

Co-Evolution of Genomic Structure and Selective Forces Underlying Sexual Development and Reproduction

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Key Words

Adaptation · Environmental and temperature-dependent sex determination · Genomic organization · Genotypic sex determination · Natural selection · Reptile genome evolution · Sex chromosomes · Sex ratio · Sexual conflict · Sexual selection

Abstract

Genomic structure affects the expression and evolution of phenotypes via its effect on genomic function. One example is the presence of sex chromosomes and the development of the sexual phenotype. Multiple forces account for the evolution of genomic structure and function, some acting synergistically and some in an antagonistic manner, in a co-evolutionary process between genomic architecture and environmental effects at different time scales. Here I review the evolution of sex chromosomes and how they affect sex determination, sex ratios, sexual selection, and sexual conflict, at the same time that these phenomena influence the evolution of genome organization. Because of this reciprocal interaction, the need to correctly identify sex chromosome systems in order to understand the causes and consequences of their evolution is emphasized. Importantly, it is argued that the existence of taxa lacking sex chromosomes poses a challenge to current evolutionary models and a unique opportunity to test them empirically using reptiles as a model system.

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How genomic architecture affects the development of phenotypes has been a persistent question that permeates many areas of biological research. One exemplary process is the development of the sexual phenotype which has long been the target of study, and where emerging views that combine information from many disparate disciplines are also providing an integrated understanding of how genomic structure and function respond to environmental forces at ecological and evolutionary time scales. Of particular importance is the co-evolution that takes place between sex chromosomes and sexual development, sex ratios, sexual conflict, and sexual selection. These forces can have a synergistic or antagonistic effect in the evolution of genomic structure and function. Here I review this co-evolutionary interaction and argue that reptiles with their variation in genomic structure constitute an excellent study system to test the significance of sex chromosomes in the evolution of these phenomena, and to revisit current theoretical models about the causes and consequences of genome evolution.

Sex Chromosome Systems

One of the most striking features of genome structure with respect to sexual development is the presence of sex chromosomes, given that they house sex-determining genes. Sex determination is recognized as the irreversible

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commitment to the male or female developmental fate, which can be initially triggered by genetic factors such as those contained in sex chromosomes (GSD: genotypic sex determination) or by environmental factors (environmental sex determination) such as temperature (TSD: temperature-dependent sex determination) [Valenzuela and Lance, 2004; Valenzuela, 2008a]. Thus, sex chromosomes are the keepers of genetic master triggers responsible for activating the developmental cascade that directs a bipotential embryo to a male or a female fate. Sex chromosome systems vary throughout the tree of life and include male (XX/XY or XX/XO) and female (ZZ/ZW) heterogamety found in animals and plants [Ohno, 1967; Charlesworth, 1996, 2002; Pires-DaSilva, 2007; Lan et al., 2008; Yin et al., 2008]. Some more complex variants of these sex chromosome systems also exist, with some remarkable examples in amphibians (e.g. XXAA♂/XYAA♀/XAA^Y♀ in *Eleutherodactylus riveroi* [Schmid et al., 2003]), fish (e.g. X₁X₂Y/X₁X₁X₂X₂ in *Eigenmannia* [Henning et al., 2008]), mammals (e.g. X₁X₁X₂X₂X₃X₃X₄X₄X₅X₅/X₁Y₁X₂Y₂X₃Y₃X₄Y₄X₅Y₅ in *Ornithorhynchus anatinus* [Grutzner et al., 2004]), as well as invertebrates (e.g. X₁X₂X₃X₄X₅Y/X₁X₁X₂X₂X₃X₃X₄X₄X₅X₅ in *Malthonica ferruginea* [Kral, 2007]) and plants (e.g. X₁X₂Y₁Y₂, XY₁Y₂ in *Humulus* [Matsunaga and Kawano, 2001]).

