Trends in Genetics

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REVIEWS

Review

Diversity and Determinants of Meiotic Recombination Landscapes

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Despite the universal importance of meiotic recombination for generating genetic diversity, numbers and distribution of recombination events along chromosomes vary among species, genotypes within species, and between sexes. Some interspecies differences stem from the diversity of genome size and composition among eukaryotes. Large-genome species, such as humans and most crops, display recombination landscapes that are different from those of small-genome yeasts. Chromatin patterns, including histone modifications and DNA methylation, are also responsible for interspecies differences as well as differences between the sexes. Finally, despite the overall recombination pathway conservation, there are species-specific components that result in distinct recombination patterns. Consequently, characteristics that are defining for the recombination landscape and universally shared by all eukaryotes remain largely to be discovered.

Highlights

Meiotic recombination is initiated by double-strand break (DSB) formation in chromosomal DNA at a large number of sites in the genome; however, few DSBs, generally one to two per chromosome, result in the formation of crossovers.

Despite evolutionary conservation of recombination mechanisms, there are substantial differences in recombination landscapes among species as well as among genotypes and sexes within species.

Recombination landscapes often differ between male and female meioses with regard to the number of recombination events, their overall distribution along chromosomes, and fine-scale location relative to genes and chromatin features.

Meiotic recombination events occur in open chromatin regions but specific characteristics of chromatin at recombination sites vary among species.

Ability to modify recombination landscapes is of interest to breeding, as many crop species with large and complex genomes exhibit little recombination in large portions of their chromosomes.

Meiotic Recombination

Meiotic recombination is a major force in evolution and a facilitator of plant and animal breeding. However, despite the universal importance of recombination, recombination landscapes, measured by the number and distribution of recombination events in the genome, vary among species as well as among genotypes within species and between sexes. Recent studies have made major inroads into the understanding of the mechanistic bases behind recombination landscape variation. Some of the differences can be ascribed to the overall diversity of genome size and composition among eukaryotes. Proteins controlling the recombination pathway also exhibit interspecies differences, despite the overall conservation of meiotic recombination mechanisms among eukaryotes [1]. In this review, we explore observations on recombination landscape variation in plants, animals, and fungi, with a goal of identifying aspects that are shared as well as those that are divergent among species.

Meiotic recombination is initiated by the formation of double-strand breaks (DSBs) in chromosomal DNA (Figure 1). This process is accomplished by an evolutionarily conserved protein complex that includes the topoisomerase-like protein SPO11 [2]. The complex interacts with a number of accessory proteins, which may function in recruiting SPO11 to specific recombination sites and are not as widely conserved as SPO11. In most species studied, DNA overhangs created by resection of the ends of DSBs, which are present at a large number of genomic locations (Table 1, Key Table), are thought to guide homologous **chromosome pairing** (see Glossary) by invading double-stranded DNA in the search for sequence homology [3]. Subsequently, some DSBs are processed to form **crossovers (COs)**. There are two distinct CO types (Figure 1). Class I COs are formed by a meiosis-specific group of proteins called ZMM and are subject to **CO interference** [2]. Class II COs do not exhibit interference and are formed by another set of proteins that includes MUS81. Proteins involved in class II CO formation also

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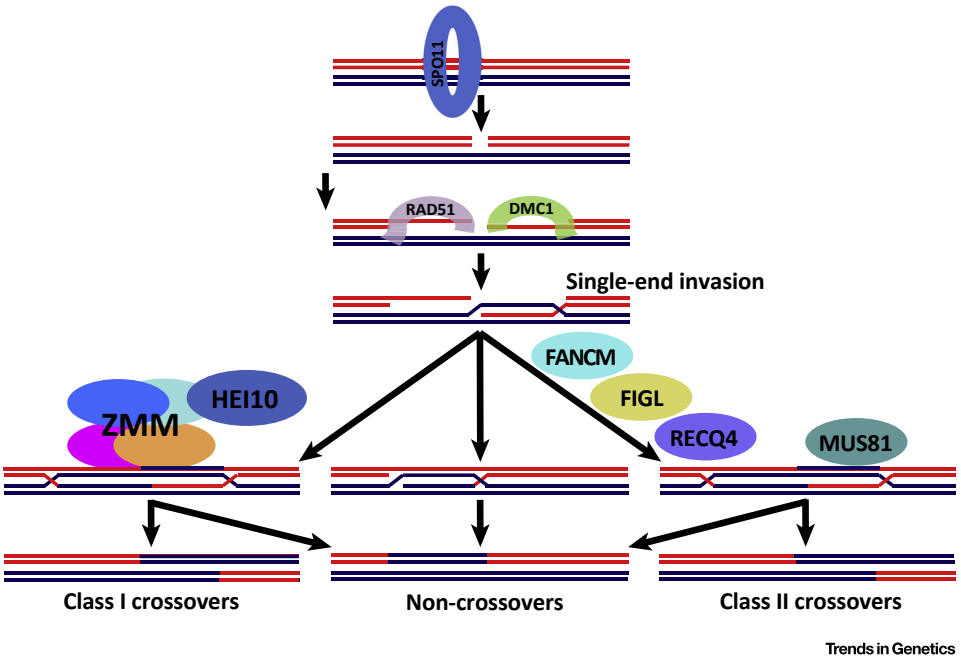

