Journal of Reproduction and Development, Vol. 59, No 5, 2013

SRD Young Investigator Award 2012

Roles of Cohesin and Condensin in Chromosome Dynamics During Mammalian Meiosis

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Abstract. Meiosis is a key step for sexual reproduction in which chromosome number is halved by two successive meiotic divisions after a single round of DNA replication. In the first meiotic division (meiosis I), homologous chromosomes pair, synapse, and recombine with their partners in prophase I. As a result, homologous chromosomes are physically connected until metaphase I and then segregated from each other at the onset of anaphase I. In the subsequent second meiotic division (meiosis II), sister chromatids are segregated. Chromosomal abnormality arising during meiosis is one of the major causes of birth defects and congenital disorders in mammals including human and domestic animals. Hence understanding of the mechanism underlying these unique chromosome behavior in meiosis is of great importance. This review focuses on the roles of cohesin and condensin, and their regulation in chromosome dynamics during mammalian meiosis.
Key words: Chromosome, Cohesin, Condensin, Meiosis, Oocyte

(**J. Reprod. Dev.** 59**:** 431**–**436, 2013)

Meiosis

Meiosis is an essential sexual reproduction process for producing haploid cells from diploid parental cells. For reducing chromosome number by half, meiosis is different from mitosis in some features. Firstly, the regulation of cell cycle is different: the S phase is followed by a single round of cell division in the mitotic cell cycle, whereas it is followed by two rounds of cell division in the meiotic cell cycle. Secondly, chromosomes behave uniquely in meiosis. In mitotic division, sister chromatids, which are replicated in the S phase, separate in anaphase (Fig. 1A). On the other hand, in the first meiotic division (meiosis I), homologous chromosomes pair, juxtapose (synapse) and recombine with their partners in the prophase in parallel with assembly of the synaptonemal complex (SC). Then, homologous chromosomes are segregated towards opposite poles of the spindle at anaphase I by the dissolution of arm cohesion while sister chromatids are kept attached at centromere regions. Finally, the two sisters are segregated at anaphase in meiosis II (Fig. 1A). Meiosis-specific molecules as well as modification of the mitotic system accomplish this series of meiotic events.

Cohesins

In mitosis, two sister chromatids that are duplicated in the S phase must be kept attached until anaphase for faithful chromosome segregation. A multi-subunit protein complex called cohesin, which is well conserved from yeasts to mammals, plays a pivotal role in sister chromatid cohesion [1]. In mammalian somatic cells, cohesin consists of four subunits, SMC1α, SMC3, RAD21 and either one of STAG1/SA1 or STAG2/SA2 (Table 1). From its rig-like structure, it is assumed that the cohesin complex may embrace two replicated sister chromatids (Fig. 1B). At the onset of anaphase, a protease called Separase cleaves RAD21, a kleisin subunit named after "bridge" in Greek, thereby allowing sister chromatids to separate and move towards the opposite spindle poles. In addition to mitotic cohesin subunits, mammals have several meiosis-specific subunits [2–6] (Table 1). So far, four meiosis specific cohesin subunits, SMC1β, REC8, RAD21L and STAG3/SA3 have been found. These meiosis-specific subunits form complexes with the mitotic cohesin subunits, making at least four types of cohesin complexes in addition to the canonical ones [5].

Homologous chromosome synapsis and recombination in prophase I

In most organisms, the pairing, synapsis and recombination of homologous chromosomes occur in parallel with the formation of the SC, which is a proteinaceous structure unique to meiosis [7]. After pre-meiotic DNA replication, the meiotic prophase is divided into four stages according to the assembly and disassembly of the SC. The axial element (AE) of the SC starts to assemble at the leptotene stage. Then, at the zygotene stage, homologous chromosomes start to synapse. At the pachytene, synapsis is completed, and the AEs are now called lateral elements of the SC. The SC is disassembled at the diplotene stage. Essentially, all of the cohesin subunits so far examined are reported to localize along the axial (lateral) element of the SC, but the timing of association and dissociation to the AEs

Received: June 12, 2013
Accepted: June 13, 2013
Published online in J-STAGE: July 8, 2013

