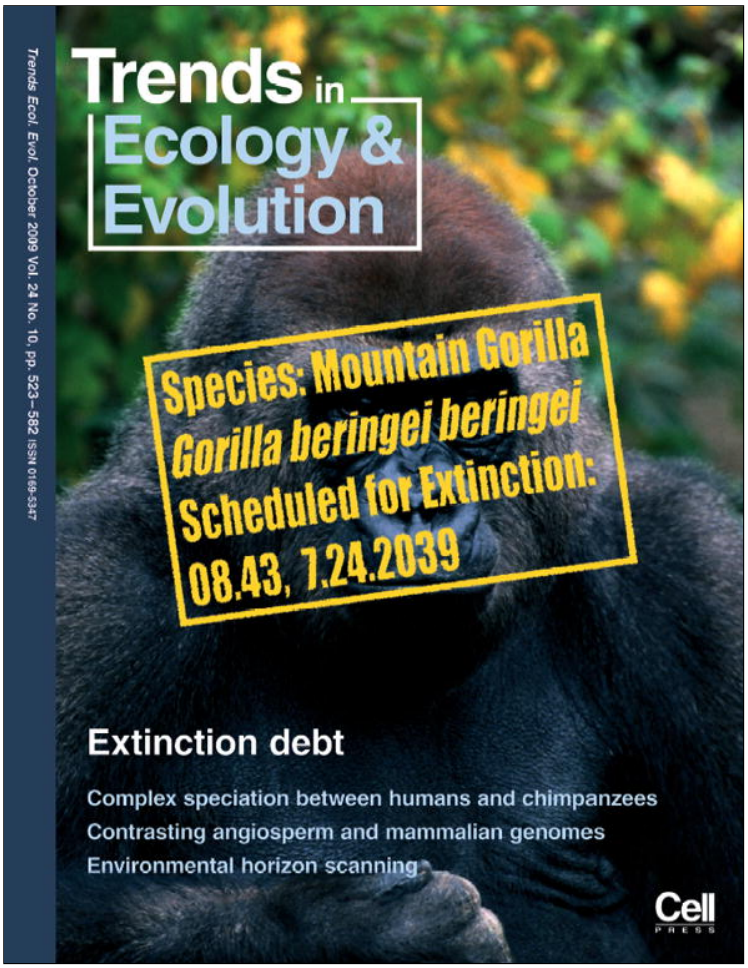

Review

Cell PRESS

Contrasting evolutionary dynamics between angiosperm and mammalian genomes

Eduard Kejnovsky[1], Ilia J. Leitch[2] and Andrew R. Leitch[3]

[1] Institute of Biophysics, The Academy of Sciences of the Czech Republic, Kralovopolska 135, 612 65 Brno, Czech Republic
[2] Jodrell Laboratory, Royal Botanic Gardens, Kew, Richmond, Surrey TW9 3AB, UK
[3] School of Biological and Chemical Sciences, Queen Mary University of London, London E1 4NS, UK

Continuing advances in genomics are revealing substantial differences between genomes of major eukaryotic lineages. Because most data (in terms of depth and phylogenetic breadth) are available for angiosperms and mammals, we explore differences between these groups and show that angiosperms have less highly compartmentalized and more diverse genomes than mammals. In considering the causes of these differences, four mechanisms are highlighted: polyploidy, recombination, retrotransposition and genome silencing, which have different modes and time scales of activity. Angiosperm genomes are evolutionarily more dynamic and labile, whereas mammalian genomes are more stable at both the sequence and chromosome level. We suggest that fundamentally different life strategies and development feedback on the genome exist, influencing dynamics and evolutionary trajectories at all levels from the gene to the genome.

Exploring differences between eukaryotic genomes

The search for characters that unify distantly related eukaryotes is a powerful way to resolve species relationships, biochemical pathways, genetic mechanisms, sequence structures and functions. Such studies reveal that even distantly related eukaryotes, separated by over 100 million years of evolution, can share the same genes arranged in blocks, often in the same order. Such similarities that unify eukaryotes, however, obscure fundamental differences in the dynamics and evolution of DNA between different groups. This review explores genomic differences between mammals and angiosperms (Tables 1 and 2), two groups for which the most extensive genomic data from multiple species exist, and suggests that their genomes are undergoing radically different modes of evolution.

The timing of the split between these groups is controversial, but current estimates suggest that it occurred 1000–2000 million years ago (mya) [1]. Given their very long period of independent evolution, major differences in genome organization and evolution between the groups are to be expected. Nevertheless, exploring these differences can shed light on factors shaping the genomes of mammals and angiosperms.

Corresponding author: Leitch, A.R. (a.r.leitch@qmul.ac.uk).

Angiosperms and mammals differ in global genomic architecture

At the whole genome level (e.g. organization of DNA in the chromosome, diversity in chromosome number and genome size) there are substantial differences between mammals and angiosperms. These are explored below and summarized in Table 1.

Glossary

R- and G-Banding: Cytogenetic procedures designed to band chromosomes so that they can be individually identified. In humans it is possible to generate over 1000 characteristic bands across the karyotype (Figure 1a).
Chromosome painting: In mammals, DNA from an individual chromosome can be isolated, labelled and used as a probe to paint that specific chromosome on a metaphase spread. Chromosome-specific paints are now available for several mammalian species and for each of the 24 chromosome types comprising the human karyotype (Figure 1b,c).
Conserved non-coding sequences (CNSs): Conserved sequences for which the functions are not clear; some might be involved in long-distance regulation of developmental genes (including over many megabases of DNA).
DNA C-values or genome size: This refers to the amount of DNA in the nuclear genome. It is usually given as the 1C value, which is the amount of DNA in the unreplicated gametic nucleus. Genome size databases are available for mammals (http://www.genomesize.com/) and angiosperms (http://data.kew.org/cvalues/homepage.html).
Epigenetics: The regulation of gene expression via cytosine methylation, histone modifications or processing of RNA (see also RNA interference).
Genomic imprinting: The regulation of genes in development depending on their parental origin.
Polyploidy (or whole-genome duplication): A process whereby the entire chromosome complement is multiplied, so that dividing cell types contain more than two sets of chromosomes (as in a diploid). Evolution can mask polyploid events through, for example, chromosome fusion or DNA loss. Ancient polyploidy (palaeopolyploidy) can then be inferred only by analyses of duplicated gene copies.
Synteny and collinearity: When the same cluster of genes occurs together in related taxa or in duplicated blocks within a genome, this is known as synteny. When these genes are also in the same or similar order, they are considered to be collinear.
Recombination: The exchange of DNA between different DNA regions or strands involved in, for example, meiosis, DNA repair, chromosome translocations and DNA insertion and deletion (Box 1).
Retrotransposons and retrotransposition: Retrotransposons are mobile elements that can, or once could, amplify via copy-and-paste mechanisms using an RNA intermediate; the mechanism is called retrotransposition. Retrotransposons can be divided into two groups. (a) The long terminal repeat (LTR) retrotransposons (e.g. *gypsy* and *copia* superfamilies, which are abundant in angiosperms). (b) Non-LTR retrotransposons including LINEs (long interspersed nuclear elements) and non-autonomous SINEs (short interspersed nuclear elements), which are most common in mammals.
RNA interference (RNAi): This is a mechanism involved in the processing of RNA into small RNA fragments, e.g. microRNA (miRNA), small interfering RNA (siRNA) and piwi-interacting RNA (piRNA) for gene regulation, heterochromatinization, suppression of transposable element mobility and defense against external nucleic acids.

