Mechanisms of stress response in the root stem cell niche

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Highlight

Environmental stress preferentially induces death of stem cells and their early descendants, which temporally stimulates the division of quiescent center cells but restricts or stops stem cell division.
Abstract

As plants are sessile organisms unable to escape from environmental hazards, they need to adapt for survival. The stem cell niche in the root apical meristem is particularly sensitive to DNA damage induced by environmental stresses such as chilling, flooding, wounding, UV, and irradiation. DNA damage has been proven to cause stem cell death, with stele stem cells being the most vulnerable. Stress also induces the division of quiescent center cells. Both reactions disturb the structure and activity of the root stem cell niche temporally; however, this preserves root meristem integrity and functioning long-term. Plants have evolved many mechanisms that ensure stem cell niche maintenance, recovery, and acclimation, allowing them to survive in a changing environment. Here, we give an overview of the cellular and molecular aspects of stress responses in the root stem cell niche.

Keywords: auxin, DNA damage, regeneration, ROS, stem cell niche, stress, quiescent center
Root stem cell niche structure and dynamics

The root apical meristem (RAM), consisting of proliferating cells at the root tip, maintains root growth and development throughout the plant life cycle (reviewed by Jiang and Feldman, 2005). The RAM harbors a stem cell niche, the specific microenvironment that provides signals that block cell differentiation (reviewed by Laux, 2003; Stahl and Simon, 2005; Aichinger et al., 2012; Perilli et al., 2012). Stem cells (initials) in the root are maintained around a group of mitotically inert quiescent center (QC) cells. The QC of angiosperms varies in size among different plant species, from as few as four cells in Arabidopsis (*Arabidopsis thaliana*) to hundreds of cells in maize (*Zea mays*) (Clowes, 1956, 1958; Dolan et al., 1993).

Mitotically active initials, capable of unlimited self-renewal and giving rise to differentiating descendants, circumscribe the QC. Figure 1 portrays the classical stem cell niche architecture of *Arabidopsis thaliana*. Stele stem cells (SSCs) located proximally to the QC generate the stele; stem cells lateral to the QC (CESC) form the endodermis and cortex, with adjacent stem cells forming the epidermis and lateral root cap (ESC); and columella stem cells (CSC) are located below the QC (Dolan et al., 1993). Root stem cells divide asymmetrically (formative cell division), giving rise to a new stem cell plus a daughter cell that differentiates after a limited number of symmetric cell divisions (Stahl and Simon, 2005; De Smet and Beeckman, 2011). CESC show a division pattern comprising first anticlinal symmetric and second periclinal asymmetric divisions. ESC undergo two variants of formative cell division: they first divide periclinally, producing a new ESC and a LRC daughter cell; the new ESC then divides anticlinally, producing the epidermis daughter cell (Willemsen et al., 2008; De Smet and Beeckman, 2011).

Experiments with QC laser ablation (Xu et al., 2006) showed that positional information rather than QC cell identity specifies the location and size of the stem cell niche. Thus, the structure of the stem cell niche changes during root development despite stereotypical cell division patterns. In some plants, e.g., *Sinapis alba*, *Vicia faba*, and *Malva sylvestris*, the QC is absent from the root apex at germination and is organized later during root growth (Clowes, 1958, 1961, 1978). In other plants, including Arabidopsis, the QC is specified during embryogenesis but can be quickly restored upon injury after germination. The duration of the QC mitotic cycle is long but not infinite (Rahni and Birnbaum, 2019). QC daughter cells usually become CSC (Cruz-Ramirez et al., 2013); however, clonal analysis shows that QC cells can potentially replace all stem cells in the meristem (Kidner et al., 2000). Cell divisions in the QC accelerate upon meristem ageing, disturbing the stem cell niche structure (Wein et al., 2020; Timilsina et al., 2019). It is unclear whether meristem ageing is part of an inherent developmental program or is the consequence of accumulating stress.

Specific cellular stress responses in the root stem cell niche

Upon severe or prolonged stress, the stem cell niche shows two specific cellular responses: activation of QC cell divisions and death of root stem cells (Fig. 2A). Clowes described QC activation upon high dosage irradiation in the middle of the 20th century (Clowes 1959, 1963). However, the specific vulnerability of root stem cells and their programmed cell death (PCD) as a result of various stresses has been discovered only recently (Fulcher and Sablowski, 2009; Furukawa et al., 2010; Heyman et al., 2013; Hong et al., 2017).

