Regulation of Root Apical Meristem Development

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Abstract

The establishment of the Angiosperm root apical meristem is dependent on the specification of a stem cell niche and the subsequent development of the quiescent center at the presumptive root pole. Distribution of auxin and the establishment of auxin maxima are early formative steps in niche specification that depend on the expression and distribution of auxin carriers. Auxin specifies stem cell niche formation by directly and indirectly affecting gene activities. Part of the indirect regulation by auxin may involve changes in redox, favoring local, oxidized microenvironments. Formation of a QC is required for root meristem development and elaboration. Many signals likely pass between the QC and the adjacent root meristem tissues. Disappearance of the QC is associated with roots becoming determinate. Given the many auxin feedback loops, we hypothesize that roots evolved as part of an auxin homeostasis mechanism.

Contents

INTRODUCTION

In this review we focus on the developmental biology of roots, with an emphasis on the root apical meristem of Angiosperms. Several excellent reviews (Aeschbacher et al. 1994; Casson & Lindsay 2003; Jiang & Feldman 2003; Jürgens 2001; Scheres & Wolkenfelt 1998; Scheres et al. 1994, 1996, 2002) and articles (Aida et al. 2004, Benfey et al. 1993, Dolan et al. 1993, Friml et al. 2003) documenting our increased understanding of the molecular controls of root development, particularly with regard to auxin controls of root development in *Arabidopsis*, have recently appeared. Here we build on those reviews, expand the number of species considered, and propose a model that integrates many of these observations. In the development of this model, we believe it instructive to consider current thinking on the evolutionary origin of roots.

RAM: root apical meristem

THE EVOLUTIONARY ORIGIN OF ROOTS

The earliest evidence for roots associated with vascular plants comes from fossil lycopods, which were extant in the early- to mid-Devonian period, about 400 mya. In these seedless plants, the rooting structures appear little different morphologically from the shoot system, reflecting the hypothesized origin of the root as a product of a embryonic shoot dichotomy. In this scenario, the root meristem was transformed from a shoot meristem (Gensel & Edwards 2001). Thus, precocious occurrence of the root-shoot dichotomy may be viewed as a mechanism for inserting root formation into embryogeny and thereby suggests that there exists a correlation between the morphology of the mature root system and embryo morphology, as postulated by Goebel (1928). In another part of this scenario, transformation of a shoot apex into a root apex was associated with the shoot system's adaptive requirements, most probably anchorage and the absorption of water and nutrients. Current molecular efforts may eventually elucidate the mechanisms underlying this hypothesized evolutionary push for shoot meristem transformation. Recent investigations of mutations affecting both root and shoot meristems would support this transformation theory (Ueda et al. 2004), as do the similarities in the expression of *SCR* and *WOX* genes in both root and shoot meristems (Haecker et al. 2004, Wysocka-Diller et al. 2000). On the other hand, molecular data may also suggest a de novo

origin of the embryonic root without the need for any dichotomy. The ability to profile and compare global gene expression patterns in root and shoot meristems may help in deciding whether roots originated de novo or whether root and shoot systems differentiated from a single, homologous organ system.

MORPHOLOGICAL AND ANATOMICAL LANDMARKS

Much of the recent and most exciting data on embryonic primary-root development come from *Arabidopsis thaliana*. As a consequence, the root anatomy of this species is well-characterized both in relation to mutants and with regard to cell- and tissue-specific expression of many genes (Casson & Lindsey 2003 and references therein). But findings from other species, especially maize and pea, have also impacted greatly our understanding of root development (Clowes 1978, Jiang & Feldman 2003).

At the very tip of most roots is the RC (**Figure 1**), which serves to protect the underlying root meristem as the root advances through the soil. With the exception of a few species in highly specialized families, such as the Podostemaceae—in which the RC is reduced in size or absent during some portion of root ontogeny (Rutishauser 1997, Suzuki et al. 2002)—a RC is otherwise always present (von Guttenberg 1968), thereby pointing to nontrivial, central roles for it. Just proximal to the RC is the RAM. In many species such as *Arabidopsis* and maize, a discrete boundary, the RC junction, is recognized between the RC and the RAM (**Figure 1**). Roots maintaining this type of architecture are said to show "closed" organization, as contrasted with those in species such as pea, in which no sharp boundary is discerned between the RC and the root proper. This latter type of root is described as having "open" organization (Clowes 1981, 1982). Recent work suggests that an organizational state that is intermediate between open and closed, termed "intermediate open," was the ancestral organizational state of Angiosperm RAMs (Groot et al. 2004). But no matter what the architecture (open, closed, or intermediate), all Angiosperm RAMs consist of files of cells that converge to a small group of cells located just proximal to the RC proper (**Figure 1**). Because of their location, cells situated at the point of file convergence were long considered to function as the initial cells for the root. Another important conclusion, derived from lineage analyses, was that in roots showing closed organization, maintenance of the RC and formation of new RC cells could be traced to a set of initials that functioned solely in the production of new RC derivatives. This contrasted with RAMs showing open organization, where files of several different cell types converged to a common group of initials; this suggested that more than one cell/tissue type is produced from a common initial cell(s) (Cutter 1971). Much effort has been directed at determining the minimum number of initial cells, which taken together are said to form the promeristem (Clowes 1954). Based on lineage analyses, early researchers concluded that the promeristem was quite small, perhaps consisting of 20 cells or less (**Figure 1*c***) (Clowes 1954, 1961).

This notion of a small number of initials was challenged by Clowes (1954), who showed that the promeristem was broad and consisted of a relatively large number of cells. Using radiolabeled DNA precursors and autoradiography, Clowes demonstrated that cells positioned at the point of lineage convergence were relatively inactive mitotically (**Figure 2**). He termed this region of slowly dividing cells the QC (Clowes 1956, 1975). We now know that the QC is a ubiquitous feature of all Angiosperm RAMs for at least part or all of their ontogeny. Clowes's proposal of a group of mitotically inactive cells at the point of lineage convergence completely upset all previous ideas of the promeristem (Clowes 1956). The presence of a QC meant that the functioning initials in a growing root were not located at the point of lineage convergence, and hence necessitated a

Auxin: from the very first mitotic division of the zygote, gradients of auxin, a plant hormone, guide patterning of the embryo into the parts that will become the plant's organs. The most important auxin produced by plants is indole-3-acetic acid (IAA)

RC: root cap

QC: quiescent center. Located just proximal to the RC, the QC is a collection of slowly dividing stem cells that spend long periods in G1

