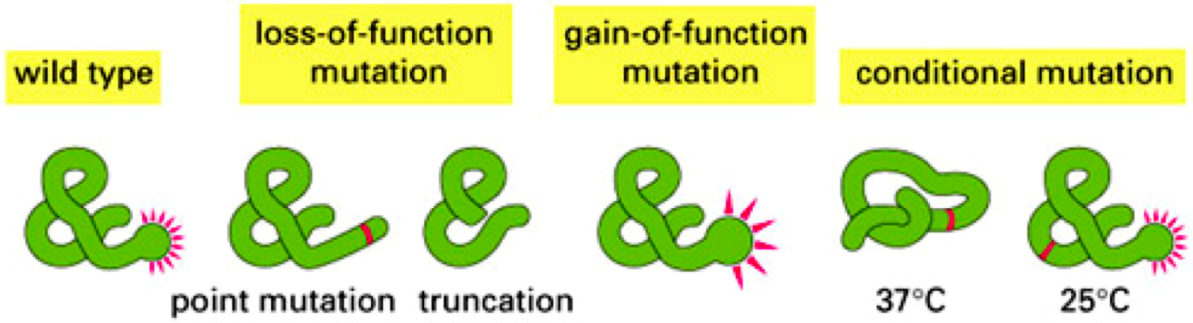
Mutations: molecular basis of alleles

- different alleles (varieties of a gene): due to slight differences in DNA sequence

- types of mutations:
→ **loss-of-function**: mutation blocks or impairs function of protein
→ **gain-of-function**: mutation adds some new function, or "over-function"
→ **conditional mutation**: effect (loss or gain) only under certain conditions

- all mutations can be either disadvantageous or advantageous for survival in changing environment (evolution by selection)



Examples of how mutations can generate recessive vs. dominant phenotypes

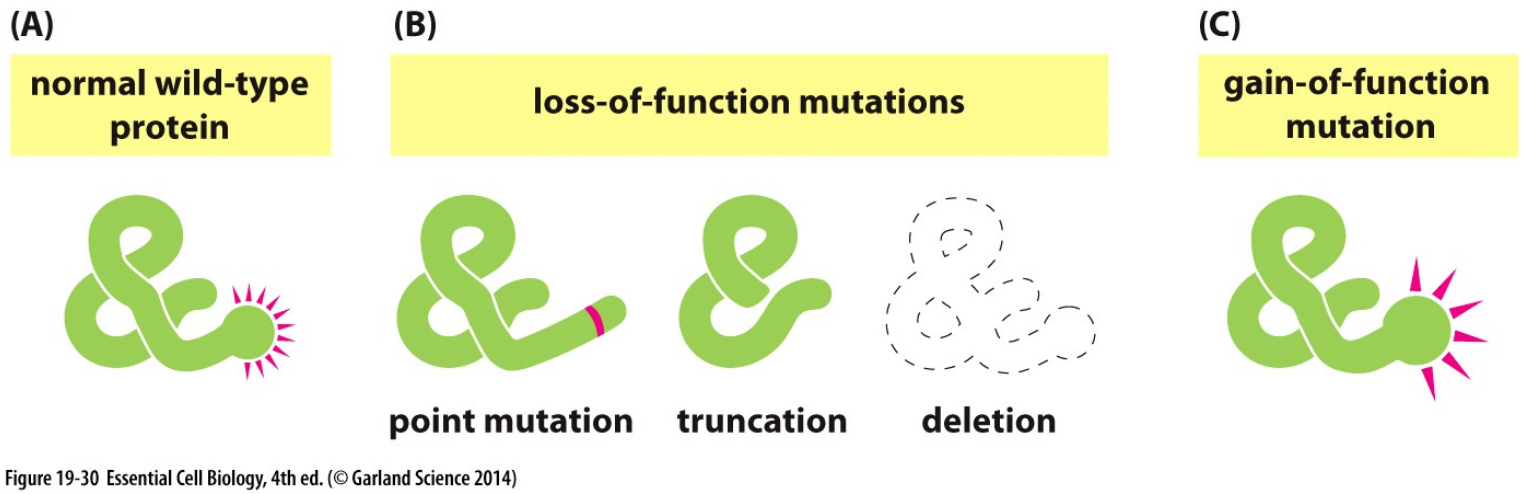


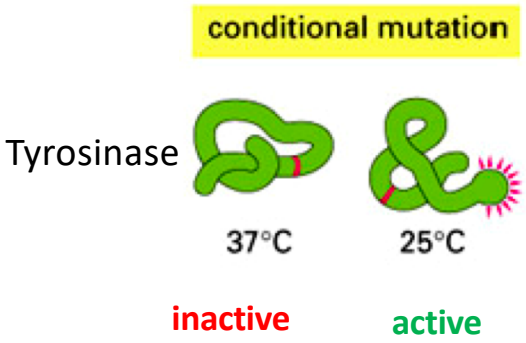
Figure 19-30 Essential Cell Biology, 4th ed. (© Garland Science 2014)

Phenotype resulting from the mutation :

usually recessive

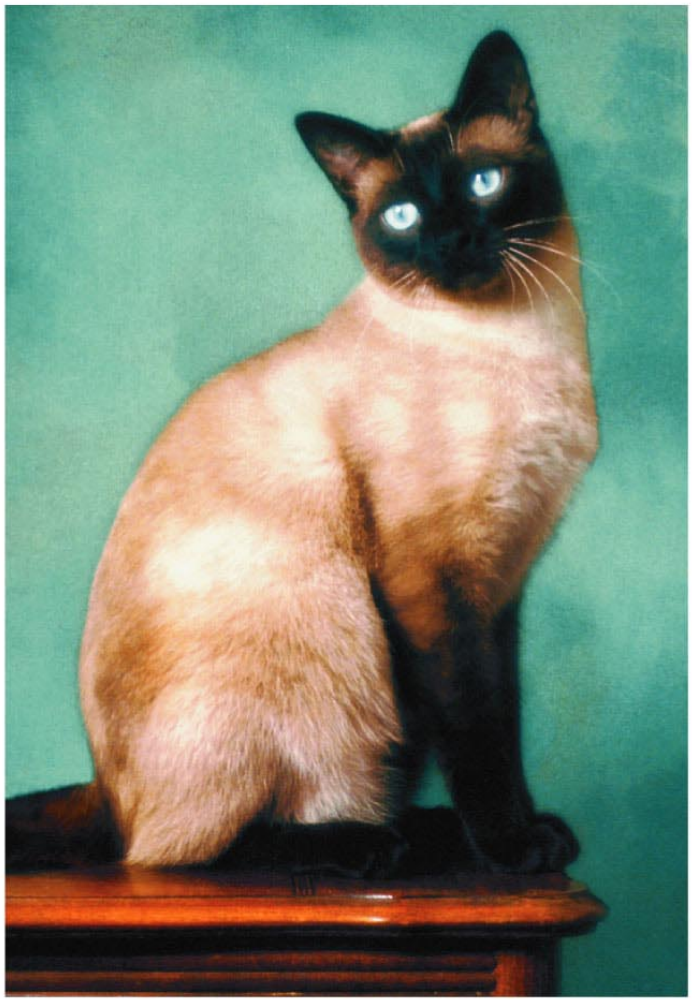
usually dominant

The same gene can be affected by a loss-of-function or a gain-of-function mutation.



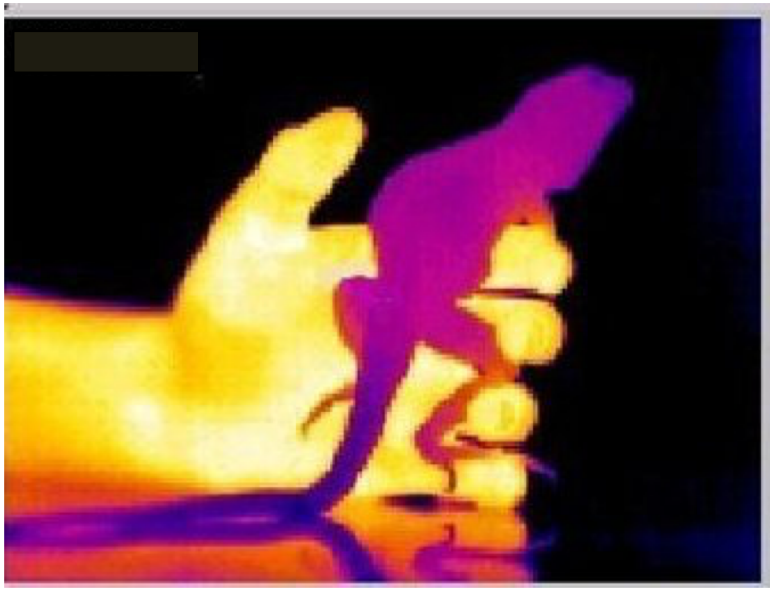
(a) A Himalayan rabbit

(b) A Siamese cat

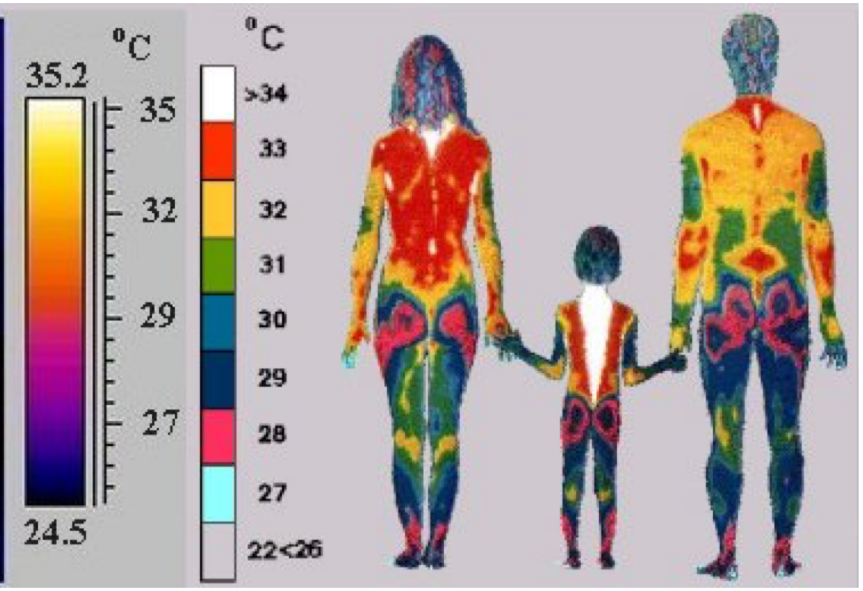


Both show dark fur color on the snout, ears, and paws. These patches are due to the effect of a **temperature-sensitive allele** responsible for pigment production.