Figure 1. Simplified Diagram of the Meiotic Recombination Pathway. Only proteins mentioned in this review are depicted. For simplicity, only one chromatid for each chromosome is shown.

facilitate DNA repair via homologous recombination in somatic cells, suggesting that the class II CO pathway serves predominantly as an emergency repair system in meiotic recombination. Mutating genes encoding class II pathway proteins leads to higher CO numbers but may also result in genome instability, such as chromosome breakage [4]. DSBs that do not become CO sites are repaired as **non-COs**, some of which encompass **gene conversions**.

General Recombination Landscape Features and its Diversity among Species

In most species, relatively few DSBs result in COs and there are only one or two COs per **bivalent**. Most of these COs are class I, whereas the class II pathway is responsible for formation of only 5% to 20% of COs [5,6]. There are substantial differences among species in the fraction of DSBs repaired as COs and the number of COs per chromosome (Table 1). The highest CO frequencies are found in fission yeast, which exhibits on average 15 COs per chromosome pair [7]. These differences may stem from the diversity of meiotic mechanisms among species. For example, fission yeast only exhibits the interference-insensitive class II COs and lacks the MSH4 and MSH5 proteins, which other species utilize in the class I CO pathway [8]. *Caenorhabditis elegans* and females of *Drosophila melanogaster* have relatively few DSBs per meiosis and low DSB/CO ratios (Table 1) [9,10]. In these species, DSBs are formed after **homologous chromosomes** pair and chromosome pairing proceeds through largely recombination-independent mechanisms that rely on interactions among specific chromosome sites called pairing centers [11,12].

Recombination events are not randomly distributed across the genome but tend to form distinct hotspots. Some species, including *Drosophila* females and *C. elegans*, likely lack **recombination hotspots** [13,14] but it is not clear which specific recombination mechanisms

Glossary

Allopolyploid: organism containing more than two sets of chromosomes as a result of interspecific hybridization as a part of polyploidization.
Autopolyploid: organism containing multiple sets of chromosomes from within the same species.
Bivalent: pair of homologous chromosomes formed during meiosis.
Chromatin immunoprecipitation (ChIP): technique to identify genome sites occupied by specific proteins. Chromatin is fragmented and fragments bound by a protein of interest are purified using an antibody raised against the protein. The purified fragments can then be sequenced or identified using PCR.
Chromosome pairing: process of juxtaposition of homologous chromosomes during the prophase of meiosis. In most species studied (except *C. elegans* and females of *Drosophila*), homologous chromosome pairing follows the initiation of meiotic recombination and is dependent on recombination progression.
CO interference: mechanism preventing formation of two COs in close proximity to each other.
Crossover (CO): reciprocal exchange of large chromosome segments between chromatids of homologous chromosomes.
Cytosine methylation: type of DNA methylation common in animals and plants. In plants, DNA can be methylated at CG, CHG, and CHH sites (where H is any nucleotide other than cytosine). Only CG methylation is found in animal cells.
Disomic inheritance: meiotic behavior typical for diploid (i.e., non-polyploid) organisms.
Gene conversion: non-CO region encompassing a DNA sequence polymorphism between the parental chromosomes in which the original sequence has been replaced by the sequence of the other parental chromosome.
Histone methylation: type of chromatin modification found and animals, fungi, and plants and thought to control chromatin and gene functioning. Tri-methylation of lysine residues in the H3 histone at positions 4 (H3K4me3) and 36