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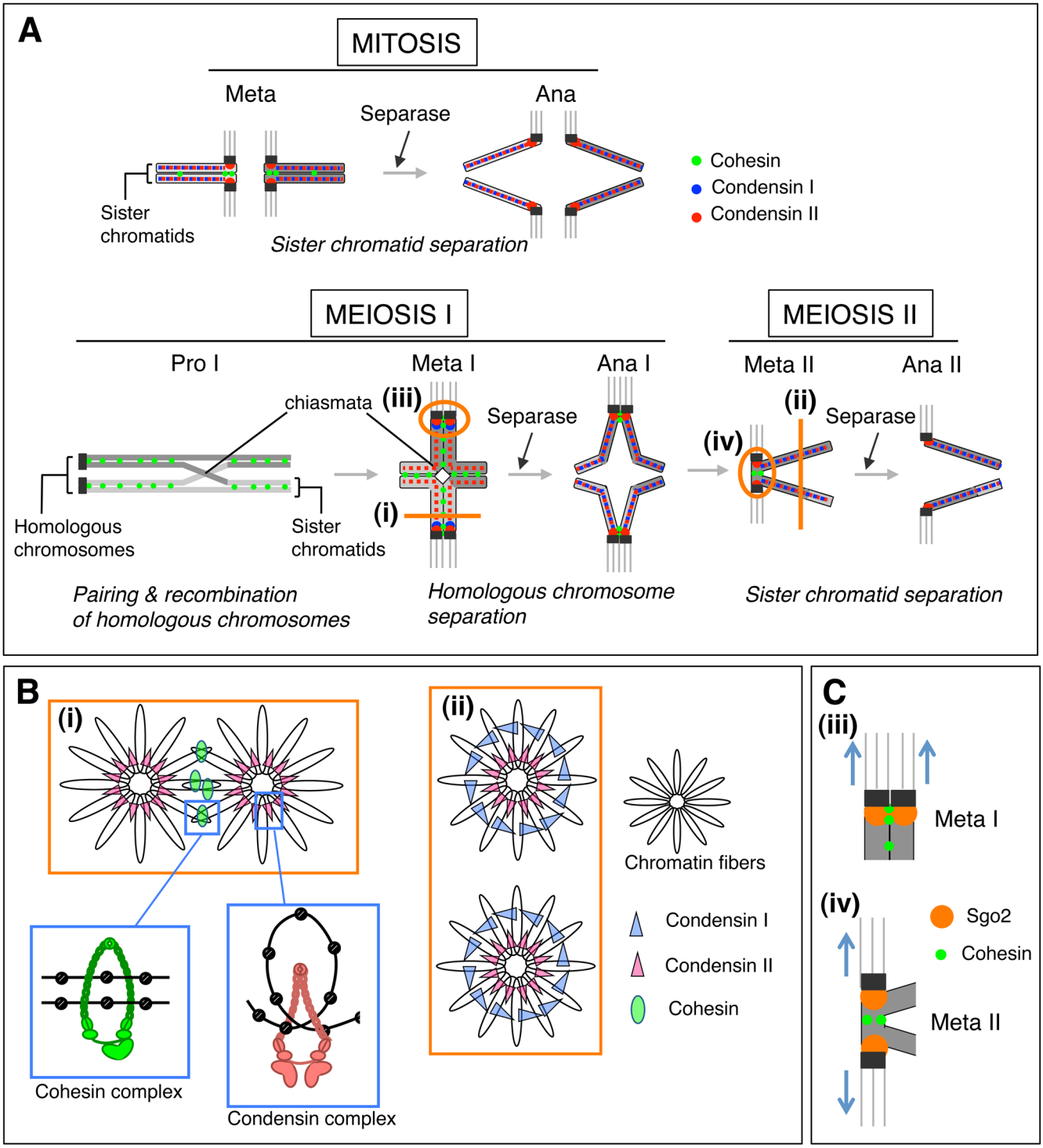

Fig. 1.

differs among cohesin subunits. For example, meiosis-specific cohesin subunit RAD21L localizes along the AEs in early stages of prophase I (indicated by arrows in Fig. 2), whereas RAD21 is present along AEs in the later stages (indicated by arrowheads in Fig. 2). Furthermore, there are several discrepancies about the timing of expression of each cohesin subunit in mammalian meiosis as discussed in several reviews [8, 9], making it difficult to comprehend the whole yet precise view of meiotic cohesin dynamics.

