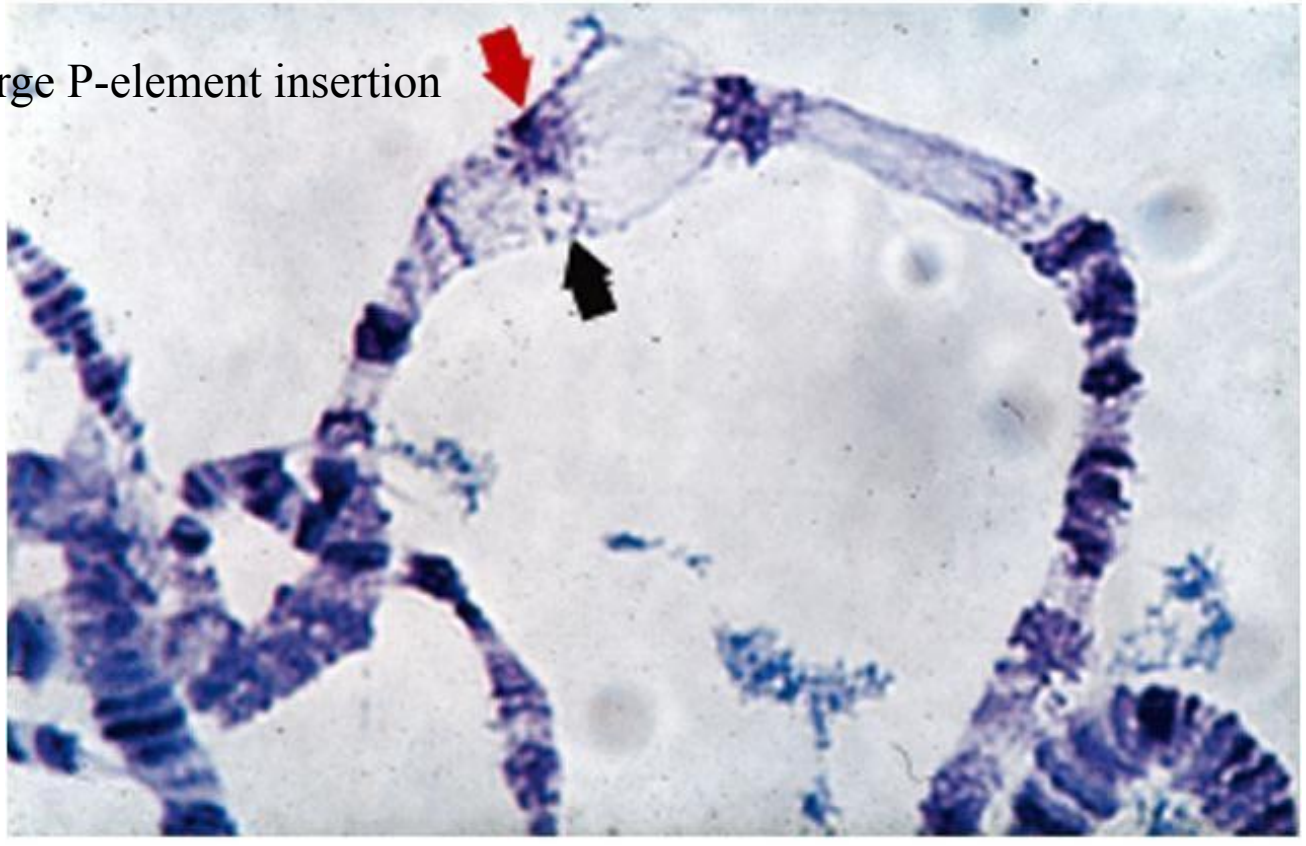
Kromozom Yapı Değişimleri



Fare kromozomları insan kromozomlarının 170 parçaya kırılması ile oluşturulabiliyor.

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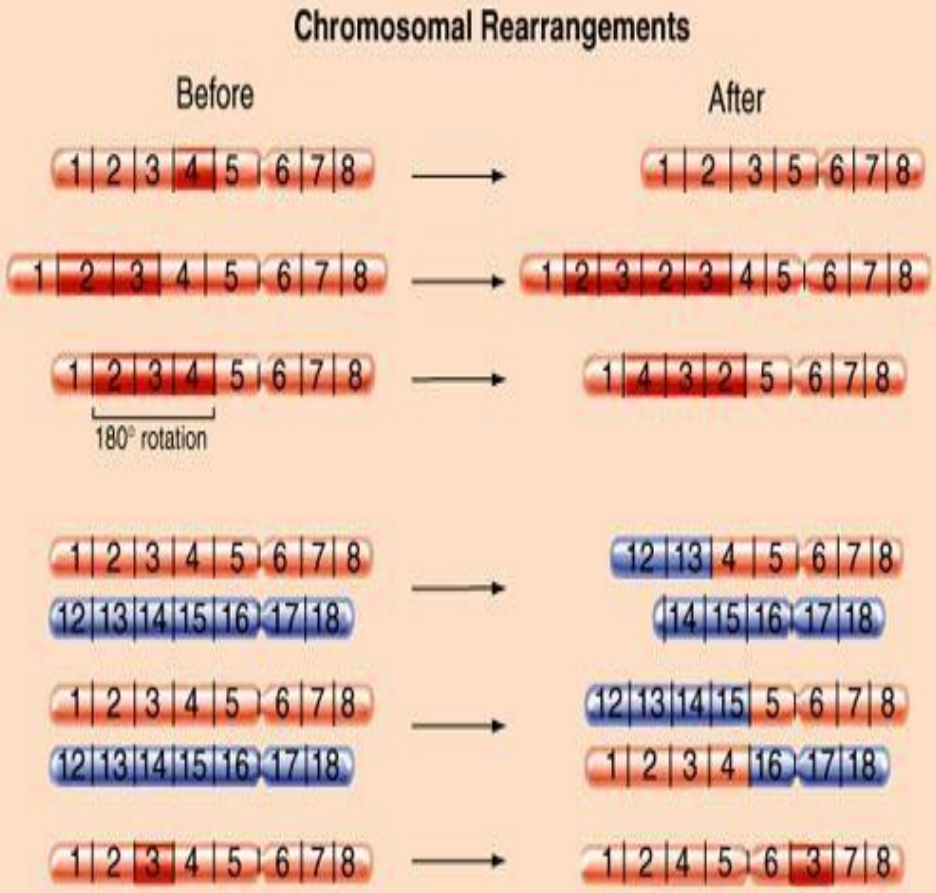
TABLE 13.1 Chromosomal Rearrangements and Changes in Chromosome Number



Deletion: Removal of a segment of DNA

Duplication: Increase in the number of copies of a chromosomal region

Inversion: Half-circle rotation of a chromosomal region

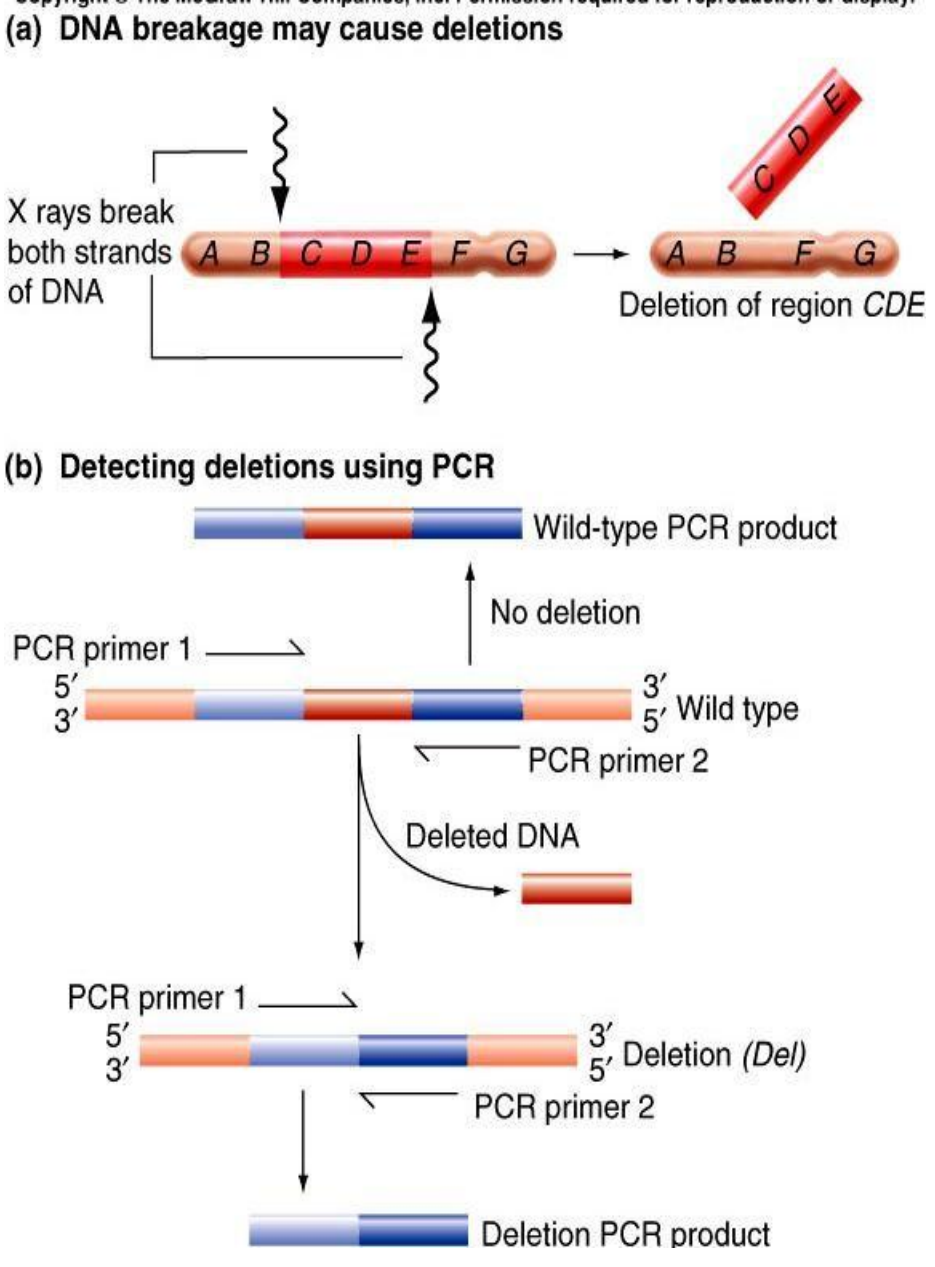
Translocations:

Nonreciprocal: Unequal exchanges between nonhomologous chromosomes

Reciprocal: Parts of two nonhomologous chromosomes trade places

Transposition: Movement of short DNA segments from one position in the genome to another

Delesyon

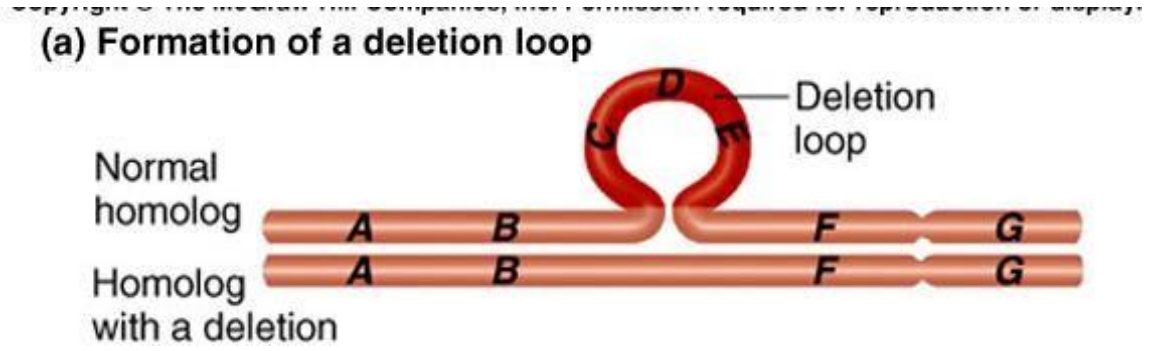

(a) DNA breakage may cause deletions
X rays break both strands of DNA
A B C D E F G
C D E
A B F G
Deletion of region CDE
(b) Detecting deletions using PCR
Wild-type PCR product
No deletion
PCR primer 1
5′
3′
3′
5′
Wild type
PCR primer 2
Deleted DNA
PCR primer 1
5′
3′
3′
5′
Deletion (Del)
PCR primer 2
Deletion PCR product

Delesyon heterozigot halde fenotipi değiştirebilir.

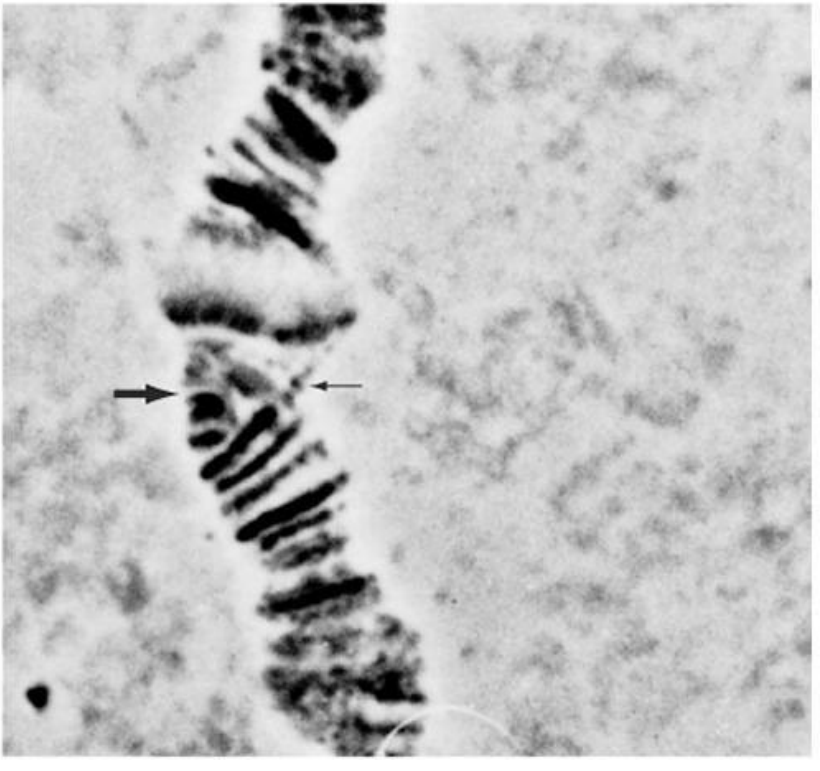
Wild type
(two copies of *Notch*$^{+}$)