Infrared thermography



Gecko are “cold blooded” exothermic

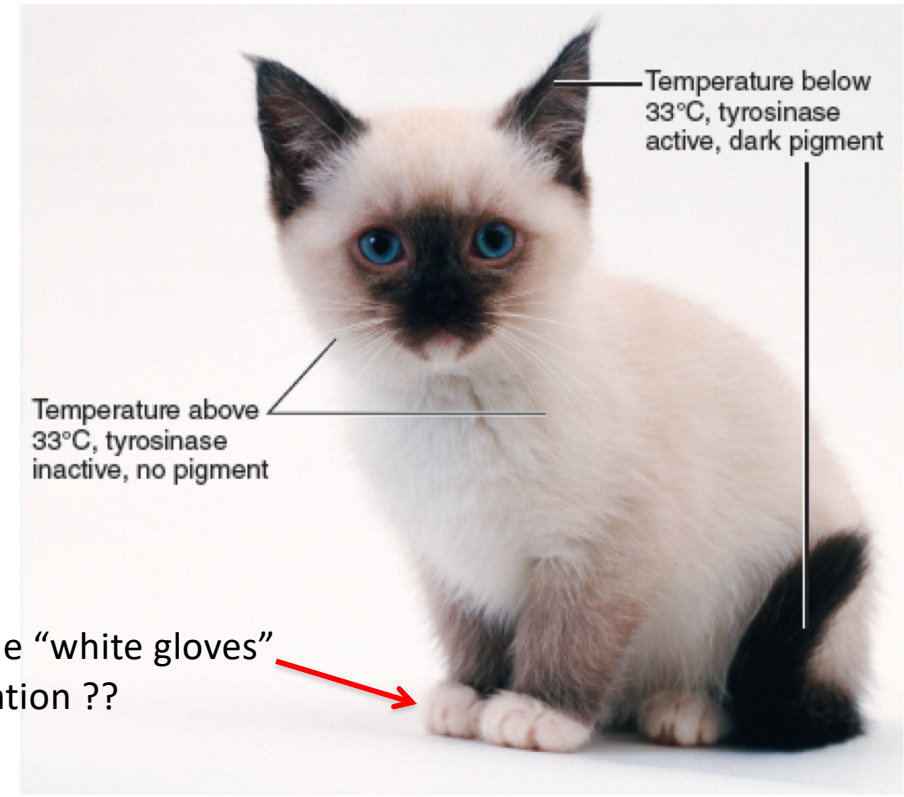


Surface temperature varies

Woman’s fingers : 27 °C

Thermography would show that the dark areas are colder (< 33°C)

The tyrosinase gene of this cat has been sequenced :



Note the “white gloves”
Explanation ??

Figure 12.14 Siamese cat. The pattern of coat color is due to an allele that encodes a temperature-sensitive form of the enzyme tyrosinase.

The pattern distribution is due to a transition mutation from G→A in the 2nd exon of a tyrosinase gene, resulting in replacement of **glycine** by **arginine**.

Point mutation (a deletion cannot be conditional !)

Effect of environment on phenotype :

1. Hydrangea (Hortensias)

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2. Himalayan rabbit

Ice bag

Germ-line cells and somatic cells

- when oocyte and sperm fuse: **zygote** (fertilized egg)
- gametes are produced from diploid precursor cells: **germ-line**
  by a specialized cell division: **meiosis**

Definition of gamete :
cell whose fate is to fuse with another gamete.

Greek gamos = union, marriage

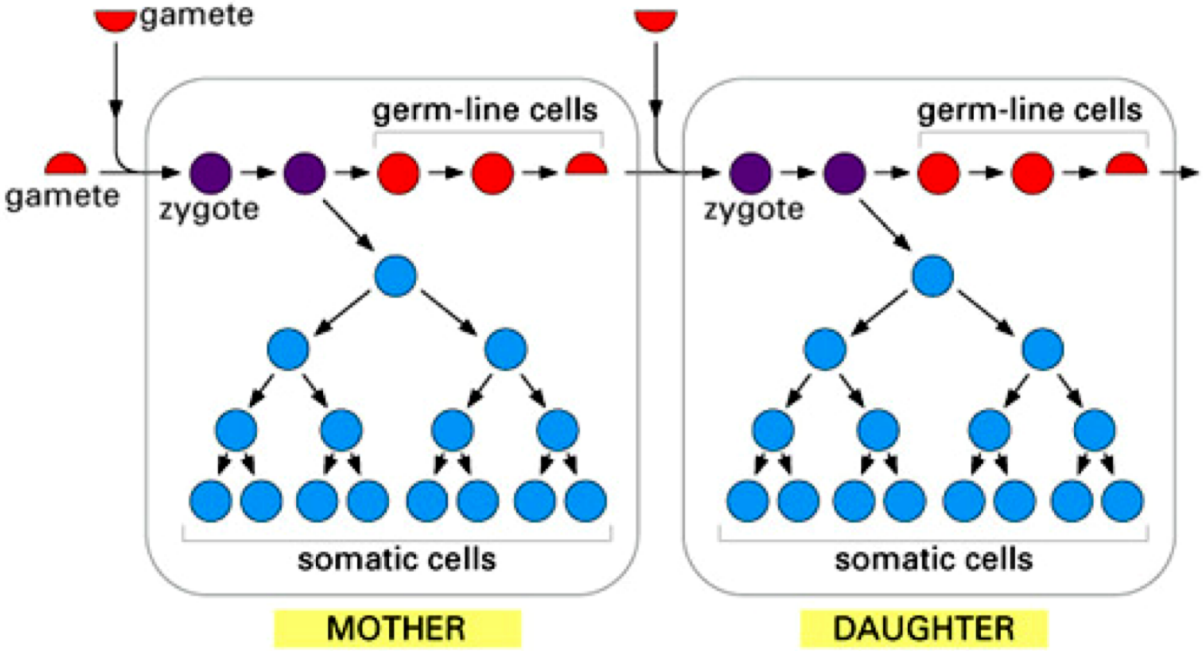


Figure 20-5 Essential Cell Biology, 2/e. (© 2004 Garland Science)

somatic cells vs. germ-line cells

When a mutation occurs
(***de novo*** mutation) :

in a somatic cell → somatic mutation

in a germ-line cell → germ-line mutation

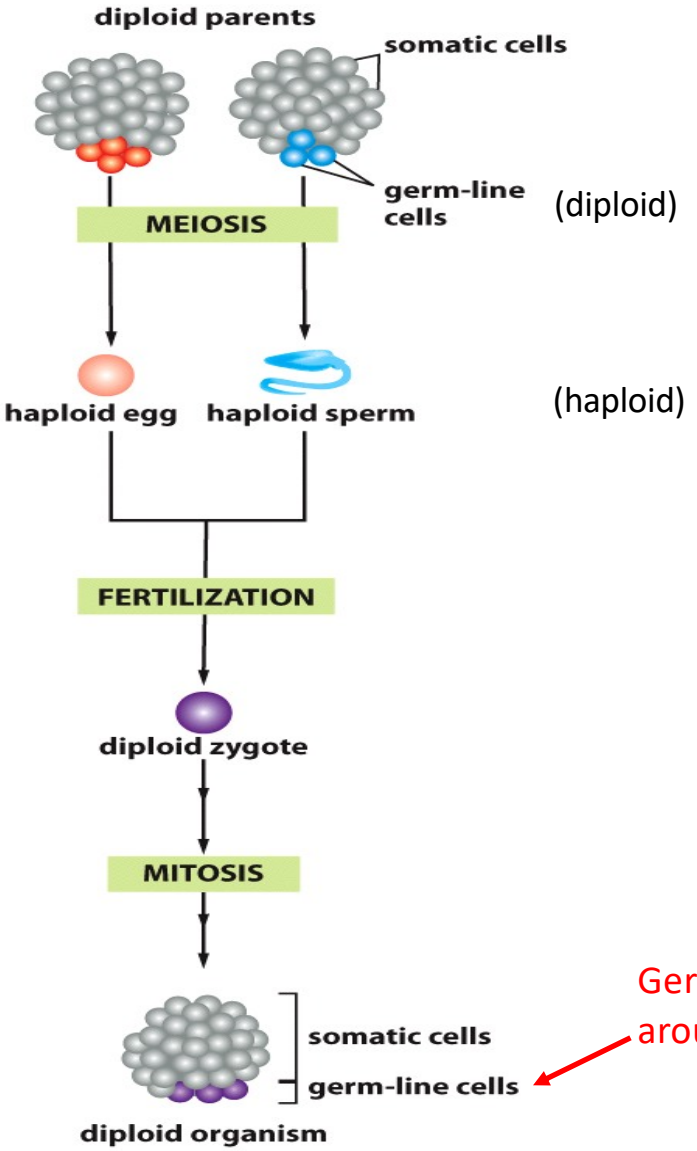


Figure 19-5 Essential Cell Biology, 4th ed. (© Garland Science 2014)

Most multicellular organisms reproduce sexually.

