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EVOLUTIONARY SIGNIFICANCE OF GENOMIC CONFLICT

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ABSTRACT

Genomic conflict arises when some selfish genetic elements such as transposons, homing endonucleases, driving chromosomes, heritable microorganisms etc. in the eukaryotic genome are transmitted at a rate much higher than expected, regardless of the effect on fitness of the host. Conflict may occur between genomes (including paternal-maternal and parental-zygotic conflicts) or within genomes (between cytoplasmic and nuclear genes or sex chromosomes and autosomes). In the present article, we will focus on evolutionary role of genomic conflict behind the unexpected complexity of mechanisms of sex determination, diversity of genome, speciation and extinction of eukaryotic populations among plants and animals.

Keywords: genomic conflict; eukaryotes; transposon; sex determination; speciation

INTRODUCTION

The concept of genomic conflict or genetic conflict took birth from two closely related ideas in evolutionary biology, first that the natural selection operates on individual genes rather than on the individual organism (levels of selection), and second that some genetic elements in the eukaryotic genome are selfish or parasitic, i.e. gain a transmission advantage through a well known phenomenon called meiotic drive. Genetic conflict occurs when such a selfish gene or ultraselfish gene or parasitic DNA in an organism is not transmitted by the Mendelian pattern of inheritance, and favors its own propagation regardless of the effect on fitness of the host. In many species of animals and plants, selfish genetic elements (SGEs) in the genome are transmitted at a rate much higher than others, and are either neutral or detrimental to the organism (Burt and Trivers 2006). Based on location in the genome, SGEs can be present in the nucleus or in the cytoplasmic organelles or parasitic microorganisms. While on his studies on B chromosomes, Ostergen (1945) recognized that selection may operate in different directions on different parts of the genome. The discovery of meiotic drive chromosomes in several species (Sandler and Novitski , 1957) also stimulated consideration of the gene as the level of selection. Genomic conflict may occur at two basic levels, within genome viz. intragenomic (between different genetic elements in an individual organism involving cytoplasmic and nuclear genes, or sex chromosomes and autosomes), and between genomes viz. intergenomic (between genetic elements of different individuals who interact over a particular phenotype, including paternal-maternal and parental-zygotic conflicts). For example, in cases of sex determination among

eukaryotes, there is potential conflict between maternally expressed sex determining genes and embryonically expressed genes.

Genomic conflict is an important evolutionary force behind the unexpected diversity of genetic mechanisms of sex determination among plants and animals. The sex determining system in eukaryotes is much influenced by parental sex ratio genes, parental effect sex determiners and zygotic sex determiners. The present article is an attempt to discuss the theory of genomic conflict in relation to the evolution of sex and sex determining mechanisms, diversity of genome, speciation and extinction of eukaryotic populations among plants and animals.

MEIOTIC DRIVE AND SELFISH GENETIC ELEMENTS

Meiotic drive also called segregation distortion is a mechanism by which a heterozygous locus segregates at a frequency greater than the expected Mendelian frequency in more than half of the functional gametes by destroying or disabling the homologous chromosome. For example, *sd* complex in fruitfly (*Drosophila melanogaster*), t-locus in mouse (*Mus musculus*) and sk gene in fungus (*Neurospora sp.*) etc. behave as sex-ratio distorters, because they cause a sex-ratio bias in the offspring of the host individual. There are various mechanisms of meiotic drive. Many of these reduce the quantity of functional sperm, while others do not cause destruction of gametes, but rather use the asymmetry of meiosis in females. Meiotic drive alleles are able to spread through a population as long as their increase in transmission outweighs the reduction in fertility. SGEs may occur either at multiple locations or at unique sites in the genome of the host organisms. Many of SGEs are nuclear genes such as transposable elements, segregation distorters and supernumerary (B) chromosomes, while others are cytoplasmic genes of either a cellular organelle such as mitochondria and chloroplasts, or belong to genomes of parasitic microorganisms such as *Wolbachia*. According to the mechanism of spread, SGEs have been categorized into four types (see below).

