptor BAK1 and downstream signaling.
events (Asai et al., 2002; Boller and Felix, 2009). It is worth mentioning that flagellin-FLS2-based immunity is transient by nature and has often been viewed as a small increment of the total effective immunity executed through plant immune systems (Jones and Dangl, 2006). On the contrary, CLV3p-FLS2 mediated immunity seems to result in complete removal of Pst DC3000 in the SAM, whereas fb2 and cv3 mutants showed some susceptibility to bacterial infection (Lee et al., 2012a). However, the multiplicity of Pst DC3000 in susceptible SAM of fb2 or cv3 mutant plants is lower than in a typical compatible infection in Arabidopsis (Segonzac et al., 2012). This sluggish bacterial growth in the SAM may be due to the compactness of the meristematic tissues leading to reduced space for the optimal bacterial multiplication, as compared with apoplastic compartments in plants. Alternatively, there might exist CLV3p-FLS2 independent protection mechanisms in susceptible SAM. Owing to the scarcity of detailed literature on stem-cell-triggered immunity in plants, the underlying mechanism delineating how Pst DC3000 fails to dampen CLV3p-FLS2 mediated immunity in the SAM remains to be determined. We suggest the following hypotheses to address the lack of effectiveness of Pst DC3000 effectors in breaching CLV3p-FLS2 mediated immunity in the SAM:

(i) Unlike apoplastic fluid, which is analogous to hrp inducing medium (Zwieseler-Volllick et al., 2002; Rico and Preston, 2008), the SAM microenvironment may not be favorable for the expression of bacterial genes implicated in Type III secretion system (TSS), responsible for the delivery of bacterial effectors into the plant cell;
(ii) The distinction between PAMPs and effectors sometime cannot strictly be maintained (Thomma et al., 2011), therefore CLV3p may also be recognized by cellular receptors (R-genes) analogous to those of TSS delivered bacterial effectors and may execute Effector-Triggered-Immunity (ETI), which is higher in magnitude than PTI (Jones and Dangl, 2006);
(iii) Whereas hypersensitive response (HR) and systemic resistance through meristems have already been demonstrated against infection of Phytophthora infestans (Orłowska et al., 2012), the impetus of such responses might be strong enough to prevent bacterial infection in the SAM as compared to other parts of the plant. These different hypotheses merit detailed experimental clarification in the future.

Once fully explored, the introduction of CLV3p mediated immunity at novel locations in plant could be a smart solution to improve plant protection against pathogens, thus avoiding too high growth cuts. However, to engineer this pathway in vegetative plants such as leaves, root, and stem, developmental complications of spatial and temporal nature may arise. To counter such problems, context dependent inducible gene expression systems would be a solution (Rushston et al., 2002; Grofkinsky et al., 2011). Genetically modified plants expressing the CLV3p peptide under the control of an elicitor or a pathogen inducible promoter will drive transgene expression only at the onset of pathogen infection. Nevertheless, unforeseen complexities such as gene silencing and non-specific traits in transgenic plants remain valid concerns.

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