0169-5347/$ – see front matter doi:10.1016/j.tree.2009.04.010 Available online 6 August 2009

Table 1. Major differences in genome organization between angiosperms and mammals

Phenomenon	Angiosperms	Mammals	References
Chromosome structure			
R- and G-bands	Absent	Present; used extensively to compare karyotypes between species; R-bands are SINE-rich and G-bands are LINE-rich	[2,6,86,87]
C-bands	Present, labelling heterochromatin	Present, labelling heterochromatin	[2,6,86,87]
Chromosome-specific painting	Very limited application, only successfully applied to certain chromosome types (e.g. sex and B chromosomes)	Widely applicable across mammals species	[9]
Conserved non-coding sequences (CNS)			
Average CNS size	20–30 bp	69–>100 bp	[7,88]
Relative conservation	Relatively less highly conserved, degrading quickly over evolutionary time	More highly conserved, degrading more slowly over evolutionary time	[7,88]
Average density of CNS in genome	3 CNS/gene although 27% of genes not associated with CNSs	17.7 CNS/gene, all analyzed genes associated with CNSs	[7,88]
Distribution in genome	Intergenic	Mostly within introns and intergenic regions	[7,88]
Genes			
Occurrence of multigene families	Large multigene families common (in *A. thaliana*, 37.4% of genes occur in families with >5 members whereas 35% are single)	Fewer, smaller multigene families (in humans 1.4% of genes occur in families with > 5 members whereas 86.4% are single)	[7]
Average gene length (introns+exons)	2.9 kb (mean for *A. thaliana* and *O. sativa*)	43.5 kb in humans	[89]
Average intron length	270 bp (mean for *A. thaliana* and *O. sativa*)	5.5 kb in humans	[89]
Average total intron length	1.64 kb (mean for *A. thaliana* and *O. sativa*)	42 kb in humans	[89]
Average total exon length	1.35 kb (mean for *A. thaliana* and *O. sativa*)	1.49 kb in humans	[89]
Genome size and chromosome number			
Range in genome size	~2000-fold from 1C = 0.063 pg in *Genlisea margaretae* to 1C = 127.4 pg in tetraploid *Fritillaria assyriaca* (based on 5770 species with C-value measurements, Figure 2)	Five-fold, from 1C = 1.73 pg in *Miniopterus schreibhersi* to 1C = 8.4 pg in *Tympanocytomys barrerae* (based on ~400 species, Figure 2)	[13,85]
Range in chromosome number	From $2n = 4$ in five species to $2n = 640$ in *Sedum suaveolens*.	From $2n = 6$ in female *Muntiacus muntjak* to $2n = 134$ in *Diceros bicornis*	[90]
Mitochondrial DNA			
Average size of mitochondrial genome	Variable in size, ranging from 200 to over 2000 kb	Narrow range e.g. 16.5 kb in humans (mean size for vertebrates is ~17 kb with low SD)	[91–93]
Number of protein genes in mitochondria	27 in *A. thaliana*	13 in humans	[92]
Percentage of nuclear genome occupied by NUMTs	0.171% in *A. thaliana* and 0.097 % in *O. sativa*	0.016% in humans, 0.002% in *Mus musculus* and 0.0002% in *Rattus norrvegicus*	[93,94]
Retrotransposable elements			
Predominant type of element	LTR retrotransposons belonging to *copia* and *gypsy* superfamilies; individual elements range from a few hundred bases to 25 kb with 10^3–10^5 copies, contributing up to 80% of the genome (depending on genome size)	Non-LTR retrotransposons LINEs and SINEs are predominant; in the human genome these two classes comprise over 33% of the DNA; the SINE element *Alu* has the highest copy number, with >1 million copies	[44,45,95,96]
Diversity of retroelements	Large range in copy number and diversity of families present in the genome	Generally mammalian genomes are characterized by a low diversity of retroelement families.	[96]
Tandem repeats			
Rate of sequence homogenization	Complete replacement of subtelomeric repeats in 3 million years (data from *Nicotiana*)	Little change in great ape centromeres repeats over 7 million years	[97,98]

Table 2. Important mechanisms contributing to differences in genomic structure between angiosperms and mammals

Phenomenon	Angiosperms	Mammals	References
Polyploidy and interspecific hybridization			
Incidence of polyploidy	Frequent occurrence; most (maybe all) species have evidence of polyploidy in their ancestry and some, e.g. *Brassica napus*, have undergone four rounds of polyploidy over this time frame	Absent in mammals, only one controversial report of a polyploid rodent	[17,99]
Frequency of interspecific hybridization	At least 25% of species	~6% of species	[18]
Recombination			
Rates of recombination	Higher and more variable	Lower and less variable	[25]
Linkage map recombination frequency	*Arabidopsis thaliana*, 2.6 cM/Mb	Human, 1.22 cM/Mb	[29,30]
Occurrence of chromosomal translocations	Large number in some lineages including microshuffling, e.g. comparative linkage map analysis reveals ~10 chromosome rearrangements between *A. thaliana* and *A. lyrata*, which diverged just ~5 mya and ~90 translocation since *A. thaliana* and *B. nigra* diverged 14–24 mya	Small number of large translocations, e.g. chromosome painting reveals one chromosomal translocation between human and great apes (diverged ~5 mya) and only 14 between mouse and rat (diverged 10–20 mya) even though rodents have one of the highest rates of chromosome evolution in mammals	[26–28]
Retrotransposition			
Retroelement insertion	Higher frequency of insertion events; (a) in *Gossypium* amplification of retroelements has expanded the genome 3-fold in some lineages, accumulating e.g. >50 000 copies of the *Gorge 3* LTR retroelement in the last 5–10 million years; (b) 80% of the *Zea mays* genome is composed of retroelements, most inserted in the last 1–3 million years	Lower frequency of insertion events; divergence of the great apes is associated with amplification of *Alu* elements, with an estimated 5000 *Alu* insertions in the African great ape lineage over ~5–10 million years	[95,100]
Retroelement half-life	<1–6 million years (*Oryza sativa*), <2 million years (*Z. mays*)	We are unaware of comparable data	[36,43,100]
Gene silencing			
Epigenetic regulation of genes	Genes activated by cytosine demethylation	Genes silenced by cytosine methylation	[101]
Genomic imprinting	Restricted to endosperm	Used extensively during development	[65,66]
Global epigenetic repatterning associated with gametogenesis	No	Yes	[65,66]
RNAi-directed DNA methylation (RdDM) and RNA-dependent polymerase (RdRP)	Present	Not described in mammals	[102,103]
miRNA targets	Usually considered to require near perfect sequence complementarity of miRNAs to particular genes, predominantly targeting intergenic regions	Lower complementarity of miRNAs influencing a broader set of genes, predominantly targeting introns	[56,57,102,104,105]
Silencing mechanism of miRNA	Pre- and post-transcriptional level silencing, the former through heterochromatinization	Regulation at post-transcriptional level, with only limited evidence for regulation at DNA level	[56,57,102,104,105]
Role of miRNA silencing	Viral defence, heterochromatinization, silencing of mobile elements	Cell differentiation and development; a role in suppressing mobile elements is unclear	[56,57,102,104,105]

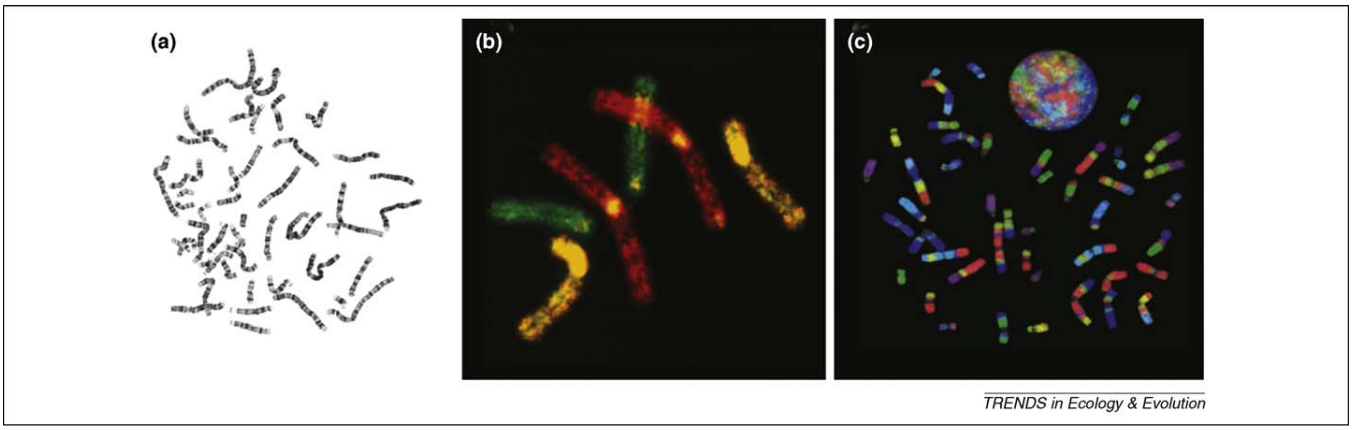

Figure 1. Cytogenetic banding and chromosome painting. (a) Human metaphase showing G-bands enabling the identification of individual chromosomes (used with permission from Mr R. Palmer). (b) Chromosome painting using whole chromosome paints derived from Indian muntjac to metaphases of the same species {reprinted with permission from Oxford University Press (Human Molecular Genetics) [84], copyright 1998} (c) Human metaphase probed with gibbon chromosome paints {reprinted with permission from Macmillan Publishers Ltd (Nature Reviews Genetics) [8], copyright 2007}.