1. Transposable Elements

Mobile transposable elements (TEs) or transposons are self-replicating genes with ability to move from one to other positions in the genome, and therefore, accumulate in several copies in an organism. They are often called 'jumping genes' or 'parasitic DNA' after discovery by Barbara McClintock in 1944 in maize. TEs comprise over 50% of the maize genome, 45% of the human genome and 15% of the *Drosophila (D) melanogaster* genome. Various known families of TEs constitute about 47% of genome in *Aedes aegypti* mosquito. The *P element* spread through most of the global *D. melanogaster* populations within a few decades after a natural acquisition from *D. willistoni*. Although transposons might occasionally induce beneficial mutations, their spread is mostly explained by their ability to replicate in the genome as 'genomic parasites' (Charlesworth et al., 1994).

2. Segregation and Post-Segregation Distorters

Each gene of a diploid organism has equal probability (50%) of ending up into functional gametes; however, sometimes certain genes are consistently overrepresented among the products of meiosis. Two well-studied examples are segregation distorter (sd) complex found in an inversion on chromosome 2 of *D. melanogaster*, and the t-locus in mice (discussed below). Segregation distorters are easily detected when occur on the sex chromosomes, because a sex-ratio bias is observed as a result of an excess of gametes with either the X chromosome (X drive against Y) or the Y chromosome (Y drive against X). In the case of the t-locus in mice, for instance, certain t-alleles are homozygous lethal, and others are homozygous sterile owing to

their coupling to deleterious recessive genes in the inverted complex. The presence of deleterious effects in the homozygous condition explains the persistent population polymorphism for sd-and t-loci. Supernumerary B chromosomes represent another class of segregation distorters. These are non-essential linear chromosomes widespread in eukaryotes including both plants and animals; not homologous with any member of the normal (A) chromosome set; morphologically and structurally different from the A chromosomes; and are transmitted at higher than expected frequencies due to preferential segregation at meiosis, and therefore, accumulation in progeny genome as selfish or parasitic chromosomes.

Some SGEs behave as post-segregation distorters, as these come in action after fertilization and the commencement of development. Many of these act by killing individuals that have not received the SGE and are analogous to post-segregation-killing plasmids, such as pIK137 in *Escherichia coli* (Cooper and Heinemann, 2000), and Medea locus in the flour beetle *Tribolium castaneum* (see below), while other may cause cytoplasmic incompatibility due to maternally inherited bacterium *Wolbachia* (which is widespread in insects, arachnids (spiders), crustaceans and nematodes). The Medea gene causes the death of progeny from heterozygous mothers that do not inherit it as observed in the flour beetle (*Tribolium castaneum*) (Beeman et al., 1992). The Medea encodes both a maternally-expressed toxin and a zygotically-expressed antidote. The toxin causes the death of all progeny lacking the Medea allele.

3. Cytoplasmic Sex-Enhancing Elements

In contrast to nuclear genes, cytoplasmic genes are often inherited uniparentally through female gametes, and therefore, selection on such genes in panmictic populations favors the variants that increase allocation to the sex that can transmit them (females) over the sex that cannot (males) (Cosmides and Tooby, 1981). Examples include mitochondria that induce cytoplasmic male sterility in plants, cytoplasmic microorganisms that kill males, feminize hosts and induce parthenogenesisand.

4. Converting Elements

Gene conversion is a rare event and generally occurs in a minority of meioses (Bengtsson, 1986). However, in homing endonuclease genes (HEGs), gene conversion occurs frequently and is heavily biased in one direction (Gimble and Thorner, 2000). HEGs are more stable, being restricted to one genomic location, and are capable of population invasion from a very low initial frequency. These convert their rival allele into a copy of themselves, and are thus inherited by nearly all meiotic daughter cells of a heterozygote cell. The rival allele without the HEGs is cleaved by a sequence-specific homing endonuclease and the double-strand break is repaired by homologous recombination (gene conversion) using the allele containing HEGs as template. Both homologous chromosomes will contain the HEGs after repair (Sinkins and Gould, 2006).