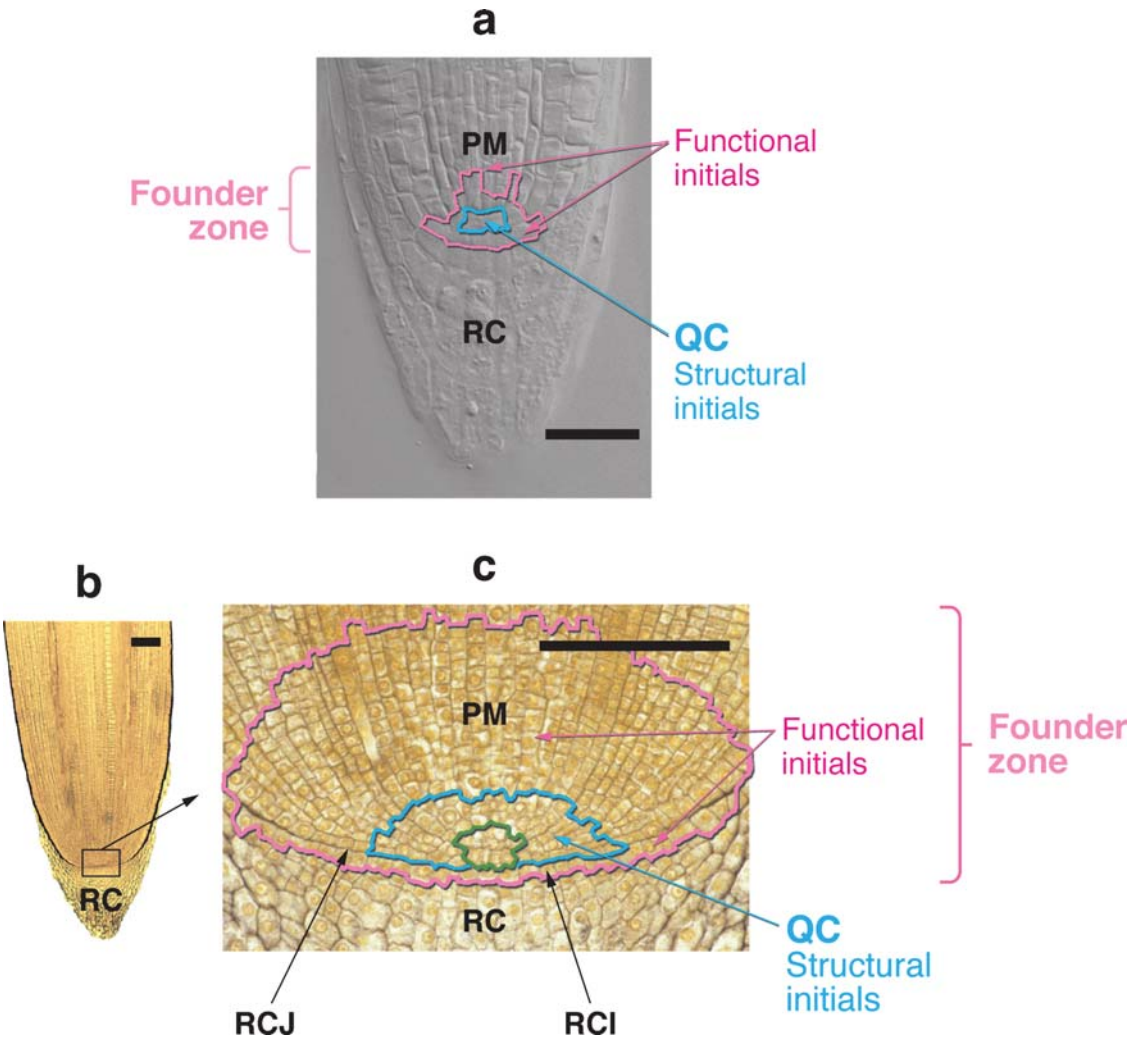

Figure 1

(*a*) RAMs of *Arabidopsis thaliana* and (*b*,*c*) *Zea mays* showing the location of various cell populations. For *b* and *c*, note the convergence of cell files to a small number of cells, circumscribed in green (the originally designated promeristem). QC, quiescent center; PM, proximal meristem; RC, root cap; RCI, root cap initials; RCJ, root cap junction. Scale bar = 100 μm.

reconsideration of these initials' location. From the autoradiographs, Clowes also deduced that the mitotically active initials comprising the promeristem circumscribed the QC and that the location of these initials could shift as the QC enlarged or diminished in size (**Figure 2**). In this sense, a cell is an initial not because of any inherent properties but because of its position within the RAM and, more specifically, because of its position in relation to the QC. Hence, if the promeristem is considered to be the total collection of initials encircling the QC, then the promeristem is not permanent.

Although the QC lately has attracted much attention (Aida et al. 2004, Haecker et al. 2004, Ueda et al. 2004), its role in root development remains obscure. The development

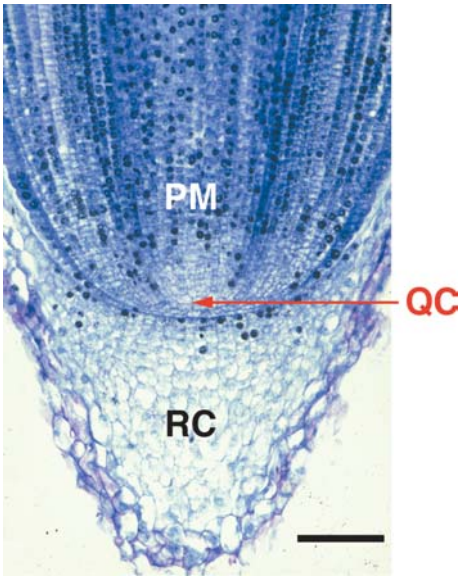

Figure 2

Autoradiograph of a *Zea mays* root apex supplied with ^{3}H-thymidine to indicate which cells are synthesizing DNA and thus able to divide. Black "dots" demarcate cells incorporating the radiolabel. Note the absence of labeled cells at the point of lineage convergence, in the region designated the QC. Most new derivatives in a growing root occur just proximal to the QC in the proximal meristem. QC, quiescent center; PM, proximal meristem; RC: root cap. Scale bar = 100 μm.

and interpolation of a zone of low mitotic activity within a region of meristematic activity raises a number of questions, including questions as to the reason for and consequences of rapidly dividing and quiescent cells being located adjacent to each other. Here, upon reviewing the literature on the QC, we conclude that the QC is central to root development and that it serves as an "integrator" for many processes and events requisite for meristem establishment and maintenance. Hence, the QC will be a focus for this review.

CONCEPT OF STEM CELLS

A number of researchers suggest that QC cells should be viewed as stem cells because of their apparent ability for unlimited proliferation, self-maintenance, and self-renewal (Barlow 1997, Ivanov 2004). Barlow (1997) hypothesizes that in roots with large QCs, such as maize, the QC is composed of cells showing varying degrees of "stemness" (Cai et al. 2004), including variations in their ability to divide (or not divide) as well as their states of differentiation and self-renewal. Hence, he suggests that we consider QC cells as constituting part of "founder zones" within which exist cells displaying gradations or gradients in the traits that define a cell as a stem cell. Within the founder zone, lineages converge to "initials" (**Figure 1**), which, because they divide infrequently, appear compromised as to the active providing of new cells. To reconcile this apparent contradiction, Barlow distinguishes between two types of initials: "structural" and "functional." Functional initials are considered the rapidly dividing cells encircling and abutting directly onto the surfaces of the QC. Functional initials comprise the promeristem and because of their rapid rates of division, they serve as the source for most new derivatives in a growing root. Structural initials, on the other hand, are viewed as cells which divide relatively infrequently. Such divisions, when they do occur, result in additions to, and often replacement of, the functional initials (Barlow 1997). How the balance of structural and functional initials is maintained is not known. However, the recent application of the stem cell niche concept (Aida et al. 2004, Laux 2003)—the notion that stem cells are controlled by local environments known as niches—may offer some insight. This concept has already been usefully applied to animals (Spradling et al. 2001). When applied to the QC, this concept suggests that the cells comprising the QC acquire or express stem cell features not because of any preexisting properties but rather because of the particular microenvironment that defines the stem cell niche. Thus, for root meristems it is probably correct to consider founder zones and stem cell niches as either partly or completely overlapping (**Figure 1**).

Stem cells: undifferentiated cells with the capacity for unlimited proliferation, self-maintenance, and self-renewal

Stem cell niche: a microenvironment in which cells are maintained as stem cells

IAA: indole-3-acetic acid

Polar auxin transport: the unidirectional, energy-requiring movement of auxin from the shoot to the root tip

As Spradling et al. (2001) note, a niche can exist in the absence of resident stem cells. Clearly, understanding the developmental mechanisms that activate or silence niches is an important challenge, and with regard to root development, we have begun to make some progress. In maize roots from which the terminal half-millimeter is surgically excised (i.e., both the RC and QC are removed), a new root meristem will re-form, but only after the development of a new QC (Feldman 1976). Insight into QC redevelopment has come from work showing that stem cell niche reestablishment is auxin-IAA dependent. Inhibiting polar auxin transport prevents both stem cell niche reestablishment and reformation of the QC (Sabatini et al. 1999). More recent work using molecular markers specific to the QC (Friml et al. 2002, Sabatini et al. 1999) has shown that long-term exposure of *Arabidopsis* roots to auxin transport inhibitors induces ectopic QC formation (Sabatini et al. 1999), which further supports the notion that auxin is central to stem cell niche development. Linking the establishment of this niche with the formation of the QC is and will continue to be an active research thrust.