***Del* / +**
(one copy of *Notch*$^{+}$)

Delesyonlu kromozomların eşleşmesi



(b) A deletion loop in *Drosophilia* polylene chromosomes



Mayozda eşleşme

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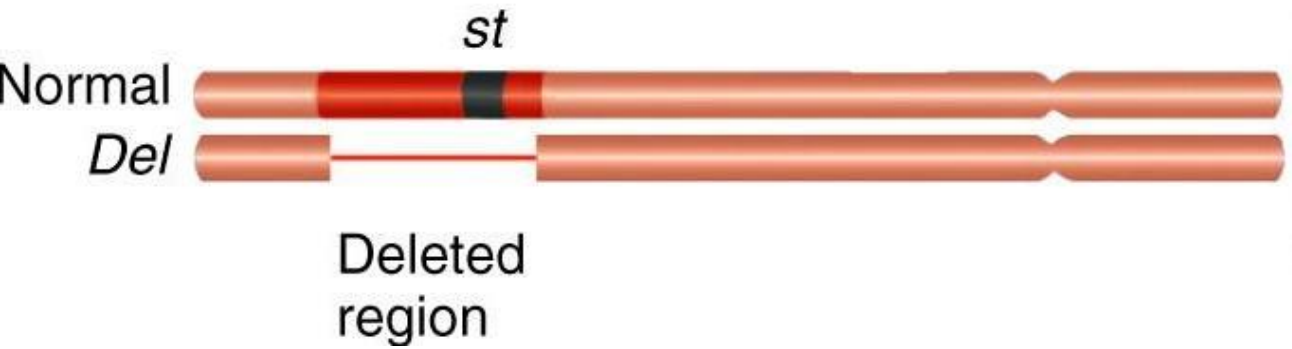
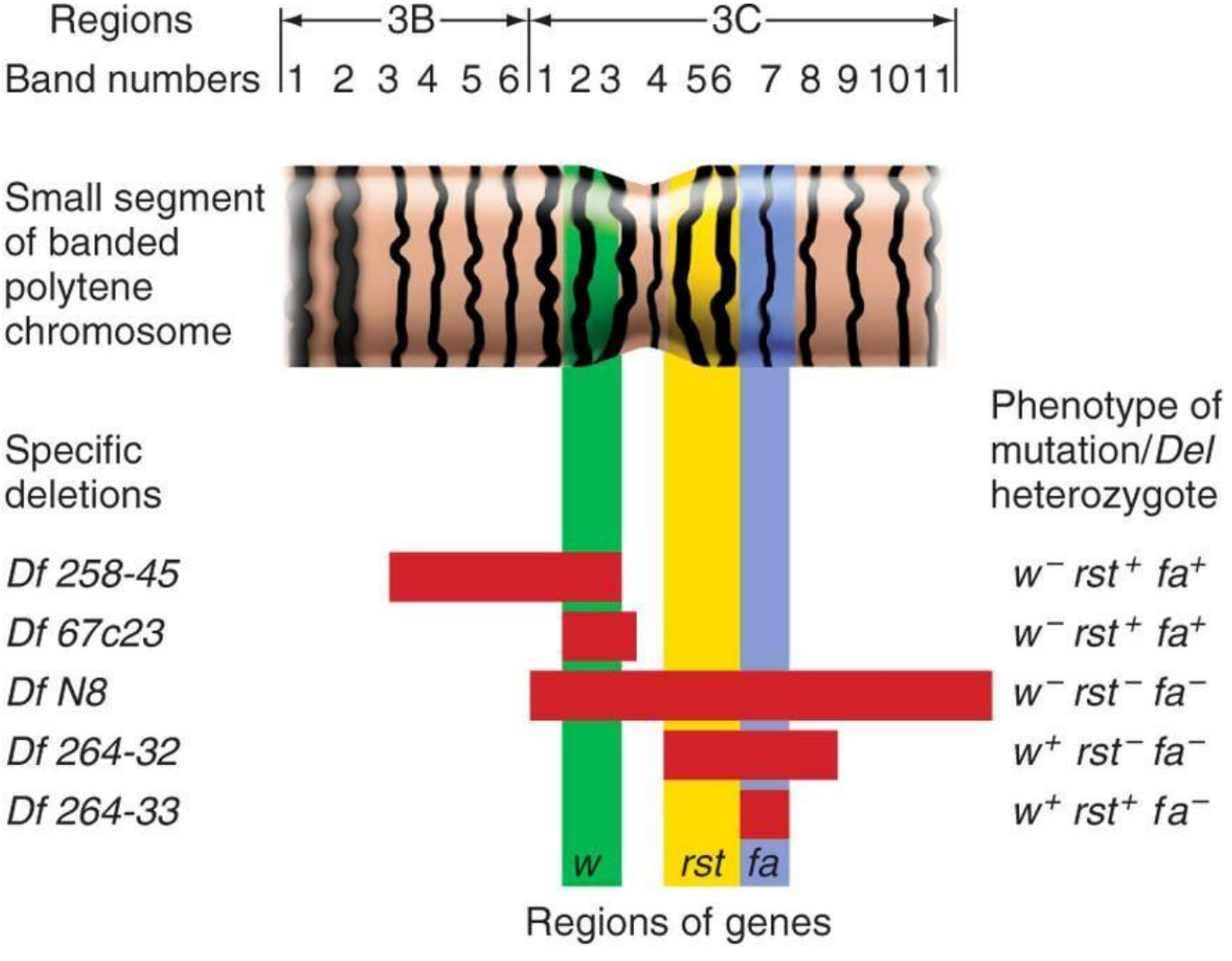
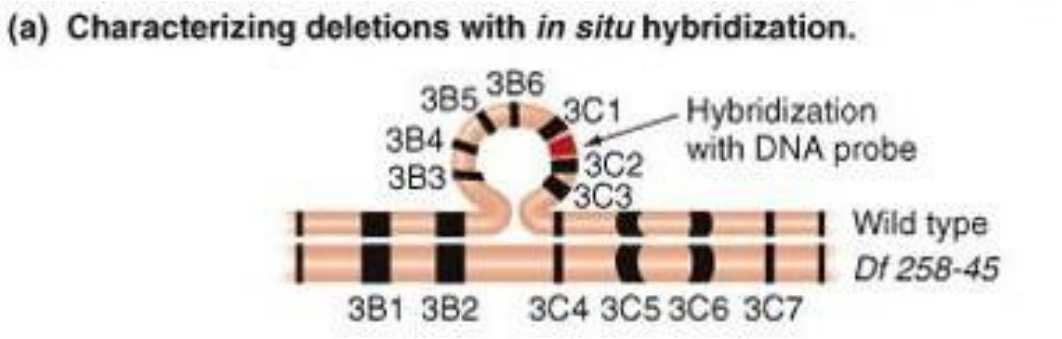


Deletion has uncovered the mutant gene. Phenotype is scarlet (mutant).

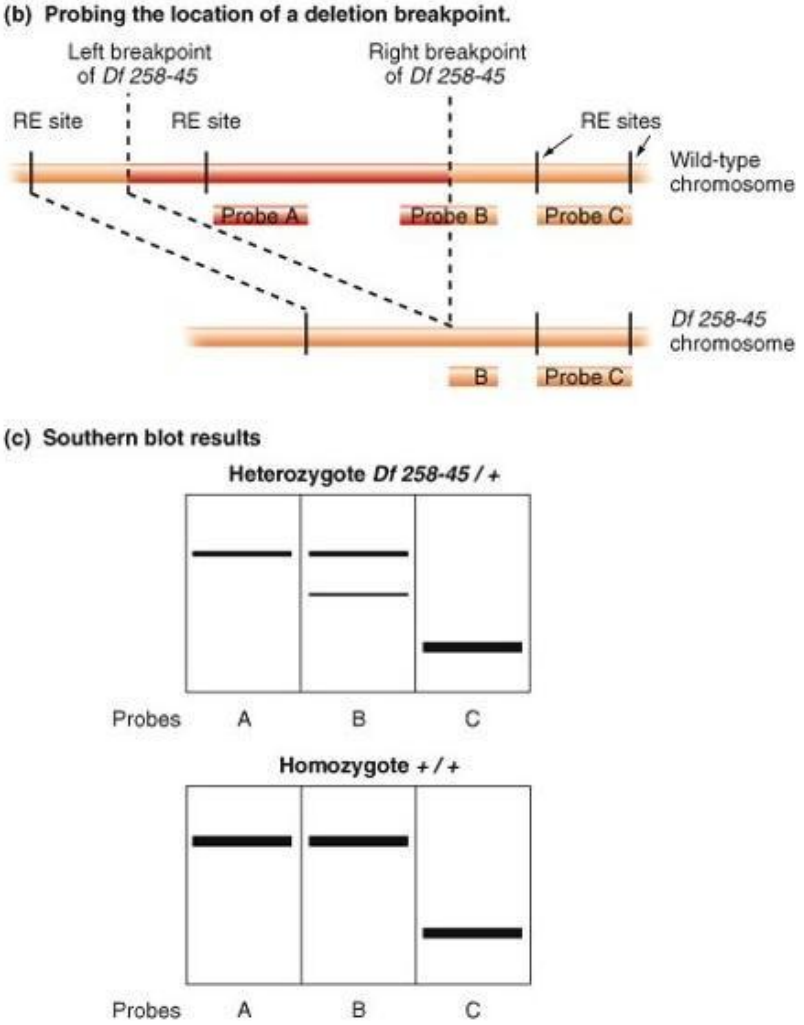
Genetik haritalamada delesyonların kullanımı



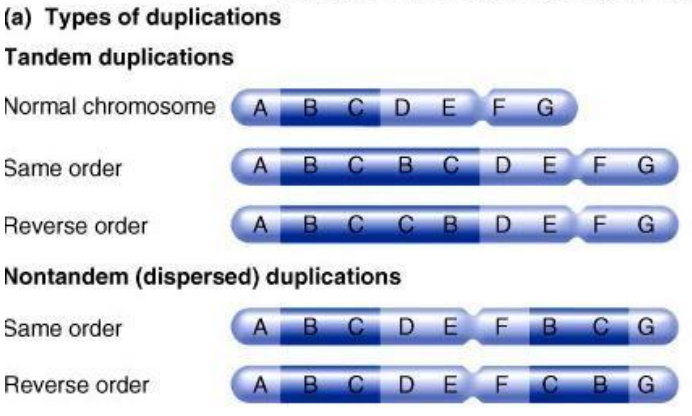
Delesyon haritalamasında moleküler yöntemler de kullanılabilir (*in situ* melezleme)

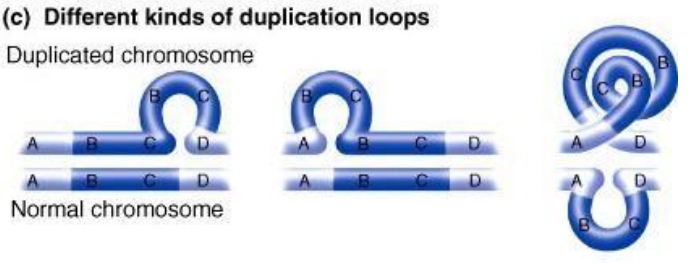


Delesyon haritalamasında Southern blot



Duplikasyonlar

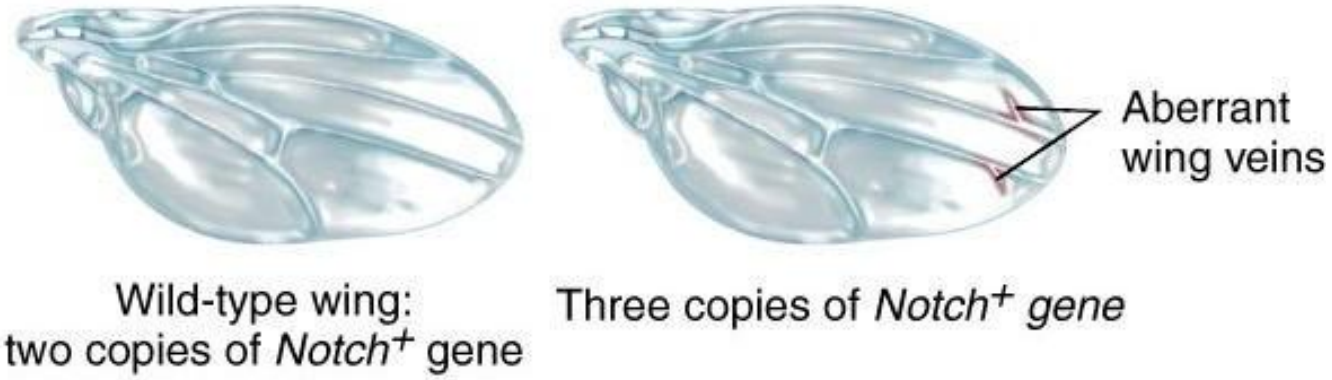




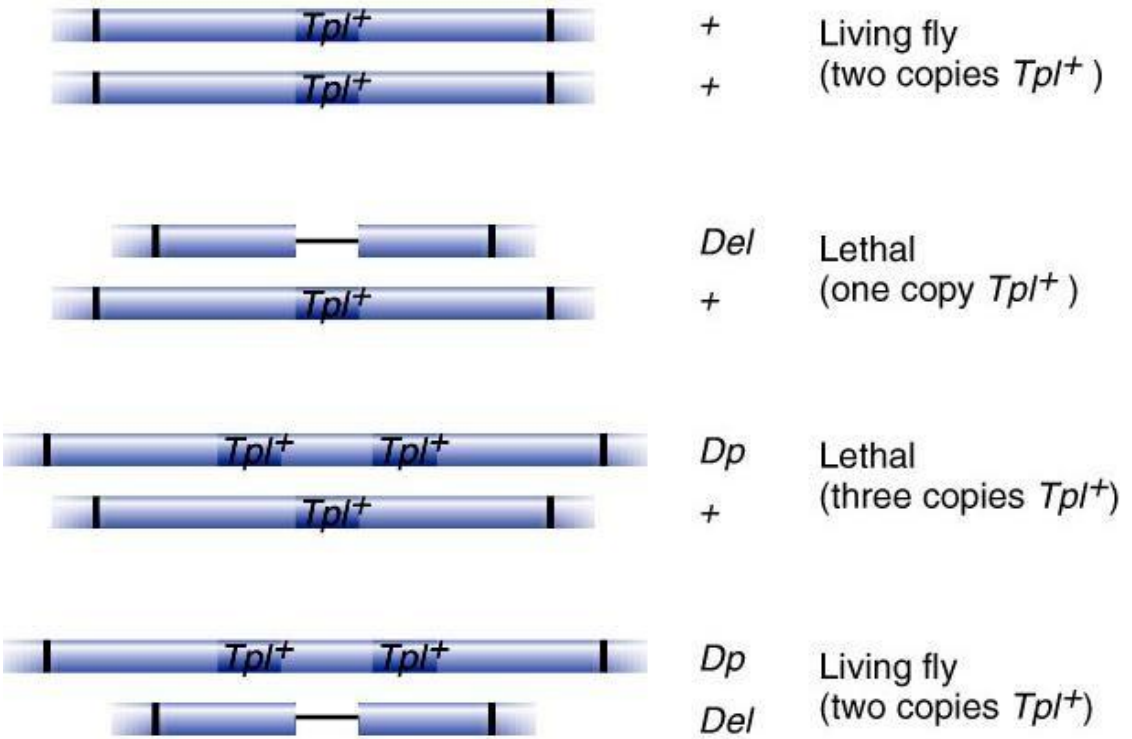
Mayozda Kromozom eşleşmesi

DNA replikasyonu sırasında
Homolog olmayan krossin over'ler

(a) Duplication heterozygosity can cause visible phenotypes.



(b) For rare genes, survival requires exactly two copies.



Genotype of X chromosomes

Wild type

Bar

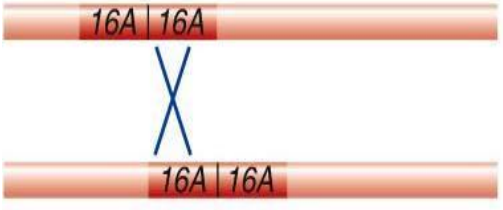
Double-Bar

Phenotype

Wild-type eye

Double-Bar eye

Out-of-register pairing during meiosis in a Bar-eyed female

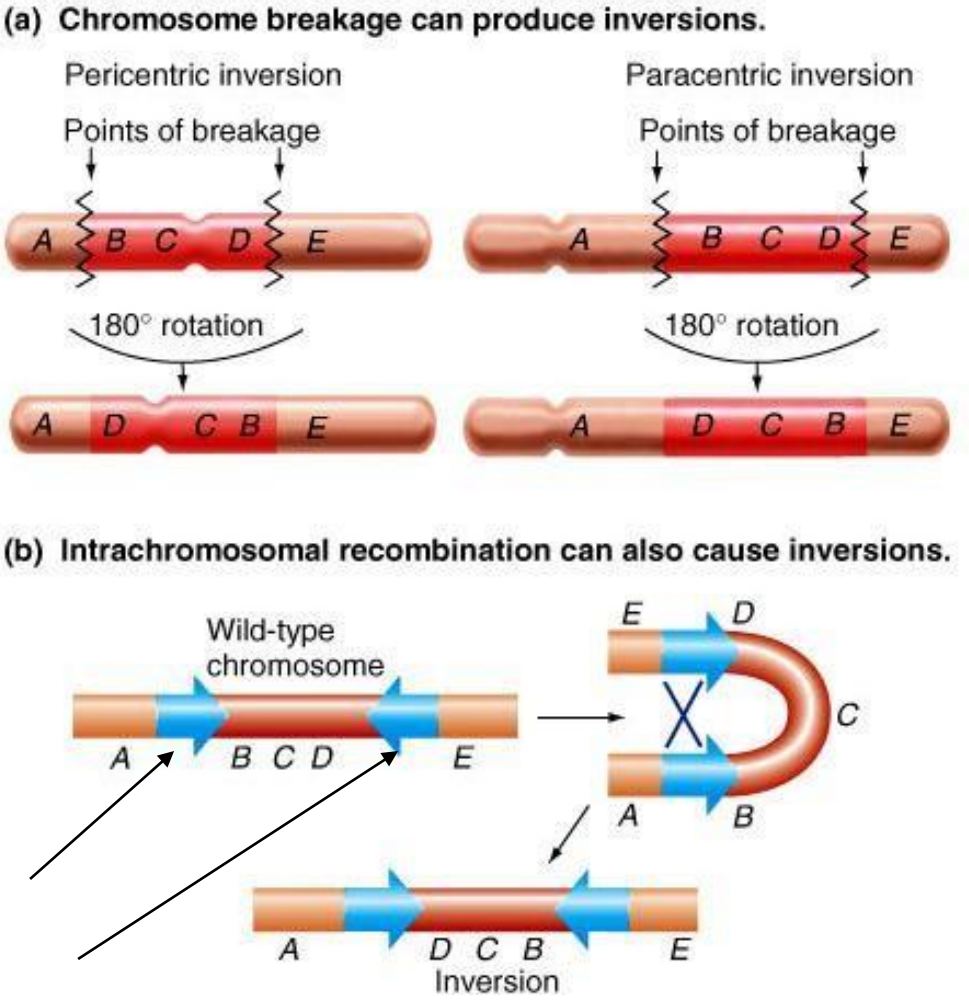


Gene copy number decreased

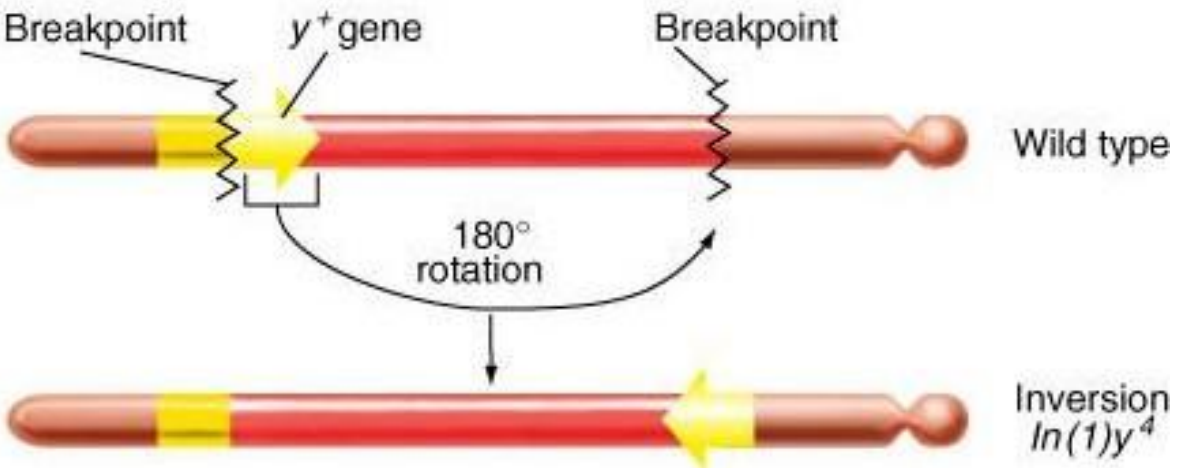
Gene copy number increased

Gen aileleri örn. Hemoglobin genleri duplikasyonla oluşur.