OVERVIEW OF SEX DETERMINATION IN EUKARYOTES

Sex determining mechanisms are extremely diverse among plants and animals. In hermaphroditic species, both sperm (microgamete) and egg (macrogamete) are produced within the same individual, whereas in dioecious (or gonochoristic) species separate sexes (male and female) perform the above functions. There are various mechanisms of sex determination in dioecious species including haplodiploidy (haploid males and diploid females produced from unfertilized and fertilized eggs respectively), paternal genomic loss (sex determined by loss of paternal chromosomes after fertilization), male heterogamety (heteromorphic XY males and

homomorphic XX females), female heterogamety (ZW females and ZZ males), polygenic sex determination, environmental sex determination, and a variety of other mechanisms (Bull, 1983). Sex determination can even differ markedly within a species and between closely related species. For example, platyfish (*Xiphophorus maculatus*) can have either male heterogamety or female heterogamety (Kallman, 1973). Further, sex determining genes in one species may not be involved in sex determination in related species (Graves, 1995). In addition, mechanisms that appear to be the same can differ markedly in the underlying genetics. For example, male heterogametic systems is based upon dominant male determiners on the Y chromosome in mammals), while upon a genic balance between factors on the X chromosome and autosomes in *Drosophila* species. Recent studies have shown that genes involved in sex determination evolved rapidly in eukaryotes (Walthour and Schaeffer, 1994). For example, SrY gene in mammals shows unusually fast sequence evolution (Whitfield et al., 1993). There are two important evolutionary questions to the above observation, firstly "Why are sex determining mechanisms so diverse?" and secondly "How do sex determining mechanisms change over species?" It is most probable that, sex determining mechanisms change when some factors (or genes) destabilize an existing system of sex determination, leading to the evolution of a new mechanism. Therefore, it is essential to focus and discuss the factors that potentially destabilize sex determining mechanisms in eukaryotes over evolutionary time.

GENOMIC CONFLICT AND SEX DETERMINATION

Genomic conflict is an inherent quality of sex determining systems in plants and animals. For example, cytoplasmic genes (e.g. mitochondria, plastids and cytoplasmic microorganisms) inherited through the egg cytoplasm, but not through sperm, are selected to produce strongly female biased sex ratios to increase their transmission to future generations (Cosmides and Tooby, 1981). In contrast, nuclear genes (e.g. autosomal genes on non-sex chromosomes) are generally selected to produce a balance in the sex ratio (Fisher, 1930). As a result, cytoplasmic and nuclear autosomal genes are selected to "push" sex determination in different directions. There is considerable evidence of conflict between nuclear autosomal and cytoplasmic genes for sex determination (Hurst, 1993). Further, conflict over sex determination can also occur between genes on sex chromosome and autosomes, and between parental and offspring expressed genes. Coevolutionary interactions among these conflicting selective components may provide a "motor" for evolutionary change in sex determination (see Figure 1).

1. Parental Sex Ratio Genes

Parental influence over sex ratio of offspring occurs in a broad range of species with male heterogamety, as seen in fruitflies, mosquitoes and lemmings. In such cases, parental sex ratio genes cause sex chromosome meiotic drive that alters the ratio of functional X and Y (or Z and W) carrying gametes, but does not directly affect the zygotic sex determining mechanism. Parental influences on sex ratio are common in haplodiploid insects where unfertilized eggs develop into males, and fertilized eggs develop into females. In such cases, females manipulate the sex ratio among progeny by altering the probabilities that the egg is fertilized (Godfray, 1994). Another mechanism of parental effects on sex ratio selection is differential allocation of resources to male and female progeny (more resources to offspring of one sex e.g. males) to alter selection acting upon zygotic sex determiners. In species (terrapins and western painted turtle) with environmental sex determination, the parent can influence sex among progeny by selecting oviposition sites to affect how selection operates upon environmental sex determining genes expressed in the zygote. Recent studies have shown that some birds such as the Seychelles warbler (Komdeur et al., 1997) alter sex ratio among progeny based upon available resources.

