BIO-373

Genetics & Genomics

Chromosome variation

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Plan

1. Variations in chromosome numbers
    1.1 monosomy and trisomy
    1.2 euploidy and polyploidy

2. Variations in chromosome structure or content
    2.1 Deletions
    2.2 Duplications
    2.3 Inversions
    2.4 Translocations

1. Variations in chromosome number

TABLE 8.1 **Terminology for Variation in Chromosome Numbers**

Term	Explanation
Aneuploidy	$2n \pm x$ chromosomes
Monosomy	$2n - 1$
Disomy	$2n$
Trisomy	$2n + 1$
Tetrasomy, pentasomy, etc.	$2n + 2$, $2n + 3$, etc.
Euploidy	Multiples of n
Diploidy	$2n$
Polyploidy	$3n$, $4n$, $5n$, . . .
Triploidy	$3n$
Tetraploidy, pentaploidy, etc.	$4n$, $5n$, etc.
Autopolyploidy	Multiples of the same genome
Allopolyploidy (amphidiploidy)	Multiples of closely related genomes

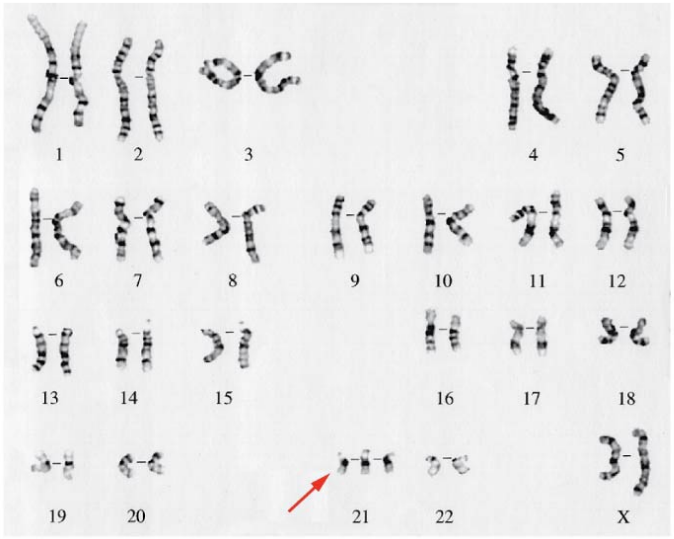
Monosomy

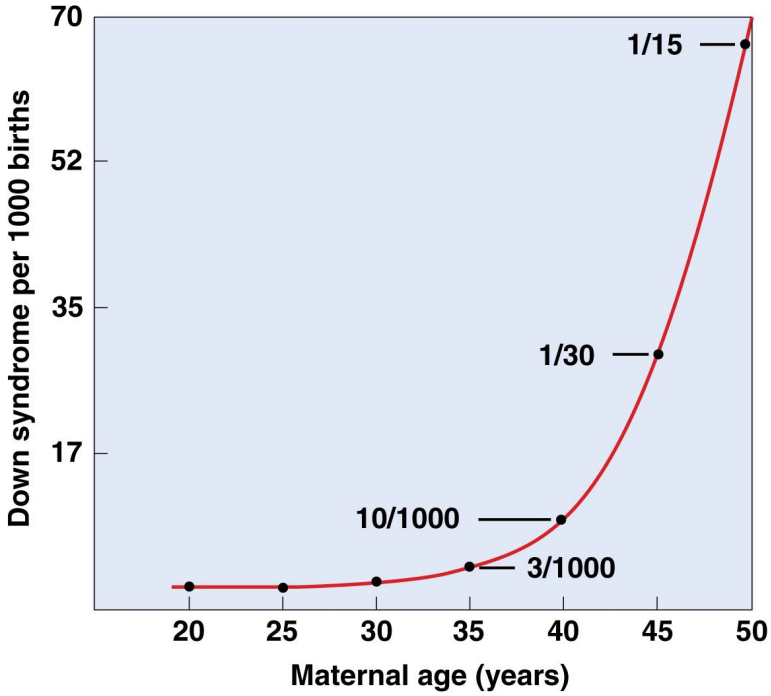
- $2n - 1$ chromosomes
- Unmasks recessive lethal alleles leading to **haploinsuffiency** (i.e. one copy is not sufficient for survival)
- Monosomies for autosomes are always lethal

