Available online at www.sciencedirect.com

ScienceDirect

Current Opinion in Plant Biology

Coordination of plant cell growth and division: collective control or mutual agreement?

Robert Sablowski

Plant tissue growth requires the interdependent cellular processes of cytoplasmic growth, cell wall extension and cell division, but the feedbacks that link these processes are poorly understood. Recent papers have revealed developmentally regulated coupling between plant cell growth and progression through both mitotic cycles and endocycles. Modeling has given insight into the effects of cell geometry and tissue mechanics on the orientation of cell divisions. Developmental inputs by auxin have been highlighted in the control of cell turgor, vacuole function and the microtubule dynamics that underlies oriented growth and division. Overall, recent work emphasizes growth and proliferation as processes that are negotiated within and between cells, rather than imposed on cells across tissues.

Address
Cell and Developmental Biology Department, John Innes Centre, Norwich Research Park, Norwich NR4 7UH, UK

Corresponding author: Sablowski, Robert (robert.sablowski@jic.ac.uk)

Current Opinion in Plant Biology 2016, **34**:54–60

This review comes from a themed issue on **Cell biology**

Edited by **Keiko Sugimoto** and **Arp Schnittger**

http://dx.doi.org/10.1016/j.pbi.2016.09.004

Introduction

Both in plants and animals, organ growth can tolerate wide variations in cell proliferation through compensatory changes in cell size and shape, supporting the idea that cell growth and division are controlled in parallel by external signals that co-ordinate cell behavior at the tissue and organ level [1,2]. At the same time, growth and cell cycle progression appear to be connected by homeostatic feedback loops within each cell [3,4,5••] and this intracellular coordination would be expected to modify responses to external signals. The relative importance of external and intracellular integration of the processes required for cell and tissue growth is unclear in all multicellular organisms.

In plants, the rate and direction of cell growth depend on the balance between turgor pressure and the resistance of the cell walls to tensile stress [6,7]. As the walls yield to turgor pressure, the larger cell volume is occupied through a combination of increased macromolecular synthesis and enlargement of vacuoles (Figure 1) [8]. During the proliferative stage, the enlarged cell eventually divides in a particular direction. The coordinated processes of cell growth and division also respond to external signals, such as nutrient availability and mechanical stress [9,10], and to developmental control, typically mediated by hormones and localized expression of transcription factors [11]. Here, I review recent insights on the intracellular mechanisms that coordinate plant cell growth and division, how these mechanisms respond to external inputs and how integration within each cell feeds back on the growth of tissues and organs. I focus on meristems and organ primordia, where cell growth and division coexist, discussing initially the coordination of rates, then directions of cell growth and division.

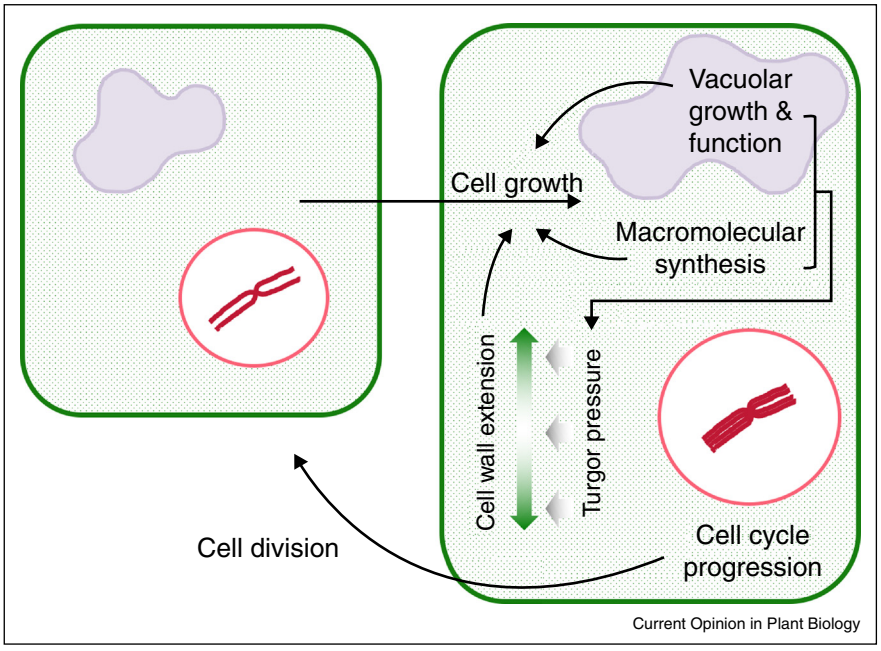
Coordination between rates of growth and cell cycle progression

As mentioned above, turgor pressure is the mechanical driver for plant cell growth. It is often assumed that turgor is constant, but this is not always the case: the emergence of lateral root primordia is facilitated by softening of cell walls in the overlying cortex and epidermis [12] and by localized regulation of turgor mediated by aquaporins [13]. It has recently been shown that during the earliest stages of lateral root emergence, enlargement of pericycle cells is accommodated by an auxin-induced reduction in the size of neighboring endodermal cells, presumably requiring turgor changes; without this accommodating response, the lateral root cannot develop [14••].

