

# Meiosis

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## INTRODUCTION

Meiosis is the specialized pair of cell divisions that alter the genetic content of the nucleus from  $2n$  (diploid) to  $1n$  (haploid) and lead to the production of gametes. Following a premeiotic S phase, homologous chromosomes pair and synapse. This is followed by meiotic recombination and subsequent chiasmata formation between the paired homologous chromosomes. Chromosome pairing and the formation of chiasmata ensure the bipolar attachment of homologous chromosomes to the spindle, which is required for the reductional division of meiosis I that leads to the separation of homologs. This is followed by a modified cell cycle lacking an S phase. A second, equational division leads to the separation of sister chromatids and a halving of the chromosome number per cell. The general progression of meiosis is highly conserved, and is thus similar in yeast, humans, and plants.

## PLANTS AS MODEL SYSTEMS FOR STUDYING MEIOSIS

The availability of large numbers of cells undergoing meiosis (meiocytes) in anthers has made plants excellent models for studying meiosis. Maize is one of the few organisms with a large genome where pairing and synapsis is amenable to analysis by a combination of cytological, genetic, and molecular techniques. The features of meiosis in *Arabidopsis*, at least at a cytological level, are conventional and comparable to those of other plants, but it has been the ease of gene discovery in this organism that has led to the adoption of *Arabidopsis* for meiosis research.

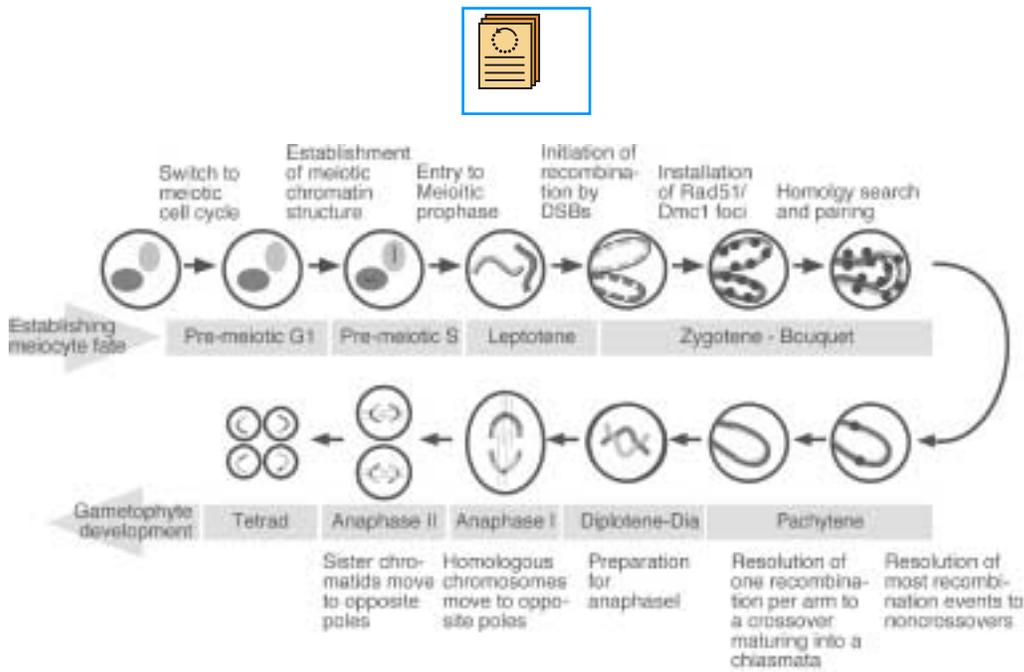
## CHROMOSOME BEHAVIOR DURING MEIOTIC PROPHASE

The accurate segregation of chromosomes at the first division of meiosis requires that homologous chromosomes pair and recombine with each other to form bivalents (Fig. 1). The pairing and crossing over of

homologous chromosomes occurs in the extensive prophase of meiosis. Dramatic changes in chromosome behavior and morphology during meiotic prophase have been used to subdivide the prophase into stages: leptotene, zygotene, pachytene, diplotene, and diakinesis.<sup>[1–3]</sup> In leptotene, the decondensed clouds of chromatin are organized into long, thin fibers by the assembly of a proteinaceous core—the axial element—onto the chromosomes. During zygotene, homologous chromosomes pair and begin to tightly associate, or synapse, along their length when the central element of the synaptonemal complex (SC) is installed between the homologous chromosomes. By pachytene, SC formation is complete and meiotic recombination between homologs is resolved. In diplotene, the synaptonemal complex disassembles and chiasmata, which are responsible for holding the homologous chromosomes together, are visible. Finally, in diakinesis, the chromosomes undergo a final stage of chromosome condensation just prior to metaphase.

## TELOMERES CLUSTER ON THE NUCLEAR ENVELOPE AT THE BEGINNING OF MEIOTIC PROPHASE

Before chromosomes synapse during zygotene, the nucleus becomes highly polarized by the formation of the telomere bouquet (Fig. 1). The ends of the chromosomes become tightly clustered together on the inner surface of the nuclear envelope, resulting in a structure resembling a bouquet of flowers. The close relationship between the telomere clustering and chromosome pairing has led to the suggestion that the bouquet may help to facilitate pairing. By coaligning the ends of the chromosomes, homologous regions of the chromosomes are vectorially aligned and within the same region of the nucleus. In addition, the clustering of telomeres on the nuclear envelope may serve to restrict the homology search to a much smaller volume of the nucleus. Consistent with this potential role is the general observation that synapsis is typically initiated near the telomeres. Mutants defective in bouquet formation show delay in the progression of meiosis and severe defects in pairing and synapsis.<sup>[4]</sup>



**Fig. 1** A diagram showing the key stages and main molecular events in meiosis. Only one homologous chromosome pair is shown, and each homologous chromosome (two sister chromatids) is a different shade of gray. The Rad51/Dmc1 foci are shown as nodules on the extended prophase chromosomes.

