Balancing Parental Contributions in Plant Embryonic Gene Activation

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Little is known about chromatin remodeling events immediately after fertilization. A recent report by Autran et al. (2011) in *Cell* now shows that chromatin regulatory pathways that silence transposable elements are responsible for global delayed activation of gene expression in the early *Arabidopsis* embryo.

Sexual reproduction in most flowering plants requires two fertilization events: one to produce the embryo and another to produce the nutritive endosperm. Unequal parental contributions to the messenger RNA (mRNA) pool in endosperm have been studied for many years, with most attention focused on uniparental gene expression (Raissig et al., 2011). This phenomenon is a result of genomic imprinting, the differential marking of paternal or maternal alleles with DNA methylation, or histone modifications by Polycomb complex proteins (Raissig et al., 2011). A single gene imprinted in the maize embryo was recently described, but the extent of imprinting in plant embryos is thus far unclear (Raissig et al., 2011). However, a phenomenon that shares some features with imprinting—delayed activation of the paternal allele in the early embryo—has been reported in the model plant *Arabidopsis thaliana* (Vielle-Calzada et al., 2000). In a recent study published in *Cell*, Autran et al. (2011) provide evidence that maternal transcripts predominate for the majority of genes in the early *Arabidopsis* embryo, with a gradual transition to increased paternal contribution. The authors also identify maternally controlled chromatin regulatory pathways that regulate this phenomenon that are distinct from those in control of genomic imprinting.

Autran et al. (2011) took advantage of two polymorphic *Arabidopsis* strains to quantify maternal and paternal transcripts in very early (2- to 4-cell) stage embryos and later, though still early, globular stage embryos. The authors found that maternal transcripts of about 85% of all genes with informative polymorphisms were overrepresented in 2- to 4-cell stage embryos. Paternal contribution was greater in the globular embryo, with 48% maternally biased genes. Experiments with six marker lines revealed that the timing of paternal allele activation was highly variable between different genes. Because the authors could not distinguish mRNA deposited in the egg cell from newly transcribed zygotic maternal mRNA, whether delayed gene activation affects only the paternal chromosomes, or the entire zygote, is unclear. A recent study indicates that early *Arabidopsis* embryo development can proceed despite low levels of new transcription by RNA polymerase II (Pillot et al., 2010), suggesting that both alleles of many genes are transcriptionally quiescent, analogous to early animal development (Tadros and Lipshitz, 2009). How the timing of this gene activation is regulated remains a mystery, but Autran et al. (2011) provide some important clues through the pathways they implicate in mediating zygotic activation of paternal genes.

Dimethylation of histone H3 at lysine 9 (H3K9me2) is found in *Arabidopsis* transposable elements and is associated with transcriptional silencing (Feng et al., 2010). H3K9me2 is closely linked with DNA methylation by CHROMOMETHYLASE 3 (CMT3). CMT3 and KRYPTONITE (KYP), the enzyme responsible for much of H3K9me2 in *Arabidopsis*, each bind to the modification made by the other protein, forming an autocatalytic feedforward loop (Feng et al., 2010). Autran et al. (2011) found that a maternally inherited mutation in KYP substantially accelerated zygotic activation of paternal genes, resulting in a paternal contribution to the mRNA pool in 2- to 4-cell embryos that is similar to that of wild-type globular embryos. Maternally inherited *kyp* and *cmt3* mutations also accelerated activation of paternally inherited marker transgenes. Notably, paternally inherited *kyp* mutations had no effect on zygotic gene activation. These findings suggest specific maternal control through H3K9 methylation in the temporal regulation of zygotic genes. The implication of CMT3 and KYP in this context is surprising, as neither H3K9me2 nor CMT3-mediated DNA methylation is normally found at genic regions (Feng et al., 2010). KYP and CMT3 are antitransposon weapons that induce transcriptional silencing of foreign genomic parasites: their use to transiently delay the expression of most embryonic host genes seems akin to settling a domestic dispute with firearms. However, some recent results suggest that KYP and CMT3 activity at genes is not so farfetched. Indeed, a mutation in an enzyme that removes H3K9me2 leads to extensive DNA and histone hypermethylation of genes, which is suppressed by mutation of either KYP or CMT3 (Inagaki et al., 2010). Thus, the balance between H3K9 methylation and demethylation may influence gene activation timing in the early embryo.

In addition to KYP and CMT3, Autran and colleagues (2011) observed that maternal mutations in RNA-directed DNA methylation (RdDM) pathway genes also led to more rapid activation of paternal genes. RdDM targets DNA methylation by the DRM family of methyltransferases through RNA interference (Feng et al., 2010). Like KYP and CMT3, this pathway targets transposons and other repetitive sequences for silencing and is associated with small RNAs that are 24 nucleotides long. Such small RNAs generally do not target genic regions, but Autran et al. (2011) found that *Arabidopsis* ovules are an exception, with particular enrichment of small RNA target sequences at genes that are activated more rapidly by a

maternal *kyp* mutation. The involvement of a second transposon-targeted pathway in zygotic gene activation suggests that regulation of genes and transposons may not be as distinct as previously thought.

Autran et al. (2011) also identified maternally inherited mutations that delayed activation of paternally inherited marker transgenes. Two were in genes encoding components of the histone chaperone complex CAF1, and two others were in genes encoding histone H3.3, a variant of histone H3. Recent work has shown that histone H3 inherited from either parent is replaced within hours of fertilization by zygotic H3 in *Arabidopsis* (Ingouff et al., 2010). This process may facilitate zygotic gene activation and may be mediated by CAF1. However, it is not obvious how CAF1, which functions to assemble nucleosomes following DNA replication, may interact with H3.3, which has been implicated in replication-independent histone exchange (Clapier and Cairns, 2009). CAF1 and H3.3 may influence gene expression independently, or CAF1 might play a plant-specific role in H3.3 deposition. At least one of the genes encoding H3.3 identified by Autran et al. (2011) is transcribed within hours of fertilization (Ingouff et al., 2010), but as the gene is expressed from both parental genomes, how a maternally inherited mutation would impact activation of paternally inherited genes remains unclear. This same H3.3 gene is abundant in egg cells, however, suggesting that the earliest stages of zygotic chromatin remodeling may utilize maternally contributed H3.3 (Ingouff et al., 2010). This early remodeling is unlikely to involve CAF1, as it is not expressed in the egg cell or zygote before the first cell division (Ingouff et al., 2010).

The globally delayed activation of zygotic genes described by Autran et al. (2011) appears quite distinct from genomic imprinting: different chromatin pathways are involved, and both sets of alleles may be similarly affected. The evolutionary logic behind the two phenomena may nevertheless be similar. The most popular explanation for imprinted gene expression is conflict between parental genomes over resource allocation to the developing embryo (Raissig et al., 2011). Delayed activation of zygotic genes allows early embryonic development to be largely controlled by maternal transcripts deposited in the egg. A similar explanation has been proposed for the increased ploidy in endosperm, which is typically triploid due to fusion of two haploid maternal nuclei prior to fertilization by haploid sperm but can contain as many as fourteen sets of maternal chromosomes in some plants (Baroux et al., 2002). Such radical strategies may not be viable in the embryo, leading to the development of a more subtle tug of war that still involves very potent repressive pathways involved in transposon silencing. How proteins typically reserved for establishing less dynamic chromatin states regulate zygotic gene activation remains to be elucidated.

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