DNA damage-mediated death of root stem cells is triggered by UVB and gamma irradiation (Furukawa et al., 2010), X-rays, and radiomimetic drugs such as bleomycin and zeocin (Fulcher and
Sablowski, 2009; Heyman et al., 2013). Notably, the PCD response of the root stem cells is cell type-specific. SSCs are especially prone to entering the PCD pathway (Fulcher and Sablowski, 2009; Heyman et al., 2013; Cahner et al., 2020). In addition to SSCs, high-concentration, long-term (24 h) zeocin treatment kills CSCs and QC cells (Fulcher and Sablowski, 2009); bleomycin also triggers death of CSCs (Cahner et al., 2020). Chilling stress induces root stem cell death; however, in most cases, columella stem cell daughters are sacrificed to ensure survival of stem cells (Hong et al., 2017).

In contrast to stem cells, QC cells are highly tolerant of DNA damage agents, dying only after exposure to acute stress (Fulcher and Sablowski, 2009; Furukawa et al., 2010). Instead, stress signals activate cell division machinery in the QC, accelerating the cell cycle (reviewed by Heyman et al., 2014). Thus, the QC serves as a reservoir of cells able to restore root growth in the case of significant damage. Mitotic activation of the QC occurs following root cap cutting (Jiang et al., 2003; Ivanov et al., 2011; Bystrova et al., 2015), chilling stress (Clowes and Stewart, 1967; Barlow and Rathfelder, 1985), flooding-induced hypoxia (Mira et al., 2020), Pb-induced toxicity stress (Kozhevnikova et al., 2007), and heat exposure (Clowes and Wadekar, 1989; Kidner et al., 2000; Heyman et al., 2013).

Sacrificing root stem cells undergoing PCD allows the RAM to survive severe stress (Fulcher and Sablowski, 2009). A plausible role for the stem cell death response is maintaining the genetic material of rapidly dividing cells undamaged to sustain tissue patterning. It is likely that for symplostically growing plant tissues, either slowly dividing QC cells or dedifferentiated tissues are best able to replenish stem cells with compromised DNA.

Below, we discuss the mechanisms that provoke stress-induced changes in stem cell niche activity and help this region withstand unfavorable conditions (Fig. 2).

**Mechanisms behind root stem cells susceptibility to DNA damage**

Accumulating evidence suggests that severe stress leads to DNA fragmentation in root stem cells and their early descendants (Fulcher and Sablowski, 2009; Furukawa et al., 2010; Mironova and Xu, 2019). DNA breaks in stem cells cause DNA replication stress and are particularly disruptive when a cell undergoes mitosis, leading to chromosomal aberrations and mutations. The root stem cell-specific DNA replication stress mechanism is associated with DNA topoisomerases (Zhang et al., 2016) (Fig. 2B). DNA TOPOISOMERASE1 (TOP1) is essential for the survival of SSCs, which appear to be particularly sensitive to torsional stress during DNA replication. DNA topoisomerases relax DNA supercoils by introducing temporary single- or double-strand breaks (Champoux, 2001).

Two cell cycle checkpoint kinases, ATAXIA TELANGIECTASIA MUTATED (ATM) and ATM AND RAD3-RELATED (ATR), transmit DNA damage signals in plant cells (Abraham, 2001; Garcia et al., 2003; Culligan et al., 2004). ATM responds to double-strand DNA breaks (Bensimon et al., 2011), while ATR transmits signals about single-strand DNA breaks (Flynn and Zou, 2011). The NAC family transcription factor SUPPRESSOR OF GAMMA RESPONSE1 (SOG1) is phosphoactivated by ATM to trigger the DNA damage response (Yoshiyama et al., 2013). In plant stem cells, SOG1 governs the key cell death pathway induced by high-intensity UVB radiation, X-rays, and radiomimetic drugs (Furukawa et al., 2010; Fulcher and Sablowski, 2009). The SOG1 downstream cascade that triggers cell death remains largely unknown; however, many direct targets of SOG1 have been discovered recently (Ogita et al., 2018; Ryu et al., 2018).
Several mechanisms that restrict uncontrolled stem cell death exist. The MEDIATOR (MED) complex subunit (MED18) protects root meristem cells from DNA damage-mediated cell death; med18 mutants show spontaneous death of vascular initials and their daughters (Raya-González et al., 2018). Besides cell death, the SOG1-dependent pathway also mediates stem cell survival following stress-induced DNA damage by inhibiting cell cycle progression at the G2/M checkpoint (Furukawa et al., 2010; Yoshiyama et al., 2013). Temporal cell cycle arrest prevents the mitotic catastrophe that might happen if DNA is left unrepaired. ATR regulates cell cycle arrest at the G2/M checkpoint in response to irradiation (Culligan et al., 2004) and aluminum (Al) (Rounds and Larsen, 2008; Sjogren et al., 2015). Temporal inhibition of CSC division occurs upon chilling stress; when it finally divides, the CSC daughter tends to undergo PCD (Hong et al., 2017).

