Recombination-Independent Mechanisms and Pairing of Homologous Chromosomes during Meiosis in Plants

Olivier da Ines, Maria Gallego, Charles White

Molecular Plant • Volume 7 • Number 3 • Pages 492–501 • March 2014 REVIEW ARTICLE

Recombination-Independent Mechanisms and Pairing of Homologous Chromosomes during Meiosis in Plants

Olivier Da Ines, Maria E. Gallego, and **Charles I. White**[1]

Génétique, Reproduction et Développement, UMR CNRS 6293, Clermont Université, INSERM U1103, 63171 Aubière, France

ABSTRACT Meiosis is the specialized eukaryotic cell division that permits the halving of ploidy necessary for gametogenesis in sexually reproducing organisms. This involves a single round of DNA replication followed by two successive divisions. To ensure balanced segregation, homologous chromosome pairs must migrate to opposite poles at the first meiotic division and this means that they must recognize and pair with each other beforehand. Although understanding of the mechanisms by which meiotic chromosomes find and pair with their homologs has greatly advanced, it remains far from being fully understood. With some notable exceptions such as male *Drosophila*, the recognition and physical linkage of homologs at the first meiotic division involves homologous recombination. However, in addition to this, it is clear that many organisms, including plants, have also evolved a series of recombination-independent mechanisms to facilitate homolog recognition and pairing. These implicate chromosome structure and dynamics, telomeres, centromeres, and, most recently, small RNAs. With a particular focus on plants, we present here an overview of understanding of these early, recombination-independent events that act in the pairing of homologous chromosomes during the first meiotic division.

Key words: meiosis; homolog pairing; chromatin; centromeres; telomeres.

INTRODUCTION

Meiosis is the specialized eukaryotic cell division that reduces the chromosome complement by half. The two successive divisions of meiosis are preceded by a single round of DNA replication. Errors in chromosome segregation during these two divisions lead to aneuploidy, which may have dramatic effects such as infertility and birth defects (Hassold and Hunt, 2001). During the second meiotic division, as in mitosis, proper sister chromatid segregation is ensured by centromeric cohesion established at the preceding S-phase. In contrast, accurate segregation of homologous chromosomes during the first meiotic division relies upon exchange of genetic material between homologous chromosomes (crossing-over) and chromatid cohesion distal to the crossover. These exchanges require homologous chromosome recognition and pairing, synaptonemal complex assembly (synapsis) and homologous recombination, and ensure proper and successful homolog segregation during meiosis.

With some exceptions (e.g. *Drosophila*; see review by McKee et al., 2012) chromosomes are not paired in somatic cells, and so each chromosome must find and pair with its homolog at the entry into meiosis. This involves a step in which chromosomes are aligned and brought into close proximity, followed by homology recognition and synapsis (Burgess, 2002; McKee, 2004; Pawlowski and Cande, 2005; Zickler, 2006; Barzel and Kupiec, 2008; Zetka, 2009; Bhalla and Dernburg, 2008; Tiang et al., 2012). How chromosomes find their homologous partner (homology search) during prophase of the first meiotic division is a major and long-standing question in eukaryotic genetics. Studies in many organisms show that homolog recognition and pairing depend upon recombination. In particular, SPO11-mediated DNA double-strand breaks (DSB) initiate recombination during meiotic prophase I and are required for efficient homolog pairing in most eukaryotes, including plants. This role of recombination in homolog pairing has been well described in recent reviews (Wells et al., 2006; Bhalla and Dernburg, 2008; Bozza and Pawlowski, 2008; Ding et al., 2010; Tiang et al., 2012). Exceptions to this

[1] To whom correspondence should be addressed. E-mail chwhite@univ-bpclermont.fr, tel. 33-473407752, fax 33-473407777.

doi:10.1093/mp/sst172, Advance Access publication 28 December 2013

Received 16 October 2013; accepted 17 December 2013

rule of the dependence of homolog synapsis on recombination do however exist: for example, although *Drosophila* and *Caenorhabditis elegans* do carry out SPO11-induced meiotic recombination, this is not required for homolog pairing and synapsis (Dernburg et al., 1998; McKim et al., 1998). Likewise, a number of budding yeast and *Arabidopsis* mutants defective for homologous recombination still show residual homolog pairing activity (Weiner and Kleckner, 1994; Rockmill et al., 1995; Leu et al., 1998; Tsubouchi and Roeder, 2003; Bleuyard and White, 2004; Li et al., 2004, 2005; Ronceret et al., 2009; Stronghill et al., 2010; Da Ines et al., 2012), and this implies the existence of recombination-independent mechanisms in homologous chromosome pairing.

As for any process involving DNA interactions, homologous chromosome pairing is intricately linked to the complex organization of the chromosomes and the nucleus. In this review, we present an overview of the early, recombination-independent events that promote homologous chromosome pairing during the first meiotic division, with a particular focus on plants.

ROLES OF CHROMATIN DYNAMICS AND REMODELING IN PAIRING OF HOMOLOGOUS CHROMOSOMES

During the first meiotic prophase, chromosomes condense, align with their partners and recombine, and partially decondense before entering metaphase. Homologous chromosome recognition and pairing thus involve interactions between DNA molecules in the context of these dynamic changes in chromatin and chromosome conformation. Early work in maize showed that chromosome pairing is associated with progressive changes in chromatin organization, with analyses of chromosome morphology and distribution permitting association of pairing with extensive chromatin rearrangements (Dawe et al., 1994). Dramatic structural reorganization was observed at the onset of pairing, with elongation of knob heterochromatin, increase in surface complexity and in total chromosome volume, suggesting that efficient homologous chromosome pairing relies on active movement of chromosomes and on a specialized chromatin and nuclear architecture (Dawe et al., 1994). Studies in wheat also provide strong evidence for a role of chromatin remodeling in homologous chromosome pairing (Prieto et al., 2004, 2005; Colas et al., 2008). Each chromosome of hexaploid wheat has both homologous and homeologous partners with which it can potentially pair in meiotic prophase. Proper chromosome segregation and fertility thus depend upon the restriction of pairing to homologs, and the exclusion of homeologous associations. In wheat, when a chromosome recognizes its homolog (and not another chromosome), a localized conformational change in adjacent chromatin is triggered in both partners. This process further facilitates recognition and pairing of homologous versus homeologous chromosomes and is affected by the P*h1* locus (Prieto et al., 2005; Greer et al., 2012). First identified in the 1950s as a dominant mutation that permits homeolog pairing (Okamoto, 1957; Riley and Chapman, 1958; Sears and Okamoto, 1958), *Ph1* has been recently shown to be a cluster of defective cyclin-dependent kinase (CDK)-like genes with similarity to mammalian Cdk2 (Greer et al., 2012). The authors argue that absence of *Ph1* alters heterochromatin decondensation through regulation of Cdk2-type activity and histone H1 phosphorylation, leading to reduction in the ability to distinguish homologous from homeologous chromosome pairing (Prieto et al., 2005; Greer et al., 2012). In accordance with this, application of okadaic acid (a drug inducing chromosome condensation and affecting phosphorylation of histone H1) can phenocopy the effect of the absence of *Ph1* on pairing (Knight et al., 2010).

