Who, where, how many?

The control of cell division, patterning and differentiation must be tightly coordinated during development. Crisanto Gutierrez and colleagues have now forged a link between these process with the identification of GEM, a chromatin regulator that controls both cell division and cell fate in *Arabidopsis* (*Nature* **447**, 213–217; 2007).

Expression of the *GL2* gene in *Arabidopsis* roots determines whether or not cells produce hairs. Its expression is under tight spatial control: it is present in cells that touch one cortical cell, but is absent in cells that touch two cortical cells. Cell division also controls the symmetry of these hair- and non-hair-producing cells to give a characteristic pattern in the root. The first link between cell fate and cell division was observed in plants that overexpressed CDT1, a component of the pre-replication complex that controls initiation of DNA replication in eukaryotes; these plants exhibited increased cell division and increased *GL2* mRNA levels. Gutierrez and colleagues have now identified the novel factor GEM (*GL2* expression modulator) in a yeast two-hybrid study using CDT1 as bait. It is expressed ubiquitously in *Arabidopsis*, and does not show homology to any known sequence. To assess its function, the authors generated plants with reduced *GEM* mRNA expression (*gem-1*) and overexpressed GEM (*GEM^{OE}*). Analysis of these strains showed that GEM restricted cell division and negatively regulated *GL2* expression, suggesting that it might specify cell fate.

Through a comprehensive series of experiments Gutierrez and colleagues defined how GEM regulates *GL2* expression – by functioning as part of the transcriptional complex that represses *GL2* expression. Pulldown experiments showed that GEM interacted with TTG1, a component of this complex, and a yeast three-hybrid assay revealed that TTG1 disrupted the CDT1–GEM interaction. This competition for binding of GEM to TTG1 and CDT1 is crucial for control of both cell division and cell specification, the latter through effects on *GL2* expression.

Changes in histone modifications alter the expression of root-patterning genes, prompting the authors to examine whether GEM might also alter these chromatin marks. They found that manipulating levels of GEM did indeed alter levels of acetylated K9 and K14 residues on histone 3 (H3K9acK14ac) at the *GL2* promoter, corroborating the

View of the *Arabidopsis* root epidermis (the root tip is not shown) showing two distinct cell types: atrichoblasts (A) and trichoblasts (T), organized in cell files, which will become non-hair and hair cells, respectively. Atrichoblasts express the homeobox *GL2* gene, whereas trichoblasts do not. The cell division rate is higher for trichoblasts resulting in a file that contains more cells along its length.

evidence that GEM negatively regulates *GL2* expression. GEM was also shown to regulate the level of H3K9me3, which is associated with active euchromatin in *Arabidopsis*.

Interestingly, the group speculate that *Arabidopsis* GEM maybe functionally equivalent to animal geminin — CDT1-mediated formation of pre-replication complexes at DNA replication origins is inhibited by geminin, which has not been identified in yeast or plants. Given the lack of amino-acid homology between GEM and geminin, and that the authors show that GEM interacts with CDT1 to mediate chromatin modification and gene expression, a possibly analogy between the function of GEM and geminin in DNA replication and cell-fate decisions warrants further investigation.

Taken together, the group show that GEM regulates cell division, modulates the expression of a cell-fate determining gene, and maintains correct histone modifications at this gene, thus linking the complex regulation of fate, location and division.

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