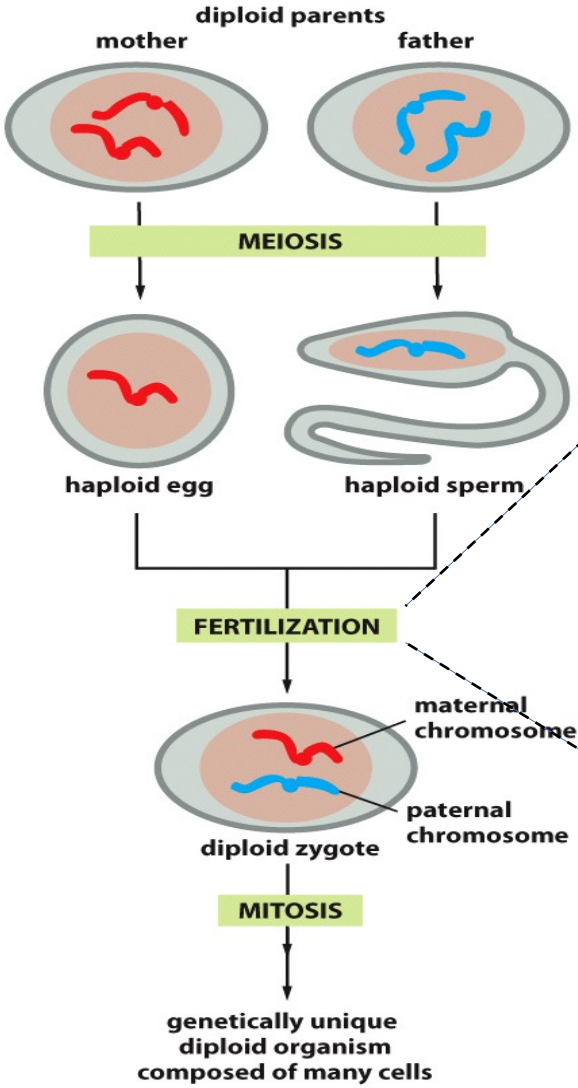
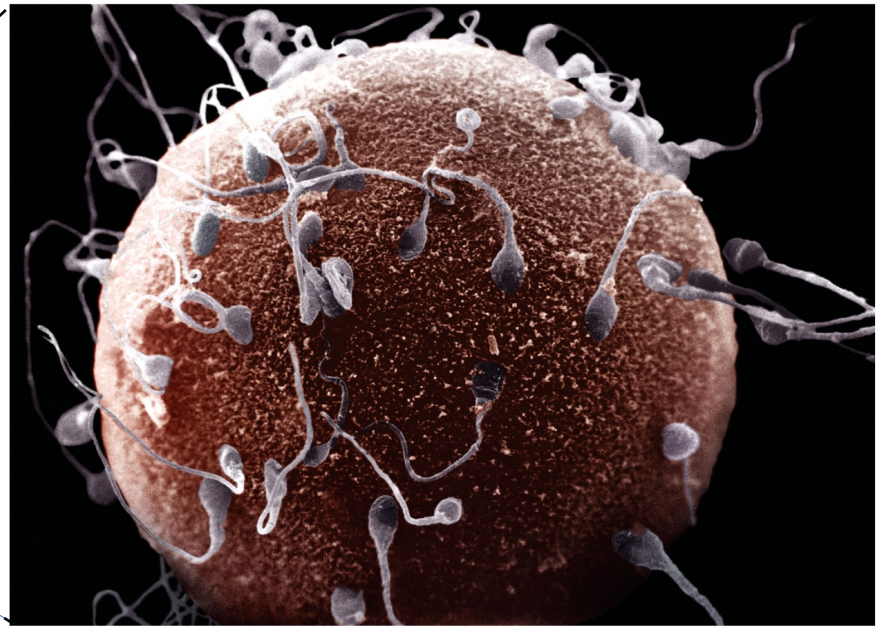


Figure 19-4 Essential Cell Biology, 4th ed. (© Garland Science 2014)



fertilization of egg by sperm

Overview: Meiosis vs. Mitosis

Tutorial 9.2
Tutorial 10.1

unique

In spermatogenesis meiosis I lasts 24 days

Meiosis II is similar to a mitosis

In spermatogenesis meiosis I lasts 24 hours

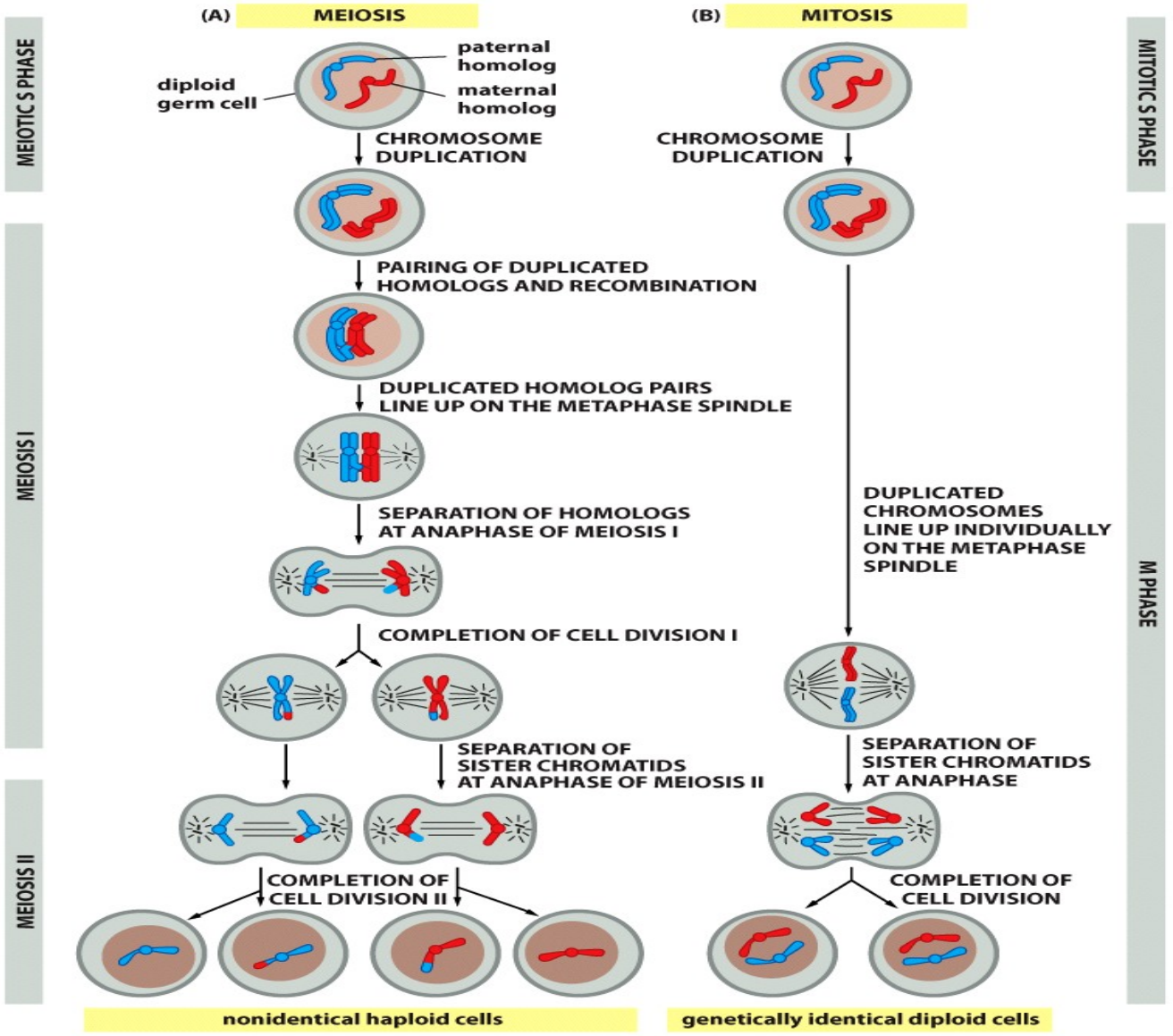


Figure 19-7 Essential Cell Biology, 4th ed. (© Garland Science 2014)