Chromosomes: more compartmentalized in mammals than angiosperms

Fundamental differences in the structure of mammalian and angiosperm chromosomes were probably first observed with the development of cytogenetic banding (Figure 1a). In mammals, R- and G-bands, which represent domains (or isochores) of different gene densities and sequence character (particularly the predominant retrotransposons that they contain [2]) (Table 1), are highly conserved enabling karyotypes to be compared (e.g. cetaceans diverging ~30 mya have near identical G-banding patterns [3,4]). The occurrence of bands suggests that many of the sequences comprising mammalian chromosomes are organized into compartments that have remained relatively stable over long evolutionary time frames. The evolutionary stability is also reflected in the widespread occurrence of conserved non-coding sequences (CNSs), which are scattered throughout the mammalian genome [5].

Similar analyses in angiosperms, however, have consistently failed to reveal such compartmentalization and genome stability. R- and G-bands have not been detected [6] and CNSs are fewer in number, smaller in size and degrade more quickly over evolutionary time compared with mammals (Table 1) [7]. Together these data point to a more fluid and less compartmentalized organization of DNA in angiosperms compared with mammals.

Further organizational differences have been highlighted by chromosome painting techniques that identify individual chromosomes (Figure 1b). Chromosome painting across a range of mammalian species (Figure 1c) has revealed astonishing stability in chromosome structure over millions of years of mammalian divergence, facilitating predictions of the ancestral mammalian karyotype [8]. The data suggest that mammalian chromosome divergence is characterized by relatively few rearrangements of large genomic segments [8].

Chromosome painting, however, like R- and G-banding, has failed in angiosperms. The paints do not localize to individual chromosomes, but instead label much of the genome. Only unusual chromosomes occurring in some species (e.g. sex or B chromosomes) are preferentially

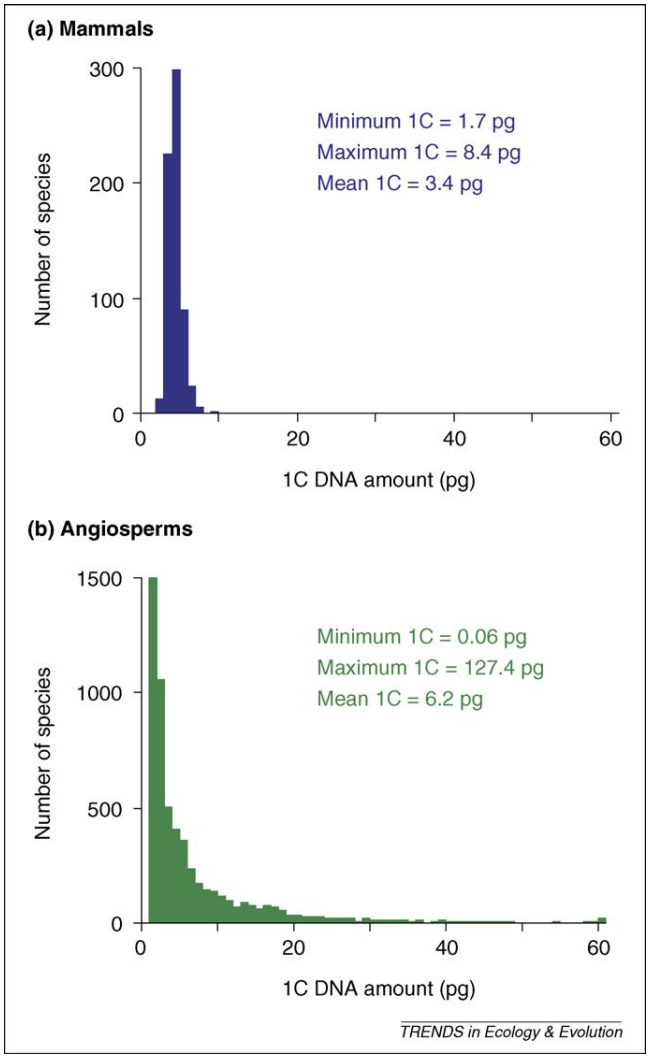

Figure 2. Histograms showing the distribution of genome sizes in mammals and angiosperms. (a) Data for mammals (data for ca. 400 species (656 estimates) taken from the Animal Genome Size database [85]) and (b) angiosperms (data for 5770 species from the Plant DNA C-values database [13] plus additional data not yet incorporated into the database; values for 19 species which are >1C = 60 pg have been binned at 60 pg).

painted because of the accumulation of some repetitive sequences [9,10]. The failure of this technique points to a more dispersed, genome-wide distribution of repeats in angiosperms. To determine the frequency of chromosomal rearrangements in angiosperm evolution, comparative linkage maps have been used. These reveal more chromosomal translocations and local reshuffling of short DNA segments in angiosperms than in mammals, particularly in non-coding regions [11,12] (Table 2).

Genome size and chromosome number: angiosperms have greater diversity than mammals

There are considerable differences in the range and distribution of genome sizes (DNA C-values) and chromosome numbers (Table 1). Angiosperms have a particularly large range of genome sizes (c. 2000-fold) [13] and chromosome numbers ($2n = 4$ to $2n = 640$). This contrasts with the narrower range of genome sizes (five-fold) (Figure 2) and chromosome numbers ($2n = 6$ to $2n = 134$) in mammals.

Such ranges need to be considered in the context of the ages of the groups. The origin of angiosperms is ~140–180 mya and there are now approximately 250 000 species [14], whereas the common ancestor of eutherian mammals evolved ~93 mya [15] and there are approximately 5400 species. Nevertheless, the younger age of mammals is unlikely to be the reason for the reduced diversity of their genomes. Our analysis of the Plant DNA C-values database identified over 60 families and 70 genera with genome sizes varying more than five-fold [13]. Indeed, Orchidaceae, considered to have arisen 110 mya, have genome sizes that range over 160-fold [16]. Collectively these data point to fewer constraints on genome size and chromosome number evolution in angiosperms compared with mammals.

Mechanisms responsible for differences

At the global scale, the picture emerging is that the angiosperm genome is less compartmentalized and more labile than the mammalian genome. We propose that the reasons lie in different activities of four mechanisms primarily responsible for genome divergence: polyploidy, recombination, retrotransposition and gene silencing.

Polyploidy and interspecific hybridization are more important in the divergence of angiosperms than mammals

Polyploidy and interspecific hybridization have played significant roles in the divergence of angiosperms. Indeed, most (maybe all) species have at least one round of polyploidy in their ancestry [17] and at least 25% of species show evidence of interspecific hybridization (Table 2) [18]. In contrast, polyploidy has not played a role in the divergence of mammals, although it is generally recognized that there were two rounds of polyploidy early in vertebrate evolution [19]. The incidence of hybridization is also lower (~6%, [18]). Perhaps angiosperms form hybrids more readily because their gametes are released with only limited targeting systems, in contrast to the internal fertilization and complex mating behaviour of mammals, which limit opportunities for interspecific crosses. Furthermore, through clonal growth, angiosperm hybrids and polyploids can build up numbers of individuals without much, or any, fertility, an option unavailable to mammals.

Polyploidy leads to increases in genome size and gene and allele diversity [20] and, together with local duplications, results in large multigene families in angiosperms [7]. Gene duplication might release functional constraints on copies, enabling them to evolve new or tissue-specific functions, to form pseudogenes or to be deleted [21]. However, many duplicate copies (up to 30% of genes in *Arabidopsis thaliana*) are retained and are perhaps "connected" to generate balanced amounts of gene products in relation to other duplicated genes [22]. Polyploidy and interspecific hybridization can also trigger genetic and epigenetic changes to the genome [23,24]. One consequence of recurrent polyploidy and hybridization in angiosperms is ongoing genome restructuring, inhibiting the establishment of a highly compartmentalized genome.

