Chromosome mutations

are variations in:

1. **Chromosome structure (chromosomal rearrangements)**
    - **deletions**
    - **duplications**
    - **translocations**
    - **inversions**
    - **transpositions**
2. **Chromosome number**
    - **aneuploidy**
    - **abnormal euploidy**

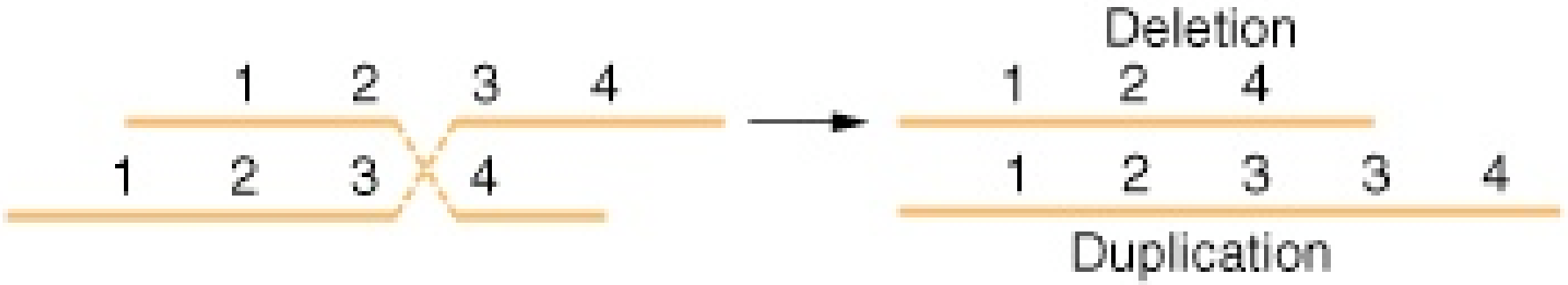
Chromosomal rearrangements

consequence of chromosome breaks

possible causes:

1. high-energy (ionizing) radiation
   - X-rays
   - □, □, and □emissions (from man-made or natural radioactive sources)
   - cosmic rays
2. “spontaneous”
   - unequal crossing over
   - mitotic recombination

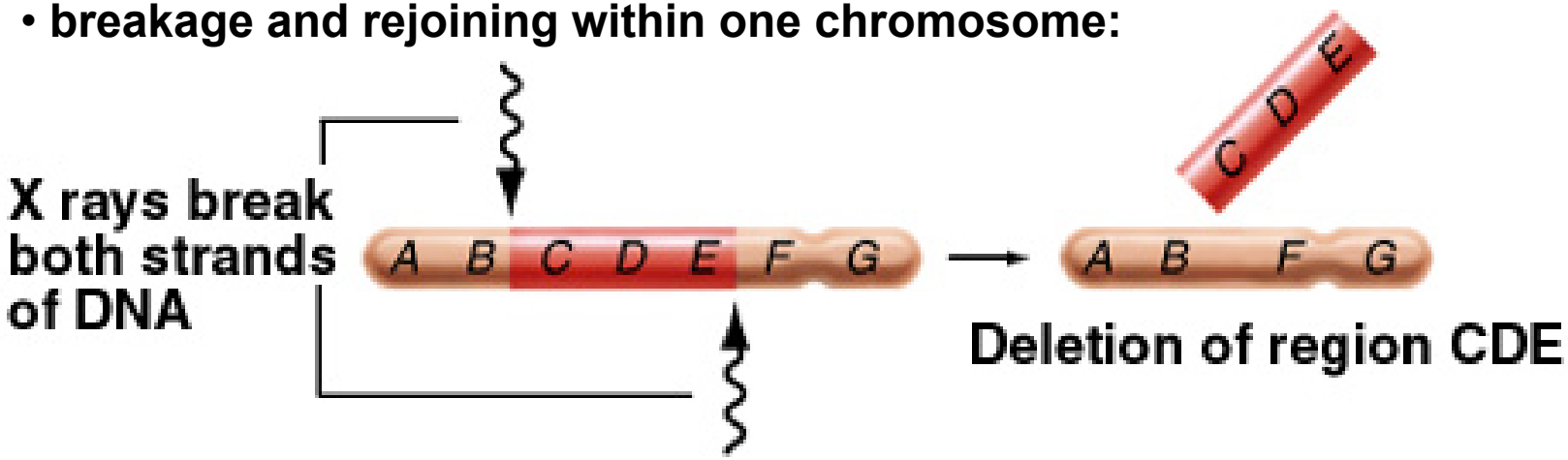
Unequal crossing-over



Deletions

= deficiencies = losses of chromosome segments

- can occur terminally or internally, e. g. caused by…
  - breakage and rejoining within one chromosome:



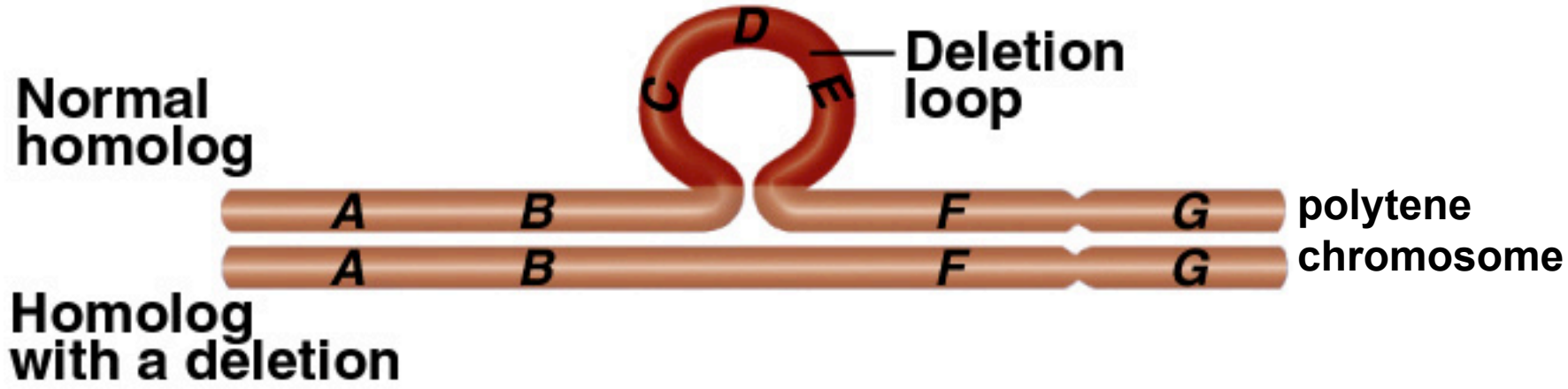
Consequences of deletions

- almost always lethal when homozygous
- often also lethal when heterozygous

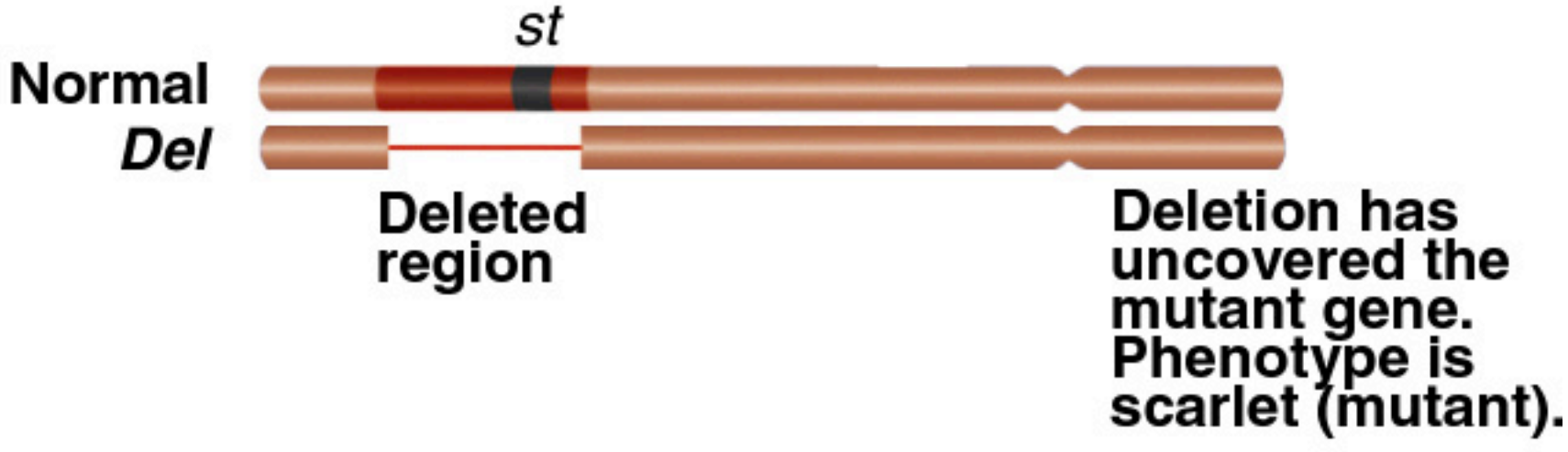
- example of a viable deletion in humans: *Cris-du-chat* syndrome
    - terminal deletion of short arm of one chromosome #5
    - can be seen in karyotype analysis as loss of bands/interbands
    - leads to mental retardation

How deletions can be identified….

