Animal Cells and Systems
Vol. 16, No. 6, December 2012, 438–446

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Reanalysis of Ohno's hypothesis on conservation of the size of the X chromosome in mammals

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(*Received 3 May 2012; received in revised form 16 July 2012; accepted 22 August 2012*)

In 1964, Susumu Ohno, an evolutionary biologist, hypothesized that the size of X chromosome was conserved in mammalian evolution, and that this was based on chromosomal length. Today, unlike Ohno's method which was based on estimated lengths, we know the exact lengths of some mammalian sequences. The aim of this study was to reanalyze Ohno's hypothesis. In mammalian species, variation in the length of the X chromosome is greater than in the autosomes; however, this variation is not statistically significant. This means that differences in chromosomal length occur equally in the X chromosome and in the autosomes. Interspersed nuclear elements and genetic rearrangements were analyzed to maintain the same variance between the length of the X chromosome and the autosomes. The X chromosome contained fewer short interspersed elements (SINEs) (0.90 on average); however, it did contain more long interspersed elements (LINEs) than did autosomes (1.56 on average). An overall correlation of LINEs and SINEs with genetic rearrangements was observed; however, synteny breaks were more closely associated with LINEs in the autosomes, and with SINEs in the X chromosome. These results suggest that the chromosome-specific activities of LINEs and SINEs result in the same variance between the lengths of the X chromosome and the autosomes. This is based on the function of interspersed nuclear elements, such as LINEs, which can inactivate the X chromosome and the reliance of non-autonomous SINEs on LINEs for transposition.

Keywords: LINE; mammals; Ohno's hypothesis; SINE; X chromosome

Introduction

In mammals, males have X and proto-Y sex chromosomes that are differentiated from an autosomal pair (Ross et al. 2005). There is no recombination between these sex chromosomes, and the sex-determining SRY gene is isolated, which results in a progressive degradation of the Y chromosome (Graves et al. 2006; Yang et al. 2011). As a result, unlike the diploid chromosomes in the autosomes, the sex chromosomes are classified into two atypical groups: XY in males and XX in females. The Y chromosome contains a handful of genes with specialized functions in male sex determination and reproduction (Graves et al. 2006). This highlights the importance of dosage compensation for X-linked gene products.

Dosage compensation is important on two fronts. First, to achieve equal amounts of genetic product in both sexes, a dosage compensation-related X-linked gene is created by inactivation of one of the two X chromosomes (Lyon 1961; Heard and Disteche 2006). Second, dosage compensation is used to double the product output rate of each X-linked gene to eliminate both haploinsufficiency and the damaging effects of monosomic expression of the X chromosome (Ohno 1967; Nguyen and Disteche 2006). Both of these functions of dosage compensation are widely accepted by biologists, have formed the foundation of sex chromosome-related research, and are often referred to as 'Ohno's law.' Wolf, a colleague of Ohno, first coined the phrase, 'Ohno's law' in 1998, and stated that the finding of a roughly equal X chromosome-to-autosome ratio and a similar absolute size of the X chromosome in various mammalian species prompted the speculation that the X chromosome was conserved during mammalian evolution and retained the genetic constitution of a common ancestor (Wolf 1998). Ohno discovered that the original X chromosomes of a common ancestor were maintained intact by most, if not all, placental mammals (Ohno 1969). This discovery was based on measurements of X chromosomes from 'two-dimensional measurements of chromosomes' in which the X chromosomes of placental mammals (human, cow, donkey, horse, cat, dog, and mouse) were all similar in size and formed little more than 5% of the haploid set (Ohno et al. 1964). To highlight the consistency in the absolute size of the mammalian X chromosome, Ohno proposed that X chromosome-to-autosome translocation during evolution had caused an incompatibility with speciation (Fujita et al. 2011). The part of the X chromosome translocated to the autosome is not properly inactivated by the X chromosome inactivation mechanism, and it acts locally and *in cis* (White et al. 1998; Sharp et al. 2002; Lee 2009). This renders it incapable of satisfying the desirable dosage compensation and results in an imbalanced X-linked gene expression. Nor is it able to satisfy the dosage compensation when *in trans*. An imbalanced expression of the chromosome often has a negative effect on the phenotype (Epstein 2007). A dosage imbalance such as

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ISSN 1976-8354 print/ISSN 2151-2485 online

http://dx.doi.org/10.1080/19768354.2012.724709
http://www.tandfonline.com

monosomy is not well tolerated in mammals (Birchler et al. 2005). To agree with the dosage compensation model hypothesized by Ohno, two arguments are needed; first, the X chromosome has to be conserved among species; second, X-linked gene expression must be doubled or hypertranscribed.