This is due to either preferential segregation of Z or W chromosomes during meiosis (a parental sex ratio affect) or to maternal modification of zygotic sex determination (see below).

2. Parental Effect Sex Determiners

These genes are expressed in the parent, but function within the developing zygote to determine its sex. However, in terms of selection, parental effect sex determining genes are subject to the same selection pressures as sex ratio genes because they are expressed in the parent. Parental effect sex determiners can be either maternal or paternal in origin. Most maternal effects are due to the products (e.g. mRNA or proteins accumulated during oogenesis in the developing egg) which are typically important in early development because in most organisms the zygotic genes are not expressed during early mitotic divisions. Therefore, gene products placed in the egg by the mother could have major effects on sex determination in the developing zygote. In *D. melanogaster*, for example, daughterless (*da* gene transcript), a maternal effect nuclear gene product placed in eggs, is involved in sex determination (Cline, 1980). However, action of the maternal *da* product occurs during early development of the zygote (after meiosis), where the transcribed protein activates the Sex-lethal gene (*Sxl*), resulting in female development.

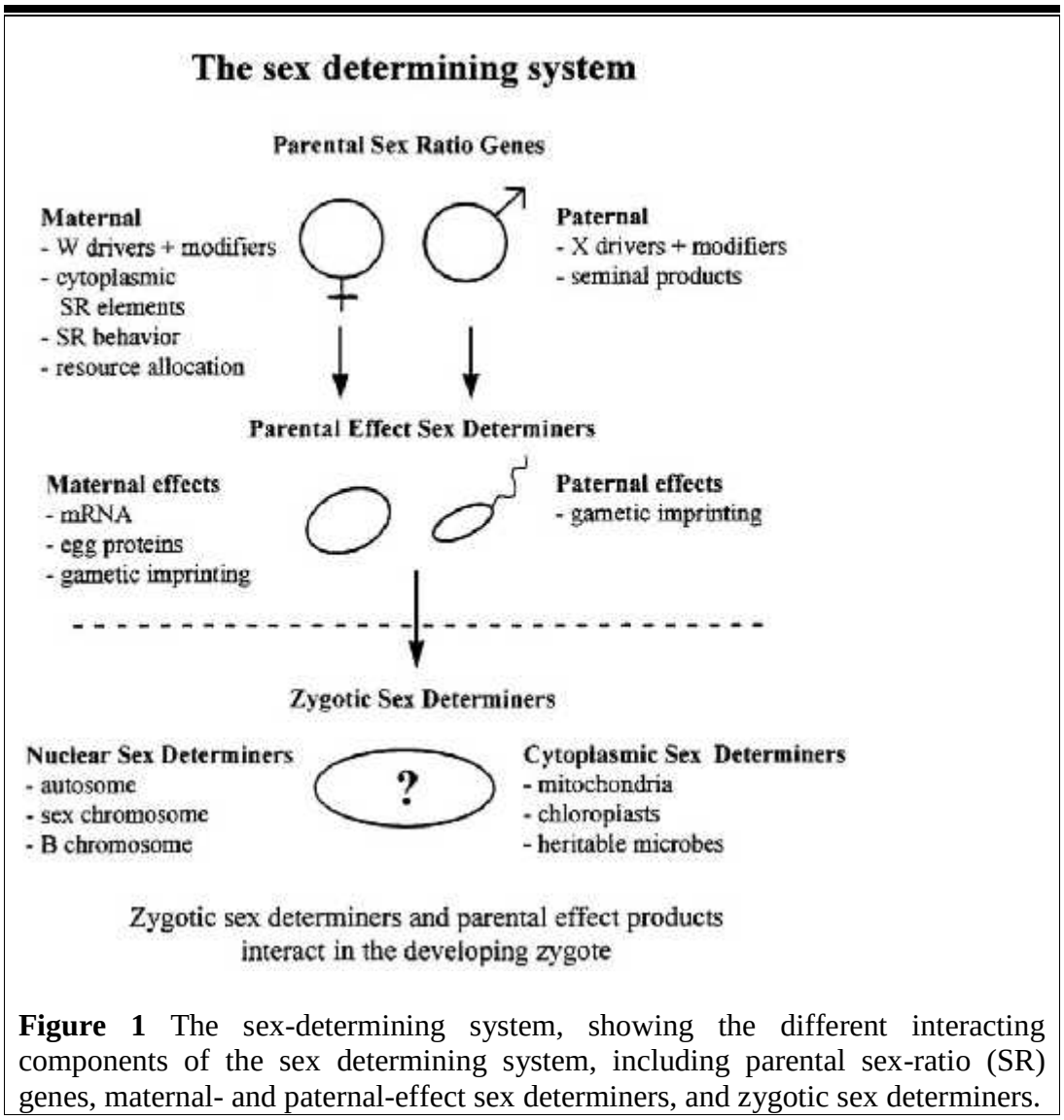

Figure 1 The sex-determining system, showing the different interacting components of the sex determining system, including parental sex-ratio (SR) genes, maternal- and paternal-effect sex determiners, and zygotic sex determiners.

3. Zygotic Sex Determiners

Examples of zygotic sex determiners include *SrY* in mice and humans, *Sex lethal* in *D. melanogaster* (Steinemann-Zwicky et al., 1990), and the *xol* and *sdc* genes in *C. elegans* (Hodgkin, 1990). In both *D. melanogaster* and *C. elegans*, the primary sex-determining signal is the X : A ratio. Multiple X numerator elements are present on the X chromosome, and a regulatory cascade involving several genes determines somatic sex (Hodgkin, 1990). The evolution of X : A systems appears to be associated with the evolution of dosage compensation.

GENOMIC CONFLICT SYSTEMS IN EUKARYOTES