Surprisingly, reports on the effects of local and global chromatin modifications on homolog pairing are very limited in the model plant *Arabidopsis thaliana*. Mutation of *SWI1*, a gene of unknown molecular function involved in sister chromatid cohesion and chromosome remodeling events, has been shown to affect chromosome pairing (Mercier et al., 2003; Boateng et al., 2008). Less condensed chromosomes were observed in *swi1* mutants and this was related to altered distribution of acetylated histone H3 and dimethylated histone H3 (H3K4me2) (Boateng et al., 2008). Alterations in histone modification patterns were also found in the *Arabidopsis ask1* mutant (Yang et al., 2006). ASK1 is the *Arabidopsis* SKP1 homolog, a component of the SCF ubiquitin ligase, and is implicated in a number of early meiotic nuclear reorganization events (Wang and Yang, 2006; Yang et al., 2006; Zhao et al., 2006; Yang et al., 2009). Absence of ASK1 affects acetylated histone H3 and H3K9me2 distribution patterns. These modifications in chromatin structure further lead to alterations in rDNA and nucleolar organizer regions, continued telomere association with the nucleolus, and prolonged chromosome attachment to the nuclear membrane and the nucleolus. These, in turn, result in defects in homolog pairing and chromosome segregation (Yang et al., 2006, 2009).

These data thus suggest that histone modifications, which play a central role in chromatin organization, are instrumental for meiotic chromosome pairing. Recent studies have shown that chromosomal distributions of histone H3 modifications during meiosis diverge in plants and animals (Manzanero et al., 2000) but also between dicots (*A. thaliana*) and monocots (*Aegilops* sp. and *Secale cereale*) (Oliver et al., 2013), highlighting the importance of chromatin remodeling in meiotic chromosome recognition and pairing in plants. How these remodeling events are involved is not currently understood, but one may speculate that they might act to modulate the functioning of the homologous recombination machinery in meiotic chromosome recognition and pairing.

DNA methylation is another important epigenetic mark regulating a wide range of biological processes (He et al.,

2011; Vanyushin and Ashapkin, 2011). Evidence for roles of DNA methylation in meiotic chromosome pairing are however scarce. In the natural autotetraploid *Arabidopsis arenosa*, immunolocalization of 5-methylcytosine (5-mC) showed DNA methylation in both euchromatic and heterochromatic regions during meiotic prophase I, contrasting with the staining restricted to chromocenters in vegetative nuclei (Carvalho et al., 2010). 5-mC is, however, excluded from rDNA loci in meiotic prophase I and the authors correlate this with the quadrivalent associations of the Nucleolus Organiser Regions (NORs) observed at early leptotene in this species (Carvalho et al., 2010).

A ROLE FOR HETEROCHROMATIC REGIONS IN HOMOLOG PAIRING

There is strong evidence that euchromatic and heterochromatic regions behave differently with respect to meiotic chromosome pairing. That heterochromatin regions are instrumental for homologous chromosome pairing during meiosis was initially demonstrated in *Drosophila* (Hawley et al., 1992; Dernburg et al., 1996; Karpen et al., 1996; Renauld, 1997). In female *Drosophila*, pairing and segregation of the fourth and the X chromosomes occurs without crossovers. This achiasmate pairing has been shown to depend on pairing of heterochromatic regions. In *Drosophila* males, heterochromatin, and especially rDNA, plays an important role in X–Y chromosome disjunction. Indeed, it has been shown that deletion or insertion of rDNA regions significantly affects pairing of the X and Y chromosomes and more precisely that a few copies of the *Drosophila* rDNA intergenic spacer regions are sufficient to promote chromosome pairing (McKee and Karpen, 1990; McKee et al., 1992; McKee, 1996). In the nematode *Caenorhabditis elegans*, meiotic chromosome pairing is initiated at particular pairing centers characterized by repeated DNA sequences. Each chromosome is characterized by a specific family of repeated sequences, which vary in length but have similar 12-bp core sequences. These heterochromatic repeat sequences are located near the ends of the chromosomes and are recognized by specific Zinc-finger DNA-binding proteins ZIM1-3 and HIM-8, which establish homologous chromosome associations (MacQueen et al., 2005; Phillips and Dernburg, 2006; Phillips et al., 2009; Zetka, 2009; Tsai and McKee, 2011).

In plants, there are no fully understood examples of heterochromatin-based mechanisms involved in meiotic chromosome pairing. However, several studies suggest that specific chromosomal regions (such as centromeres or telomeres, see below) play important roles in this process. Studies in maize showing that certain chromosome segments exhibit high crossover frequencies independently of their chromosomal locations suggest the existence of pairing centers outside of centromeres and telomeres (Maguire, 1986). The presence of short regions of synapsis and pairing of chromosomes have also been reported in several *Arabidopsis* recombination defective mutants (Bleuyard and White, 2004; Vignard et al., 2007; Ronceret et al., 2009; Stronghill et al., 2010; Da Ines et al., 2012). Although a whole-genome analysis of this pairing has not been carried out throughout the genome, it is clear that limited pairing of homologs does occur in these mutants (Bleuyard and White, 2004; Vignard et al., 2007; Ronceret et al., 2009; Stronghill et al., 2010; Da Ines et al., 2012). In the absence of key recombination proteins such as SPO11, RAD51, DMC1, XRCC3, or PHS1, pairing of 5S rDNA loci has been observed with up to 45% of this occurring between homologous chromosomes (Bleuyard and White, 2004; Ronceret et al., 2009; Da Ines et al., 2012). Similarly, recombination-independent pairing of NORs has been observed in *Arabidopsis* (Stronghill et al., 2010; Da Ines et al., 2012). *Arabidopsis* has two NOR-bearing chromosomes: chromosomes 2 and 4. These NORs are thought to be 'sticky' and Fluorescent *In Situ* Hybridization (FISH) analyses in *Arabidopsis* wild-type plants have shown that the two NORs are very frequently associated as one large knob (Ross et al., 1996; Fransz et al., 1998; Pecinka et al., 2004). Interestingly, this characteristic association of the nucleolar heterochromatin is also observed in absence of recombination (Stronghill et al., 2010; Da Ines et al., 2012). Analysis of meiosis in the absence of AHP2, the *Arabidopsis* homolog of yeast Hop2, showed that pairing and synapsis are severely disrupted in such mutants. However, pairing was found in the short arms of chromosomes 2 and 4, and led to normal synapsis of these NOR-bearing chromosome arms (Stronghill et al., 2010). Although the role of this NOR-driven pairing in wild-type plants remains to be determined, these observations strongly suggest that NORs may act as pairing sites in *Arabidopsis*. Examples of this are seen in several mutants with reduced crossing-over formation but which have a tendency to maintain crossing-over on the NOR-bearing chromosomes. The fraction of interference-insensitive crossovers is also reduced on these NOR-bearing chromosomes (Ji et al., 1999; Sanchez Moran et al., 2001; Lam et al., 2005; Drouaud et al., 2007). As mentioned above, this mechanism is not restricted to plants and NOR-driven chromosome pairing behavior is seen in *Drosophila* and has been reported for the sex chromosomes of North African rodent *Lemniscomys barbarus* (Stitou et al., 1997).