With regard to the doubling of X-linked gene expression, there are arguments for and against the up-regulated X-linked genes causing disomic expression levels to balance those between autosomes. DNA microarray analysis of *C. elegans* and the mouse showed that the transcription level patterns of the X chromosomes of both species were similar, not only in male and female soma, but also in the X chromosome and autosomes, which showed that X chromosome expression was elevated in somatic cells (Gupta et al. 2006). This mirrored the results obtained by Nguyen and Disteche (2006), who demonstrated a global transcriptional output ratio of X chromosome to autosomes in adult male and female tissues. However, RNA-sequencing analysis, which is more sensitive than microarray analysis, revealed an X chromosome-to-autosome ratio in humans and mice of ~ 0.5 instead of ~ 1, which challenges the doubling seen in dosage compensation (Xiong et al. 2010).

It may be that only a subset of X-linked genes are compensated (Yang et al. 2011), and, therefore, the concept of dosage compensation by hypertranscription remains to be proved.

This questions Ohno's hypothesis of conservation of the X chromosome among mammalian species. To date, no direct research has been carried out on Ohno's hypothesis, which states that the size of the X chromosome is more conserved in mammals and that this corresponds to the size of the autosome. There is a tendency to assume that autosomes contain more diverse genes and have more variation in their sequence lengths than X chromosomes, because gene loss and gain events are thought to occur more frequently (Anopriyenko and Zakian 2004; Bakloushinskaya 2009; Rodriguez Delgado et al. 2009). It is therefore necessary to fully understand the processes of chromosomal length conservation or change for both X chromosomes and autosomes. This study aims to re-examine Ohno's hypothesis of mammalian chromosomal lengths.

We hypothesize the variation between the lengths of X chromosomes and autosomes among mammals. This can be evaluated by comparing an X chromosome group with an autosome group.

Materials and methods

Mammalian chromosome sizes

The chromosome sizes of 14 species of mammals (human, chimp, orangutan, rhesus monkey, marmoset, mouse, rat, rabbit, cat, dog, horse, pig, sheep, and cow) were obtained from the UCSC Genome Browser database (Fujita et al. 2011) (Table 1). We calculated the total autosomal length for 9 randomly selected species of the 14 species to compare the lengths of the X chromosome group with those of the autosome group (Kim et al. 2008). The chromosome sizes were analyzed, and the length of each chromosome group (X chromosome group and the total length of the autosome group of each species) was divided by its mean value. All statistical tests were performed using the 'R' statistical package (Hornik 2011).

Repeat elements and synteny breaks

The positions of long interspersed elements (LINEs), short interspersed elements (SINEs), and synteny breaks obtained from the UCSC Genome Browser database were used to analyze the relationship between rearrangements and repeat elements. Synteny breaks were identified by a border around each rearrangement of blocks. The number of synteny blocks was counted to ascertain the number of synteny breaks. Annotation data were processed using the Python programming language (Van Rossum and Informatica 1995).

To examine the association between synteny breaks and non-long terminal repeat (non-LTR) retrotransposons (LINEs and SINEs), each chromosome was divided into 10 megabase-pair lengths, the number of synteny blocks, LINEs, SINEs, and L1 elements in each chromosome section was counted and normalized, and the correlation between synteny blocks, LINEs, and SINEs was evaluated.

Results and discussion

Chromosome length conservation

We randomly selected 9 of the 14 mammalian species (Table 1). Our research focused on the following species: human, marmoset, mouse, rabbit, cat, dog, horse, pig, and cow.