Interestingly, in applying the niche concept to *Arabidopsis*, Aida et al. (2004) do not believe the four-celled *Arabidopsis* QC is composed of stem cells. Rather, they view the QC as an organizing center that, through the production and local distribution of a signal, maintains as stem cells the adjacent, rapidly dividing initial cells. If we accept that a stem cell must divide, at least occasionally, then under the experimental conditions used by most researchers, the *Arabidopsis* QC indeed does not appear to be composed of stem cells. There are no reports of the QC cells dividing under the conditions under which *Arabidopsis* plants are normally grown (Fujie et al. 1993). However, if *Arabidopsis* plants are exposed to elevated temperatures (30–42°C) for varying periods (5–180 min), QC cells activate and replace, at different rates, the surrounding stem cells (Kidner et al. 2000). More recently Baum et al. (2002) concluded that the four cells comprising the *Arabidopsis* QC "do divide initially after germination and apparently continue to divide during subsequent root growth until the primary root reaches its final length." They further noted that whereas divisions within the QC may be rare during early stages of seedling root growth (stages used by most investigators), they are relatively more frequent in older roots. Thus, given the criteria by which stem cells are typically defined, including the capacity for occasional, asymmetric divisions—where one daughter cell may differentiate—and the capacity of QC cells to respond (activate) under certain conditions in which neighboring cells are lost or destroyed (Barlow 1997, Cai et al. 2004, Kidner et al. 2000), we conclude that the four cells comprising the *Arabidopsis* QC are most certainly stem cells and should be regarded as structural initials as opposed to the surrounding functional initials (which Aida et al. regard as *the* stem cells) (Aida et al. 2004, Sablowski 2004). Significantly, this conclusion means that *Arabidopsis* root development is not so different from that of larger roots in other members of the Cruciferae, which have much larger QCs (Cutter 1971). As well, this conclusion is central to understanding determinate growth in roots, both in *Arabidopsis* and in other species, as we discuss below.

TOWARD AN UNDERSTANDING OF QC FORMATION

Cells occupying the QC niche begin acquiring QC-specific molecular characters very early in embryogenesis (Friml et al. 2002). In *Arabidopsis*, the QC's origins can be traced to divisions of the upper hypophysis derivative, which generates four nascent QC cells located just proximal to the RC junction, at the pole of the stele (**Figure 3**). It is postulated that sometime thereafter, the cell cycles of these cells lengthen, mostly because G1 is prolonged. Quiescence is, significantly, not an all-or-nothing state but rather a continuum. In roots with small QCs, such as *Arabidopsis*, each of the four QC cells can be at the same state

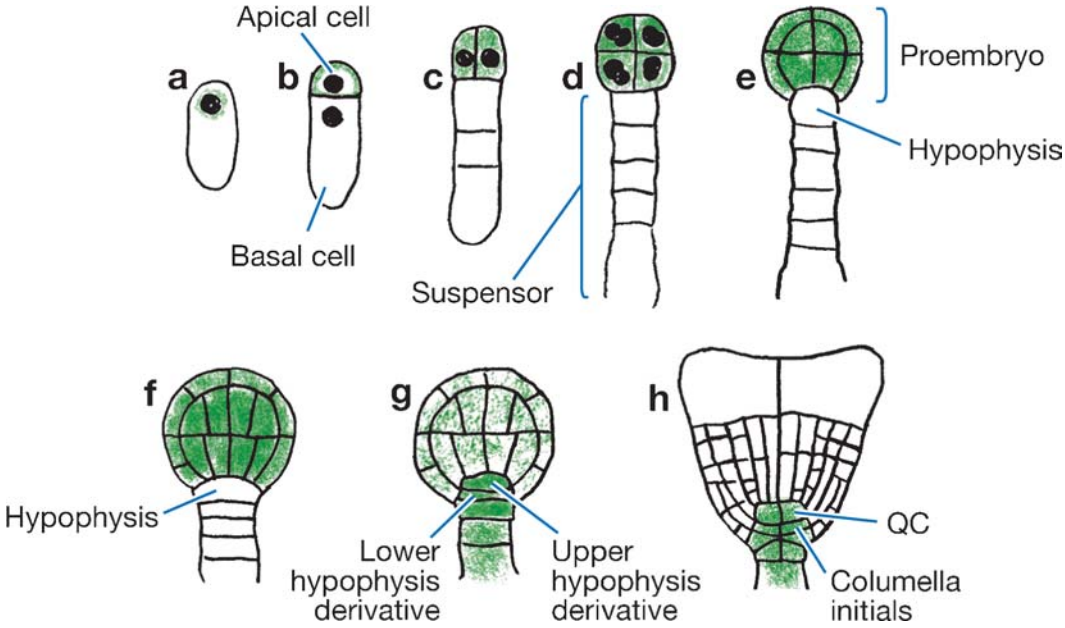

Figure 3

Schematic diagram of the early stages of *Arabidopsis* embryogenesis [after Hanstein (1870)]. Green shading indicates the distribution of auxin at various stages of embryo development; the darker the green, the more auxin [after Friml et al. (2003)].

of quiescence. However, in roots with considerably larger QCs, such as maize (with 600–1000 QC cells) (Clowes 1961), the degree of quiescence probably varies with position in the QC: Cells located at the point of lineage convergence are at the "deepest" level of quiescence and divide the least frequently, whereas cells located toward the proximal (basal) face of the QC divide more frequently (Barlow & MacDonald 1973). These differences in the state of quiescence again emphasize the fact that root meristem cells express certain characteristics because of their position in the meristem and not because these cells are inherently different from other cells in the root meristem.

Definitive data are now lacking on the timing of formation of the stereotypical (functional) QC. However, expression of *WOX5* (encoding a putative homeodomain transcription factor) in early globular (16-cell) embryos led Haecker et al. (2004) to conclude that QC identity is specified early in hypophysis formation. As well, other putative transcription factors, including *SHORT-ROOT*, *SCARECROW*, and *PLETHORA* (*PLT1* and *PLT2*) appear to be required for QC identity and specification and are expressed early in root development (Aida et al. 2004, Di Laurenzio et al. 1996, Helariutta et al. 2000, Sabatini et al. 2003, Wysocka-Diller 2000). *PLT1*, which is transcribed in response to auxin, is expressed as early as the eight-cell globular embryo stage, whereas *PLT2* is expressed in slightly older globular embryos. Through the generation of double and triple mutants, Aida et al. (2004) were able to show that *PLT* and *SCR/SHR* work via parallel pathways that appear to converge to a subset of target QC-specific promoters. *PLT* genes are not involved with auxin accumulation but rather act downstream of auxin, as indicated by the fact that auxins "cannot bypass the requirement for the *PLT* genes" (Aida et al. 2004). Additionally, the expression of a number of so-far uncharacterized QC-specific markers (QC25,

CLV: CLAVATA
WUS: WUSCHEL

QC46) has been detected in early heart-stage embryos (Aida et al. 2004, Friml et al. 2002). In summary, we can now conclude that the beginnings of QC specification can be traced to the 8–16-cell embryo.

