Review

About PAR: The distinct evolutionary dynamics of the pseudoautosomal region

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Sex chromosomes differ from other chromosomes in the striking divergence they often show in size, structure, and gene content. Not only do they possess genes controlling sex determination that are restricted to either the X or Y (or Z or W) chromosomes, but in many taxa they also include recombining regions. In these 'pseudoautosomal regions' (PARs), sequence homology is maintained by meiotic pairing and exchange in the heterogametic sex. PARs are unique genomic regions, exhibiting some features of autosomes, but they are also influenced by their partial sex linkage. Here we review the distribution and structure of PARs among animals and plants, the theoretical predictions concerning their evolutionary dynamics, the reasons for their persistence, and the diversity and content of genes that reside within them. It is now clear that the evolution of the PAR differs in important ways from that of genes in either the non-recombining regions of sex chromosomes or the autosomes.

Evolution and structure of sex chromosomes

In organisms with genetic sex determination, the chromosomes on which the sex-determining loci reside often display distinctive features, including striking divergence in size, structure and gene content between the homologs. Suppressed recombination between the X and Y chromosomes (or Z and W) appears to mediate this divergence, which probably initiates around the sex-determining region (SDR; Glossary) and expands in a stepwise fashion to include larger segments of each sex chromosome (Figure 1). Without recombination, the sex chromosomes are free to diverge from one another over time, leaving few if any traces of their homologous origins. Deleterious mutations

Glossary

Achiasmate: meiosis that does not involve recombination between a pair of chromosomes (lacking chiasmata).
Dioecious: a sexual system where male and female reproductive functions occur in different individuals.
Hermaphroditism: a sexual system where male and female functions occur in the same individual.
Heterogametic sex: the sex that is heterozygous at the sex-determining region (males in XY species; females in ZW species)
Identity disequilibrium: a genetic association whereby individuals that are heterozygous at one locus are more likely to be heterozygous at another locus than would be expected from the allele frequencies, with the same holding for homozygotes.
Inbreeding depression: a reduction in fitness of inbred individuals – individuals whose parents are more related than a comparison group. The opposite of outbreeding depression.
Meiotic drive: a bias whereby one allele is more likely to be inherited than the alternative allele among the offspring of a heterozygous individual.
Outbreeding depression: a reduction in fitness in outbred individuals – individuals whose parents are less related than a comparison group. The opposite of inbreeding depression.
Overdominance: a form of selection where heterozygotes have higher fitness than homozygotes.
Pseudoautosomal region (PAR): the region of the genome partially linked to the site(s) at which sex is determined genetically; recombination in the PAR maintains homology between the sex chromosomes in the heterogametic sex.
Sex-determining region (SDR): the region of the genome completely linked to the site(s) at which sex is determined genetically.
Sex-ratio distorter gene: a gene that controls the degree of meiotic drive of the X versus Y (W versus Z). A stable polymorphism could occur at such genes, where one allele drives the X more than the alternative allele and becomes associated with the X.
Sex-specific selection: a form of selection where the fitness of a genotype differs between males and females. Sex-specific selection includes not only sexually antagonistic selection but also cases where selection acts in the same direction in males and females.
Sexual dimorphism: a difference in phenotype between males and females.
Sexually antagonistic selection: selection that acts in opposite directions in males and females, favoring different alleles.
Strata: different regions of the sex chromosomes that were subsumed into the non-recombining SDR at different times in the past; homologous sequences on the X and Y show different levels of divergence depending on the age of their strata.

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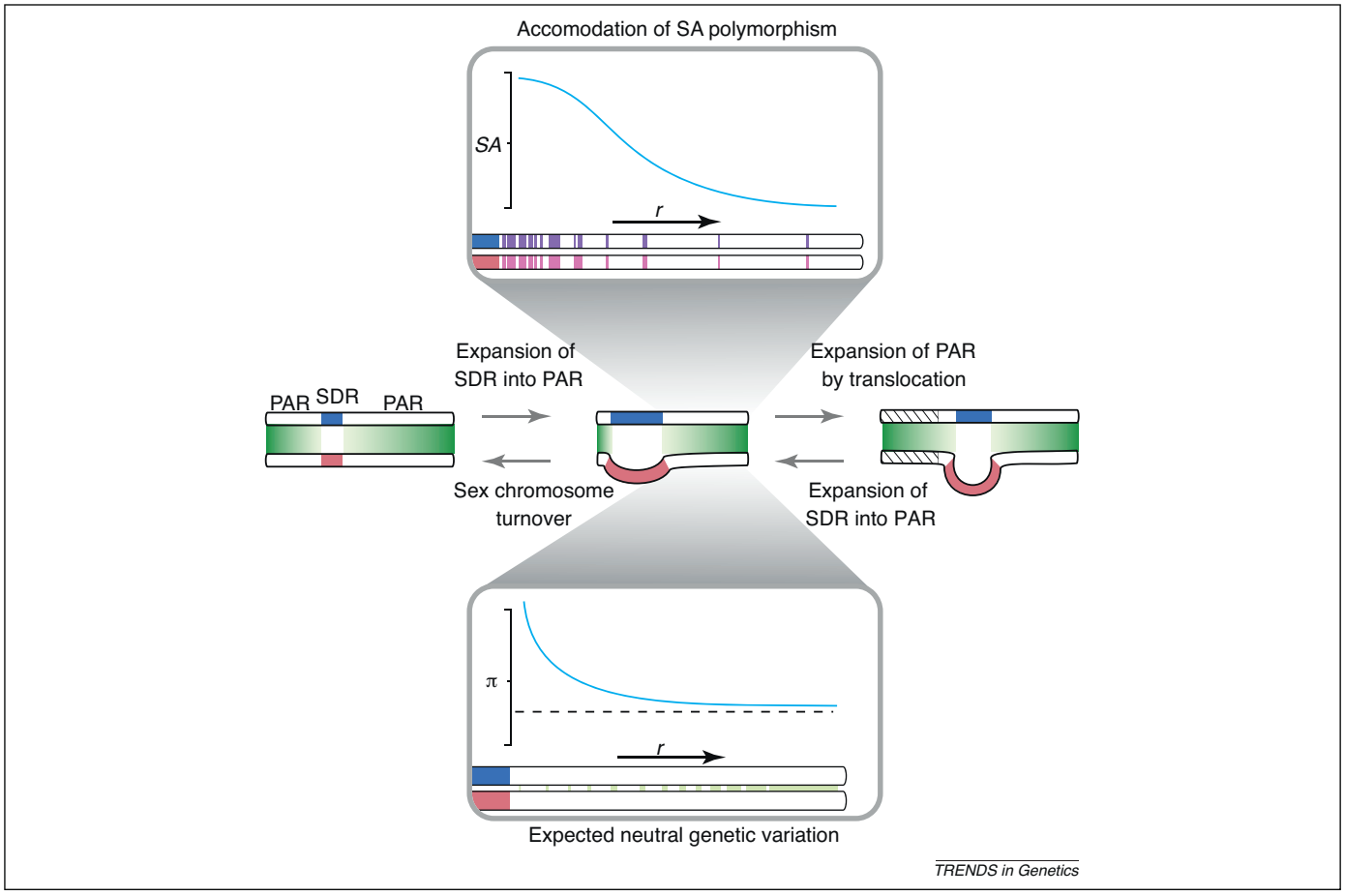