SOG1 targets numerous genes responsible for cell cycle regulation at the G2/M transition, including cyclin-dependent kinase (CDK) inhibitors KIP-RELATED PROTEIN 6 (KRP6), SIAMESE-RELATED (SMR) SMR4,5,7, and WEE1 (Ogita et al., 2018). KRP and SMR bind to CDK–cyclin complexes and inhibit their kinase activity (Van Leene et al., 2010; Yi et al., 2014). WEE1 kinase phosphorylates and inactivates the CDKs that mediate the G2/M-phase cell cycle transition (De Schutter et al., 2007). Direct targets of SOG1, homologous TF-coding genes ANAC044 and ANAC085, play a crucial role in G2/M cell cycle arrest upon DNA damage response (Takahashi et al., 2019). Similar to sog1 mutants, the stem cell niche of anac044 and anac085 mutant plants is tolerant to DNA damaging agents. However, the increased tolerance of anac044/085 mutants is associated with G2/M checkpoint control, rather than through increased DNA repair. ANAC044/ANAC085 are essential in regulating protein accumulation of the R1R2R3-type Myb transcription factors (MYB3R), which mediate G2/M-specific genes expression both positively and negatively. Notably, that myb3r3 and myb3r5 mutants, which cannot induce G2/M arrest upon DNA damage response, also show less zeocin-induced stem cell death (Chen et al., 2017). Interestingly, that ANAC044/ANAC085 have been implicated in the regulation of stress-specific function, mediating heat-stress, but not osmotic-stress-induced G2/M arrest (Takahashi et al., 2019).

DNA damage-activated backup plan: QC cell divisions

DNA damage-induced cell death activates regeneration programs in the stem cell niche, consequently inducing divisions in the QC (Heyman et al., 2013, 2014). The transcription factor ETHYLENE RESPONSE FACTOR 115 (ERF115) is the master regulator of damage-induced regenerative processes. Under non-stress conditions, ERF115 is only expressed in dividing QC cells, serving as a rate-limiting regulator of divisions in the QC (Heyman et al., 2013). Under stress, ERF115 is activated in the QC, around dead cells, and in the endodermis. This activation induces restorative cell divisions (Heyman et al., 2016; Zhou et al., 2019; Canher et al., 2020). ERF115-dependent activation of QC cell division is detected in response to heat stress, wounding, and nematode infection (Heyman et al., 2013; Zhou et al., 2019).

ERF115 is not a direct target of SOG1; rather, it is induced in the stem cell niche as a result of SOG1-dependent PCD (Johnson et al., 2018). ERF109, a close homolog of ERF115, is quickly induced after cell ablation and triggers ectopic ERF115 expression around the dead cells, activating regeneration processes in the meristem (Heyman et al., 2016; Zhou et al., 2019). ERF115 recruits the regulatory circuit SCARECROW (SCR) - SHORT ROOT (SHR) - RETINOBLASTOMA-RELATED (RBR), which guides asymmetric cell division of root stem cells (Paquette and Benfey, 2005; Cruz-Ramírez et
ERF115 binds to and inhibits RBR activity (Zhou et al., 2019). This blocks RBR-SCR interaction and allows for QC cell division. ERF115 also forms a heterodimer with PHYTOCHROME A SIGNAL TRANSDUCTION1 (PAT1) to mediate restorative cell divisions, e.g., stem cell niche recovery upon root tip excision (Heyman et al., 2016). One putative PAT1-ERF115 target is WOUND INDUCED DEDIFFERENTIATION1 (WIND1), a key factor promoting plant cell dedifferentiation (Iwase et al., 2011; Heyman et al., 2016). Co-expression of PAT1 with ERF115 hyperinduces WIND1. Another potential target of ERF115 is the AUXIN RESPONSE FACTOR 5 (ARF5), a major regulator of auxin signaling in root development (Canher et al., 2020). The ARF5 upstream region possesses ERF115 binding sites, and its expression corresponds with ERF115 level.