In his research, Ohno noticed that the X chromosome remained the same size compared to the autosomes which were of different sizes and were divergent across many mammalian species. However, in order to ascertain whether indeed the X chromosome is more conserved than autosomes, the length of the autosomes had to be measured; these lengths were indeed not conserved. This gives a null hypothesis that the same frequency of deletions and duplications must have occurred during speciation. Therefore, to compare the differences in length, autosomal lengths within species should be totaled. It is also not viable to compare the lengths separately since chromosome shuffling creates

Table 1. Chromosome lengths of mammalian genome sequences obtained from the UCSC Genome Browser database.

Order	Family	Species	Genome sequence length (bp)	
			X-chromosome	Autosome
Primates	*Hominidae*	Human (*Homo sapiens*)[a]	155,270,560	2,881,033,286
		Chimpanzee (*Pan troglodytes*)	156,848,144	2,963,472,556
		Orangutan (*Pongo pygmaeus abelii*)	156,195,299	2,873,295,730
		Rhesus (*Macaca mulatta*)	153,947,521	2,709,717,664
	Callitrichidae	Marmoset (*Callithrix jacchus*)[a]	142,054,208	2,625,311,106
Rodentia	*Muridae: Murinae*	Mouse (*Mus musculus*)[a]	166,650,296	2,472,342,367
		Rat (*Rattus norvegicus*)	160,699,376	2,558,181,645
Lagomorpha	*Leporidae*	Rabbit (*Oryctolagus cuniculus*)[a]	111,700,775	2,136,051,329
Carnivora	*Felidae*	Cat (*Felis catus*)[a]	145,558,876	2,727,085,831
	Canidae	Dog (*Canis familiaris*)[a]	126,883,977	2,318,226,206
Perissodactyla	*Equidae*	Horse (*Equus caballus*)[a]	124,114,077	2,242,939,370
Artiodactyla	*Suidae: Suinae*	Pig (*Sus scrofa*)[a]	125,871,292	2,136,613,509
	Bovidae: Caprinae	Sheep (*Ovis aries*)	129,136,099	2,655,612,385
	Bovidae: Bovinae	Cow (*Bos taurus*)[a]	88,516,663	2,545,896,661

[a]Those selected for the analysis of nine species.

variety in mammals. We have therefore totaled the length of the autosomes from each species in order to compare the length of an X chromosome group with that of an autosome group.

The lengths of the X chromosomes and autosomes follow a reasonably normal distribution pattern based on a Q–Q plot (Supplementary Figure 4).[1]

We determined whether the variation in X chromosomal length was smaller than that of the autosomes, indicating that the X chromosome was conserved. We summed the autosomal length and normalized it by dividing it by the mean autosomal length of the species. X chromosomes were also normalized by their mean value. No significant conservation of X chromosomal length was observed; instead, the length variation of X chromosomes was greater (Figure 1a). This observation was mirrored by the Kernel density estimation of the X chromosome and autosomes (Figure 1b). The probability density function of the autosomes had a higher density peak and a narrower range of lengths.

We ran two variance tests to verify the significant differences between the variation within the X chromosome and autosome groups. To establish variance homogeneity, a modified robust Brown-Forsythe Levene-type test (Levene 1960; Weisberg and Fox 2010), based on the absolute deviation from the median, was carried out. The null hypothesis was not rejected, and we were unable to accept the alternative hypothesis; there was a difference between the deviations within each chromosome group ($p = 0.294$). An F-test carried out to compare the two variances also did not allow us to accept the alternative hypothesis ($F = 2.7569$, $p = 0.1729$). Both the tests resulted in no significant differences in the variance between the lengths of mammalian X chromosomes and autosomes.

Subsequently, we decided to use the full set of 14 mammal species, since it is possible that some differences may be detected over the 10–20 million years during which the mouse and rat branches diverged (Springer et al. 2003), as this is a reasonable measurement of evolutionary change. The resulting graph (Supplementary Figure 1) shows a wider dispersion than the nine species; however, the results of the F-test ($F = 2.7569$, $p = 0.1558$) were identical to those conducted using the nine species.

The differences visible on the graph are not insignificant. Due to the use of such a small sample size (9 and 14), the statistical powers of the tests are relatively low (Lo and MacKinlay 1989), resulting in no rejection of the null hypothesis. It is presumed that variance in the length of the mammalian X chromosome is greater than that in the autosomes. Even if the results are not statistically valid, they do show that there is no difference between the variance in the length of the X chromosome and autosomes in mammals. Therefore, the length of the X chromosome is not likely to be conserved relative to autosomes among mammal species.