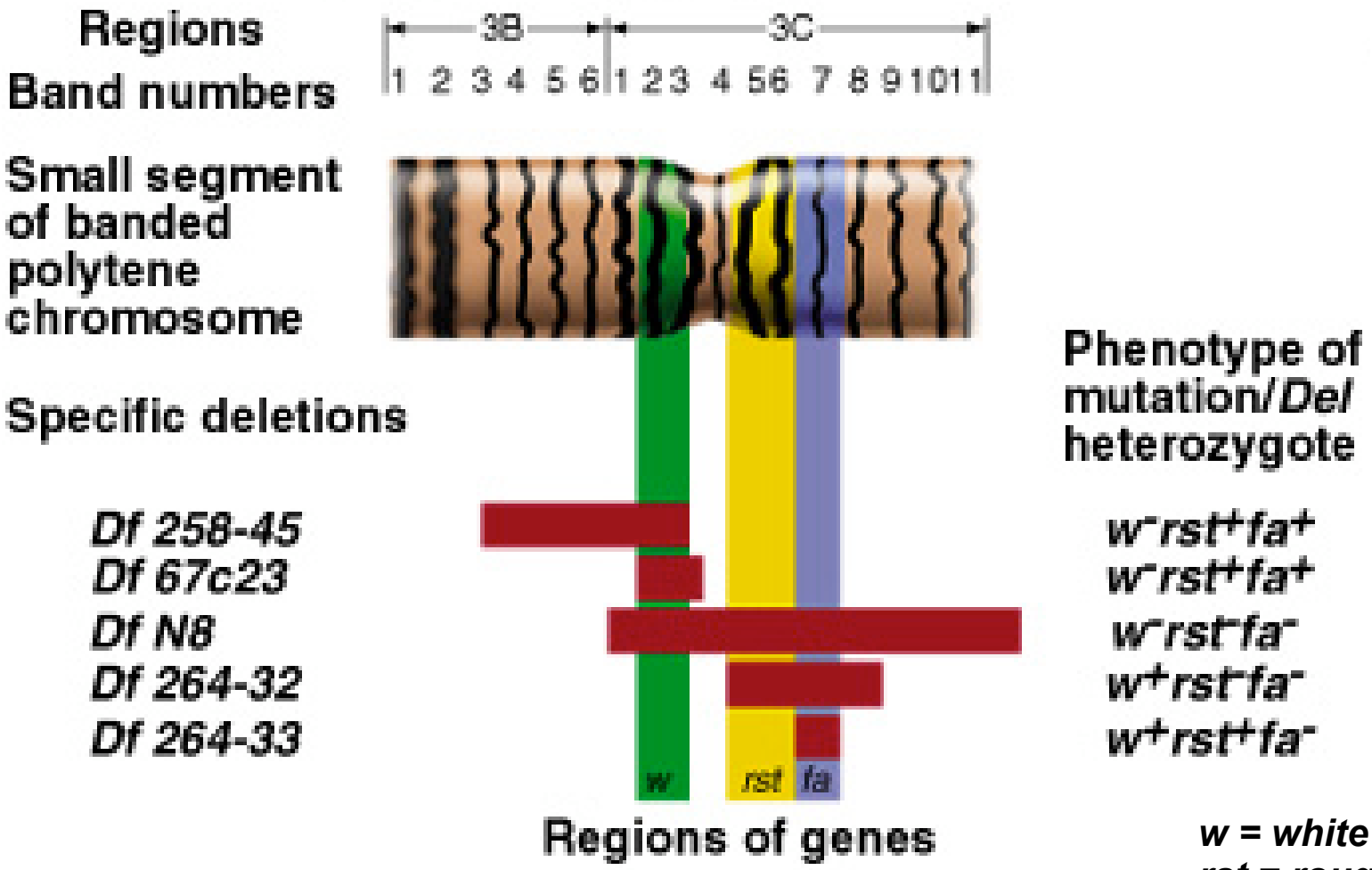
by finding a visible change in chromosome structure:



by the fact that deletions "uncover" genes:

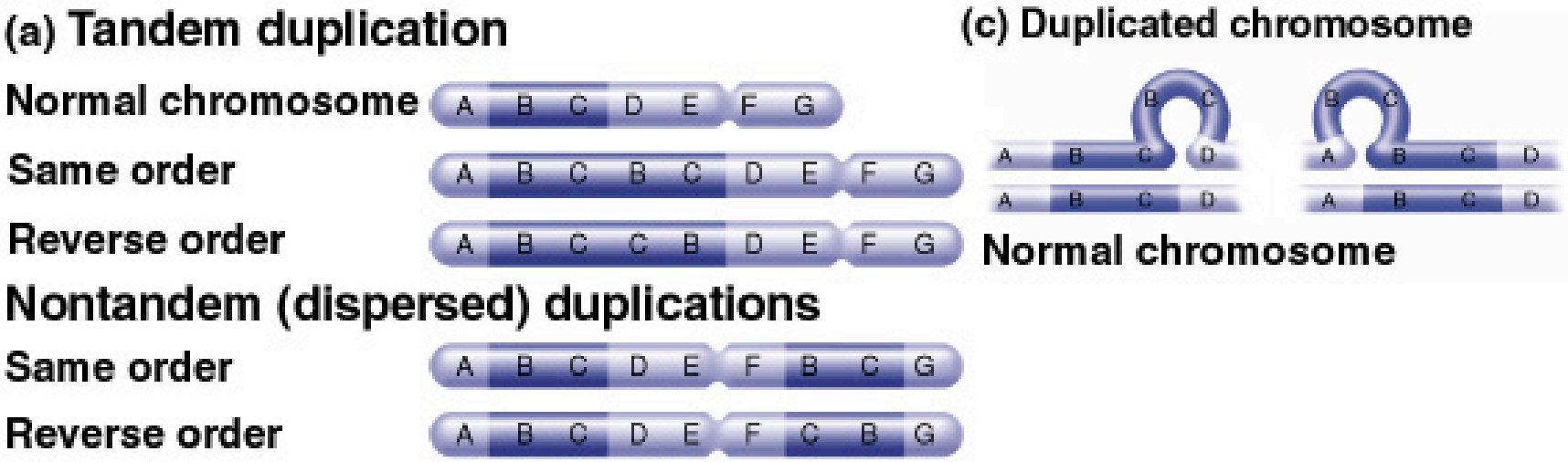


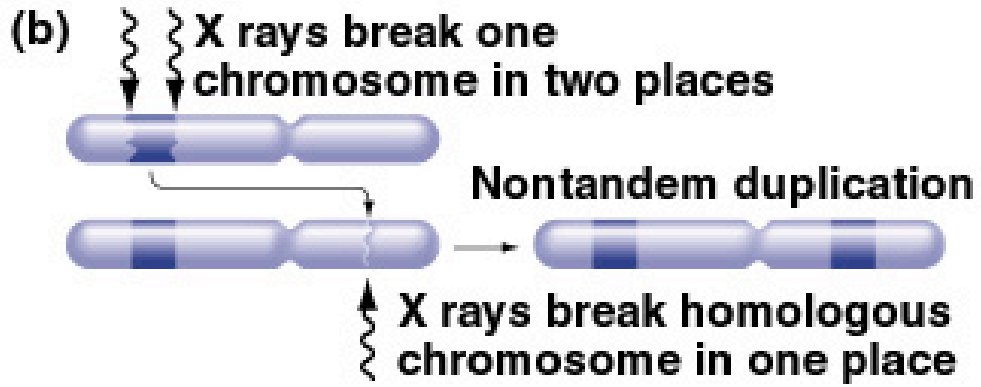
Mapping genes with deletions



w = white
rst = roughest
fa = facet

Duplications





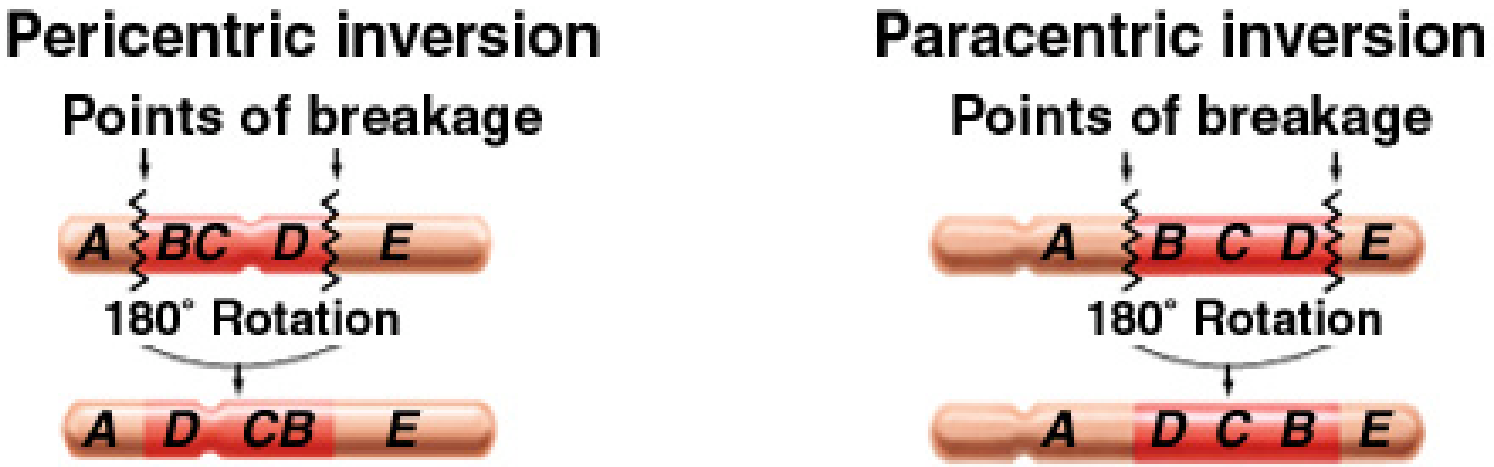
Consequences of duplications

- most duplications have no phenotypic consequence
- sometimes effects can be seen due to increased gene dosage

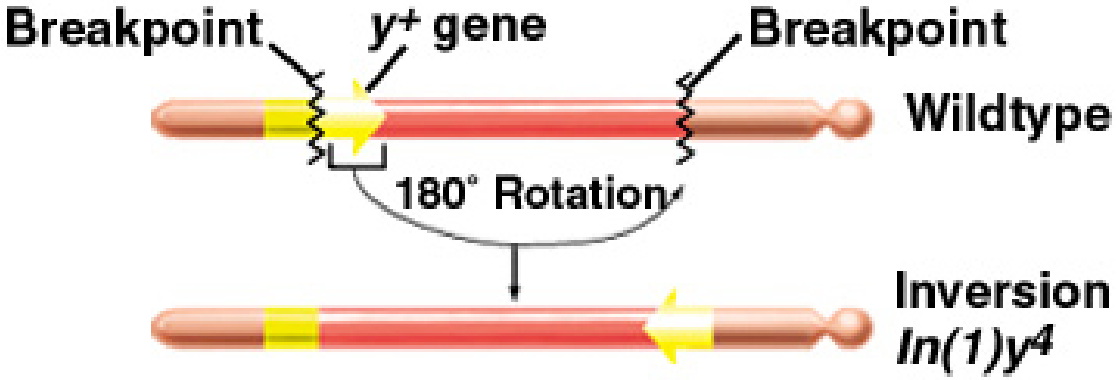
- play a very important role in evolution:
  - increase gene number
  - evolution of new genes (paralogs!)

Inversions

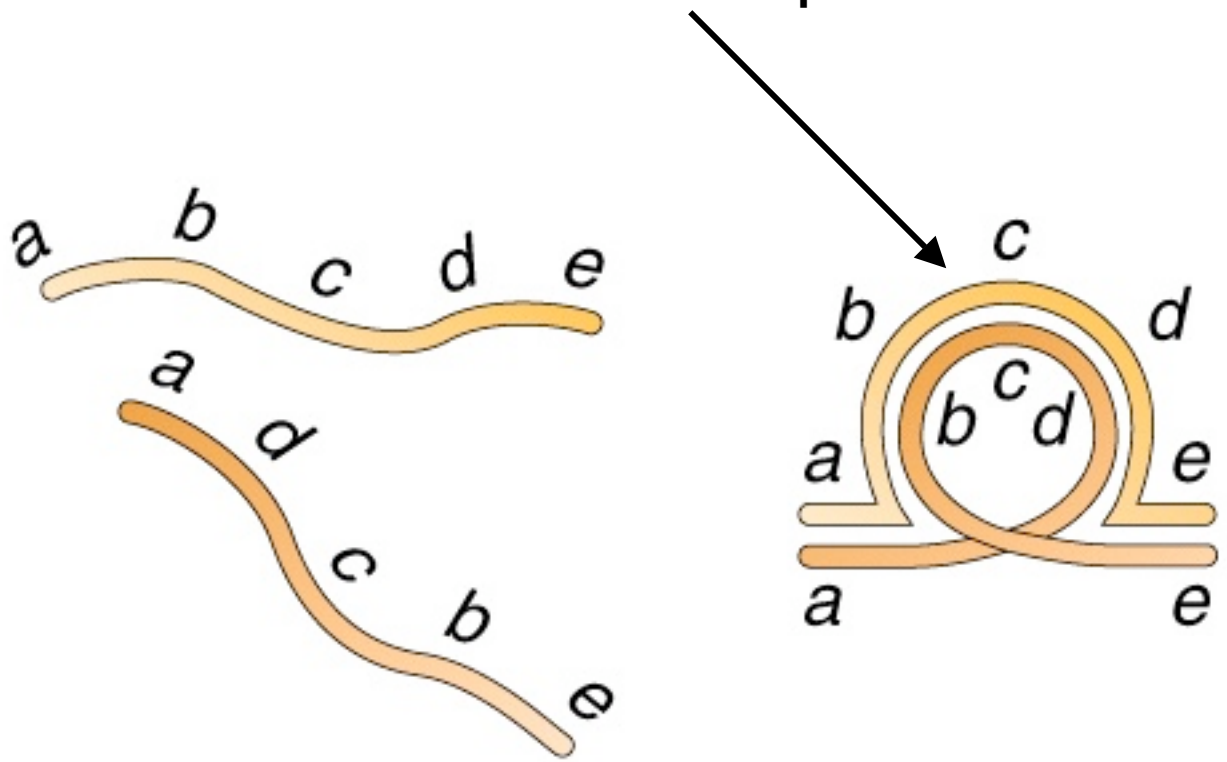
result from insertion of a chromosome fragment in reverse orientation:



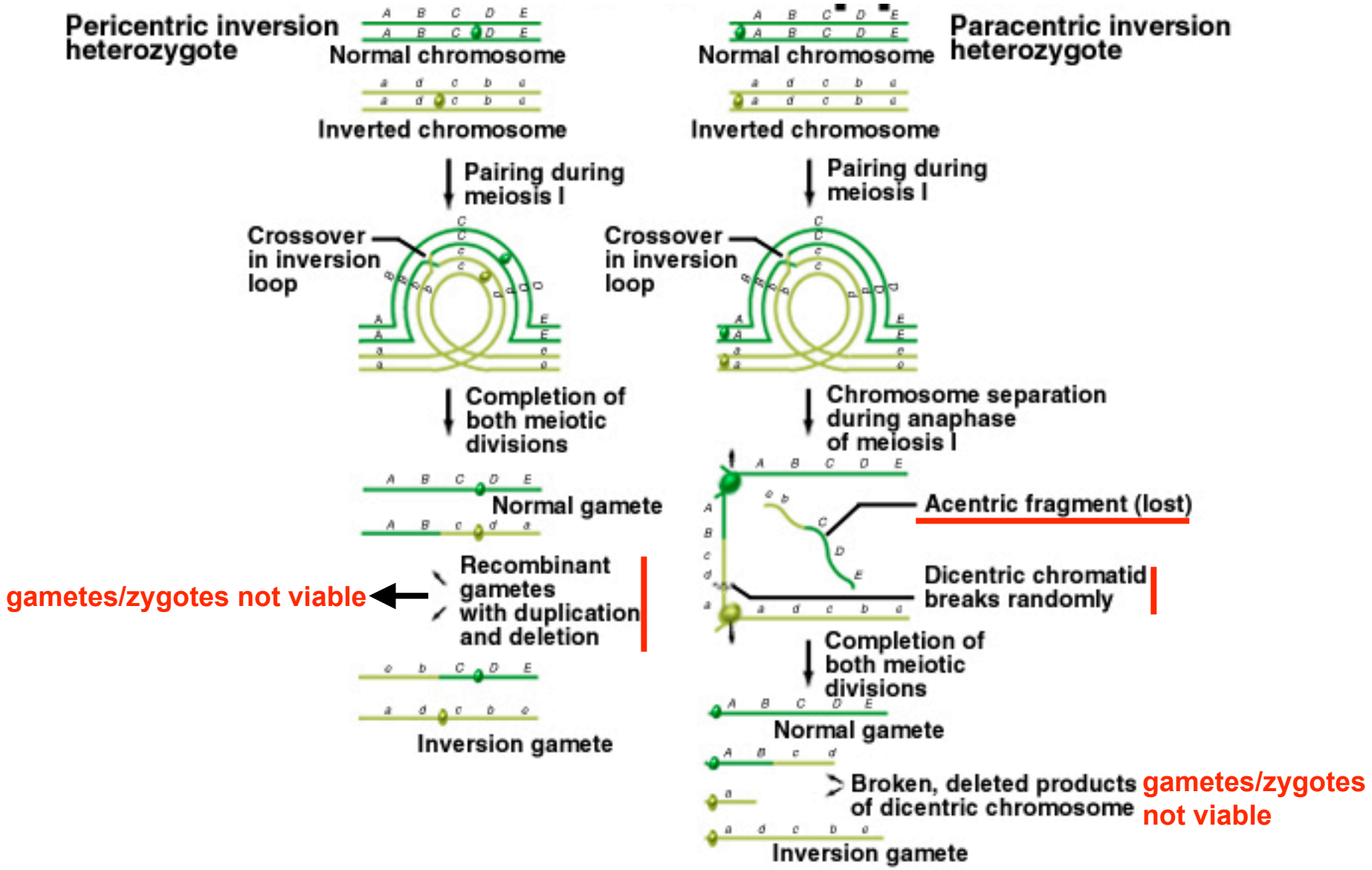
- **usually no phenotypic consequences**
- **can sometimes lead to a mutant phenotype:**