Despite limited understanding of meiotic cohesin dynamics, it is obvious that they play an important role in meiotic prophase

Table 1. Subunits of cohesin and condensin complexes in mammals

	Type	SMC subunits		Non-SMC subunits		
Cohesin	Mitotic*	SMC1α	SMC3	RAD21	STAG1/SA1, STAG2/SA2	
	Meiotic	SMC1β	SMC3	REC8, RAD21L	STAG3/SA3	
Condensin	I	SMC2	SMC4	CAP-H	CAP-D2	CAP-G
	II	SMC2	SMC4	CAP-H2	CAP-D3	CAP-G2

In mammals, not only meiotic but also mitotic cohesin subunits are expressed during meiosis, at least at some stages. Thus, in this sense, it seems better to call "mitotic" cohesin subunits as "ubiquitous" cohesin subunits.

Fig. 1. (A) Spatiotemporal dynamics of cohesin and condensins I and II in mitotic and meiotic divisions. In mitosis, cohesin maintains sister chromatid cohesion mainly at centromeres, while most cohesin is removed from chromosome arms until metaphase (meta). Condensins I and II are recruited to the chromatid axes and participate to construct mitotic chromosomes. Sister chromatids separate from each other by the action of Separase to cleave a cohesin subunit, RAD21, at anaphase (ana). In meiosis, homologous chromosomes pair, juxtapose, and recombine with their partners in prophase I (pro I). Theoretically, cohesin localizing arm regions distal to chiasmata contributes to the physical connection between homologous chromosomes. At metaphase I (meta I), meiotic cohesin containing REC8 maintains sister chromatid cohesion at both centromeres and chromosome arms. At this stage, condensin I localizes at the vicinity of centromeres, while condensin II localizes along chromatid axes. At anaphase I (ana I), cohesin along arms is removed by the action of Separase, while centromeric cohesin is protected. In parallel, condensin I becomes localized along arms. At the onset of anaphase II (ana II), the remaining cohesin at centromeres is now cleaved by the action of Separase. (B) Cross-sectional views of chromosomes along lines (i) and (ii) in Fig. 1A are shown. In the insets, the models of how cohesin and condensin complexes regulate the higher structure of chromosomes are proposed; cohesin complexes are thought to hold nucleosomes from sister chromatids, whereas condensin may connect the separate segments of the nucleosome of a single chromatid. (C) Localization of Sgo2 and cohesin containing REC8 around centromeres, indicated by ellipses (iii) and (iv) in Fig. 1A, is shown. When sister kinetochores are pulled towards the same spindle poles at meta I, no or little tension is exerted between the kinetochores. In such a case, Sgo2 is localized close to the centromeric cohesin. When sister kinetochores are pulled towards opposite directions at metaphase II (meta II) (or in mitotic metaphase), tension is exerted between the kinetochores. In this situation, Sgo2 relocates from the inner centromere to the outer kinetochores. This relocation of Sgo2 leads to spatial separation from centromeric cohesin, thereby stopping its protective function of centromeric cohesion.

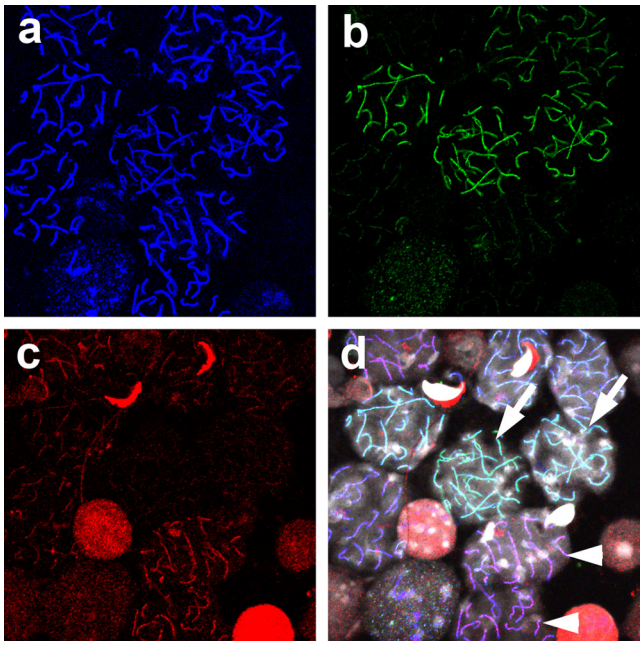

Fig. 2. Differentially expressed cohesin subunits during meiotic prophase I. Newly identified cohesin subunit RAD21L (green), the canonical mitotic cohesin subunit RAD21 (red), and the synaptonemal complex protein SYCP3 (blue) are immunofluorescently labeled in mouse testicular cells. DNA (silver) was counterstained with DAPI. (a) SYCP3, (b) RAD21L, (c) RAD21, (d) merged image. It is noteworthy that RAD21L, but little RAD21, is detected along the synaptonemal complex in some spermatocytes (arrows), and vice versa in other spermatocytes (arrowheads).