Specificity of meiosis I : pairing of homologous chromosomes

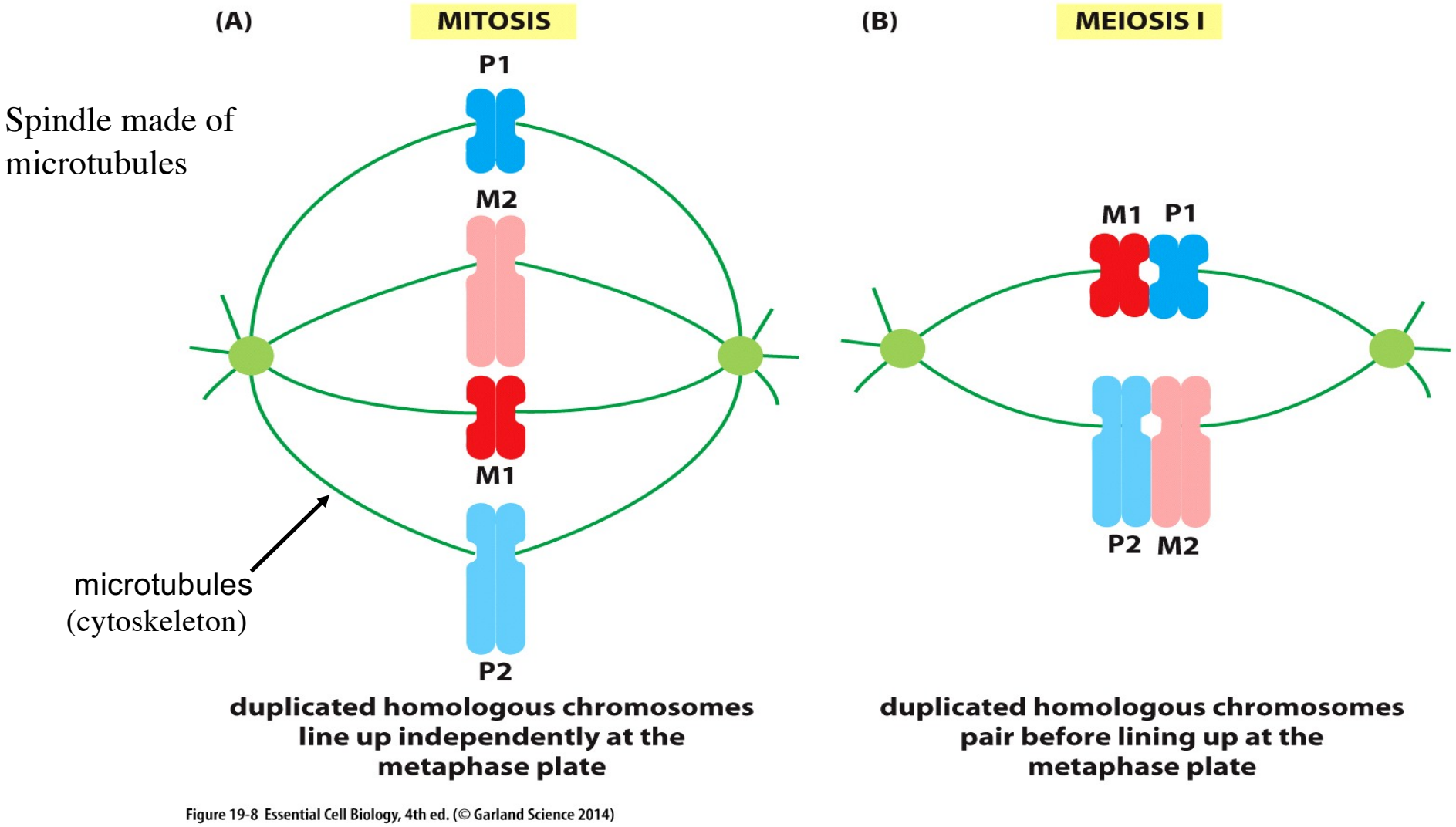
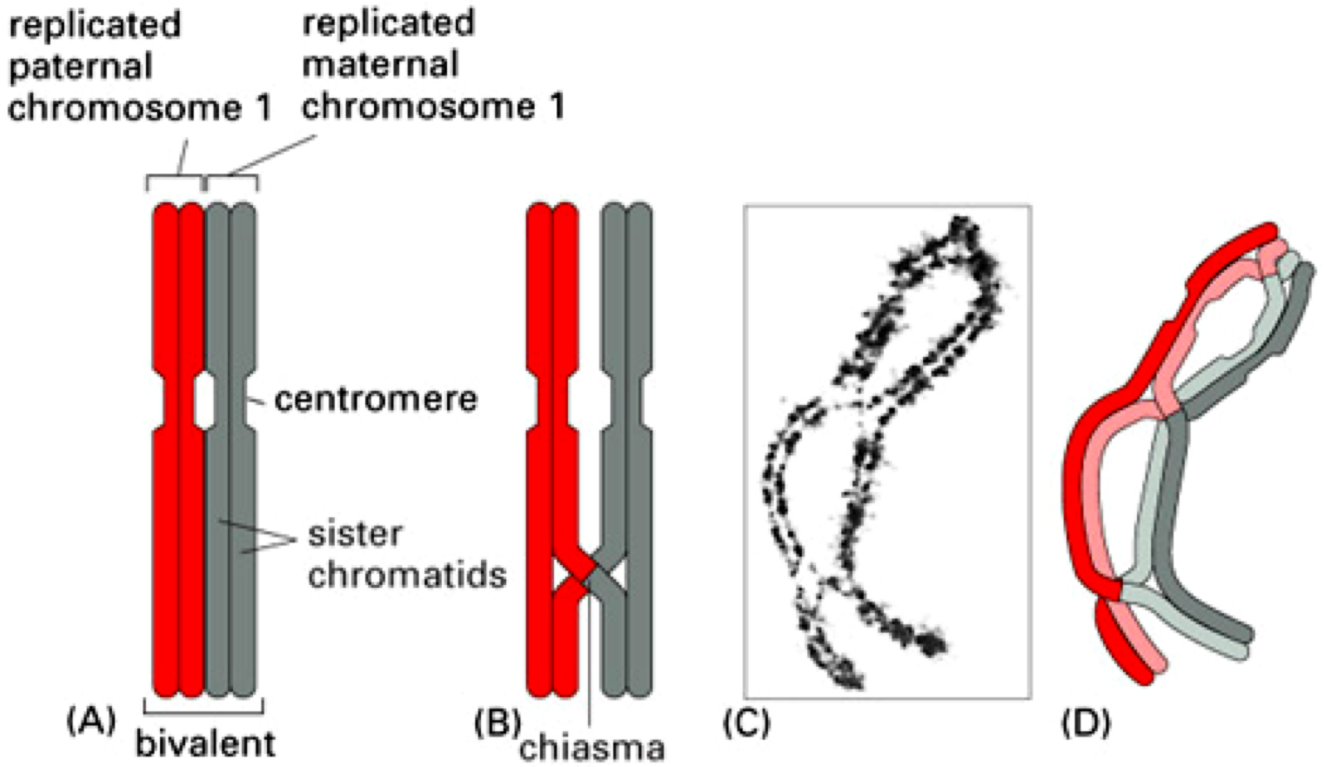


Figure 19-8 Essential Cell Biology, 4th ed. (© Garland Science 2014)

Homologous recombination between paired homologs

Meiosis I



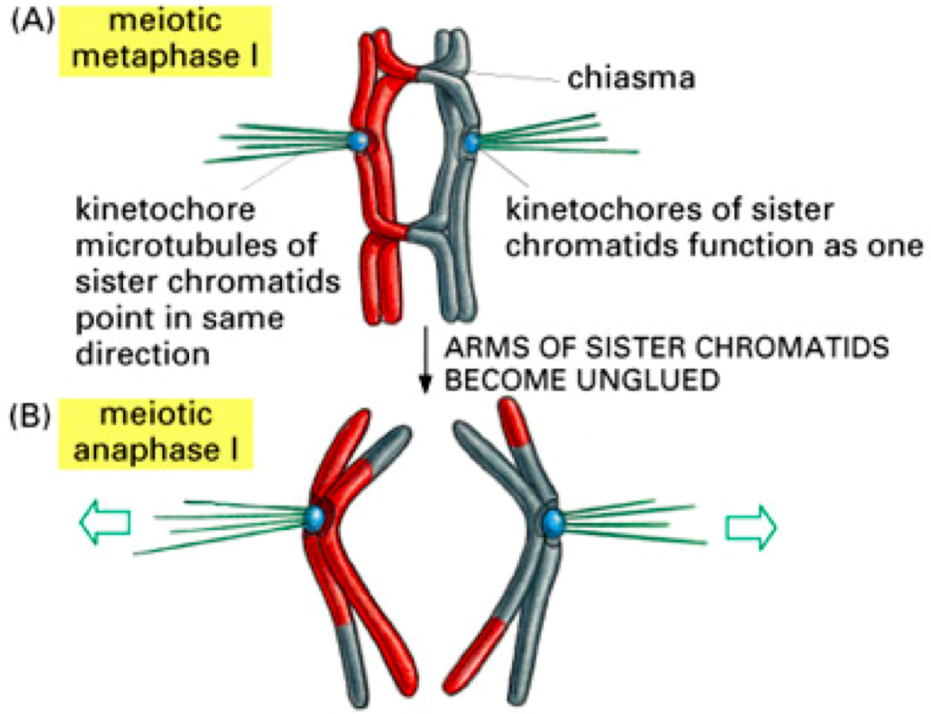
Observation under a microscope

Schematic rendering

Figure 20-7 Essential Cell Biology, 2/e. (© 2004 Garland Science)

Crossing-overs during meiotic division I

1. exchange of parts of chromosome
2. correct positioning for anaphase of division I
   (segregation of maternal and paternal homolog)