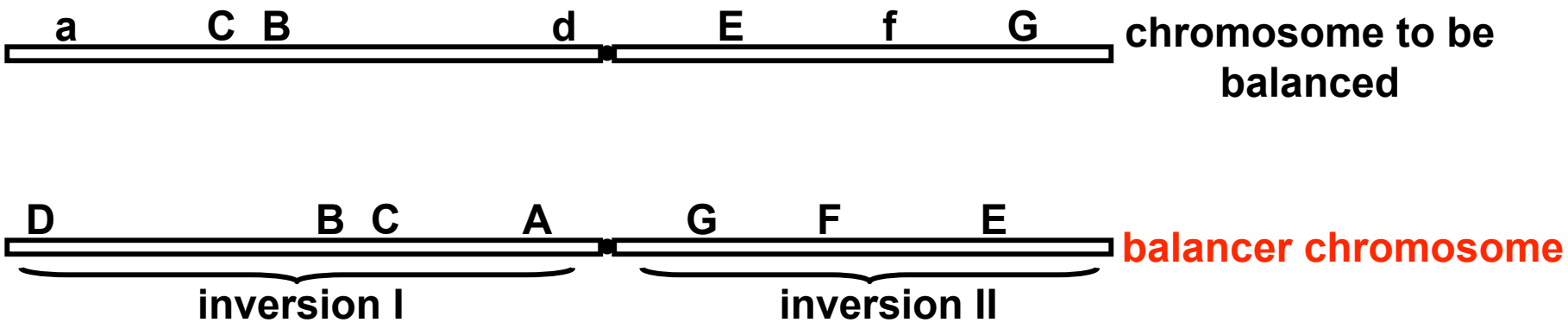
Inversion chromosome pairs with normal chromosome under formation of an inversion loop



Inversions suppress genetic recombination by crossing-over



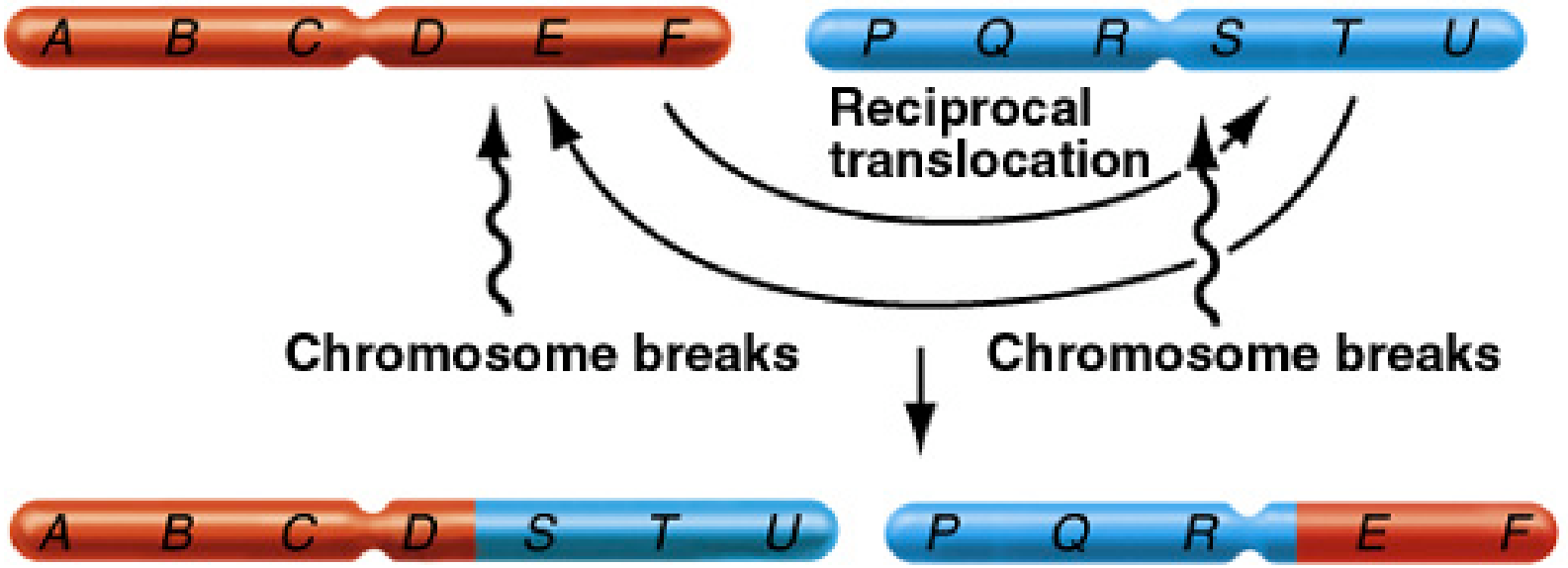
Inversions are used to “balance” chromosomes



Translocations

= attachments of chromosome fragments to non-homologous chromosomes

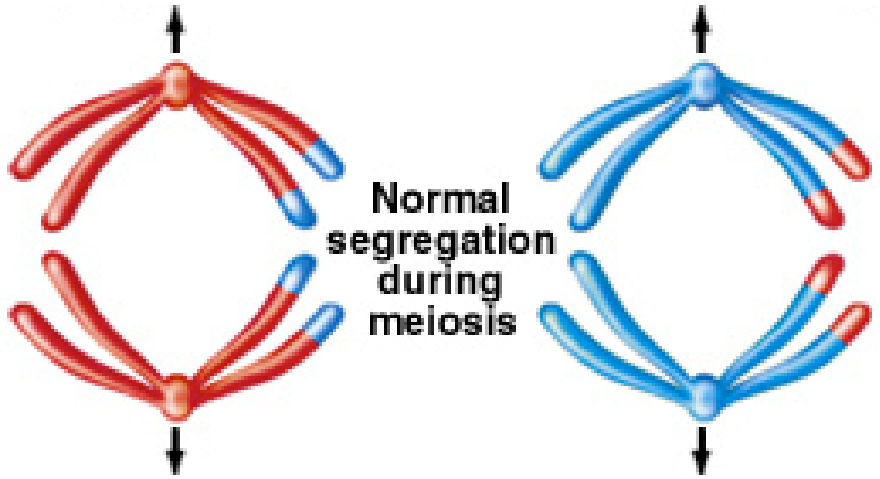
- **reciprocal translocations arise from exchange of chromosome fragments between non-homologous chromosomes:**



- **non-reciprocal translocations arise from attachment of chromosome fragment to a non-homologous chromosome; lead to duplications and deletions in progeny**

Consequences of translocations

- usually none in homozygotes; genetic material is neither lost nor gained:

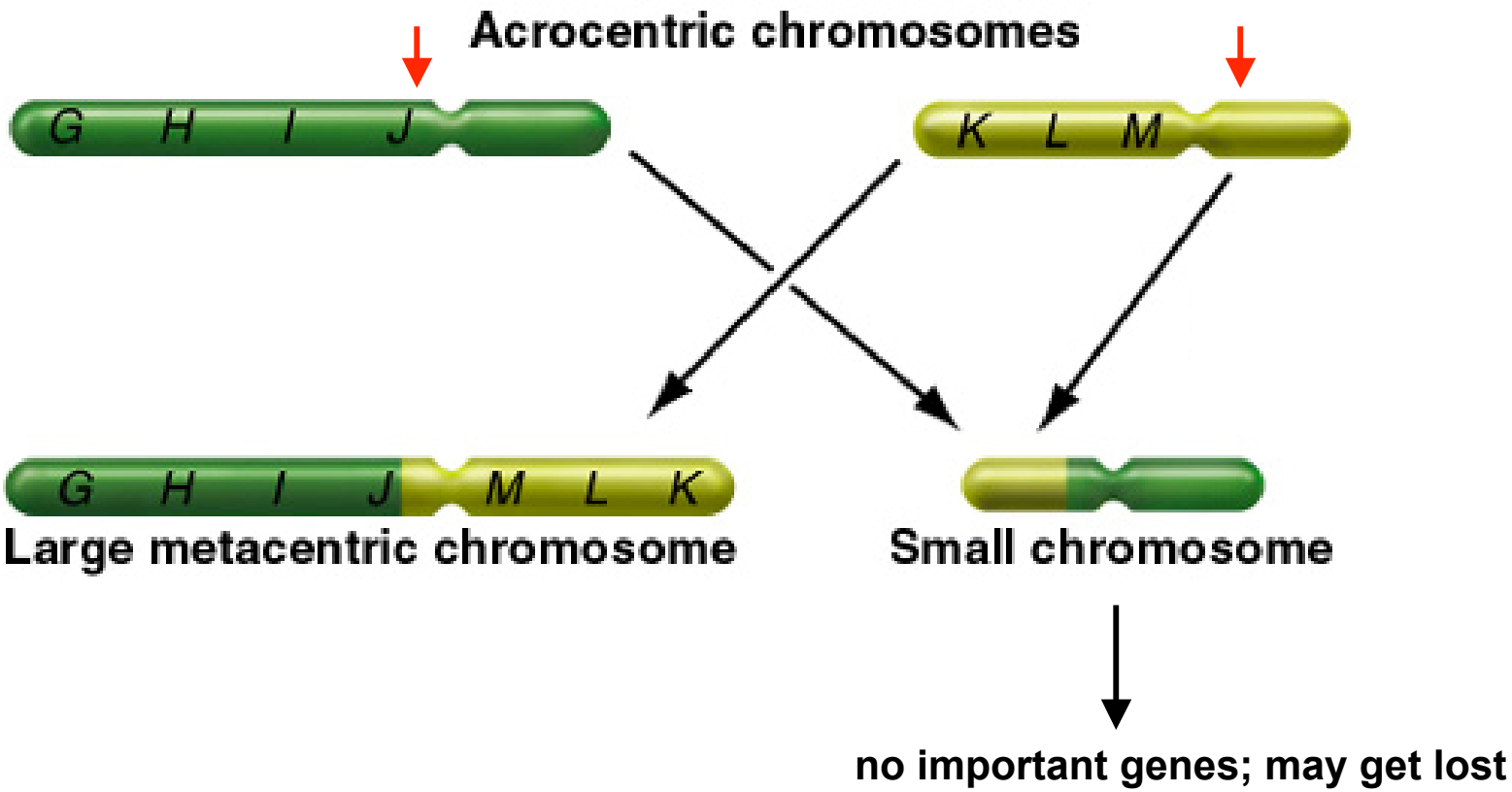


- none in heterozygotes if translocation chromosomes segregate together ("balanced" translocation); if translocation chromosomes are separated, genetically imbalanced gametes result with deletions or duplications; zygotes produced by these gametes are not viable

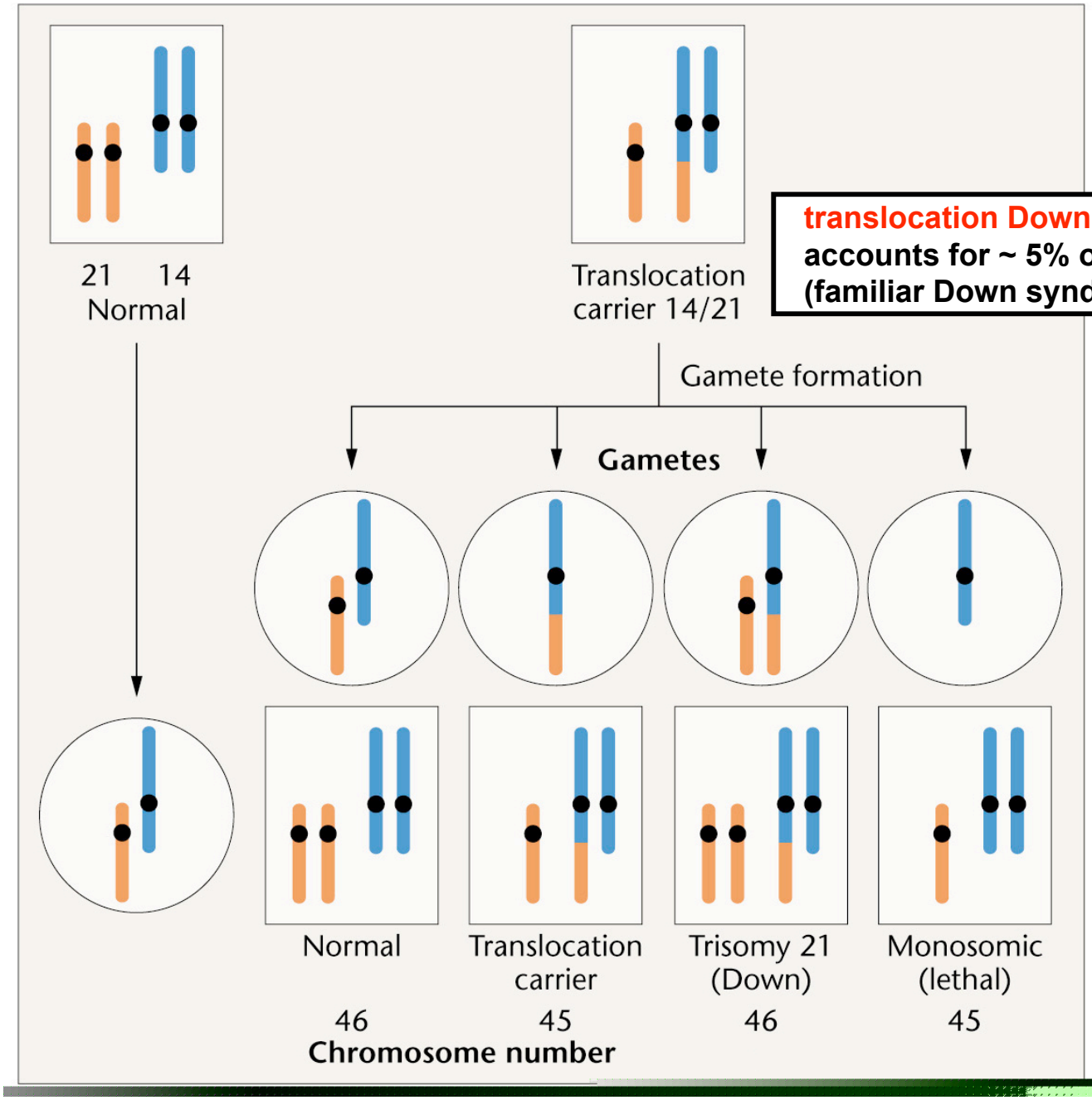
→ semisterility

Robertsonian translocation or centric fusion

= fusions of two acrocentric chromosomes after short arms broke off



How a Robertsonian translocation can lead to Down syndrome



translocation Down syndrome accounts for ~ 5% of all cases (familiar Down syndrome)