## CHROMOSOME PAIRING AND SYNAPSIS

In some organisms, such as the hexaploid wheat and *Drosophila*, the pairing of homologous chromosomes occurs prior to meiosis. However, in many other organisms such as maize, oat, humans, and mice, homologous chromosomes are not associated with each other until zygotene. Regardless of when chromosomes pair, a major question in meiosis is, how do the homologous chromosomes identify and associate with each other? The axial cores of the synaptonemal complex do not appear to contain the information for distinguishing homology because they will synapse randomly in a haploid organism undergoing meiosis.<sup>[3]</sup> The general consensus is that the homology search is DNA-based, which accounts for the correct pairing of chromosome inversions, translocations, and alien chromosomes. In most organisms, including plants, a successful homologous chromosome pairing is linked to the progression of the meiotic recombination pathway, initiated by the action of the topoisomerase Spo11 to generate DNA double-strand breaks (DSBs).<sup>[2]</sup> Mutants lacking Spo11 or other components of the meiotic recombination pathway that act at subsequent steps show serious defects in homologous chromosome pairing.

In a number of species, the chromosome homology search and synapsis are closely coupled during the zygotene stage. Electron microscopy has revealed the presence of large numbers of small, electron-dense spheres associated with synapsing chromosomes during this stage. These nodules, called early recombination nodules,

contain recombination enzymes and are predicted also to function in the chromosome homology search.<sup>[2,3]</sup>

## MEIOTIC RECOMBINATION

Homologous recombination fulfills a number of critical biological functions, including maintaining genetic diversity, repairing DSBs. Stabilizing interactions between homologous chromosomes in the form of chiasmata, promoting proper disjunction, healing a number of types of DNA damage, and removing undesirable mutational load. Because meiosis is a specialized type of cell division and the meiotic recombination machinery is largely derived from the machinery responsible for mitotic recombination and DNA repair in somatic cells, the meiotic and somatic recombination pathways share many components. However, a number of meiotic recombination-specific components also have been identified. Meiotic recombination is initiated by the introduction of DSBs on chromosomes by the topoisomerase Spo11 (Fig. 1). The DSBs are then resected and subsequently repaired by a protein complex containing two homologs of the *E. coli* RecA protein, Rad51 and Dmc1. These two recombination proteins are some of the most studied elements of meiotic recombination and have also been proposed to play roles in the pairing of homologous chromosomes.<sup>[5]</sup> The Rad51/Dmc1 complex forms distinct foci on chromosomes during the meiotic prophase I, which are thought to mark the positions of DSBs. In maize, there are about 500 Rad51 foci in zygotene when





chromosomes are pairing, located mostly on unpaired chromosomes. By early pachytene, when pairing and synapsis are complete, there are only about 10–20 foci, which corresponds well to the number of meiotic cross-overs in maize.

## METAPHASE I AND II CHROMOSOME SEGREGATION

The reductional separation of homologous chromosomes at the first division of meiosis (MI) requires that homologous chromosomes recombine with each other and form bivalents. Since chiasmata hold the homologs together until the metaphase/anaphase transition during MI, failure to undergo recombination results in the inappropriate attachment of chromosomes to the spindle and their inaccurate segregation, leading to aneuploidy. Sister chromatid cohesion at the centromere and arms proximal to the chiasmata is maintained during the first meiotic division (MI) but is dissolved during the second meiotic division (MII), permitting the separation of sisters. During the MI reductional division, the kinetochores of both sister chromatids face the same spindle pole, and the kinetochores of one homolog face toward one pole while the kinetochores of the other homolog face the other pole. Often, sister kinetochores are fused to form a single structure. Following anaphase of MI, the two sisters end up at the same spindle pole. During the MII equational metaphase, sister kinetochores face the opposite spindle poles, ensuring that when sister chromatid cohesion is released at anaphase, the sister chromatids will move to opposite spindle poles and end up in different daughter cells.<sup>[3]</sup>

## THE IMPORTANCE OF UNDERSTANDING MEIOSIS FOR THE CROP SCIENTIST

Meiosis requires DNA replication and chromosome condensation, homologue pairing and recombination, sister chromatid cohesion and homologue attachment, and spindle assembly and chromosome segregation. Many genes are expected to participate in these events, some of which will be unique to meiosis, whereas others are likely to be involved in other cellular processes. Therefore, understanding gene functions in meiosis will provide new insights into the molecular control of many basic cellular events in plants. Furthermore, knowledge about the genes controlling meiosis also has several potential applications in plant breeding. Such applications would include: 1)

developing strategies for acquiring apomixis in maize and other grasses; 2) allowing manipulation of the level of genetic recombination in breeding programs, for example in wide hybrid crosses and for the introgression of quantitative trait loci (QTL) from exotic germplasm; 3) altering genetic incompatibility between species, thus permitting wide hybrid crosses and making it possible to select for desired traits from a broader gene pool; and 4) developing new methods for manipulating transgene integration in random or homologous transformation methods.

## CONCLUSION

Meiosis is a highly specialized cell cycle leading to halving of the chromosome number per cell, which is required for the formation of gametes. Homologous chromosomes must pair and recombine, forming bivalents, in order for meiotic chromosome segregation to occur properly.

## ARTICLES OF FURTHER INTEREST

- Chromosome Structure and Evolution*, p. 273
- Cytogenetics of Apomixis*, p. 383
- Female Gametogenesis*, p. 439
- The Interphase Nucleus*, p. 568
- Male Gametogenesis*, p. 663
- Mitosis*, p. 734

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