Conservation of gene contents has been reported by many biologists (Quilter et al. 2002; Raudsepp et al. 2004; Murphy et al. 2007). A recent study on elephant X chromosomes found that the gene contents and order of human and elephant genes were identical (Rodriguez Delgado et al. 2009). In contrast to X chromosomes, autosomes have undergone global genome rearrangement phases and have been shuffled (O'Brien et al. 1999). For example, in carnivores, the

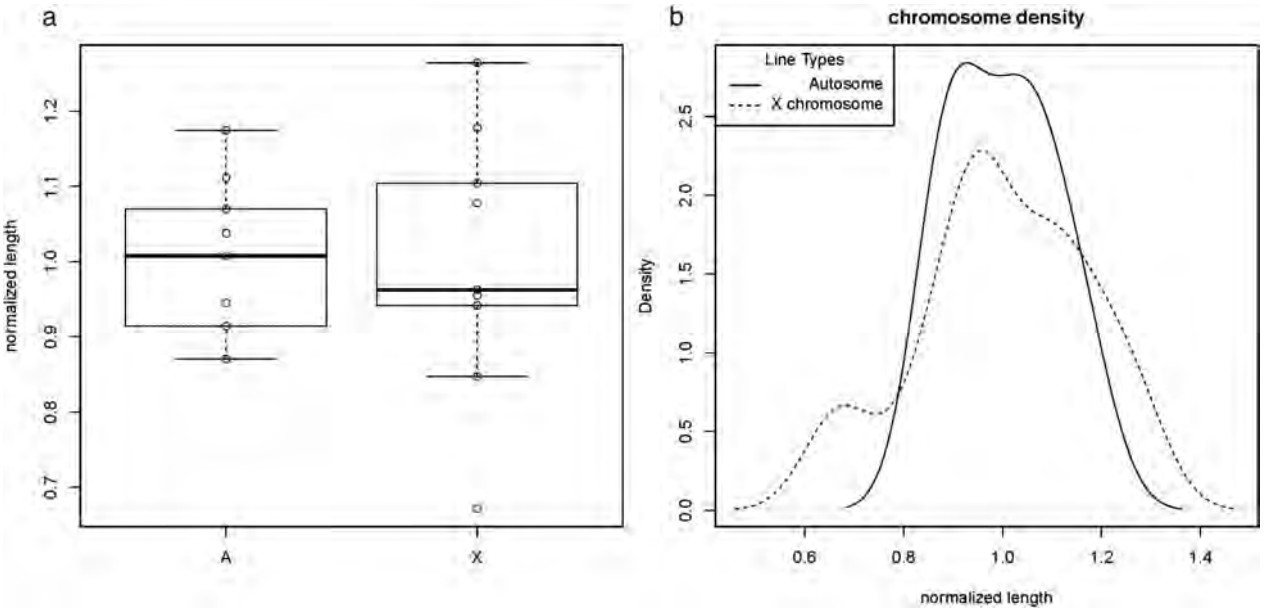


Figure 1. Comparison of normalized lengths between the X chromosomes and autosomes; (a) Box plot of normalized lengths of each chromosome group. The scatter plot shows the range of error differences. There was a discrepancy between the length of the X chromosomes and autosomes, in which the X chromosomes are wider; (b) Estimated Kernel density of the X chromosome (dashed line) and the autosome (solid line). The probability density function of the autosomes has a higher density peak and a narrower length range.

red fox has $2N = 36$ chromosomes and a dog has $2n = 78$ chromosomes (Wayne et al. 1987). However, our results showed a similar or even larger deviation in the length of X chromosomes compared to autosomes.

It is intriguing that Ohno's reported X chromosome-to-autosome ratios were consistently around the 5% level (Ohno et al. 1964). The X chromosome-to-autosome ratio based on sequence length had a similar mean value of 5.438143%, with a group range of 4.8–5.9%, except for the mouse, rat and cow, which were outliers (Supplementary Table 1 and Supplementary Figure 2).