Transposition

= movement of DNA elements from one site in the genome to another

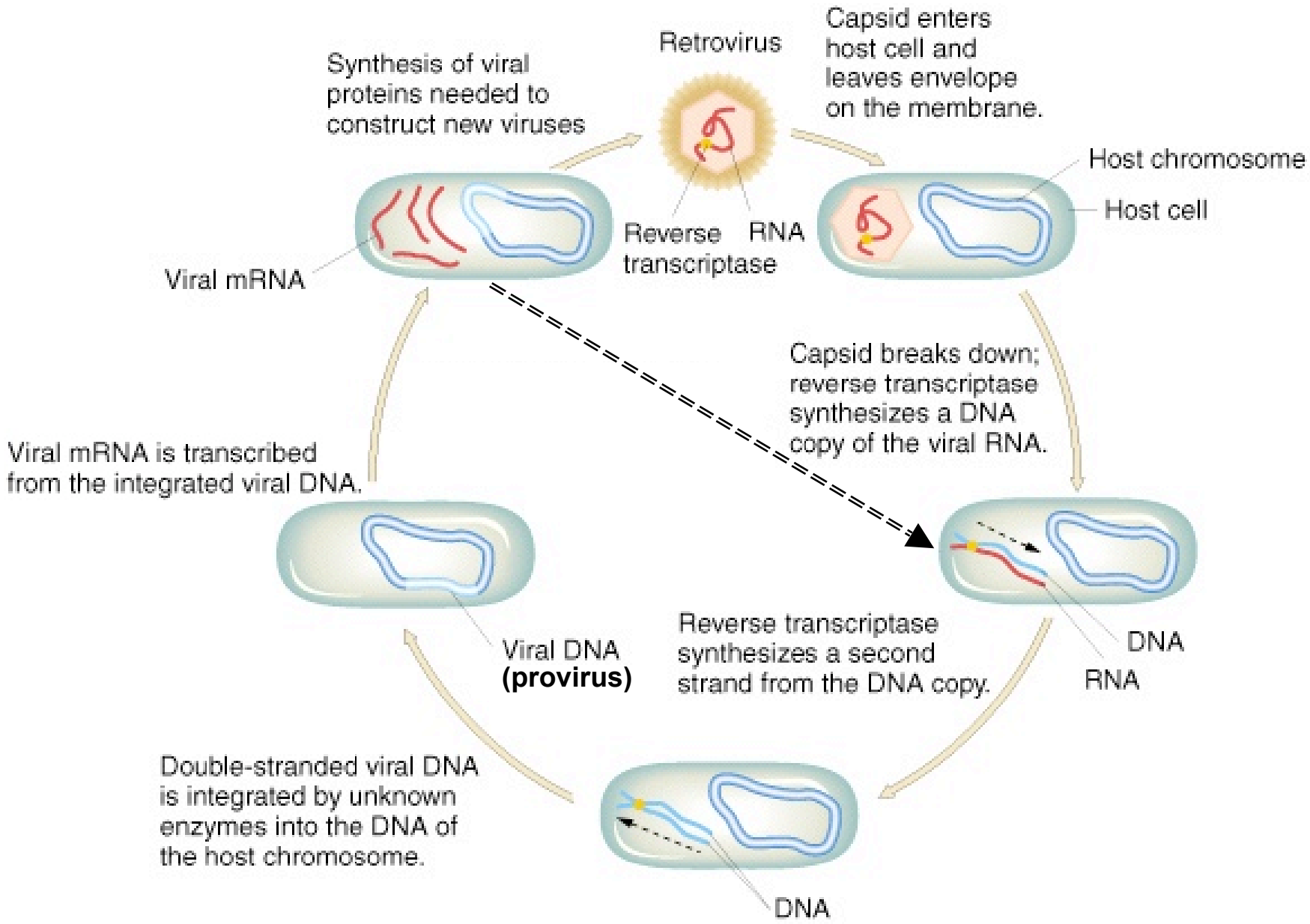
- **transposable elements = transposons:**
  - **some related to viruses (transposons & viruses: mobile genetic elements)**
  - **found in all organisms (bacteria to humans)**
  - **have no obvious function (are dispensible)**

    → are considered as "selfish" DNA
  - **impact on evolution of genomes**
  - **can be used as transformation vectors and for mutagenesis**
  - **2 main classes:**

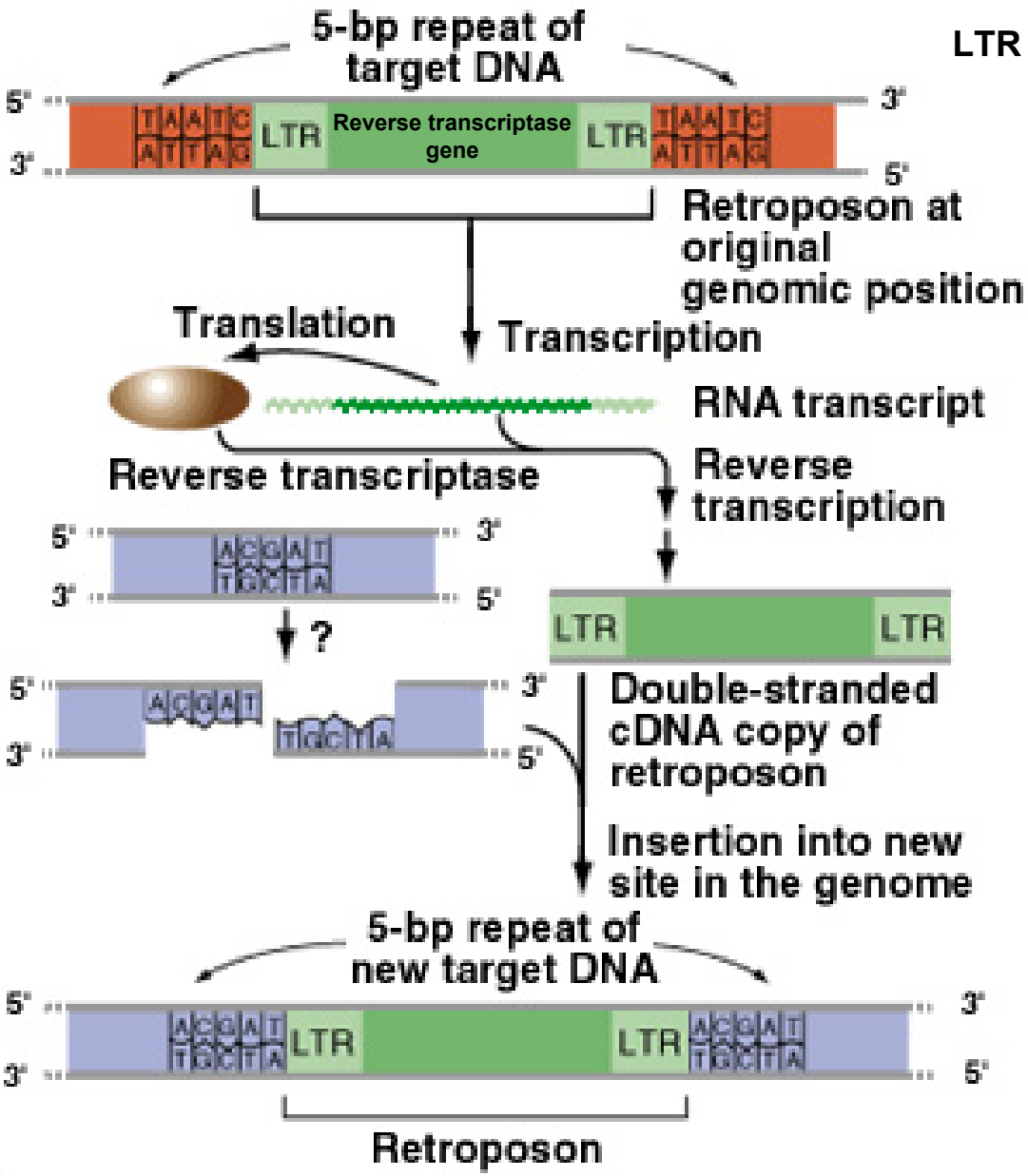
    1. retrotransposons (= retroposons)

    2. DNA-only transposons

Life cycle of a retrovirus



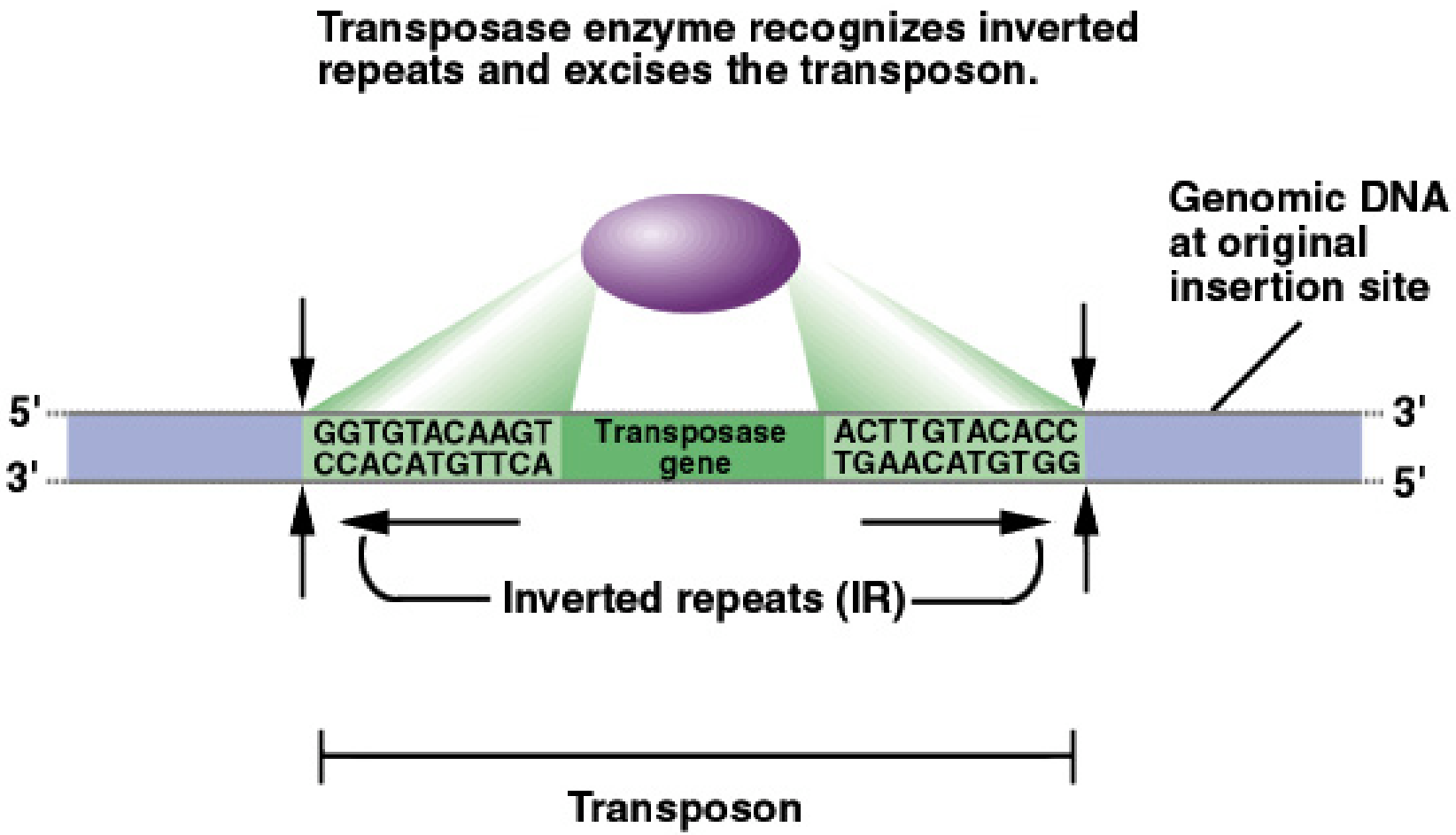
Retrotransposons (retroposons) transpose via RNA intermediate