Reptiles possess a variety of sex-determining mechanisms [Valenzuela and Lance, 2004; Organ and Janes, 2008] making them an ideal group to study the co-evolution between genomic structure and function in directing sexual development. Squamates possess XX/XY, ZZ/ZW, and homomorphic sex chromosomes thus far undetectable with classic cytogenetic techniques [reviewed in Pokorna and Kratochvil, 2009]. Within squamates, Serpentes have exclusively a ZZ/ZW system while lizards exhibit both male and female heterogamety, and a single amphisbaenian has been shown to possess a ZZ/ZW mechanism [Cole and Gans, 1987]. The ancestral state for squamates remains unclear as some studies suggest it may have been TSD with lack of sex chromosomes [Janzen and Krenz, 2004; Pokorna and Kratochvil, 2009], while other reconstructions yield XY as the ancestral system [Organ and Janes, 2008]. Within archosaurs, all birds possess ZZ/ZW [Solari, 1994].

In turtles, only eight cases of heteromorphic sex chromosomes have been reported. These include six XX/XY systems in *Acanthochelys radiolata* [McBee et al., 1985], *Staurotypus salvinii* and *S. triporcatus* [Bull et al., 1974], *Siebenrockiella crassicollis* [Carr and Bickham, 1981], *Chelodina longicollis* [Ezaz et al., 2006], and *Emydura macquarii* [Martinez et al., 2008], plus two ZZ/ZW in-

stances in *Kachuga smithii* [Sharma et al., 1975], and *Pelodiscus sinensis* [Kawai et al., 2007]. Most of these examples are macro-sex chromosomes with the exceptions of *Chelodina longicollis*, the first known case of micro-sex chromosomes in turtles [Ezaz et al., 2006] and more recently, *Pelodiscus sinensis* [Kawai et al., 2007]. Micro-sex chromosomes are an unusual mechanism in reptiles only found so far outside of turtles in the agamid lizard, *Pogona viticeps* (ZZ/ZW) [Ezaz et al., 2005]. These last 3 findings underscored the functional importance of previously underappreciated micro-chromosomes as indicated by Bull [1983], and opened the question about the prevalence of micro-chromosomes in GSD reptiles as cryptic sex chromosomes that are only detectable with high resolution cytogenetic techniques such as comparative genome hybridization. Lastly, most turtles studied thus far, all crocodylians, *Sphenodon*, and numerous lizards exhibit TSD [Deeming, 2004; Ewert et al., 2004; Harlow, 2004; Nelson et al., 2004; Valenzuela, 2004a; Pokorna and Kratochvil, 2009], a system whose evolution has evaded full scientific explanation [reviewed in Valenzuela, 2004b].

Steps in Sex Chromosome Evolution

The sex chromosome mechanisms mentioned above, even when of the same type, are evolutionarily highly labile and have arisen independently multiple times [Valender and Lahn, 2006]. Sex chromosome evolution appears to follow a series of well-described steps [reviewed in Charlesworth, 1991; Bachtrog, 2006; and Engelstadter, 2008], and are briefly summarized here. The process begins by the appearance of a sex-determining gene (or the neo-functionalization of a previously existing gene into a sex-determining role) in an ancestral autosome [Ohno, 1967; Charlesworth, 1991]. This is followed by reduced recombination around the region containing the sex-determining genes (likely to avoid the production of suboptimal genotypes [Charlesworth and Charlesworth, 2000]), which permits the accumulation of sexually antagonistic genes that in turn favors further reduced recombination in a positive feedback loop [Rice, 1987; Rice, 1992]. Lower recombination enables the accumulation of deleterious mutations in the heterogametic sex chromosome through one or more processes. One potential process is that when recombination is low, selection is inefficient at purging deleterious mutations in the heterogametic chromosome under their heterozygous state, because the lower effective population size experienced