I. So far, several knockout mice have been produced for *in vivo* functional analysis of meiotic cohesin subunits. In general, depletion of meiosis-specific cohesin subunits, such as SMC1β, REC8 and RAD21L, causes meiotic blockage prior to the pachytene stage due to errors in pairing or the synaptic process in male mice. In SMC1β−depleted spermatocytes, formation of AEs is partially defective, with AEs markedly shortened and chromatin loops more extended [10, 11]. In REC8-depleted spermatocytes, AEs are formed and partially synapsed [12], but the synapsis occurs between sister chromatids rather than homologous chromosomes [13]. In RAD21L-depleted spermatocytes, AEs are fragmented and poorly aligned, and synapsis occurs between nonhomologous chromosomes [14]. Furthermore, it has been shown very recently that mice lacking both REC8 and RAD21L fail to assemble their AEs, revealing that these two meiosis-specific kleisins are essential for the assembly of AEs [15]. Notably, the phenotypes in female meiosis differ among these knockout mice. REC8-null neonatal ovaries are devoid of oocytes and ovarian follicles, indicating that REC8-depleted oocytes never proceed beyond prophase I [13]. In contrast, SMC1β-depleted oocytes are highly-error prone but proceed to metaphase II [10]. Surprisingly, it has been reported that RAD21L-deficient females are fertile but develop an age-dependent sterility [14]. The reason why these cohesin subunit-deficient female mice exhibit such different phenotypes is unknown and remains to be solved.

Homologous chromosome separation in anaphase I

Sister chromatid separation in mitosis is triggered by the activation of anaphase-promoting complex/cyclosome (APC/C) [16]. The activation of APC/C involves the association of its activator Cdc20. APC/C^{Cdc20} ubiquitinates its target proteins, Cyclin B and Securin, thereby inducing degradation of the molecules by proteasome. The degradation, in turn, brings about activation of Separase, which cleaves a kleisin subunit, RAD21[17, 18]. In meiosis I, homologous chromosomes rather than sister chromatids separate in anaphase. Thus, in the early studies using *Xenopus* oocytes, the mechanism governing cell cycle progression to anaphase was thought to be different between mitosis and meiosis [19, 20]. However, in later studies using mouse oocytes, it has been strongly argued that the pathway from APC/C^{Cdc20}-dependent degradation of target proteins to activation of Separase is also utilized for homologous chromosome separation in meiosis I [21–23]. Microinjection of anti-REC8 antibody, which prevents REC8 from dissociating from chromosomes, into oocytes at the germinal vesicle stage (GV) and metaphase II stage inhibits homologous chromosome separation and sister chromatid separation, respectively [24]. Furthermore, metaphase I-arrested oocytes from mice carrying REC8 that can be cleaved artificially by TEV protease (*$REC8^{TEV/TEV}$*) undergo disjunction of both homologous chromosomes and sister chromatids upon exposure to TEV protease, although *$RAD21^{TEV/TEV}$* oocytes are not affected by TEV protease, demonstrating that cohesin containing REC8 but not RAD21 is responsible for maintaining sister chromatid cohesion at both centromeres and arm regions in meiosis [25]. From these studies, it seems reasonable to conclude that meiotic cohesin containing REC8 maintains sister chromatid cohesion until metaphase I and that the Separase-dependent cleavage of arm REC8 at anaphase I and centromeric REC8 at anaphase II leads to homologous chromosome separation and sister chromatid separation, respectively (Fig. 1A).