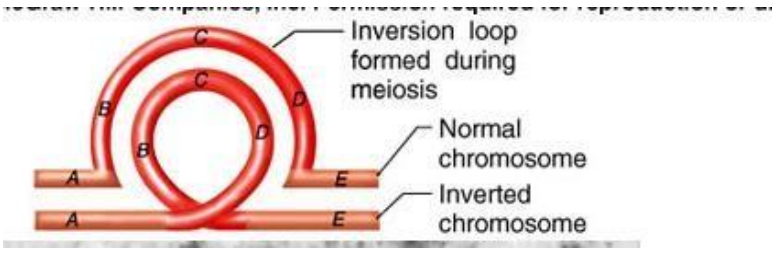
İnversiyon

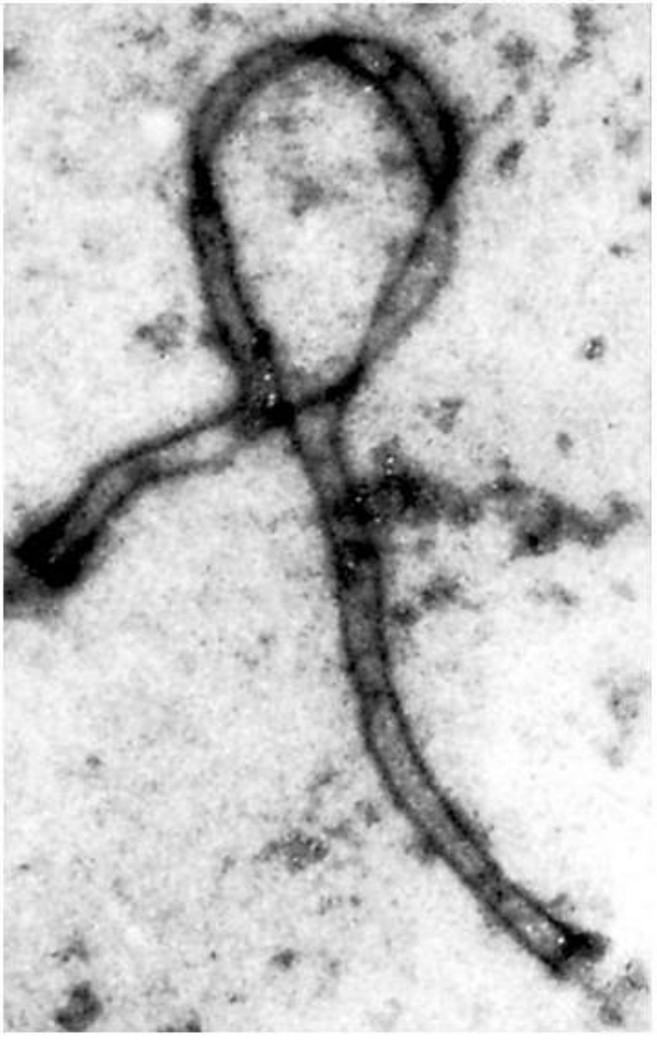

(a) Chromosome breakage can produce inversions.
Pericentric inversion
Points of breakage
A B C D E
180° rotation
A D C B E
Paracentric inversion
Points of breakage
A B C D E
180° rotation
A D C B E
(b) Intrachromosomal recombination can also cause inversions.
Wild-type chromosome
A B C D E
E D C A B
A D C B E
Inversion

(c) Inversions can disrupt gene function.

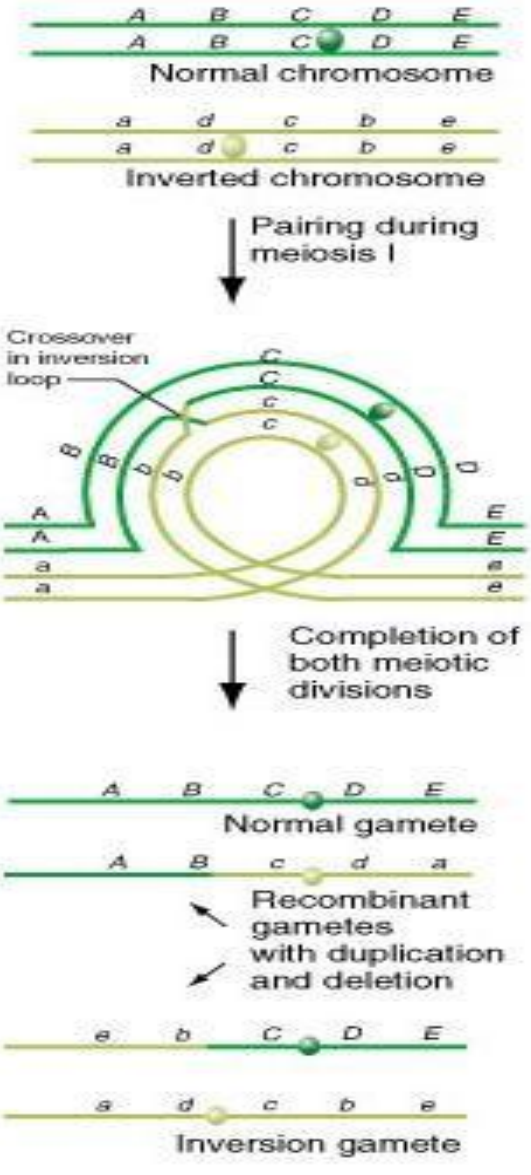


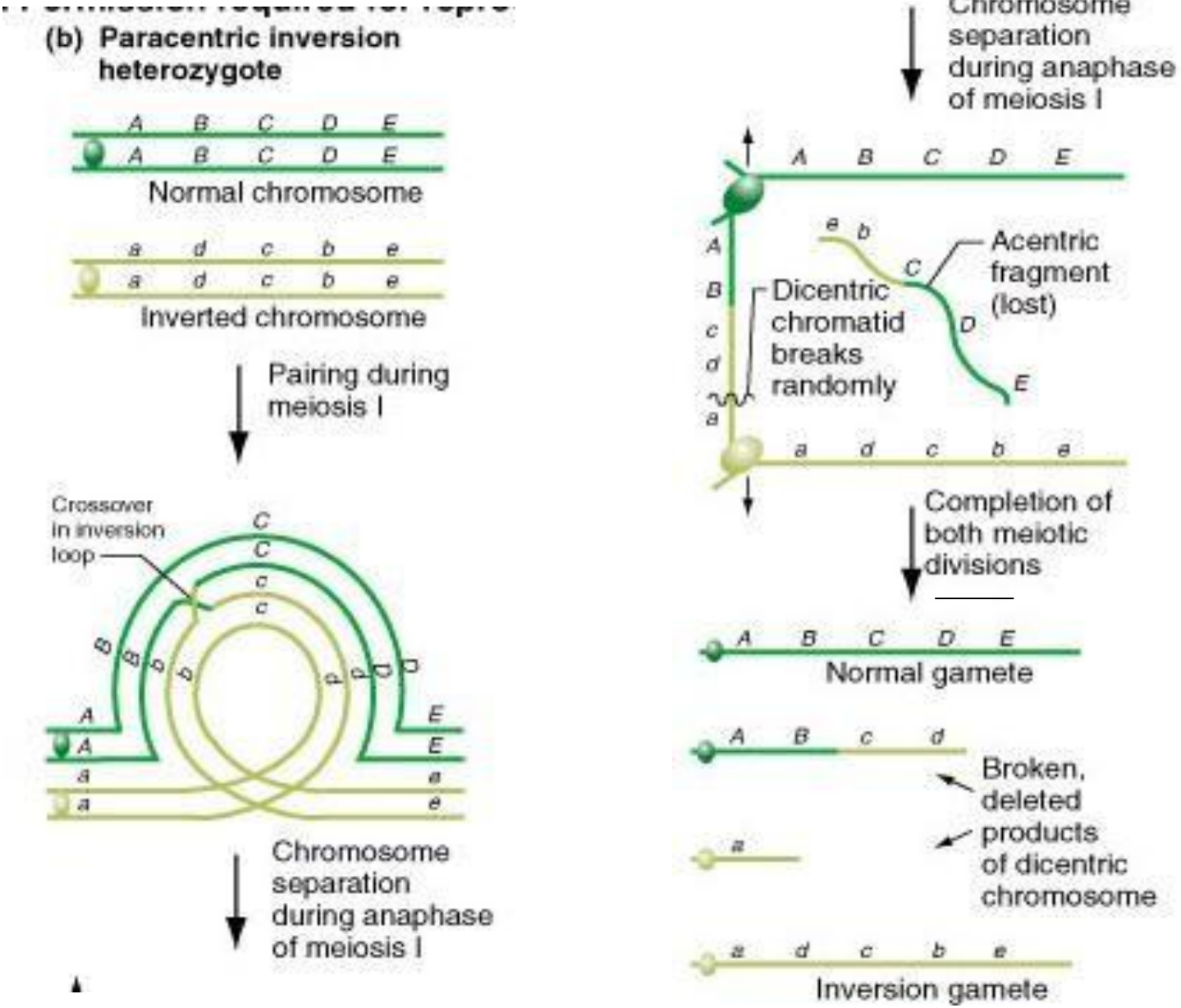
Inversiyon loop

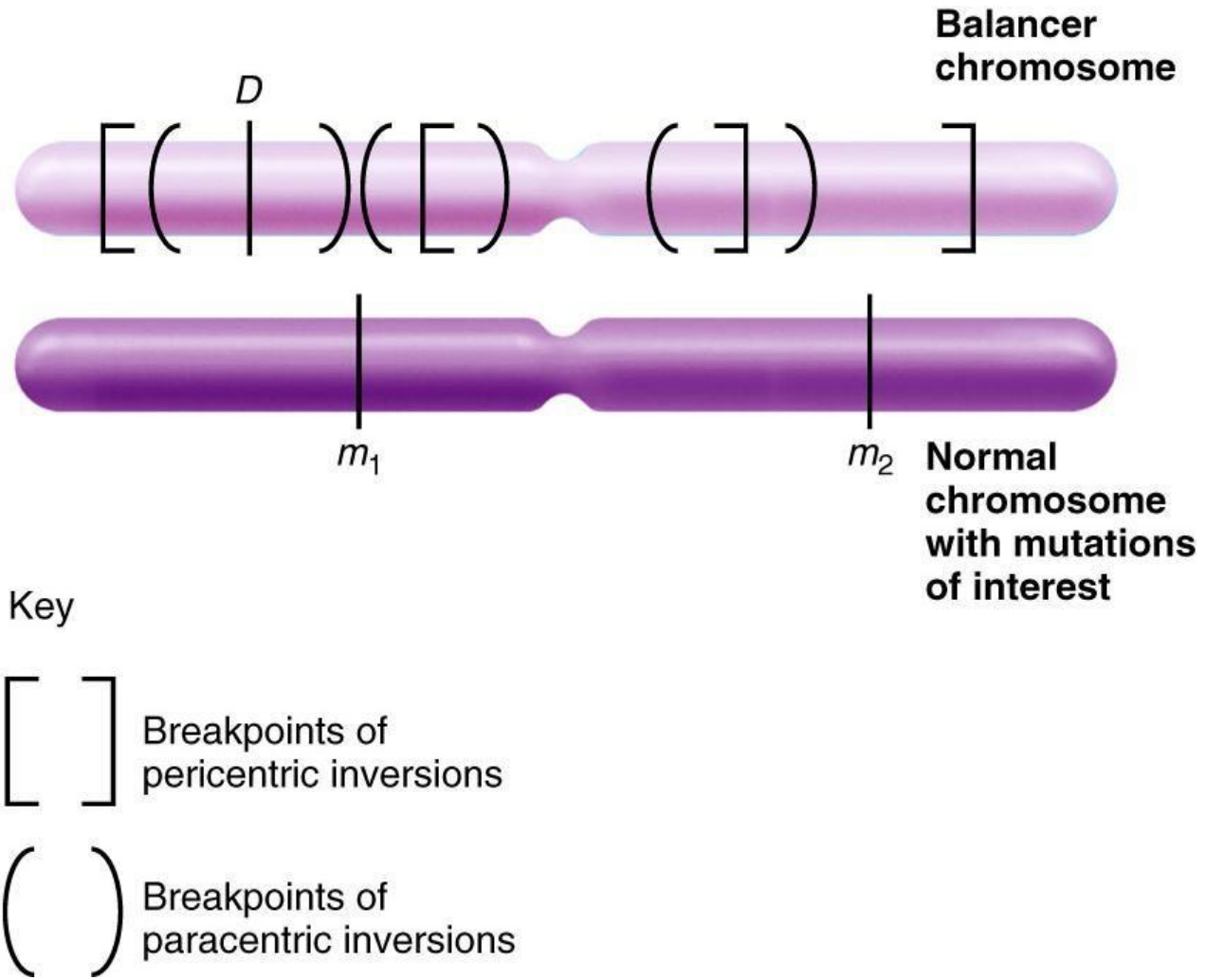




(a) Pericentric inversion heterozygote

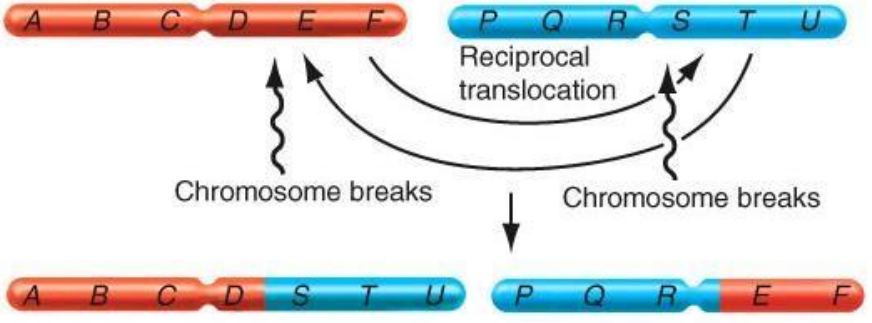



(b) Paracentric inversion heterozygote
A B C D E
A B C D E
Normal chromosome
a d c b e
a d c b e
Inverted chromosome
Pairing during meiosis I
Crossover in inversion loop
Chromosome separation during anaphase of meiosis I
Chromosome separation during anaphase of meiosis I
Acentric fragment (lost)
Dicentric chromatid breaks randomly
Completion of both meiotic divisions
Normal gamete
Broken, deleted products of dicentric chromosome
Inversion gamete