Figure 1. The life cycle of PAR. Regions of the sex chromosomes are demarcated as a recombining PAR or a non-recombining SDR, with green shading indicating increasing genetic distance (*r*) to the SDR. Accumulation of sexually antagonistic (SA) variation is expected at PAR sites, especially near the boundary with the SDR. Neutral sites are also expected to display greater divergence between PAR regions linked to the X and Y [44], indicated by pairwise diversity (π). Suppression of recombination between the sex chromosomes expands the SDR into the PAR, subsuming SA variation. Alternatively, the PAR expands through translocation of autosomes to the sex chromosomes. The cycle can begin again through the invasion of a new sex-determining locus on another chromosome.

are more likely to accumulate and beneficial mutations are less likely to establish within the SDR that is restricted to the heterogametic sex, and genetic degeneration is therefore expected [1,2]. This likely accounts for the commonly observed loss of genes on the Y or W.

In many species recombination persists in one or more regions of the sex chromosomes. This could be because recombination is essential for proper pairing and segregation during meiosis, because the advance of the region of recombination suppression was halted by selection, or for other unrecognized reasons. The recombining regions of sex chromosomes are known as PARs. Homologous pairing and recombination in the diploid PARs of X and Y (or Z and W) maintain their sequence homology (unlike genes in the SDR). Genes in the PARs thus share important features with autosomal genes and are often said to exhibit 'autosomal inheritance' (e.g. [3]). However, because they are linked to the SDR, their evolutionary dynamics are expected to differ from those of autosomal genes.

The sex-biased inheritance of PAR genes has important implications for the outcome of selection on genes whose expression affects fitness in males and females differently – whether selection acts in opposite directions in males and females (i.e. sexual antagonism), or with different intensity in the two sexes; i.e. sex-specific selection. With male heterogamety, for example, alleles carried by the male-determining (Y) chromosome are more often transmitted to sons than to daughters, and vice versa for the X. Distinct selection pressures in males and females can cause divergence in frequencies between the alleles carried by X and Y chromosomes, and this could favor recombination suppression, leading to expansion of the non-recombining SDR and concomitant diminution of the PAR (Figure 1). Even so, recombination can persist within PARs over extended periods of evolutionary time, often at levels higher than elsewhere in the genome.

In this review we briefly summarize what the distribution and structure of PARs in dioecious animals and plants can tell us about PAR evolution. We review theoretical predictions concerning the evolution of suppressed recombination on sex chromosomes, the corresponding contraction of the PAR, and potential reasons for the persistence of the PAR. We then summarize theory that predicts conditions under which polymorphism can be maintained in the PAR. A key conclusion from the theoretical work is that the evolutionary dynamics of the PAR cannot be considered autosomal or indeed even intermediate between the non-recombining SDR and autosomes. We end by asking what types of genes are found in the PAR in species studied to date, and suggest areas in which further research is required.

The evolving PAR

High-resolution genetic maps of PARs are lacking in all but a handful of species. Even in extensively mapped species, such as chickens, the PAR is largely uncharacterized. Most information about the size and content of PARs thus comes from mammals. Because mammals share the same ancestral sex chromosome pair [4], comparisons between divergent lineages can provide insight into the evolutionary transitions that have taken place in the PAR. Even though mammalian sex chromosomes are much more conserved than those in other groups such as fish and amphibians, the PARs have undergone several changes.