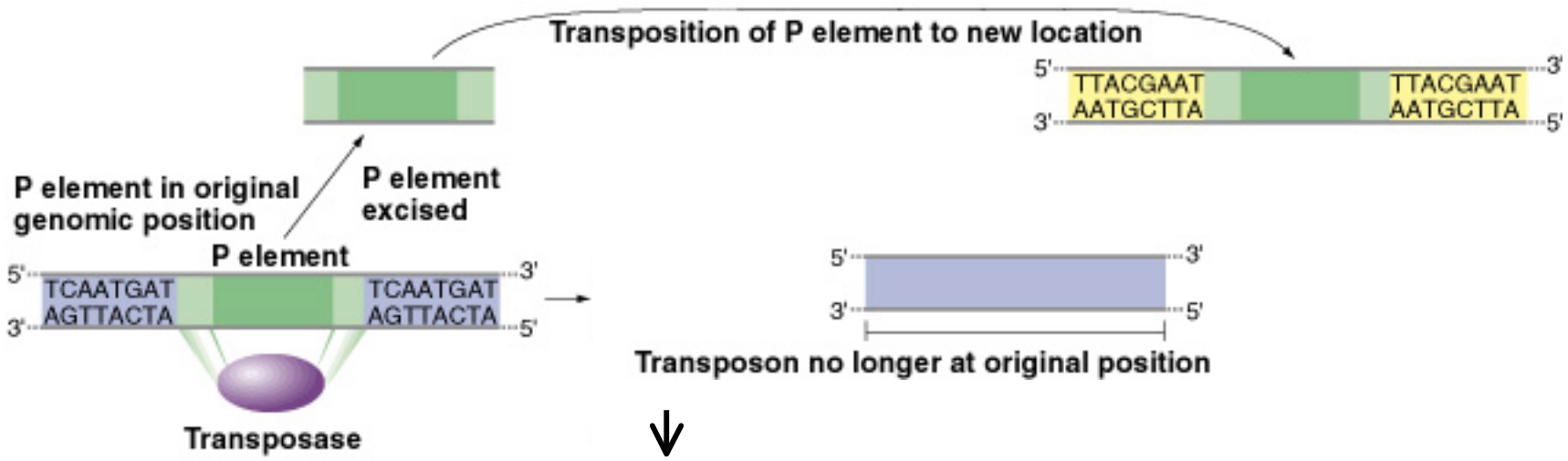
LTR = long terminal repeat

→ retroposon remains in place and new copy inserts into other location

DNA-only transposons



P-elements in *Drosophila*



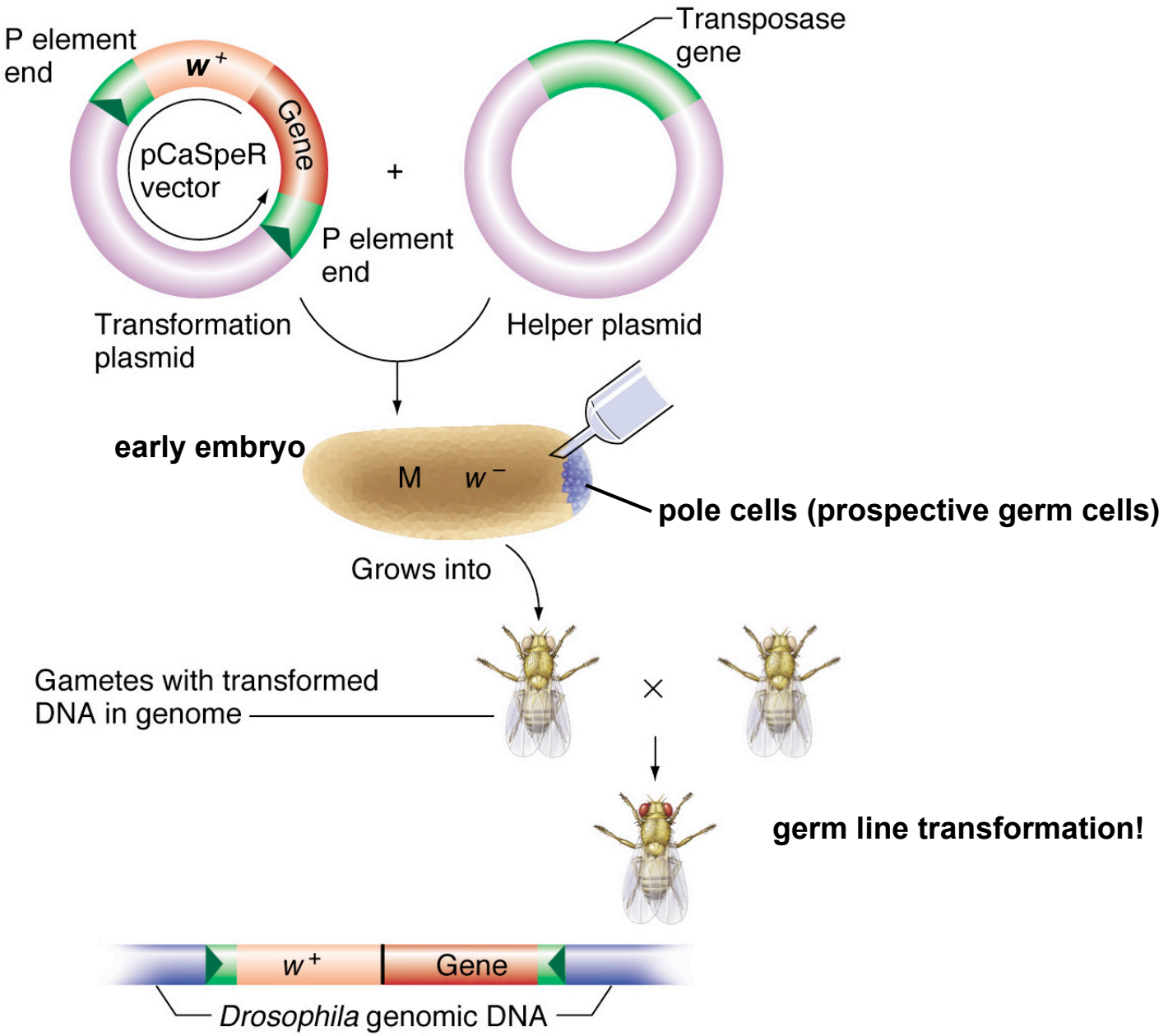
↓

excision can be imprecise

↓

deletion

P-element transformation



Changes in chromosome number

Aneuploidy

= change in the number of single chromosomes (but not in the number of sets)

	Karyotype	Examples (humans)
Monosomy	2n - 1	Turner (45, XO); loss of an autosome is lethal
Trisomy	2n + 1	Trisomy 21 (Down syndrome), 18, 13; Klinefelter (47, XXY), Triple-X (47, XXX), XYY males (47, XYY)
Nullisomy	2n - 2	not viable in diploids