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Genetic shuffling

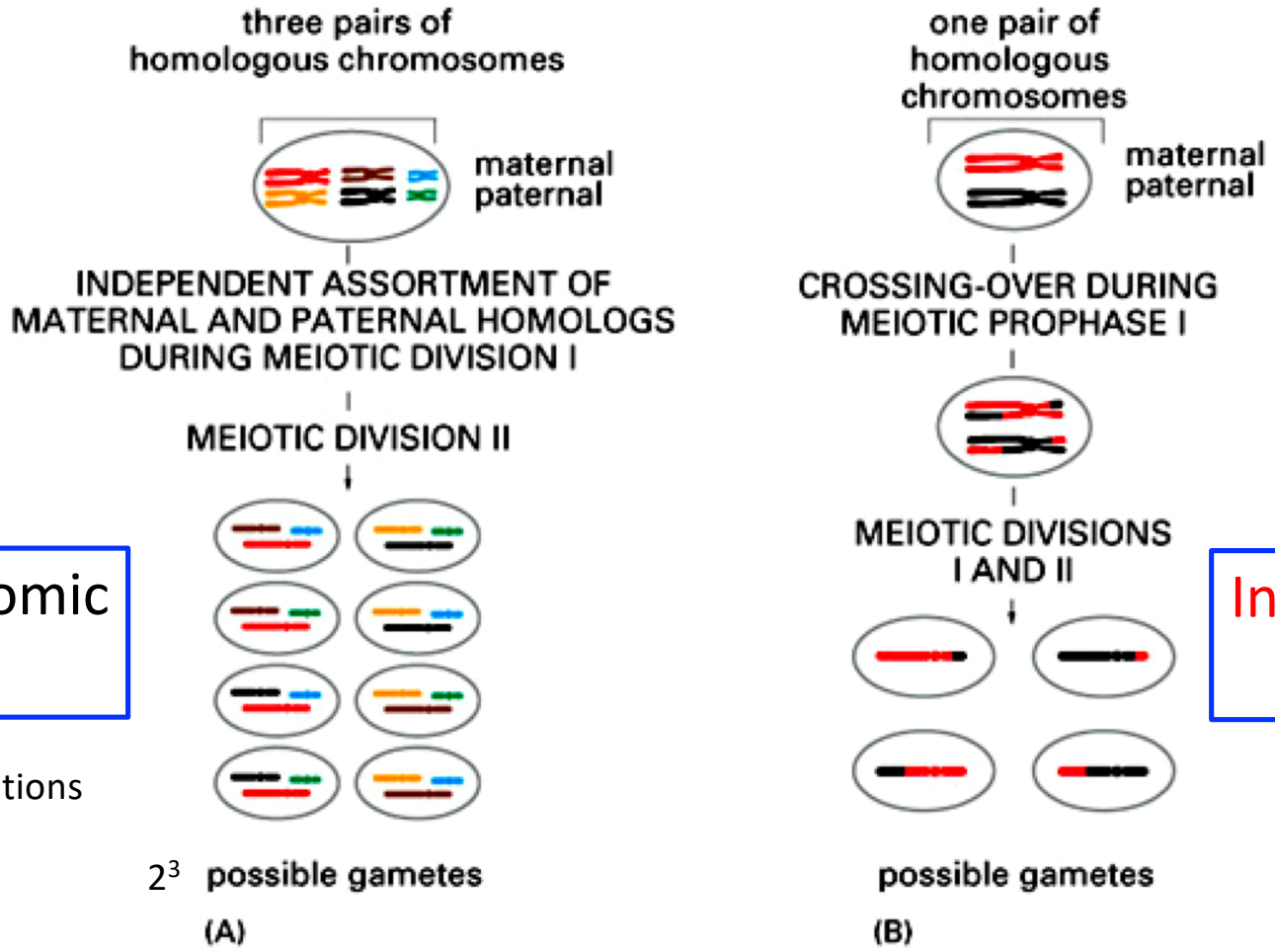


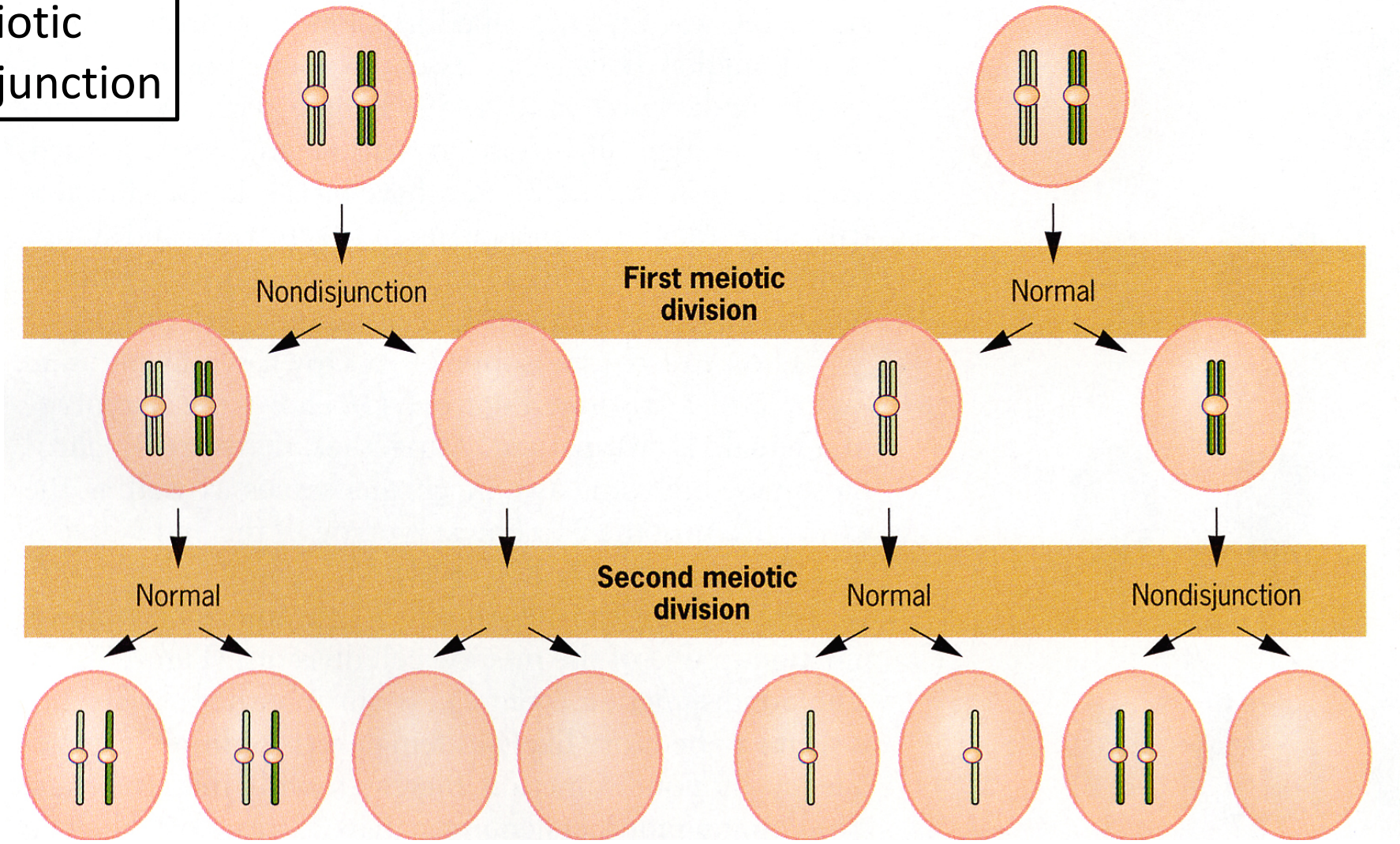
Figure 20-11 Essential Cell Biology, 2/e. (© 2004 Garland Science)