Our results show that the length of the X chromosome is not likely to be conserved relative to that of autosomes among mammalian species, and, like Ohno's observations, the ratio between the lengths of X chromosome and autosome remains constant. This indicates that the changes in the chromosomal length are equally likely to occur in the X chromosome as in autosomes, and this raises the question as to how similar changes in length are possible for the sex chromosomes and autosomes.

Genetic rearrangements and repeat elements

Chromosomal rearrangements, or mutations, are widespread events that change the positions of parts of the chromosome. This is in contrast to point mutations, which cause substitutions, insertions, or deletions of single nucleotides. Chromosomal rearrangements usually produce a new arrangement of the gene order or change the genome contents (Zhao and Bourque 2010). These large genomic rearrangements can be analyzed using methods to identify orthologous genes across different genomes. However, genes represent only a small fraction of the chromosomes on which they reside, and in order to align matched genomic pairs, chromosomes use homologous marks that are not restricted to genes but correspond to genomic fractions. These homologous fractions are known as synteny blocks (Zhao and Bourque 2010), and the break points of continuous synteny blocks created by genomic rearrangement are called synteny breaks.

Large genomic rearrangements occur in two ways: (1) via Robertsonian translocations (ROBs) at chromosomal breakpoint regions and (2) via genomic alterations caused by transposable elements (TEs).

ROBs in the balanced form include the movement of extensive parts of a chromosome to another chromosome, but without any loss of genetic information, and resulting in no difference in the amount of genetic material. This preserves the length of the chromosomes.

TEs constitute a major part of the interspersed repetitive DNA that covers 50% of the vertebrate genome. TEs are capable of shifting to other locations within the genome by means of conservative transposition, or in most cases, by replicative transposition,

where a copy of the TE is made in the new position (White et al. 1998). In mammals two representative TEs are present: LINEs and SINEs. As non-LTR retrotransposons, LINEs have autonomous activity and SINEs are dependent on LINEs (Graves et al. 2006).

A clear association between TE copy density and synteny breaks was reported in Lepidoptera (d'Alencon et al. 2010), where the synteny breaks are indicators of genomic rearrangement. This finding confirmed that genomic rearrangements occur due to the transposition of TEs. Furthermore, long interspersed nuclear element 1 (LINE1 or L1 element), which is the only active LINE (Ross et al. 2005), is known to affect genome reshaping, including genomic rearrangements. Han reported that L1 created variation in the human genome by L1 recombination-associated deletions (L1RADs), in which L1RAD mechanisms mediate repairs of double-strand breaks (DSB) in DNA (Han et al. 2008). These events were observed in human and chimpanzee lineages and occurred 73 times in chromosomes 16 and 21. The total amount of human DNA deleted was estimated to be $\sim$450 kbp (Han et al. 2008). Similarly, Alu elements, a major component of SINEs in humans, are reported to be capable of creating genomic deletions by unequal homologous recombination. Since the divergence of humans and chimpanzee lineages, $\sim$400 kbp has been lost from human DNA (Sen et al. 2006). These indicate that LINEs and SINEs can reduce the size of the chromosomes.

Additionally, TEs are capable of creating segmental duplications (SDs) (Bourque 2009). TEs trigger double-strand DNA breaks, and their translocations create unequal crossovers between TEs on homologous chromosomes, which results in duplications and deletions (Stankiewicz and Lupski 2002). In primates, the genome re-arrangements created by the actions of LINEs and SINEs are closely linked to SDs (Bailey and Eichler 2006). It is therefore possible that non-LTR retrotransposons (LINEs and SINEs) play a role in chromosome lengthening.

Contrary to ROBs, re-arrangements by non-LTR retrotransposons can affect the size of the chromosome, which is why we chose to investigate the roles of LINEs and SINEs in chromosomal length alteration.

LINE, SINE, sequence lengths, representative fraction of the genome sequence, and fraction ratio of the X chromosome to the autosomes are shown in Table 2 and Figure 2. The average X chromosome-to-autosome fraction ratio was 0.90 in SINEs and 1.56 in LINEs (1.69 in L1 elements). This indicates that SINEs are distributed almost equally among the X chromosome and autosomes, and that LINEs are 1.5$\times$ more common in the X chromosome than in autosomes. These results mirror those previously found in humans (Ross et al. 2005), where the Alu family of SINEs was less common, but where the LINE L1 family was found at much higher numbers in the X chromosome.