in these species could be responsible for this absence. Both DSBs and COs are known to form hotspots. Genome-wide CO hotspot patterns have been elucidated in several species of plants, animals, and fungi (Figure 2). In contrast, DSB hotspots have only been studied in a handful of species [15–20]. CO hotspot distribution does not always mirror DSB hotspot distribution. This trend is particularly obvious in species with large and complex genomes, including mammals and plants (Figure 2). Whereas COs tend to be in or in the vicinity of genes, DSBs are frequently found outside of gene regions. In maize, nearly three-quarters of meiotic DSBs are in repetitive DNA, predominantly in *Gypsy*-class retrotransposons [19]. DSB formation in transposons was also found in *Arabidopsis*, whose genome contains several-fold less repetitive DNA than that of the maize genome. In *Arabidopsis*, however, DNA transposons of the Helitron, *mariner*, MuDR, *pogo*, and Tc1 families are the primary targets of DSB formation in repetitive genome regions [20]. In budding yeast, meiotic DSBs are detected in Ty class retrotransposons [21]. In general, however, DSBs present in repetitive DNA rarely lead to CO formation.

Chromosomal Mechanisms Limiting CO Number and Location

The high DSB/CO ratio observed in most species (Table 1) points to the existence of mechanisms limiting CO number. One such mechanism is CO interference, which affects both CO number and distribution [21]. However, even with interference, the number of COs per chromosome could be potentially higher, as evidenced by experiments showing recombination increases in *Arabidopsis* as a result of overexpression of the *HEI10* gene promoting class I CO formation [22]. It is generally assumed that increasing recombination frequency would be evolutionarily beneficial by bringing more genetic diversity [23]. Absence of recombination causes accumulation of detrimental alleles, which, in the extreme, is hypothesized to lead to mutational meltdown [24]. Thus, the CO number could represent a balance between fitness-driven benefits of recombination and genome stability [4,23]. Despite its plausibility, this hypothesis is contradicted by the lack of genome instability observed in mutants with moderately increased recombination frequencies [4,22]. Moreover, a population's ability to purge detrimental alleles depends on, in addition to recombination frequency, the effective population size (N_e), which varies widely among species, and even between different genome locations within species [25] in ways not similar to the variation of the recombination frequency. This evidence suggests that other factors, for example, those related to intrinsic features of the recombination pathway or population's adaptation to local conditions, limit recombination frequency [23].

In addition to the CO number limitations, there are limits to CO position, manifested by regions universally devoid of COs. In all species examined, COs are absent from centromeres, which are defined as chromosome regions known to be the sites of microtubule attachment during cell division. In large-genome species of animals and plants, such as maize and barley, fairly extensive chromosome stretches around centromeres, called pericentromeric regions, also exhibit limited COs (Figure 2). CO suppression in the middle parts of chromosomes is observed in some cases also in plant and animal chromosomes with off-center centromeres, including telocentric chromosomes [26]. Hence, the CO suppression pattern in maize, barley, and other large-genome species, may be caused by extensive chromosome length rather than centromere presence.

The molecular bases behind pericentromeric CO suppression may vary among species. In budding yeast, COs at the centromere are prevented by a kinetochore protein complex Ctf19, which blocks DSB formation [27]. This complex is conserved in eukaryotes and similar mechanisms may operate in other species, such as mouse, humans, and *Arabidopsis*, which also lack DSBs in centromeric regions. However, the mechanism in maize and barley must be

(H3K36me3) is frequently found in active chromatin and promoters of highly expressed genes. In contrast, di-methylation of lysine 9 in the H3 histone (H3K9me2) is associated with transcriptionally silenced chromatin.

Homoeologous chromosomes: pair of chromosomes that are similar but not identical and are present in an organism as a result of hybridization between closely related species.

Homologous chromosomes: pair of chromosomes in which each chromosome comes from a different parent.

Hypomorphic allele: mutant allele with a reduced function.

Multivalent: group of more than two chromosomes, homologous, homoeologous, or non-homologous, found during meiosis.