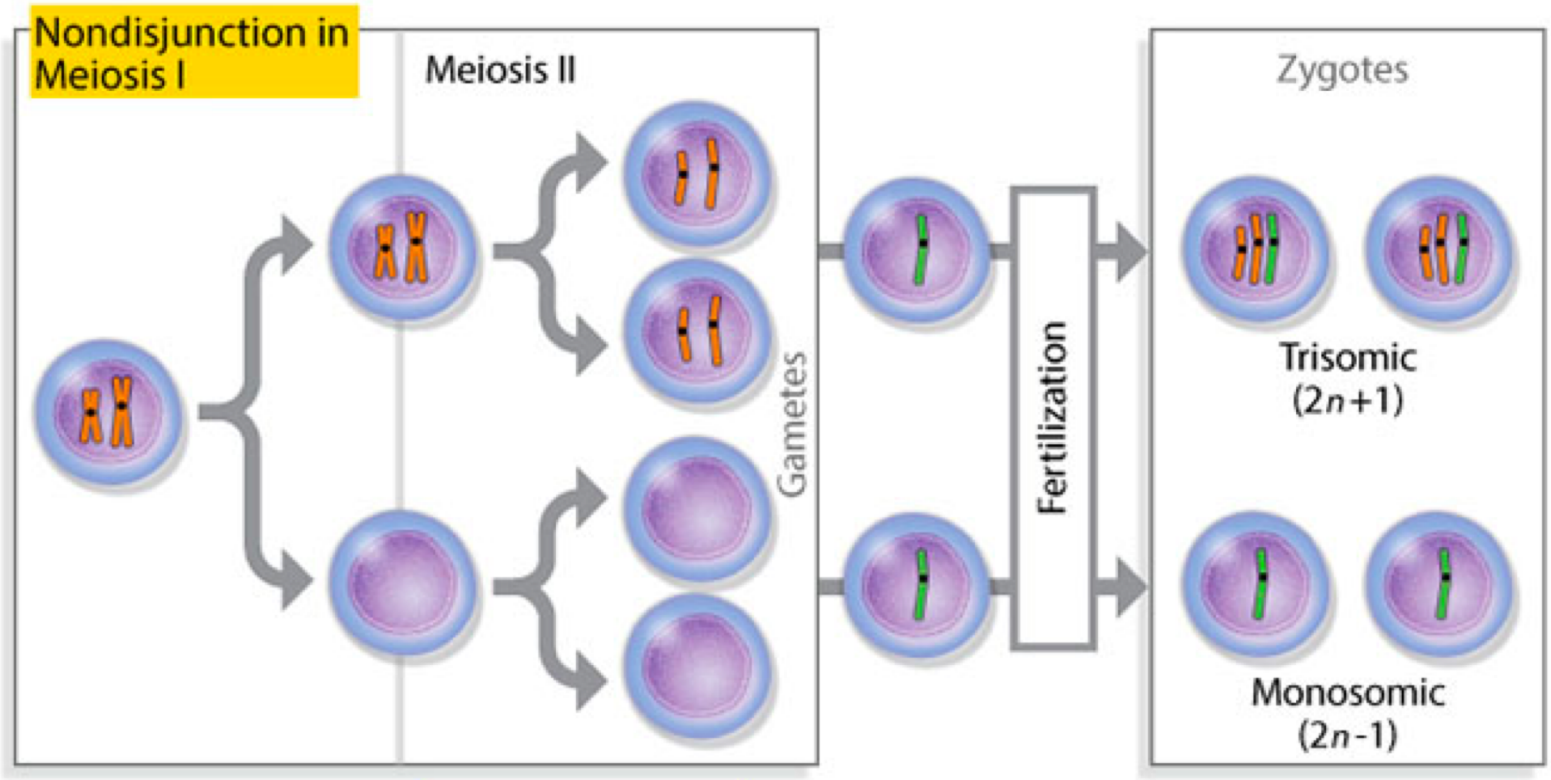
Interchromosomic shuffling

2^{23} different combinations

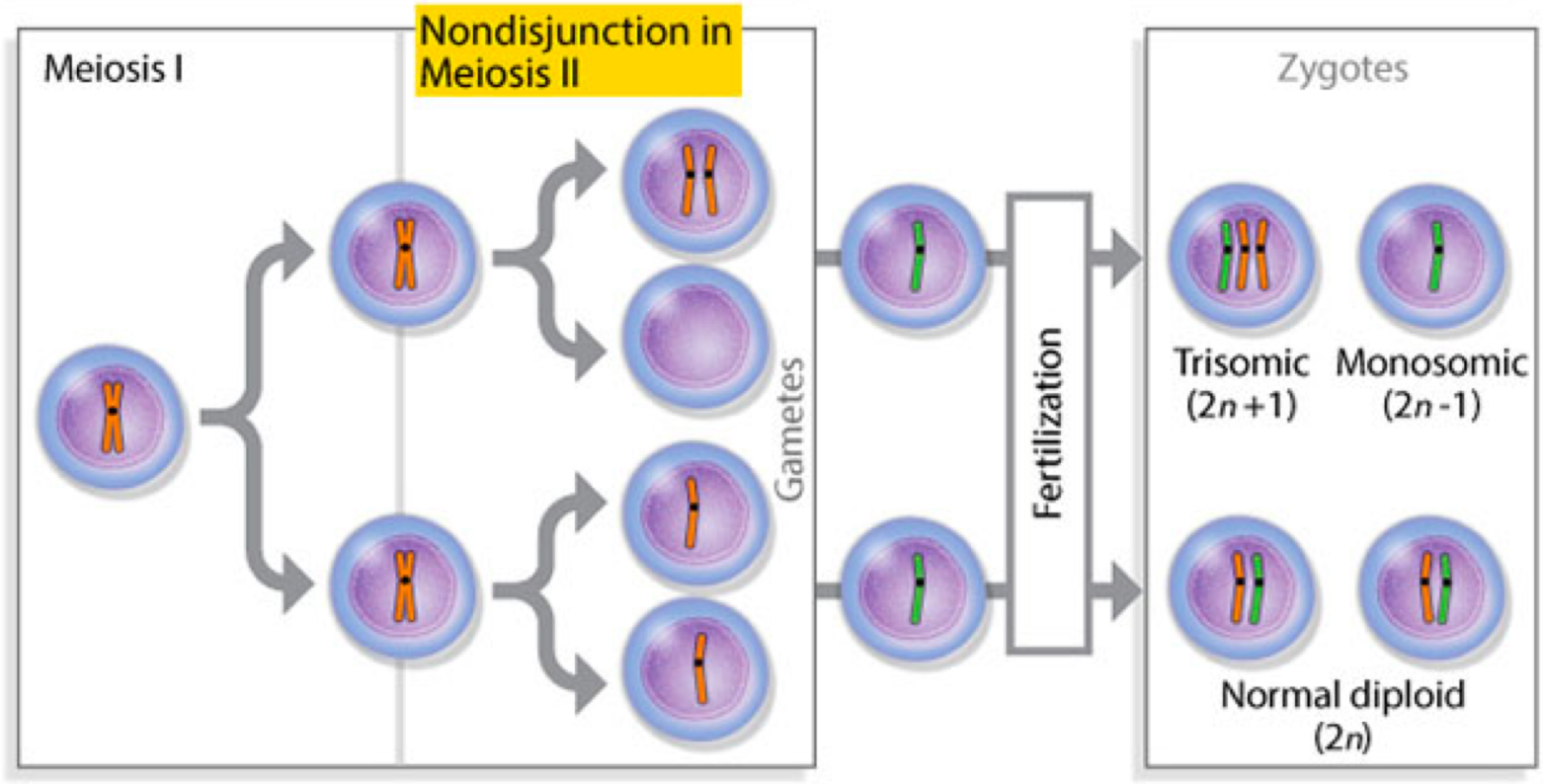
Intrachromosomic shuffling

Meiotic nondisjunction

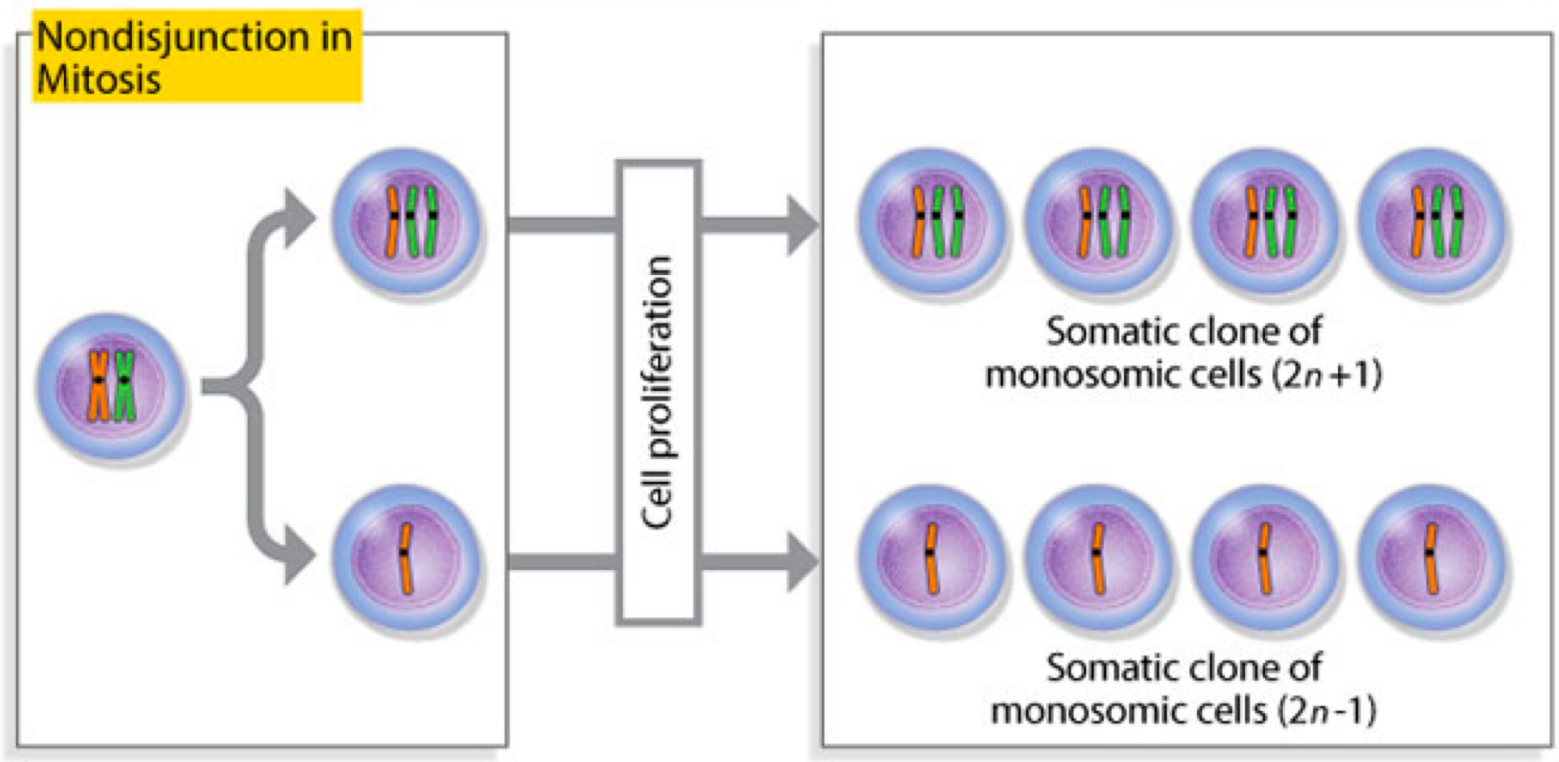




Miko, I. (2008) Mitosis, meiosis, and inheritance. Nature Education 1(1):206



Miko, I. (2008) Mitosis, meiosis, and inheritance. Nature Education 1(1):206



Miko, I. (2008) Mitosis, meiosis, and inheritance. Nature Education 1(1):206

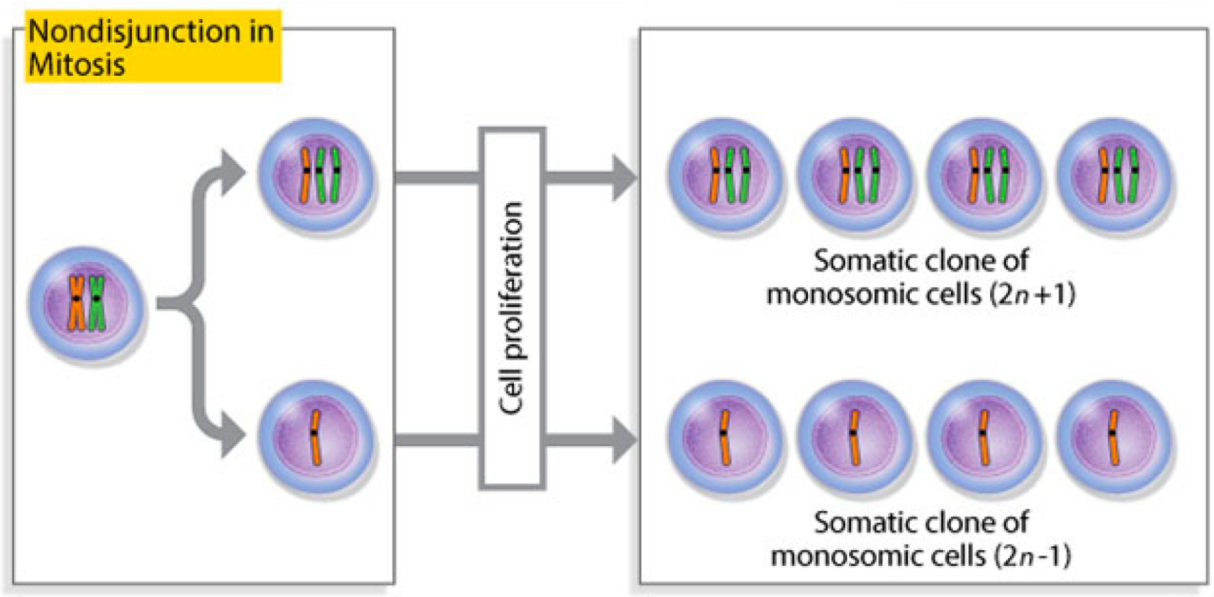
Table 3.4 Parental origin of meiotic error leading to aneuploidy

Chromosome abnormality		Paternal (%)	Maternal (%)
Trisomy 13		15	85
Trisomy 18		10	90
Trisomy 21		5	95
45,X	Turner	80	20