MAINTENANCE OF THE QC AND STEM CELL NICHE

Once the stem cell niche is determined and the QC consequently developed, how is the niche (QC) maintained? Is the QC solely dependent on auxin? As Cai et al. (2004) note, a common problem faced by all stem cell populations is how they balance the number of differentiated cells with the maintenance of an adequate pool of self-renewing stem cells. Drawing from parallels with animals, Barlow (1997) suggests that the most straightforward way of viewing this balance in the QC (both structural and functional initials) is to consider that as cells leave the stem cell population, they in turn regulate the proliferative rate of the "true" stem cells. Such interactions between the stem cell niche and derivative, proliferating cells imply that communication exists between these various regions and thus point to future research directions.

In this regard, recent work demonstrating molecular controls for the location and number of stem cells in the shoot meristem of *Arabidopsis* may offer insights about similar controls in root meristems. In *Arabidopsis* shoot meristems, control of the size and positioning of the stem cell niche involves two-way signaling between the stem cells and an adjacent, underlying population of cells comprising the organizing center (Sablowski 2004). To maintain this balance, the CLV pathway, which restricts the number of stem cells, is balanced by WUS, a homeodomain transcription factor secreted by cells that constitute the underlying organizing center (Clark et al. 1997, Mayer et al. 1998). A feedback loop between these two proteins is part of the mechanism maintaining shoot meristem homeostatis (Brand et al. 2000, Carles & Fletcher 2003). In roots of *Arabidopsis*, overexpression of *CLE19*, which encodes a CLV3 homolog, causes a diminution in the size of the root meristem (Casamitjana-Martínez et al. 2003). This suggests that CLE19 functions by overactivating an endogenous CLV-like pathway involved in root meristem maintenance. Interestingly, overexpression of *CLE19* in the root meristem via the RCH1 promoter reduces meristem size without affecting either QC specification (QC-specific markers are still correctly expressed) or stem cell maintenance (Casamitjana-Martínez et al. 2003). However, when *CLE19* is placed under regulation of the CaMV35S promoter, the QC in the primary root disappears and the root meristem is fully differentiated (Fiers et al. 2004). Thus, although there is evidence of a role for *CLV3*-like genes operating in the root meristem, a pathway similar to the CLV/WUS feedback loop has not been found to date in *Arabidopsis* roots (Sablowski 2004). Although the CLV pathway has not yet been shown to operate in roots, it is clear that, as in shoots, many factors are likely involved in regulating root meristem organization (Sabatini et al. 2003).

THE CENTRAL ROLE OF AUXIN

One of the most satisfying conclusions to come from work with *Arabidopsis* root mutants is the central role of the plant hormone, auxin (IAA), in root development. Recent work demonstrates that auxin influences root development and specification from the earliest stages of embryogenesis (Hamann et al. 1999, 2002). In a truly landmark paper, Friml and others (2003) report that after division of the zygote of *Arabidopsis*, auxin accumulates in the smaller apical derivative (**Figure 3**). The auxin maximum remains apically positioned throughout the development of the preglobular embryo. However, by the 32-cell stage and apparently coincident with the initial expression of certain QC-specific markers, the auxin maximum shifts basally to the most distal (uppermost) cells of the suspensor, which includes the hypophysis, the progenitor of the QC. Some time after the QC is established,

the auxin maximum moves yet again to precursors of the columella initials (Sabatini et al. 1999). Changes in location of the auxin maximum are correlated with the distribution and redistribution of members of the PIN protein family, putative auxin efflux carriers of which at least four are expressed during *Arabidopsis* embryogenesis (Aida et al. 2002). Particular attention was drawn to the cellular distribution of PIN1, PIN4, and PIN7, whose locations shift during the early stages of embryo development. This led Friml et al. (2003) to postulate that the repositioning of the efflux carriers underlies and accounts for changes in auxin distribution and in the relocation of the auxin maximum. Further, Friml et al. (2003) suggest that auxin gradients may be reversed and that maxima may shift, not only because of changes in the location of the auxin transporters, but also because rates of auxin efflux may differ among the transporters.

In this model, therefore, specification of the root occurs as a consequence of a PIN1- and PIN4-dependent accumulation of auxin. In evaluating this model, it is worthwhile to consider the origins of this auxin. Friml et al. (2003) suggest that the auxin in preglobular embryos originates either in the suspensor or externally, perhaps in the embryo sac. However, by the globular stage and coincident with a change in the expression pattern of the PIN-dependent transporters, the embryo most likely begins auxin production in the apical region (Friml et al. 2003). Moreover, as the embryo matures, auxin production likely continues and increases at the apical end. Genes mediating the auxin response, including *BODENLOS* (which affects sensitivity to auxin) (Hamann 2001, Hamann et al. 1999, 2002), *MONOPTEROS* (which encodes an auxin response factor affecting polar auxin transport) (Aida et al. 2002, Berleth & Jürgens 1993, Hardtke & Berleth 1998), and *AUXIN RESISTANT1* (which affects the auxin response by mediating ubiquitination) (Leyser et al. 1993), have mutants that do not form an embryonic root. For two of these mutants, *monopterous* (*mp*) and *bodenlos* (*bdl*), initial regulation by auxin of root meristem development may be direct. For *mp* mutants, the first recognizable morphological effects of the mutation are seen at the octant stage of embryogenesis, in which four rather than two tiers of embryonic cells are formed. For *bdl* mutants, defects are first observed at the two-cell proembryo stage, in which the apical cell undergoes a transverse rather than longitudinal division.

Auxin efflux carriers: transmembrane proteins inserted in localized portions of the plasma membrane that preferentially move auxin out of the cell

SPECIFICATION AND DIFFERENTIATION OF THE HYPOPHYSIS

The specific controls in *Arabidopsis* for the division of the upper hypophysis derivative into the four-celled QC are not known (**Figure 3**). However, an early role for auxin is suggested. Mutations of the *HOBBIT* gene cause the hypophysis to develop incorrectly, which disrupts QC development (Willemsen et al. 1998). Moreover, *hobbit* mutants show a reduction in auxin reporter gene expression and accumulate the AXR3/IAA17 repressor of auxin responses, which supports a role for auxin in the earliest stages of root meristem specification (Blilou et al. 2002). Additionally, the *pin*7-mutant *Arabidopsis* lines show abnormal, premature divisions of the hypophysis. Finally, both the shift of PIN1 to the basal face of the hypophysis and the repositioning of the auxin maximum from the QC point to a role for auxin in the control of hypophysis mitoses. But why establish such high levels of auxin in these cells? Is it possible that a certain auxin threshold must be reached before the hypophysis can develop further and form the QC? And if so, are these auxin-regulated events dependent mainly on the positioning (and repositioning) of the PIN proteins (specifically PIN4)? If yes, what then regulates both these efflux carriers' positioning and subsequent shift in position in the hypophysis and its descendants? Possibly auxin directs or canalizes its own movement by regulating the repositioning of its own carriers. The canalization theory (Berleth & Sachs 2001, Sachs 2000) considers this mechanism and is based