TELOMERE DYNAMICS AND INTERACTION WITH THE NUCLEAR ENVELOPE

During premeiotic interphase, chromosomes are separated and they must thus be brought into close proximity to assess homology and engage in pairing. Telomere movement clearly plays an important role in meiotic chromosome pairing and telomeres are believed to be the initiation site for pairing and synapsis in a number of organisms. In many

species, telomeres are dispersed in early meiosis but, at the leptotene-zygotene transition, they move and cluster to form the telomere 'bouquet', in which telomeres are attached to the inner surface of the nuclear envelope and grouped on one face of the nucleus (Scherthan, 2001; Bass, 2003; Harper et al., 2004; Naranjo and Corredor, 2008; Roberts et al., 2009). The clustering of telomeres occurs at the nuclear envelope near the microtubule organizing center (MTOC) in *C. elegans*, the spindle pole body in fungi or the centrosome in animals. The resulting bouquet arrangement and oscillation of the chromosomes facilitate alignment of chromosome arms and this is thought to play an important role in the initiation of homolog pairing (Scherthan, 2001; Bass, 2003; Harper et al., 2004; Roberts et al., 2009). The coincident formation of the telomere bouquet with the initiation of pairing is also suggestive of a direct role of the bouquet in meiotic chromosome pairing. Moreover, analyses of telomere mutants show that meiotic chromosome pairing is impaired (although not abolished) when bouquet formation is defective (Cooper et al., 1998; Trelles-Sticken et al., 2000; Liu et al., 2004; Trelles-Sticken et al., 2005). Importantly, telomere clustering is still observed in recombination defective mutants (e.g. *spo11* and *rad50S*), demonstrating that the formation of the bouquet is a recombination-independent event (Trelles-Sticken et al., 1999).

Telomeres also seem to play an important role in homolog pairing in plants. Most plants form a bouquet, which is formed coincidently with the initiation of chromosome pairing (Bass et al., 1997; Martinez-Perez et al., 1999; Bass et al., 2000; Corredor et al., 2007; Higgins et al., 2012; Phillips et al., 2012; Wen et al., 2012). However, the bouquet is not well defined and the site where telomeres are attached is not clear (reviewed in Harper et al., 2004; Roberts et al., 2009). Studies in maize have led to the identification of the *pam1* (plural abnormalities of meiosis 1) gene that is required for telomere clustering and homolog pairing (Golubovskaya et al., 2002). Absence of Pam1 affects telomere clustering and, hence bouquet formation, and leads to defects in chromosome synapsis. Interestingly, normal loading of the key recombinase RAD51 is observed in *pam1* plants, suggesting that recombination is not affected and that defects observed in pairing result from a defective telomere bouquet (Golubovskaya et al., 2002). Telomere bouquet formation in rye or wheat-rye additions is disrupted by application of the microtubule-depolymerizing agent colchicine, which also hampers pairing and synapsis (Loidl, 1990; Cowan and Cande, 2002; Cowan et al., 2002; Corredor and Naranjo, 2007).

Surprisingly, the situation appears different in *Arabidopsis*, where a loose clustering resembling a bouquet, rather than classical bouquet, is observed (Armstrong et al., 2001; Yang et al., 2006; Roberts et al., 2009). During interphase and early meiosis in *Arabidopsis*, telomeres appear to associate with the nucleolus. At the onset of leptotene, telomeres pair, dissociate from the nucleolus, and become dispersed but confined to one hemisphere of the nucleus. This atypical telomere clustering has been suggested to facilitate homolog pairing (Armstrong et al., 2001) and appears recombination-independent. Indeed, absence of recombination proteins, such as the ATM kinase, the RAD51 paralog RAD51C, or the synaptonemal complex (SC) axial element protein ASY1, has no effect on telomere clustering in *Arabidopsis* (Armstrong et al., 2001; Li et al., 2005; Roberts et al., 2009). There is, however, no clear evidence that telomere clustering is actively involved in homolog pairing in *Arabidopsis*. *Arabidopsis* meiotic telomere pairing is not affected by colchicine treatment (Roberts et al., 2009) and analyses show normal SC formation in late-generation telomerase mutants (with very short or absent telomeres), suggesting that telomere pairing is dispensable for homolog pairing and subsequent synapsis (Roberts et al., 2013). The authors propose that, rather than telomere pairing, it is the localization of telomeres to the nucleolus that is important for homolog pairing in *Arabidopsis* (Roberts et al., 2009, 2013).

Indeed, although telomere bouquet configuration diverges between species, telomere attachment to a particular nuclear region seems to be an important and conserved characteristic. The SUN and KASH families of proteins have been recently identified as key players in connecting chromosomes to the nuclear envelope and thereby promoting chromosome movements (Hiraoka and Dernburg, 2009). The crucial role of these proteins in telomere-led movement was initially characterized in fission yeast (Chikashige et al., 2006, 2007) but they are widely conserved and a role of these proteins in telomere attachment has been suggested in other organisms, particularly mouse (Ding et al., 2007; Boateng et al., 2013) and plants (Murphy and Bass, 2012; Roberts et al., 2013).

Early homologous chromosome pairing independent of DNA DSB has been reported in mice (Boateng et al., 2013). This early pre-DSB homolog pairing is dependent on presence of the SPO11 protein but not on its ability to cleave DNA and introduce DSB. Interestingly, the authors also showed that this early chromosome pairing also requires binding of the telomeres to the nuclear envelope by the protein SUN1 and is further stabilized by recombination. Plants also possess several SUN domain proteins (Graumann et al., 2010) and a role for these in telomere clustering and homolog pairing has been shown in maize (Murphy and Bass, 2012). Five SUN-domain proteins have been identified in *Arabidopsis* but their potential involvement in meiotic pairing has not yet been established (Graumann et al., 2010, 2013). Elucidating the role of chromosome movements in meiotic pairing and synapsis is becoming a very active area of research in plants. To date, most of our knowledge comes from FISH analyses, which necessarily only provide frozen images of a dynamic process. Live imaging may provide complementary as well as alternative answers to these mechanisms. For instance, imaging of chromosome dynamics in live maize meiocytes using 3-D microscopy very elegantly showed that nuclear and chromosome

movement are extremely dynamic during meiotic process and mostly telomere-led (Sheehan and Pawlowski, 2009).

ROLE OF CENTROMERES IN PAIRING OF HOMOLOGS

Centromeres have emerged as important players in chromosome pairing and interactions between centromeric regions in early meiotic prophase have been reported in many organisms (reviewed in Stewart and Dawson, 2008). The exact role of these interactions remains to be determined but, in general, it is believed that they lead to pre-alignment of homologs, facilitating the homology scanning process and the efficiency of homologous chromosome pairing.