Mammalian sex chromosomes have small PARs. For instance, human sex chromosomes have two very small PARs (PAR1 and PAR2), one at each end of the X–Y pair, and together comprising only 4.6% of the Y chromosome. PAR1 is common to most eutherian mammals, with a gene order that has been fairly well-conserved since its addition, within the last 105 million years, to the pre-existing sex chromosomes that are shared with marsupials [4,5]. However, the boundary between PAR1 and the non-recombining region has shifted over evolutionary time [6], and both the size and gene content of PAR1 differ among humans, chimps, ruminants, horses and dogs [7–10]. This implies that genes within the ancestral PAR have been differentially subsumed into the non-recombining regions in different mammalian lineages. In contrast to PAR1, PAR2 is exclusive to humans, and therefore represents a more recent addition to the sex chromosomes [11]. The very small mouse PAR (less than 1% of the length of the Y chromosome) also appears to be of recent origin [12]. The size and genetic content of the PAR can also vary within species, for example among inbred strains of mice [13]. The mouse PAR also exhibits a high frequency of *de novo* genomic rearrangements, with variants that can differ by hundreds of kilobases [14].

In species whose sex chromosomes evolved more recently than those of mammals, the PARs appear to be physically larger (Box 1, Table I), albeit with great variation in PAR sizes, from 15.8% of the chromosome pair in the threespine stickleback [15] to 83% in the papaya [16]. However, no consistent correlation between the age and the extent of recombining regions of sex chromosome pairs is evident, as reviewed in [17,18]. By contrast, there is an intriguing taxonomic pattern ($P < 0.05$; two-sided Fisher's exact test) in the distribution of one versus two PARs: of the species studied to date, 12 of 14 plants have two PARs, compared with 13 of 26 animal species, which tend to have older sex chromosome systems (Table S1 in the supplementary material online). Clearly, more data are needed on the relative size of the PAR and the age of the corresponding sex chromosomes, analyzed within a phylogenetic context.

Analysis of patterns of sequence divergence indicates that the expansion of the non-recombining region, and the contraction of the PAR(s), involves discrete steps that create 'evolutionary strata,' where each stratum exhibits a distinct level of divergence between homologous genes, as in human sex chromosomes [19]. For example, analyses in birds suggest that one stratum is ancient, with recombination having ceased ~132–150 mya, before the radiation of modern birds [20,21], and the second and third strata formed more recently at ~71–99 mya and 47–57 mya, respectively [21]. Similar patterns of evolutionary strata, with different times since recombination suppression, are evident in mammals [19,22], plants [23–25], and *Drosophila* [26,27].

It is important to stress that not all species have a PAR. The PAR is absent in marsupials, whose sex chromosome pairing is achiasmate [5]. A PAR is necessarily absent in groups that lack recombination in the heterogametic sex, such as Diptera and Lepidoptera [28,29]. Even in the absence of male recombination, the evolutionary dynamics of a PAR are intriguingly recapitulated by a segregating rearrangement involving the X chromosome in the fly *Drosophila americana*, providing occasional recombination in females for genes subject to sex-linked transmission in males [30]. Although the PAR allows the maintenance of meiotic pairing and exchange in many species, in those without a PAR other mechanisms ensure correct segregation of sex chromosomes.

Suppressing PAR recombination

Comparative analyses indicate frequent expansion of the non-recombining region by suppression of recombination in the PAR. This process could initiate at the sex-determining locus, thus establishing the SDR. One of the simplest models for suppressed recombination assumes that two loci interact to determine sex. In this model, recombination between the two loci produces sterile intersexual individuals, such that selection favors modifier alleles or structural rearrangements that reduce the rate of recombination [31]. Consistent with this idea, the evolution of separate sexes from hermaphroditism is generally thought to require two or more loci, separately conferring male sterility and female sterility, such that recombination produces sterile individuals [32]. More generally, loci that do not themselves influence sex determination, but that rather influence fitness differentially between the sexes, could also select for reduced recombination between the sex chromosomes to strengthen linkage with the SDR.

An early idea for the suppression of recombination on sex chromosomes proposed that if male heterozygotes at a given locus are particularly fit, this locus would evolve tighter linkage with the SDR [33]. The reasoning was that XY males must be heterozygous in the SDR and therefore might be more likely to be heterozygous outside the SDR, a genetic association known as identity disequilibrium. Without such an association, suppressed recombination does not evolve [34]. Inbreeding is one mechanism that can generate a positive genetic association in heterozygosity (as well as in homozygosity) among loci. Indeed, it has been shown that fusions bringing overdominant loci into linkage with the SDR do spread provided that inbreeding is present [35]. Essentially, heterozygosity at the SDR (XY) protects linked loci in the PAR from homozygosity when relatives mate and produce offspring, thus reducing the severity of inbreeding depression [35].

The relevant genetic association, where a focal locus is more likely to be heterozygous in the heterogametic sex, can also arise when alleles differ in frequency between male and female gametes. Under random mating, an

Box 1. High rates of recombination within PAR

In species requiring at least one crossover for proper chromosome segregation during meiosis, physically small PARs are expected to have high recombination rates per physical map length compared to the rest of the genome, as observed in humans (Table I). As a corollary, recombination rates in the PAR are predicted to be higher in the heterogametic sex relative to the homogametic sex. This is because recombination is restricted to the PAR of the heterogametic sex but can occur freely along the length of the sex chromosomes in the homogametic sex. Empirical data are broadly consistent with this expectation (Table II). The recombination rate is 12.5-fold greater in males than females in human PAR1 [69], 7-fold greater in the mouse PAR [40], and nearly 10-fold greater in the heterogametic sex relative to the homogametic sex just outside the SDR in both the blood fluke [70] and the Japanese medaka [71]. Of the seven additional animal and three plant species with relevant data, however, recombination rates are only slighted elevated – less than 2.5-fold ($n = 3$ animals; 2 plants) or even lower in the heterogametic sex ($n = 4$ animals; 1 plant) (Table II).