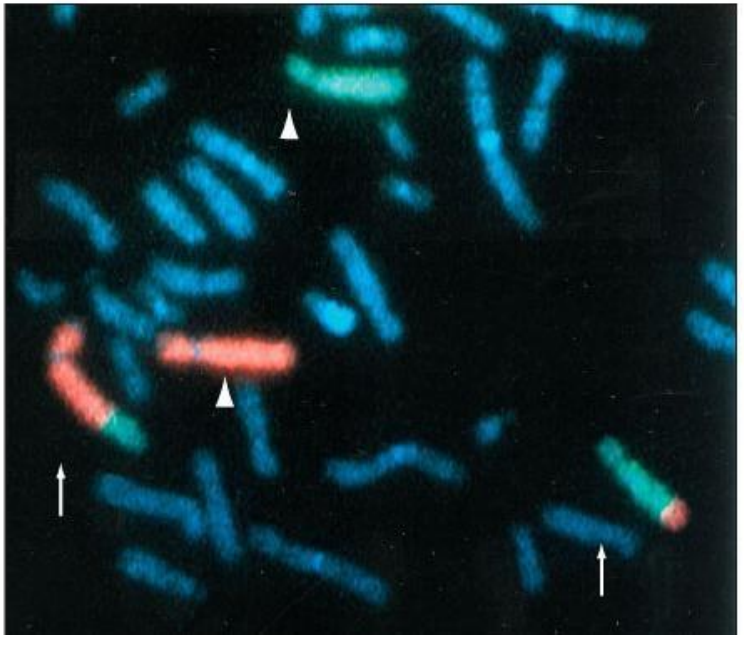

Balancer chromosome
D
m_1
m_2
Normal chromosome with mutations of interest
Key
Breakpoints of pericentric inversions
Breakpoints of paracentric inversions

Resiprokal translokasyon

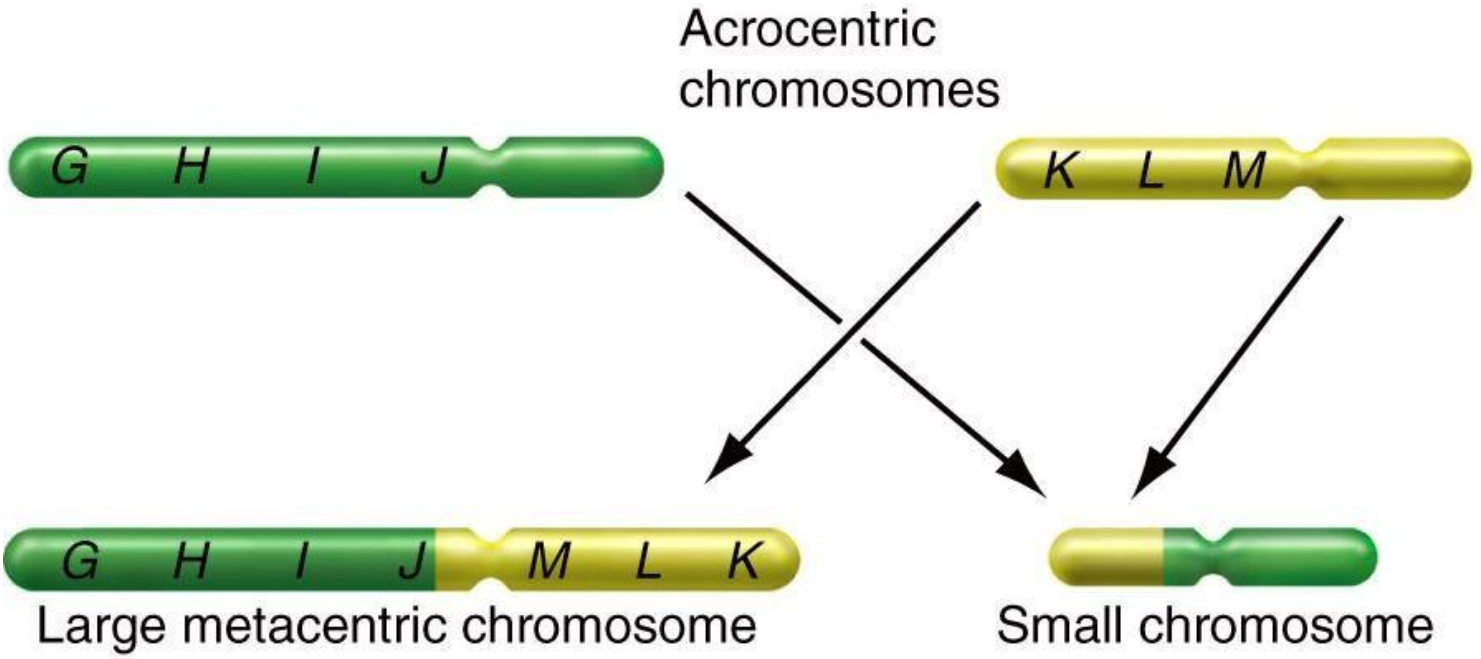
(a) Two chromosome breaks can produce a reciprocal translocation.



(b) Chromosome painting reveals a reciprocal translocation.

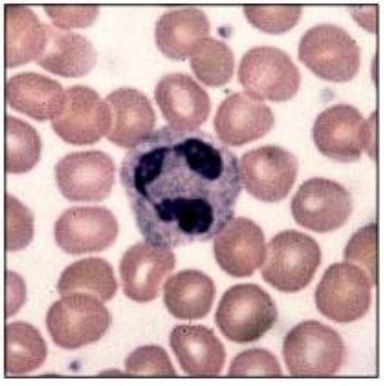


Robertsonian translokasyonu

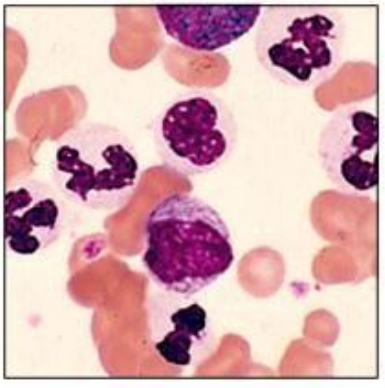


A Robertsonian translocation

(a) Leukemia patients have too many white blood cells.

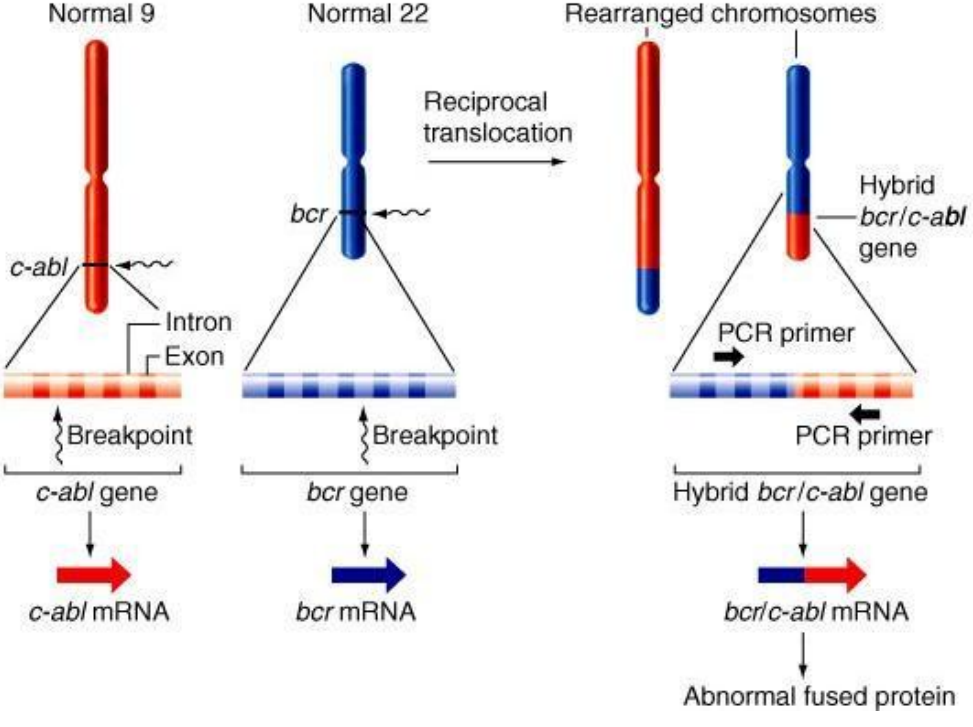


Normal

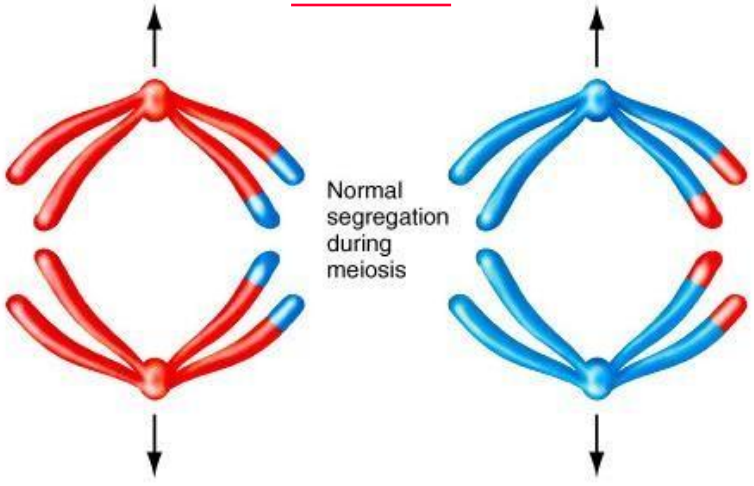


Leukemic

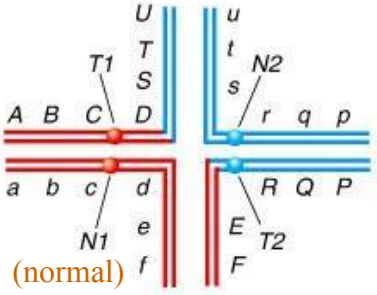
(b) The genetic basis for chronic myelogenous leukemia.



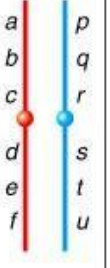
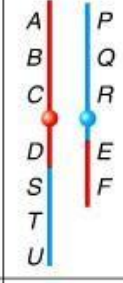
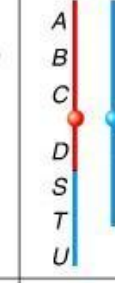
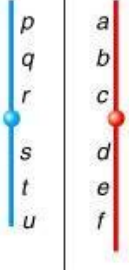
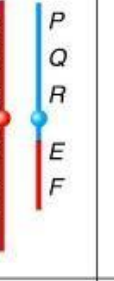
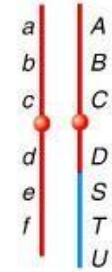
(a) Segregation in a translocation homozygote



(b) Chromosome pairing in a translocation heterozygote

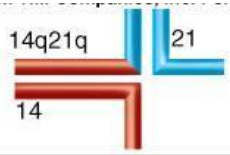


(c) Segregation in a translocation heterozygote

Segregation pattern	Alternate		Adjacent - 1		Adjacent - 2 (less frequent)	
Gametes	Balanced *N1 + N2*	Balanced *T1 + T2*	Unbalanced *T1 + N2*	Unbalanced *N1 + T2*	Unbalanced *N1 + T1*	Unbalanced *N2 + T2*
						
Type of progeny when mated with normal *abcdefpqrstu* homozygote	*abcdef pqrstu*	*ABCDEF PQRSTU*	(no E, F) None surviving	(no S, T) None surviving	None surviving	None surviving

(d) Semisterility in corn

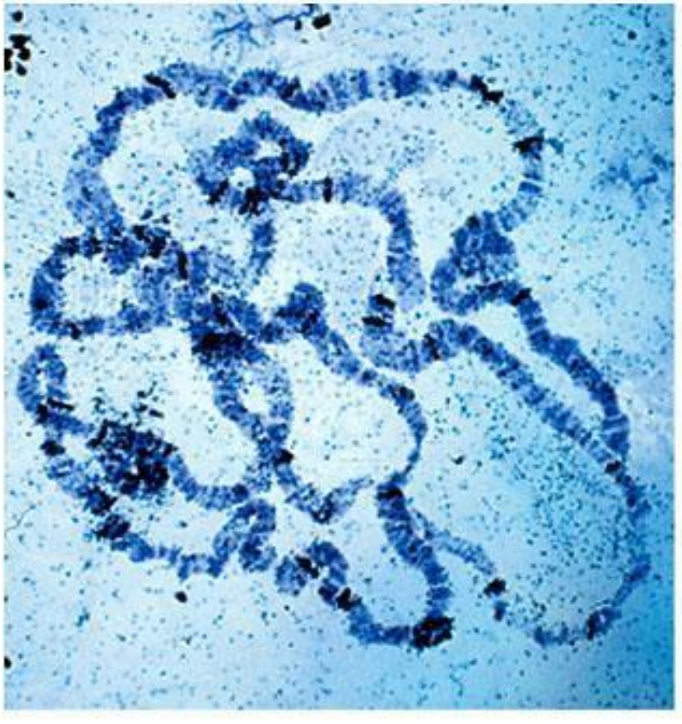
Translokasyonlu Down



Segregation pattern	Alternate		Adjacent-1		Adjacent-2	
Gametes	21 14 Balanced normal	14q21q Balanced Robertsonian translocation	21 14q21q Unbalanced	14 Unbalanced	14 14q21q Unbalanced	21 Unbalanced
Fertilization with normal gamete	Normal phenotype	Normal phenotype (carrier)	Down syndrome	Lethal	Lethal	Lethal

Transpospozisyon: Küçük DNA parçalarının hareketi

copia TE

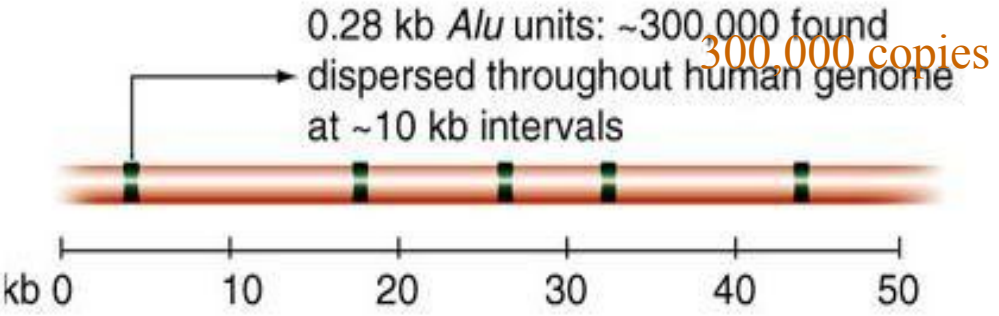


Transpozabl elementler

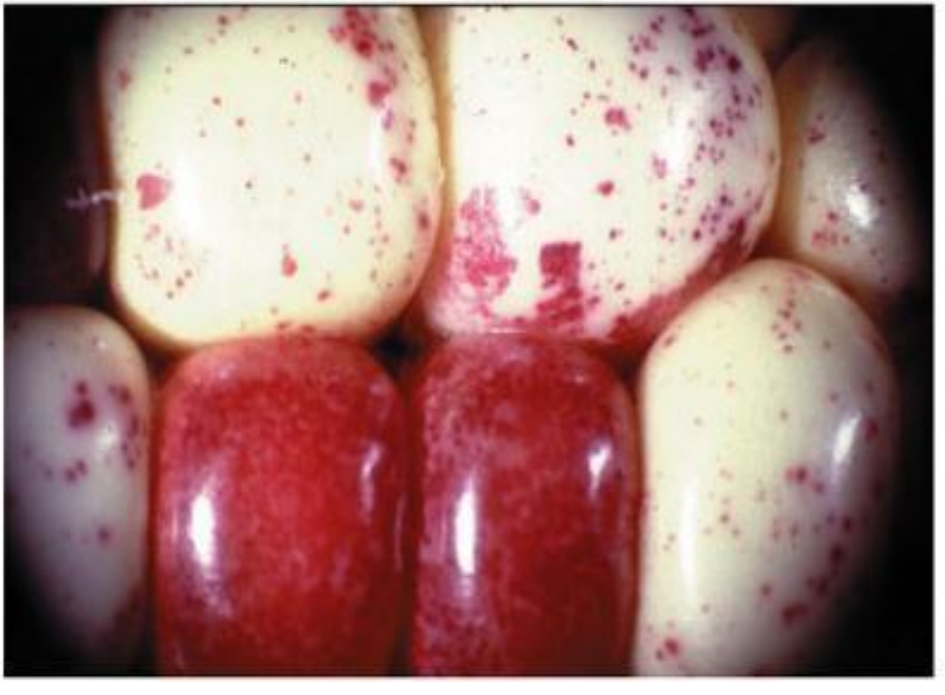
Genom içersinde hareket edebilen DNA parçaları

1. 50-10,000 bp
2. Kopya sayısı 1 den 100e ve 1000e kadar değişir
3. Memelilerde TEs: LINES (L1) ve SINES (Alu)

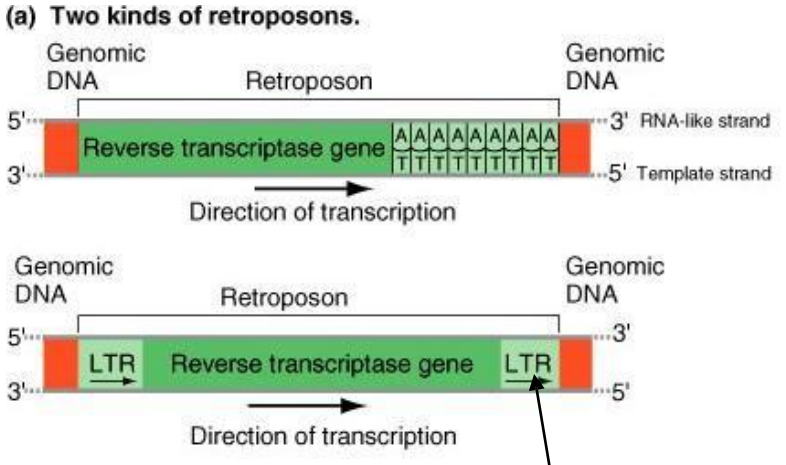
(a) *Alu* SINEs in the human genome.