Centromere association in the absence of recombination has been reported in budding yeast, fission yeast, *Drosophila*, and plants (Church and Moens, 1976; Karpen et al., 1996; Martinez-Perez et al., 1999; Ding et al., 2004; Tsubouchi and Roeder, 2005; Takeo et al., 2011; Tanneti et al., 2011; Da Ines et al., 2012; Phillips et al., 2012; Wen et al., 2012). In female *Drosophila*, centromeres cluster into one or two masses during early meiotic prophase independently of recombination and synapsis is first initiated at centromeres, followed by initiation at euchromatic sites (Takeo et al., 2011; Tanneti et al., 2011). Strong evidence for a role of centromeres in mediating recombination-independent pairing also comes from analyses in budding yeast. Centromere coupling, the association between centromeres of non-homologous chromosomes, was first described in budding yeast (Kemp et al., 2004; Tsubouchi and Roeder, 2005). In early meiotic prophase, centromeres associate in pairs in a dynamic, recombination-independent manner and this can be sufficient to mediate proper chromosome segregation (Kemp et al., 2004; Tsubouchi and Roeder, 2005; Bardhan et al., 2010; Obeso and Dawson, 2010). This process of centromeric coupling is dependent upon the SC component Zip1 and the cohesin protein Rec8, but not on Spo11. In contrast, the transition between non-homologous centromere coupling and pairing of centromeres of homologous chromosomes necessitates SPO11 protein and, hence, initiation of meiotic recombination (Tsubouchi and Roeder, 2005; Tsubouchi et al., 2008; Bardhan et al., 2010; Obeso and Dawson, 2010). Thus, centromere coupling, or pairing of centromeres of non-homologous chromosomes, precedes homologous interactions, which are then stabilized by SPO11-dependent homologous recombination mechanisms.

In order to ensure correct chromosome segregation, these non-homolog associations must be eliminated and pairing of centromeres of homologous chromosomes stabilized by homologous recombination. A recent study in yeast shows that this process is regulated through phosphorylation/dephosphorylation of serine 75 of the Zip1 protein by Mec1 (ATR) kinase and PP4 phosphatase (Falk et al., 2010). PP4, which is active throughout meiotic prophase, dephosphorylates Zip1 and this permits non-homologous centromere interactions. Initiation of meiotic recombination through DSB formation leads to activation of Mec1, which phosphorylates Zip1, thereby disrupting non-homologous centromere associations. This results in a dynamic centromere coupling/pairing process, which continues until all DSB are repaired and homologous chromosomes are paired (Falk et al., 2010).

Coupling of centromeres of non-homologous chromosomes has also been described in *Arabidopsis* (Da Ines et al., 2012). *Arabidopsis* centromeres are not paired during meiotic interphase, but cluster at leptotene/zygotene, and this is followed by pairwise centromere coupling (Armstrong et al., 2001; Da Ines et al., 2012, and references therein). The possible dependence of this centromere coupling on ZYP1 (homolog of yeast Zip1) has not been directly tested in *Arabidopsis*, but meiotic non-homologous centromere association is dependent on the presence of the cohesion protein REC8 (Cai et al., 2003) and does not require SPO11-induced recombination (Da Ines et al., 2012). Initiation of recombination by SPO11 is needed for the transition to homologous centromere pairing, as is the meiosis-specific recombinase DMC1 (Da Ines et al., 2012). These observations of the action of the recombination machinery at or near the centromeres are of particular importance to plant breeders, given the strong bias of meiotic crossing-over to centromere-distal regions in major crop plants.

Centromere coupling is also observed in other plants (Church and Moens, 1976; Martinez-Perez et al., 1999; Phillips et al., 2012; Wen et al., 2012; Zhang et al., 2013). Allohexaploid wheat has seven pairs of chromosomes derived from each of three related ancestral genomes, resulting in 42 chromosomes in a diploid cell. Each chromosome of hexaploid wheat has thus both one homologous and four homeologous partners with which it can potentially pair. Centromeres associate non-homologously in floral tissues and, prior to entry into meiosis, these associations switch to homologous pairs in a Ph1-dependent process (Martinez-Perez et al., 1999, 2000, 2001; Griffiths et al., 2006). It is proposed that this early premeiotic centromeric association mediates the sorting of homologs/homeologs essential for proper homologous chromosome pairing in polyploids (Moore and Shaw, 2009). The exact roles the centromeres play in this process, however, remain uncertain and other work has suggested that centromere pairing is a consequence of telomere driven pairing in wheat (Corredor et al., 2007).

Centromeres thus clearly play roles in chromosome pairing and synapsis in a number of organisms. In this context, it is important to take into account the fact that centromere structure varies considerably between organisms (ranging from 125 bp in *Saccharomyces cerevisiae* to the highly repeated DNA of up to several megabases in length found in multicellular eukaryotes). The specificities of centromere DNA and chromatin structure on meiotic centromere association and pairing, and the roles of this in initiating homolog synapsis and of recombination in stabilizing and extending

these interactions into chromosome arms remain, however, far from being fully understood.

NON-CODING RNA AND HOMOLOGOUS CHROMOSOME PAIRING

Non-coding small RNAs have emerged as essential regulators of genome function and, as such, have been found to play roles in multiple developmental and physiological processes (Chen, 2012), including DNA repair and homologous recombination (Wei et al., 2012; Chowdhury et al., 2013). Recently, a role of non-coding RNA in homologous chromosome pairing has been demonstrated in the fission yeast *Schizosaccharomyces pombe* (Ding et al., 2012). The authors report that the *sme2* locus pairs earlier than other loci in a recombination-independent manner (Ding et al., 2012). The *sme2* gene encodes a meiosis-specific non-coding RNA (mei-RNA), which binds two RNA-binding proteins, Mei2 and Mmi1. These transcripts accumulate at the *sme2* loci and are responsible for the pairing of these homologous loci. Deleting the *sme2* locus eliminates pairing while insertion at other chromosomal regions enhances robust pairing of these regions (Ding et al., 2012).

To date, there is no experimental evidence to support the notion that non-coding RNA may mediate homologous chromosome pairing in plants. However, homologs for the *Mei2* gene encoding RNA-binding protein have been identified in *Arabidopsis* and mutants of the corresponding genes display meiotic defects (Kaur et al., 2006). Non-coding RNAs are abundant in *Arabidopsis* male meiocytes (Yang et al., 2011), but their possible roles in the meiotic division cycle have not yet been demonstrated.

CONCLUSIONS AND PERSPECTIVES

Recognition and pairing of homologous chromosomes during meiosis are clearly facilitated by early, recombination-independent events. In addition to the roles of telomeres and centromeres, it is becoming increasingly apparent that meiotic chromosome pairing and segregation are controlled by a number of epigenetic mechanisms. Striking recent examples of this in plants are seen in recent genome-wide studies on the impact of chromatin modifications such as H2A.Z, histone H3 Lys4 trimethylation, or cytosine methylation on meiotic crossover distribution in *Arabidopsis* (Melamed-Bessudo and Levy, 2012; Mirouze et al., 2012; Yelina et al., 2012; Choi et al., 2013). Extensive chromatin changes occur during the process of chromosome pairing and specificities of chromosome structure appear to actively influence this process, particularly within heterochromatin regions. The roles of centromeres, telomeres, heterochromatic/euchromatic regions, chromatin modifications, and non-coding RNAs on homolog pairing and recombination are far from being fully understood and promise exciting advances in the future studies.

FUNDING

This work was partly financed by a European Union research grant (FP7-KBBE-2008-227190), the Centre National de la Recherche Scientifique, the Universite Blaise Pascal, the Universite d'Auvergne and the Institut National de la Sante et de la Recherche Medicale. No conflict of interest declared.