Of course, males and females often differ in overall rates of recombination, and this might make it difficult to discover effects specific to the PAR [72,73]. Finer-scale mapping could reveal heterogeneity in recombination across the PAR (most linkage maps analyzed to date are low resolution). For example, a high-resolution map of the papaya sex chromosome revealed that there is a 7-fold increase in the sex-averaged recombination rate in both PARs relative to the genome average [16]. A similar pattern appears in *Populus*, where the region adjacent to the SDR contains recombination hotspots in parents of both sexes [74].

Table I. Relative physical and genetic size of PARs

	SD system	PAR physical size (% chromosome)	PAR genetic size (% chromosome)	cM/Mb PAR	cM/Mb genome wide[a]	References
Human PAR1	XY	2.7 Mb (4.1%)	50 cM (96.2%)	18.52	1.13	[69,75]
Human PAR2		0.33 Mb (0.5%)	2 cM (3.8%)	6.06	1.13	
Threespine stickleback	XY	3.2 Mb (15.8%)	60.2 cM (100%)	9.71	2.24	[15,76]; C.L.P. unpublished
Blood fluke PAR1[a]	ZW	9 Mb (14.8%)	32 cM (13.7%)	3.56	4.09	[70]
Blood fluke PAR2[a]		25 Mb (41.2%)	143.3 cM (61.3%)	5.73	4.09	
Papaya[a,b]	XY	42 Mb (83%)	145 cM (100%)	7.5	2.87	[16]

SD, sex determination.

[a]Sex-averaged map.

[b]Papaya have two PARs but the data are combined here.

Table II. Relative rates of recombination in PARs

Species	SD system	Heterogametic sex (cM)/ homogametic sex (cM)	Fold change	Ref.
Vitis vinifers x *V. riparia* Grapevine	Monogenic	50.4/35.7	1.41	[56]
Fragaria virginiana Virginian strawberry	ZW	35.3/43.6	0.81	[77]
Fragaria chiloensis Beach strawberry	ZW	74.9/68.7	1.09	[78]
Schistosoma mansoni Blood fluke	ZW	N/A	9.90	[70]
Culex tarsalis Mosquito	XY	11.8/50.0 26.3/50.0	0.24 0.53	[79]
Penaeus monodon Black tiger shrimp	ZW	19.0/10.0	1.90	[80]
Takifugu rubripes Tiger pufferfish	XY	30.8/35.7	0.86	[81]
Gasterosteus aculeatus Threespine stickleback	XY	60.2/45.8	1.31	[15]; C.L.P., unpublished
Oreochromis aureus Blue tilapia	ZW	16.0/19.0	0.84	[82]
Oryzias latipes Japanese medaka	XY	18.4/2.2	9.20	[71]
Oryzias luzonensis	XY	15.5/50.0	0.31	[83]
Ambystoma tigrinum Tiger salamander	ZW	30.2/13.6	2.22	[84]
Homo sapiens Human	XY	50.0/4.0	12.5	[69,75]
Mus musculus Mouse	XY	26.8/3.9	6.87	[40]

N/A, not available; SD, sex determination

initially unlinked focal locus has been shown to evolve complete linkage with the SDR whenever selection causes the sexes to differ in allele frequency at the focal locus, assuming that the population was initially at equilibrium [34]. Because PAR loci close to the SDR are especially prone to exhibit sex differences in allele frequency ([36]; Figure 2), these results suggest that suppressed recombination should be even more likely to evolve between the

