receptors rapidly diffuse within the continuous network of dendritic ER but are confined by increased ER complexity at branch points of dendrites and near dendritic spines. The spatial range of receptor mobility is rapidly restricted by phosphoinositide-linked metabotropic glutamate receptor signaling, which is linked to intracellular Ca^{2+} release via inositol (1,4,5) trisphophate (IP_3) receptor channels, through a mechanism involving protein kinase C and the ER sheet protein CLIMP63. The morphological changes in local zones of ER have the effect of compartmentalizing ER export and also correspond to sites of new dendritic branches [18]. It will be particularly important to assess any role for XendoU in such Ca^{2+}-dependent processes, and small-molecule inhibitors effective against XendoU in the low micromolar range provide additional tools for such studies [12].

In future studies, investigations of the function of EndoU proteins *in vivo*, particularly within cells in tissues such as the central nervous system, will be of particular interest. Though these proteins are known to be aberrantly expressed in human diseases, such as cancer, loss of function may similarly be related to disease. In fact, many proteins involved in shaping the ER network are mutated in neurological disorders, including hereditary spastic paraplegia and hereditary sensory neuropathy [19,20]. It will be interesting to probe any links of EndoU mutations to human neurological disease.

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Symmetric Development: Transcriptional Regulation of Symmetry Transition in Plants

Symmetry breaking and re-establishment is an important developmental process that occurs during the development of multicellular organisms. A new report determines that transcription factors regulate a symmetry transition event in plants by modifying the direction of auxin transport. This provides one of the first mechanistic descriptions of a transition from bilateral to radial symmetry in plants.

Liam Dolan

Two flattened leaf-like structures fuse to form the bilaterally symmetrical carpel in the *Arabidopsis thaliana* flower. Early in development, the organ is bilaterally symmetrical along its entire length. Then, a symmetry-breaking event occurs in cells in the distal regions which become committed to radialization. These tissues in the distal region develop into the radially symmetric style, a specialized structure that develops a papillate surface (stigma) to which pollen adhere during reproduction. Thus, a symmetry transition event occurs during the formation of a key structure in the life cycle of a flowering plant.

The major discovery of Moubayidin and Østergaard, published recently in *Current Biology* [1], is that the basic helix-loop-helix proteins SPATULA (SPT) and INDEHISCENT (IND) are necessary and sufficient for the establishment of a radially symmetric style from bilaterally symmetric tissue in the distal region of the young

carpel. The authors report that the development of a radially symmetric style is defective in mutants that lack *SPT* function and there is a complete loss of radial symmetry at the distal region of carpels in *spt ind* double mutants. This synergistic effect on radialization is consistent with the hypothesis that the activities of both genes are required for radialization of the distal regions of carpels during style development.

Perhaps the most remarkable observation reported in the paper is that induced ectopic expression of *IND* is sufficient for radialization. This was demonstrated by ectopically expressing *IND* in leaves (Figure 1). Wild-type leaves are flattened laminar structures with distinct upper and lower surfaces and current models suggest that the laminar outgrowths occur where the upper and lower surfaces meet (Figure 1A). Induction of high levels of *IND* expression in a leaf transforms this flattened structure into a cylindrical organ with radial symmetry (Figure 1B). These data demonstrate that *IND* is sufficient for the bilateral to radial symmetrical transition during the development of lateral organs. Furthermore, the radialization caused by *IND* overexpression requires *SPT* function, supporting the conclusion that both *SPT* and *IND* proteins act to promote the formation of radial symmetry. Taken together, *SPT* and *IND* can be considered to be necessary and sufficient for the establishment of the radial symmetry in the style.

During early wild-type development, two local maxima (foci) of auxin response develop on opposite sides of the distal regions of the carpel where the future style will develop. These foci drive apical–basal growth and result from the polar transport of auxin from the proximal regions of the carpel to the distal regions by PIN-FORMED1 (PIN1) protein, which is preferentially localized on the distal face of cells — polar localization of PIN auxin efflux proteins defines the direction of polar auxin transport. It follows that the foci are strongly reduced in *pin1-5* mutants in which the polar transport of auxin from the proximal regions to the distal regions is decreased. The role of the local production of auxin in the formation of these foci has been ruled out because their appearance is not dependent on local auxin synthesis.