REFERENCES

Armstrong, S.J., Franklin, F.C., and Jones, G.H. (2001). Nucleolus-associated telomere clustering and pairing precede meiotic chromosome synapsis in *Arabidopsis thaliana*. J. Cell Sci. **114**, 4207–4217.

Bardhan, A., Chuong, H., and Dawson, D.S. (2010). Meiotic cohesin promotes pairing of nonhomologous centromeres in early meiotic prophase. Mol. Biol. Cell. **21**, 1799–1809.

Barzel, A., and Kupiec, M. (2008). Finding a match: how do homologous sequences get together for recombination? Nat. Rev. Genet. **9**, 27–37.

Bass, H.W. (2003). Telomere dynamics unique to meiotic prophase: formation and significance of the bouquet. Cell Mol. Life Sci. **60**, 2319–2324.

Bass, H.W., Marshall, W.F., Sedat, J.W., Agard, D.A., and Cande, W.Z. (1997). Telomeres cluster *de novo* before the initiation of synapsis: a three-dimensional spatial analysis of telomere positions before and during meiotic prophase. J. Cell Biol. **137**, 5–18.

Bass, H.W., Riera-Lizarazu, O., Ananiev, E.V., Bordoli, S.J., Rines, H.W., Phillips, R.L., Sedat, J.W., Agard, D.A., and Cande, W.Z. (2000). Evidence for the coincident initiation of homolog pairing and synapsis during the telomere-clustering (bouquet) stage of meiotic prophase. J. Cell Sci. **113(Pt 6),** 1033–1042.

Bhalla, N., and Dernburg, A.F. (2008). Prelude to a division. Annu. Rev. Cell Dev. Biol. **24**, 397–424.

Bleuyard, J.Y., and White, C.I. (2004). The *Arabidopsis* homologue of Xrcc3 plays an essential role in meiosis. Embo J. **23**, 439–449.

Boateng, K.A., Bellani, M.A., Gregoretti, I.V., Pratto, F., and Camerini-Otero, R.D. (2013). Homologous pairing preceding SPO11-mediated double-strand breaks in mice. Dev. Cell. **24**, 196–205.

Boateng, K.A., Yang, X., Dong, F., Owen, H.A., and Makaroff, C.A. (2008). SWI1 is required for meiotic chromosome remodeling events. Mol. Plant. **1**, 620–633.

Bozza, C.G., and Pawlowski, W.P. (2008). The cytogenetics of homologous chromosome pairing in meiosis in plants. Cytogenet Genome Res. **120**, 313–319.

Burgess, S.M. (2002). Homologous chromosome associations and nuclear order in meiotic and mitotically dividing cells of budding yeast. Adv. Genet. **46**, 49–90.

Cai, X., Dong, F., Edelmann, R.E., and Makaroff, C.A. (2003). The *Arabidopsis* SYN1 cohesin protein is required for sister chromatid arm cohesion and homologous chromosome pairing. J. Cell Sci. **116**, 2999–3007.

Carvalho, A., Delgado, M., Barao, A., Frescatada, M., Ribeiro, E., Pikaard, C.S., Viegas, W., and Neves, N. (2010). Chromosome

and DNA methylation dynamics during meiosis in the autotetraploid *Arabidopsis* arenosa. Sex Plant Reprod. **23**, 29–37.

Chen, X. (2012). Small RNAs in development—insights from plants. Curr. Opin. Genet. Dev. **22**, 361–367.

Chikashige, Y., Haraguchi, T., and Hiraoka, Y. (2007). Another way to move chromosomes. Chromosoma. **116**, 497–505.

Chikashige, Y., Tsutsumi, C., Yamane, M., Okamasa, K., Haraguchi, T., and Hiraoka, Y. (2006). Meiotic proteins bqt1 and bqt2 tether telomeres to form the bouquet arrangement of chromosomes. Cell. **125**, 59–69.

Choi, K., Zhao, X., Kelly, K.A., Venn, O., Higgins, J.D., Yelina, N.E., Hardcastle, T.J., Ziolkowski, P.A., Copenhaver, G.P., Franklin, F.C., et al. (2013). *Arabidopsis* meiotic crossover hot spots overlap with H2A.Z nucleosomes at gene promoters. Nat. Genet. **45**, 1327–1336.

Chowdhury, D., Choi, Y.E., and Brault, M.E. (2013). Charity begins at home: non-coding RNA functions in DNA repair. Nat. Rev. Mol. Cell Biol. **14**, 181–189.

Church, K., and Moens, P.B. (1976). Centromere behavior during interphase and meiotic prophase in *Allium fistulosum* from 3-D, EM reconstruction. Chromosoma. **56**, 249–263.

Colas, I., Shaw, P., Prieto, P., Wanous, M., Spielmeyer, W., Mago, R., and Moore, G. (2008). Effective chromosome pairing requires chromatin remodeling at the onset of meiosis. Proc. Natl Acad. Sci. U S A. **105**, 6075–6080.

Cooper, J.P., Watanabe, Y., and Nurse, P. (1998). Fission yeast Taz1 protein is required for meiotic telomere clustering and recombination. Nature. **392**, 828–831.

Corredor, E., and Naranjo, T. (2007). Effect of colchicine and telocentric chromosome conformation on centromere and telomere dynamics at meiotic prophase I in wheat-rye additions. Chromosome Res. **15**, 231–245.

Corredor, E., Lukaszewski, A.J., Pachon, P., Allen, D.C., and Naranjo, T. (2007). Terminal regions of wheat chromosomes select their pairing partners in meiosis. Genetics. **177**, 699–706.

Cowan, C.R., and Cande, W.Z. (2002). Meiotic telomere clustering is inhibited by colchicine but does not require cytoplasmic microtubules. J. Cell Sci. **115**, 3747–3756.

Cowan, C.R., Carlton, P.M., and Cande, W.Z. (2002). Reorganization and polarization of the meiotic bouquet-stage cell can be uncoupled from telomere clustering. J. Cell Sci. **115**, 3757–3766.

Da Ines, O., Abe, K., Goubely, C., Gallego, M.E., and White, C.I. (2012). Differing requirements for RAD51 and DMC1 in meiotic pairing of centromeres and chromosome arms in *Arabidopsis thaliana*. PLoS Genet. **8**, e1002636.

Dawe, R.K., Sedat, J.W., Agard, D.A., and Cande, W.Z. (1994). Meiotic chromosome pairing in maize is associated with a novel chromatin organization. Cell. **76**, 901–912.

Dernburg, A.F., McDonald, K., Moulder, G., Barstead, R., Dresser, M., and Villeneuve, A.M. (1998). Meiotic recombination in *C. elegans* initiates by a conserved mechanism and is dispensable for homologous chromosome synapsis. Cell. **94**, 387–398.

Dernburg, A.F., Sedat, J.W., and Hawley, R.S. (1996). Direct evidence of a role for heterochromatin in meiotic chromosome segregation. Cell. **86**, 135–146.

Ding, D.Q., Haraguchi, T., and Hiraoka, Y. (2010). From meiosis to postmeiotic events: alignment and recognition of homologous chromosomes in meiosis. Febs J. **277**, 565–570.