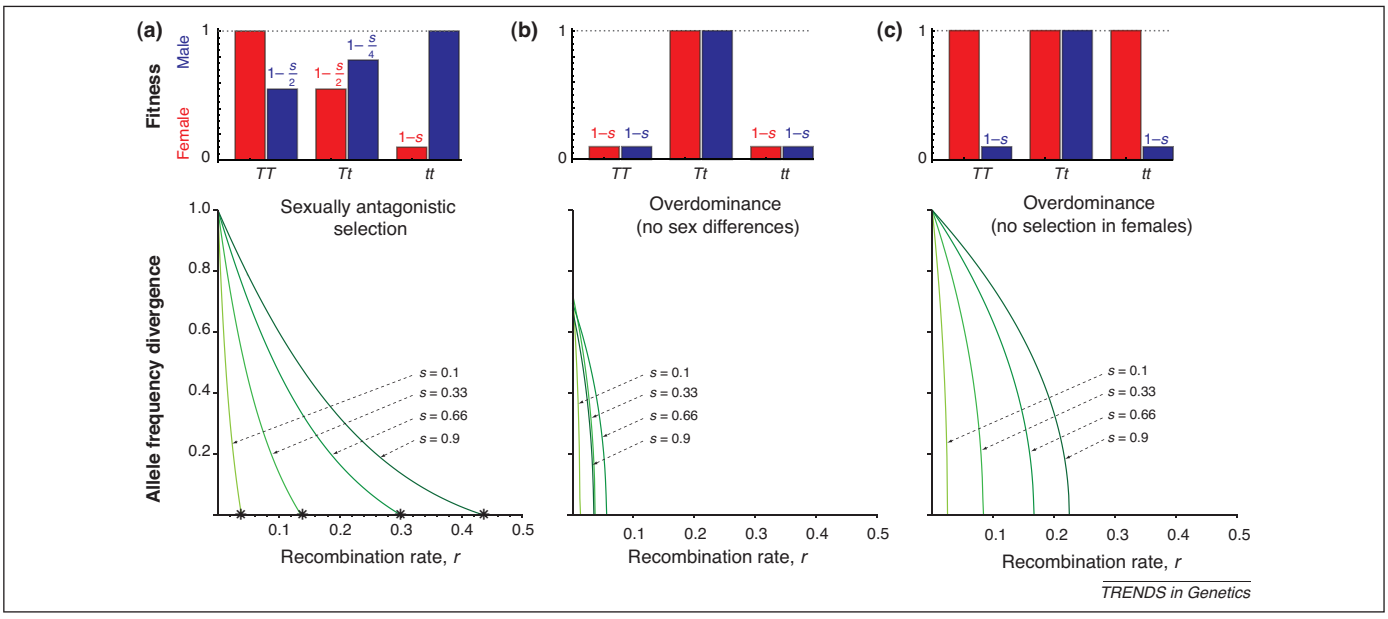

Figure 2. Allele frequency divergence between X and Y. For example, when fitness depends on the genotype at a trait locus bearing two alleles, *T* and *t*, as illustrated by the top panels, allele *T* equilibrates to different frequencies on the X and Y as illustrated in the bottom panels, showing frequency of *T* on the X minus that on the Y. **(a)** With sexually antagonistic selection, the female-benefit allele (*T*) rises to higher frequency on the X than on the Y, which helps maintain polymorphism (*r* less than the stars). **(b)** With overdominance (no sex differences in fitness), allele frequencies can also diverge; here, the *T* allele is more common on the X, but the reverse equilibrium is equally plausible. Because *T* is more common on the X and *t* on the Y, males are more likely to be high-fitness heterozygotes. **(c)** Even without selection in females and overdominance only in males, allele frequencies can diverge, again promoting the production of high-fitness heterozygous males. Polymorphism is always maintained in cases **(b)** and **(c)** because of the overdominance, but male and female allele frequencies equalize when **(b)** $r > (1–s)s/(8–6\ s)$ and **(c)** $r > s/4$. Fitnesses (above) are illustrated for females (red) and males (blue). *s* refers to the strength of selection, with the histograms illustrating $s = 0.9$; *r* refers to the recombination rate between the selected locus and the SDR.

SDR and linked PAR genes. This recombination suppression could in turn bring loci that were initially distant from the PAR boundary into tighter linkage with the SDR (Figure 1), allowing their allele frequencies to diverge between the two sexes and fueling a cycle of continued recombination suppression. PARs that happen to have high recombination rates per physical distance at the junction with the SDR, however, could break this cycle and thus be more stable over evolutionary time. This is a worthy area for future theoretical development.

A recent analysis that did not require the initial population to be at equilibrium showed that tighter linkage between a focal locus and the SDR evolves whenever the average selection coefficient acting on an allele differs in males and females, whether or not allele frequencies differ between them [37]. Of course, sex-specific selection typically leads to sex differences in allele frequency [37], but this result indicates that a difference in selection acting on alleles in males versus females is sufficient to drive recombination suppression in the PAR. Interestingly, this prediction applies whether selection acts in opposite directions in males and females (sexually antagonistic selection) or in the same direction but with differing strengths.

The key insight from these analyses is that it is not necessarily the production of heterozygotes nor sexually antagonistic selection, *per se*, that drive the non-recombining region to expand into the PAR. Instead, if selection favors one allele more in males than in females, tighter linkage with the Y-linked SDR (through translocations, fusions, or recombination modification) is favored simply because future carriers of the allele are then more likely to be males. A similar force favors tighter linkage between an allele favored in females with the X, although the force is weaker due to the presence of X in both sons and daughters [34,37].

Why do PARs persist?

The above theoretical synthesis suggests that the PAR should evolve towards zero recombination. However, some PARs, such as those in eutherian mammals, have been maintained over substantial periods of evolutionary time. Why then is the PAR not lost?

One compelling reason in many species is simply that the PAR is needed for proper segregation of the sex chromosomes during meiosis [38–40]. The requirement for at least one crossover for proper segregation can result in unusually high recombination rates per base within PAR regions (Box 1, Table I), accomplished in mouse meiosis by molecular mechanisms that are distinct from the autosomes [41]. An important consequence of elevated recombination in the PAR is that distal regions of the PAR could approach autosomal inheritance patterns, with an equal chance of being transmitted to either sex.

Another possibility is that PARs persist as a result of classical forces that favor recombination, such as Hill–Robertson effects, avoidance of Muller's ratchet, and negative epistasis among loci [42,43]. Although these forces are likely weak when restricted to PAR alone, they could potentially become relevant when selection for recombination suppression is also weak. A further possibility is that loci subject to outbreeding depression, where heterozygotes are on average less fit, might evolve looser linkage with the SDR, thereby reducing heterozygosity in the heterogametic sex if there is inbreeding. Alternatively, if the SDR experiences meiotic drive at a rate controlled by a

sex-ratio distorter gene that lies within the PAR, increased recombination evolves if genes modifying recombination are loosely linked to the SDR [42]; this presumably occurs because a modifier allele that increases recombination benefits from equalizing the sex ratio among its descendants. Suppressed recombination tends to evolve, however, if the genes modifying recombination are tightly linked to the SDR [42], which apparently occurs because modifiers that suppress recombination become genetically associated with the sex chromosome that is driven by the particular distorter allele found on each chromosome.