Non-CO: type of DNA repair in which the DSB is patched-up either through DNA synthesis or unwinding of CO intermediates by a helicase.

Polyploidization: process of whole-genome duplication or other levels of multiplication leading to formation of a polyploid organism.

Recombination hotspot: chromosome segments a few kb in length showing elevated (generally fivefold higher than the genome-wide average) recombination rates.

Key Table

Table 1. Comparison of the Main Features of Recombination Hotspots in Selected Species Frequently Used in Studies on Meiotic Recombination

Species	Genome size	Chromosome no.	Average DSB no.	Average CO no.	Most common DSB location	Most common CO location	DNA sequence motifs	Recombination sites are associated with			Refs
								H3K4me3	Nucleosome depletion	Reduced DNA methylation	
Saccharomyces cerevisiae (budding yeast)	12.1 Mb	16	175	90	Gene promoters	Gene promoters	None	Yes	Yes	n/a[a]	[16,48,80]
Schizosaccharomyces pombe (fission yeast)	13.8 Mb	3	60	36	All genome regions	All genome regions	None	No	No	n/a[a]	[7,18]
Drosophila melanogaster[b]	123 Mb	4	23	5.5	n/a	Genes	Many diverse motifs	Not known	Yes	Not known	[8,45]
Arabidopsis thaliana	135 Mb	5	300 (male)	10 (male) 6 (female)	Gene promoters and terminators	Genes	DSB/CO CO CO	No (DSBs) Yes (COs)	Yes	Yes	[20,44,46]
Zea mays (maize)	2.4 Gb	10	500	18	All genome regions	Genes	DSB CO	No (DSBs) Yes (COs)	Yes	Yes	[19,43]
Mus musculus (laboratory mouse)	2,8 Gb	20	250	23 (male) 27 (female)	Intergenic	Intergenic	Different PRDM9 alleles bind different DNA motifs, e.g.,	Yes	Yes	Yes	[17,35]
Homo sapiens (human)	3.3 Gb	23	150 (male) 350 (female)	50 (male) 70 (female)	Intergenic	Intergenic	Different PRDM9 alleles bind different DNA motifs, e.g.,	Yes	Yes	No (at local scale)	[15,31,32,49]

[a]There is no significant level of cytosine methylation in budding and fission yeasts.
[b]*Drosophila* males and chromosome 4 in females are not known to undergo recombination. DSB patterns have not been studied in this species.

