

## LECTURE 32

### GENETICS OF INVERSIONS

#### A. Pairing of inversion genotypes:

1. Characteristic inversion loops form only in chromosomal heterozygotes of both para- and pericentric inversions. Based on the inversion loop, one can determine the type (para- or pericentric) and size of the inversion. Note that pairing of homologues in either chromosomal homozygote is “normal.”

#### B. Genetic consequences of inversions:

The critical genetic consequences of inversions stem from events that occur during meiosis I when chromosomes are at the four-strand (tetrad) stage. These consequences are a function of crossing over between chromosomes with different gene arrangements, i.e., in chromosomal *heterozygotes*. Note, however, that there is a genetic “consequence” of an inversion in the general sense that gene order has been altered. In the following, crossing over is considered in chromosomal (structural) heterozygotes.

##### 1. Paracentric inversions:

a) No crossing over: Only parental types (two *st* chromosomes and two *in* chromosomes) are recovered.

##### b) Single crossovers:

(i) Outside the inversion loop: There is no consequence other than the “normal” marker exchange expected from crossing over.

(ii) Within the inversion loop: A dicentric bridge and an acentric fragment are generated.

(a) The acentric fragment is often “lost” during cell division, and if so, there is no consequence. If the acentric fragment ends up in a gamete, there is duplication and deficiency for genetic material, resulting inevitably in zygotic (developmental) lethality.

(b) The dicentric bridge is generally visible at anaphase I and “signals” the occurrence of a single crossover within the loop of a paracentric inversion. The dicentric bridge ultimately will fragment somewhere along its length. Products of this breakage that end up as gametes are generally deficient for genetic material and will result in zygotic (developmental) lethality.

2. Pericentric inversions:

- a) No crossing over: The result is the same as for paracentric inversions.
- b) Single crossovers:
  - (i) Outside the inversion loop: The result is the same as for paracentric inversions.
  - (ii) Within the inversion loop: Chromosomes that are duplicated *and* deficient for genetic material are generated.
    - (a) The combination of duplication and deficiency of genetic material almost always results in zygotic (development) lethality.

3. Synopsis of genetic effects of inversions:

- a) Crossing over (recombination, actually) is suppressed within the interval defined by the inversion.
  - (i) Single crossovers within the inversion loop in both (para- and pericentric) inversion heterozygotes generate gametic chromosomes that are duplicated and/or deficient for genetic material, typically resulting in zygotic lethality during early development.
  - (ii) Only *parental* chromatids (one *st* and one *in*) are recovered in the next generation.
  - (iii) The two chromosomal sequences (i.e., *st* and *in*) contained between the inversion break points are maintained intact (i.e., not broken up by crossing over) and may be treated as if they were alleles at a single genetic locus.
  - (iv) Inversions historically are called “crossover suppressers.” This is a misnomer, as recombination (not crossing over) is actually suppressed.
- b) Inversions permit the build-up and maintenance of *co-adapted gene complexes*.
  - (i) The region of a chromosome contained within the break points of an inversion may contain alleles at genes that confer increased fitness when they occur together. Natural selection thus could favor chromosomal mechanisms that insured the co-occurrence of these alleles within a zygote (individual of the next generation).
  - (ii) Random crossing over in this case would be inadaptive, as intact, adaptively beneficial complexes of alleles would be broken up by recombination.
  - (iii) Inversions would thus help build-up and maintain such complexes of alleles (referred to as “co-adapted gene complexes.”)