Trisomy

- $2n + 1$ chromosomes
- The addition of a chromosome is slightly less deleterious than the loss of a chromosome ➔ results more often in viable organisms
- Still, most trisomies for autosomes are lethal, and often found in spontaneously aborted fetuses
- Only exceptions in humans:
  - **Down syndrome** (trisomy 21; ~1 in 1,000 birth)
  - **Edwards syndrome** (trisomy 18; ~1 in 5,000 birth)
  - **Patau syndrome** (trisomy 13; ~1 in 10,000 birth)
  - **Triple X syndrome** (trisomy X; ~1 in 1,000 birth)

Trisomy 21 – Down syndrome





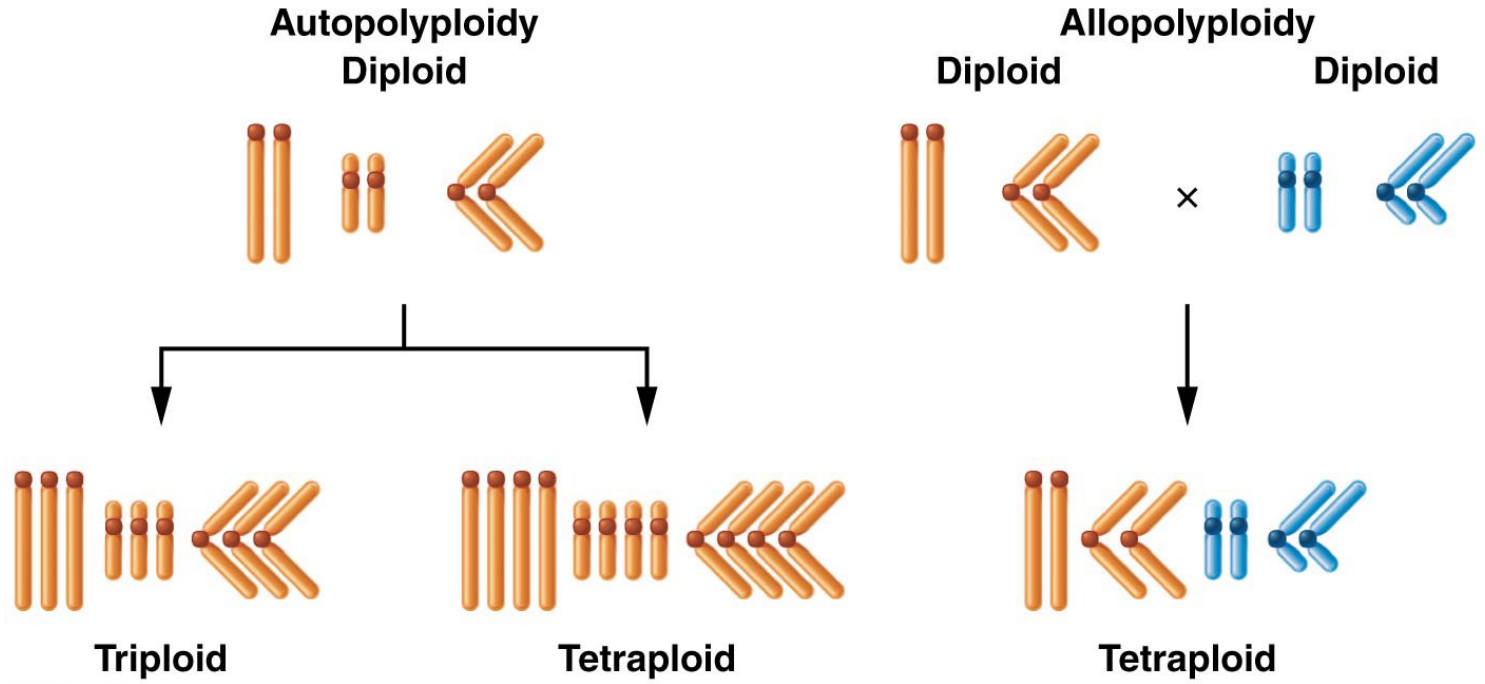
- Results from nondisjunction of chromosome 21 during meiosis, or rarely from translocation of chromosome 21 (familial form)
- increased incidence with increasing maternal age

Polyploidy

- More than two multiples of haploid chromosomes found, very prevalent in plants
  - **Triploid** - 3*n* chromosomes
  - **Tetraploid** - 4*n* chromosomes
  - **Pentaploid** - 5*n* chromosomes
  - Etc.