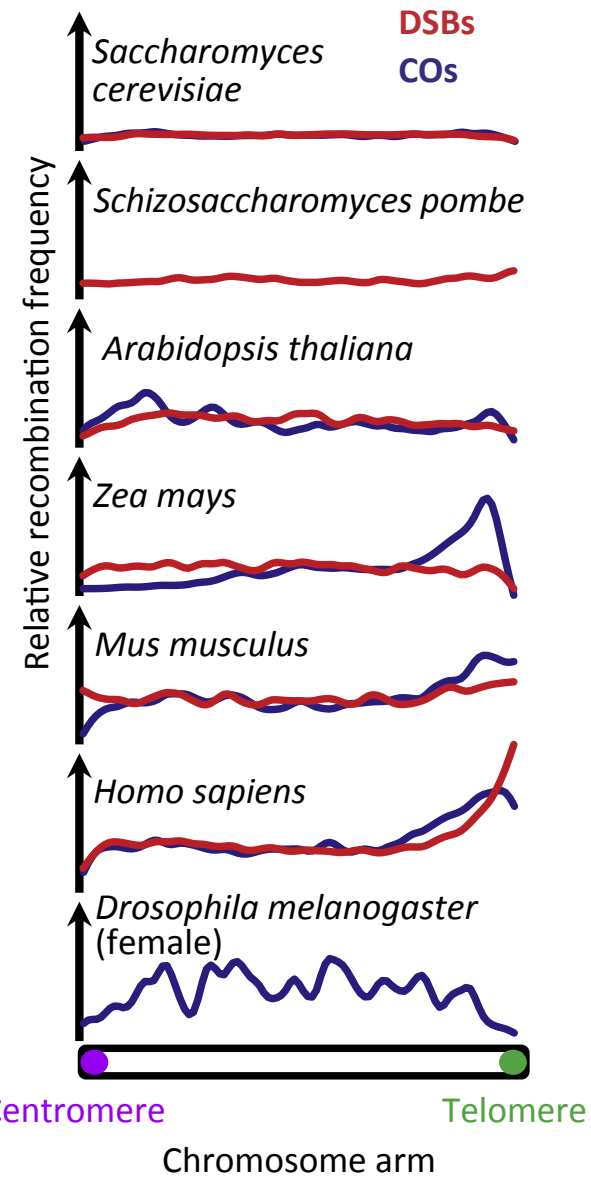

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Figure 2. Comparison of Distribution Patterns of Double-Strand Breaks (DSBs) and Crossovers (COs) along Chromosomes in Selected Species Frequently Used in Recombination Research. The species included are budding yeast [16,86], fission yeast [18], Arabidopsis [20,48], maize [19,47], mouse [17,87], human [15,88], and *Drosophila* females [89]. There is no published DSB landscape for *Drosophila melanogaster* or genome-wide CO landscape for *Schizosaccharomyces pombe*. DSB and CO patterns for each species are averages for all chromosomes (except for sex chromosomes in mouse, humans, and *Drosophila*, in which only very small chromosome segments engage in CO formation, and chromosome 4 of *Drosophila*, which lacks COs altogether). Only long chromosome arms are depicted, as short arms exhibit extreme size variation among the seven species analyzed. Chromosome arms were divided into the same number of bins in each species and average numbers of DSBs and COs were calculated for each bin. X-axes represent bins ordered from centromere (left) to telomere (right). Y-axes depict normalized numbers of DSBs and COs in each X-axis bin.

different, as these species do show DSBs in pericentromeric regions despite the lack of COs [19,28]. It is proposed that the basis of the phenomenon in barley is earlier DNA replication and DSB formation in distal chromosome regions compared with pericentromeric regions [28]. The earlier appearance of DSBs in distal regions may lead to preferential placement of COs near chromosome ends, as earlier DSBs are thought to be more likely to result in COs [28,29]. The different recombination dynamics in distal versus centromeric chromosome regions may also be linked to the formation of the telomere bouquet, a cytological structure found in many species, including budding and fission yeasts, mouse, barley, and maize, which consists of telomeres of all chromosomes clustering on the nuclear envelope [30]. The bouquet forms in early meiotic prophase I, at the time when DSBs are being repaired and homologous chromosomes start pairing.

Proteins Shaping Recombination Patterns in Populations

A number of proteins are known to affect recombination landscapes in mutant studies but relatively few of them have been shown to cause recombination pattern variation in natural populations. The best studied example of the latter is PRDM9, which controls recombination hotspot recognition in many metazoans [31]. PRDM9 binds specific DNA sequence motifs through a polydactyl zinc finger domain, and catalyzes **histone methylation** at the H3K4 and H3K36 residues, creating an open-chromatin environment favorable for DSB formation [32]. The DNA-binding domain of PRDM9 is one of the fastest evolving protein domains in eukaryotes. In humans, there are hundreds of distinct *PRDM9* alleles recognizing degenerate C-rich motifs 13 to 39 bp in length, depending on the allele, which are located within recombination hotspots [33]. The various alleles have different frequencies. For example, the most widespread variant A exists in ~86% of Europeans and 50% of Africans [34]. Similar allelic diversity is present in mouse, in which 57 zinc finger domain variants of PRDM9 were found in an analysis of just 14 different inbred lines [35]. The allele-specific preference for distinct hotspots results in fine-scale differences of DSB and CO patterns among individuals, although the overall recombination patterns along chromosomes are similar. PRDM9-controlled variation is responsible for 40% of all CO distribution variation in humans [33]. The rapid evolution of PRDM9 is propelled by hotspot erosion because of gene conversions at the PRDM9 DNA sequence motifs. As a result, there is little similarity in hotspot location between humans and chimpanzees [36]. Interestingly, the main role of PRDM9 seems to be shifting recombination away from gene regulatory regions, rather than simply allowing recombination to take place. Mouse mutants lacking PRDM9 still recombine but recombination shifts predominantly to gene promoters and enhancers, where H3K4me3 presence is associated with gene transcription [37].