Protection of centromeric cohesion in meiosis I

When homologous chromosomes separate in anaphase I, sister chromatid cohesion must be maintained at centromere regions to ensure sister chromatid separation in meiosis II. In yeast and *Drosophila*, a family of protein called Shugoshin [26] or MEI-S332 [27], is essential for the protection of centromeric cohesion. In mammals, two Shugoshin isoforms, Sgo1 and Sgo2, protect centromeric cohesin from Separase-independent cohesin removal during prophase in somatic cells [28, 29]. But, it was unknown whether either one or both of Sgos is responsible for the protection of centromeric cohesion from Separase-dependent cleavage in meiosis. Both Sgo1 and Sgo2 are localized at centromeres in mouse oocytes. Using RNAi methods in mouse oocytes, it has been proved that Sgo2, but not Sgo1, plays an essential role in protection of centromeric cohesion in meiosis I [30]. In yeast, phosphorylation of REC8 by casein kinase 1δ/ε is prerequisite for its cleavage by separase, and Shugoshin (Sgo1)-protein phosphatase 2A (PP2A) counteracts its action at centromeres in meiosis I [31, 32]. In mammals, Sgo2 is also responsible for centromeric localization of protein phosphatase 2A. Thus, it is very likely that mammalian Sgo2 recruits protein phosphatase 2A to centromeres, which may prevent separase from cleaving REC8 through its dephosphorylation in meiosis I. Importantly, in both mitosis and meiosis II, protection of centromeric cohesion is prerequisite for faithful chromosome segregation until metaphase but is harmful at anaphase onset. To explain the contradictory nature of centromeric cohesion, it is proposed that tension-dependent relocalization of shugoshin from the inner centromere to the outer kinetochores makes Shugoshin inert by anaphase onset in both mitosis and meiosis II [30] (Fig. 1C).

Condensin

Condensin is a multi-subunit protein complex that plays primary roles in chromosome assembly and segregation in eukaryotes [33]. It is thought that condensin promotes chromosome compaction by linking two distant segments of a single chromatid in contrast to cohesin holding two sister chromatids (Fig. 1B). There are two types of condensins, namely condensin I and condensin II, among eukaryotes. In HeLa cells, the two condensin complexes are differentially regulated during the cell cycle: condensin I is in the cytoplasm, whereas condensin II is in the nucleus in interphase [34]. As chromatin condenses to make chromosomes in prophase, condensin II becomes concentrated to the axes of chromosomes. Only after nuclear envelope breakdown (NEBD), condensin I becomes accessible to the mitotic chromosomes. Thus, it is believed that condensin II initiates the first step of chromosome assembly in prophase and that condensin I then participates in the second step in collaboration with condensin II after NEBD.

Construction of bivalent chromosomes from prophase I to metaphase I

Compared with the mitotic roles of condensins, little is known about their meiotic roles, especially in mammals. So far, there are only a few reports for condensin in mammalian meiosis. The first

report concerning localization of condensin I in mouse spermatocytes showed that condensin I was mainly localized around telomere regions with a faint staining along chromatid axes [35]. The second one showed only the expression of some subunits of condensin I and condensin II by western blotting in pig oocytes [36]. The most recent study was performed to gain a comprehensive view of the expression, localization and potential functions of condensin I and condensin II in mouse oocytes [37]. In fully-grown GV oocytes, condensin I is present in the cytoplasm, while condensin II is localized in the nucleus. Notably, at metaphase I, condensin II becomes localized along chromatid axes of bivalent chromosomes, while condensin I is concentrated around centromeres and is not stably associated with chromosome arms. Thus, the dynamics of condensins are different between mitosis and meiosis I (Fig. 1A). What causes this difference? In contrast to mitosis, in which most cohesin is removed from chromosome arms in prophase, a substantial amount of cohesin remains associated with chromosome arms until metaphase to keep homologous chromosomes linked in meiosis I. The occupancy of cohesin along arms might interfere with loading and/or stable association of condensin I (Fig. 1B). From another point of view, cohesin along arms might give the solidity to bivalent chromosomes in place of condensin I until metaphase I. In this sense, it is noteworthy that condensin I becomes detectable along chromosome arms at the same time as the majority of cohesin is removed from them in anaphase I. The stable association of condensin I after anaphase I is likely to reinforce their rigidity, as proposed for chromosome segregation in mitotic anaphase [38]. It is proposed from the microinjection of antibodies against condensin subunits into mouse oocytes that condensins may play multiple roles in meiotic chromosome dynamics including chromosome individualization, sister chromatid resolution (chromatid axis formation), chromosome separation, and monopolar attachment of sister kinetochores.