Origin of polyploidy

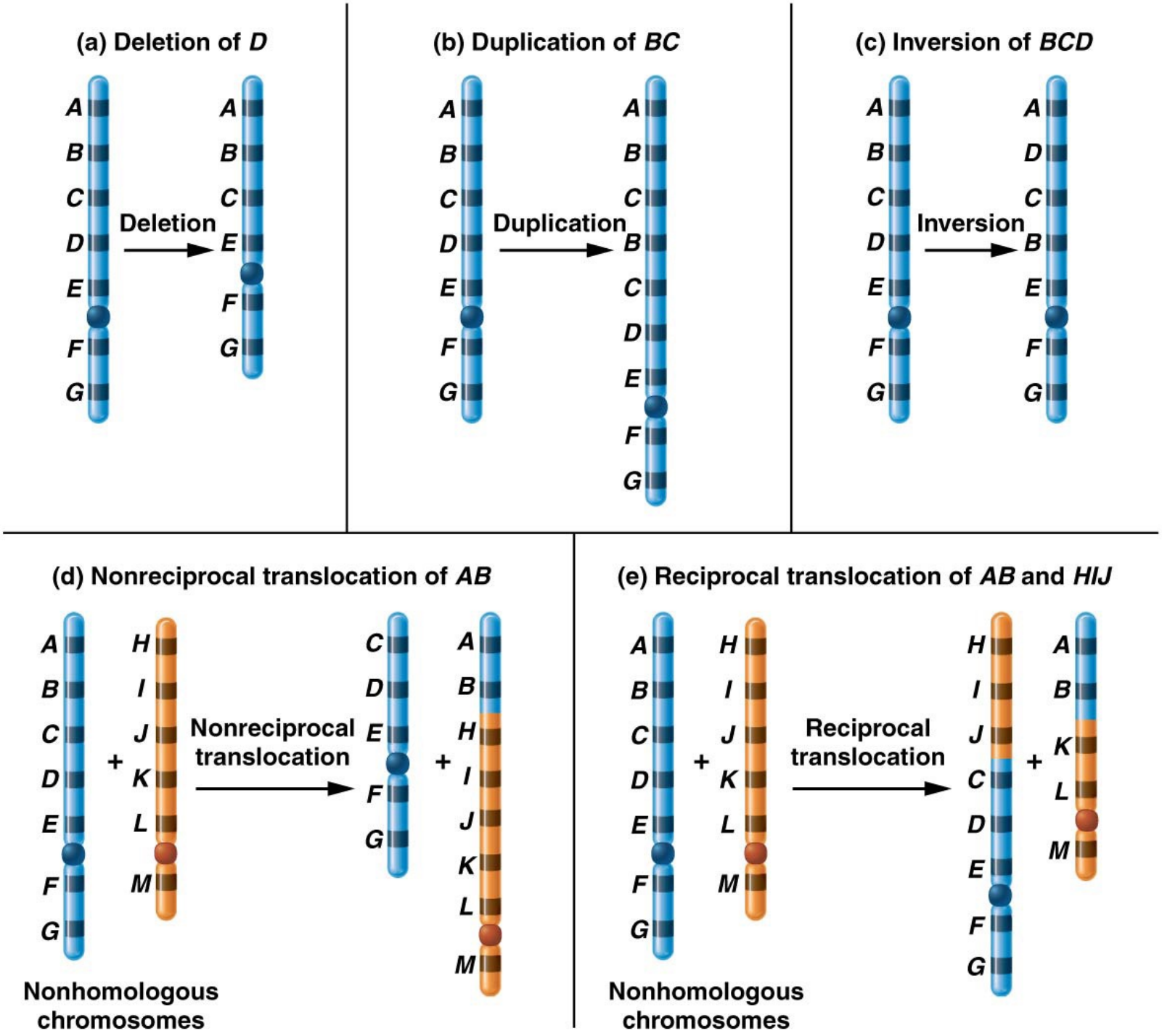
- Addition of one or more sets of chromosomes identical to haploid complement of same species (**autopolyploidy**)
- Combination of chromosome sets from different species as consequence of hybridization (**allopolyploidy**)