**Not merely a by-product: the crucial role of ROS in the stem cell niche**

Stress-induced changes in stem cell niche activity also rely on changes in the distribution of reactive oxygen species (ROS). A by-product of aerobic metabolism, ROS are highly reactive molecules that can induce DNA damage, protein oxidation, and lipid peroxidation (reviewed by Gill and Tuteja, 2010; Huang et al., 2019). ROS exist in ionic and molecular states: ionic forms include hydroxyl radicals (OH•) and superoxide anions (O2•−); molecular forms include hydrogen peroxide (H2O2) and singlet oxygen (1O2). An antioxidant system consists of ROS scavenger enzymes and non-enzymatic low molecular metabolites (ascorbic acid, ASC; reduced glutathione, GSH; carotenoids; flavonoids, proline) that counteract uncontrolled oxidation (Conklin and Barth, 2004; Schafer and Buettner, 2001; reviewed in Jiang and Feldman, 2005). Cellular redox potential is determined by the contribution of different redox couples and ROS and is controlled by a delicate balance between ROS production and scavenging (reviewed by Lee et al., 2019).

Cellular redox potential plays a critical role in regulating cell proliferation. In the stem cell niche, QC cells have a more highly oxidized status than surrounding stem cells (Jiang et al., 2003; Jiang and Feldman, 2005), which is essential for maintenance of QC dormancy (reviewed by Huang et al., 2019; Eljebbawi et al., 2020). Indeed, miao mutants deficient in plastid-localized GR2 enzyme, which is part of the plant antioxidant system, exhibit a partial loss of QC identity mediated by a perturbed auxin maximum (Yu et al., 2013). Knockout of VITAMIN C DEFECTIVE 1 (VTC1), a rate-limiting gene affecting the quantity of ascorbic acid, results in elevated H2O2 levels that increase the number of QC cells and periclinal divisions in the root meristem (Kka et al., 2018). It is noteworthy that both reducing the oxidative status of the QC and treating roots with exogenous H2O2 leads to QC activation (Jiang et al., 2003; Kong et al., 2018).

Stress conditions such as heat, cold, drought, heavy metals, and pathogens rapidly disturb the redox balance by inducing ROS accumulation in plant tissues (Lee et al., 2012; Kawarazaki et al., 2013; Kim and Hwang, 2014; Zhao et al., 2018). While ROS bursts under severe stress conditions can cause intense oxidative stress, sometimes leading to whole-organ death, under moderate stress conditions, ROS activate signaling pathways that trigger adaptive stress response programs. A well-described example of ROS-mediated damage and adaptation in the stem cell niche is flooding-induced hypoxia. Maintaining well-balanced, low levels of ROS is crucial for root meristem survival under hypoxia conditions (Sasidharan et al., 2018). Hypoxia-induced accumulation of ROS and nitric oxide (NO) causes QC cell division and death of meristematic root cells (Mira et al., 2016). A decline
in either O₂ or NO leads to expression of core hypoxia genes and hypoxia acclimation (Gibbs et al., 2011, 2018).

**Pivotal role of auxin in root stem cell niche maintenance**

The auxin concentration maximum defines QC identity and maintains stem cell niche integrity (Jiang and Feldman, 2005). Auxin biosynthesis, conjugation, oxidation, and, most critically, transportation networks work together to generate and support the auxin maximum in the stem cell niche. Maintaining a dynamic balance in auxin patterning helps plants withstand the rigors of environmental stress.

Environmental cues commonly affect root growth plasticity by influencing auxin biosynthesis, transport, and signaling (Pierik and Testerik, 2014; Korver et al., 2018). Despite different stresses having specific targets in these auxin pathways, sometimes outside the meristem, all of them potentially influence stem cell niche activity to some extent. Stress-induced messages that affect the shoots are delivered to the root meristem by long-distance auxin transport; short-distance auxin transport consequently alters auxin levels in the root stem cell niche. For example, iron deficiency decreases auxin transport from shoots to roots in rice (Sun et al., 2017). Mathematical modeling suggests that the rate of auxin inflow into the root meristem is a critical parameter affecting the maintenance of the auxin maximum (Mironova et al., 2010).