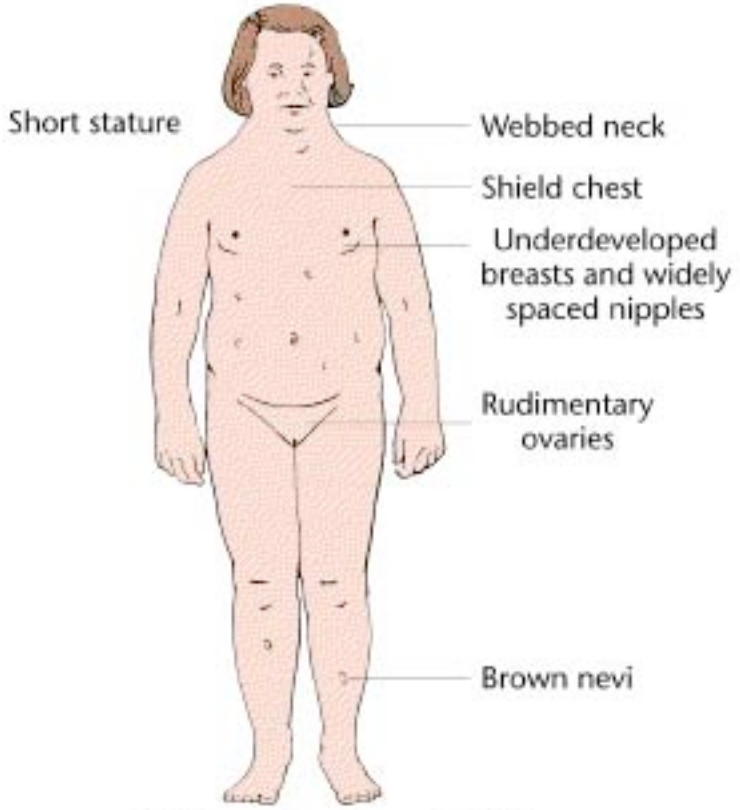
(abnormal) Euploidy

= change in the number of chromosome sets

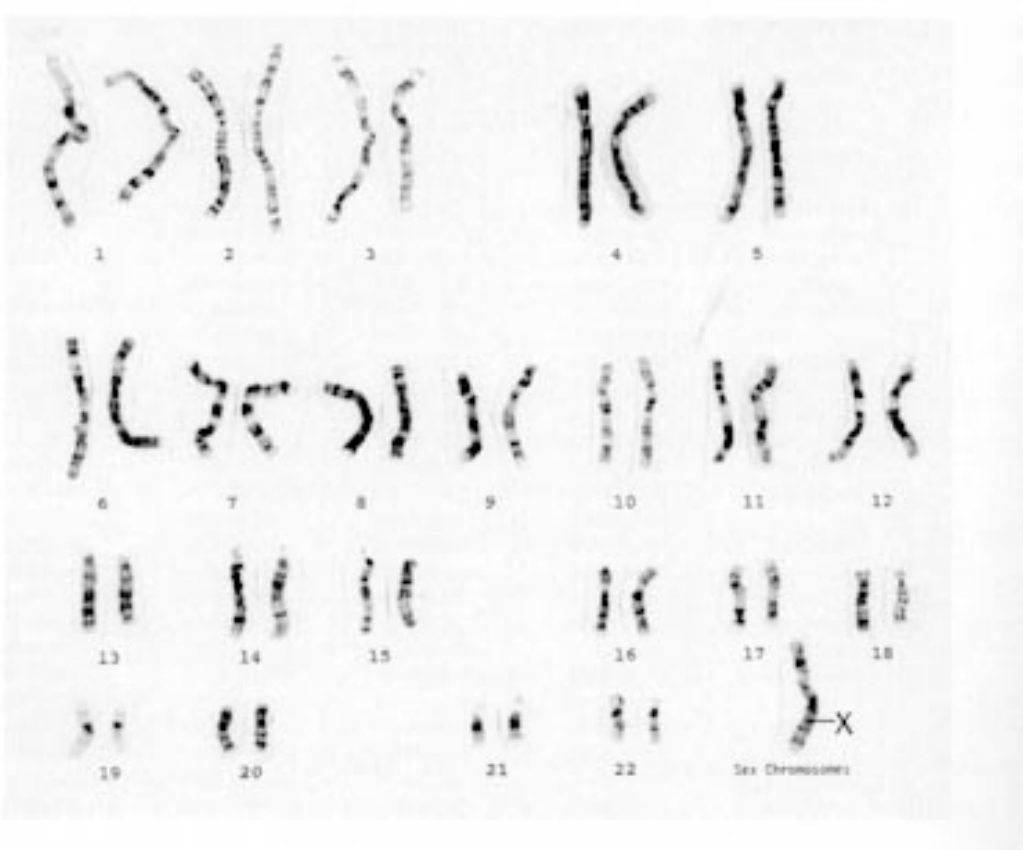
Diploid	2n
Polyploid (Triploid, Tetraploid etc.)	3n, 4n etc.

- is not viable in humans; many plants polyploid

Turner Syndrome (45, X)



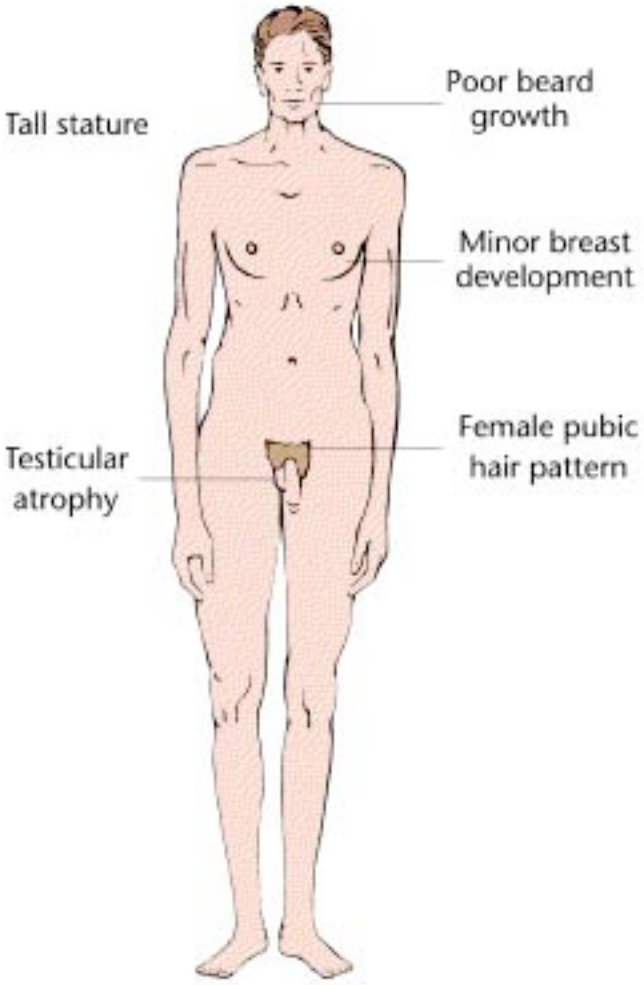
(b) Turner Syndrome (45,X)



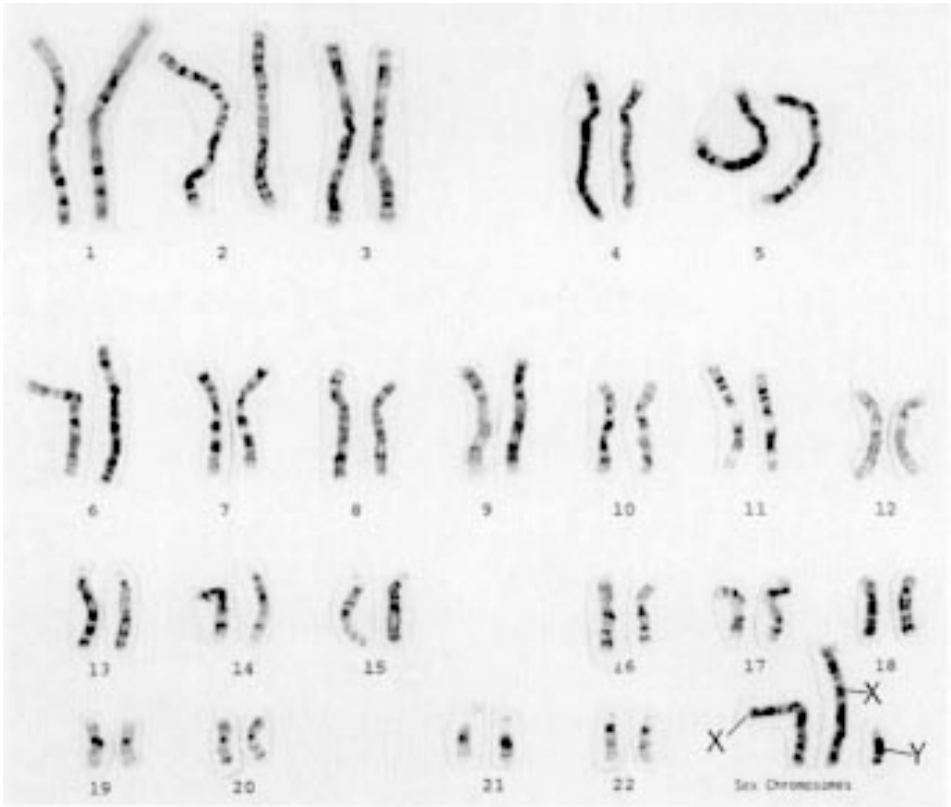
- sterile females

1 in 3000 female births

Klinefelter Syndrome (47, XXY)



(a) Klinefelter Syndrome (47,XXY)



2 in 1000 male births

- sterile males

Down Syndrome (47, +21)