The transition from bilateral to radial symmetry is preceded by a change in auxin distribution driven by PIN auxin efflux carriers in the distal regions where the style develops. This is demonstrated by imaging the changes in the spatio-temporal expression of auxin signaling and transport reporters. Over time, the two foci of auxin signaling coalesce to form a ring, and this is likely to be the result of non-polar membrane localization of PIN proteins in this region — PIN1, PIN3 and PIN7 are localized on surfaces of the cell and therefore auxin transport by PINs will occur over the entire cell surface and will not be polarized.

The transition from the state where there are two foci of local auxin signalling (bilateral symmetry) to the state where there is a ring of cells with detectable local auxin signalling (radial symmetry) passes through a 4-foci state, which requires the activity *SPT* and *IND*.

Having demonstrated that *SPT* and *IND* are necessary and sufficient for the symmetry transition and having shown that auxin distribution undergoes a bilateral-to-radial transition at the apex, Moubayidin and Østergaard then set out to link these heretofore separate processes during the formation of radial symmetry.

The Østergaard lab had previously demonstrated that SPT and IND act by directly repressing expression of the *PINOID* (*PID*) gene, which encodes a protein that regulates PIN protein localization [2,3]. PID is an AGC3-type protein kinase that phosphorylates PIN proteins resulting in their polar localization to a single face of the cell while the localization of the non-phosphorylated forms of PINs is not polar (the proteins are located in membranes on all faces of the cell).

PID expression is excluded from cells in the developing style of the wild type through the repressive activity of *SPT* and *IND*; *PID* is expressed in the developing style of *spt* mutants. Therefore, it is formally possible that the lack of radial symmetry in *spt ind* double mutants results from the derepression of PID activity in the cells of the developing style which in turn maintains polar localization of PIN and bilateral symmetry.

This hypothesis was tested in two ways. First, the authors expressed a version of PIN1 that mimics the phosphorylated form that is produced by the activity of PID. Expression of this phosphorylation mimic in a *pin1* mutant background disrupts the development of radial symmetry and results in the formation of a bilaterally symmetrical style similar to the *spt ind* double mutant. This is consistent with the model that PID-mediated PIN1 phosphorylation and the subsequent non-polarized PIN1 localization is required for the development of radial symmetry in the style. Second, the authors observed that the phosphorylation-resistant form of PIN1 suppresses the loss of style radial symmetry seen in *spt* mutants. This result indicates that *SPT* and *IND* control auxin flux through *PID* during the development of radial style symmetry. Taken together, these data are consistent with the hypothesis that repression of PID-mediated polar localization of PIN1 by *SPT* and *IND* is required for the symmetry transition during style development.

Moubayidin and Østergaard have discovered the precise mechanism in which symmetry transitions occur

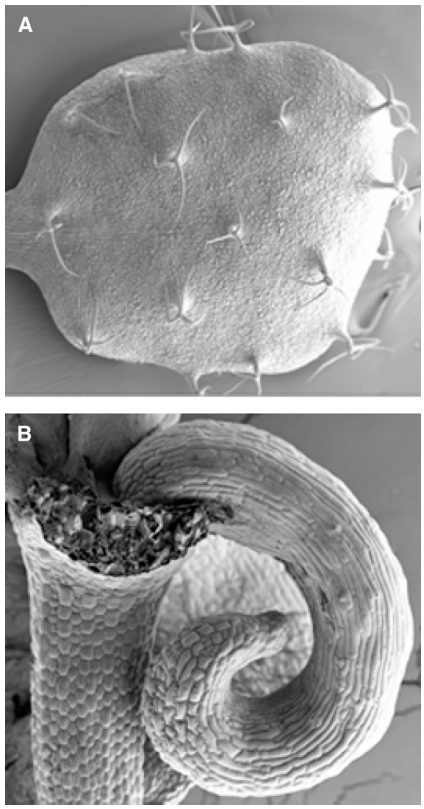

Figure 1. Ectopic expression of *IND* in leaves is sufficient to program the development of radially symmetrical organs.

(A) Wild-type leaf with characteristic flattened leaf lamina (dorsal-ventral symmetry). (B) Leaf in which *IND* has been activated ectopically resulting in the formation of a cylindrical organ (radial symmetry). Images courtesy of Laila Moubayidin and Lars Østergaard.

during style formation. Given the many roles played by auxin in development, it will be intriguing to see if similar mechanisms control the reorganization of symmetry during the development of other organs.

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