QC activation and root meristem exhaustion upon severe stress often correspond to depletion of auxin in the stem cell niche (Fig. 3). A decrease in activity of the auxin response marker DR5 might also indicate the maladaptive status and vulnerability of the stem cell niche to stress. Low-potassium (K⁺) conditions slightly decrease DR5 signal in the QC, corresponding with an acceleration of QC cell division under control conditions; this phenotype is greatly enhanced in the *kup9* mutant defective in K⁺ and auxin efflux from the endoplasmic reticulum (Zhang et al., 2020). Chilling stress causes a decrease in DR5 activity in the QC, contributing to induction of CSC division and CSC daughter death (Hong et al., 2017) (Fig. 3A, B). Generally, a decrease in QC-localized DR5 signal corresponds strongly with misexpression of auxin transporters from PIN-FORMED or AUX/LAX families.

Local auxin biosynthesis in the stem cell niche has less influence on QC maintenance than PIN-mediated transport, but helps the plant to rapidly enhance auxin levels in the root tip upon stress. Expression of the *TRYPTOPHAN AMINOTRANSFERASE OF ARABIDOPSIS 1* (*TAA1*) gene encoding an auxin biosynthesis enzyme is enhanced upon Al exposure (Yang et al., 2014a), leading to auxin accumulation in the root tip. Auxin biosynthesis via TAA/TAR enzymes is essential for the root meristem response to the stress hormone ethylene (Brumos et al., 2018). Enhanced auxin biosynthesis rates are also observed at the site of root tip injury (Matosevich et al., 2020).

Dead cells affect auxin patterning via disruption of PIN-mediated auxin transport routes in the meristem (Canher et al., 2020). Bleomycin-mediated SSCs death leads to rapid accumulation of auxin around the dead cells without activating auxin biosynthesis (Fig. 3D). Auxin accumulation in the endodermis promotes replenishment of SSCs via an ERF115-dependent pathway. As another example, DNA damage-induced CSC daughter death partially blocks lateral auxin redistribution in the columella, leading to auxin accumulation in the QC upon chilling stress (Hong et al., 2017).
Intriguingly, plants with sacrificed CSC daughters and boosted auxin levels in the QC not only recover faster from chilling stress but also withstand accompanying freezing, drought, and even genotoxic zeocin treatments better than those plants not sacrificing these cells. Moreover, auxin protects stem cells against zeocin-induced cell death (Hong et al., 2017).

**The stem cell niche does not live by auxin alone: other plant hormones**

Although a change in auxin patterning precedes division of the QC cells (Jiang et al., 2003), the QC is activated by exposure to ethylene (Ortega-Martinez et al., 2007), jasmonic acid (JA) (Zhou et al., 2019), salicylic acid (SA) (Pasternak et al., 2019), cytokinin (Zhang et al., 2013), and brassinosteroids (BRs) (Lozano-Elena et al., 2018) (Fig. 2C). Cytokinin negatively regulates the auxin influx carrier LAX2 in the meristem, with the lax2 mutant showing reduced auxin levels in the stem cell niche and ectopic divisions in the QC (Zhang et al., 2013). The morphogenetic role of low-level exogenous SA is determined by its dose-dependent control of auxin transport and biosynthesis (Pasternak et al., 2019). Exposure to low-level SA leads to stem cell niche enlargement via activation of PIN1 and TAA1 and inhibition of PIN2 and PIN7. Another explanation of hormone-induced division of QC cell is precocious RAM ageing. Prolonged treatments with relatively high concentrations of exogenous hormones are typically used to induce division of QC cells, which might be stressful for the stem cell niche. QC cell divisions occur more frequently in ageing plants than in younger plants (Timilsina et al., 2019).

The response and acclimation of the root stem cell niche to stress also rely on hormone-specific effects that are independent of auxin. Restricted ethylene diffusion in compacted soil or upon flooding leads to ethylene accumulation in the root tip, which helps the meristem to adapt to the stress (Hartman et al., 2019; Pandey et al., 2021). Ethylene signaling activates NO scavenging by PHYTOGLOBIN1 (PGB1), which is essential for acclimating the meristem to flooding-induced hypoxia (Hartman et al., 2019). PGB1 reduces NO levels and stabilizes ERFVII transcription factor proteins, which help the stem cell niche to withstand hypoxia. PGB1 is also essential for adaptation to water deficit (Mira et al., 2017).