upon the view that small, local differences in auxin concentration can be amplified by a self-reinforcing accumulation mechanism, which results in local auxin elevation and depletion in surrounding tissue. Can we use this theme of self-reinforcement to understand changes in the positioning of the auxin maximum at different stages of embryogenesis? Is auxin canalization linked with a repositioning of the efflux carriers? Friml et al. (2004) suggest that the localization of PIN proteins toward either the apical or basal end of cells depends, in part, on the level of expression of PINOID (PID), a serine-threonine kinase. Overexpression of PID causes a basal to apical relocalization of PIN and a consequent reduction of auxin in primary root tips. Moreover, if the *PID* gene is attached to a promoter primarily active in young embryos, globular- and heart-stage embryos are unable to establish an auxin maximum in the hypophysis. This results in a misspecification of the hypophysis. Most intriguing is that auxin itself controls cellular PID levels (Benjamins et al. 2001), which thereby suggests a feedback mechanism by which auxin regulates its own distribution. In the context of embryogenic root meristem organization, the accumulation of auxin in the apical cell following the first zygotic division (Friml et al. 2003) may be in response to an auxin feedback loop. If correct, the challenge is to discover the earliest steps of this auxin self-regulation. The elucidation of the role of PID is an important step toward realizing this goal (Friml et al. 2004). As well, the demonstration that other proteins, such as GNOM, influence localization of auxin efflux carriers (Steinmann et al. 1999), suggests the existence of other targets (proteins or genes) for auxin feedback and self-regulation. Taken together, substantial evidence now points to the likelihood that root specification is an auxin-dependent/linked process that begins early in the chain of events leading to QC formation. Significantly, however, high auxin levels do not always translate into quiescence. For example, the columella initials are the most rapidly cycling cells in the mature root yet have the highest auxin levels. Thus, high auxin per se does not cause cells to divide more slowly. Rather, auxin regulation of cell division likely depends both on auxin levels in a cell or group of cells and these cells' position in the root, especially position in relation to the QC and stem cell niche. In this regard, Blilou et al. (2005) have recently proposed a way in which auxin accumulation is linked to root specification; PIN proteins restrict *PLT* expression and in turn *PLT* genes maintain *PIN* transcription.

While specification of the uppermost suspensor cell as the hypophysis appears required for *Arabidopsis* embryonic root meristem initiation and organization (Friml et al. 2003), there are a large number of species in which the root meristem organizes without forming a hypophysis (von Guttenberg 1968). Examples include pea (*Pisum sativum*) (Tiegs 1912) and many grasses (e.g., maize) in which root meristem formation occurs from an irregular mass of embryonic parenchyma tissue within which the root pole organizes (von Guttenberg 1968). It is unknown whether the fact that a hypophysis is not required for embryonic root meristem development implies that a polar auxin gradient is also absent in embryos lacking a hypophysis. However, we consider this unlikely and rather posit that apical-basal auxin gradients are central to root meristem organization in all Angiosperms whether or not a hypophysis develops in the embryonic root.

A ROLE FOR THE QC IN THE ESTABLISHMENT, MAINTENANCE, AND ELABORATION OF PATTERNS

What does the QC do? The origins of the QC, or at least the temporal expression of some QC-specific genes early in root embryogenesis, suggests a role for the QC in root meristem establishment, but there is not yet much evidence to support this view. The evidence is mostly correlative: In embryos in which a QC fails to form, patterning of the primary

root meristem is disrupted (Friml et al. 2002). There is considerable evidence, however, that in mature roots a QC is essential for normal root growth (Feldman & Torrey 1976). By exposing roots to environmental extremes such as cold (Barlow & Adam 1989) or radiation (Clowes 1959), or by culturing roots in media supplemented with varying levels of nutrients (Feldman & Torrey 1976), QC size can be altered and meristem architecture affected. Exactly how these treatments lead to a change in QC size, that is, induce some QC cells to divide, is not known. In some cases it seems likely that QC cells are activated indirectly in response to environmental damage to the adjacent, rapidly dividing initials, which again suggests that a balance exists between the stem cells comprising the QC and the rapidly dividing initials. Damage to the initials thus shifts this balance, which is restored by activation of the QC and replacement of the damaged initials. Other evidence pointing to the necessity of the QC in the maintenance of root meristem organization comes from surgical approaches, including laser ablation. Destruction of one or more of the four *Arabidopsis* QC cells alters the developmental fate of contacting initial cells (van den Berg et al. 1997). In maize, excising the QC (and the RC) leads to a reorganization of the remaining root meristem tissue (Feldman 1976). A new root meristem will re-form, but only *after* a new QC begins to re-form (Feldman 1976). This suggests that it is not the cells occupying the QC niche that are special, but rather the niche that is special. Interestingly, if additional proximal root tissue (>0.5 mm in maize) is also excised with the QC, a new QC niche cannot re-form. Hence, the damaged root meristem is not replaced, which suggests that the "new" distalmost cells may have lost their competence to respond to auxin (Sabatini et al. 1999).

Changes in QC size and shape correlate with changes in tissue (vascular) patterns. Feldman & Torrey (1976) reported that as a consequence of shifting the location of the basal (proximal) edge of the QC, the PM is moved into a wider or narrower region of the root, further from and closer to the RC, respectively. These researchers showed that maize roots with small QCs had simpler vascular patterns and that an increase in QC size (upon moving the edge of the PM to a wider region of the root) corresponded to an increase in vascular complexity. They thus proposed that the QC influences root tissue patterns through alterations in its size.

PM: proximal meristem. In an actively growing root, the collection of dividing cells overlaying the basal (proximal) face of the QC. Through the proliferative activity of the proximal meristem, new root derivatives form

ROOT DETERMINATION AND THE QC AND STEM CELL NICHE

Although we tend to think of individual roots (and their root meristems) as having the potential for unlimited growth, most roots in fact have a limited lifetime (Chapman et al. 2003, Varney & McCulley 1991 and references cited therein). In some special instances, however, individual roots can be quite long-lived, such as those of certain Gymnosperms, which can live for more than one year (Wilcox 1962), and for roots of certain species that can be maintained for long periods in tissue culture (Torrey 1958). But this behavior is the exception. Roots of most species, including those of *Arabidopsis*, become determinate when they are four to five weeks old (Barlow 1997, Baum et al. 2002). In wildtype *Arabidopsis*, root determination is preceded by an activation of the structural initials (the QC) resulting in a change from closed to open in apical meristem architecture. Ultimately, the four cells comprising the QC are no longer distinct and found in their usual position, just proximal to the RC, are "disorganized," vacuolated cells (Baum et al. 2002). The stem cell niche has been lost; having become determinate, the root ceases to grow. Barlow (1997) suggests that we may view this determination essentially as a loss of the QC's ability to divide and thereby replenish the functional initials. How might we view the underlying causes of determination? If, as suggested, the niche is primarily dependent on auxin, then perhaps insufficient auxin accumulates to maintain the niche? Or perhaps in older root meristems,

there is a lessening of the inhibitory effects of the QC cells on the differentiation of the neighboring functional initials (van den Berg et al. 1997), which thereby upsets the balance between functional and structural initials and leads to determination. Perhaps, too, one might consider possible parallels with the model of stem cell termination proposed for the conversion of cells in a vegetative shoot meristem to part of a floral meristem (Lenhard et al. 2001).

An extreme example of root determination is found in species of the Podostemaceae, in which roots either never form or abort very early during embryogenesis (Rutishauser 1997, Suzuki et al. 2002). A number of known mutations that underlie similar phenoypes in *Arabidopsis* [e.g., *axr6* (Hobbie et al. 2000), *short-root* (Helariutta et al. 2000), *monopterous* (Hardtke & Berleth 1998), *rfc3* (Horiguchi et al. 2003), and *root meristemless* (Cheng et al. 1995)] show premature root determination, which directs us to an examination of the underlying genetic controls of root determination. In particular, in the *rml* mutant of *Arabidopsis*, the root meristem forms normally during embryogenesis only to disorganize shortly after germination. Because the *RML* gene encodes the first enzyme of glutathione (GSH) biosynthesis, gamma-glutamylcysteine synthetase, it has been suggested that this mutation causes meristem disorganization by interfering with a redox-regulated G1/S transition of the cell cycle. This would lead to an imbalance in the stem cell population (Vernoux et al. 2000). These efforts thus point to candidate genes whose homologues may underlie the determinate root phenotypes, as in the Podostemaceae.