Monopolar attachment of sister kinetochores

Injection of an antibody against condensin subunits causes severe defects in kinetochore direction in meiosis I even when the antibody is injected into mouse oocytes arrested at metaphase I, suggesting that condensin may contribute to both establishment and maintenance of monopolar attachment of sister kinetochores in mouse oocytes [37]. How might condensins contribute to the process? The distance between sister kinetochores was not affected by the antibody injection, thus excluding the possibility that condensins might be involved in the process linking sister kinetochores. It is proposed that condensins contribute to assembling a specialized structure of centromeric chromatin that helps the juxtaposed sister kinetochores be directed and connected to the same spindle pole. Since condensin I is enriched around centromeres at metaphase I, it is suggested that condensin I may have a specific contribution to monopolar attachment of sister kinetochores. Interestingly, it has been reported that condensin I is physically and functionally associated with some of the subunits of monopolin complex which is responsible for monopolar attachment of sister kinetochores in budding yeast meiosis [39–41]. Therefore, condensin I might help construct a centromeric platform that ensures that two sister kinetochores behave as if they were a single one.

Potential role(s) in meiotic prophase I

It has been reported in budding yeast that condensin I has multiple roles in meiotic events, such as chromosome compaction, SC assembly, homologous pairing, processing of double strand breaks and resolution of recombination-dependent chromosome links [42]. Furthermore, a recent study in *C. elegans* revealed that the establishment of a higher-order chromosome structure by condensin I regulates crossover number and distribution [43]. So far, there is no report concerning possible functions of condensins in pairing and recombination of homologous chromosome in mammals.

Conclusions

Recent studies reveal that meiosis-specific cohesins as well as the centromeric protector shugoshin contribute to the unique chromosome segregation in meiosis I, in which homologous chromosomes segregate with sister chromatids kept attached. But how meiosis-specific cohesin subunits fulfill their special roles in meiosis, such as AE formation, synapsis and recombination between homologous chromosomes, remains to be solved at a mechanistic level. Condensins I and II play crucial roles in construction and segregation of meiotic chromosomes, but their individual functions remain elusive. Recent studies show that cohesin, condensin and their relatives are involved in a wide variety of chromosomal functions and their regulation, such as genomic imprinting, dosage compensation, and human congenital disorders [33, 44]. It is fascinating to investigate unidentified roles of cohesin and condensin during gametogenesis and early embryonic development in mammals.

Acknowledgments

I would like to thank all the collaborators contributing to the works deserving an SRD Young Investigator Award. I am very grateful to Dr T Miyano for being a reference for the award and for his critical reading of the manuscript. This study was supported by Grant-in-Aids for Young Scientists (A) (23688036) to JL.

References

1. **Peters JM, Tedeschi A, Schmitz J.** The cohesin complex and its roles in chromosome biology. *Genes Dev* 2008; **22**: 3089–3114. [Medline]
2. **Revenkova E, Eijpe M, Heyting C, Gross B, Jessberger R.** Novel meiosis-specific isoform of mammalian SMC1. *Mol Cell Biol* 2001; **21**: 6984–6998. [Medline]
3. **Prieto I, Suja JA, Pezzi N, Kremer L, Martinez AC, Rufas JS, Barbero JL.** Mammalian STAG3 is a cohesin specific to sister chromatid arms in meiosis I. *Nat Cell Biol* 2001; **3**: 761–766. [Medline]
4. **Lee J, Iwai T, Yokota T, Yamashita M.** Temporally and spatially selective loss of Rec8 protein from meiotic chromosomes during mammalian meiosis. *J Cell Sci* 2003; **116**: 2781–2790. [Medline]
5. **Lee J, Hirano T.** RAD21L, a novel cohesin subunit implicated in linking homologous chromosomes in mammalian meiosis. *J Cell Biol* 2011; **192**: 263–276. [Medline]
6. **Ishiguro K, Kim J, Fujiyama-Nakamura S, Kato S, Watanabe Y.** A new meiosis-specific cohesin complex implicated in the cohesin code for homologous pairing. *EMBO Rep* 2011; **12**: 267–275. [Medline]
7. **Page SL, Hawley RS.** The genetics and molecular biology of the synaptonemal complex. *Annu Rev Cell Dev Biol* 2004; **20**: 525–558. [Medline]
8. **Firooznia A, Revenkova E, Jessberger R.** From the XXVII North American Testis Workshop: the function of SMC and other cohesin proteins in meiosis. *J Androl* 2005; **26**: 1–10. [Medline]
9. **Suja JA, Barbero JL.** Cohesin complexes and sister chromatid cohesion in mammalian

meiosis. *Genome Dyn* 2009; **5**: 94–116. [Medline]