2. Variation in chromosome structure or content

Alterations of chromosomes

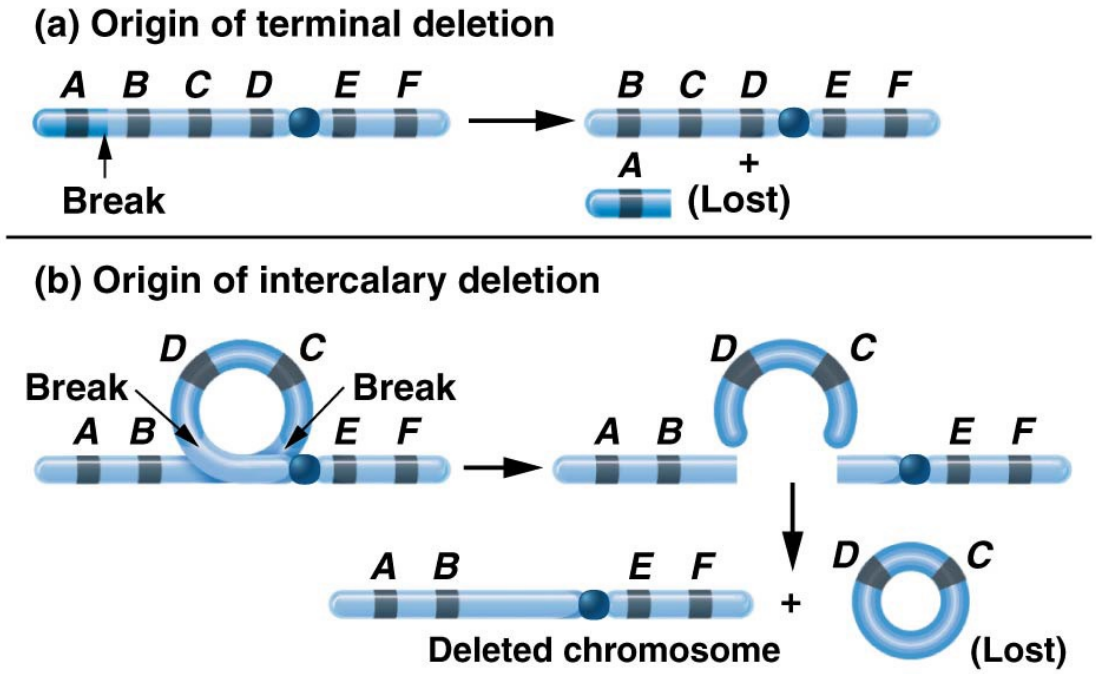
- **Deletions and duplications**
  - Total amount of genetic information in chromosome changes
- **Inversions and translocations**
  - Genetic material remains the same but rearranged


(a) Deletion of D
A
B
C
D
E
F
G
Deletion
A
B
C
E
F
G
(b) Duplication of BC
A
B
C
D
E
F
G
Duplication
A
B
C
B
C
D
E
F
G
(c) Inversion of BCD
A
B
C
D
E
F
G
Inversion
A
D
C
B
E
F
G
(d) Nonreciprocal translocation of AB
A
B
C
D
E
F
G
+
H
I
J
K
L
M
Nonreciprocal translocation
C
D
E
F
G
+
A
B
H
I
J
K
L
M
Nonhomologous chromosomes
(e) Reciprocal translocation of AB and HIJ
A
B
C
D
E
F
G
+
H
I
J
K
L
M
Reciprocal translocation
H
I
J
C
D
E
F
G
+
A
B
K
L
M
Nonhomologous chromosomes