by such genes allows drift to drive them to fixation [Nei, 1970]. Deleterious mutations also accumulate by Muller's ratchet, by background selection (which can have a synergistic effect on Muller's ratchet), by 'weak-selection Hill-Robertsonian effects', or by the genetic hitchhiking provided by mutations that are favored by selection [reviewed in Charlesworth and Charlesworth, 2000]. Such genetic load can lead to the genetic degeneration (loss of gene function) of the heterogametic sex chromosome which may be followed by its physical degeneration (loss of genes) as with the Y chromosome of mammals [Rice, 1996]. This process can thus result in the formation of two morphologically dissimilar sex chromosomes, exhibiting distinct patterns of heterochromatin accumulation and deletions [Ohno, 1967; Vallender and Lahn, 2004; Waters et al., 2007]. The degeneration of the heterogametic sex chromosome may cause its extinction [Graves, 2002; Graves, 2006], and a new pair of sex chromosomes may be formed de novo by the reiteration of the same process [Charlesworth et al., 2005; Just et al., 2007], or by the translocation of an ancestral sex-determining gene onto an autosome [Van Doorn and Kirkpatrick, 2007]. Examples of nascent sex chromosomes are known in both animals [e.g. Almeida-Toledo et al., 2000; Peichel et al., 2004; Just et al., 2007] and plants [e.g. Liu et al., 2004; Ming et al., 2007]. The degeneration of the heterogametic sex chromosome may also elicit the evolution of dosage compensation mechanisms [Bull, 1983; Charlesworth, 1996]. Interestingly, similar steps leading to the formation of large chromosomal regions of reduced recombination in strata with discrete evolutionary history as occurs in animal and plant sex chromosomes are also detected in basal life forms such as fungi [Hood et al., 2004; Fraser and Heitman, 2005].

It should be noted however that degeneration of the heterogametic sex chromosome is not ubiquitous [e.g. Sites et al., 1979]. On the one hand, recently derived Y (or W) chromosomes at the early stages of evolution are expected to show little or no morphological degeneration and reduced recombination, which may explain the presence of homomorphic sex chromosomes in many taxa [Bull, 1983; Solari, 1994; Volff and Schartl, 2001; Liu et al., 2004; Vallender and Lahn, 2004; Gorelick, 2005]. On the other hand, extreme differentiation between sex chromosomes and degeneration of the heterogametic sex chromosome might not be the only, or the inevitable, evolutionary trajectory. For instance, some species are known to possess larger Y chromosomes than the X as occurs in some *Drosophila*, polychaetes, frogs, plants, and turtles [Lewis and John, 1963; Sato and Ikeda 1992; Solari, 1994;

Matsunaga and Kawano, 2001; Martinez et al., 2008]. Ohno [1967] considered the presence of a larger W chromosome than the Z an evolutionary 'dead end' resulting from the accidental crossing-over between the Z and the W after the latter had experienced a pericentric inversion. More recently however, increases in the size of the Y chromosome or expansion of specific regions compared to the X have been identified in some plants and fish, and may be the result of within-chromosome duplications, or the insertion of transposable elements or autosomal sequences [Ming and Moore, 2007]. Furthermore, homomorphic or scarcely differentiated sex chromosomes are found in some ancient vertebrate lineages [e.g. Pigozzi and Solari, 1999; Nakamura, 2009] and are presumably ancient systems themselves [Pigozzi and Solari, 1999; Mank and Ellegren, 2007]. If true, higher homomorphism may not always represent the early and transitory stage in the evolution of recently formed sex chromosomes, but might instead be an evolutionarily stable state. What prevents the evolution of heteromorphic sex chromosomes in such ancient systems remains unknown.

Forces behind Sex Chromosome Evolution

Genome structure in terms of the presence, content and divergence of sex chromosomes is influenced by selective forces acting at different levels of organization. Besides the factors described previously, these forces include selection on sex allocation, sexual conflict, and sexual selection, among others. Reciprocally, the presence and evolution of sex chromosomes affect these processes with important fitness effects which have a significant influence on speciation and extinction. Thus an important co-evolutionary interplay occurs between fundamental aspects of genomic architecture and these reproductive phenomena. For instance, selection favoring the transition from monoecy to dioecy in ancestral organisms may have driven the evolution of sex chromosomes in primitive systems [Charlesworth, 1991] and the development of more elaborate sexual dimorphisms beyond anisogamy [Rice, 1984]. Intralocus conflict exists when a gene is beneficial to one sex and detrimental to the other [Bonduriansky and Rowe, 2005]. Chromosomal sex determination permits the accumulation of genes in the heterogametic sex chromosomes (Y or W) that benefit the heterogametic sex (XY males or ZW females), even at the expense of the homogametic sex [e.g. Roldan and Gomendio, 1999]. On the other hand, sexual selection can have a significant influence in the evolution of sex chromosomes. Namely,