10. **Revenkova E, Eijpe M, Heyting C, Hodges CA, Hunt PA, Liebe B, Scherthan H, Jessberger R.** Cohesin SMC1 beta is required for meiotic chromosome dynamics, sister chromatid cohesion and DNA recombination. *Nat Cell Biol* 2004; **6**: 555–562. [Medline]
11. **Novak I, Wang H, Revenkova E, Jessberger R, Scherthan H, Hoog C.** Cohesin Smc-1beta determines meiotic chromatin axis loop organization. *J Cell Biol* 2008; **180**: 83–90. [Medline]
12. **Bannister LA, Reinholdt LG, Munroe RJ, Schimenti JC.** Positional cloning and characterization of mouse mei8, a disrupted allelle of the meiotic cohesin Rec8. *Genesis* 2004; **40**: 184–194. [Medline]
13. **Xu H, Beasley MD, Warren WD, van der Horst GT, McKay MJ.** Absence of mouse REC8 cohesin promotes synapsis of sister chromatids in meiosis. *Dev Cell* 2005; **8**: 949–961. [Medline]
14. **Herrán Y, Gutierrez-Caballero C, Sanchez-Martin M, Hernandez T, Viera A, Barbero JL, de Alava E, de Rooij DG, Suja JA, Llano E, Pendas AM.** The cohesin subunit RAD21L functions in meiotic synapsis and exhibits sexual dimorphism in fertility. *EMBO J* 2011; **30**: 3091–3105. [Medline]
15. **Llano E, Herran Y, Garcia-Tunon I, Gutierrez-Caballero C, de Alava E, Barbero JL, Schimenti J, de Rooij DG, Sanchez-Martin M, Pendas AM.** Meiotic cohesin complexes are essential for the formation of the axial element in mice. *J Cell Biol* 2012; **197**: 877–885. [Medline]
16. **Nasmyth K.** How do so few control so many? *Cell* 2005; **120**: 739–746. [Medline]
17. **Uhlmann F, Wernic D, Poupart MA, Koonin EV, Nasmyth K.** Cleavage of cohesin by the CD clan protease separin triggers anaphase in yeast. *Cell* 2000; **103**: 375–386. [Medline]
18. **Hauf S, Waizenegger IC, Peters JM.** Cohesin cleavage by separase required for anaphase and cytokinesis in human cells. *Science* 2001; **293**: 1320–1323. [Medline]
19. **Taieb FE, Gross SD, Lewellyn AL, Maller JL.** Activation of the anaphase-promoting complex and degradation of cyclin B is not required for progression from Meiosis I to II in *Xenopus* oocytes. *Curr Biol* 2001; **11**: 508–513. [Medline]
20. **Peter M, Castro A, Lorca T, Le Peuch C, Magnaghi-Jaulin L, Doree M, Labbe JC.** The APC is dispensable for first meiotic anaphase in *Xenopus* oocytes. *Nat Cell Biol* 2001; **3**: 83–87. [Medline]
21. **Amanai M, Shoji S, Yoshida N, Brahmajosyula M, Perry AC.** Injection of mammalian metaphase II oocytes with short interfering RNAs to dissect meiotic and early mitotic events. *Biol Reprod* 2006; **75**: 891–898. [Medline]
22. **Kudo NR, Wassmann K, Anger M, Schuh M, Wirth KG, Xu H, Helmhart W, Kudo H, McKay M, Maro B, Ellenberg J, de Boer P, Nasmyth K.** Resolution of chiasmata in oocytes requires separase-mediated proteolysis. *Cell* 2006; **126**: 135–146. [Medline]
23. **Terret ME, Wassmann K, Waizenegger I, Maro B, Peters JM, Verlhac MH.** The meiosis I-to-meiosis II transition in mouse oocytes requires separase activity. *Curr Biol* 2003; **13**: 1797–1802. [Medline]
24. **Lee J, Okada K, Ogushi S, Miyano T, Miyake M, Yamashita M.** Loss of Rec8 from chromosome arm and centromere region is required for homologous chromosome separation and sister chromatid separation, respectively, in mammalian meiosis. *Cell Cycle* 2006; **5**: 1448–1455. [Medline]
25. **Tachibana-Konwalski K, Godwin J, van der Weyden L, Champion L, Kudo NR, Adams DJ, Nasmyth K.** Rec8-containing cohesin maintains bivalents without turnover during the growing phase of mouse oocytes. *Genes Dev* 2010; **24**: 2505–2516. [Medline]
26. **Kitajima TS, Kawashima SA, Watanabe Y.** The conserved kinetochore protein shugoshin protects centromeric cohesion during meiosis. *Nature* 2004; **427**: 510–517. [Medline]