2.1 Deletions

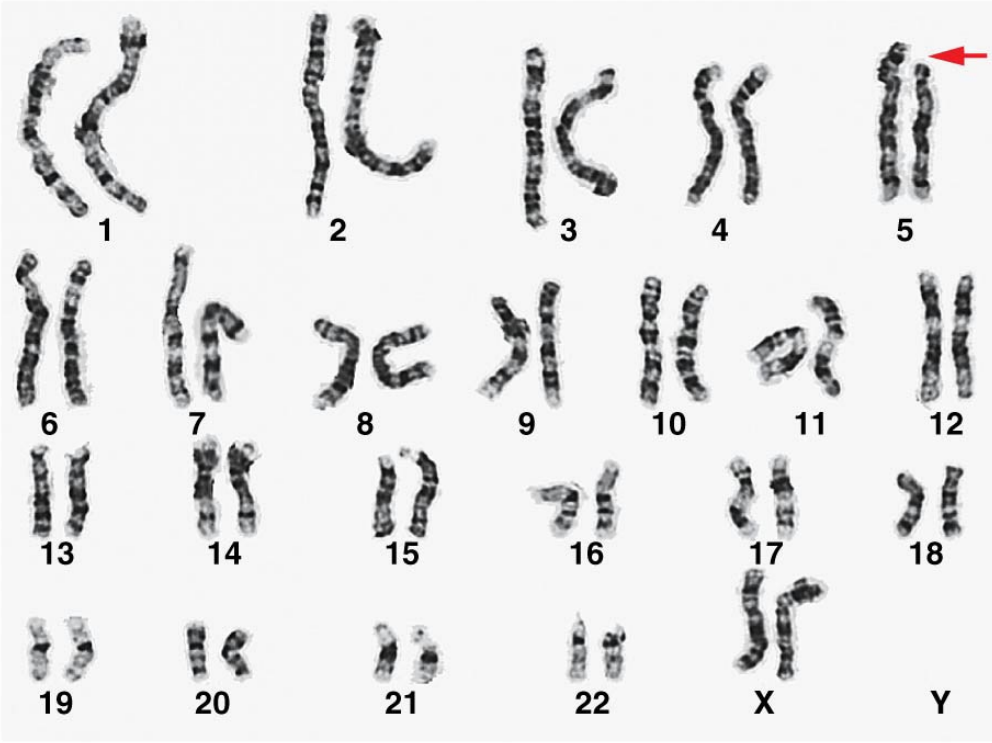
Deletions

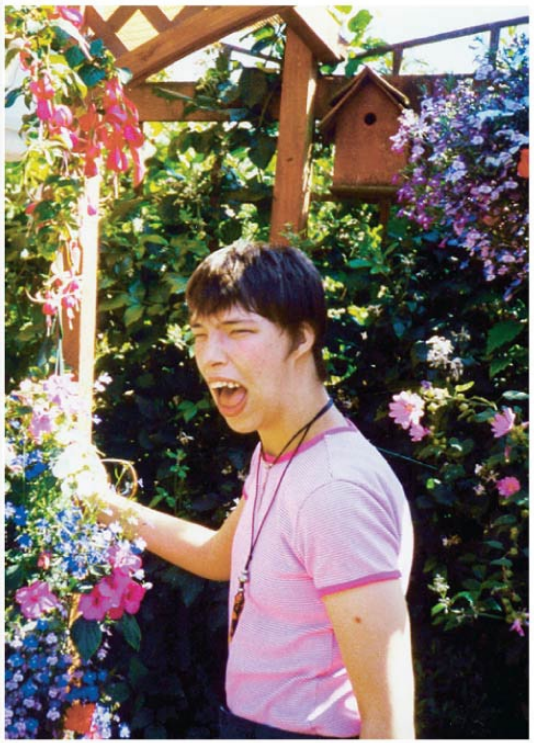
- Missing regions of chromosome, due to **chromosome breaks** in one or more places
- Two types, depending on localization:
  - **Terminal** deletion (near a telomere)
  - **Intercalary** deletion (inside a chromosome)



Example of disease due to terminal deletion

- **Cri-du-chat syndrome**
  - Deletion of a segment in the small terminal portion of chromosome 5
  - 1/50’000 live births
  - Specific cry, cognitive impairment, anatomical malformations