Recombination: shuffling, incorporation and elimination of DNA occurs more rapidly in angiosperms than mammals

Recombination plays a role in genome evolution because of its involvement in, for example, genomic rearrangements (chromosomal fusions, inversions and translocations), insertions (including organellar DNA), and repair and deletions of DNA sequences (Box 1). Much evidence suggests that recombination rates are higher and activity more variable in angiosperms than in mammals (Table 2) [25], thus leading to differences in genome structure and long-term stability. The higher recombination frequencies are reflected in the greater number of translocations that can occur during species divergence [26–28] and higher linkage map recombination frequencies reported in angiosperms compared with mammals [29,30]. Differences in recombination frequencies are also reflected in different frequencies of illegitimate DNA insertions into the genome via recombination (Box 1). This process provides a constant supply of DNA from a variety of sources from both within and outside the genome, e.g. transposable elements and mitochondrial and plastid DNA. Integration of mitochondrial DNA into the nuclear genome, perhaps involving both homologous and non-homologous recombination, can generate large segments or mosaics of organellar DNA [31]. Such integration occurs more frequently in angiosperms than in mammals [32], generating a higher proportion of nuclear mitochondrial sequences (NUMTs) (Table 1). Plastid DNA also integrates into the angiosperm nucleus; indeed ~18% of nuclear genes in *A. thaliana* are of cyanobacterial (plastid) origin [33].

The insertion of DNA is intimately associated with DNA repair processes [34] for which differences might also exist. In experiments in which protoplasts of tobacco and human HeLa cells were transfected with linear DNA sequences, DNA repair was less precisely regulated and error-prone in tobacco [35].

Increases in genome size generated by newly inserted DNA and polyploidy are counteracted by DNA deletions, a process also requiring the recombination machinery (Box 1). The rates of DNA loss from angiosperm genomes can be astonishingly high. It has been estimated that the half-life of a range of retroelements in *Oryza sativa* (rice)

Box 1. Different roles of DNA recombination in genome evolution: translocations, insertions and deletions

Recombination is the exchange of DNA segments between strands and is usually initiated by double-strand DNA breaks that can be induced naturally or occur accidentally. The process can generate variability in the genome because it results in DNA shuffling, e.g. chromosomal translocations (Figure Ia) and DNA insertions (Figure Ib) and eliminations (Figure Ic). DNA from a variety of sources (e.g. retroelement, plastid, organelle, viral or bacterial DNA) can be inserted into a chromosome illegitimately (ectopic recombination). DNA insertions and eliminations together result in genome turnover.

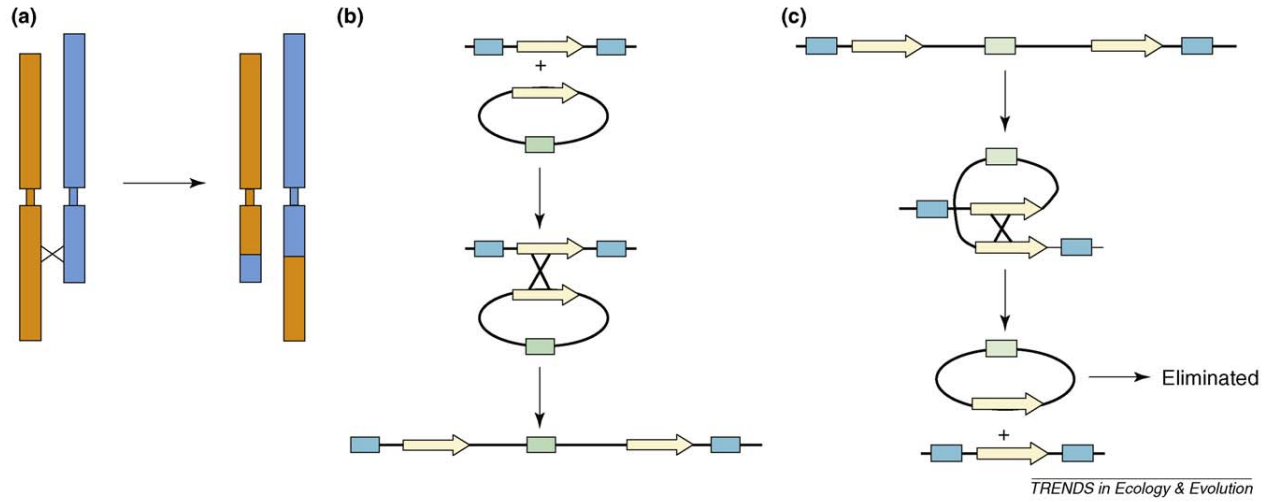

Figure I. DNA recombination. (a) Recombination leading to chromosomal translocations. Recombination between non-homologous chromosomes (brown and pale purple) at X results in two hybrid chromosomes. (b) Recombination leading to DNA insertions. Recombination can insert DNA sequences (circle of DNA) into a linear chromosome (straight DNA). Homologous recombination at X requires some sequence similarity between the donor and recipient DNA strands (arrows), generating a recombinant chromosome that contains structural features of both the target and donor sequences (blue and pale green boxes and arrows). (c) Recombination leading to DNA elimination from a linear chromosome. This occurs through alignment of two identical or similar sequences (arrows) along the chromosome, perhaps brought about as a natural part of chromosome folding or through the twisting of DNA strands. Once aligned, recombination at X leads to the elimination of DNA (circle of DNA). This might occur between, for example, the long terminal repeats (arrows) of an LTR retroelement, resulting in elimination of most of the element but leaving behind a solo LTR.

is less than a few million years (Table 2) [36] and 80% of nuclear insertions of plastid genes might disappear within one million years [37]. Although we are unaware of similar data for mammals, it is noteworthy that chromosome paints remain effective between species despite ~93 million years of divergence [8,15], suggesting the conservation of non-coding DNA sequences over long time frames.

Higher recombination rates in angiosperms than in mammals result in more translocations, enhanced integration of sequences, faster DNA deletion and more error-prone DNA repair. Recombination will blur genome substructure more extensively in angiosperms than mammals and contribute to a more dynamic and fluid genome structure. However, it is not clear what causes the difference in recombination rates. It might relate to the higher proportion of repetitive DNA in angiosperms (particularly in species with large genomes), providing multiple substrates for homologous recombination. Indeed, long terminal repeat (LTR) retrotransposons, which are abundant in angiosperms but not mammals (see below and Table 1), are good substrates for ectopic recombination because the LTRs can recombine, leaving behind solo LTRs [38] (Box 1). The larger number of multigene families [7] in angiosperms than in mammals (Table 1) might also provide more sites for homologous recombination. In addition, the size of mammalian and angiosperm genes might play a role. The average total exon lengths are similar, but typically the entire gene is larger in mammals owing to greater intron lengths [39] (Table 1). Indeed mammalian introns form a substantial component of non-coding DNA [40], unlike angiosperms, for which most non-coding DNA is intergenic. In *Drosophila melanogaster* an inverse correlation exists between intron length and recombination frequency per kilobase of DNA [41], perhaps because of a selective advantage conferred by recombining exons separated by short introns [42]. If this relationship holds for angiosperms and mammals, the shorter introns of angiosperms might also contribute to higher recombination frequencies.

Retroelements are more mobile and diverse in angiosperms than mammals

In both angiosperms and mammals the most significant and abundant mobile elements are retrotransposons, which are major determinants of genome structure and evolution. Angiosperms contain predominantly LTR retrotransposons belonging to the *copia* and *gypsy* superfamilies [43]. Within these there is massive diversity, with thousands or tens of thousands of elements contributing up to 80% of the genome in some species [44]. LTR retrotransposons are less abundant, diverse and active in mammals. Instead the non-LTR retrotransposon classes LINEs (long interspersed nuclear elements) and non-autonomous SINEs (short interspersed nuclear elements) predominate [45]. Angiosperms have higher background levels of retrotransposition than mammals, often caused by bursts of activity associated with hybridization, polyploidy [46,47]

or stress [48]. However, they can also have a short half-life, as already mentioned [36,38].