To investigate the relationship between LINEs, SINEs, and genomic rearrangements, we examined the association between synteny breaks and non-LTR retrotransposons (LINEs and SINEs).

The correlation between synteny blocks, LINEs, and SINEs is shown in Figure 3, and the normalized density of synteny breaks, LINEs, and SINEs on each chromosome was merged as shown in Supplementary Figure 3. Overall, synteny breaks and LINEs tended to match each other in the autosomes of seven mammalian species, except for the mouse and marmoset. However, in the cat autosome, the association of LINEs and SINEs with synteny breaks was surprisingly clear. In the human autosome, LINEs and SINEs were both matched to synteny breaks on chromosomes 4 and 8, and synteny breaks correlated more to LINEs than to SINEs on chromosome 7. However, in contrast, on the first half (0–130 Mbp) of chromosome 5, synteny breaks correlated more to SINEs than to LINEs. This pattern of association of interspersed nuclear elements with synteny breaks was similar in other autosomes and in the autosomes of other mammalian species. LINEs, however, correlated to synteny breaks globally, except for in the mouse and marmoset autosomes.

The association between LINEs and SINEs with synteny breaks was also observed in X chromosomes; however, synteny breaks tended to correlate more with SINEs rather than LINEs. SINEs also correlated more closely with synteny breaks in the cat, dog pig, human, marmoset, and cow. In horse and rabbit, the density of the SINEs and synteny breaks changed equally, when compared with those of the mouse, which is unusual when there is a relatively low association between interspersed nuclear elements and synteny breaks. In the mouse X chromosome, however, LINEs were correlated with synteny breaks. SINEs and LINEs of the horse and rabbit were highly correlated with each other. In *C. elegans* and yeast, large-scale rearrangements containing enriched repetitive sections of DNA are common (duplications and transposons) (Eichler and Sankoff 2003), and our results show a similar tendency in nine mammalian species.

We suspect that L1 elements are involved in X chromosome inactivation because SINEs and synteny breaks are closely correlated in the X chromosome. As mentioned previously, because the sex chromosomes evolved into two types of chromosomes (X and Y), dosage compensation for X-linked genes has been essential for survival. In dosage compensation, X chromosome inactivation occurs, silencing one female

Table 2. Sequence length and fraction of the genome of SINEs, LINEs, and L1 elements in nine mammalian species.

Species		Sequence length		Fraction of the genome sequence (%)		X chromosome to autosome fraction ratio
		X chromosome	Autosome	X chromosome	Autosome	
SINE	Cat	9,959,224	188,833,672	6.84	6.92	0.99
	Cow	13,258,682	409,714,586	14.98	16.09	0.93
	Dog	13,688,403	238,361,286	10.79	10.28	1.05
	Horse	8,158,723	165,527,084	6.57	7.38	0.89
	Human	16,110,567	374,758,497	10.38	13.01	0.80
	Marmoset	14,116,018	347,624,970	9.94	13.24	0.75
	Mouse	10,008,501	194,124,295	6.01	7.85	0.76
	Pig	16,439,680	310,073,718	13.06	14.51	0.90
	Rabbit	21,253,274	405,362,696	19.03	18.98	1.00
LINE	Cat	20,628,532	282,572,155	14.17	10.36	1.37
	Cow	25,659,899	524,779,399	28.99	20.61	1.41
	Dog	42,222,175	424,497,957	33.28	18.31	1.82
	Horse	38,953,237	488,798,495	31.39	21.79	1.44
	Human	50,991,068	575,161,891	32.84	19.96	1.64
	Marmoset	43,131,737	527,047,944	30.36	20.08	1.51
	Mouse	57,980,941	463,595,712	34.79	18.75	1.86
	Pig	37,271,969	412,538,139	29.61	19.31	1.53
	Rabbit	25,587,618	342,361,247	22.91	16.03	1.43
L1	Cat	17,288,465	212,333,285	11.88	7.79	1.53
	Cow	16,173,938	289,372,717	18.27	11.37	1.61
	Dog	38,260,272	343,609,622	30.15	14.82	2.03
	Horse	32,425,232	362,097,953	26.13	16.14	1.62
	Human	45,235,679	462,365,371	29.13	16.05	1.82
	Marmoset	38,406,683	436,489,610	27.04	16.63	1.63
	Mouse	57,037,165	452,070,015	34.23	18.29	1.87
	Pig	32,906,261	338,942,838	26.14	15.86	1.65
	Rabbit	22,927,085	300,560,810	20.53	14.07	1.46