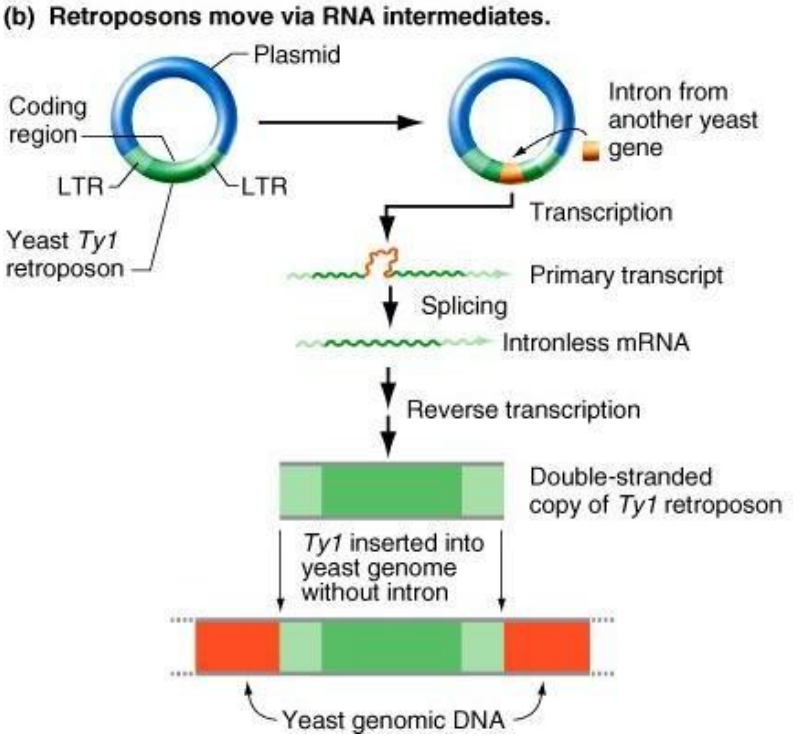


(b) TEs cause mottling in corn.



Retropozonlar: RNA ara moleküllerinin transkripsiyonu ile oluşurlar.





Retrovirus (RNA tümor virüsü)

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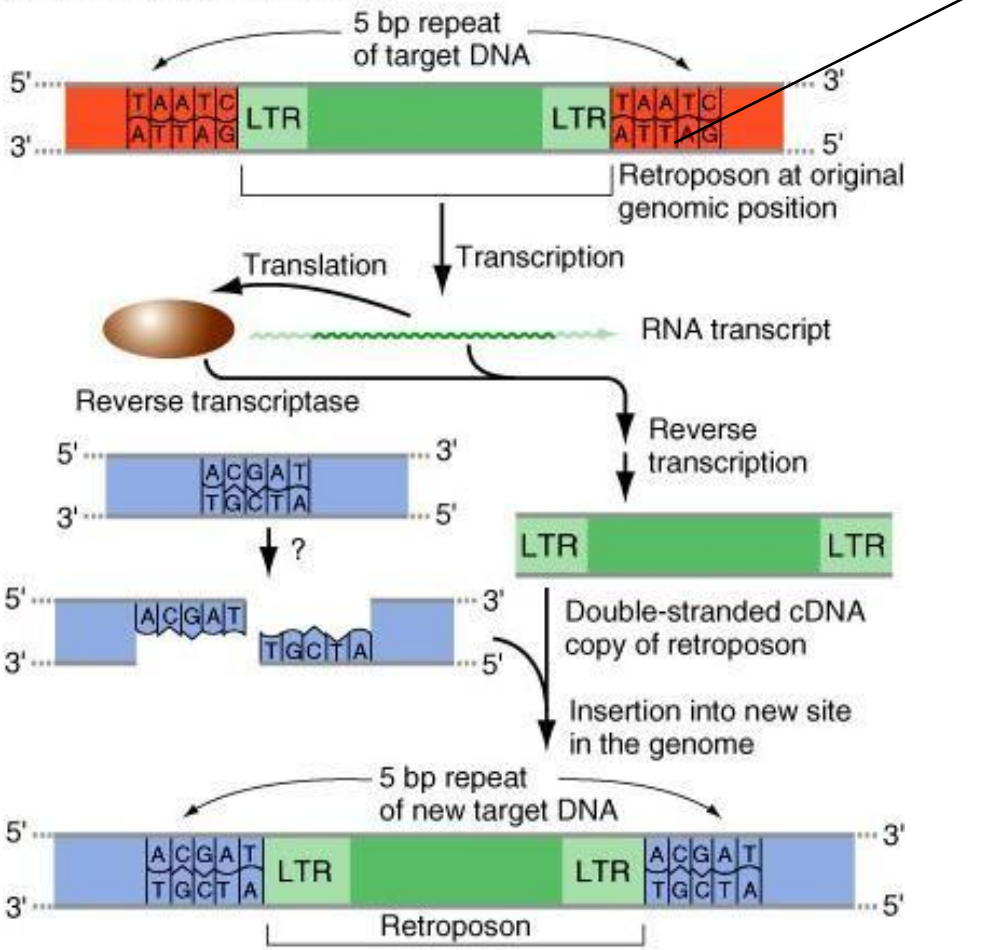
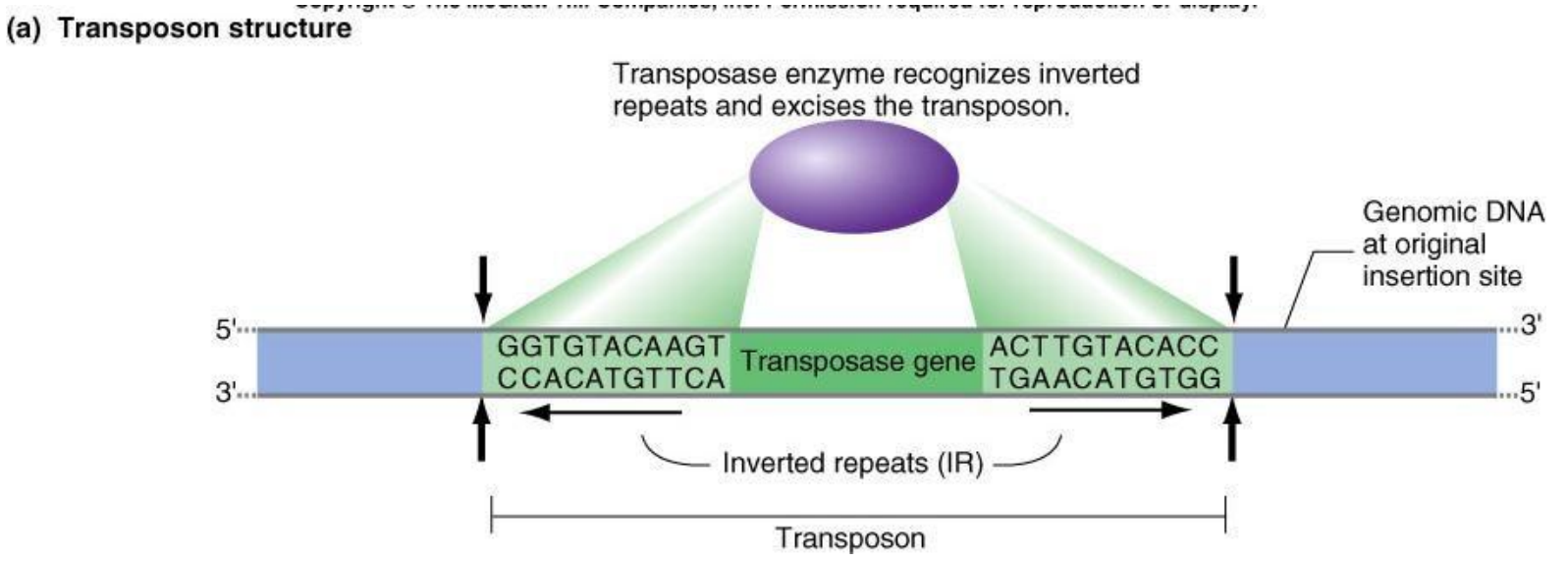
(c) How retroposons move.



Transpozonlar



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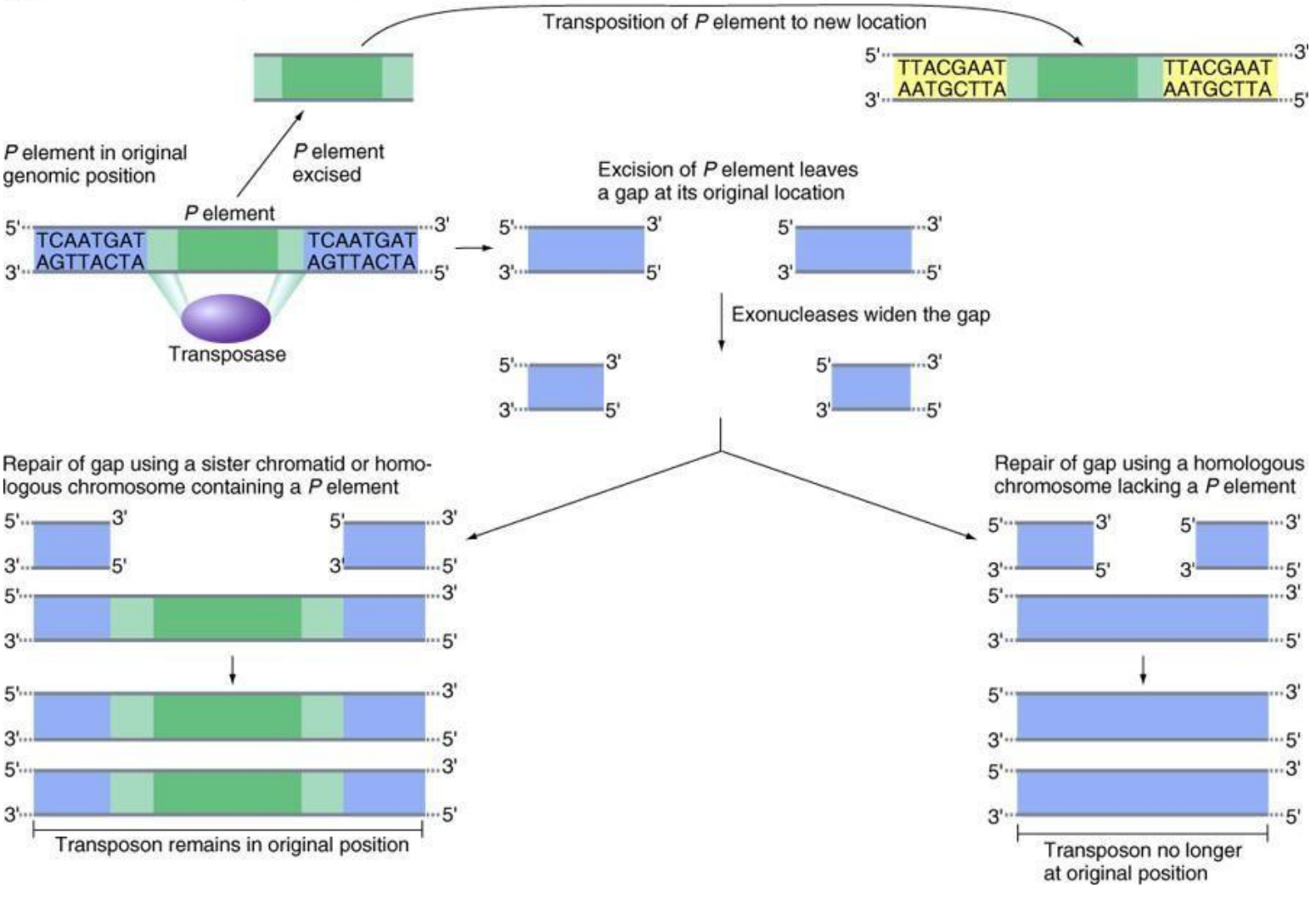
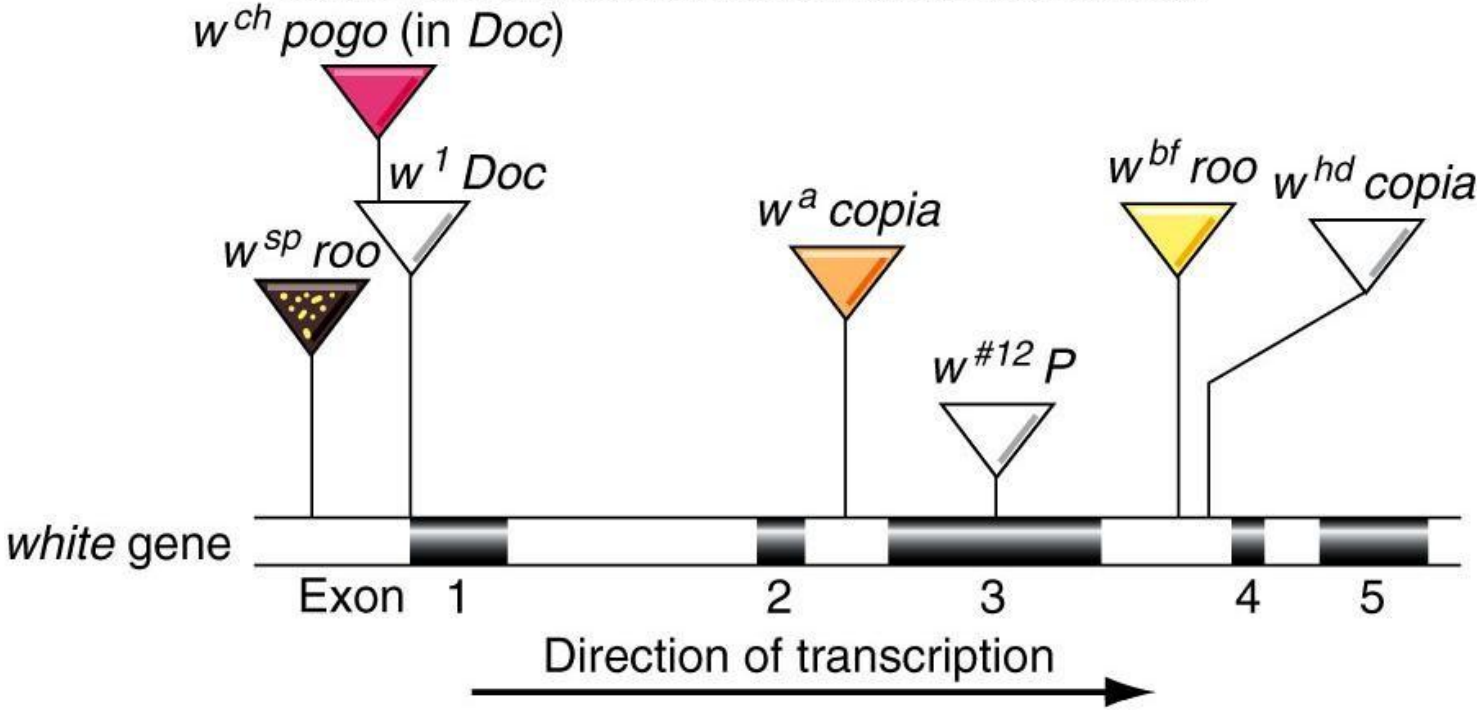
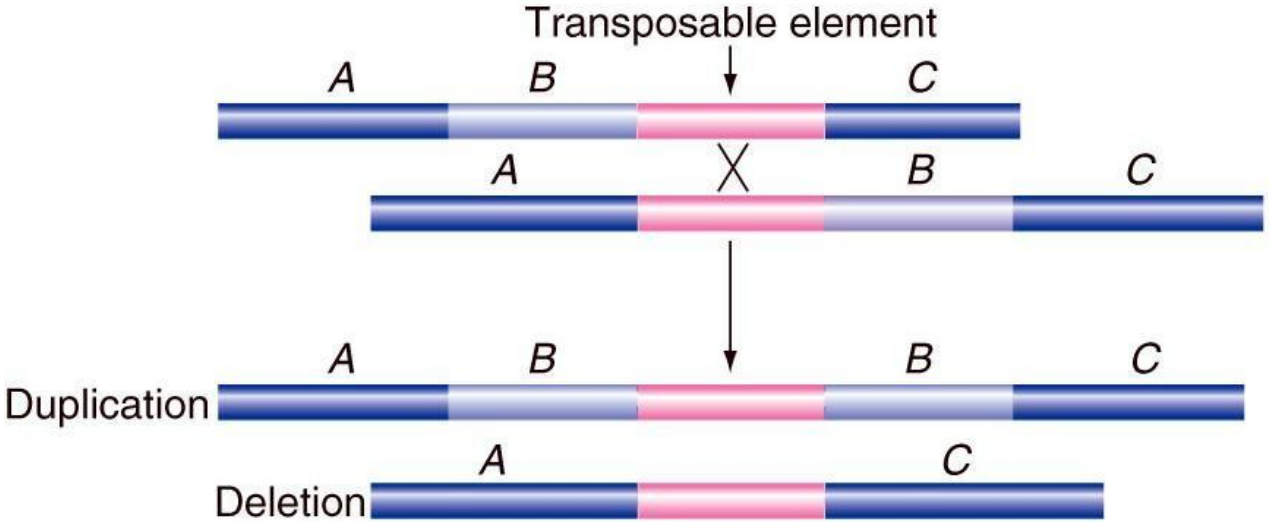
(b) How *P* element transposons move




w ch pogo (in Doc)
w 1 Doc
w sp roo
w a copia
w bf roo
w hd copia
w #12 P
white gene
Exon 1
2
3
4
5
Direction of transcription

(a) Unequal crossing-over between TEs.