The increased cell volume associated with turgor-driven wall extension is occupied by a combination of macromolecular synthesis and vacuolar growth. In the root meristem, auxin has been shown to limit the enlargement of late meristematic cells through rapid post-transcriptional increase in the abundance of vacuolar SNARE proteins, which control vacuolar morphology [15•]. These auxin-induced changes were mediated by the actin cytoskeleton and reduced the volume of the vacuole relative to that of the cell [16••]. The auxin-dependent changes in vacuole morphology were proposed to regulate cytosol density during cellular expansion [16••]; if this is the case, vacuolar function might also be expected to be coordinated with overall macromolecular synthesis (Figure 2).

Ultimately, cell growth depends on macromolecular synthesis, which is coordinated by the conserved

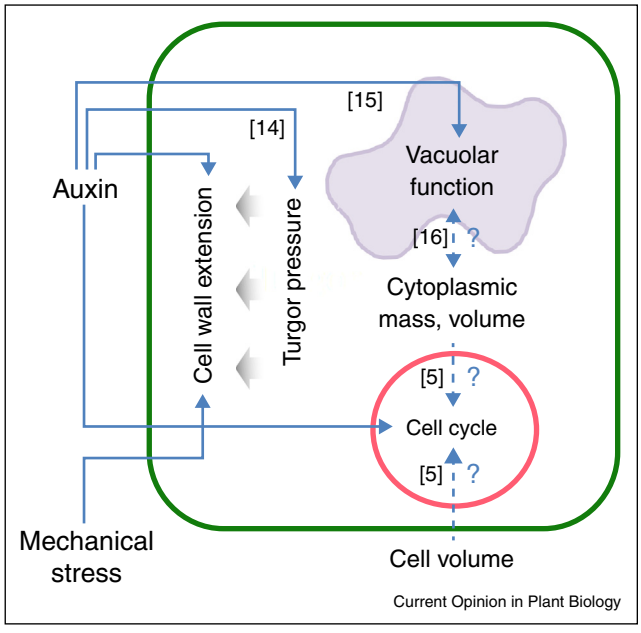
Figure 1



Overview of the coordinated cellular processes required for meristem and organ primordium growth.

Ser/Thr kinases TOR and SnRK1 [10]. When sufficient sugar is available, TOR promotes meristem activity and organ growth not only through its conserved role in promoting macromolecular synthesis, but also through direct regulation of the cell cycle regulator E2Fa and potentially through control of cell wall remodeling [17–19]. At the same time, high sugar levels lead to inhibition of the SnRK1 kinase, which promotes catabolism and inhibits cell cycle progression [20]. Recently, a link emerged between SnRK1 and the differential growth that establishes the boundaries between the meristem and emerging organs [21]: overexpression of the catalytic subunit of SnORK1 (AtKIN10) caused organ fusions [22] and AtKIN10 directly interacted with the transcription factor PETAL LOSS, which controls organ boundary development [23].

Figure 2



External inputs (solid blue arrows) and internal feedbacks (dashed blue arrows) in the coordination of cellular processes required for growth. Question marks indicate hypothetical feedbacks. Numbers correspond to recent papers relevant to the interactions shown

When nutrients are not limiting, overall meristem activity is high, but the growth rate of neighboring cells within the meristem and developing organs is surprisingly variable [5••,24••]. Detailed analysis in developing sepals suggested that growth curves are similar in neighboring cells, but shifted and scaled by size [25]. This local heterogeneity of growth rates is affected by microtubule dynamics, which probably mediates cellular responses to the mechanical stress that builds up during tissue growth [24••]. Presumably the response of individual cells to local stress leads to variable growth rates through changes in cell wall extensibility [9,26,27]. However, it remains unknown whether vacuolar function and turgor pressure might also be locally regulated and whether different rates of cell enlargement are accompanied by variation in biosynthetic rates.

Over time, variable cellular growth rates combined with the imprecision of cell divisions [5••,28] would be

expected to increase variability in cell sizes, but meristem cell sizes remain uniform for extended periods. In yeast and in at least some animal cell types, uniform cell sizes are maintained by checkpoints that link cycle progression to growth [1,3,4,29]. Computer simulations and recovery from perturbation of cell sizes suggested that a feedback between cell size and cell cycle progression also operates in the shoot meristem [5••]. This raises the question of why uniform cell sizes should matter. In unicellular organisms, the reasons proposed relate to cell physiology, which is affected by the ratio between cell volume and surface [4,30]. In the meristem, an additional function could be to achieve the spatial resolution required to pattern structures at a scale comparable to cell sizes, such as organ boundaries [5••].

