Mitosis–meiosis transition, the regulation of the means to sexual reproduction

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Reduction of chromosome number through meiosis is a central event that facilitates sexual reproduction in eukaryotes. In addition to providing an opportunity for genetic reassortment, it makes the transition from diploid somatic to haploid gametic phase. Whereas cellular differentiation is established during initial stages of development in animal systems, no true germline is set aside in early embryogenesis in plants, where both vegetative and generative parts are derived from meristems during growth and differentiation[1,2]. As such, the regulation of mitotic to meiotic transition is the most vital event in the life of a plant. Although, the basic control mechanisms that strictly regulate cyclin-dependent kinases for temporal progression through the cell cycle are remarkably well understood[3,4], no definite information on molecular identity of signals that regulate the switch from mitosis to meiosis is yet available. Lately, some data on the development of cell lineage involved in these events are beginning to emerge[5].

Creation of germline *de novo* and initiation of meiosis in plants

Unlike animals, there are no primordial germ cells in plants, therefore, plants differ in strategy to recruit cells into the meiotic pathway. Plant meiocytes arise *de novo* from germline formed from sub-epidermal cells in the anthers and ovules. Within the primordia destined to form anthers and ovules, a few sub-epidermal cells assume an archesporial function, giving rise to the male or female functional germline[5]. Several genes important for the specification of reproductive cell types[6–8] and the mitotic–meiotic switch[9,10] have now been identified. The *Sporocyteless/Nozzle (SPL/NZZ)* gene of *Arabidopsis*[6,7] encodes a nuclear protein with limited homology to the MADS box domain, which seems likely to be a transcription regulator involved in early germline specification[5]. Similarly, the *Multiple Archesporial Cells 1 (MAC 1)* gene of maize also appears to be important in the transition from hypodermal to sporogenous cells[8].

Loci implicated in the mitotic to meiotic switch in plants have been identified in the *ameiotic1* (*am1*) mutant of maize[9], and possibly in the *switch* (*swi1*) mutant[10] of *Arabidopsis*. The *am1* locus is crucial for the initiation of both male and female meiosis; *am1* meiocytes, instead of entering the meiotic prophase, carry out a mitosis-like division and degenerate. *SWI-1* has been proposed to regulate the switch from mitosis to meiosis in *Arabidopsis* ovules, because *swi1* archesporial cells undergo an extra mitotic division before entering meiosis in ovules. The phenotypes of additional alleles of *swi1*, and the testing of meiotic reporters in *swi1* ovules, should reveal how this gene might control the mitotic–meiotic switch. The molecular analysis of loci of this type, and the expression patterns of genes crucial for cell-type specification and meiotic initiation, are beginning to show how reproductive cells establish the signal network necessary to enter the meiotic pathway[5].

Built-in property to determine chromosome reduction

Meiotic reduction in chromosome number depends on a distinctive attachment of chromosomes to the spindle as well as distinctive regulation of the cohesion between sister chromatids[11]. The pattern of attachment in the first meiotic division is different from attachment in somatic mitosis. Of the two stages of meiosis, the reduction in chromosome number is attained in meiosis I, but meiosis II which brings about just genetic assortment is in fact architecturally analogous to mitosis. As such, the two stages of meiosis can offer architectural insight into the factors that transcend mitosis–meiosis developmental organization.

In mitosis, sister kinetochores lie back-to-back and capture microtubules from opposite poles; as a result, sister chromatids move to opposite poles during anaphase. In the first meiotic division, however, sister chromatid kinetochores lie side-by-side, and they capture microtubules from the same spindle pole; as a result, sister kinetochores move to the same pole during anaphase I. The meiosis II chromosomes behave like mitotic chromosomes; sister kinetochores are back-to-back during metaphase II, they capture microtubules from opposite poles and move to opposite poles during anaphase II. This requires that meiosis I chromosomes attach to the spindle differently than meiosis II chromosomes and that they regulate chromosome cohesion differently. In order to elucidate the chromosome cohesion and segregation in the two situations, Paliulis and Nicklas[12] designed an ingenious experiment to fuse meiosis I spermatocytes with meiosis II spermatocytes in grasshopper. They observed that chromosomes placed onto the spindle of a different meiotic division always behaved as they would have on their native spindle. Chromosomes attach to the spindle and divide according to chromosome type, suggesting that the patterns for attachment of spindle and regulation of cohesion are built into the chromosome itself. It has been further suggested that regulation of chromosome cohesion may be linked to differences in the arrangement of kinetochores in the two meiotic divisions. An obvious analogy could accordingly be drawn between meiotic and mitotic kinetochore organization in a dividing cell. Candidates for centromere cohesion molecule are now being identified. Changes in cohesion subunits are responsible for differences between chromosome segregation in mitosis and meiosis, and a single change in chromosomal protein may be enough to cause the altered pattern of chromosome segregation[13,14].

Telomere proteins and pairing initiation

Telomeres consist of simple TTTAGGG consensus repeat associated with proteins that play an important role in replication, cellular proliferation and ageing[2]. Besides

these vital functions telomeres perform in vegetative cells, they have been implicated as key players in the initiation of the pairing process during meiosis. An essential role for telomeres in the reductional division is underlined by the observation that deletion of telomeres and the resulting rearrangement of linear chromosomes into rings is compatible with the vegetative growth, but obstructs meiosis and hence sexual reproduction[15,16]. Further, it has been observed that telomere distribution pattern observed in pre-meiotic vegetative cell is altered with the onset of bouquet formation in order to initiate homologue alignment. It has been convincingly shown in budding yeast that telomeres play an important role for homologue search and alignment in synaptic meiosis[17]. The telomeric protein exclusively involved in meiosis of budding yeast has now been identified as Ndj1p/Tam1p. Cells deficient for this protein show reduced efficiency in homologue recognition and increased occurrence of nonrecombinant chromosomes. An exhaustive study conducted on DNA/immuno-*in situ* cytological localization of telomeric DNA and proteins suggests that Ndj1p is the first telomeric protein that is required for bouquet formation in a synaptic organism[18], hence it could be the key player in mitotic–meiotic transition.

Whence meiosis

Meiosis is at the heart of sexual reproduction. Necessary genomic and functional information as to how this may have occurred in the first place is beginning to emerge. An attempt has been made to reconstruct the events that may have permitted the development of sexual reproduction in an ancient eukaryotic ancestor. Accordingly, a 'core meiotic recombination machinery' has been defined[19]. As recombination occurs at a much higher frequency during meiosis than during vegetative/somatic growth, it is surmised that an important step in the development of meiosis was the generation of means to greatly stimulate the frequency of recombination. The core machinery might apparently have been adapted from vegetative DNA metabolism functions to promote a high frequency of crossover recombination between homologous chromosomes during prophase of meiosis I. This stimulation of interhomologue crossing over was critical for the emergence and evolutionary success of sex[19]. In *Saccharomyces cerevisiae* stimulation of recombination during meiotic prophase is accomplished by deliberate introduction of double-stranded breaks (DSBs) in DNA, and the culprit most directly responsible for making these breaks is the Spo11 enzyme. The presence of Spo11 orthologues in virtually all eukaryotes, and its homologous proteins even in *Archaebacteria*, indicates that the Spo11-generated DSBs are the initiating lesions for most, if not all, meiotic recombination[20], and hence the signal candidate for the emergence of meiosis on the planet.

Understanding the linkage between unique features of mitosis and meiosis and unraveling the clusters of different signal transduction pathways and cell-cycle checkpoints could enable us to manipulate the vegetative or reproductive phase. This would have far-reaching consequences in manoeuvring the biological resources for the benefit of mankind.

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