(b) Two transposons can form a large, composite transposon.

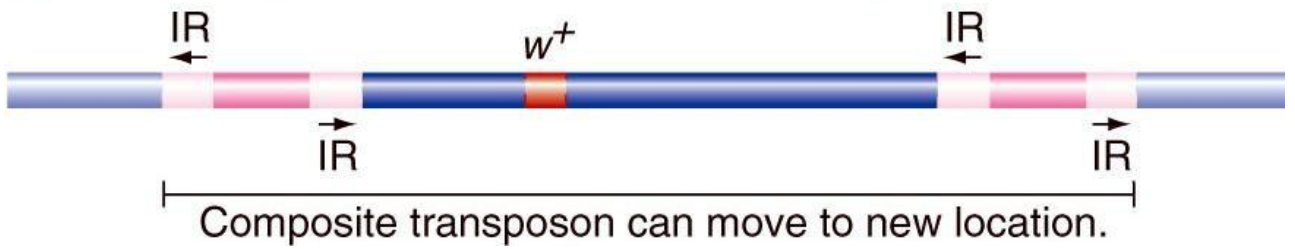


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TABLE 13.1 Chromosomal Rearrangements and Changes in Chromosome Number

Changes in Chromosome Number

Euploidy: Cells that contain only complete sets of chromosomes

Diploidy (2*x*): Two copies of each homolog

Monoploidy (*x*): One copy of each homolog

Polyploidy: More than the normal diploid number of chromosome sets

Triploidy (3*x*): Three copies of each homolog

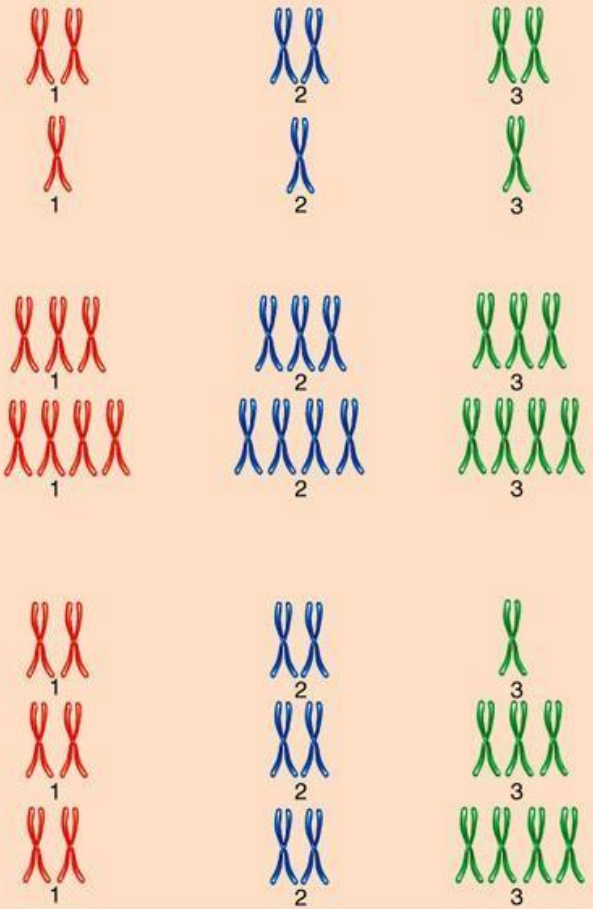
Tetraploidy (4*x*): Four copies of each homolog

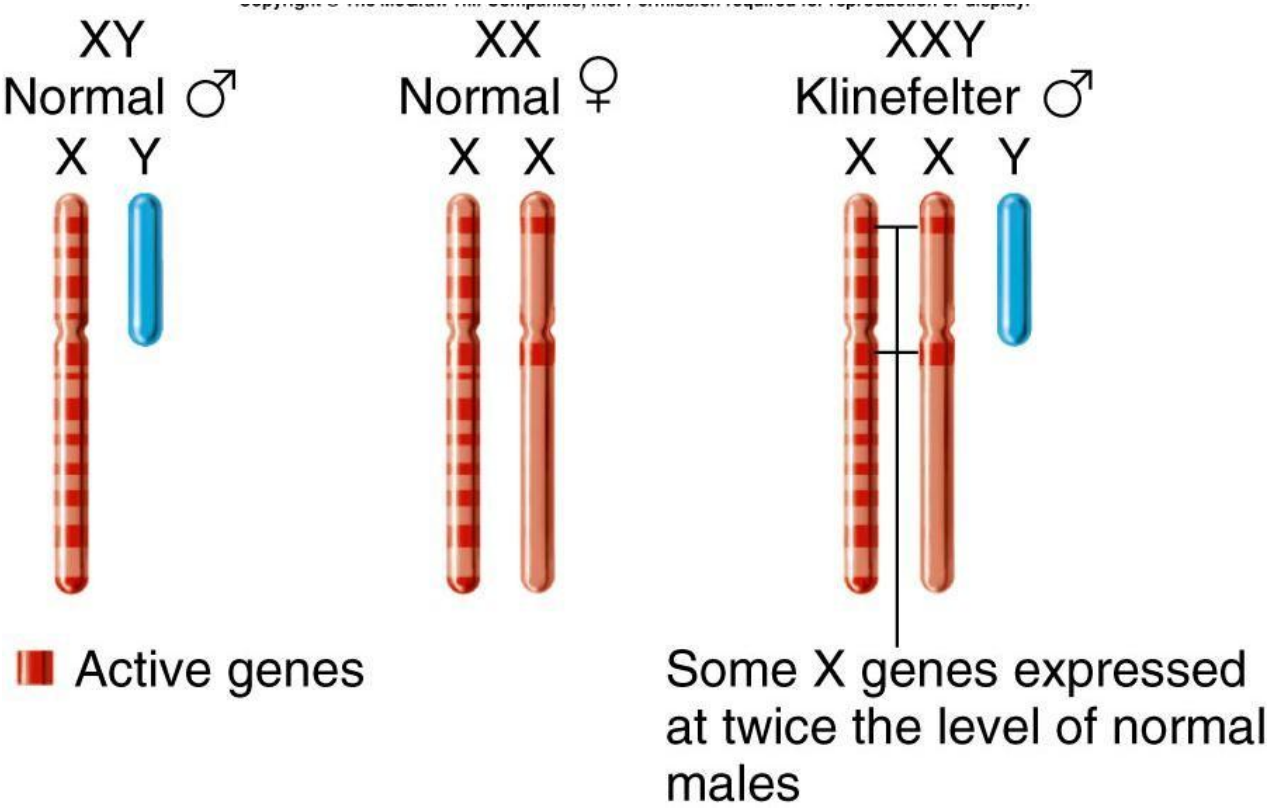
Aneuploidy: Loss or gain of one or more chromosomes producing a chromosome number that is not an exact multiple of the haploid number

Monosomy (2*n* − 1)

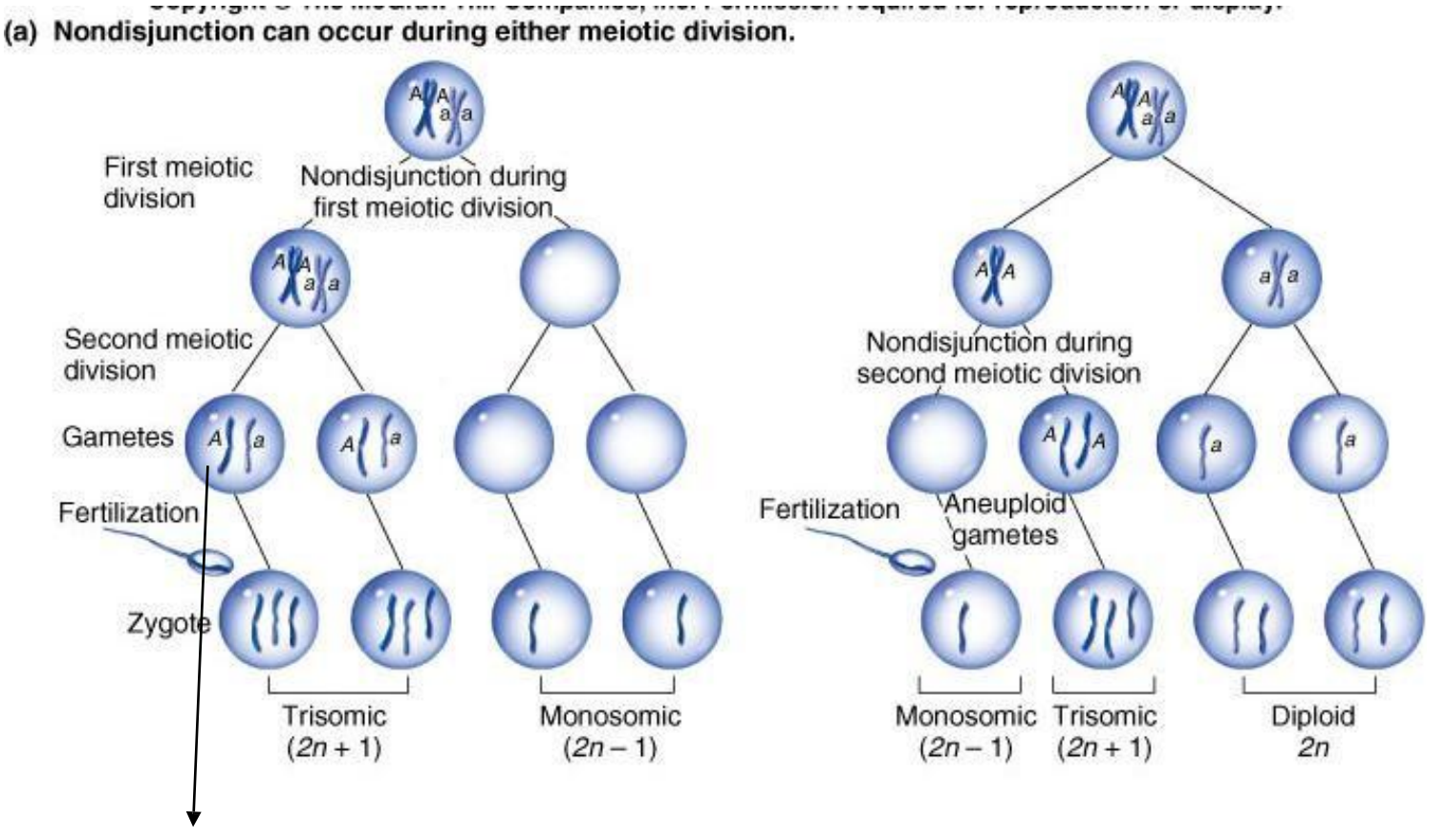
Trisomy (2*n* + 1)

Tetrasomy (2*n* + 2)




XY
Normal ♂
X Y
XX
Normal ♀
X X
XXY
Klinefelter ♂
X X Y
Active genes
Some X genes expressed at twice the level of normal males