As in animals, it remains unclear how plant cells could assess their size and feed back the information on cell cycle progression (Figure 2). It will be important to determine what aspect of size (e.g. cell volume, cytoplasmic volume or cell surface area [29]) best correlates with cell cycle progression. A potential molecular mechanism is illustrated by recent work in budding yeast, with dilution of a cell cycle inhibitor whose synthesis rate does not scale with cell volume [31••]. In the unicellular alga *Chlamydomonas*, cell growth in the light is followed by multiple rounds of rapid division in the light, restoring the initial cell size; in this case, accumulation of a variant cyclin-dependent kinase during light growth determined the subsequent number of divisions and consequently the final cell size [32••].

In contrast to the meristem, differentiating organs show a wide range of cell sizes and shapes, suggesting that the mechanisms that link cell growth to cell cycle are developmentally regulated. Accordingly, the coordination between cell size and S-phase entry changes at the transition from meristem to organ identity [33], and cell sizes diverge in developing sepals due to variability in cell cycle length and in the switch to endocycles [34]. The shift to endocycles is caused by selective inhibition of mitosis, while allowing repeated re-entry into S-phase; the consequent increase in cell ploidy is believed to increase the physiologically sustainable cell size [35]. Consistent with this permissive role of endoreduplication, the transition to endocycles precedes cell enlargement in the root meristem [36]. However, like the coupling between the mitotic cycle and cell size, the relation between endocycles and cell size appears to be developmentally regulated and dependent on cell type [37].

Coordination between oriented growth and division

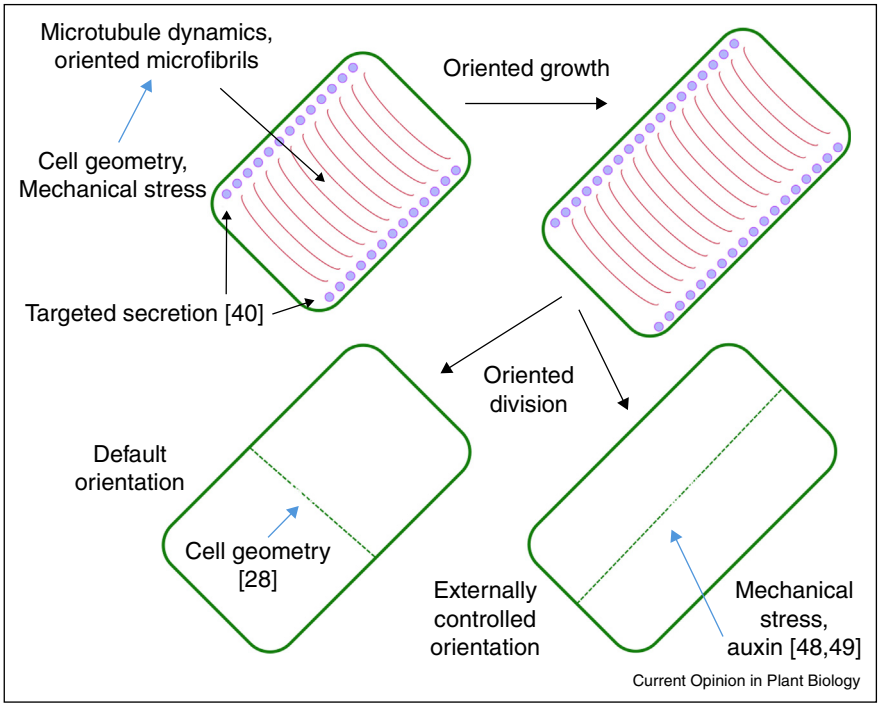
Morphogenesis depends not only by on the rates, but also the directions of growth [38]. Directional cell growth is influenced by the deposition of cellulose microfibrils, which increase tensile strength in the direction along which they are laid down [7]. The deposition of cellulose microfibrils is in turn guided by the orientation of cortical microtubules, which serve as tracks for the cellulose synthase complexes that produce the microfibrils [39]. In addition to the established role of cellulose microfibrils, a novel mechanism that controls oriented cell growth has been revealed: targeted vesicle traffic to the edges of cell walls (i.e. to the intersection of wall facets) was required for anisotropic growth in root and leaf primordia, suggesting that edges have a special role in cell wall mechanics [40••]. Like the pattern of microfibril deposition, this targeted secretion depended on microtubule arrays, although in this case the actin cytoskeleton was also involved [40••] (Figure 3).