selection acting on sexually antagonistic genes via inter- and intralocus sexual conflict favors their accumulation in the heterogametic sex chromosome (Y or W) [Rice, 1987; Rice, 1992; van Doorn, 2009; but see Mank and Ellegren, 2009a] thus affecting sex chromosome composition, which in turn can influence reproductive traits. In a recently reported example, sex chromosome content in the form of sexually antagonistic genetic variation that is X-linked was shown to influence female mate choice and female-induced sex ratio biases [Connallon and Jakubowski, 2009]. Sex ratio biases can also result from sex chromosome drive as documented in mammals, flies, and plants [Werren and Beukeboom, 1998; Jaenike, 2001]. Moreover, differences between sex chromosomes and autosomes can lead to the recently described zygotic-drive, a process somewhat resembling meiotic-drive where competition occurs among siblings of the opposite sex rather than among gametes [Rice et al., 2008].

Whether males or females are the heterogametic sex affects the relative likelihood of occurrence of various evolutionary mechanisms (good-genes or Fisher's runaway models) of sexual selection [Kirkpatrick and Hall, 2004a]. Furthermore, what sex is heterogametic has important consequences on genome organization because sexual conflict via maternal-effect genes in ZZ/ZW systems has a stronger effect on the degeneration of the heterogametic sex chromosome (W) than sexual selection, due to the combined effect that females have on both egg allocation and sex determination, unlike in XX/XY systems [Miller et al., 2006]. Additionally, the presence of female heterogamety (ZZ/ZW or ZZ/ZO) may permit the development of more extreme conspicuous secondary sexual characters in males and associated female preferences than male heterogametic systems [Reeve and Pfennig, 2003; Albert and Otto, 2005].

Finally, the evolution of neo-sex chromosomes by the translocation of an ancestral (perhaps degenerate) sex chromosome into a pair of autosomes could cause profound changes in the *cis*- and *trans*-regulation of the genes contained in these chromosomes [e.g. Carvalho and Clark, 2005] as it can break existing syntenic blocks and generate new ones. The translocation of autosomal regions onto sex chromosomes will have the same effect. Indeed, several explanations have been proposed for the conservation of syntenic blocks. One states that the requirement for a temporal order of expression keeps the cluster intact [e.g. Patel, 2004], and another that the regulatory elements must stay linked to the genes they regulate [e.g. Ahituv et al., 2005]. The conservation of syntenic blocks has been documented but it is hardly ubiqui-

tous, as significant and rapid evolutionary changes in chromosomal rearrangements occur [e.g. Matsuda et al., 2005; Richards et al., 2005]. Importantly, if any of the genes within the rearranged chromosomal region are ecologically important, such as would be the case of sex-determining genes contained in sex chromosomes, translocations or fissions could cause the evolutionary split of the lineages possessing and lacking the chromosomal rearrangement. Chromosome speciation has been documented in a number of taxa [e.g. Masly et al., 2006] and the process responsible for the spread and fixation of large chromosomal mutations has stimulated much theoretical debate [White, 1968; Ayala and Coluzzi, 2005; Coghlan et al., 2005]. However, recent work has demonstrated the role of neo-sex chromosome formation in the speciation of stickleback fish via the effect of courtship genes that contribute to reproductive isolation, thus providing empirical evidence that sex chromosome turnover can function as a driver of the speciation process [Kitano et al., 2009].

What Happens When Sex Chromosomes Are Lacking?