Nondisjunction in meiotic recombination results in aneuploidy



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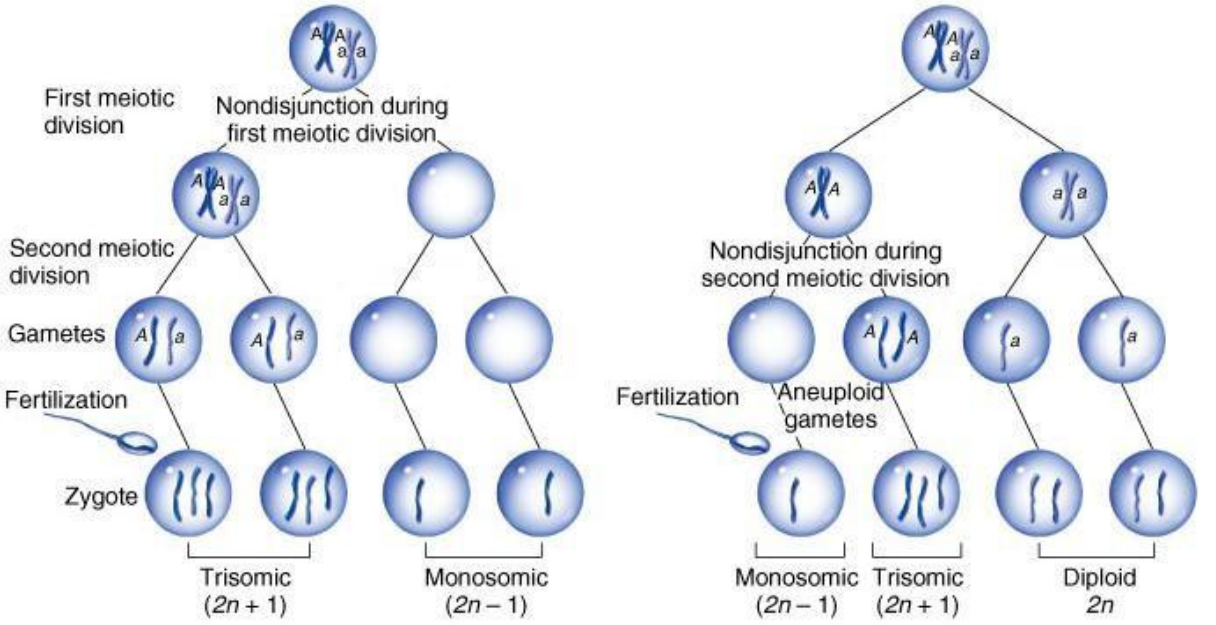
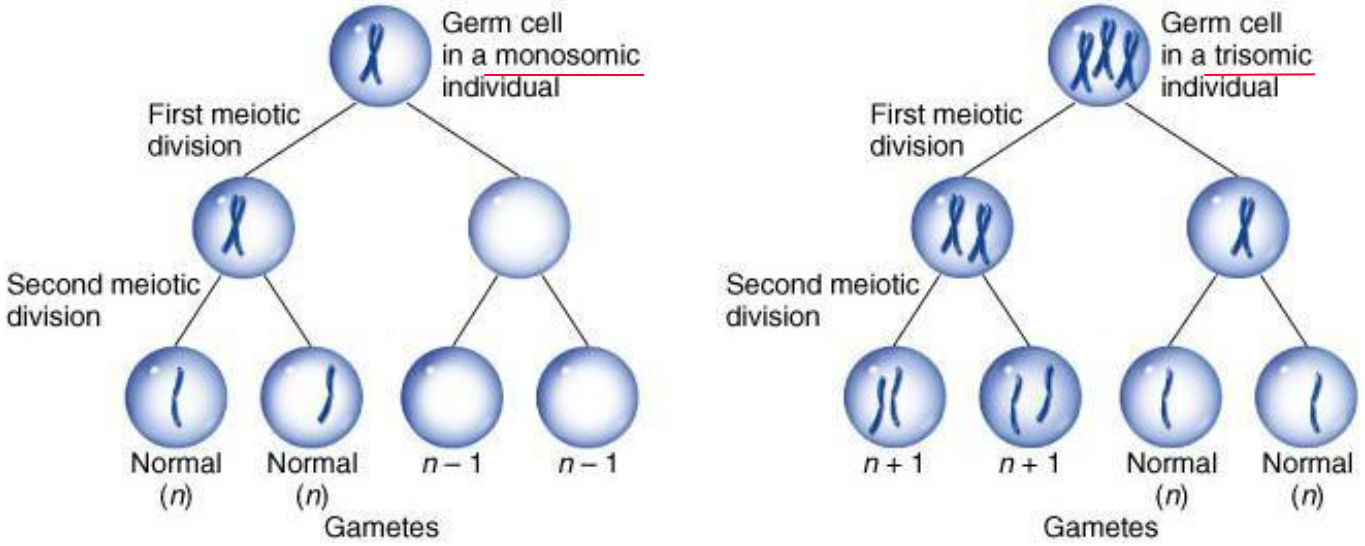
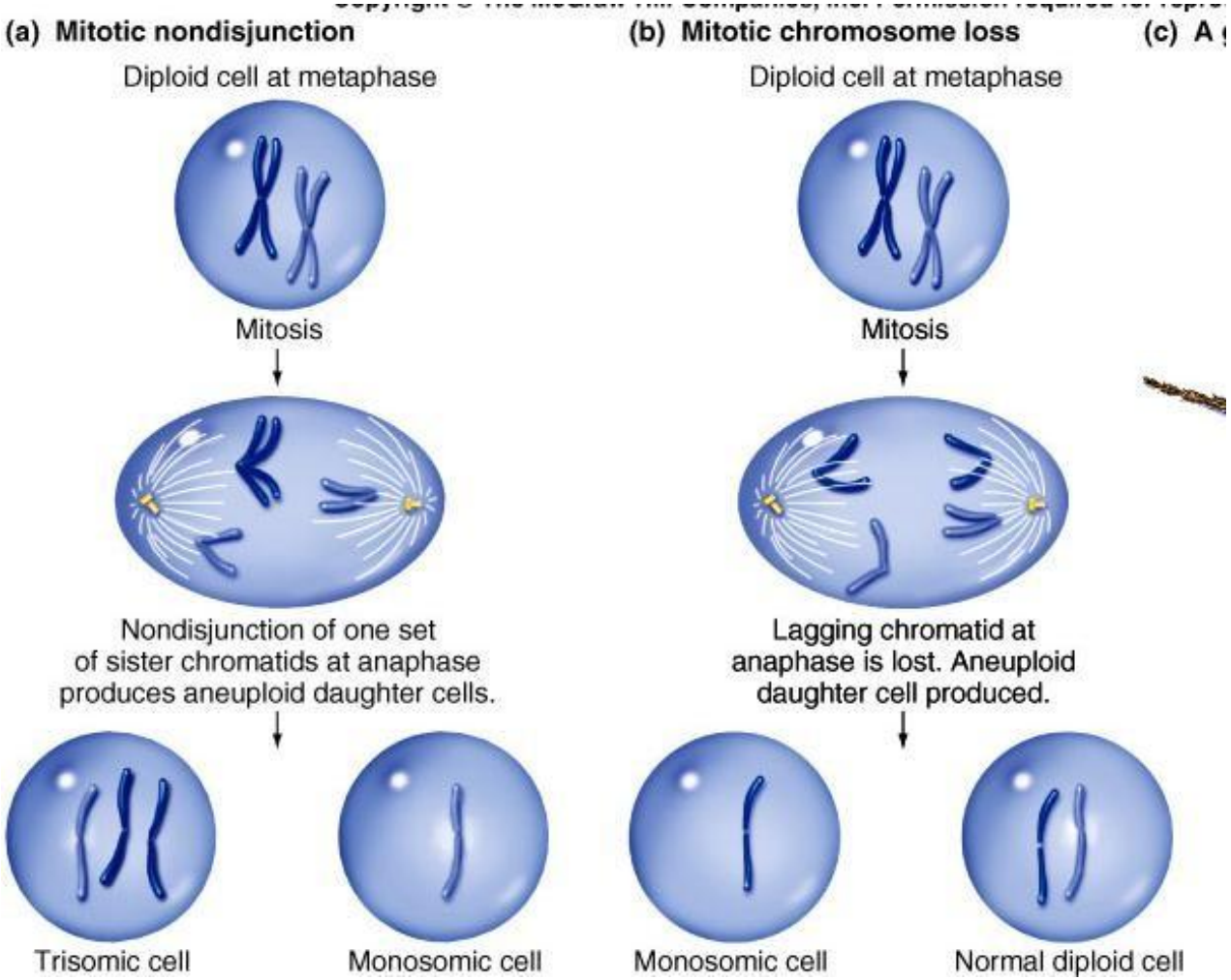
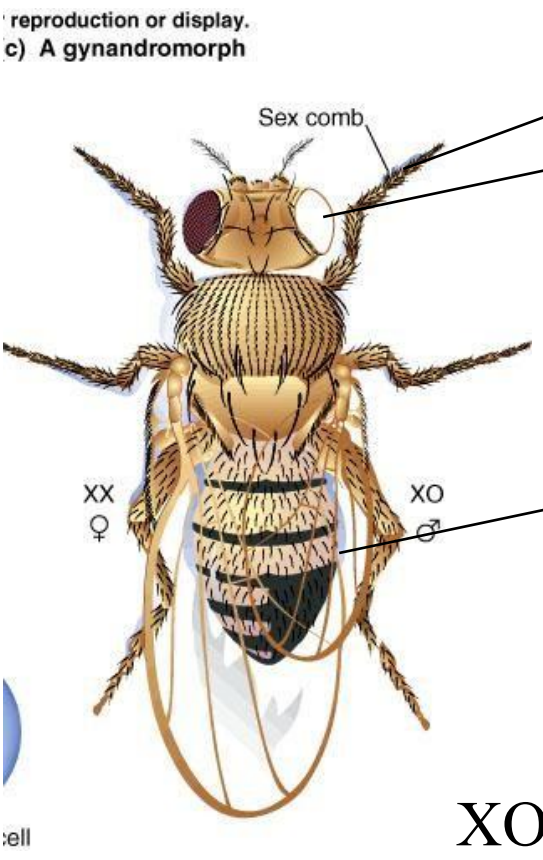
(a) Nondisjunction can occur during either meiotic division.



(b) Aneuploids beget aneuploid progeny.




(a) Mitotic nondisjunction
Diploid cell at metaphase
Mitosis
Nondisjunction of one set of sister chromatids at anaphase produces aneuploid daughter cells.
Trisomic cell
Monosomic cell
(b) Mitotic chromosome loss
Diploid cell at metaphase
Mitosis
Lagging chromatid at anaphase is lost. Aneuploid daughter cell produced.
Monosomic cell
Normal diploid cell



Male-specific

White eye

Minute wing

XX

XO

$X^{w+m+} X^{w-m-}$

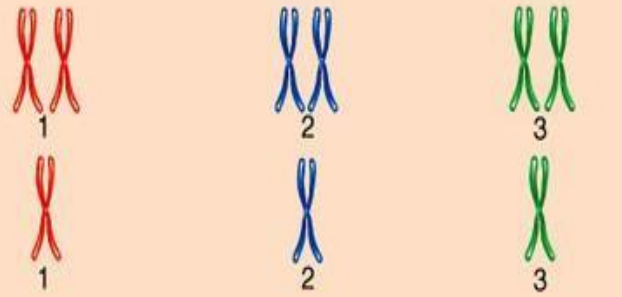
$X^{w-m-} O$

Changes in Chromosome Number

Euploidy: Cells that contain only complete sets of chromosomes

Diploidy (2*x*): Two copies of each homolog

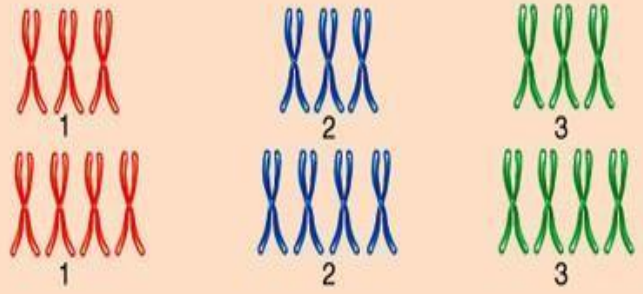
Monoploidy (*x*): One copy of each homolog



Polyploidy: More than the normal diploid number of chromosome sets

Triploidy (3*x*): Three copies of each homolog

Tetraploidy (4*x*): Four copies of each homolog



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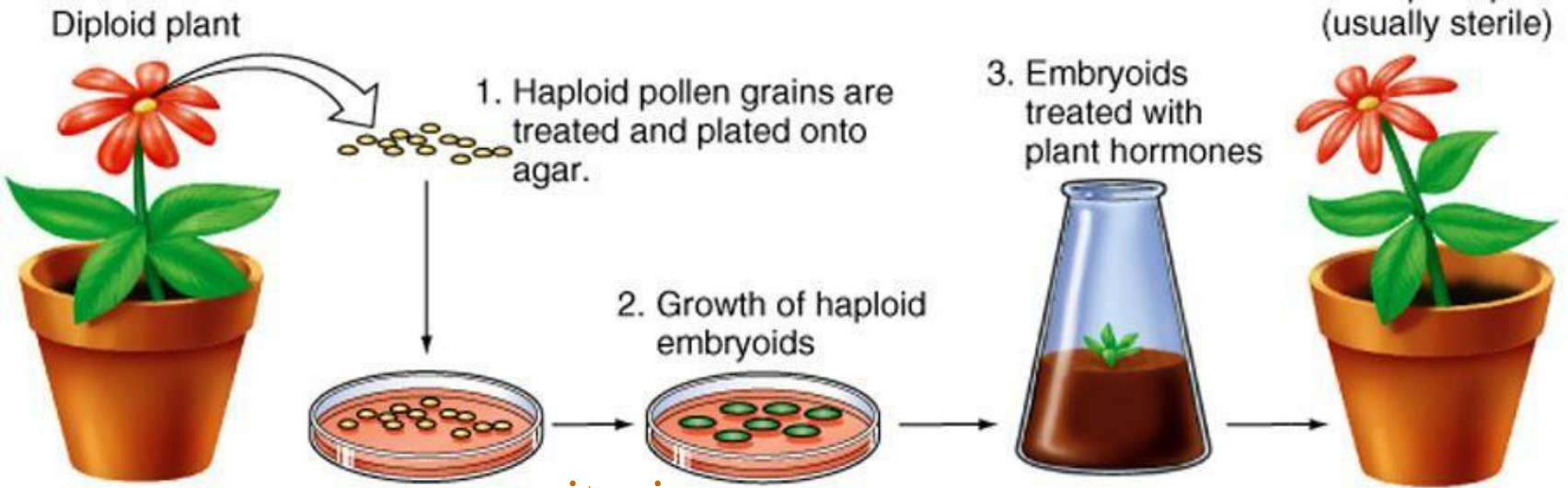
(a) How to create a monoploid plant



mitosis

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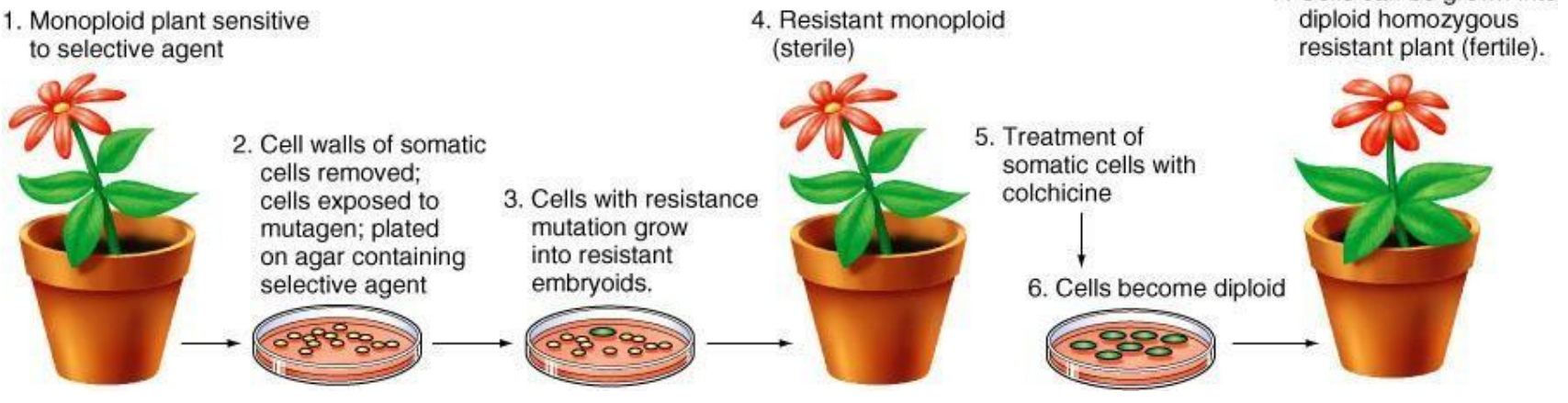
(b) Using monoploid plants to select for herbicide resistance



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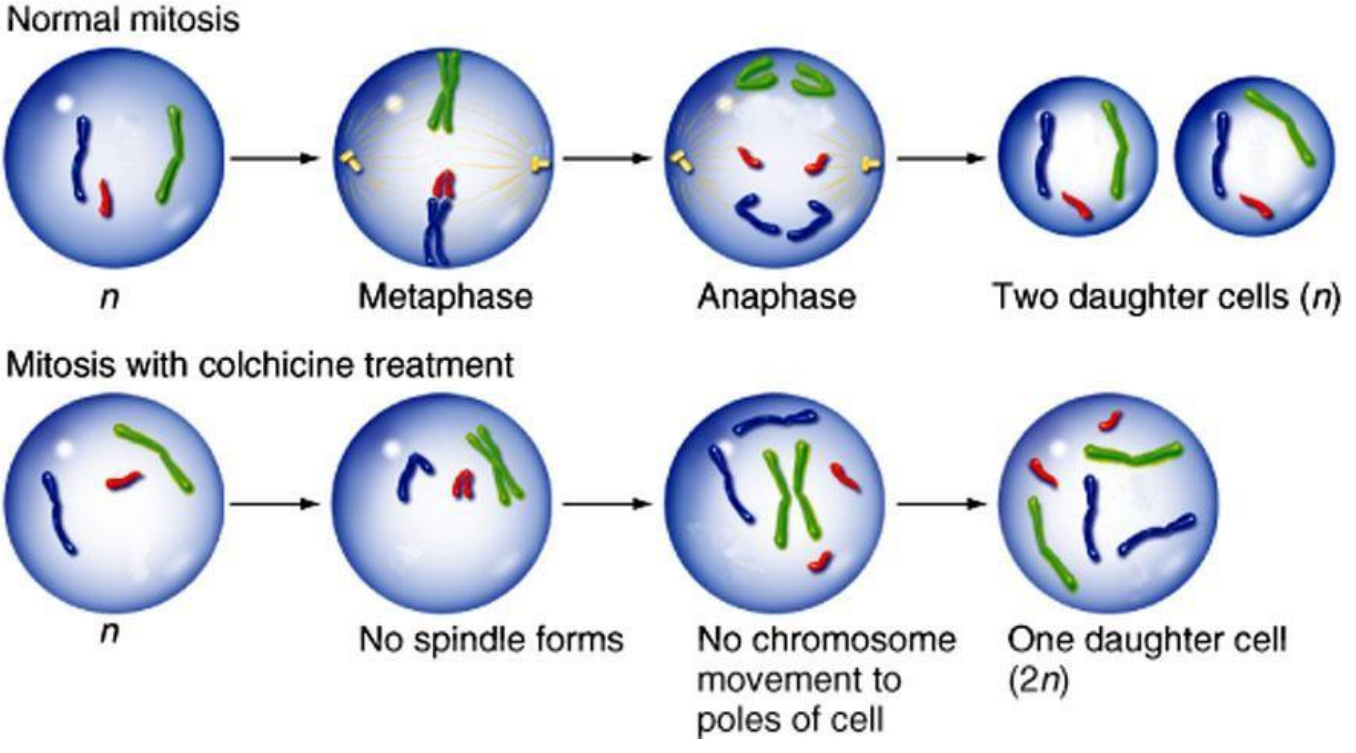
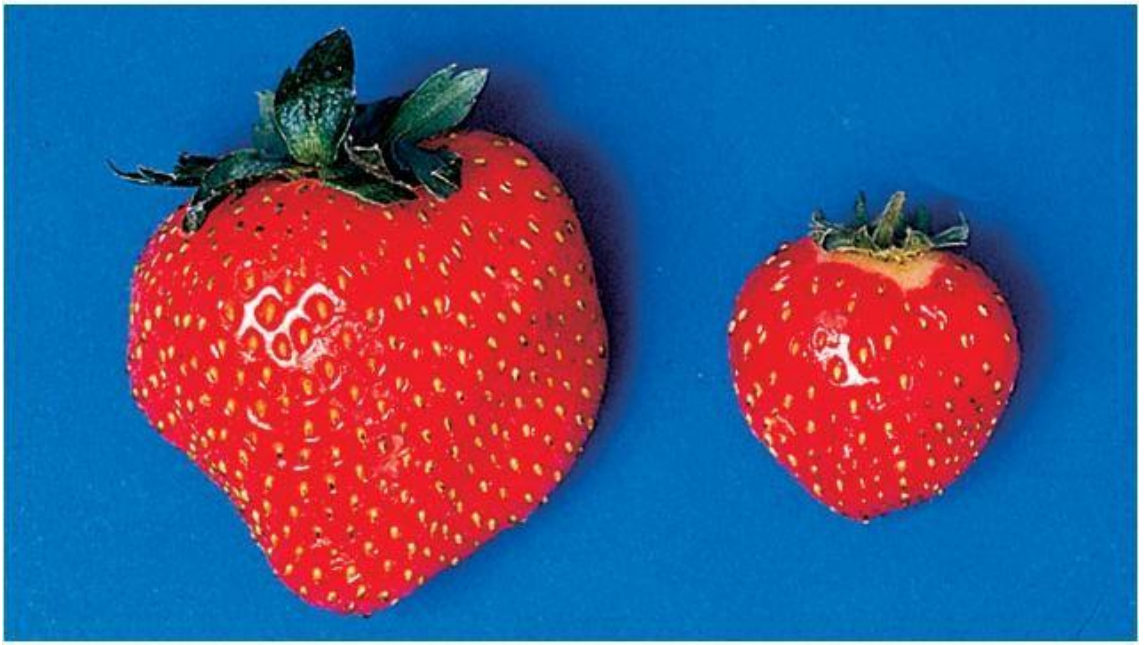
(c) Using colchicine to double chromosome numbers