The dynamic and self-organizing properties of microtubule arrays make them, and consequently the direction of cell growth, highly sensitive to external inputs. One of these external influences is mechanical stress, which results in part from the growth of connected cells within the tissues [9,26,27], and recent work has shown how cells integrate mechanical stress conditioned by their own shape [41•]. Mechanical stress also influences oriented growth by altering auxin transport independently of the microtubule arrays [26,42]. Auxin accumulation, which can result from altered transport, disrupts microtubule arrays to promote isotropic cell growth during primordium emergence [43••]. The emerging picture is that multiple feedback loops coordinate cell wall mechanics, microtubule dynamics and auxin transport and to regulate oriented growth of cells and tissues.

Cell cycle is connected to oriented growth through the placement of cell division planes. It is generally accepted that in the absence of external cues, plant cells divide by default along the smallest possible plane that produces equally-sized daughter cells [28,44]. In practice, however, individual cells often deviate from this general rule. To describe and simulate realistic cell division patterns, statistical image analysis has been combined with models including a stochastic component [28,44,45]. This stochastic component may reflect the underlying molecular mechanism. It has been proposed that the cell division plane is determined by tensile microtubule strands that radiate from the nucleus and are stabilized on the shortest path to the cell walls [46], and microtubule dynamics may explain how alternative division planes may be selected, corresponding to local minimal areas [44]. The involvement of microtubule arrays both in responses to mechanical stress and in connecting cell division plane to cell geometry suggests that both processes converge competitively on the regulation of microtubule dynamics [47].

The geometrical and biophysical rules mentioned above are considered to operate by default during proliferative growth, but they can be overridden by chemical signaling. This is observed most clearly in asymmetric, formative

Figure 3



Overview of cellular processes required for oriented cell growth and division. Blue arrows correspond to inputs that affect oriented cell behavior; numbers in brackets correspond to relevant recent papers.

cell divisions, which give rise to different cell types. During early embryogenesis, numerous divisions do not follow the default geometric rules described above for proliferative growth. These asymmetric divisions require auxin signaling and correlate with the acquisition of different cell fates [48••]. Presumably auxin re-orients cell division by altering the dynamics of microtubule arrays as discussed above, but the molecular details remain unknown.

By changing cell connectivity, intercellular communication and cell fate, asymmetric divisions are expected to have major effects on subsequent development, as shown by recent work on vascular patterning in the growing embryo, in which an auxin-induced source of cytokinin induces periclinal cell divisions in neighboring cells to create vascular progenitors [49•]. This work also suggested that correct patterning depends on the initial cell geometry, which originated from a symmetry-breaking division very early in embryogenesis.

What remains unclear, however, is to what extent oriented divisions impact on the mechanics of tissue growth. A causative role for oriented divisions has been suggested based on periclinal divisions seen in subepidermal cells before the outgrowth of leaf primordia [50,51]. On the other hand, classic work on the maize *tangled-1* mutant, in which the orientation of cell divisions is disrupted, showed relatively modest effects on leaf size and shape [52]. More recent work on the development of pitcher leaves in the carnivorous plant *Sarracenia purpurea* has suggested that changes in the orientation of cell division in subepidermal layers cause differences in primordium growth that initiate the formation of the pitcher [53]. It remains difficult, however, to exclude that oriented divisions are a response to mechanical stress within the tissues, which could result from regulation of growth through cell wall mechanics.

New walls are expected to bear load and alter the distribution of mechanical stress, at least locally. Although it has been considered that the placement of new walls has little effect on overall tissue mechanics, simulations have shown that the rules to orient new cell divisions do affect the local variability of growth and the overall tissue growth [6,47]. The placement of cell walls also determines the overall shape of daughter cells, and mechanical models have shown how the shape of individual cells can influence patterns of tissue growth [54]. The cumulative effect that a regulated pattern of cell divisions can have on tissue growth remains unclear and is an important topic for future work.

Conclusions and perspectives

The details of how different growth processes interact within and across cells is important are important for our

understanding of how the size and shape of plant organs are genetically determined. An extreme view, articulated by Kaplan in the 1990s, is that subdivision of organs into cells provides physiological support, allows cell specialization and may have mechanical consequences, but rates and orientations of tissue growth are controlled chiefly by supra-cellular cues [55]. Many current models of plant morphogenesis embrace a similar view, partly due to the difficulties of implementing spatial models of organ growth with cellular resolution [6]. The work reviewed here emphasizes growth as a process of negotiation within and between cells, in which internal coordination of metabolism, cell wall functions and cell cycle progression are integrated with mechanical and chemical signals operating across tissues. The outcome of this intracellular integration, in turn, feeds back on the directions and rates of tissue growth and on patterning. Quantitative imaging of cell behavior combined with computational models that specify the properties and interactions of individual cells [56•] will be key for future progress in this area.

Acknowledgments

Work in the RS laboratory is supported by Biotechnology and Biological Sciences Research Council grants BB/J007056/1 and BB/J004588/1.