X chromosome, and L1 elements – which comprise most of the LINEs – function as a part of the X chromosome inactivation machinery. During X chromosome inactivation, LINEs are expelled from the inactive X chromosome, and L1 elements make up a silencing core along with Xist (X-inactive specific transcript) RNA, SATB1 (special AT-rich sequence-binding protein-1) protein, and the polycomb complex

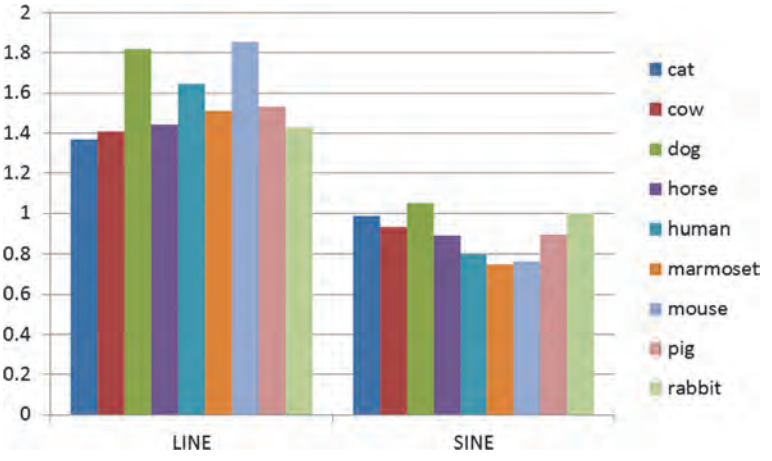
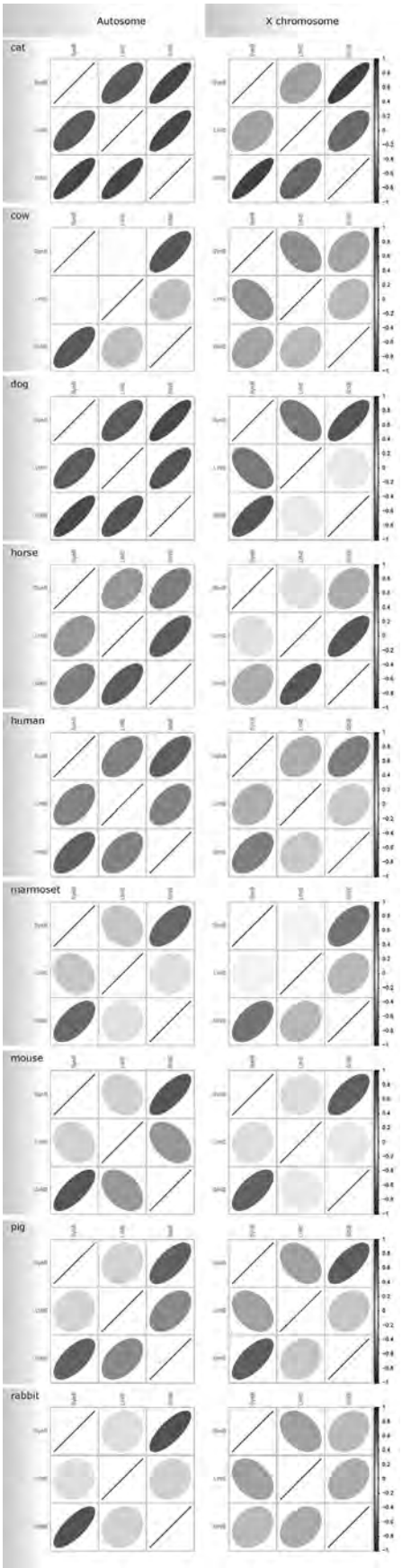


Figure 2. Fraction ratio of X chromosome to autosome of LINEs and SINEs in nine mammalian species. SINEs are almost equally distributed on X chromosomes (average of 0.90-fold) and autosomes. LINEs are more frequent in X chromosomes (average of 1.56-fold) than in autosomes.