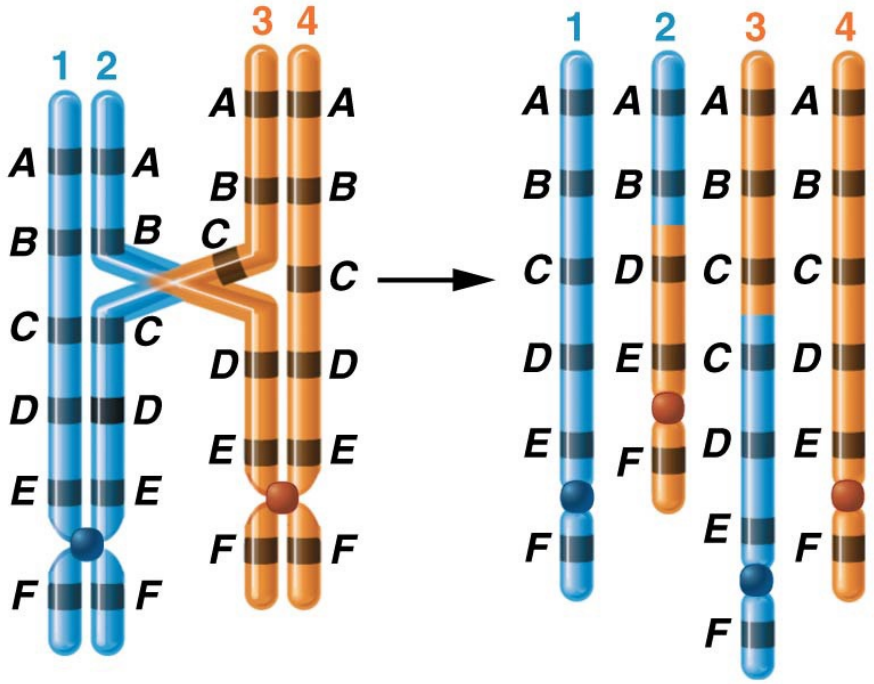




2.2 Duplications

Duplications

- Repeated segment of a chromosome ➔ a single locus is present more than once in genome
- Arise from **unequal crossing over** between synapsed chromosomes during meiosis



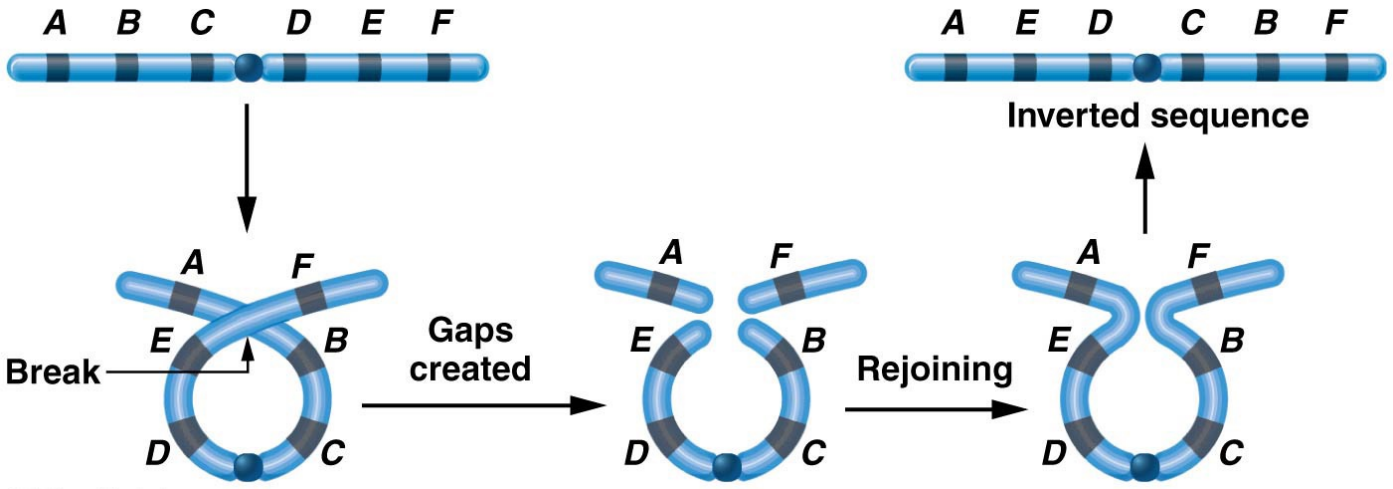
Duplications

- **Gene duplications and evolution**
  - Major source of new genes
  - Hypothesis supported by discovery of genes with substantial amount of DNA sequence in common, but distinct gene products

2.3 Inversions

Inversion

- Rearrangement of linear gene sequence: segment of chromosome turned 180° within chromosome
- No loss of genetic information
- Requires two breaks in chromosome, followed by reinsertion of the inverted segment
- May result from chromosomal looping



Types of inversions

- **Paracentric inversion**
  - Does not change lengths of two arms of chromosome
  - Centromere not part of inverted segment
- **Pericentric inversion**
  - Centromere is part of inverted segment
  - Does change lengths of two arms of chromosome