References and recommended reading

Papers of particular interest, published within the period of review, have been highlighted as:

- • of special interest
- •• of outstanding interest

1. Lloyd AC: **The regulation of cell size**. *Cell* 2013, **154**:1194-1205.

2. Horiguchi G, Tsukaya H: **Organ size regulation in plants: insights from compensation**. *Frontiers Plant Sci* 2011:2.

3. Kafri R, Levy J, Ginzberg MB, Oh S, Lahav G, Kirschner MW: **Dynamics extracted from fixed cells reveal feedback linking cell growth to cell cycle**. *Nature* 2013, **494**:480-483.

4. Ginzberg MB, Kafri R, Kirschner M: **On being the right (cell) size**. *Science* 2015, **348**:1245075.

5. •• Serrano-Mislata A, Schiessl K, Sablowski R: **Active control of cell size generates spatial detail during plant organogenesis**. *Curr Biol* 2015, **25**:2991-2996.

The authors investigated whether cell growth feeds back on cell cycle progression to maintain uniform cell sizes in the shoot meristem. Measurement of the sources of size variability and computer simulations indicated that the distribution of cell sizes in the meristem was consistent with coupling of growth and division in individual cells. Transient perturbation of cell size by expression of the cell cycle inhibitor KRP4 was followed by rapid recovery of cell sizes due to frequent division. Altered cell sizes caused by gain and loss of KRP4 function did not affect growth rates, but disrupted the development of organ boundaries and floral organ number, suggesting that cell size is important for patterning in the meristem.

6. Ali O, Mirabet V, Godin C, Traas J: **Physical models of plant development**. *Ann Rev Cell Dev Biol* 2014, **30**:59-78.

7. Braidwood L, Breuer C, Sugimoto K: **My body is a cage: mechanisms and modulation of plant cell growth**. *New Phytol* 2014, **201**:388-402.

8. Sablowski R, Carnier Dornelas M: **Interplay between cell growth and cell cycle in plants**. *J Exp Bot* 2013. http://dx.doi.org/10.1093/jxb/ert354.

9. Sassi M, Traas J: **When biochemistry meets mechanics: a systems view of growth control in plants**. *Curr Opin Plant Biol* 2015, **28**:137-143.

10. Xiong Y, Sheen J: **Novel links in the plant TOR kinase signaling network**. *Curr Opin Plant Biol* 2015, **28**:83-91.

11. Hepworth J, Lenhard M: **Regulation of plant lateral-organ growth by modulating cell number and size**. *Curr Opin Plant Biol* 2014, **17**:36-42.

12. Vilches-Barro A, Maizel A: **Talking through walls: mechanisms of lateral root emergence in *Arabidopsis thaliana***. *Curr Opin Plant Biol* 2015, **23**:31-38.

13. Peret B, Li G, Zhao J, Band LR, Voss U, Postaire O, Luu D-T, Da Ines O, Casimiro I, Lucas MI *et al.*: **Auxin regulates aquaporin function to facilitate lateral root emergence**. *Nat Cell Biol* 2012, **14**:991-998.

14. •• Vermeer JE, von Wangenheim D, Barberon M, Lee Y, Stelzer EH, Maizel A, Geldner N: **A spatial accommodation by neighboring cells is required for organ initiation in Arabidopsis**. *Science* 2014, **343**:178-183.

The authors showed that very early during lateral root emergence, the overlying endodermal cells shrank to make space for the expanding primordium, but without loss of cell integrity. This process was necessary for primordium emergence and depended on auxin signaling within the endodermis. Expression of a dominant negative regulator of auxin responses (*shy2-2*) in the endodermis blocked outgrowth of the underlying pericycle cells before the first cell divisions leading to lateral root development. Signaling between the expanding endodermis and the pericycle cells did not appear to involve auxin transport and may be mediated instead by mechanical stress.

15. • Löfke C, Dünser K, Scheuring D, Kleine-Vehn J: **Auxin regulates SNARE-dependent vacuolar morphology restricting cell size**. *eLife* 2015, **4**:e05868.

In the epidermis of the root meristem, auxin inhibits cell expansion. This work revealed that auxin causes rapid changes in vacuolar morphology, preceding changes in cell size. These effects were TIR-dependent, involved rapid (15–30 min) post-transcriptional increase in the abundance of SNARES in the vacuolar membrane, were partly mediated by the Q-SNARE VTI11 and required phosphatidylinositol signaling.

16. •• Scheuring D, Löfke C, Krüger F, Kittelmann M, Eisa A, Hughes L, Smith RS, Hawes C, Schumacher K, Kleine-Vehn J: **Actin-dependent vacuolar occupancy of the cell determines auxin-induced growth repression**. *Proc Natl Acad Sci U S A* 2016, **113**:452-457.

This paper revealed a role for the actin cytoskeleton in controlling plant cell size. Changes in vacuolar morphology and size induced by auxin (see [15•]) were associated with an increase in the density of actin filaments surrounding the vacuoles. 3D analysis of vacuolar morphology showed that auxin induced constriction of vacuoles, rather than fragmentation. Disruption of the actin cytoskeleton prevented the auxin-induced changes in vacuole morphology and restored cell expansion.