27. **Kerrebrock AW, Moore DP, Wu JS, Orr-Weaver TL.** Mei-S332, a *Drosophila* protein required for sister-chromatid cohesion, can localize to meiotic centromere regions. *Cell* 1995; **83**: 247–256. [Medline]
28. **Kitajima TS, Sakuno T, Ishiguro K, Iemura S, Natsume T, Kawashima SA, Watanabe Y.** Shugoshin collaborates with protein phosphatase 2A to protect cohesin. *Nature* 2006; **441**: 46–52. [Medline]
29. **McGuinness BE, Hirota T, Kudo NR, Peters JM, Nasmyth K.** Shugoshin prevents dissociation of cohesin from centromeres during mitosis in vertebrate cells. *PLoS Biol* 2005; **3**: e86. [Medline]
30. **Lee J, Kitajima TS, Tanno Y, Yoshida K, Morita T, Miyano T, Miyake M, Watanabe Y.** Unified mode of centromeric protection by shugoshin in mammalian oocytes and somatic cells. *Nat Cell Biol* 2008; **10**: 42–52. [Medline]
31. **Katis VL, Lipp JJ, Imre R, Bogdanova A, Okaz E, Habermann B, Mechtler K, Nasmyth K, Zachariae W.** Rec8 phosphorylation by casein kinase 1 and Cdc7-Dbf4 kinase regulates cohesin cleavage by separase during meiosis. *Dev Cell* 2010; **18**: 397–409. [Medline]
32. **Ishiguro T, Tanaka K, Sakuno T, Watanabe Y.** Shugoshin-PP2A counteracts casein-kinase-1-dependent cleavage of Rec8 by separase. *Nat Cell Biol* 2010; **12**: 500–506. [Medline]
33. **Hirano T.** Condensins: universal organizers of chromosomes with diverse functions. *Genes Dev* 2012; **26**: 1659–1678. [Medline]
34. **Ono T, Losada A, Hirano M, Myers MP, Neuwald AF, Hirano T.** Differential contributions of condensin I and condensin II to mitotic chromosome architecture in vertebrate cells. *Cell* 2003; **115**: 109–121. [Medline]
35. **Viera A, Gomez R, Parra MT, Schmiesing JA, Yokomori K, Rufas JS, Suja JA.** Condensin I reveals new insights on mouse meiotic chromosome structure and dynamics. *PLoS One* 2007; **2**: e783. [Medline]
36. **Lisková L, Susor A, Pivonkova K, Saskova A, Karabinova P, Kubelka M.** Detection of condensin I and II in maturing pig oocytes. *Reprod Fertil Dev* 2010; **22**: 644–652. [Medline]
37. **Lee J, Ogushi S, Saitou M, Hirano T.** Condensins I and II are essential for construction of bivalent chromosomes in mouse oocytes. *Mol Biol Cell* 2011; **22**: 3465–3477. [Medline]
38. **Gerlich D, Hirota T, Koch B, Peters JM, Ellenberg J.** Condensin I stabilizes chromosomes mechanically through a dynamic interaction in live cells. *Curr Biol* 2006; **16**: 333–344. [Medline]
39. **Tóth A, Rabitsch KP, Galova M, Schleiffer A, Buonomo SB, Nasmyth K.** Functional genomics identifies monopolin: a kinetochore protein required for segregation of homologs during meiosis I. *Cell* 2000; **103**: 1155–1168. [Medline]
40. **Johzuka K, Horiuchi T.** The cis element and factors required for condensin recruitment to chromosomes. *Mol Cell* 2009; **34**: 26–35. [Medline]
41. **Brito IL, Yu HG, Amon A.** Condensins promote coorientation of sister chromatids during meiosis I in budding yeast. *Genetics* 2010; **185**: 55–64. [Medline]
42. **Yu HG, Koshland DE.** Meiotic condensin is required for proper chromosome compaction, SC assembly, and resolution of recombination-dependent chromosome linkages. *J Cell Biol* 2003; **163**: 937–947. [Medline]
43. **Mets DG, Meyer BJ.** Condensins regulate meiotic DNA break distribution, thus crossover frequency, by controlling chromosome structure. *Cell* 2009; **139**: 73–86. [Medline]
44. **Wood AJ, Severson AF, Meyer BJ.** Condensin and cohesin complexity: the expanding repertoire of functions. *Nat Rev Genet* 2010; **11**: 391–404. [Medline]