2.4 Translocations

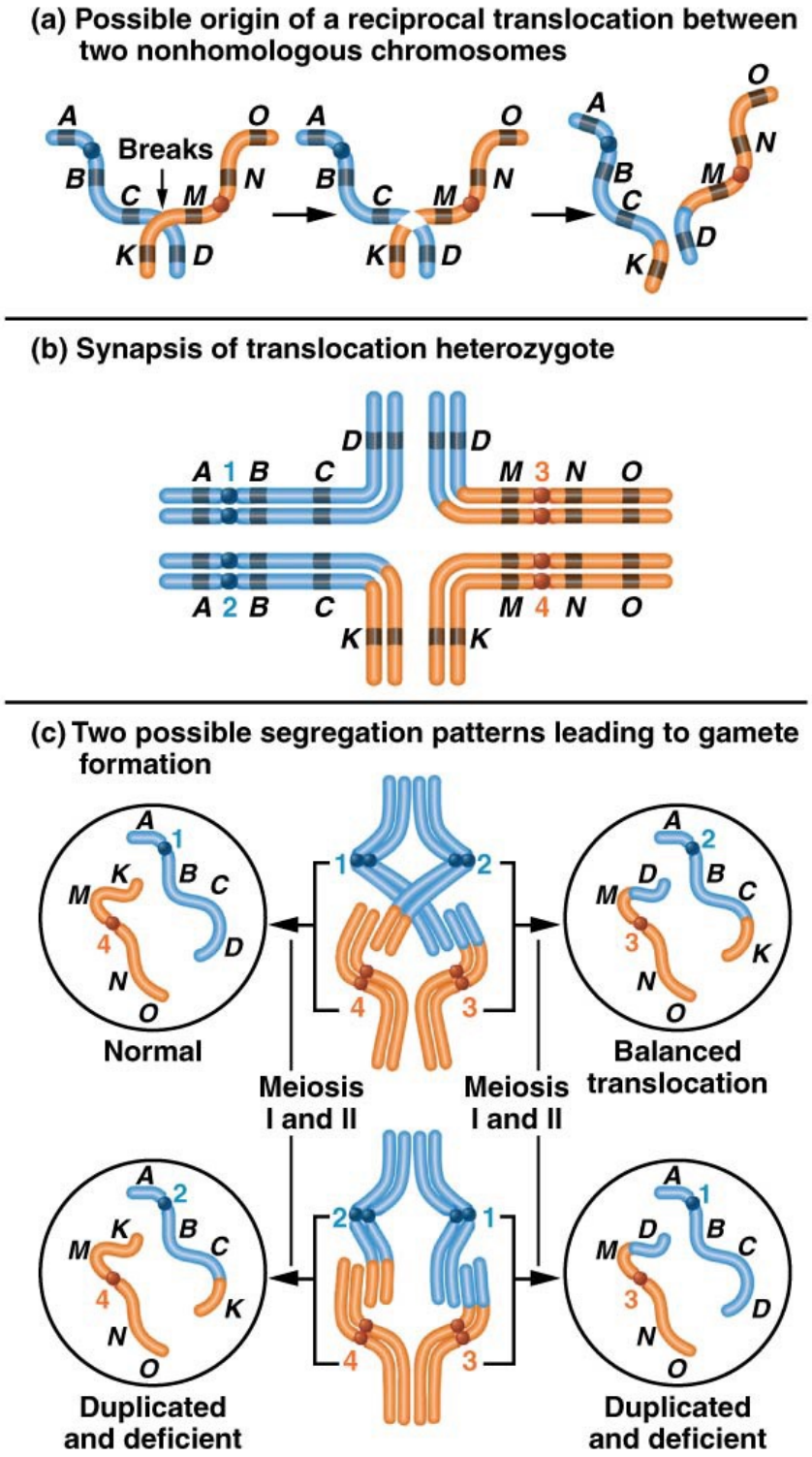
Translocations

- Movement of chromosomal segment to new location in genome
  - **Non-reciprocal** translocation
  - **Reciprocal** translocation
- No loss of genetic information
- Problems during gamete formation

Reciprocal translocations

- Exchange of segments between 2 nonhomologous chromosomes
- Leads to unusual synapsis configuration during meiosis