17. Montané M-H, Menand B: **ATP-competitive mTOR kinase inhibitors delay plant growth by triggering early differentiation of meristematic cells but no developmental patterning change**. *J Exp Bot* 2013, **64**:4361-4374.

18. Xiong Y, McCormack M, Li L, Hall Q, Xiang C, Sheen J: **Glucose-TOR signalling reprograms the transcriptome and activates meristems**. *Nature* 2013, **496**:181-186.

19. Leiber R-M, John F, Verhertbruggen Y, Diet A, Knox JP, Ringli C: **The TOR pathway modulates the structure of cell walls in Arabidopsis**. *Plant Cell* 2010, **22**:1898-1908.

20. Gazzarrini S, Tsai AY-L: **Trehalose-6-phosphate and SnRK1 kinases in plant development and signaling: the emerging picture**. *Front Plant Sci* 2014, **5**:119.

21. Žádníková P, Simon R: **How boundaries control plant development**. *Curr Opin Plant Biol* 2014, **17**:116-125.

22. Tsai AYL, Gazzarrini S: **AKIN10 and FUSCA3 interact to control lateral organ development and phase transitions in Arabidopsis**. *Plant J* 2012, **69**:809-821.

23. O'Brien M, Kaplan-Levy RN, Quon T, Sappl PG, Smyth DR: **PETAL LOSS, a trihelix transcription factor that represses growth in *Arabidopsis thaliana*, binds the energy-sensing SnRK1 kinase AKIN10**. *J Exp Bot* 2015, **66**:2475-2485.

24. •• Uyttewaal M, Burian A, Alim K, Landrein B, Borowska-Wykret D, Dedieu A, Peaucelle A, Ludynia M, Traas J, Boudaoud A *et al.*: **Mechanical stress acts via katanin to amplify differences in**

growth rate between adjacent cells in Arabidopsis. *Cell* 2012, **149**:439-451.

25. Tauriello G, Meyer HM, Smith RS, Koumoutsakos P, Roeder AHK: **Variability and constancy in cellular growth of Arabidopsis sepals**. *Plant Physiol* 2015, **169**:2342-2358.

26. Sampathkumar A, Yan A, Krupinski P, Meyerowitz EM: **Physical forces regulate plant development and morphogenesis**. *Curr Biol* 2014, **24**:R475-R483.

27. Bozorg B, Krupinski P, Jönsson H: **Stress and strain provide positional and directional cues in development**. *PLoS Comput Biol* 2014, **10**:e1003410.

28. Shapiro BE, Tobin C, Mjolsness E, Meyerowitz EM: **Analysis of cell division patterns in the Arabidopsis shoot apical meristem**. *Proc Natl Acad Sci U S A* 2015, **112**:4815-4820.

29. Pan KZ, Saunders TE, Flor-Parra I, Howard M, Chang F: **Cortical regulation of cell size by a sizer cdr2p**. *eLife* 2014, **3**:e02040.

30. Schmoller KM, Skotheim JM: **The biosynthetic basis of cell size control**. *Trends Cell Biol* 2015, **25**:793-802.

31. •• Schmoller KM, Turner J, Kõivomägi M, Skotheim JM: **Dilution of the cell cycle inhibitor Whi5 controls budding-yeast cell size**. *Nature* 2015, **526**:268-272.

A novel molecular mechanism is proposed to links cell cycle progression to cell size in budding yeast. The Cln3 cyclin-Cdk1 kinase controls progression from G1 to S-phase by inactivating the Whi5 transcriptional repressor. The concentration of Whi5 decreases during the cell cycle, until a threshold is reached that allows progression to S-phase. The initial Whi5 concentration in a cell depends on the size of its mother cells: smaller mother cells generate small daughters with higher Whi5 levels, leading to a longer G1 phase and consequently cell size correction. A key aspect of this mechanism is that Whi5 is synthesized at a constant rate, in contrast to the majority of other genes, whose transcription and translation rates scale with the general biosynthetic capacity of the cell, which in turn reflects cell size.

32. •• Li Y, Liu D, López-Paz C, Olson BJSC, Umen JG: **A new class of cyclin dependent kinase in Chlamydomonas is required for coupling cell size to cell division**. *eLife* 2016, **5**:e10767.

In *Chlamydomonas reinhardtii*, cells grow in the light, then stop growing but cycle rapidly through S and M phases in the dark. The number of cycles in the dark reflects the size of the mother cell at the end of the light period and restores cells to their initial size. A mutant screen for perturbed restoration of cell sizes revealed a novel cyclin-dependent kinase (CDKG1), which regulates the number of mitotic cycles. The number of cycles depended on the initial amount of CDKG1, which was proportional to the size of the mother cell. CDKG1 regulates activity of the retinoblastoma (RB) pathway, which had previously been implicated in cell size control in Chlamydomonas.