In species that lack PRDM9, including yeast and plants, as well as birds and dogs, most COs are formed in gene promoters, which exhibit an open-chromatin environment independently of recombination [19,20,38,39]. In these species, recombination hotspot locations are much more evolutionarily stable. Hotspots in budding yeast exhibit considerable overlap with those in *Saccharomyces paradoxus*, even though the two lineages are at least ten times more divergent than humans and chimpanzees [40].

Two other well-studied proteins, HEI10 and RNF212, affect recombination landscapes by influencing the decision of which recombination intermediates become COs. HEI10 is a meiotic E3 ubiquitin ligase mediating the final steps of CO formation [41,42]. HEI10 affects CO number rather than distribution and has been identified as a recombination controller in several species. In the *Arabidopsis* Col x Ler hybrid, genetically controlled differences in *HEI10* expression level account for ~57% of CO variation [41]. Overexpressing *HEI10* in *Arabidopsis* resulted in a twofold CO number increase, with the additional COs located in the already recombination-rich

chromosome regions. RNF212 is a SUMO ligase found in animals but absent from plants [41,42]. In mouse, HEI10 and RNF212 have antagonistic effects on CO formation [42]. In human population studies, allelic variation in *RNF212* was found to be responsible for 2%–4% of the overall CO frequency variation [43].

Some recombination regulators are found to act only in very specific situations. A set of meiotic genes identified in tetraploid *Arabidopsis arenosa* [44] is thought to reduce CO rates specifically in response to polyploidy (see Polyploidy section). These genes predominantly encode proteins involved in chromosome axis formation and synapsis, and may limit CO numbers by increasing CO interference [45].

In addition to the genes found to affect natural populations, there is a large number of others known to affect the CO landscape but only in experimental populations. For example, in *C. elegans*, *HSH5* and a *HEI10* homolog *ZHP3*, were found to affect CO patterns [46]. In *Arabidopsis*, dramatic increases in class II COs, up to eightfold, were achieved by mutating termed antirecombination genes, such as *FANCM*, *FIGL1*, and *RECQ4*, whose products work to disassemble CO intermediates to promote non-CO formation [4] (Figure 1).

DNA Sequence

A number of studies associate the location of recombination events with the presence of specific DNA sequences. Already mentioned are the sequence motifs recognized by PRDM9. Species that lack PRDM9, such as maize, *Arabidopsis*, or *Drosophila*, also exhibit DNA sequence motifs enriched at recombination sites (Table 1). However, it is generally not known how these sequence motifs function and their involvement in recombination may be indirect. In maize, a guanine/cytosine (G/C)-rich sequence motif (Table 1) was found in studies using **chromatin immunoprecipitation (ChIP)** with the DSB marker RAD51 [19]. The motif is present at ~20% of DSB hotspots but is much more frequent (~70%) at hotspots in genic regions, which are more likely to produce COs. A similar motif was identified at maize CO sites [19,47]. The latter also resembles a CO motif from *Arabidopsis* [19,48], suggesting that the two species may have similar hotspot recognition mechanisms. CO-associated sequence motifs are also found in species that lack recombination hotspots. In *Drosophila*, there is a large number of CO sequence motifs, which is suggested as the reason why this species lacks recombination hotspots [49]. Over 97% of COs possess at least one CO sequence motif, with the most abundant motif present at 43% of CO sites.

Chromatin

Recombination hotspots in all eukaryotes are characterized by local epigenetic conditions indicative of open chromatin [16,18–20,47,48,50]. In all species, except fission yeast, both DSBs and COs occur at nucleosome-depleted sites. Sliding away of nucleosomes is thought to be needed to allow access of recombination proteins to DNA [51]. Also in all species studied, recombination hotspots are to some degree associated with the presence of H3K4me3. H3K4me3 is one of the products of PRDM9 activity upon binding to its target sites [32,33]. As a result, DSB hotspots in mouse colocalize with H3K4me3 [17]. Recombination in budding yeast is also thought to require H3K4me3 and DSB hotspots in this species overlap H3K4me3 sites [52]. In plants, the relationship between H3K4me3 sites and recombination may be more tenuous than in yeast and mammals. In *Arabidopsis* and maize, COs tend to colocalize with H3K4me3 sites [47,50] but DSBs do not show a strong association with elevated H3K4me3 [19,20]. Studies in *Arabidopsis* show also a link between recombination and the presence of a histone variant H2A.Z, which is frequently found in gene promoters and is responsible for nucleosome mobility [50].