Given the important differences that exist in the evolutionary trajectories and relative rates of evolution of sex chromosomes and autosomes [Charlesworth et al., 1987; Kirkpatrick and Hall, 2004b], and given that sex chromosomes have significant consequences for the evolution of phenomena such as sexual dimorphisms, sexual conflict, sex ratio evolution, speciation and extinction as described above [e.g. Berry and Shine, 1980; Rice, 1984; Lindholm and Breden, 2002; Valenzuela et al., 2003; Edwards et al., 2005; Saether et al., 2007], a logical question ensues. Namely, what happens with all these processes that are so profoundly affected by the presence and evolution of sex chromosomes when a species lacks sex chromosomes altogether? In this respect, a complementary issue should be noted here as it is critical to answering this question appropriately. It is essential to correctly identify the sex chromosome systems when they exist if we are to understand their evolution and the evolution of sex-related traits. Therefore, distinguishing species that do indeed possess sex chromosomes from those that lack them [Valenzuela et al., 2003] is a crucial step in this direction, and not a simple matter of semantics [contra Sarre et al., 2004]. Particularly, as described above, theory predicts that the evolution of the fundamental traits and processes such as sexual dimorphisms, sexual conflict, sex ratio

evolution, speciation and extinction occurs differently in species that exhibit strict chromosomal sex determination, in those that possess sex chromosomes but are susceptible to environmental factors that distort Mendelian sex ratios, and in those that may have strict environmental sex determination in the complete absence of sex chromosomes [Valenzuela et al., 2003]. Thus, although a continuum clearly exists from taxa with strict GSD, through taxa that have GSD systems increasingly sensitive to environmental perturbations, to species with strict environmental sex determination [see fig. 1 in Valenzuela et al., 2003], and although the gene regulatory network underlying sexual development is composed of numerous elements common to all vertebrates [Place and Lance, 2004; Valenzuela, 2008a, b], whether the species possesses or lacks sex chromosomes has a biological and evolutionary relevance that is far from trivial and should not be ignored. This realization will help us understand the potential adaptive significance not only of the extremes of this continuum, but importantly, of sex chromosome systems that are susceptible to environmental influences [Bull, 2008].

Reptiles as a Model System

Reptiles are an ideal group to answer this question because of the variation they exhibit in sex-determining mechanisms among closely related taxa, including sex chromosome systems and environmental mechanisms. While tests about the importance of genomic architecture on the evolution of these fundamental phenomena have relied for the most part on examining or contrasting taxa with male and female heterogamety, a complementary approach using TSD and GSD reptiles will greatly enhance our knowledge in this area. For instance, we can examine the evolution of sexual dimorphism, sex allocation, sexual conflict, and sexual selection in reptiles that possess sex chromosomes and compare with those species that lack them. A research approach that addresses these questions would test the theoretical models in this area and provide critically needed empirical evidence for their biological significance.

While sex ratio evolution under TSD versus GSD in reptiles has received extensive attention, the explicit effect of the absence or presence of sex chromosomes on sexual dimorphism, sexual conflict, and sexual selection has remained understudied. The following are some of the questions that could be derived from theoretical expectations and tested directly using reptiles:

(1) Do TSD reptiles truly lack sex chromosomes? Given that modern cytogenetic techniques have enabled the discovery of otherwise cryptic sex chromosome systems in reptiles that showed no detectable dimorphism by classic methods [Ezaz et al., 2005, 2006], the theoretical assumption that one extreme of the continuum of the sex-determining mechanisms is represented by reptiles that lack sex chromosomes should be empirically tested. On the one hand, if sex chromosomes were found in TSD taxa, we should then ask why the theoretical extreme of a pure TSD system without sex chromosomes has not been attained in nature, as its absence would challenge current knowledge about the evolution of sex-determining mechanisms [Bull, 1983; Valenzuela, 2004b; Bull, 2008; Georges et al., 2010]. On the other hand, if sex chromosomes are truly lacking in TSD taxa, then we should ask the following questions.

(2) Does the absence of sex chromosomes prevent the development of sexual dimorphisms to the extent that they are achieved in the presence of sex chromosomes?

(3) How do the mechanisms underlying the ontogenetic development of sexual dimorphism differ among species with and without sex chromosomes?

(4) Is sexual conflict or sexual selection weaker in the absence of sex chromosomes?