Retroelement amplification by retrotransposition and removal by ectopic recombination lead to retroelement turnover. We suggest that both processes are more frequent in angiosperms (Table 2), contributing to a loss of genome substructure and higher rates of genome divergence compared with mammals [49]. Nevertheless, recombination between retroelements does occur in mammals. Indeed, it is estimated that at least 0.3% of human genetic diseases occur because of unequal recombination between *Alu* elements (SINE class of non-LTR retrotransposons) [50].

Collectively, recombination and retrotransposition lead to homogenization of sequences between and within chromosomes, although rates are generally thought to be higher within chromosomes (intrachromosomal homogenization) [51–53]. In mammals this would contribute to the divergence of chromosomes and the formation of a compartmentalized structure. However, in angiosperms the rates of intrachromosomal and interchromosomal homogenization are similar, perhaps because of high levels of retrotransposition and ectopic recombination between chromosomes [54], leading to a less well-structured genome. Lower frequencies of intrachromosomal recombination [55] would have the same outcome, but this is less likely in angiosperms because of considerable interchromosomal mobility of repetitive sequences [54].

Is gene silencing more focussed in angiosperms than mammals?

There is evidence of fundamental differences in gene silencing and defence mechanisms between angiosperms and mammals (Table 2). In mammals, there is low complementarity of miRNAs to their targets and thus individual miRNAs can influence a broad set of genes or sequences across the genome, a mechanism thought to facilitate regulation and fine-tuning of gene expression [56]. In angiosperms, it is generally thought that interactions are more specific, resulting in more focused and localized effects, although recent data for *A. thaliana* question these assertions [57].

Our understanding of RNAi is in its infancy but is growing rapidly. Recent models suggest that miRNAs might have evolved from siRNA involved in transposable element suppression [58]. Given that there are higher levels of nuclear DNA insertions (e.g. plastid and mitochondrial DNA) and retrotransposition in angiosperms than in mammals, this might suggest different RNAi activities (e.g. roles of siRNA, piRNA) in element suppression. Indeed the abundance, copy numbers and diversity of retrotransposons in angiosperms suggest that individual elements have frequently escaped silencing regulation in the divergence of the group. This is despite RNAi-directed DNA methylation (RdDM) and RNA-dependent RNA polymerase (RdRP), currently only known in angiosperms, which presumably evolved to limit such activity.

What are the causes and consequences of such different modes of genome evolution?

Evolutionary processes such as selection and genetic drift influence the mode and activity of mechanisms that are primarily responsible for generating patterns of genome structure. Here we explore how differences in developmental processes and life strategies might feed back on these mechanisms to generate the different genome organizational patterns observed in angiosperms and mammals (summarized in Figure 3).

Genome structure and development

Do fundamental differences in development drive genomic differences between angiosperms and mammals? Angiosperms have three developmental features that are absent in mammals: (1) alternation of generations resulting in two distinct life phases, the haploid gametophyte (embryo sac and pollen) and the sporophyte (diploid); (2) double fertilization in most species, forming a zygote (sporophyte) and a triploid endosperm that nourishes the zygote; and (3) the absence of a sequestered germ line [59].

A consequence of alternation of generations and double fertilization is that many genes must function in three different dosages: single dosage (gametophyte), double dosage (zygote) and triple dosage (endosperm). Further complexity arises from multiple rounds of polyploidy in the recent and/or ancient evolutionary history of angiosperms [17]. This tolerance to different ploidy levels in somatic dividing cells might predispose angiosperms to germ line polyploidy and perhaps explains why it is so prevalent in angiosperms.

The sequestration of a germ line early in mammalian development means that there are relatively few cell divisions leading to gamete formation, particularly in oogenesis [60] (Table 2). By contrast, there is no sequestration of the germ line in angiosperms; instead, gametes are formed from somatic cells in the apical meristems. Even ephemeral species such as *A. thaliana* with short generation times (7 weeks) undergo many hundreds of divisions between the seeds of one generation and those of the next [61]. For the majority of angiosperms this number is likely to be order(s) of magnitude larger. Because the number of mutations and cell divisions are positively correlated [62], there are many more opportunities for mutations to arise compared with mammals. Furthermore, whereas the mammalian germ line is largely protected from the environment, the angiosperm germ line is vulnerable to environmental stresses that can also stimulate mutations and retrotransposition [48].

Angiosperms are characterized by plasticity in their development, resulting in a high degree of phenotype variability, even between individuals of the same species. Morphology is also greatly influenced by environmental conditions and individuals in different habitats can express different phenotypes [63]. In evolution, this plasticity can be reflected in rapid morphological divergence, as observed, for example, in the silverswords of Hawaii, for which species have diverged into small rosette-forming plants, shrubs, vines and large trees within six million years [64]. In contrast to angiosperms, mammals have a highly constrained development that is controlled by well-tuned and coordinated developmental pathways. Among these, genomic imprinting is important for development and arises through global repatterning of DNA methylation during gametogenesis. In angiosperms, genomic imprinting is exhibited by

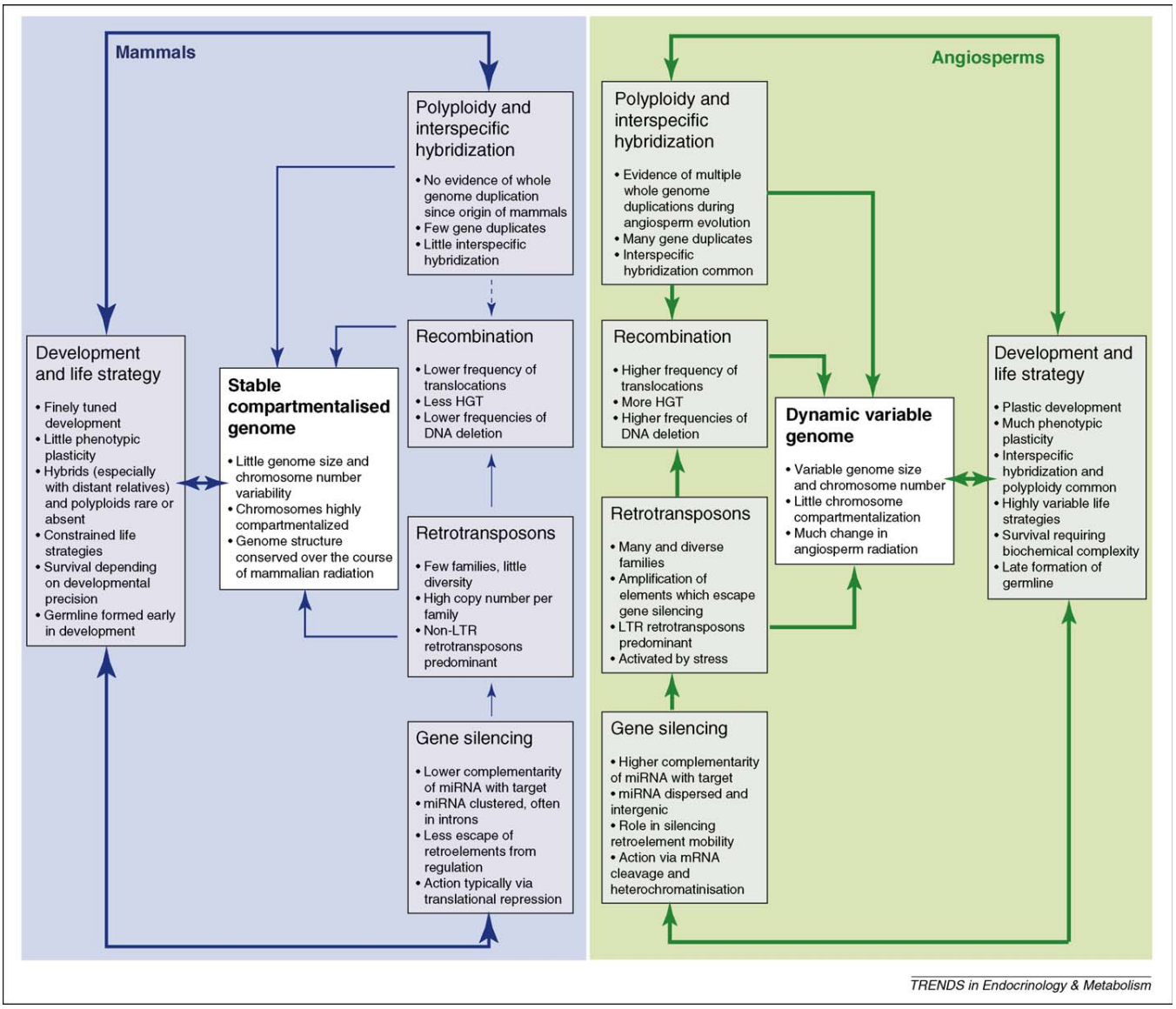

Figure 3. Different interrelationships and their relative strengths, represented by the direction and thickness of the arrows, between mechanisms generating genomic change and the life strategy options and developmental constraints in mammals and angiosperms. HGT refers to Horizontal Gene Transfer, the integration of DNA from sources outside of the nucleus.

only some genes of the endosperm, a tissue that does not contribute to the germ line [65,66]. Potentially, global repatterning would trigger catastrophic release of elements already largely responsible for high rates of genome divergence (e.g. retrotransposons). In any case, advantages conferred by developmental plasticity in angiosperms might provide little selective pressure for the evolution of genomic imprinting.