Although determination of roots is generally viewed as an "ending" of root function, in some instances, the determination process can also be considered a "beginning." For example, in some palms (e.g., *Cryosophila*), the first-order roots produced on the trunk become determinate and are converted into protective spines (Tomlinson 1990). Other examples of determinate spine roots occur at the nodes of some bamboos. How this transformation and determination occur, especially in regard to already well-characterized meristem landmarks such as the QC, has recently been explored in roots of cacti (e.g., *Pachycereus* and *Stenocereus*) by Rodríguez-Rodríguez et al. (2003). These researchers showed that shortly after germination, the primary root becomes determined, which leads to the formation and outgrowth of many branch roots requisite for seedling establishment (Dubrovsky 1997). In this determination process, a QC disappears at or shortly after germination. Rodríguez-Rodríguez et al. (2003) thus concluded that maintenance of typical meristem architecture and indeterminate growth are impossible in the absence of a QC. Toward an understanding of the mechanism of determination, Rodríguez-Rodríguez et al. (2003) suggest similarities between their observations and those regarding defects in *Arabidopsis* roots caused by mutations of either *HOBBIT* (Blilou et al. 2002, Willemsen et al. 1998) or *PINOID* (Bennett et al. 1995, Christensen et al. 2000, Friml et al. 2004). Because a mutation of *PINOID* results in increased auxin efflux in *Arabidopsis* roots, Rodríguez-Rodríguez et al. (2003) treated the developing (not-yet-determined) cacti roots with the auxin transport inhibitor NPA to ascertain whether they could rescue the cacti roots and maintain the indeterminate state. They were unsuccessful. This may be explained by the recent finding that PINOID overexpression leads to meristem disorganization and auxin reduction at the root tip, which suggests that cacti roots may become determinate because of too little and not too much auxin (Friml et al. 2004). Supporting this suggestion are reports that the terminal differentiation of primary-root meristems of 35S::*PID* seedlings is preceded by a reduction in the expression of auxin-responsive reporter genes (Benjamins et al. 2001). Although little is known of the molecular mechanisms leading to QC disappearance and root determination, that *PLT* expression is required for maintenance of both the QC and normal

meristem architecture may mean that molecular events underlie the indeterminate state of roots. Aida et al. (2004) explored this possibility by making double mutants in *Arabidopsis* of this two-gene family (*plt1 plt2*), which showed that lateral root meristems disorganized and terminally differentiated shortly after their initiation.

THE ROLE OF THE RC IN MERISTEM ESTABLISHMENT AND MAINTENANCE

Because division of the hypophysis simultaneously produces derivatives that are the progenitors for both the QC and RC, the question arises as to the requirement of a RC for meristem establishment. In the absence of a RC, would a root meristem organize? Two types of indirect evidence suggest that a RC is central to primary root meristem establishment and maintenance. First, no capless primary (embronic-in-origin) roots exist in nature (von Guttenberg 1968). While it is true that lateral roots of some highly derived species lack a RC (Hiyama et al. 2002, Suzuki et al. 2002), there are no reports of embryonic roots developing without a RC. Second, no capless, embryonically formed roots have been reported from *Arabidopsis* mutant screens. This may simply be coincidental since in *Arabidopsis*, any mutation affecting the hypophysis would be expected to impact development of both the RC and root meristem (Willemsen et al. 1998). To the contrary, we conclude that the simultaneous origin of the progenitors of both the RC and QC is not coincidental and points to a developmental linkage between the RC and QC that is established early in embryogenesis. Additional evidence of the interdependence of the RC and QC comes from experiments in which the RC can be excised (via a tear in the columella initials) (Feldman 1977, Lim et al. 2000). As a consequence of RC removal, the QC activates and meristem architecture is dramatically altered (Feldman 1976). In this regard, one would predict that destruction of RCIs, employing the same approach used to ablate QC and other root tip cells (van den Berg et al. 1995, 1997), would also activate the QC. The recent report that transgenic toxin expression in RCs leads to alterations in root meristem activity reinforces the notion of the RC's importance in overall meristem function (Tsugeki & Federoff 1999), in part by affecting lateral auxin redistribution (Blilou et al. 2005). As well, reports that RC border cells in pea affect meristem activity and gene expression provide additional evidence for a regulatory role for the RC in root meristem function (Woo et al. 1999).

RCI: root cap initial

Experimental data thus show that the RC is required not only for meristem establishment but also for meristem maintenance. While at this time we can only speculate about the nature of this regulation, the shift of the auxin maximum during early embryogenesis to the columella initials suggests that the nascent RC may function as a positional marker that defines where the new QC will re-form. The recent report that RCs are short-lived in determinate roots of certain cacti (Rodríguez-Rodríguez et al. 2003) supports this suggestion. It also raises the intriguing possibility that root determination may have its origins in changes in the RC that could translate into changes in the positioning and degree of the auxin maximum. Given the fact that a small amount of auxin can create a sink and cause more auxin to move toward this sink (Feldman 1981), the shift in the auxin maximum to the columella initials may be an outcome of the development of an auxin sink in the RC. In this regard, studies on the timing and distribution (and redistribution) in the RCs of PIN and PINOID should be very informative (Friml et al. 2004).

COMMUNICATION IN THE ROOT MERISTEM

The coordinated activities and developmental links between the RC and the QC point to a two-way communication between these two populations. Not only does the RC

communicate with the QC (as shown by decapping experiments) (Feldman 1976, Lim et al. 2000) but, as suggested from laser-ablation experiments, the QC communicates with the RC (van den Berg et al. 1995, 1997). In *Arabidopsis*, ablation of one or more QC cells causes the adjacent, rapidly cycling columella cells to cease dividing and instead undergo differentiation (van den Berg et al. 1995). Although the nature of this hypothesized two-way communication is not known, we have a few clues. One of the more intriguing comes from maize roots, which increase slightly their rate of growth following cap excision (L.J. Feldman, personal observations). As well, the increase in mitoses in the QC and the differentiation of membrane-bound starch grains in the terminal-most QC cells following cap excision (Barlow 1974) suggest that signals from and processes in the RC are important in the maintenance of both quiescence and the undifferentiated status of QC cells. We can thus conclude that these signals, whether originating in or redistributed by the RC, play important roles in balancing cell division and differentiation in the root meristem. At this point, while we can only speculate as to the nature of such communication and positional information, the communication mechanism surely involves auxin in part. Upsetting auxin transport perturbs the balance between the QC and RC and can result in the QC penetrating and displacing the original cap (Jiang et al. 2003). Also, given the high levels of oxidative stress in the QC (Jiang et al. 2003), one could hypothesize a role for free radicals in short-range communication as has already been shown for plant responses to pathogens (Laloi et al. 2004, Wojtaszek 1997). In addition, the recent demonstration of the requirement of SCARECROW (SCR) for QC specification suggests that interactions such as those of WUS/CLV in the shoot may operate in root meristems in balancing proliferation and differentiation (Doerner 2003, Sabatini et al. 2003). Sabatini et al. (2003) postulate that SCR activity in the QC is important in maintaining function in the surrounding stem cells (functional initials). *SCR* activity is regulated by SHORT-ROOT, a transcription factor that originates in the stele (Benfey et al. 1993, Helariutta et al. 2000). Thus, taken together, these observations provide specific evidence for short-range communication feedback loops between the various cell types comprising the root meristem. Additionally, this work (Sabatini et al. 2003) focuses attention on communication between the QC and the cells bordering on the proximal (basal) face of the QC, the proximal meristem (PM) (**Figures 1**, **2**). Damaging the PM by exposing roots to environmental extremes activates the QC, which results in a replacement of the damaged PM cells and a re-formation of the QC (Barlow & Adam 1989). It would be interesting to view this damage and activation in *Arabidopsis* in relation to *SCR* and *SHR* activity. In this regard, activation of the QC might provide insight into the unidentified signals believed to move from the QC as a result of *SCR* action (Sabatini et al. 2003). The challenge now is to determine the interplay, or feedback, between QC-, RC-, and PM-derived signals and to show which of these act as positional signals and thereby promote or inhibit cell-type specific differentiation.