Abscisic acid (ABA) has a specific role in the stem cell niche, i.e., maintaining the stem cell niche in a juvenile state and ensuring QC dormancy (Zhang et al., 2010). ABA treatment suppresses cell division in the meristem for long periods without loss of meristem function. At least partially, ABA exerts its role on meristematic activity by modulating auxin transportation and signaling (Zhang et al., 2010; Promchuea et al., 2016; Rowe et al., 2018). However, ABA-mediated production of ROS in mitochondria is also crucial for maintaining stem cell niche activity and the auxin response maximum (Yang et al., 2014b). Furthermore, SA promotes ROS accumulation in the stem cell niche (Wang et al., 2021).

Noteworthy, salt stress initiates an increase in ABA and a decrease in BR signaling in the inner tissues; these events are followed by activation of JA and derepression of BR pathways (Geng et al., 2013). These observations indirectly support the idea that the QC is temporally protected under early stress response but later on its cells divide to replenish the damaged cells. BRs recruit BRI1-EMS-SUPPRESSOR 1 (BES1) – BRASSINOSTEROIDS AT VASCULAR AND ORGANIZING CENTER (BRAVO) – ERF115 signalling module to control QC cell divisions (Vilarrasa-Blasi et al., 2014).
Recent studies demonstrated that JA plays a pivotal role in stem cell niche regeneration (Zhou et al., 2019). Wounding leads to JA accumulation that rapidly induces transcription of *ERF109*. *ERF109* stimulates CYCD6;1 expression in the endodermis and QC and triggers *ERF115* expression in the stele. Methyl jasmonate pre-treatment to induce *ERF115* expression before cell ablation promotes faster replenishment of dead cells. JA and auxin synergistically activate the SCR-SHR-RBR pathway to guide restorative cell divisions when roots are cut, penetrate the soil, or are infected with nematodes.

**Conclusion**

Figure 2 summarizes major pathways of stress-induced responses in the root stem cell niche. This roadmap is certainly incomplete, missing multiple condition-specific crosstalk and feedback routes between the major pathways. For example, H$_2$O$_2$ treatment activates *ERF115*-mediated QC cell division independently of cell death signaling (Kong et al., 2018); *ERF115* enhances auxin signaling via the ARF5/MP transcription factor, and ARF5/MP, in turn, promotes the *ERF115* pathway (Canher et al., 2020); and reduction of QC oxidation status corresponds with auxin depletion (Jiang et al., 2003). DNA damage response, ROS, auxin distribution, the *ERF115*-mediated cascade, and hormonal signaling are all interconnected, facilitating plant adaptation to numerous adverse conditions. Identifying key components of the root stem cell niche response to stress will help scientists to sustain, select, or bioengineer plants that effectively tolerate particular stresses, thus widening the scope of sustainable agriculture.
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Author Contribution

J.X. and V.M conceptualized the idea of the review. E.V.U. and V.M. collected data and drafted paper. E.V.U. prepared figures. E.V.Z. and J.X. revised and edited the manuscript. All authors read and approved the submitted version.
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Figure 1. The root stem cell niche in Arabidopsis.

Figure 2. Pathways of the stem cell niche response to stress. The summary (A) and the details about DNA damage (B) and hormonal (C) stress responses. The processes are in boxes, the proteins are colored blue. SA – salicylic acid, CK – cytokinins, JA – jasmonic acid, ABA – abscisic acid, BR – brassinosteroids, Eth – ethylene, ROS – reactive oxygen species.

Figure 3. Auxin dynamics in the stem cell niche in response to stress. (A) Auxin maximum in the QC maintains stem cell niche integrity. (B) Auxin levels in the meristem are depleted in response to different stresses (e.g., chilling stress at 4°C; Hong et al., 2017), resulting in loss of QC identity and precocious divisions in the stem cell niche. (C) Re-establishment of auxin maximum in the QC occurs after chilling-stress-specific CSC daughter death (Hong et al., 2017). (D) Bleomycin-induced cell death of SSCs and their daughters causes auxin accumulation around the wound, activating restorative cell divisions (Canher et al., 2020).
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