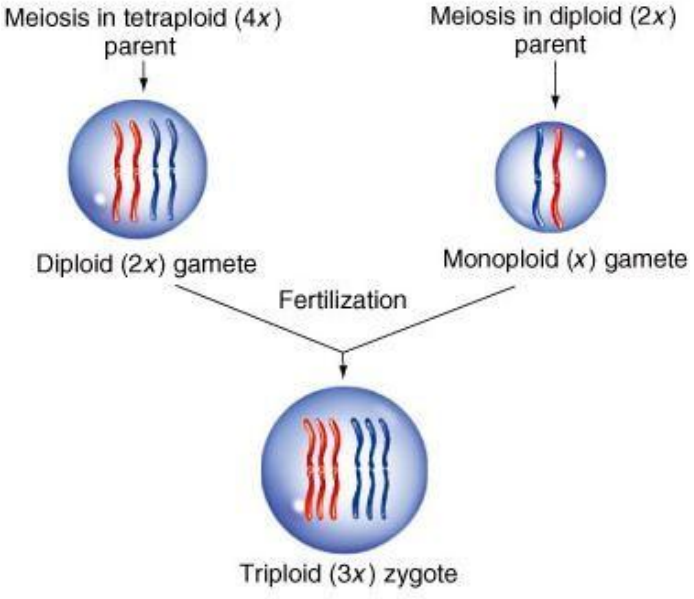


8X

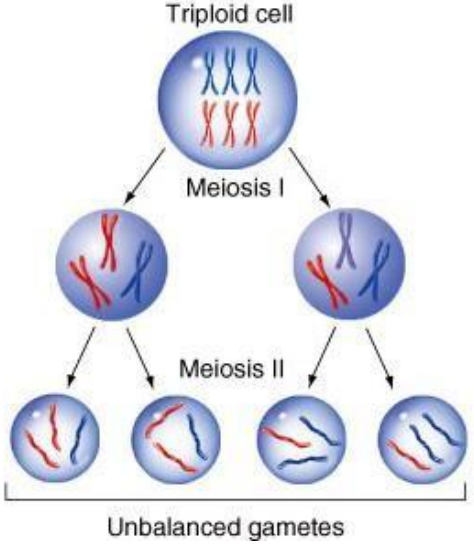


2X

(a) Formation of a triploid organism



(b) Meiosis in a triploid organism



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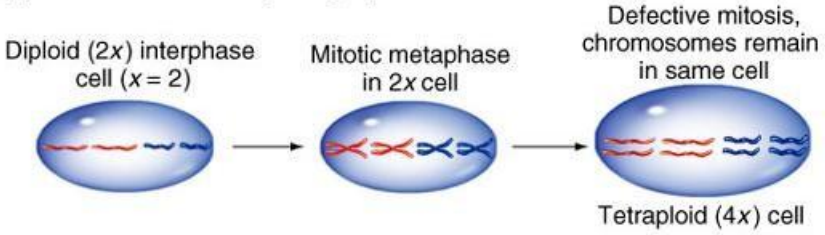
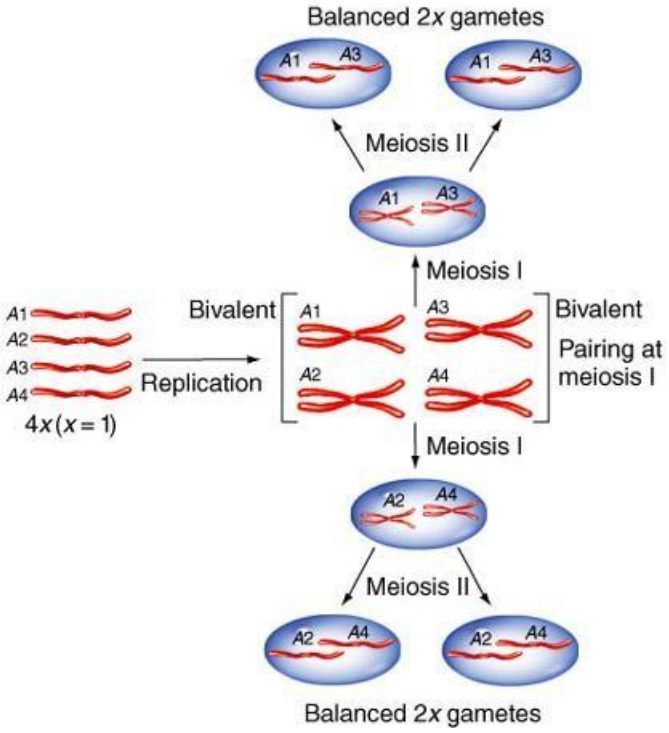
(a) Generation of tetraploid (4*x*) cells



(b) Pairing of chromosomes as bivalents



(c) Gametes formed by *A A a a* tetraploids

Chromosomes	Pairing	Gametes produced by random spindle attachment
1. *A* 2. *A* 3. *a* 4. *a*	1 *A* 3 *a* 2 *A* 4 *a* **or** 1 *A* 4 *a* 2 *A* 3 *a*	1 + 3 *A a* 2 + 4 *A a* **or** 1 + 4 *A a* 2 + 3 *A a*
	1 *A* 2 *A* 3 *a* 4 *a* **or** 1 *A* 4 *a* 3 *a* 2 *A*	1 + 2 *A A* 3 + 4 *a a* **or** 1 + 4 *A a* 2 + 3 *A a*
	1 *A* 2 *A* 4 *a* 3 *a* **or** 1 *A* 3 *a* 4 *a* 2 *A*	1 + 2 *A A* 3 + 4 *a a* **or** 1 + 3 *A a* 2 + 4 *A a*

Total:
8*A a*:2*A A*:2*a a* = 4*A a*:1*A A*:1*a a*

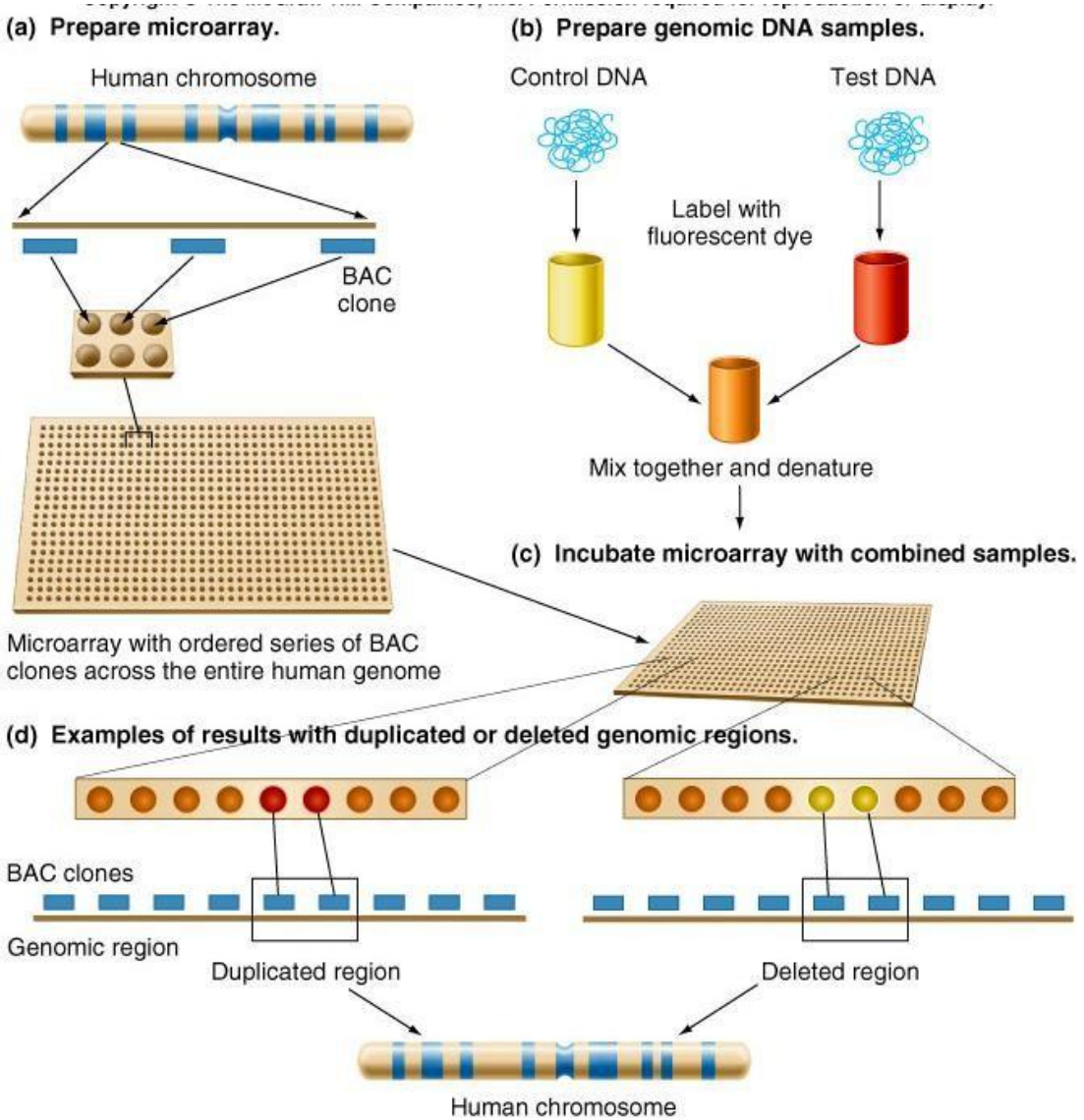

(a) Prepare microarray.
Human chromosome
BAC clone
Microarray with ordered series of BAC clones across the entire human genome
(b) Prepare genomic DNA samples.
Control DNA
Test DNA
Label with fluorescent dye
Mix together and denature
(c) Incubate microarray with combined samples.
(d) Examples of results with duplicated or deleted genomic regions.
BAC clones
Genomic region
Duplicated region
Deleted region
Human chromosome

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TABLE 13.2 Aneuploidy in the Human Population

Chromosomes	Syndrome	Frequency at Birth
Autosomes		
Trisomic 21	Down	1/700
Trisomic 13	Patau	1/5,000
Trisomic 18	Edwards	1/10,000
Sex chromosomes, females		
XO, monosomic	Turner	1/5,000
XXX, trisomic	X inactivation	1/700
XXXX, tetrasomic	Limited fertility	
XXXXX, pentasomic		
Sex chromosomes, males		
XYY, trisomic	Normal	1/10,000
XXYY, tetrasomic	Klinefelter	1/500
XXXY, tetrasomic		
XXXXY, pentasomic		
XXXXXY, hexasomic		

About 0.4% of all babies born have a detectable chromosomal abnormality that generates a detrimental phenotype.

Fig. 13.34

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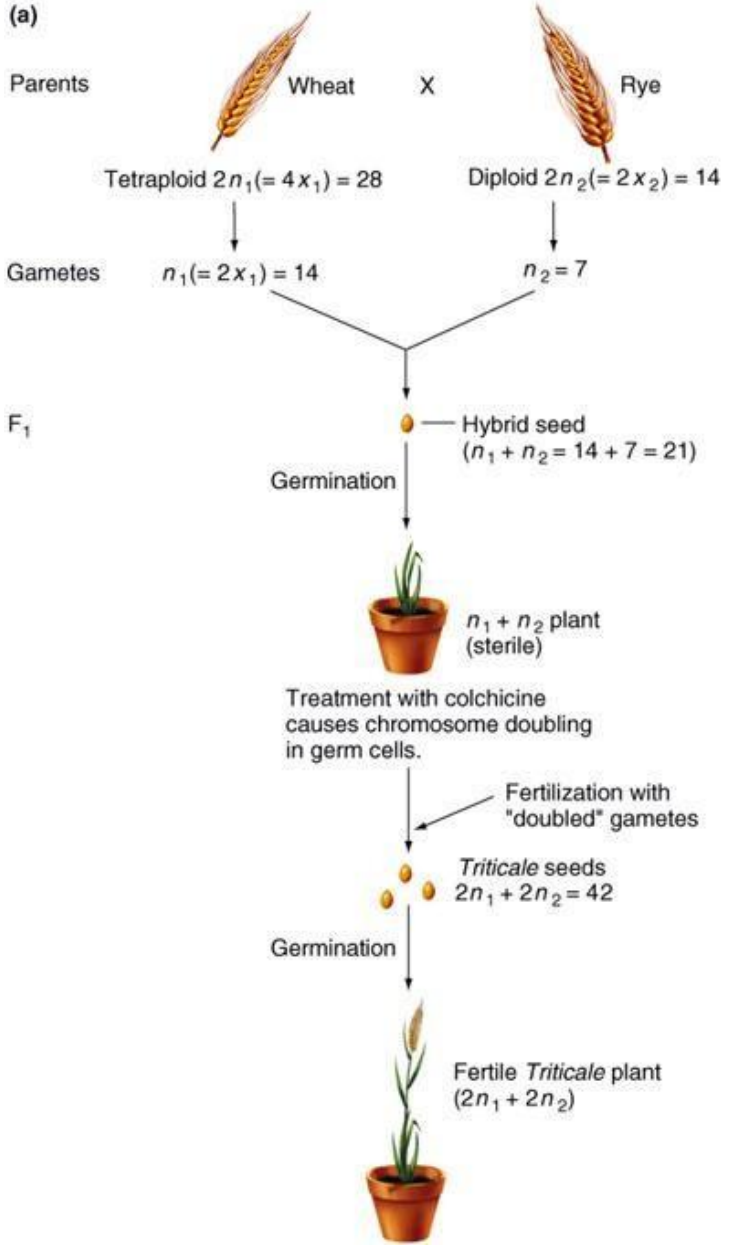


“B” Kromozomları

“Accessory”, “supernumerary”, “additional” kromozomlar, “**selfish genetic elements**”

Normal kromozom yapısı “A”

“B” kromozomları

- küçük

-Bitkiler ve hayvanlar aleminde çeşitli sayılarda

-1300 den fazla bitkide
- 500 hayvanda
-çeşitli mantarlarda

-genetik olarak in aktif, gelişim için elzem değil, çok az bazen de hiç fenotipik

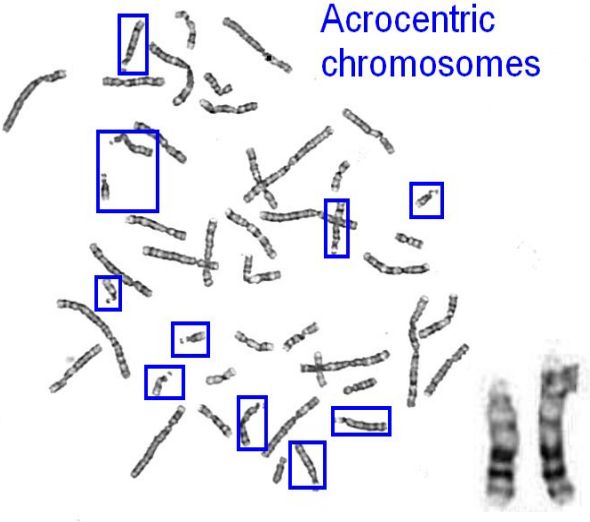
-Yaşamsal değil, bir tür içersinde bazı bireylerde oluşur

- Gametogenez sırasında veya sonrasında oluşur

Bazı organizmalarda:

-heterokromatik görünümde (deeply staining)

-light staining with telomeric and centromeric region of heterochromatin



Çavdar, mısır; akrosentrik

Parazitik eşek arısında; submetasentrik

Allium cernuum; metasentrik

Her hücrede bulunmaz

Mitotik aktif somatik ve germ hücrelerinde rastlanır

Triticum tripsacoides : B kromozomu kök ucu hücrelerinde yok, fakat present polen anahücrelerinde var

Crepis capillaris : 2 B kök ucu vegetatif hücrelerde

4 B Germ hücrelerinde

-işlevsel rRNA genleri(NOR lokus)taşırlar

-A kromozomlarının eşleşmesini

-Kiasma oluşumunu

-genetik rekombinasyonu etkilerler

- **Gen anlatımı DNA metilasyonu ile ilişkilidir.**