1. Meiotic-Drive Chromosome

Meiotic-drive chromosomes are segregated in a non-Mendelian fashion ending up into 70–100% of gametes (Sandler and Novitski, 1957), as observed in from several mammals and insect groups including fruitflies, mosquitoes, and butterflies. When selection favors meiotic drive loci present on the sex chromosomes (which may also occur on autosomes), it is referred as sex chromosome drive. The best known examples are sd-complex in *Drosophila*, and the t-locus in *Mus* (discussed below). Meiotic-drive sex chromosomes are easily recognized because they have an immediate effect on the sex ratio of offspring. Most examples include driving X chromosomes typically referred to as Sex-Ratio (SR) chromosomes. Driving Y chromosomes are rare, probably because of their stronger driving capacity leading to fast extinction of the host. Meiotic drive sex chromosomes would quickly lead to extinction of carrier populations in absence of countering selections (Hamilton, 1967; Lyon, 1991) at the gene, individual, and group levels. At the individual level, driving sex chromosomes often reduce male fertility through dysfunction of gametes carrying the non-driving sex chromosome homolog (Policansky and Ellison, 1970). If driver genes residue in chromosomal inversions, females may also have reduced fitness as well (James and Jaenike, 1990). Countering selection generally favors alleles on the autosomes and the non-driving sex chromosome that suppress the meiotic drive of the SR chromosome. There is considerable evidence that X-chromosome drive selects for repressors on the Y chromosome and autosomes. In species with recombination on the sex chromosomes, selection on linked genes can favor either enhancement of drive or suppression of drive, depending on how tightly linked the gene is and whether linkage disequilibria are maintained (Wu, 1983). Many B chromosomes (discussed above) have an increased transmission in gametes (transmission drive), by which the chromosomes are maintained within populations despite the fitness costs they impose on the host (Nur, 1977). One striking example of a sex-ratio distorting B chromosome is the psr chromosome in *N. vitripennis* described below.