Finally, PAR might persist dynamically, with new PARs arising via translocations, only to be subsumed over time into the SDR (Figure 1). Translocations to the PAR are particularly favorable for regions of the genome experiencing sex differences in selection, including sexually antagonistic selection [34,37]. Such translocations facilitate allele frequency divergence between males and females (Figure 2) and could explain neo-PAR regions, such as PAR2 in humans. Further data and theoretical work are needed to assess the relevance of these forces for the persistence of PARs.

Maintenance of variation in the PAR

Linkage to the SDR alters the evolutionary dynamics of PAR genes compared to autosomal genes, with important effects on the maintenance of variation and on associations between single nucleotide polymorphisms (SNPs) and the sex of an individual. Even for neutral PAR sites, linkage to the SDR causes unusual patterns of genetic variation [44]. For example, expected heterozygosity between pairs of alleles is elevated when comparing X-linked and Y-linked alleles (Figure 1) but reduced when comparing two Y-linked alleles. Selection can further exaggerate these patterns in the following ways.

First, sex linkage dramatically alters the conditions under which a polymorphism is stable under sexually antagonistic selection. Selection acts in opposing directions in males and females on a myriad of traits, including body size and shape, as well as life-history characteristics such as lifespan and fertility schedules [45]. As summarized in Box 2, sexually antagonistic selection can maintain a polymorphism at any genomic location. With autosomal inheritance, however, variation will be maintained only if heterozygotes have higher fitness than homozygotes, averaged across males and females. By contrast, polymorphism at loci within the region of an X that does not recombine with the Y will be maintained if a female-benefit allele is sufficiently dominant in females, assuming that the Y has degenerated so that males are hemizygous. PAR genes can maintain variation even more readily, especially when linkage to the SDR is tight (Box 2, Figure I).

Second, sex linkage facilitates the development of associations between alleles and the X or Y chromosome, generating allele-frequency differences between the sexes. This explains why it is easier to maintain polymorphism in the PAR under sexually antagonistic selection, because female-benefit and male-benefit alleles become genetically associated with the X and Y, respectively (Figure 2a). Surprisingly, it is possible for alleles in the PAR to diverge in frequency on the X and Y even when every genotype has the same fitness in males and females [36]. For instance, substantial differences in allele frequency between the X and Y build up in PAR genes sufficiently linked to the SDR when selection is overdominant with identical fitnesses in males and females (Figure 2b), whether homozygotes are equal in fitness as illustrated or not (Supplementary material online). These puzzling predictions are explained by the fact that alleles at PAR loci can spend different amounts of time linked to the X or Y. In particular, genetic associations develop whereby one allele occurs more often in females and the other in males, making the production of heterozygous offspring more likely.

The stable persistence of sex differences in allele frequencies without sex differences in selection has interesting implications. First, sexual dimorphism could arise without sex differences in selection. For example, if a trait allele *T* becomes associated with the X chromosome and an alternative allele, *t*, with the Y, females will more often display the *TT* phenotype than males, whereas males will more often display the *tt* phenotype than females, even if *TT* and *tt* individuals are equally fit (the opposite might equally occur). In essence, the two sexes specialize on different strategies (alleles), in the absence of sex-specific fitness differences. Second, when equilibrium frequencies differ between the two sexes, selection can drive the allele frequencies in opposite directions in males and females, and thus have the appearance of sexually antagonistic selection, even though the fitness of each genotype is the same in the two sexes.

One further example serves to emphasize the unique dynamics within the PAR. If selection acts only in males, with lower fitness in homozygotes relative to heterozygotes, one might expect the equilibrium frequency of the trait allele, *T*, to be the same in females and males. However, if linkage to the SDR is sufficiently tight, this is not true. Instead, one allele again becomes associated with the X chromosome and becomes more frequent than the other allele in females (Figure 2c; [36]), even though it does not benefit females.

Three major predictions regarding loci on PAR follow from the above theory. First, polymorphisms should be more prevalent at loci in the PAR closer to the SDR (Figure 2; Box 2). Second, the frequency of alleles in the two sexes (or associated with the X and Y) should often differ, especially when closely linked to the SDR, but this cannot be taken as evidence of sexually antagonistic selection (Figure 2). And third, it is generally easier to maintain a sexually antagonistic polymorphism in the PAR than on an autosome (Box 2). Interestingly, it can also be easier to maintain polymorphism within the PAR than within the SDR because degeneration within the SDR makes the Y less likely to evolve male-benefit alleles [36]. Thus, perhaps counter-intuitively, the conditions for maintaining a polymorphism in the PAR are not intermediate between those for genes on the autosomes and on the non-recombining portions of the sex chromosomes.

What types of genes are found on the PAR?

