CROSSING –OVER: Mechanism and its significance

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Crossing over is the exchange of genetic material between non sister chromatids of homologous chromosomes during meiosis, which results in new allelic combinations in the daughter cells.

During prophase I of meiosis, homologous chromosome align with each other and exchange genetic material, so that some of the resultant chromosomes are recombinants – containing a mixture of genes derived from the maternal as well as the paternal chromosomes.
The image is a representation of one set of homologous chromosomes, with genes being represented by different letters of the alphabet. The genes on one chromosome are shown using capital letters and that on the homologous pair using small letters. Two of the four daughter cells formed after this crossing over event have a recombinant chromosome that is neither completely derived from the mother nor the father. The image also demonstrates that genes that are in close physical proximity to one another on the chromosome are likely to be inherited together, while those that are farther away might get independently assorted during meiosis.

During prophase I, of Meiosis, chromosome condensation occurs and duplicated chromosomes with attached sister chromatids, are initially seen as long thin threads. As condensation proceeds, homologous chromosomes are brought together because of the similarity in structure and centromere position. A protein structure called the synaptonemal complex also plays an important role. At this point, chromosomes are anchored to the nuclear envelope. Now, recombination occurs between non-sister chromatids of homologous chromosomes. This is observed microscopically as a crossing over event between bivalent chromosomes (a pair of two chromosomes) with a tetrad structure (their duplicated sister chromatids are also visible). Towards the end of prophase I, homologous chromosomes now appear to ‘repel’ each other. The nuclear envelope is no longer clearly visible and the cell then moves on to metaphase and anaphase to complete the first stage of meiosis.
Crossing—over begins at Pachytene stage, after the synapsis of the homologous chromosomes has occurred in zygotene stage of Prophase I of Meiosis

**Mechanism of Crossing—Over:**

On a molecular level, crossing over begins with a double strand break in one of the DNA molecules. This double strand break can occur naturally through agents like radiation or carcinogens, or through the action of specific proteins. Enzymes, exonucleases, that remove nucleotides from the 5’ end of DNA, act on this break and remove short stretches of nucleotides in the 5’ -> 3’ orientation from both the strands. This leads to two hanging single-stranded rejoins that get coated with proteins that catalyze recombination, also known as recombinases. These enzymes catalyze the invasion of single strand regions into sequences that are suitable for base pairing. The close proximity of non-sister chromatids during prophase I, allows this single-stranded region to use the sequence on the homologous chromosome. The first invading strand behaves like a primer and synthesizes a double stranded region for itself using one strand of its non-sister chromatid as a template. This leads to its complementary strand getting displaced and base pairing with the second single stranded region that was initially generated by the exonuclease. Ultimately, this results in two strands being exchanged with the formation of a cross-like structure called the Holliday junction. This is named after the scientist who first proposed that such a junction could explain both crossing over and another phenomenon called
gene conversion where a **heterozygous** gene locus becomes homozygous during **cell division**. Holliday junctions can also be seen microscopically as ‘chiasma’ towards the end of prophase I, which continue to be visible till the end of **anaphase I**. Holliday junctions are stabilized and resolved through proteins that modulate genomic manipulation which are known as MSH4 and MSH5.

In the image, the events after strand invasion that lead to crossing over and Holliday junction formation are given on the right.

**Importance of Crossing-Over**

Crossing over increases the variability of a **population** and prevents the accumulation of deleterious combinations of alleles, while also allowing some parental combinations to be passed on to the offspring. This way, there is a balance between maintaining potentially useful allelic combinations as well as providing the opportunity for variation.
and change. It provides the way of micro evolution. Linkage map and genetic maps are constructed on the basis of Crossing-Over.

**Types of crossing over**

1. **Somatic crossing over**
   - Pairing of homologous chromosomes occurs in germinal cells but some times in somatic cells. Somatic crossing over is reported in *Drosophila* by **Curt Stern (1935)**. Somatic crossing over occurs rarely.

2. **Meiotic crossing over or germinal crossing over**
   - This type of crossing over takes place in germinal cells during gametogenesis.

**Kinds of Crossing Over**
- Single crossing over (only one chiasmata is formed)
- Double crossing over (two chiasmata are formed)
- Multiple crossing over (more than two chiasmata are formed)