47,XXX		5	95
47,XXY	Klinefelter	45	55
47,XYY		100	0

Frequency of different types of nondisjonction :

Trisomie	Origine (%)				
	Méiotique				Mitotique → mosaic
	Paternelle		Maternelle		
	MI	MII	MI	MII	
15	-	15	76	9	-
16	-	-	100	-	-
18	-	-	33	56	11
21	3	5	65	23	4
XXY	46	-	38	14	2
XXX	-	6	60	16	18

Tableau II. ***Origine des trisomies.*** MI : méiose I ; MII : méiose II (adapté de [5]).



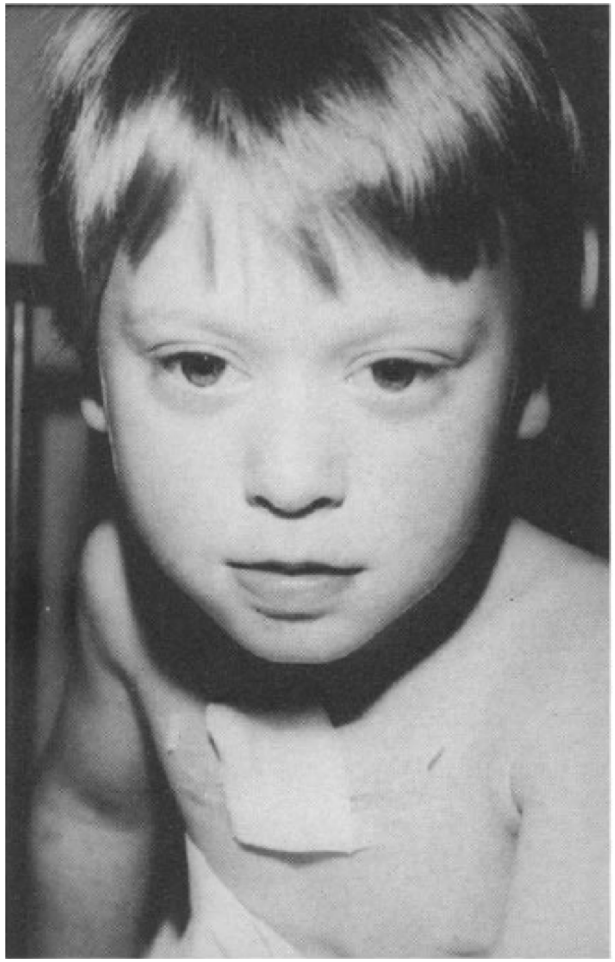
x % of her cells are normal (46, XX)
100-x % of her cells are trisomic (47, XX +21)

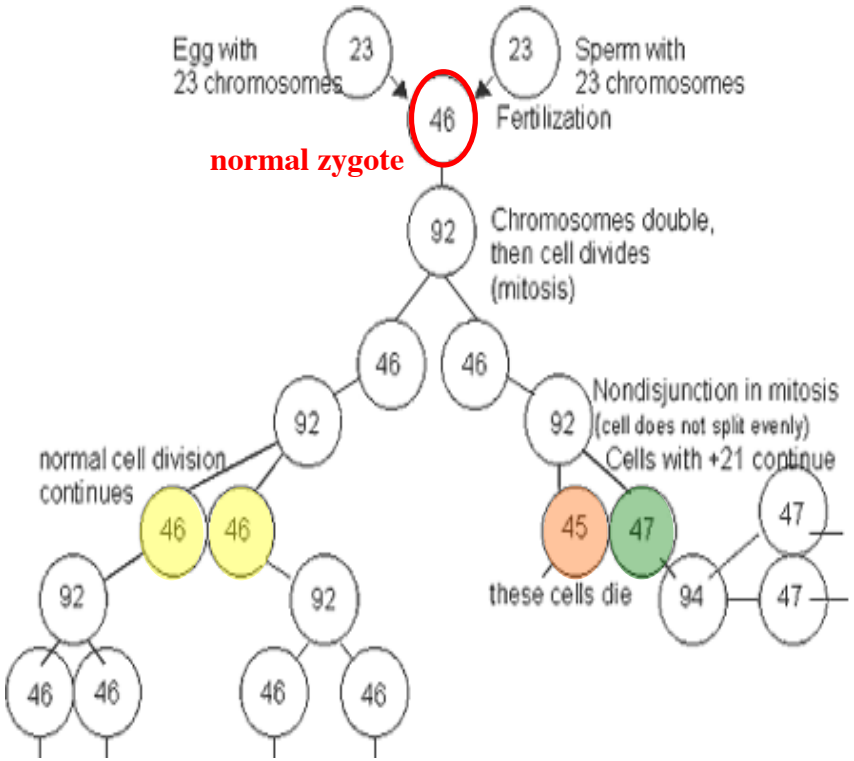
Chromosomal mosaic

46,XY cells

+

47,XY+21cells





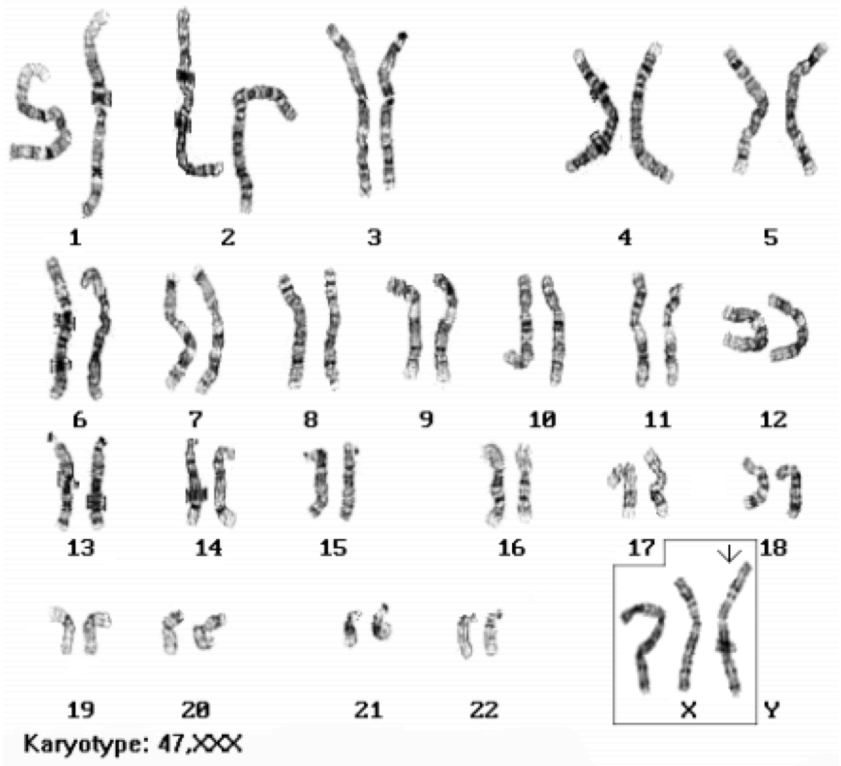
17 ans

Bérénice borne 1991

188 cm

17 ans

Caryotype :



