Sex Chromosome Evolution

1. Sex Determination

Almost all life forms undergo some type of sexual reproduction (defined as genetic exchange between individuals) and many species have two morphologically distinct sexes, males and females. The way the sexes are determined varies among taxa. Some examples:

a) Environmental sex determination – males and females are genetically identical. Sex is determined by environmental conditions. Example: in turtles and crocodiles, sex is determined by the temperature at which the eggs are reared. In sea turtles, low temperature (below 27 C) = male, high temperature (above 31 C) = female, intermediate or fluctuating temperatures produce a mix of males and females.

b) Haplodiploidy – females develop from fertilized eggs and are diploid. Males develop from unfertilized eggs and are haploid. Example: honey bees.

c) Male heterogamety – sex is determined by sex chromosomes. Females are XX and males are XY. Males are heterogametic. Example: humans, *Drosophila*

d) Female heterogamety - sex is determined by sex chromosomes. Females are ZW and males are ZZ. Females are heterogametic. Example: birds, butterflies

2. Origin of sex chromosomes

Sex chromosomes (XY or ZW) are thought to derive from an ancestral pair of autosomes, one of which gained a sex-determining locus. Over time, sexually antagonistic mutations (mutations that are beneficial to one sex, but deleterious to the other) are expected to accumulate on the chromosome bearing the sex-determining locus. This should favor suppression of recombination between the two chromosome copies. Eventually, the lack of recombination leads to the degeneration of the sex-specific chromosome (Y or W).

3. *Drosophila* sex chromosomes

Like humans, *Drosophila* has an XY sex determination system. The Y is highly degenerated and contains only 12 protein-coding genes that are required for male fertility. The X, on the other hand, has over 2,000 genes, many of which are essential for viability. Gene density on the X is similar to that of the autosomes. In *Drosophila*, the X contains about 16% of the genes in the genome, while the Y contains less than 0.1%.

4. Sex-biased gene content

Microarray and RNA-seq experiments have found that sex-biased genes (genes with higher expression in one sex than the other) are not randomly distributed across the *Drosophila* genome. Male-biased genes tend to be under-represented on the X ("demasculinization"), while female-biased genes tend to be over-represented on the X ("feminization"). Some tissues show an exception to this pattern. For example, in the brain there is an excess of male-biased genes on the X.

5. Special evolution of the X chromosome

There are two evolutionary "effects" that are specific to the X chromosome:

a) Fast-X effect: an expected increase in the rate of adaptive evolution on the X chromosome due to the fixation of recessive, beneficial mutations in hemizygous males. This effect is observed in *Drosophila*.

b) Large-X effect: the X is enriched for loci that cause hybrid incompatibilities, such as hybrid male sterility, suggesting that the X plays a disproportionately large role in speciation – at least in the evolution of postzygotic reproductive isolation. This effect is observed in hybrids of *Drosophila* species.

6. Special regulation of the X chromosome

There are two regulatory mechanisms specific to the X chromosome in male *Drosophila*.

a) X chromosome dosage compensation: in male somatic tissues, expression of the single X chromosome in up-regulated approximately two-fold. This balances expression with autosomal genes and with the 2 copies of the X in females. The up-regulation occurs through the specific binding of an RNA/protein complex (Dosage Compensation Complex, DCC) to many locations across the male X chromosome. Dosage compensation does not appear to occur in the male germline.

b) Suppression of X expression in the male germline: in the male germline, the expression of the X chromosome is suppressed. This is similar to what occurs in mammals and is also referred to as meiotic sex chromosome inactivation (MSCI).

Suppression of the X chromosome can be demonstrated using reporter genes that are expressed specifically in the testes and comparing the expression of autosomal vs. X-linked copies of the reporter genes.

Suppression of the X occurs in testes, but not in other tissues. The degree of suppression depends on the expression level of the gene (that is, how strongly its regulatory sequences induce expression in testes).

Although most other types of tissue-specific genes are underrepresented on the X chromosome, reporter gene experiments indicate that they are not subject to X suppression. For example, genes expressed in accessory gland are under-represented on the X. However, accessory gland specific reporter genes show no evidence of X suppression.

In contract to other tissue-specific genes, ovary-specific genes are over-represented on the X, which is consistent with feminization of the X chromosome. However, there does not appear to be a chromosome-wide mechanism to up-regulate the X in the female germline.

The X chromosome is not an inherently bad environment for tissue-specific expression. It is possible to get highly tissue-specific expression of X-linked reporter genes.