What We Know Thus Far

As mentioned above, the evolution of sex ratio under TSD in contrast to GSD in reptiles has been intensively investigated. Indeed, it was the observation of biased sex ratios that drove the original discovery of TSD in reptiles [Charnier, 1966] which was followed by the empirical and theoretical work of many researchers in an attempt to study its prevalence, proximate mechanism, and adaptive significance [e.g. Pieau, 1971; Charnov and Bull, 1977; see Bull, 2004 for a historical account; reviewed in Valenzuela and Lance, 2004]. Space constraints prevent a full description here. Sex ratio evolution when the environment reverses the effect of sex chromosomes or when sex chromosomes are absent can be very dynamic, moving from balanced to highly biased proportions of males or females. Whether these plastic systems are dominated by environmental vagaries or by Fisherian forces via frequency-dependent selection, depends on ecological circumstances and evolutionary constraints [Fisher, 1930; reviewed in Bull, 1983; Charnov and Bull, 1989; Valenzuela, 2004b; Bull, 2008]. But what about phenomena beyond sex ratio that are so strongly influenced by the presence of sex chromosomes?

Sexual dimorphism has been documented in reptiles for a number of traits, including body size, coloration, and several reproductive behaviors [e.g. Berry and Shine, 1980; Brana, 1996; Wikelski and Trillmich, 1997; Morbey and Ydenberg, 2001; Butler and Losos, 2002; Shine, 2003; Cox et al., 2007; Husak and Fox, 2008]. Interestingly, TSD turtles show greater sexual dimorphism in body size in general than do GSD turtles [Ceballos et al. unpublished]. For instance, the most extreme sexual size dimorphism (the average adult female size being 1.6 to 2.5 times larger than that of males) is found in some of the *Graptemys*, *Kachuga*, *Pseudemys*, *Trachemys*, *Malaclemys*, and *Podocnemis* turtles (all TSD), with only two of the *Apalone* turtles (GSD) reaching intermediate dimorphism (1.7–1.8) [e.g. Ernst and Barbour, 1989; Gibbons and Lovich, 1990; Stephens and Wiens, 2008]. Assuming that TSD turtles do indeed lack sex chromosomes, this observation would appear to challenge the prediction that sex chromosomes are fundamental for the development of sexual dimorphism. Furthermore, it has been proposed that the evolution of TSD was favored as a mechanism that permits the development of adaptive sexual size dimorphism in reptiles [Head et al., 1987], although results from empirical tests remain equivocal [Ewert et al., 1994; reviewed in Valenzuela, 2004b]. Additionally, sexually dimorphic performance in species with contrasting sex chromosome systems (male and female heterogamety) have been documented [Van Damme et al., 2008], and encompass traits that may be under sexual selection [Husak and Fox, 2008]. Furthermore, complex sexual dimorphic patterns among closely related *Anolis* and among ecomorphs that share the same sex chromosome mechanism exist, though they may not be the result of sexual selection alone [Butler and Losos, 2002]. It should be noted that losses of sexual dimorphism in reptiles over evolutionary time have occurred in some instances [Wiens, 2001]. Sexual selection is present in reptiles with and without sex chromosomes via female and male choice, direct male competition, and potentially via sperm competition [e.g. Pearse and Avise, 2001; Butler and Losos, 2002; Shine, 2003; Poschadel et al., 2006; Baird et al., 2007; Husak and Fox, 2008; Irschick et al., 2008; Van Damme et al., 2008; Uller and Olsson, 2008]. Likewise, sexual conflict is also found in reptiles in the presence and absence of sex chromosomes [e.g. Shine, 2003; Calsbeek and Bonneaud, 2008; Fitze and Le Galliard, 2008; Uller and Olsson, 2008; King et al., 2009]. Recent work on GSD reptiles indicated that sexual conflict may favor biased sex ratio under facultative sex allocation [Alonzo and Sinervo, 2007] and mediate the effect that sex ratios have on sexual selection act-

ing on sexual size dimorphism, ultimately also affecting speciation [Fitze and Le Galliard, 2008].