PRC2 (Polycomb Repressive Complex 2; this includes Eed, Suz12, RbAp48, and the catalytic subunit Ezh2). The L1 elements are then silenced on the inactive X chromosome (Ringrose and Paro 2004; Zhao et al. 2008; Chow et al. 2010). Despite the arrival of the Y chromosome, LINEs remain part of the X chromosome inactivation machinery, and it is possible that SINEs, rather than LINEs, are more involved in the synteny breaks on the X chromosome.

It is therefore reasonable to suggest that the uneven distribution of LINEs and SINEs in the mammalian X chromosome, and their differing roles, are responsible for the wider variance in the length on the X chromosome than on autosomes.

Alu elements also effect changes in sequence lengths (Boissinot et al. 2001). L1 elements are more common in the X chromosome than in autosomes, and the alleles containing the L1 elements were possibly lost from the X chromosome rather than from the autosomes. However, the autosomes suffer more from deleterious effects than does the X chromosome, and the lower number of Alu sequences on the X chromosome is thought to be due to these deleterious effects.

SINEs and non-autonomous transposons do not encode a functional reverse transcriptase protein and rely on the LINE machinery for transposition (Lander et al. 2001). Therefore, in X chromosomes, a higher number of LINEs affect the activity of SINEs. The X chromosome-to-autosome fraction ratios were as follows; the autosome was affected by 1 unit of LINEs and 1 unit of SINEs, and the X chromosome was affected by 1.56 (1.37–1.86) units of LINEs and 0.9 (0.75–1.05) units of SINEs (Table 2). However, in the X chromosome, the influence of LINEs on sequence length was limited, whereas that of SINEs was enhanced. This resulted in either a wider variance, or no difference at all, in the length of the mammalian X chromosome compared with the autosomes. The presence of fewer LINEs in the X chromosome may have resulted in a more conserved length.

Our results regarding LINEs and SINEs in the mouse show that synteny breaks are not correlated with LINEs, but are generally correlated with SINEs (Supplementary Figure 3). A clear association between an abrupt change in GC content and SINEs with

Figure 3. The correlation between the synteny blocks, LINEs, and SINEs on autosomes and X the chromosomes in nine mammalian species. Positive correlations are shown in blue, and negative correlations in red. The higher the correlation, the thinner the shape. Synteny breaks and LINEs match in the autosomes of seven mammalian species (except in the mouse and marmoset). SINEs and synteny breaks in the X chromosome show a close correlation.

synteny breaks has previously been reported in mice (Waterston et al. 2002). L1 elements split into two groups: immature L1, which contained more than 99% full-length L1 elements, and truncated L1, which contains the remainder of the L1 elements. Neither immature nor truncated L1 was correlated with synteny breaks (data not shown). SINEs and LINEs are generally distributed within AT- and GC-rich regions. SINEs are more common in GC-rich regions, and LINEs are more common in AT-rich regions (Lander et al. 2001). An AT- and gene-rich region is very similar to a gene-coding region, and if the coding region is susceptible to genetic changes, then this also affects the survival of the repeat elements. Further study is needed to get insight into the association between the distribution of gene-coding regions, GC-rich regions, AT-rich regions, LINEs, and SINEs in several mammalian species, if we are to understand the extraordinary association between LINEs and synteny breaks in mice. In our research, we were unable to establish the precise function of LINEs and SINEs and how they are involved in changes in the sequence length. Further research to quantify how interspersed nuclear elements alter sequences should be undertaken.

Acknowledgements

This work was supported by a grant (PJ0090192012) from Next-Generation BioGreen 21 Program, Rural Development Administration, Republic of Korea.

Note

1. Supplementary material can be found by clicking on the Supplementary Content tab at http://dx.doi.org/10.1080/19768354.2012.724709

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