33. Schiessl K, Kausika S, Southam P, Bush M, Sablowski R: **JAGGED controls growth anisotropy and coordination between cell size and cell cycle during plant organogenesis**. *Curr Biol* 2012, **22**:1739-1746.

34. Roeder AHK, Chickarmane V, Cunha A, Obara B, Manjunath BS, Meyerowitz EM: **Variability in the control of cell division underlies sepal epidermal patterning in *Arabidopsis thaliana***. *PLoS Biol* 2010, **8**:e1000367.

35. Edgar BA, Zielke N, Gutierrez C: **Endocycles: a recurrent evolutionary innovation for post-mitotic cell growth**. *Nat Rev Mol Cell Biol* 2014, **15**:197-210.

36. Hayashi K, Hasegawa J, Matsunaga S: **The boundary of the meristematic and elongation zones in roots: endoreduplication precedes rapid cell expansion**. *Sci Rep* 2013, **3**:2723.

37. Katagiri Y, Hasegawa J, Fujikura U, Hoshino R, Matsunaga S, Tsukaya H: **The coordination of ploidy and cell size differs between cell layers in leaves**. *Development* 2016, **143**:1120-1125.

38. Coen E, Rolland-Lagan A-G, Matthews M, Bangham JA, Prusinkiewicz P: **The genetics of geometry**. *Proc Natl Acad Sci U S A* 2004, **101**:4728-4735.

39. Chen X, Wu S, Liu Z, Friml J: **Environmental and endogenous control of cortical microtubule orientation**. *Trends Cell Biol* 2016 In: *http://dx.doi.org/10.1016/j.tcb.2016.02.003*.

40. •• Kirchhelle C, Chow C-M, Foucart C, Neto H, Stierhof Y-D, Kalde M, Walton C, Fricker M, Smith Richard S, Jérusalem A *et al.*: **The specification of geometric edges by a plant Rab GTPase is an essential cell-patterning principle during organogenesis in Arabidopsis**. *Dev Cell* 2016, **36**:386-400.

This work reveals that targeted secretion to the edges between cell walls controls oriented cell growth. A fusion between YFP and the Rab GTPase RAB-A5c was transported between the trans-Golgi network and cell wall edges in root and leaf primordia. This localization was lost in mature cells, correlated with the orientation of cell elongation and depended on the integrity of the microtubule and actin cytoskeletons. Live imaging and cell tracking showed that a dominant-negative version of RAB-A5c disrupted oriented cell expansion and sometimes caused rupture of cells, suggesting that their tensile strength had been compromised. A 2D finite-element model suggested that reducing stiffness of cell edges can cause radial cell expansion as seen after expression of the dominant negative version of RAB-A5c.

41. • Sampathkumar A, Krupinski P, Wightman R, Milani P, Berquand A, Boudaoud A, Hamant O, Jönsson H, Meyerowitz EM: **Subcellular and supracellular mechanical stress prescribes cytoskeleton behavior in Arabidopsis cotyledon pavement cells**. *eLife* 2014, **3**:e01967.

This paper focused on the growth of jigsaw puzzle-shaped epidermal cells to explore the links between mechanical stress, microtubule dynamics and cell wall deposition at the subcellular level. Atomic force microscopy showed that the neck regions of growing epidermal pavement cells were stiffer than lobe regions. This correlated with the microtubule alignment and increased cellulose deposition across the neck region. A finite element model with mechanically isotropic walls predicted anisotropic stress focused on the indenting regions of the pavement cells, suggesting how mechanical stress could mediate the feedback between cell shape and growth.

42. Heisler MG, Hamant O, Krupinski P, Uyttewaal M, Ohno C, Jönsson H, Traas J, Meyerowitz EM: **Alignment between PIN1 polarity and microtubule orientation in the shoot apical meristem reveals a tight coupling between morphogenesis and auxin transport**. *PLoS Biol* 2010, **8**:e1000516.

43. •• Sassi M, Ali O, Boudon F, Cloarec G, Abad U, Cellier C, Chen X, Gilles B, Milani P, Friml J: **An auxin-mediated shift toward growth isotropy promotes organ formation at the shoot meristem in Arabidopsis**. *Curr Biol* 2014, **24**:2335-2342.

Auxin was shown to trigger the emergence of floral primordia in the meristem in part by altering microtubule orientation. When primordium initiation was blocked by the auxin transport inhibitor NPA, microtubules were aligned to the meristem circumference, but became disorganized when primordia were induced by auxin treatment. Disruption of microtubule arrays with oryzalin or by a katanin mutation was sufficient to promote primordium outgrowth in apices with defective auxin transport. Finite element models of the growing apex suggested that a shift to anisotropic growth, which is associated with disorganized microtubule arrays, could amplify the effect of local cell wall loosening, which alone would not be sufficient to initiate primordium outgrowth.