The segregation distorter (sd) gene complex in fruitfly

This gene complex is found at low frequency in nearly all natural populations of the fruit fly, *D. melanogaster*. In heterozygous males carrying *sd* and a typical wild-type second chromosome (sd/sd^+), most sd^+-bearing spermatid nuclei fail to complete the histone-to-protamine transition during spermiogenesis, so that primarily sd-bearing spermatids develop properly and go on to fertilize eggs. . In heterozygous sd/sd^+ male fruitfly flies (*(D. melanogaster)*, sd gene complex manages to get into 90% of all functional sperm by the sd mechanism (the other sperm produced degenerate) (Larracuente and Presgraves, 2012)

The t-locus of the house mouse

The t-locus in house mice (*M. musculus*) has several alleles and a heterozygous male carries one of these alleles t and the normal allele T in more than 90 percent of the sperm. In the homozygous male, some of the t alleles are lethal, while others cause male sterility. Despite these disadvantages to the individual, the meiotic drive of the t alleles is so great that they reach a high frequency in many populations (Safronova and Chubykin, 2013).

The psr locus in the parasitic wasp

Paternal Sex Ratio (psr-locus) is a small B chromosome in the parasitic wasp *Nasonia vitripennis*. Males with the *psr* chromosome produce functional sperm, but after fertilization of the egg by psr-bearing sperm, psr causes supercondensation and destruction of the paternal chromosomes in early fertilized eggs, leaving only the maternal set. Because this wasp has haplodiploid system of sex determination, the effect of psr is to convert diploid (female) eggs into haploid (male) eggs that carry psr. As a result, the fertilized (diploid) egg, which normally develops into a female, instead develops into a haploid male that also carries the psr chromosome (Beukeboom et al., 2007). Unpaired supernumerary chromosomes typically have high transmission rates through haploid males (for example, near 100% in wasps) because male spermatogenesis in wasps is mitotic, but low transmission rates through females (for example, 10% in wasps). By converting females to males, psr ends up in the sex with higher supernumerary chromosome transmission rates.

2. Cytoplasmic Sex-Ratio Distorters in Animals

Conflict between cytoplasmic and nuclear genes over sex determination and sex ratios is a common and widespread phenomenon in animals. Cytoplasmic sex-ratio distorters include male-killers, primary sex-ratio distorters, feminizers, and parthenogenesis inducers. Examples of male-killing microbes include spiroplasms in *D. willistoni*, gamma proteobacteria in *Nasonia* wasps, rickettsia, spiroplasms and flavobacteria in ladybird beetles, and microsporidia in mosquitoes. Many sex-ratio distorters are cytoplasmic microorganisms that are transmitted through the egg cytoplasm but not through sperm (Hurst, 1993), to distort sex ratio toward females. *Wolbachia* is a maternally-inherited intracellular symbiontic proteobacterium that infects a wide range of arthropods and nematodes (Werren et al., 2008). It is frequently transmitted vertically from females through the eggs to the progeny; although, horizontal transfer between hosts has also been documented (Cordaux et al., 2001). *Wolbachia* is capable of inducing several interesting sex-related phenotypes (e.g. male killing, male feminization, cytoplasmic incompatibility etc.) in its hosts through reproductive alterations. All of these phenotypes distort the progeny sex ratio in favor of females thus ensuring higher transmission rate of *Wolbachia* to the next generation of hosts (White et al., 2013).

Male killing or male lethality

Male killing (MK) or male lethality (ML) is an interesting example of cytoplasmic sex-ratio distortion in animals, where male embryos (in the case of cytoplasmic inherited bacteria) or male larvae (in the case of Microsporidia) are killed to divert parental investment from males to females who can transmit these cytoplasmic elements (for instance, in ladybird beetles, infected female hosts eat their dead infected male brothers in the case of cytoplasmic inherited bacteria) (White et al., 2013).

Male feminization

Male feminization (MF) is a special case of reproductive alteration in amphipod and isopod Crustacea and Lepidoptera, in which genetic males are converted into females by cytoplasmic inherited protists (Microsporidia) or bacteria (*Wolbachia*), regardless of sex-determining nuclear genes. *Wolbachia* causes the feminization of genetic male embryos in several species of crustaceans and insects (Rousset et al., 1992), including the leafhopper *Zyginidia pullula (*Asgharian et al., 2014).

Cytoplasmic incompatibility

In many arthropods, zygotes produced by sperm from infected males and eggs from non-infected females are killed by *Wolbachia* or *Cardinium* (White et al., 2013).