Because genes linked to the SDR are more likely to maintain polymorphism (Box 2) and to exhibit sex differences in

Box 2. Sexually antagonistic selection and the maintenance of polymorphism

At a locus subject to sexually antagonistic selection, let T be a female-benefit allele (selected against in males by an amount s_m) and t be a male-benefit allele (selected against in females by an amount s_f), with fitnesses given by:

	Male trait		
Autosomal, ZZ, or PAR	*TT*	*Tt*	*tt*
Sex-linked (XY)	$X^T Y$		$X^t Y$
Male fitness:	$1 - s_m$	$1 - h_m s_m$	1
	Female trait		
Autosomal, XX, or PAR	*TT*	*Tt*	*tt*
Sex-linked (ZW)	$Z^T W$		$Z^t W$
Female fitness:	1	$1 - h_f s_f$	$1 - s_f$

The following table summarizes the conditions under which both T and t alleles can increase when rare, such that selection maintains polymorphism, at an autosomal or fully sex-linked gene, where $W^m_{x/y}$ refers to the fitness in males of genotype x relative to genotype y (e.g. $W^m_{Tt/TT} = (1 - h_m s_m)/(1 - s_m)$) and the same for $W^f_{x/y}$ in females (based on [50,51,85–87]).

	Exact	Assuming weak selection
Autosomal	$\frac{1}{2}\left(W^f_{Tt/TT} + W^m_{Tt/TT}\right) > 1$ & $\frac{1}{2}\left(W^f_{Tt/tt} + W^m_{Tt/tt}\right) > 1$	$\frac{h_f}{1-h_m} s_f < s_m < \frac{1-h_f}{h_m} s_f$
Sex-linked (XY)	$W^f_{Tt/TT}\left(\frac{1}{2} + \frac{W^m_{t/T}}{2}\right) > 1$ & $W^f_{Tt/tt}\left(\frac{1}{2} + \frac{W^m_{T/t}}{2}\right) > 1$	$2h_f s_f < s_m < 2(1 - h_f) s_f$
Sex-linked (ZW)	$W^m_{Tt/TT}\left(\frac{1}{2} + \frac{W^f_{t/T}}{2}\right) > 1$ & $W^m_{Tt/tt}\left(\frac{1}{2} + \frac{W^f_{T/t}}{2}\right) > 1$	$2h_m s_m < s_f < 2(1 - h_m) s_m$

For genes located within the PAR, Bull [88] showed that polymorphism will be maintained provided that the largest root λ of both of the following cubic equations is greater than one:

$$\lambda^3 - \lambda^2\left(W^m_{Tt/TT}(1-r) + \frac{W^f_{Tt/TT}}{2}\right) + \left(W^m_{Tt/TT}\right)^2 W^f_{Tt/TT}\left(\frac{1}{2} - r\right) = 0$$

$$\lambda^3 - \lambda^2\left(W^m_{Tt/tt}(1-r) + \frac{W^f_{Tt/tt}}{2}\right) + \left(W^m_{Tt/tt}\right)^2 W^f_{Tt/tt}\left(\frac{1}{2} - r\right) = 0$$

The qualitative behavior is illustrated in Figure I. When selection is weak relative to the recombination rate (s_m, $s_f \ll r$) or when $r = 1/2$, these conditions reduce to those found at an autosomal locus. With strong selection and/or tight recombination, however, it is always easier to maintain a polymorphism at a gene linked to the SDR ($r < 1/2$) than on an autosome. It can even be easier to maintain a polymorphism at a PAR gene than at a gene within the sex-determining region, if Y-linked genes in the SDR have degenerated but PAR genes remain functional, because in the latter case associations can develop between the Y and the allele beneficial to males (see additional details in [50,89]).

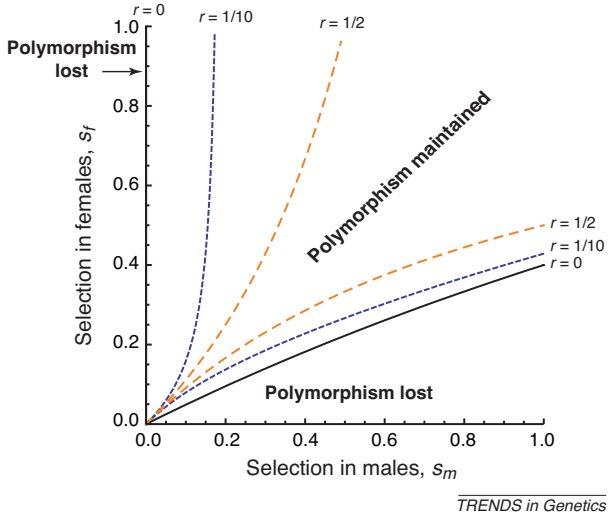

Figure I. Assuming additive selection ($h_m = h_f = 1/2$), sexually antagonistic selection at a locus maintains a polymorphism for combinations of selection coefficients in males and females that are sufficiently balanced [50,89], such that the point (s_m, s_f) falls between the pair of curves illustrated for a given recombination rate, r. The higher the recombination rate between the locus and the sex-determining region, the more restrictive this condition becomes. The conditions for $r = 1/2$ correspond exactly to those for an autosomal locus. Notice that for tight linkage, it becomes easy to maintain a polymorphism even when selection in males is much weaker than in females, because the male-benefit allele becomes genetically associated with the Y.

allele frequency (Figure 2), we would expect traits exhibiting substantial genetic variance and sex differences to map disproportionately to the PAR. Indeed, variation in many phenotypic traits has been mapped to sex chromosomes. For example, there is preferential sex-linkage of genes controlling sexually selected traits [46] and traits important for speciation [47,48]. However, few studies have sufficient resolution to determine whether the traits map to the recombining or the non-recombining regions.