- c) Inversions are expected to have negative fertility effects.
- (i) In para- and pericentric inversions, single crossovers occurring within the inversion loop generate duplicated/deficient gametes that result in zygotic lethality. Occurrence of duplicated/deficient gametes is expected to translate into a reduction in fertility in inversion heterozygotes. This assumes that the inversion is sufficiently large so that the probability of a crossover is near unity.
  - (ii) Given this expected reduction in fertility, the selective advantage (benefit) of a co-adapted gene complex must outweigh the cost of up to a 50% reduction in fertility.
  - (iii) As might also be expected, compensatory mechanisms that maintain co-adapted gene complexes but reduce the loss of fertility have evolved.
    - (a) In *Drosophila* females, for example, the acentric fragment/dicentric bridge products generated from single crossovers in paracentric inversions are preferentially shunted into polar body nuclei. Consequently, there is no reduction in fertility in female *Drosophila* heterozygous for paracentric inversions.
      - (1) Because *Drosophila* males do not generate polar bodies, there should be a reduction in fertility in males heterozygous for paracentric inversions. However, no such reduction on fertility occurs because there is no crossing over in *Drosophila* males.
      - (2) Alternatively, there is up to a 50% loss in fertility in *Drosophila* females heterozygous for a pericentric inversion, as there are no compensatory mechanisms in *Drosophila* females that reduce fertility loss in pericentric inversion heterozygotes. As might be expected, there is no reduction in fertility in *Drosophila* males (because there is no crossing over in *Drosophila* males,
    - (b) In deer mice (*Peromyscus*), there are no apparent fertility effects in individuals heterozygous for pericentric inversions. In this case, the mechanism appears to be fairly abundant pericentromeric heterochromatin that reduces the incidence of crossing over.

#### 4. What about double crossovers?

- a) An effective rule-of-thumb regarding odd- vs. even-number of multiple crossovers within an inversion loop is that an odd number of crossovers to the same chromatid will result in the duplicated/deficient chromatid situation noted previously; whereas an even number of crossovers to the same chromatid will “correct” the problem.
  - (i) One crossover within a loop and one outside the loop are effectively the same as a single crossover within the loop.

- (ii) Two crossovers within a loop generate 2-strand dco, 3-strand dco (x2), and 4-strand dco. Predictions can be made (based on the above), given the number and types of crossovers to a given chromatid within a tetrad.
- b) Double crossovers (or at least chromatids undergoing two exchanges within an inversion loop) will “break-up” co-adapted gene complexes.
  - (i) This is a fairly rare event, in that interference and “strain” caused by loop formation (resulting in partial asynapsis) reduces the probability of double crossing over.
  - (ii) Nonetheless, these rare “events” can occur and can even be adaptive.

### C. Multiple inversions:

1. Multiple inversions are when more than one inversion occurs on the same chromosome. There are three types of multiple inversions.
  - a) Adjacent: A second inversion occurs adjacent to the break points of the first inversion.
  - b) Included: A second inversion is included within the break points (limits) of the first inversion.
  - c) Overlapping: A second inversion overlaps the first inversion (i.e., one break point occurs within the first inversion)
2. Multiple inversions are extremely useful in phylogenetic inference (construction of organismal-evolutionary trees).
  - a) Example: X chromosomes of four species of *Drosophila*
    - Species #1: a d e f c b g h
    - Species #2: a b c d e f g h
    - Species #3: a d e f h g b c
    - Species #4: a b c f e d g h
  - b) Given that Species #2 is ancestral (i.e., possesses ancestral sequence)...
 

Evolutionary sequence is: #2 → #4 → #1 → #3
  - c) More typically, the ancestral species (sequence) is not known, meaning that arrows are reversible and may have side branches.

#### D. Inversions and speciation

1. In populations differing by a single inversion, matings produce “hybrids” with reduced fertility, forming a reproductive barrier between populations. Inversions thus can serve as a “reproductive-isolating-mechanism.”
2. More generally, populations may differ by more than one inversion, and if so, pairing of homologues differing by multiple inversions becomes problematic, and “hybrids” may be up to 100% infertile.
3. The concept is that major chromosome rearrangements serve (or have served) as effective reproductive-isolating mechanisms. This is reinforced by the observation that virtually all species differ by one or more major chromosomal rearrangements.