Ding, D.Q., Okamasa, K., Yamane, M., Tsutsumi, C., Haraguchi, T., Yamamoto, M., and Hiraoka, Y. (2012). Meiosis-specific noncoding RNA mediates robust pairing of homologous chromosomes in meiosis. Science. **336**, 732–736.

Ding, D.Q., Yamamoto, A., Haraguchi, T., and Hiraoka, Y. (2004). Dynamics of homologous chromosome pairing during meiotic prophase in fission yeast. Dev. Cell. **6**, 329–341.

Ding, X., Xu, R., Yu, J., Xu, T., Zhuang, Y., and Han, M. (2007). SUN1 is required for telomere attachment to nuclear envelope and gametogenesis in mice. Dev. Cell. **12**, 863–872.

Drouaud, J., Mercier, R., Chelysheva, L., Berard, A., Falque, M., Martin, O., Zanni, V., Brunel, D., and Mezard, C. (2007). Sex-specific crossover distributions and variations in interference level along *Arabidopsis thaliana* chromosome 4. PLoS Genet. **3**, e106.

Falk, J.E., Chan, A.C., Hoffmann, E., and Hochwagen, A. (2010). A Mec1- and PP4-dependent checkpoint couples centromere pairing to meiotic recombination. Dev. Cell. **19**, 599–611.

Fransz, P., Armstrong, S., Alonso-Blanco, C., Fischer, T.C., Torres-Ruiz, R.A., and Jones, G. (1998). Cytogenetics for the model system *Arabidopsis thaliana*. Plant J. **13**, 867–876.

Golubovskaya, I.N., Harper, L.C., Pawlowski, W.P., Schichnes, D., and Cande, W.Z. (2002). The pam1 gene is required for meiotic bouquet formation and efficient homologous synapsis in maize (*Zea mays* L.). Genetics. **162**, 1979–1993.

Graumann, K., Bass, H.W., and Parry, G. (2013). SUNrises on the International Plant Nucleus Consortium: SEB Salzburg 2012. Nucleus. **4**, 3–7.

Graumann, K., Runions, J., and Evans, D.E. (2010). Characterization of SUN-domain proteins at the higher plant nuclear envelope. Plant J. **61**, 134–144.

Greer, E., Martin, A.C., Pendle, A., Colas, I., Jones, A.M., Moore, G., and Shaw, P. (2012). The Ph1 locus suppresses Cdk2-type activity during premeiosis and meiosis in wheat. Plant Cell. **24**, 152–162.

Griffiths, S., Sharp, R., Foote, T.N., Bertin, I., Wanous, M., Reader, S., Colas, I., and Moore, G. (2006). Molecular characterization of Ph1 as a major chromosome pairing locus in polyploid wheat. Nature. **439**, 749–752.

Harper, L., Golubovskaya, I., and Cande, W.Z. (2004). A bouquet of chromosomes. J. Cell Sci. **117**, 4025–4032.

Hassold, T., and Hunt, P. (2001). To err (meiotically) is human: the genesis of human aneuploidy. Nature Rev. Genet. **2**, 280–291.

Hawley, R.S., Irick, H., Zitron, A.E., Haddox, D.A., Lohe, A., New, C., Whitley, M.D., Arbel, T., Jang, J., McKim, K., et al. (1992). There are two mechanisms of achiasmate segregation in *Drosophila* females, one of which requires heterochromatic homology. Dev. Genet. **13**, 440–467.

He, X.J., Chen, T., and Zhu, J.K. (2011). Regulation and function of DNA methylation in plants and animals. Cell Res. **21**, 442–465.

Higgins, J.D., Perry, R.M., Barakate, A., Ramsay, L., Waugh, R., Halpin, C., Armstrong, S.J., and Franklin, F.C. (2012). Spatiotemporal asymmetry of the meiotic program underlies

the predominantly distal distribution of meiotic crossovers in barley. Plant Cell. **24**, 4096–4109.

Hiraoka, Y., and Dernburg, A.F. (2009). The SUN rises on meiotic chromosome dynamics. Dev. Cell. **17**, 598–605.

Ji, Y., Stelly, D.M., De Donato, M., Goodman, M.M., and Williams, C.G. (1999). A candidate recombination modifier gene for *Zea mays* L. Genetics. **151**, 821–830.

Karpen, G.H., Le, M.H., and Le, H. (1996). Centric heterochromatin and the efficiency of achiasmate disjunction in *Drosophila* female meiosis. Science. **273**, 118–122.

Kaur, J., Sebastian, J., and Siddiqi, I. (2006). The *Arabidopsis*-mei2-like genes play a role in meiosis and vegetative growth in *Arabidopsis*. Plant Cell. **18**, 545–559.

Kemp, B., Boumil, R.M., Stewart, M.N., and Dawson, D.S. (2004). A role for centromere pairing in meiotic chromosome segregation. Genes Dev. **18**, 1946–1951.

Knight, E., Greer, E., Draeger, T., Thole, V., Reader, S., Shaw, P., and Moore, G. (2010). Inducing chromosome pairing through premature condensation: analysis of wheat interspecific hybrids. Funct. Integr. Genomics. **10**, 603–608.

Lam, S.Y., Horn, S.R., Radford, S.J., Housworth, E.A., Stahl, F.W., and Copenhaver, G.P. (2005). Crossover interference on nucleolus organizing region-bearing chromosomes in *Arabidopsis*. Genetics. **170**, 807–812.

Leu, J.Y., Chua, P.R., and Roeder, G.S. (1998). The meiosis-specific Hop2 protein of *S. cerevisiae* ensures synapsis between homologous chromosomes. Cell. **94**, 375–386.

Li, W., Chen, C., Markmann-Mulisch, U., Timofejeva, L., Schmelzer, E., Ma, H., and Reiss, B. (2004). The *Arabidopsis* AtRAD51 gene is dispensable for vegetative development but required for meiosis. Proc. Natl Acad. Sci. U S A. **101**, 10596–10601.

Li, W., Yang, X., Lin, Z., Timofejeva, L., Xiao, R., Makaroff, C.A., and Ma, H. (2005). The AtRAD51C gene is required for normal meiotic chromosome synapsis and double-stranded break repair in *Arabidopsis*. Plant Physiol. **138**, 965–976.

Liu, L., Franco, S., Spyropoulos, B., Moens, P.B., Blasco, M.A., and Keefe, D.L. (2004). Irregular telomeres impair meiotic synapsis and recombination in mice. Proc. Natl Acad. Sci. U S A. **101**, 6496–6501.

Loidl, J. (1990). The initiation of meiotic chromosome pairing: the cytological view. Genome. **33**, 759–778.

MacQueen, A.J., Phillips, C.M., Bhalla, N., Weiser, P., Villeneuve, A.M., and Dernburg, A.F. (2005). Chromosome sites play dual roles to establish homologous synapsis during meiosis in *C. elegans*. Cell. **123**, 1037–1050.

Maguire, M.P. (1986). The pattern of pairing that is effective for crossing over in complex B–A chromosome rearrangements in maize. III. Possible evidence for pairing centers. Chromosoma. **94**, 71–85.