We should also expect enrichment for genes exhibiting sexually antagonistic selection within segments recently transferred to the PAR, both because polymorphism is more readily maintained there (Box 2) and because translocations moving such genes to the sex chromosome are

selectively favored [34,37]. Over longer periods of evolutionary time, however, we would expect the harmful effects of expressing traits in the 'wrong' sex to be reduced [49,50], either by evolving sex-specific expression or by suppressing recombination with the SDR because tighter linkage increases the frequency of the 'right' allele in each sex (Figure 2a). For PAR genes subject to sexually antagonistic selection, which of these two routes is taken will determine the type of genes that ultimately remain in the PAR. If sexual conflict is resolved by evolving sex-limited expression [51], PAR genes could well lose polymorphism, eliminating selection for suppressed recombination and allowing such genes to persist within the PAR. By contrast, if sexual conflict is resolved by PAR genes evolving tighter linkage with the SDR [50], polymorphism will remain stable (Box 2, Figure I), and we would expect selection to continue to favor suppressed recombination until the gene becomes subsumed in the non-recombining SDR. As a result, genes that persist in older sections of the PAR should be more likely to have evolved sex-limited expression than genes that have transferred to the SDR (e.g. [52]).

To test these ideas we need to identify genes that underlie traits experiencing sexually antagonistic selection and/or sex-limited expression, determine whether they map to the PAR or SDR, and also infer the ages of these regions. Several mapping studies in plants and animals point to the existence of genes in the PAR that influence sexually dimorphic and sexually antagonistic traits, some of which might have evolved sex-limited expression (Table S2 in the supplementary material online). Three studies stand out as most informative.

In the white campion, *Silene latifolia*, quantitative trait locus (QTL) mapping for 40 sexually dimorphic traits found that all had at least one QTL in the SDR [53]. In addition, 11 QTL for 12 morphological, physiological, and life-history traits map to the PAR. Of these, eight QTL were male-specific (i.e., identified only by QTL mapping in males) and one was female-specific (i.e., identified only by QTL mapping in females) [52,53]. Overall, sex-specific QTL appear to be enriched in the PAR; of 17 sex-specific QTL, nine mapped to the PAR [53]. These data are consistent with the prediction that genes that have evolved sex-specific expression might persist in the PAR. Similarly, several morphological traits are linked to the PAR in wild strawberry (*Fragaria virginiana*, *F. chiloensis*) and grapevine (*Vitis vinifera)* [54–57]. These are suggestive patterns, but it is still largely unknown whether traits mapping to the PAR tend to exhibit sex-specific fitness effects.

Male coloration in guppies (*Poecilia reticulata*) is a classic example of a trait likely to be under sexually antagonistic selection. Males display bright color patterns that are attractive to females but that also increase risk of predation [58–62]; their expression would thus be detrimental in females. Accordingly, all the color patterns show male-limited expression. By performing genetic analysis in males, genes influencing color traits were found to be linked to the sex chromosomes: some genes are fully Y-linked, whereas others map to the PAR (reviewed in [63,64]). One study showed that color patterns within the PAR in low-predation populations were completely linked to the SDR in high-predation populations [65]. This suggests that comparisons among populations differing in their extent of sexually antagonistic selection could be useful for understanding the trafficking of traits to and from the PAR. Further empirical work is needed to determine whether such loci are likely to have passed through a phase of female expression (and hence sexual antagonism); further theoretical work is needed to determine whether environmental heterogeneity can explain this trafficking even if expression were to be male-limited.

Finally, in the threespine stickleback species complex (*Gasterosteus aculeatus*), traits important for reproductive isolation between an incipient species pair map to both the ancestral X chromosome and a neo-X chromosome formed by fusion between the ancestral Y chromosome and an autosome in one of the species [66]. The QTL for two traits map to the PAR of the neo-X chromosome; one trait is a male-limited behavior and the other is a sexually dimorphic morphological trait. Selection for linkage between the sex-determination locus and the genes underlying one or both of these traits might have contributed to selection for the Y–autosome fusion [34,67]. However, it is again not known whether selection acting on these genes is currently sexually antagonistic or whether it might have been so at the time of the fusion.

Concluding remarks

The evolution of sex chromosomes provides a fascinating case in which similar processes have affected parallel changes within independent lineages. A prominent repeated feature is the suppression of recombination, causing expansion of the SDR, and the associated degeneration of Y or W chromosomes, leading to heteromorphic chromosomes. It is thus understandable that discussion of sex-chromosome evolution often focuses on the SDR, and the PAR is barely mentioned (e.g. [68]). However, as demonstrated in this review, the evolutionary dynamics of the PAR ultimately inform the processes that underlie the formation of the SDR. Although there is much room for more theoretical work on PAR evolution, clear predictions exist, including higher polymorphism at PAR loci closely linked to the SDR, as well as counter-intuitive suggestions that PAR evolutionary dynamics are not necessarily intermediate between that of the SDR and autosomes.

Empirically, we still know very little about which genes are found in the PAR, how long they persist before being subsumed into the SDR (if indeed they are), and their expression patterns, particularly their dominance coefficients and the relative roles of sexual antagonism versus other forms of sex-specific selection, and sex-limited expression. Because of the changes that evolve in the PAR, much can be learned from comparisons between species within clades, and even in those with a well-established and evolutionarily conserved sex-chromosome system such as mammals. However, we anticipate that a great deal will also be learned from the study of PAR in plant and animal species with recently evolved sex chromosomes. Certainly, this relatively unexplored corner of the genome could prove to be far more exciting and informative about evolutionary genetic processes than its size or name might imply. In golfing parlance, the PAR is definitely better than par.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tig.2011.05.001.

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