Reduced methylation of cytosine residues in DNA is another feature of recombination sites universally shared by all studied species except yeasts, which generally lack this type of DNA methylation. In humans, reduced **cytosine methylation**, compared with the genome average, positively correlates with recombination event presence at the global scale [53]. However, the link is weaker at the local scale [54]. Reduced cytosine methylation at CG and CHG sites is also found at DSB and CO sites in maize and *Arabidopsis* [19,20,47,50]. In *Arabidopsis*, global loss of CG and CHG methylation due to mutations of methyl-transferases *MET1* and *CMT3*, respectively, increased DSB and CO formation in heterochromatic regions around the centromere [20,22,55,56]. Similar observations were made in mouse DNA methylation mutant *dnmt3l*, which showed increased DSB formation in retrotransposons [57]. However, CO numbers in the *met1* mutant as well as the *Arabidopsis ddm1* mutant, which reduces DNA methylation at all types of sites, increased predominantly in the already euchromatic regions along chromosome arms [55,58–60]. These observations suggest a more complex relationship between DNA methylation and recombination. This relationship likely involves the effects of DNA methylation on the overall chromosome structure in addition to local effects at recombination sites. Studies in *Arabidopsis* indicate that the link between DNA methylation and heterochromatin formation through H3K9 di-methylation [61] is involved in the effect that DNA methylation exerts on recombination [62].

It is not clear how recombination machinery recognizes the epigenetic state of hotspot sites, and this mechanism may be species-specific. In budding yeast, the Spp1 protein detects H3K4me3 presence and induces DSB formation by interacting with the chromosome axis [63]. However, a mouse homolog of Ssp1 is not essential for recombination, suggesting that in mouse this mechanism may operate differently [64].

Sex-Specific Differences in the Recombination Landscape

Differences in recombination frequency between male and female meioses have long been known [65–67]. Interestingly, the sex that exhibits a higher frequency varies (Table 1), even among closely related species. For example, in a mouse subspecies *Mus musculus castaneus*, females experience higher CO numbers but in a sister subspecies *Mus musculus musculus*, males have more COs [67]. Major differences in CO distribution between the sexes have also been described in several species, including mouse, humans, and *Arabidopsis*. In these cases, the species with a higher CO number typically exhibits elevated CO rates in distal chromosome regions [65,68]. In addition to the global differences, there are differences at the local scale. The latter are also observed in species in which the overall CO numbers and global distribution patterns are similar in male and female, such as maize [47]. In humans, mouse, and maize, differences in recombination hotspot usage between male and female are found [47,68,69]. In humans and mouse, most hotspots are shared by the sexes, whereas in maize the shared fraction was found to be only ~15%. In addition, studies in maize uncovered differences in hotspot locations relative to transcription start sites and transcription termination sites for COs located in gene promoters and terminators, respectively [47]. There were also disparities in CO locations relative to H3K4me3 and nucleosome occupancy patterns. Studies in *Arabidopsis* indicate differences in CO location in male and female relative to the presence of transposons and protein-coding genes as well as the G/C content [65]. Little is known, however, about the mechanistic underpinnings of the CO landscape differences between sexes. A recent study found that in mouse the differences in CO landscape stem from differences in DSB distribution [69]. At the time of DSB formation, DNA is globally demethylated in female mouse meiocytes whereas it is not in the male, which results in profound differences in recombination hotspot usage.

Polyploidy

Polyploidization events characterize the evolutionary history of eukaryotes. Following polyploidization, the **disomic inheritance** pattern is disturbed by the formation of **multivalents**, resulting in recombination between **homoeologous chromosomes** and perhaps also non-homologous chromosomes. Non-homologous COs can lead to drastic chromosomal rearrangements [70], which in some species can occur for many years after polyploidization [71]. These chromosome rearrangements are not random but result from activity of the meiotic recombination program and appear to be affected by chromosome organization features [72].