Genome structure and life strategies

Different life strategies might drive genomic differences between angiosperms and mammals (Figure 3). Mammals are capable of high levels of mobility, enabling them to find food and mates and escape disease, predation and adverse conditions. Associated with this is a highly complex, yet constrained pattern of development [67]. In contrast, the sessile nature of angiosperms means that they cannot readily escape adverse conditions, herbivores and poor environmental conditions or attract pollinators. Instead their survival depends on being able to respond to adverse conditions through biochemical complexity and developmental plasticity, the tool kit for plant survival [68,69]. This is reflected in the large number of genes (perhaps 25% of the total) involved in the production of secondary metabolites [70].

Perhaps by adopting the mammalian life strategy the genome itself becomes constrained, because genomic reorganization (e.g. via retrotransposition, polyploidy and ectopic recombination) is likely to be detrimental to a finely tuned, developmentally complex system and thus should be selected against. In contrast, the sessile life strategy of angiosperms requiring developmental plasticity might mitigate against the evolution of developmental complexity. Indeed, genomic restructuring could be an advantage to angiosperms because it can generate biochemical complexity [23,71]. For example, a major component of the abiotic and biotic stress response is the activation of retrotransposons [48] and increased frequency of recombination

[72]. Selection against such change might be less severe in angiosperms than mammals because of the robustness of their biological systems. The lack of a sequestered germ line and the large number of offspring typical of many angiosperms mean that there are many opportunities for generating variation upon which selection can act. However, the effects of genetic drift versus selection in fixing such variation is influenced by the effective population size (N_e) [73]. Whereas small N_e values for angiosperms might explain some of the variability in their genome structure (favouring the effects of drift) [73], there is no reason to suppose that angiosperm N_e values are materially smaller than those of mammals, making it unlikely that genetic drift has had a greater impact on their genome evolution.

There might be relationships between genome size and life strategy, particular in the upper limits of the c.2000-fold range of genome sizes found in angiosperms. Nucleic acids are an expensive resource for plants because nitrates and phosphates must be harvested from the environment and are frequently in limiting supply [74]. Furthermore, the time taken to replicate DNA in the cell cycle increases with genome size [75]. Consequently, angiosperms with larger genomes are more restricted in the type of life history strategies and habitats they can adopt and are less able to adapt to changing environments [74]. Indeed this might explain, in part, the highly skewed distribution of genome sizes encountered in angiosperms (Figure 2). For mammals, synthesis of DNA is not limiting because their food source has plentiful DNA and RNA. However, mammals are characterized by a narrow range of small genome sizes, perhaps to maximize energy flows for an active, dynamic life strategy. Indeed, bats have the smallest mammalian genomes recorded, perhaps reflecting their need to minimize body weight (there are significant correlations between genome size and cell size) and maximize energetics for flight (there is an inverse correlation between cell size and metabolic rate) [76].

Comparisons with other systems

Our proposed hypotheses that life strategy and development might be important determinants of genome structure need to be tested against other eukaryoytic groups. We are unaware of many fundamental differences among other vertebrates that set mammals apart from the rest, although comparable depths of data are lacking. Nevertheless, considerable effort is being expended to resolve these deficiencies and recent genomic studies in the platypus have shown that this early diverging mammal has some features similar to reptiles (e.g. abundant widespread microsatellite sequences [77]). In addition, although polyploidy is absent in mammals, it has occurred in the divergence of many groups of fish [78] and occurs in amphibians and reptiles.

Among land plants, polyploidy is common in monilophytes (ferns and horsetails, >90% of species) but is rare in gymnosperms (<5% of species). Gymnosperms are considered to be developmentally constrained in comparison with angiosperms and have less phenotypic and morphological diversity (e.g. there are no annual gymnosperms).

Comparative genome analyses and wide phylogenetic coverage do exist for insects that have constrained development and are perhaps more similar to mammals than angiosperms. Some features of their genomes are similar to those of mammals: (a) polyploidy is rare [79]; (b) among dipterans (an early diverging group, ~331 mya, [80]) chromosomes are highly structured, as revealed by banding on polytene chromosomes; (c) comparative genomic analyses of *Drosophila* and *Anopheles* revealed orthologous genes in syntenic groups [81] despite diverging >250 mya [82], and; (d) in the grasshopper *Podisma pedestris* (Orthoptera, diverged ~371 mya), ribosomal DNA sequences have escaped homogenization for millions of years [83]. However, species in Orthoptera do not produce fine-structured chromosome banding patterns as in Diptera and analysis of recombination frequencies in different insects reveals considerable variation. Whereas some (e.g. *Drosophila melanogaster*, 1.59 cM/Mb) have rates similar to those found in mammals, others are higher, with the highest rate recorded for the honey bee (*Apis mellifera*, 19 cM/Mb) which is greater even than that reported for angiosperms (Table 2) [29,30].

With increasing numbers of genome sequences from a range of eukaryotes becoming available, further and fuller comparisons between and within major groups will become possible. Thus, a clearer picture of the significance of differences between genomes will emerge. This will facilitate testing of hypotheses as to how life strategies and developmental pathways influence, or are influenced by, genome structure.

Acknowledgement

We would like to thank Mr M. Chester, Dr J. Cotton, Dr R. Hobza, Dr A. Kovarik, Dr J. Macas, Prof. R.A. Nichols, Mr S. Renny-Byfield, Prof. B. Vyskot and four anonymous referees for valuable comments. This research was supported by the NERC, grant LC06004 from the Ministry of Education and grant nos AV0Z50040507 and AV0Z50040702 from the Academy of Sciences of the Czech Republic. EK dedicates this paper to his mother, Zdenka Kejnovska.

References

1 Keeling, P.J. *et al.* (2005) The tree of eukaryotes. *Trends Ecol. Evol.* 20, 670–676
2 Costantini, M. and Bernardi, G. (2008) The short-sequence designs of isochores from the human genome. *Proc. Natl. Acad. Sci. U. S. A.* 105, 13971–13976
3 Árnason, U. (1972) The role of chromosomal rearrangements in mammalian speciation with special reference to Cetacea and Pinnipedia. *Hereditas* 70, 113–118
4 Trifonov, V.A. *et al.* (2008) Multidirectional cross-species painting illuminates the history of karyotypic evolution in Perissodactyla. *Chromosome Res.* 16, 89–107
5 Elgar, G. and Vavouri, T. (2008) Tuning in to the signals: noncoding sequence conservation in vertebrate genomes. *Trends Genet.* 24, 344–352
6 Friebe, B. *et al.* (1996) Chromosome banding methods. In *Plant Chromosomes – Laboratory Methods* (Fukui, K. and Nakayama, S., eds), pp. 123–153, CRC Press
7 Lockton, S. and Gaut, B.S. (2005) Plant conserved non-coding sequences and paralogue evolution. *Trends Genet.* 21, 60–65
8 Ferguson-Smith, M.A. and Trifonov, V. (2007) Mammalian karyotype evolution. *Nat. Rev. Genet.* 8, 950–962
9 Houben, A. *et al.* (2001) The genomic complexity of micro B chromosomes of *Brachycome dichromosomatica*. *Chromosoma* 110, 451–459
10 Kejnovsky, E. *et al.* (2009) The role of repetitive DNA in structure and evolution of sex chromosomes in plants. *Heredity* 102, 533–541