Manzanero, S., Arana, P., Puertas, M.J., and Houben, A. (2000). The chromosomal distribution of phosphorylated histone H3 differs between plants and animals at meiosis. Chromosoma. **109**, 308–317.

Martinez-Perez, E., Shaw, P., and Moore, G. (2001). The Ph1 locus is needed to ensure specific somatic and meiotic centromere association. Nature. **411**, 204–207.

Martinez-Perez, E., Shaw, P., Reader, S., Aragon-Alcaide, L., Miller, T., and Moore, G. (1999). Homologous chromosome pairing in wheat. J. Cell Sci. **112**(Pt 11**),** 1761–1769.

Martinez-Perez, E., Shaw, P.J., and Moore, G. (2000). Polyploidy induces centromere association. J. Cell Biol. **148**, 233–238.

McKee, B.D. (1996). The license to pair: identification of meiotic pairing sites in *Drosophila*. Chromosoma. **105**, 135–141.

McKee, B.D. (2004). Homologous pairing and chromosome dynamics in meiosis and mitosis. Biochim. Biophys. Acta. **1677**, 165–180.

McKee, B.D., and Karpen, G.H. (1990). *Drosophila* ribosomal RNA genes function as an X–Y pairing site during male meiosis. Cell. **61**, 61–72.

McKee, B.D., Habera, L., and Vrana, J.A. (1992). Evidence that intergenic spacer repeats of *Drosophila melanogaster* rRNA genes function as X–Y pairing sites in male meiosis, and a general model for achiasmatic pairing. Genetics. **132**, 529–544.

McKee, B.D., Yan, R., and Tsai, J.H. (2012). Meiosis in male *Drosophila*. Spermatogenesis. **2**, 167–184.

McKim, K.S., Green-Marroquin, B.L., Sekelsky, J.J., Chin, G., Steinberg, C., Khodosh, R., and Hawley, R.S. (1998). Meiotic synapsis in the absence of recombination. Science. **279**, 876–878.

Melamed-Bessudo, C., and Levy, A.A. (2012). Deficiency in DNA methylation increases meiotic crossover rates in euchromatic but not in heterochromatic regions in *Arabidopsis*. Proc. Natl Acad. Sci. U S A. **109**, E981–E988.

Mercier, R., Armstrong, S.J., Horlow, C., Jackson, N.P., Makaroff, C.A., Vezon, D., Pelletier, G., Jones, G.H., and Franklin, F.C. (2003). The meiotic protein SWI1 is required for axial element formation and recombination initiation in *Arabidopsis*. Development. **130**, 3309–3318.

Mirouze, M., Lieberman-Lazarovich, M., Aversano, R., Bucher, E., Nicolet, J., Reinders, J., and Paszkowski, J. (2012). Loss of DNA methylation affects the recombination landscape in *Arabidopsis*. Proc. Natl Acad. Sci. U S A. **109**, 5880–5885.

Moore, G., and Shaw, P. (2009). Improving the chances of finding the right partner. Curr. Opin. Genet. Dev. **19**, 99–104.

Murphy, S.P., and Bass, H.W. (2012). The maize (*Zea mays*) desynaptic (dy) mutation defines a pathway for meiotic chromosome segregation, linking nuclear morphology, telomere distribution and synapsis. J. Cell Sci. **125**, 3681–3690.

Naranjo, T., and Corredor, E. (2008). Nuclear architecture and chromosome dynamics in the search of the pairing partner in meiosis in plants. Cytogenet. Genome Res. **120**, 320–330.

Obeso, D., and Dawson, D.S. (2010). Temporal characterization of homology-independent centromere coupling in meiotic prophase. PLoS One. **5**, e10336.

Okamoto, M. (1957). Asynaptic effect of chromosome V. Wheat Inf. Serv. **5**, 6.

Oliver, C., Pradillo, M., Corredor, E., and Cunado, N. (2013). The dynamics of histone H3 modifications is species-specific in plant meiosis. Planta. **238**, 23–33.

Pawlowski, W.P., and Cande, W.Z. (2005). Coordinating the events of the meiotic prophase. Trends Cell Biol. **15**, 674–681.

Pecinka, A., Schubert, V., Meister, A., Kreth, G., Klatte, M., Lysak, M.A., Fuchs, J., and Schubert, I. (2004). Chromosome territory arrangement and homologous pairing in nuclei of *Arabidopsis thaliana* are predominantly random except for NOR-bearing chromosomes. Chromosoma. **113**, 258–269.

Phillips, C.M., and Dernburg, A.F. (2006). A family of zinc-finger proteins is required for chromosome-specific pairing and synapsis during meiosis in *C. elegans*. Dev. Cell. **11**, 817–829.

Phillips, C.M., Meng, X., Zhang, L., Chretien, J.H., Urnov, F.D., and Dernburg, A.F. (2009). Identification of chromosome sequence motifs that mediate meiotic pairing and synapsis in *C. elegans*. Nat. Cell Biol. **11**, 934–942.

Phillips, D., Nibau, C., Wnetrzak, J., and Jenkins, G. (2012). High resolution analysis of meiotic chromosome structure and behaviour in barley (*Hordeum vulgare* L.). PLoS One. **7**, e39539.

Prieto, P., Moore, G., and Reader, S. (2005). Control of conformation changes associated with homologue recognition during meiosis. Theor. Appl. Genet. **111**, 505–510.

Prieto, P., Shaw, P., and Moore, G. (2004). Homologue recognition during meiosis is associated with a change in chromatin conformation. Nat. Cell Biol. **6**, 906–908.

Renauld, H. (1997). Heterochromatin: a meiotic matchmaker? Trends Cell Biol. **7**, 201–205.

Riley, R., and Chapman, V. (1958). Genetic control of the cytologically diploid behaviour of hexaploid wheat. Nature. **182**, 713–715.

Roberts, N.Y., Osman, K., and Armstrong, S.J. (2009). Telomere distribution and dynamics in somatic and meiotic nuclei of *Arabidopsis thaliana*. Cytogenet. Genome Res. **124**, 193–201.

Roberts, N.Y., Osman, K., Franklin, F.C., Pradillo, M., Varas, J., Santos, J.L., and Armstrong, S. (2013). Telomeres in plant meiosis: their structure, dynamics and function. Annual Plant Reviews. **46**, 191–228, edited by Evans, D.E., Graumann, K., and Bryant, J.A.

Rockmill, B., Sym, M., Scherthan, H., and Roeder, G.S. (1995). Roles for two RecA homologs in promoting meiotic chromosome synapsis. Genes Dev. **9**, 2684–2695.

Ronceret, A., Doutriaux, M.P., Golubovskaya, I.N., and Pawlowski, W.P. (2009). PHS1 regulates meiotic recombination and homologous chromosome pairing by controlling the transport of RAD50 to the nucleus. Proc. Natl Acad. Sci. U S A. **106**, 20121–20126.

Ross, K.J., Fransz, P., and Jones, G.H. (1996). A light microscopic atlas of meiosis in *Arabidopsis thaliana*. Chromosome Res. **4**, 507–516.

Sanchez Moran, E., Armstrong, S.J., Santos, J.L., Franklin, F.C., and Jones, G.H. (2001). Chiasma formation in *Arabidopsis thaliana* accession Wassileskija and in two meiotic mutants. Chromosome Res. **9**, 121–128.