ROS: reactive oxygen species. ROS are molecules or ions formed by the incomplete one-electron reduction of oxygen. Reactive oxygen intermediates include singlet oxygen, superoxides, peroxides, and hydroxyl radicals. ROS participate in the regulation of signal transduction and gene expression as well as in the process of oxidative damage to nuclei acids, proteins, and lipids

REDOX REGULATION OF ROOT DEVELOPMENT

We next consider recent views on the mechanisms linking auxin to the development of the stem cell niche, the QC, and root meristem establishment. An important insight into these links has come from recent work showing that the redox status of the QC is different from that in adjacent, rapidly dividing cells: The QC has a more oxidizing environment (Jiang et al. 2003, Kerk & Feldman 1995, Kerk et al. 2000, Liso et al. 2004, Sánchez-Fernández et al. 1997). Consequently, Jiang et al. (2003) have proposed that auxin affects the cell cycle in the QC via changes in redox.

Overall cell redox is determined by the net contribution of different redox couples and ROS. In biological systems, the major

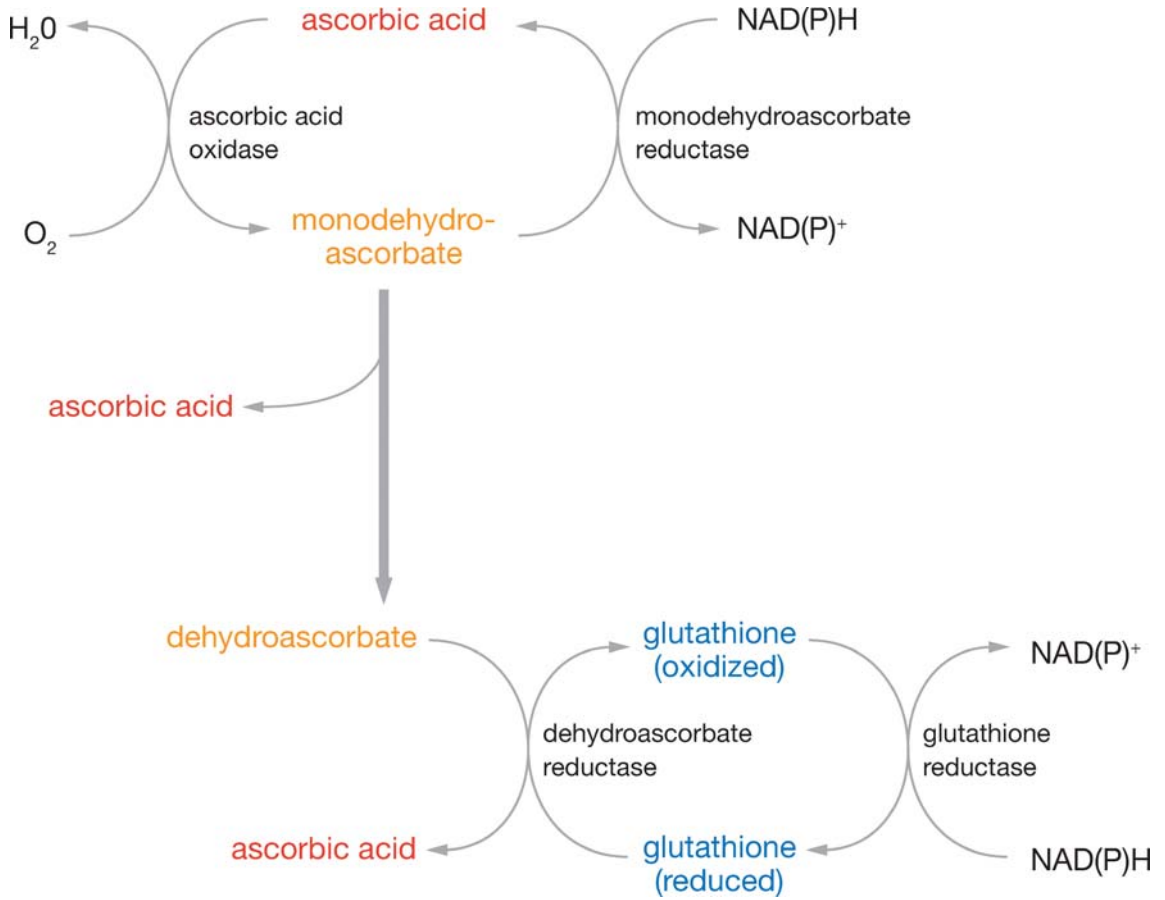

Figure 4

Ascorbate/gluthatione cycle.

(and usually most abundant) redox couples are GSH/GSSG and AA/DHA (Arrigo 1999; Arrigoni & De Tullio 2002; Banhegyi et al. 1997; Conklin & Barth 2004; De Tullio & Arrigoni 2003, 2004; Filomeni et al. 2002; May et al. 1998; Noctor et al. 2002; Potters et al. 2002, 2004; Schafer & Buettner 2001), which are biochemically interconnected via the ascorbate/glutathione cycle (May et al. 1998) (**Figure 4**). The levels and ratios of the reduced and oxidized forms of these two couples are a direct indicator of a tissue's overall redox status.

Many lines of evidence suggest that cellular redox status plays a critical role in regulating cell proliferation (Barzilai & Yamamoto 2004, den Boer & Murray 2000, Reichheld et al. 1999, Shackelford et al. 2000). In Chinese hamster ovary fibroblasts, GSH concentration has been related to the cell-cycle phase, with the lowest GSH concentration at G1, a higher concentration at S, and the greatest concentration at G2/M (Conour et al. 2004). In human colon cancer CaCo-2 cells, a change in the ratio of GSH to GSSH to favor GSSH, the oxidized form, resulted in cells arresting at G1/S (Noda et al. 2001). In plants too, changes in the absolute amounts and/or ratios of reductants/oxidants affect cell proliferation, as shown by the *rml1* mutant, in which less glutathione is synthesized because of a mutation

GSH/GSSG: $\text{glutathione}^{\text{reduced}}/\text{glutathione}^{\text{oxidized}}$

AA/DHA: ascorbate/dehydroascorbate

AAO: ascorbic acid oxidase

GR: glutathione reductase

in gamma-glutamylcysteine synthetase, the first enzyme in glutathione biosynthesis. In this mutant, the root meristem forms normally but ceases producing new derivatives shortly after germination and disorganizes (Vernoux et al. 2000). Similarly, treating cultured plant cells with a specific inhibitor of gamma-glutamylcysteine synthetase can block the plant cell cycle (Potters et al. 2004, Sánchez-Fernández et al. 1997). Addition of AA increases the rates of cell proliferation in plant cells (Kerk & Feldman 1995, Liso et al. 1988, 2004), whereas addition of the oxidized form of AA, DHA, delays cell-cycle progression (Potters et al. 2002, 2004). Reichheld et al. (1999) showed that tobacco cells in G1 were more sensitive to oxidative stress than cells in S phase; this accords similar findings with regard to mammalian cells, in which G1 progression is influenced to a large extent by extracellular signals (Hulleman & Boonstra 2001, Juliano 2003). Reichheld et al. (1999) thus proposed that redox sensing could be central to the control of cell-cycle progression under conditions of environmental stress. These observations, plus reports of relatively low levels of GSH (Jiang et al. 2003, May et al. 1998) and AA (Kerk & Feldman 1995, Liso et al. 2004) in the QC, and the observation that AA, or its immediate precursor, L-galactono-gamma-lactone, activates the QC (Kerk & Feldman 1995, Liso et al. 2004), has led to the proposal of a linkage between redox status and the arrest of QC cells in G1 (Jiang et al. 2003).