11 Bowers, J.E. *et al.* (2005) Comparative physical mapping links conservation of microsynteny to chromosome structure and recombination in grasses. *Proc. Natl. Acad. Sci. U. S. A.* 102, 13206–13211
12 Tang, H.B. *et al.* (2008) Synteny and collinearity in plant genomes. *Science* 320, 486–488
13 Bennett, M.D. and Leitch, I.J. (2005) Plant DNA C-values database release 4.0.(http://data.kew.org/cvalues/homepage)
14 Soltis, D.E. *et al.* (2008) Origin and early evolution of angiosperms. *Ann. N. Y. Acad. Sci.* 1133, 3–25
15 Bininda-Emonds, O.R.P. *et al.* (2007) The delayed rise of present-day mammals. *Nature* 446, 507–512
16 Leitch, I.J. *et al.* (2009) Genome size diversity in orchids – consequences and evolution. *Ann. Bot.* 104, 469–481
17 Soltis, D.E. *et al.* (2009) Polyploidy and angiosperm diversification. *Am. J. Bot.* 96, 336–348
18 Mallet, J. (2005) Hybridization as an invasion of the genome. *Trends Ecol. Evol.* 20, 229–237
19 Holland, L.Z. *et al.* (2008) The amphioxus genome illuminates vertebrate origins and cephalochordate biology. *Genome Res.* 18, 1100–1111
20 Soltis, P.S. and Soltis, D.E. (2000) The role of genetic and genomic attributes in the success of polyploids. *Proc. Natl. Acad. Sci. U. S. A.* 97, 7051–7057
21 Semon, M. and Wolfe, K.H. (2007) Consequences of genome duplication. *Curr. Opin. Genet. Dev.* 17, 505–512
22 Thomas, B.C. *et al.* (2006) Following tetraploidy in an *Arabidopsis* ancestor, genes were removed preferentially from one homeolog leaving clusters enriched in dose-sensitive genes. *Genome Res.* 16, 934–946
23 Chen, Z.J. (2007) Genetic and epigenetic mechanisms for gene expression and phenotypic variation in plant polyploids. *Annu. Rev. Plant Biol.* 58, 377–406
24 Adams, K.L. and Wendel, J.F. (2005) Polyploidy and genome evolution in plants. *Curr. Opin. Plant Biol.* 8, 135–141
25 Gaut, B.S. *et al.* (2007) Recombination: an underappreciated factor in the evolution of plant genomes. *Nat. Rev. Genet.* 8, 77–84
26 Stanyon, R. *et al.* (1999) Reciprocal chromosome painting shows that genomic rearrangement between rat and mouse proceeds ten times faster than between humans and cats. *Cytogenet. Cell Genet.* 84, 150–155
27 Yogeeswaran, K. *et al.* (2005) Comparative genome analyses of *Arabidopsis* spp: Inferring chromosomal rearrangement events in the evolutionary history of A. thaliana. *Genome Res.* 15, 505–515
28 Lagercrantz, U. (1998) Comparative mapping between *Arabidopsis thaliana* and *Brassica nigra* indicates that *Brassica* genomes have evolved through extensive genome replication accompanied by chromosome fusions and frequent rearrangements. *Genetics* 150, 1217–1228
29 Beye, M. *et al.* (2006) Exceptionally high levels of recombination across the honey bee genome. *Genome Res.* 16, 1339–1344
30 Singer, T. *et al.* (2006) A high-resolution map of *Arabidopsis* recombinant inbred lines by whole-genome exon array hybridization. *PLoS Genet.* 2, 1352–1361
31 Noutsos, C. *et al.* (2005) Generation and evolutionary fate of insertions of organelle DNA in the nuclear genomes of flowering plants. *Genome Res.* 15, 616–628
32 Leister, D. (2005) Origin, evolution and genetic effects of nuclear insertions of organelle DNA. *Trends Genet.* 21, 655–663
33 Martin, W. *et al.* (2002) Evolutionary analysis of *Arabidopsis*, cyanobacterial, and chloroplast genomes reveals plastid phylogeny and thousands of cyanobacterial genes in the nucleus. *Proc. Natl. Acad. Sci. U. S. A.* 99, 12246–12251
34 Triant, D.A. and DeWoody, J.A. (2008) Molecular analyses of mitochondrial pseudogenes within the nuclear genome of arvicoline rodents. *Genetica* 132, 21–33
35 Pelczar, P. *et al.* (2003) Different genome maintenance strategies in human and tobacco cells. *J. Mol. Biol.* 331, 771–779
36 Ma, J.X. *et al.* (2004) Analyses of LTR-retrotransposon structures reveal recent and rapid genomic DNA loss in rice. *Genome Res.* 14, 860–869
37 Matsuo, M. *et al.* (2005) The rice nuclear genome continuously integrates, shuffles, and eliminates the chloroplast genome to cause chloroplast-nuclear DNA flux. *Plant Cell* 17, 665–675
38 Vicient, C.M. *et al.* (1999) Retrotransposon BARE-1 and its role in genome evolution in the genus *Hordeum*. *Plant Cell* 11, 1769–1784
39 Deutsch, M. and Long, M. (1999) Intron–exon structures of eukaryotic model organisms. *Nucleic Acids Res.* 27, 3219–3228
40 Wong, GK-S. *et al.* (2000) Is "junk" DNA mostly intron DNA? *Genome Res.* 10, 1672–1678
41 Comeron, J.M. and Kreitman, M. (2000) The correlation between intron length and recombination in *Drosophila*: Dynamic equilibrium between mutational and selective forces. *Genetics* 156, 1175–1190
42 Duret, L. (2001) Why do genes have introns? Recombination might add a new piece to the puzzle. *Trends Genet.* 17, 172–175
43 Wicker, T. and Keller, B. (2007) Genome-wide comparative analysis of *copia* retrotransposons in Triticeae, rice, and *Arabidopsis* reveals conserved ancient evolutionary lineages and distinct dynamics of individual *copia* families. *Genome Res.* 17, 1072–1081
44 Kumar, A. and Bennetzen, J.L. (1999) Plant retrotransposons. *Annu. Rev. Genet.* 33, 479–532
45 Wicker, T. *et al.* (2007) A unified classification system for eukaryotic transposable elements. *Nat. Rev. Genet.* 8, 973–982
46 Liu, B. and Wendel, J.F. (2000) Retrotransposon activation followed by rapid repression in introgressed rice plants. *Genome* 43, 874–880
47 Voytas, D.F. and Naylor, G.J.P. (1998) Rapid flux in plant genomes. *Nat. Genet.* 20, 6–7
48 Grandbastien, M.A. (1998) Activation of plant retrotransposons under stress conditions. *Trends Plant Sci.* 3, 181–187
49 Lim, K.Y. *et al.* (2007) Sequence of events leading to near-complete genome turnover in allopolyploid *Nicotiana* within five million years. *New Phytol.* 175, 756–763
50 Deininger, P.L. and Batzer, M.A. (2002) Mammalian retroelements. *Genome Res.* 12, 1455–1465
51 Hood, M.E. *et al.* (2005) Repeat-induced point mutation and the population structure of transposable elements in *Microbotryum violaceum*. *Genetics* 170, 1081–1089
52 Kejnovsky, E. *et al.* (2007) High intrachromosomal similarity of retrotransposon long terminal repeats: Evidence for homogenization by gene conversion on plant sex chromosomes? *Gene* 390, 92–97
53 Krzywinski, J. *et al.* (2005) Satellite DNA from the Y chromosome of the malaria vector *Anopheles gambiae*. *Genetics* 169, 185–196
54 Zhao, X.P. *et al.* (1998) Dispersed repetitive DNA has spread to new genomes since polyploid formation in cotton. *Genome Res.* 8, 479–492
55 Lukacsovich, T. and Waldman, A.S. (1999) Suppression of intrachromosomal gene conversion in mammalian cells by small degrees of sequence divergence. *Genetics* 151, 1559–1568
56 Groszhans, H. and Filipowicz, W. (2008) Molecular biology: The expanding world of small RNAs. *Nature* 451, 414–416
57 Brodersen, P. *et al.* (2008) Widespread translational inhibition by plant miRNAs and siRNAs. *Science* 320, 1185–1190
58 Piriyapongsa, J. and Jordan, I.K. (2008) Dual coding of siRNAs and miRNAs by plant transposable elements. *RNA* 14, 814–821
59 Walbot, V. and Evans, M.M.S. (2003) Unique features of the plant life cycle and their consequences. *Nat. Rev. Genet.* 4, 369–379
60 Hurst, L.D. and Ellegren, H. (1998) Sex biases in the mutation rate. *Trends Genet.* 14, 446–452
61 Fajkus, J. *et al.* (2005) Telomeres in evolution and evolution of telomeres. *Chromosome Res.* 13, 469–479
62 Ellegren, H. (2007) Characteristics, causes and evolutionary consequences of male-biased mutation. *Proc. R. Soc. B Biol. Sci.* 274, 1–10
63 Raven, P.H. *et al.* (2005) *Biology of Plants.* (7th edn), W.H. Freeman & Co
64 Witter, M.S. and Carr, G.D. (1988) Adaptive radiation and genetic differentiation in the Hawaiian silversword alliance (Compositae, Madiinae). *Evolution* 42, 1278–1287
65 Scott, R.J. and Spielman, M. (2006) Genomic imprinting in plants and mammals: how life history constrains convergence. *Cytogenet. Genome Res.* 113, 53–67
66 Kinoshita, T. *et al.* (2008) Genomic imprinting: A balance between antagonistic roles of parental chromosomes. *Semin. Cell Dev. Biol.* 19, 574–579
67 Wheeler, B.M. *et al.* (2009) The deep evolution of metazoan microRNAs. *Evol. Dev.* 11, 50–68

