Crossing-over, its mechanism and importance

Importance

Crossing over is a general mechanism in which two DNA molecules can exchange parts (recombine). All groups of organisms possess this mechanism (bacteria, archea and eukaryotes). In eukaryotes there are two uses of crossing over, in the sense of DNA exchanging part also called “homologous recombination”:

1) Crossing over in the strict sense during pachytene of meiosis I

a) The crossover process leads to offspring having different combination of alleles from those of their parents and thus in general increases variability of offsprings by reshuffling haplotypes. The process of recombination occurs between paired homologus chromosomes inherited from both parents.

b) Serves to guide meiotic cohesins that hold the two homologous chromosomes (bivalent) together until anaphase I (This is necessary for proper attachment to spindle and proper segregation)

2) Homologous recombination in all other situations

This is a general mechanism for repair of double strand DNA breaks. Double strand DNA break repair can be for simplicity divided into homologous recombination and nonhomologous end joining (NHEJ). As can be deduced from the mechanism (see below) homologous recombination is precise and can even return lost sequence (using another copy on another chromatid or another chromosome). However, it can lead astray if the breakpoint resides in a repetitive sequence – if a wrong copy of the repetitive sequence is used for the repair, this unequal crossing over can cause insertion, deletion, duplication, inversion, reciprocal translocation etc. (maybe figure). Therefore our cells use NHEJ very often, which depends on quickly gluing together any close free (nontelomeric) DNA ends, supposing that if it is really fast, the ends that belong to each other are in proximity (before separated by diffusion). Of course this can also lead to chromosome rearrangements (if there are more breaks simultaneously in proximity) and often to small deletions or insertions at the breakpoints (which usually do not matter, if they are not in coding or important regulatory sequence).

Mechanism

double stranded DNA cut is made in one chromosome – in meiosis it is initiated by PRDM9 (PRDM9 though is only label, not the endonuclease itself), in other situation it is a result of DNA damage exonucleases create single stranded 3´overhangs these single stranded DNA overhangs invade the other chromosome (strand invasion), mediated by Rad51 (RecA in bacteria) – heteroduplex DNA is formed DNA polymerase extends the 3´ ends of the original overhangs using the other chromosome as template ligase seals the ends, forming a double Holiday junction recutting and religation of the Holiday junction can make crossover or noncrossover products. Note that the sequence flanking the site of that was initially cut or broken was deleted and replaced by sequence of the other chromosome – this is called gene conversion.