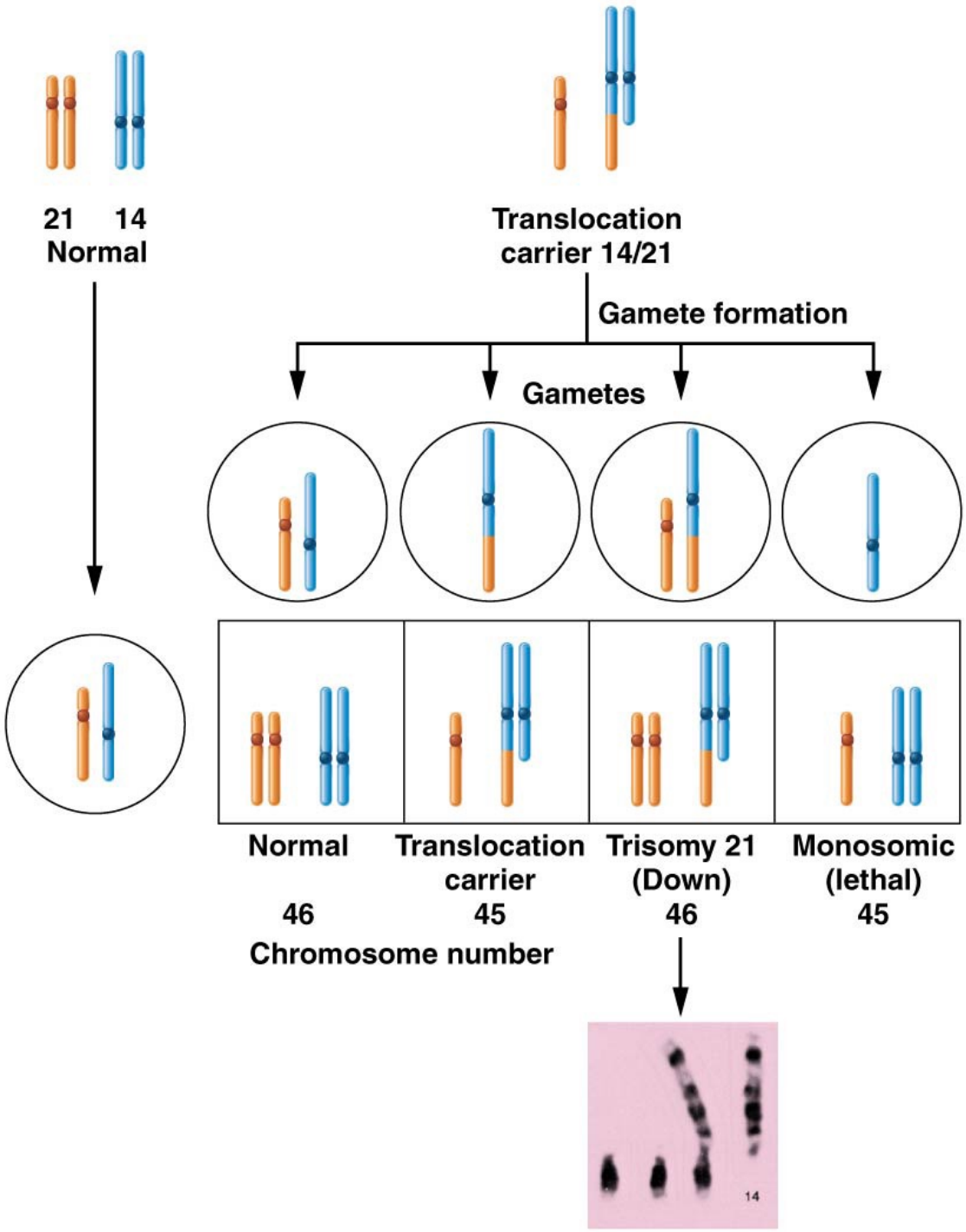
- Segregation patterns at 1st meiotic division:
  - **Alternate segregation**
    - Has complete set of genetic information
  - **Adjacent segregation**
    - Leads to gametes containing duplications and deficiencies



Robertsonian translocation

- Involves breaks at extreme ends of the short arms of two nonhomologous acrocentric chromosomes
- Small segments are lost
- A large “fusion” chromosome is created (Robertsonian translocations are also called “centric fusions”)

- Example: Familial Down syndrome


21 14
Normal
Translocation carrier 14/21
Gamete formation
Gametes
Normal
Translocation carrier
Trisomy 21 (Down)
Monosomic (lethal)
46
45
46
45
Chromosome number
14