Triple-X woman

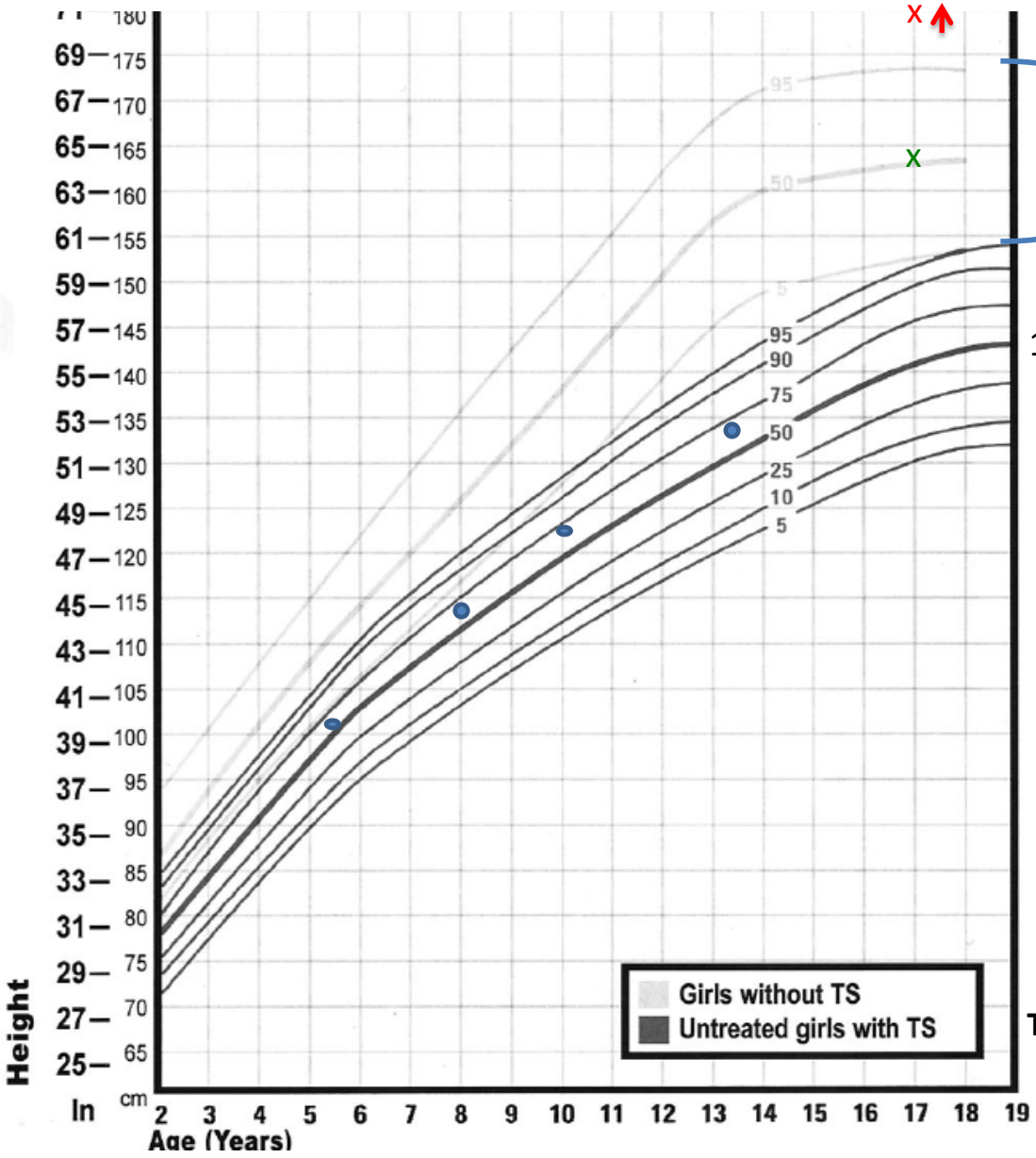
Phenotype :
- tall
- thin

2 X chromosomes are inactivated

95% : mat/mat/ pat

5% : mat/pat/pat

Growth curve



Bérénice
XXX

Normal
XX

160 cm

144 cm XO

Turner Syndrome

Importance of chromosomal dosage.

Linda HUNT (actress)

Syndrome de Turner

45, X0

145 cm

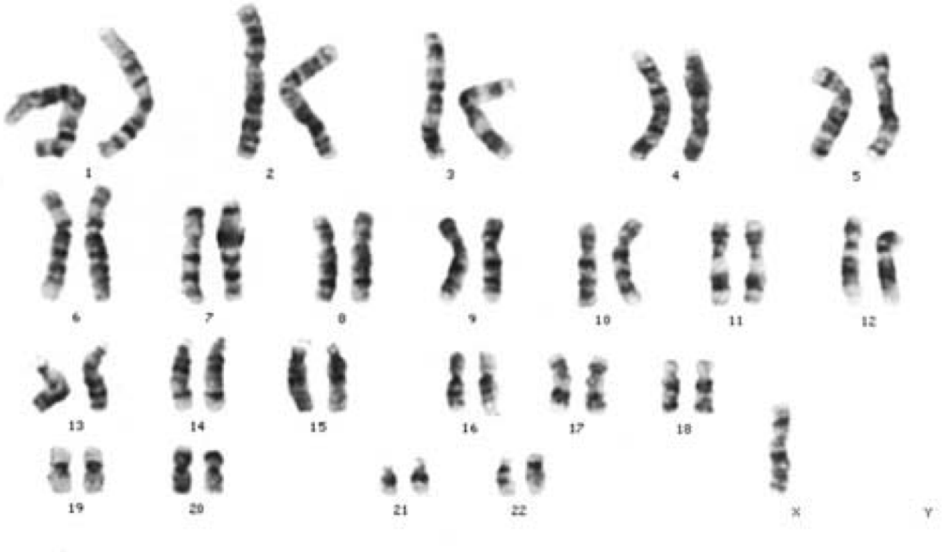
Gene SHOX :

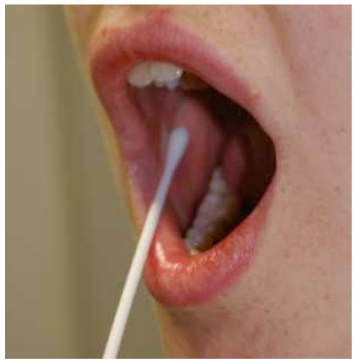
1 copy → 145 cm

2 copies → 165 cm

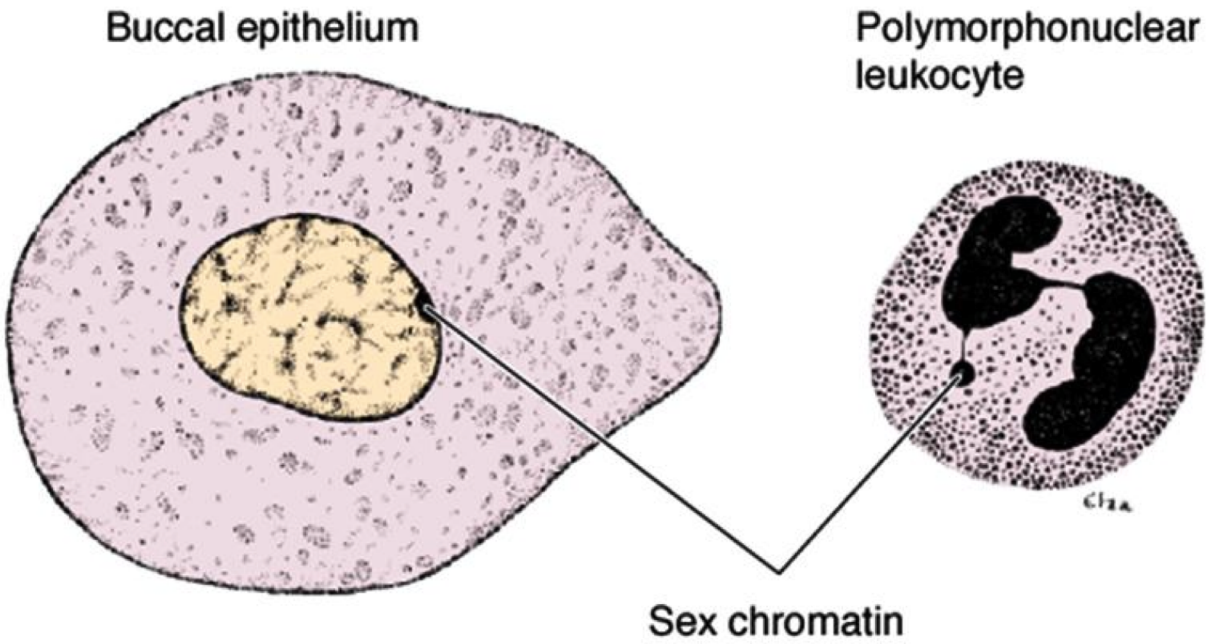
3 copies → 185 cm

The Sox gene escapes inactivation





Barr body



Blood sample

drumstick