Given this variation, targeted research in reptiles could reveal how essential are sex chromosomes in the evolution of these and related traits and phenomena, allowing a critical empirical re-evaluation of theoretical models in this field. Moreover, deciphering the relative significance of sex chromosomes on the evolution of sexual selection and sexual dimorphism is also critical because the potential role of sexual selection in speciation remains controversial [Gray and McKinnon, 2007], and sexual dimorphism might be an important driver in sex ratio evolution [Uller, 2006].

If dimorphic traits are controlled hormonally, then there should be no major difference as to whether the primary sex is initially triggered by sex chromosomes or by an environmental factor. Reptiles have been a historically important group in the research of endocrine control of dimorphic traits [Crews and Moore, 2005]. Evidence indicates that testosterone controls sexual dimorphism and other sexually selected traits in reptiles with and without sex chromosomes [Sakata and Crews, 2004; Woolley et al., 2004; Miles et al., 2007; Cox et al., 2009], as it occurs in other lower vertebrates [e.g. Mank, 2007]. Interestingly, recent experiments and comparative analyses indicate that the evolution of sexual size dimorphism might have been facilitated by evolutionary changes in the underlying effect of testosterone on body growth [Cox et al., 2009]. In this context, one can envision a scenario where the absence of sex chromosomes may have permitted the environmental control of the endocrine system under a TSD mechanism to enable the evolution of sexual size dimorphism in reptiles as proposed previously [Head et al., 1987]. This scenario may require sexual selection to play a lesser role in the evolution of sexual dimorphism given the purported effect that sex chromosomes can have on the evolution and strength of sexual selection [e.g. Reeve and Pfennig 2003; Kirkpatrick and Hall, 2004a; Albert and Otto, 2005; Miller et al., 2006]. It has recently been noted that sexually dimorphic phenotypes develop ontogenetically via differential expression of many genes whose accelerated evolution has been attributed to sexual selection but which may instead be the result of relaxed selection if they are more dispensable than genes that show stronger effects on survival and fertility [Mank and Ellegren, 2009b]. The resolution of the evolution of sexual conflict in the absence of sex chromosomes may have taken a similar route. One possibility is for TSD reptiles to utilize hormonal systems dependent on the environmentally-controlled gonadal differentia-

tion to differentially activate or suppress genes with sexually antagonistic effects. Finally, the co-evolution between sex chromosomes and dosage compensating mechanisms also requires revisiting in light of the extremely local compensation exhibited by taxa with female heterogamety [Mank, 2009]. Finally, work in GSD reptiles susceptible to thermal sex reversals has recently provided novel insight into the evolution of dosage compensation [Quinn et al., 2007].

Where Are We Now and Where Are We Headed?

In summary, much has been gained in our understanding of sex chromosome evolution in terms of the trajectory followed from their initial formation, the drivers of such processes, and the consequence of their evolution on sex-related traits and phenomena. In particular, evidence was presented to demonstrate the co-evolution between sex chromosomes and multiple fundamental biological processes, from sexual development via sex determination to sex ratios, sexual conflict, sexual selection, and ultimately speciation and extinction. However, some aspects of the existing paradigm are challenged by empirical evidence from sex chromosome systems with properties counter to theoretical models [e.g. Pigozzi and

Solari, 1999; Mank, 2009; Mank and Ellegren, 2009b], and by species lacking sex chromosomes that show phenomena purported to be largely influenced by the presence of sex chromosomes. Importantly, the existence of closely related species such as reptiles that exhibit these traits and processes in the absence of sex chromosomes provides a unique opportunity to test empirically current theoretical models and perhaps to change existing paradigms of the evolution of genome structure and function. Questioning the significance of sex chromosomes in the development and evolution of these traits and phenomena is not unprecedented, and it is hoped that studying the causes and consequences of reptilian genomic evolution continues to contribute to our understanding in this area. An exciting era of discoveries is expected from comparative research particularly given the burst of emerging genomic resources to facilitate such efforts [Modi and Crews, 2005; Janes et al., 2008; Valenzuela, 2009].

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