68 Leitch, A.R. and Leitch, I.J. (2008) Genomic plasticity and the diversity of polyploid plants. *Science* 320, 481–483
69 Wilczek, A.M. *et al.* (2009) Effects of genetic perturbation on seasonal life history plasticity. *Science* 323, 930–934
70 Szathmary, E. *et al.* (2001) *Molecular biology and evolution – can genes explain biological complexity? Science* 292, 1315–1316
71 Pearse, I.S. *et al.* (2006) Innovation in anti-herbivore defense systems during neopolypoloidy – the functional consequences of instantaneous speciation. *Plant J.* 47, 196–210
72 Lebel, E.G. *et al.* (1993) Stress-induced intrachromosomal recombination in plant somatic cells. *Proc. Natl. Acad. Sci. U. S. A.* 90, 422–426
73 Lynch, M. and Conery, J.S. (2003) The origins of genome complexity. *Science* 302, 1401–1404
74 Leitch, I.J. and Bennett, M.D. (2007) Genome size and its uses: the impact of flow cytometry. In *Flow Cytometry with Plant Cells* (Doležel, J. and et, al., eds), pp. 153–176, Wiley-VCH
75 Francis, D. *et al.* (2008) A strong nucleotypic effect of DNA C-value on the cell cycle regardless of ploidy level. *Ann. Bot.* 101, 747–757
76 Gregory, T.R. (2005) Genome size evolution in animals. In *The Evolution of the Genome* (Gregory, T.R., ed.), pp. 3–87, Elsevier
77 Warren, W.C. *et al.* (2008) Genome analysis of the platypus reveals unique signatures of evolution. *Nature* 453, 175–184
78 Le Comber, S.C. and Smith, C. (2004) Polyploidy in fishes: patterns and processes. *Biol. J. Linn. Soc.* 82, 431–442
79 Lokki, J. and Saura, A. (1980) Polyploidy in insect evolution. In *Polyploidy Biological Relevance* (Lewis, W.H., ed.), pp. 277–312, Plenum Press
80 Gaunt, M.W. and Miles, M.A. (2002) An insect molecular clock dates the origin of the insects and accords with palaeontological and biogeographic landmarks. *Mol. Biol. Evol.* 19, 748–761
81 Bolshakov, V.N. *et al.* (2002) A comparative genomic analysis of two distant Diptera, the fruit fly, *Drosophila melanogaster*, and the malaria mosquito, *Anopheles gambiae*. *Genome Res.* 12, 57–66
82 Yeates, D.K. and Wiegmann, B.M. (1999) Congruence and controversy: Toward a higher-level phylogeny of Diptera. *Annu. Rev. Entomol.* 44, 397–428
83 Keller, I. *et al.* (2006) Ribosomal DNA in the grasshopper *Podisma pedestris*: Escape from concerted evolution. *Genetics* 174, 863–874
84 Ried, T., Schrock, E., Ning, Y. and Wienberg, J. (1998) Chromosome painting: a useful art. *Hum. Mol. Genet.* 7, 1619–1626
85 Gregory, T.R. (2006) Animal genome size database, rel. 2.0.(http://www.genomesize.com)
86 Ohno, S. (2000) Conservation of linkage relationships between genes as the underlying theme of karyological evolution in mammals. In *Chromosomes in Evolution of Eukaryotic Groups (Vol. II)* (Sharma, A.K. and Sharma, A., eds), pp. 1–11, CRC Press
87 Robinson, T.J. *et al.* (2004) Cross-species chromosome painting in the golden mole and elephant-shrew: support for the mammalian clades Afrotheria and Afroinsectiphillia but not Afroinsectivora. *Proc. R. Soc. Lond. Ser. B Biol. Sci.* 271, 1477–1484
88 Freeling, M. and Subramaniam, S. (2009) Conserved noncoding sequences (CNSs) in higher plants. *Curr. Opin. Plant Biol.* 12, 126–132
89 Ren, X.Y. *et al.* (2006) In plants, highly expressed genes are the least compact. *Trends Genet.* 22, 528–532
90 Kenton, A. *et al.* (1993) Does genome organization influence speciation? A reappraisal of karyotype studies in evolutionary biology. In *Evolutionary Patterns and Processes* (Lees, D.R. and Edwards, D., eds), pp. 189–206, Academic Press
91 Gissi, C. *et al.* (2008) Evolution of the mitochondrial genome of Metazoa as exemplified by comparison of congeneric species. *Heredity* 101, 301–320
92 Palmer, J.D. *et al.* (2000) Dynamic evolution of plant mitochondrial genomes: Mobile genes and introns and highly variable mutation rates. *Proc. Natl. Acad. Sci. U. S. A.* 97, 6960–6966
93 Richly, E. and Leister, D. (2004) NUMTs in sequenced eukaryotic genomes. *Mol. Biol. Evol.* 21, 1081–1084
94 Woischnik, M. and Moraes, C.T. (2002) Pattern of organization of human mitochondrial pseudogenes in the nuclear genome. *Genome Res.* 12, 885–893
95 Batzer, M.A. and Deininger, P.L. (2002) Alu repeats and human genomic diversity. *Nat. Rev. Gen.* 3, 370–379
96 Kidwell, M.G. (2005) Transposable elements. In *The Evolution of the Genome* (Gregory, T.R., ed.), pp. 165–223, Elsevier
97 Alexandrov, I. *et al.* (2001) Alpha-satellite DNA of primates: old and new families. *Chromosoma* 110, 253–266
98 Lim, K.Y. *et al.* (2006) Comparative genomics and repetitive sequence divergence in the species of diploid *Nicotiana* section *Alatae*. *Plant J.* 48, 907–919
99 Gallardo, M.H. *et al.* (2004) Whole-genome duplications in South American desert rodents (Octodontidae). *Biol. J. Linn. Soc.* 82, 443–451
100 Rabinowicz, P.D. and Bennetzen, J.L. (2006) The maize genome as a model of efficient sequence analysis of large plant genomes. *Curr. Opin. Plant Biol.* 9, 149–156
101 Scott, R.J. and Spielman, M. (2004) Epigenetics: Imprinting in plants and mammals – the same but different? *Curr. Biol.* 14, R20–-R203
102 Matzke, M.A. and Birchler, J.A. (2005) RNAi-mediated pathways in the nucleus. *Nature Rev. Genet.* 6, 24–35
103 Ikegami, M. and Fraenkelconrat, H. (1978) RNA-dependent RNA-polymerase of tobacco plants. *Proc. Natl. Acad. Sci. U. S. A.* 75, 2122–2124
104 Lim, L.P. *et al.* (2003) Vertebrate microRNA genes. *Science* 299, 1540–11540
105 Millar, A.A. and Waterhouse, P.M. (2005) Plant and animal microRNAs: similarities and differences. *Funct. Integr. Genomics* 5, 129–135