Parthenogenesis induction

In certain haplodiploid Hymenoptera and mites, in which males are produced asexually, *Wolbachia* and *Cardinium* can induce duplication of the chromosomes and thus convert males into females.

3. Cytoplasmic Male Sterility in Plants

Cytoplasmic male sterility (CMS) is widespread (e.g. in maize, *Petunia*, rice, the common bean, and sunflower) and commonly observed phenotype in higher plants, which refers to the failure of anther or pollen development caused by a cytoplasmically inherited factor. Although all CMS plants are alike in that they are unable to produce viable pollen, the specific mechanism differs among plant species. In CMS plants, cyto-nuclear conflict between maternally inherited mitochondria inducing CMS and nuclear autosomal suppressors of cytoplasmic male sterility (CMS) is manifested by complex interactions between CMS genes and nuclear repressors of CMS (Braun et al., 1992).

ROLE OF GENOMIC CONFLICT IN EVOLUTION

Genomic conflict due to SGEs has played important roles in evolution of sex and sex-determining mechanisms, in shaping the structure of genome, speciation and extinction of eukaryotic populations as discussed below.

Evolution of Sex-determining Systems

The diversity of sex determination among eukaryotes is due to genomic conflict between non-Mendelian sex-ratio distorters and Mendelian nuclear genes. In many animals, maternally-inherited microorganisms and mitochondria are inherited uniparentally through females and therefore are selected to bias sex ratio to that sex, whereas Mendelian nuclear genes are selected to produce a balanced sex ratio to counteract the action of cytoplasmic elements. Segregation-distorting sex chromosomes that result in biased sex ratios can create strong selective pressures on Mendelian nuclear genes to counteract SGEs. This can be understood taking the example of evolution of sex determining system in the pillbug *Armadillidium vulgare* with female heterogamety (ZW females and ZZ males). However, many populations harbor a MF *Wolbachia* that converts genetic males into functional females (Rousset et al., 1992) and eliminates the W chromosome from the population. In some populations, a dominant masculinizing factor is present that overrides the action of the MF bacterium (Rigaud and Juchault, 1993).Thus, the bias in sex ratios caused by the feminizing bacterium selects for such masculinizing genes, and can effectively convert the population to male heterogamety (Mm males and mm females) from the previous female heterogametic form (Caubet et al., 2000). Thus, due to its enormous host

range, *Wolbachia* might have played a crucial role in the evolution of sex determination system and reproductive strategies in arthropods (Cordaux et al., 2011). A second example of fast evolving sex-determining mechanisms is CMS in plants such as maize and others that have mitochondrial variants (through mutations or genetic rearrangements) causing lack of the formation of anthers or pollen (Saumitou-Laprade et al., 1994). As a result, a CMS phenotype depends on the relative frequencies of CMS haplotypes and nuclear suppressors of CMS. In some cases, the suppressors of CMS can become fixed in the species; the underlying genetic structure of sex determination is then a product of the conflict between cytoplasmic and nuclear genes.

Evolution of Eukaryotic Genome

SGEs have been proposed to be responsible for the initial evolution of sex, recombination, the uniparental inheritance of organelles, genome structure, and many aspects of the design of organisms. There are two interesting evolutionary 'responses' of eukaryotic genomes to the presence of TEs: evolution of mechanisms to suppress their transposition and the occasional co-opting of TEs for beneficial functions. Eukaryotes have evolved several mechanisms for suppressing activity of TEs in the genome. Examples include the repeat-induced point mutation (RIP) and methylation induced premeiotically (MIP) in Neurospora fungi to destroy multicopy TEs (Selker, 1999), homology-dependent gene silencing in flowering plants (Jensen et al., 1999), methylation suppression of transposon expression in various eukaryotes and gene silencing by RNA interference (RNAi) (Ketting et al., 1999). RNAi is found in various organisms, and is generally believed to have evolved as a defence against double-stranded RNA viruses (Hammond et al., 2001); however, evidence from *Caenorhabditis elegans* indicates that RNAi can cause germline silencing of transposons. Widespread methylation of cytosine residues in the genome occurs in vertebrates and various plant species to reduce the rate of transposable element activity and the incidence of their associated deleterious mutations (Yoder et al., 1997). Occasionally eukaryotic genomes might 'co-opt' TEs for specific functions. Examples include telomere maintenance and aspects of the vertebrate immune system. TEs provide genetic material on which natural selection can act, and so it is not surprising that new beneficial functions for these sequences would evolve. Classical parasites (for example, viruses and bacteria) are believed to be important forces in the evolution of eukaryotes.