Scherthan, H. (2001). A bouquet makes ends meet. Nat. Rev. Mol. Cell Biol. **2**, 621–627.

Sears, E.R., and Okamoto, M. (1958). Intergenomic chromosome relationships in hexaploid wheat. Proc. X Int. Congress Genet. Montreal, Canada. pp. 258–259.

Sheehan, M.J., and Pawlowski, W.P. (2009). Live imaging of rapid chromosome movements in meiotic prophase I in maize. Proc. Natl Acad. Sci. U S A. **106**, 20989–20994.

Stewart, M.N., and Dawson, D.S. (2008). Changing partners: moving from non-homologous to homologous centromere pairing in meiosis. Trends Genet. **24**, 564–573.

Stitou, S., Burgos, M., Zurita, F., Jimenez, R., Sanchez, A., and Diaz de la Guardia, R. (1997). Recent evolution of NOR-bearing and sex chromosomes of the North African rodent *Lemniscomys barbarus*. Chromosome Res. **5**, 481–485.

Stronghill, P., Pathan, N., Ha, H., Supijono, E., and Hasenkampf, C. (2010). Ahp2 (Hop2) function in *Arabidopsis thaliana* (Ler) is required for stabilization of close alignment and synaptonemal complex formation except for the two short arms that contain nucleolus organizer regions. Chromosoma. **119**, 443–458.

Takeo, S., Lake, C.M., Morais-de-Sa, E., Sunkel, C.E., and Hawley, R.S. (2011). Synaptonemal complex-dependent centromeric clustering and the initiation of synapsis in *Drosophila* oocytes. Curr. Biol. **21**, 1845–1851.

Tanneti, N.S., Landy, K., Joyce, E.F., and McKim, K.S. (2011). A pathway for synapsis initiation during zygotene in *Drosophila* oocytes. Curr. Biol. **21**, 1852–1857.

Tiang, C.L., He, Y., and Pawlowski, W.P. (2012). Chromosome organization and dynamics during interphase, mitosis, and meiosis in plants. Plant Physiol. **158**, 26–34.

Trelles-Sticken, E., Adelfalk, C., Loidl, J., and Scherthan, H. (2005). Meiotic telomere clustering requires actin for its formation and cohesin for its resolution. J. Cell Biol. **170**, 213–223.

Trelles-Sticken, E., Dresser, M.E., and Scherthan, H. (2000). Meiotic telomere protein Ndj1p is required for meiosis-specific telomere distribution, bouquet formation and efficient homologue pairing. J. Cell Biol. **151**, 95–106.

Trelles-Sticken, E., Loidl, J., and Scherthan, H. (1999). Bouquet formation in budding yeast: initiation of recombination is not required for meiotic telomere clustering. J. Cell Sci. **112**(Pt 5), 651–658.

Tsai, J.H., and McKee, B.D. (2011). Homologous pairing and the role of pairing centers in meiosis. J. Cell Sci. **124**, 1955–1963.

Tsubouchi, H., and Roeder, G.S. (2003). The importance of genetic recombination for fidelity of chromosome pairing in meiosis. Dev. Cell. **5**, 915–925.

Tsubouchi, T., and Roeder, G.S. (2005). A synaptonemal complex protein promotes homology-independent centromere coupling. Science. **308**, 870–873.

Tsubouchi, T., Macqueen, A.J., and Roeder, G.S. (2008). Initiation of meiotic chromosome synapsis at centromeres in budding yeast. Genes Dev. **22**, 3217–3226.

Vanyushin, B.F., and Ashapkin, V.V. (2011). DNA methylation in higher plants: past, present and future. Biochim. Biophys. Acta. **1809**, 360–368.

Vignard, J., Siwiec, T., Chelysheva, L., Vrielynck, N., Gonord, F., Armstrong, S.J., Schlogelhofer, P., and Mercier, R. (2007). The interplay of RecA-related proteins and the MND1-HOP2 complex during meiosis in *Arabidopsis thaliana*. PLoS Genet. **3**, 1894–1906.

Wang, Y., and Yang, M. (2006). The *ARABIDOPSIS* SKP1-LIKE1 (ASK1) protein acts predominately from leptotene to pachytene and represses homologous recombination in male meiosis. Planta. **223**, 613–617.

Wei, W., Ba, Z., Gao, M., Wu, Y., Ma, Y., Amiard, S., White, C.I., Rendtlew Danielsen, J.M., Yang, Y.G., and Qi, Y. (2012). A role for small RNAs in DNA double-strand break repair. Cell. **149**, 101–112.

Weiner, B.M., and Kleckner, N. (1994). Chromosome pairing via multiple interstitial interactions before and during meiosis in yeast. Cell. **77**, 977–991.

Wells, J.L., Pryce, D.W., and McFarlane, R.J. (2006). Homologous chromosome pairing in *Schizosaccharomyces pombe*. Yeast. **23**, 977–989.

Wen, R., Moore, G., and Shaw, P.J. (2012). Centromeres cluster de novo at the beginning of meiosis in *Brachypodium distachyon*. PLoS One. **7**, e44681.

Yang, H., Lu, P., Wang, Y., and Ma, H. (2011). The transcriptome landscape of *Arabidopsis* male meiocytes from high-throughput sequencing: the complexity and evolution of the meiotic process. Plant J. **65**, 503–516.

Yang, X., Boateng, K.A., Strittmatter, L., Burgess, R., and Makaroff, C.A. (2009). *Arabidopsis* separase functions beyond the removal of sister chromatid cohesion during meiosis. Plant Physiol. **151**, 323–333.

Yang, X., Timofejeva, L., Ma, H., and Makaroff, C.A. (2006). The *Arabidopsis* SKP1 homolog ASK1 controls meiotic chromosome remodeling and release of chromatin from the nuclear membrane and nucleolus. J. Cell Sci. **119**, 3754–3763.

Yelina, N.E., Choi, K., Chelysheva, L., Macaulay, M., de Snoo, B., Wijnker, E., Miller, N., Drouaud, J., Grelon, M., Copenhaver, G.P., et al. (2012). Epigenetic remodeling of meiotic crossover frequency in *Arabidopsis thaliana* DNA methyltransferase mutants. PLoS Genet. **8**, e1002844.

Zetka, M. (2009). Homologue pairing, recombination and segregation in *Caenorhabditis elegans*. Genome Dyn. **5**, 43–55.

Zhang, J., Pawlowski, W.P., and Han, F. (2013). Centromere pairing in early meiotic prophase requires active centromeres and precedes installation of the synaptonemal complex in maize. Plant Cell. **25**, 3900–3909.

Zhao, D., Yang, X., Quan, L., Timofejeva, L., Rigel, N.W., Ma, H., and Makaroff, C.A. (2006). ASK1, a SKP1 homolog, is required for nuclear reorganization, presynaptic homolog juxtaposition and the proper distribution of cohesin during meiosis in *Arabidopsis*. Plant Mol. Biol. **62**, 99–110.

Zickler, D. (2006). From early homologue recognition to synaptonemal complex formation. Chromosoma. **115**, 158–174.