Fundamental cell cycle mechanisms are conserved in eukaryotes and involve as core regulators cyclins, cyclin-dependent kinases, cyclin-dependent kinase inhibitors, and the protein retinoblastoma (reviewed in De Veylder et al. 2003, Dewitte & Murray 2003, Massague 2004, Schafer 1998). Reports that oxidative stress and redox status affect the expression and/or activities of these and other cell-cycle regulators and thus lead to cell-cycle arrest highlight possible mechanisms underlying direct redox control of the cell cycle (reviewed in Barzilai & Yamamoto 2004, Boonstra & Post 2004, den Boer & Murray 2000). The general characteristics of these controls include downregulation of G1 D-type cyclins, inhibition of the ubiquitin pathway by reducing the activities of proteasome or the enzymes involved in the ubiqitination process, upregulation of CKIs, and suppresion of retinoblastoma phosphorylation (Esposito et al. 2000, Hosako et al. 2004). In plants, A-type cyclins are involved in S-phase progression (Dewitte & Murray 2003). Under oxidative stress, the expression of two A-type cyclins in BY-2 tobacco cells is downregulated and results in cell-cycle arrest at G1/S (Reichheld et al. 1999). Intriguingly, Burssens et al. (2000) showed that an A-type cyclin is not detected in the QC of the *Arabidopsis* primary root; this correlates well with the more-oxidized status of QC and the arrest of QC in G1. We thus conclude that redox directly regulates the plant cell cycle.

In plants, auxins have been linked to changes in redox (Jiang et al. 2003, Takahama 1996). High levels of auxin are correlated with the generation of H_2O_2, $O_2^{\cdot -}$, and other ROS (Joo et al. 2001, Pfeiffer & Höftberger 2001, Schopfer 2001, Schopfer et al. 2002). The mechanisms leading to ROS generation are not known but may involve free-radical generation via peroxidase-catalyzed oxidation of IAA (reviewed in Kawano 2003). ROS generation may also occur as a consequence of auxin affecting the activities of redox-associated systems (Jiang et al. 2003, Kisu et al. 1997, Pignocchi & Foyer 2003, Pignocchi et al. 2003, Takahama 1996). In this regard, upregulation by auxin of AAO in the QC (Jiang et al. 2003, Kerk & Feldman 1995) and concomitant downregulation of GR activity (Jiang et al. 2003) might possibly underlie auxin-induced changes in redox in the QC. In the QC, more AAO would lead to a rapid conversion of AA to DHA (Pignocchi & Foyer 2003, Pignocchi et al. 2003) and thereby diminish the cells' capacity to neutralize newly formed ROS (**Figure 4**) (Conklin et al. 1996, Pastori et al. 2003). As well, the concomitant, IAA-regulated reduction in GR in the QC would

reduce even further the capacity to buffer redox changes. This is because a lowering in GR activity results in less AA being regenerated (**Figure 4**). In addition, auxin may influence tissue redox status through the induction of NADH oxidase leading to the production of H_2O_2 (Liszkay et al. 2003, Morre et al. 2003). In summary, limited but convincing evidence points to ROS generation as part of the mechanism of auxin action in the QC.

Given the G1 state of most QC cells, the demonstrable oxidized redox status of the QC, and the central role for auxin in root development, a model linking auxin to quiescence and to root meristem establishment has been proposed (**Figure 5**) (Jiang et al. 2003, Kerk & Feldman 1995, Kerk et al. 2000). The key elements of this pathway are initiated early in embryogenesis with the polar accumulation of auxin at the presumptive root pole. As a consequence, mechanisms are developed to regulate auxin levels, which results not only in auxin homeostasis but the formation of a region with a relatively oxidized redox status. This leads to the accumulation of cells at the G1/S checkpoint and the origin of the QC. That a QC is specified before a root meristem organizes (Feldman 1976) and that a QC must be maintained for root meristem integrity suggests that the QC has a central role in integrating and translating auxin's biochemical and molecular effects in root organogenesis.

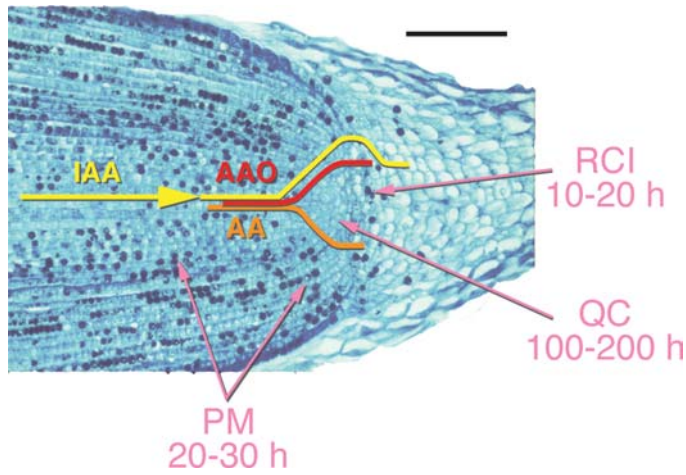

Figure 5

Schematic view of the distribution in the root apex (location of maxima and minima) of auxin (IAA), ascorbic acid oxidase (AAO), and ascorbic acid in relation to the QC. Average cell-cycle times (in hours) are indicated for various regions. PM, proximal meristem; RCI, root cap initials. Scale bar = 100 μm.

SUMMARY

The delimitation of the stem cell niche, containing both the structural initials (the QC) and the functional initials, is a defining step in root meristem organization. Upon such delimitation, a "reference point" is established and the root meristem organizes. Central to this view is the supposition that specific patterns and timing of auxin distribution are requisite for normal root development. We propose that specification involves direct and indirect interactions of auxin with essential genes (Aida et al. 2004, Reed 2001) and, as we previously have suggested, auxin-regulated, localized changes in redox (Jiang et al. 2003). Specification likely also involves an overlaying of the auxin maximum onto other morphogen gradients (Berleth 2001).

Underlying this specification, and essential for root meristem establishment, is the self-regulation by auxin of its own distribution and redistribution (Benjamins et al. 2001, Feldman 1981). We suggest that auxin effects its own transport by regulating the location and directionality of its own carriers, and thereby determines the size and position of the auxin maximum. A change in the maximum may also be accounted for by local differences in auxin synthesis and/or metabolism (Zazimalova & Napier 2003). In this regard, evidence linking auxin in the QC to high levels of auxin-metabolizing enzymes (Kerk & Feldman 1995) suggests that the "shift" of the auxin maximum from the QC to the RCI may in part be explained by auxin catabolism in the QC. Understanding why (and how) the auxin maximum is positioned and why it "pauses" in certain cells of the embryo are crucial to an appreciation of auxin-regulated meristem initiation (Uggla et al. 1996).

Finally, based on the fact that root meristems are sensitive to and very effective in metabolizing auxin (Feldman 1981), we propose that specification of the QC and stem cell niche, and subsequent root meristem organization, are inevitable developmental outcomes of the necessity to regulate auxin levels. In other words, root meristems that formed in response to auxin in turn become the mechanism for modulating auxin levels and thereby maintain auxin homeostasis. This may be a perfect feedback loop! Carrying this view to an extreme, one might even speculate that roots evolved as a consequence of plants' "need" to respond to increased levels of polarly transported auxin.

SUMMARY POINTS

1. The QC is composed of stem cells.
2. The stem cell niche is, in part, specified by auxin.
3. The stem cell niche and the QC are specified early in embryogenesis.
4. The formation of a QC is necessary for and precedes root meristem organization.
5. A QC must be maintained in order for the root meristem to remain organized and indeterminate.
6. Auxin specifies the stem cell niche and the QC by mediating localized changes in redox, preferentially favoring a more oxidizing environment.
7. The origin of roots may be linked to auxin-regulated development of oxidizing microenvironments, which culminates in root meristem establishment.

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