Host Speciation

The role of SGEs in reproductive isolation and subsequent eukaryotic speciation can be understood by *Hybrid dysgenesis*-induced transfer of TEs in hybrid crosses. TEs in such hydrids might have a role in beginning of reproductive isolation through increased rate of new chromosomal rearrangements (inversions and translocations) which are fixed in different populations with different chromosome rearrangements. For example, there is a relationship between *P*-element insertion sites and inversion breakpoints in natural populations of *D. willistoni* (Regner et al., 1996). Recent studies indicate that cytoplasmic incompatibility caused by *Wolbachia* could have a role in promoting reproductive isolation between closely related species, thus allowing divergence to continue and speciation to occur (Cordaux et al., 2011). Generally, the unidirectional cytoplasmic incompatibility (CI) is not sufficient to cause reproductive isolation between species, because horigental *gene flow* enables the bacteria to infect both species and eliminate the existing CI between them. However, other isolating mechanisms (for example, mate discrimination) in association with CI, might obstruct gene flow between the species as observed between *D. recens* and *D. subquinaria* (Shoemaker et al. 1999). However,, bidirectional cytoplasmic incompatibility (bi-CI) causes incompatibility in both

directions when two populations or species are infected with different *Wolbachia* strains. The parasitic insect genus *Nasonia* includes three closely related species; each infected with its own set of *Wolbachia* strain that cause bi-CI. The bi-CI has arisen early during speciation in this system, before the evolution of other common isolating mechanisms, such as *hybrid breakdown*, *hybrid inviability* and *hybrid sterility*, indicating the potential role of *Wolbachia* in early speciation (Bordenstein et al., 2001).

Host Extinction

There are three important studies to support the hypothesis that the fixation of meiotic drive sex chromosomes could lead to host extinction either due to a shortage of males because of a driving X chromosome, or due to a lack of females because of a driving Y chromosome through the population (Hamilton, 1967). Similar results could be predicted in case of mitochondria induced cytoplasmic male sterility, and in case of sex-ratio-distorting inherited microorganisms in host populations. In the first study, the meiotic drive sex chromosomes (using a translocation of sd to the Y chromosome) reached to fixation and eliminated *D. melanogaster* populations owing to a lack of females (Lyttle, 1977). Second study in the butterfly species *Acraea encedon* and *A. encedana*, showed that MK *Wolbachia* can reach very high frequencies in natural populations resulting in females leaving unmated (Jiggins et al., 2000). Finally, many natural populations reached to fixation due to parthenogenesis induced by *Wolbachia* strains (Stouthamer et al., 1999). Extinction of host populations due to sex-ratio distorters, however, might be avoided if the distortion is incomplete or if SGEs do not reach fixation in the population leading to population persistence. Alternatively, frequency-dependent factors or autosomal resistance genes can maintain sex-ratio distorters at intermediate prevalence.

CONCLUSIONS REMARKS

SGEs are widely distributed and make up a large part of the genome in many of eukaryotic species. In this review, we have discussed some of the evidence that indicate that SGEs have an important role in eukaryotic evolution. The potential role of genomic conflict between Mendelian nuclear genes and non-Mendelian sex distorters in evolution of sex-determination is very real, although not yet fully evaluated. Beyond their importance in the design of genome, SGEs might encourage speciation or cause host extinction. SGEs forcefully illustrate the nature of natural selection. These elements also exemplify different levels of selection, in these cases, genic selection acts in opposition to individual selection.

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