Newly formed polyploids are found to exhibit more COs than their diploid progenitors in most genera studied [73,74]. However, data from *Arabidopsis* autotetraploids show that CO numbers can decrease even within a few generations of polyploidization [75]. Established **allopolyploids** tend to maintain a higher level of recombination compared with their diploid progenitors [74,76,77]. However, established **autopolyploids** may have lower recombination rates. For example, a natural accession of autotetraploid *A. arenosa* forms 1.09 COs per bivalent compared with the diploid's 1.36 COs per bivalent. A genome scan comparing autotetraploid *A. arenosa* to diploid, revealed the meiotic genes under selection that are likely to be responsible for these differences [44]. Although specific mechanisms are not known, chromatin features such as DNA methylation and histone modifications can be altered in newly formed polyploids and these changes can persist in established polyploids [78], potentially resulting in altered recombination patterns.

Chromosome Dynamics

Early stages of meiotic prophase I coinciding with meiotic recombination are also a period of extensive chromosome dynamics, including vigorous movements of chromosomes. There are also interactions among centromeres and telomeres, observed in several species, including budding and fission yeast, maize, *Arabidopsis*, and mouse [30,79]. Although the effect of chromosome dynamics on the recombination landscape has not been vigorously examined, several studies indicate that chromosome interactions in early prophase likely affect the distribution of COs along chromosomes. Disrupting the telomere bouquet can change CO distribution by lowering the strength of interference [80]. The *Ph1* locus in polyploid wheat has been proposed to inhibit synapsis between homoeologous chromosomes by controlling premeiotic centromere clustering [81]. The *Ph1* locus also works by preventing recombination intermediates formed between homoeologous chromosomes from becoming COs [82]. The synapsis- and CO-related functions are controlled by separate genetic elements located in the *Ph1* chromosome interval [83]. Finally, a study using a **hypomorphic allele** of *SPO11* showed that lowering the DSB number increased CO rates in pericentromeric regions of *Arabidopsis* chromosomes, and hypothesized a role of centromere dynamics in this phenomenon [84].

Evolutionary Consequences of Recombination Landscapes

Recombination landscapes have profound evolutionary consequences. Specific patterns of CO distribution modulate the influence of recombination on genetic diversity. Recombination enables beneficial alleles at different loci on the same chromosome to be brought together and prevents a phenomenon known as the Hill-Robertson effect, in which a beneficial allele is coupled with a detrimental allele at a linked locus [23,85]. Heterogeneity of recombination rates along chromosomes affects the efficiency of this phenomenon. Hence, recombination landscape patterns affect the evolution of populations and genomes [26].

Intraspecies differences in recombination landscapes between male and female meioses also have interesting evolutionary consequences, as different patterns of genetic diversity are created in male versus female meioses. This phenomenon should be particularly influential

in species in which males and females produce different number of offspring and/or differ in geographical extent of gamete dispersal [47].

Concluding Remarks and Future Perspectives

The core recombination pathway components exhibit remarkable conservation among species but recombination landscapes exhibit noticeable interspecies diversity. This diversity includes differences in the number of DSBs and COs as well as their distribution. The existence of these differences poses the question of whether there are universal rules shaping recombination landscapes. DSBs as well as COs tend to be located at chromosomal sites that exhibit open chromatin characteristics. However, the only features consistently found at recombination sites in all species studied so far are reduced nucleosome occupancy at DSB and CO sites and the tendency of H3K4me3 to be present at CO sites. Such characteristics are by no means exclusive to recombination sites. Hence, additional defining features of recombination sites may lie in chromatin characteristics that have not yet been defined. Detailed studies of 3D chromatin conformation may be a fruitful avenue to discover them. It is also possible that what constitutes open chromatin depends on specific aspects of genome composition and organization in each species. Proteins linking chromatin state to the recombination machinery may be less conserved than core recombination components because they interact with genome-specific chromatin organization patterns. Studies of these proteins will allow better understanding of the aspects of hotspot recognition that are shared among species (see Outstanding Questions).

Outstanding Questions

The current knowledge of meiotic recombination mechanisms comes from studies on a handful of species. Is there an even greater diversity of recombination landscapes in species that have not been subjects of detailed studies?

Why is the crossover number per chromosome limited in most species?

What evolutionary forces create the diversity of recombination numbers and distribution patterns?

A number of genes are known to control the crossover number. Which genes limit the number of DSBs?

How and why does the DSB/CO ratio differ in different genomic locations?

Are there common chromatin features associated with recombination event locations in all eukaryotes?

How is the chromatin state recognized by the recombination machinery?

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