44. Besson S, Dumais J: **Universal rule for the symmetric division of plant cells**. *Proc Natl Acad Sci U S A* 2011, **108**:6294-6299.

45. Dupuy L, Mackenzie J, Haseloff J: **Coordination of plant cell division and expansion in a simple morphogenetic system**. *Proc Natl Acad Sci U S A* 2010, **107**:2711-2716.

46. Lloyd CW: **How does the cytoskeleton read the laws of geometry in aligning the division plane of plant cells?** *Development* 1991, **113**:55-65.

47. Alim K, Hamant O, Boudaoud A: **Regulatory role of cell division rules on tissue growth heterogeneity**. *Front Plant Sci* 2012, **3**:174.

48. •• Yoshida S, de Reuille PB, Lane B, Bassel GW, Prusinkiewicz P, Smith RS, Weijers D: **Genetic control of plant development by overriding a geometric division rule**. *Dev Cell* 2014, **29**:75-87.

Three-dimensional segmentation and statistical image analysis were used to produce a quantitative description of the patterns of cell growth and division during Arabidopsis embryogenesis. Similar to the early cleavage of animal embryos, cell volumes rapidly decreased with the first embryonic divisions but subsequently remained stable. Cell divisions that conformed to default rules based on cell geometry (see [44]) generated daughter cells with comparable fates; whereas asymmetric divisions correlated with daughter cells of different identities, based on reporter genes. Analysis of auxin response mutants showed that these asymmetric divisions depended on auxin signaling. The asymmetric

divisions generated an organized pattern of cell connectivity (defined as the amount of shared surface between each pair of cells), which could in turn influence intercellular signaling and cell fate.

49. • De Rybel B, Adibi M, Breda AS, Wendrich JR, Smit ME, Novák O, Yamaguchi N, Yoshida S, Van Isterdael G, Palovaara J: **Integration of growth and patterning during vascular tissue formation in Arabidopsis**. *Science* 2014, **345**:1255215.
This paper showed that vascular patterning in the embryo results from an auxin-induced source of cytokinin that induces periclinal cell divisions in neighboring cells. The dimeric transcription factor TMO/LHW promoted periclinal divisions during vascular development by activating cytokinin synthesis. A 2D simulation of growing and dividing cells, in which high auxin promoted cytokinin synthesis but inhibited cytokinin responses, reproduced the patterning and hormone responses seen in the wild type and in auxin or cytokinin mutants. The model also suggested that correct patterning depends on the initial cell geometry, which originated from a symmetry-breaking division in early embryogenesis.

50. Lyndon RF: **Tansley Review No. 74 control of organogenesis at the shoot apex**. *New Phytol* 1994, **128**:1-18.

51. Cunninghame ME, Lyndon RF: **The relationship between the distribution of periclinal cell divisions in the shoot apex and leaf initiation**. *Ann Bot* 1986, **57**:737-746.

52. Smith LG, Hake S, Sylvester AW: **The tangled-1 mutation alters cell division orientations throughout maize leaf development without altering leaf shape**. *Development* 1996, **122**:481.

53. Fukushima K, Fujita H, Yamaguchi T, Kawaguchi M, Tsukaya H, Hasebe M: **Oriented cell division shapes carnivorous pitcher leaves of *Sarracenia purpurea***. *Nat Commun* 2015, **6**:6450.

54. Bassel GW, Stamm P, Mosca G, de Reuille PB, Gibbs DJ, Winter R, Janka A, Holdsworth MJ, Smith RS: **Mechanical constraints imposed by 3D cellular geometry and arrangement modulate growth patterns in the Arabidopsis embryo**. *Proc Natl Acad Sci U S A* 2014, **111**:8685-8690.

55. Kaplan DR, Hagemann W: **The relationship of cell and organism in vascular plants — are cells the building-blocks of plant form**. *Bioscience* 1991, **41**:693-703.

56. • Boudon F, Chopard J, Ali O, Gilles B, Hamant O, Boudaoud A, Traas J, Godin C: **A computational framework for 3D mechanical modeling of plant morphogenesis with cellular resolution**. *PLoS Comput Biol* 2015, **11**:e1003950.
In this paper, a mathematical model was developed for the 3D interaction between cell-autonomous mechanical stress (i.e. resulting from a cell's turgor pressure and its cell wall properties) and stress imposed by its connection to surrounding cells. The model was implemented using the finite element method to calculate how tissues deform given a specified cellular structure, local cell wall properties and constant turgor. By comparing simulated shapes with the observed shapes of growing floral buds, the model was used to explore assumptions about differences in cell wall rigidity and anisotropy in organ boundaries and between the abaxial and adaxial regions of sepal primordia.