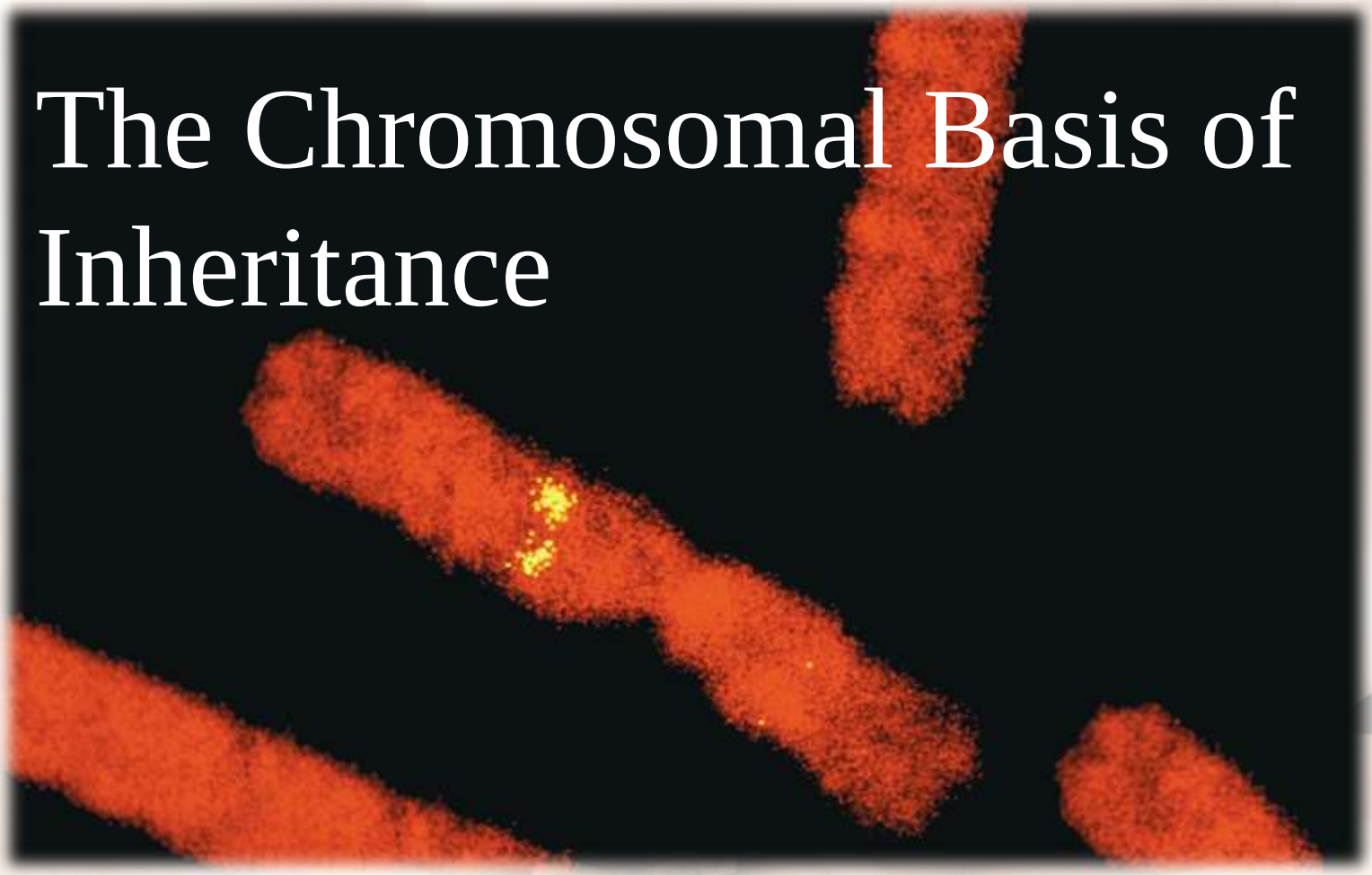
Chapter 15

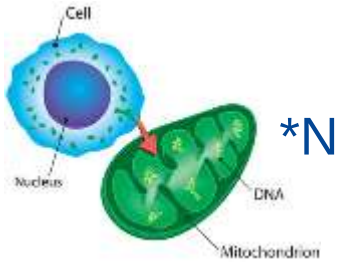


The Chromosomal Basis of Inheritance

Modified by YJ Chuang at NTHU-MS

Overview: **Locating Genes Along Chromosomes**

- Mendel's "hereditary factors" were genes, though this wasn't known at the time
- Today we can show that genes are located on chromosomes*
- The location of a particular gene can be seen by tagging isolated chromosomes with a fluorescent dye that highlights the gene



*Note: Mitochondria DNA (mtDNA) encodes 37 genes in human. mtDNA is inherited from the mother (maternally inherited).

Finding Genes on Chromosomes

- Genes are located on chromosomes

  Location of Gene on Chromosome can be visualized using certain molecular labeling techniques : **FISH** (Fluorescent *in situ* hybridization) technique

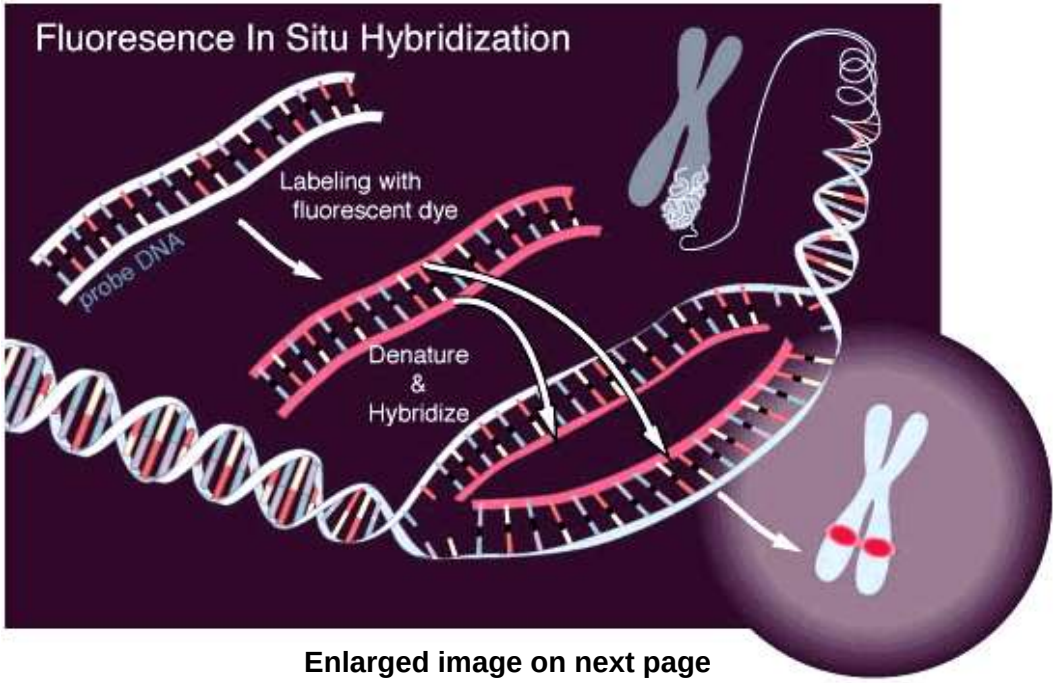
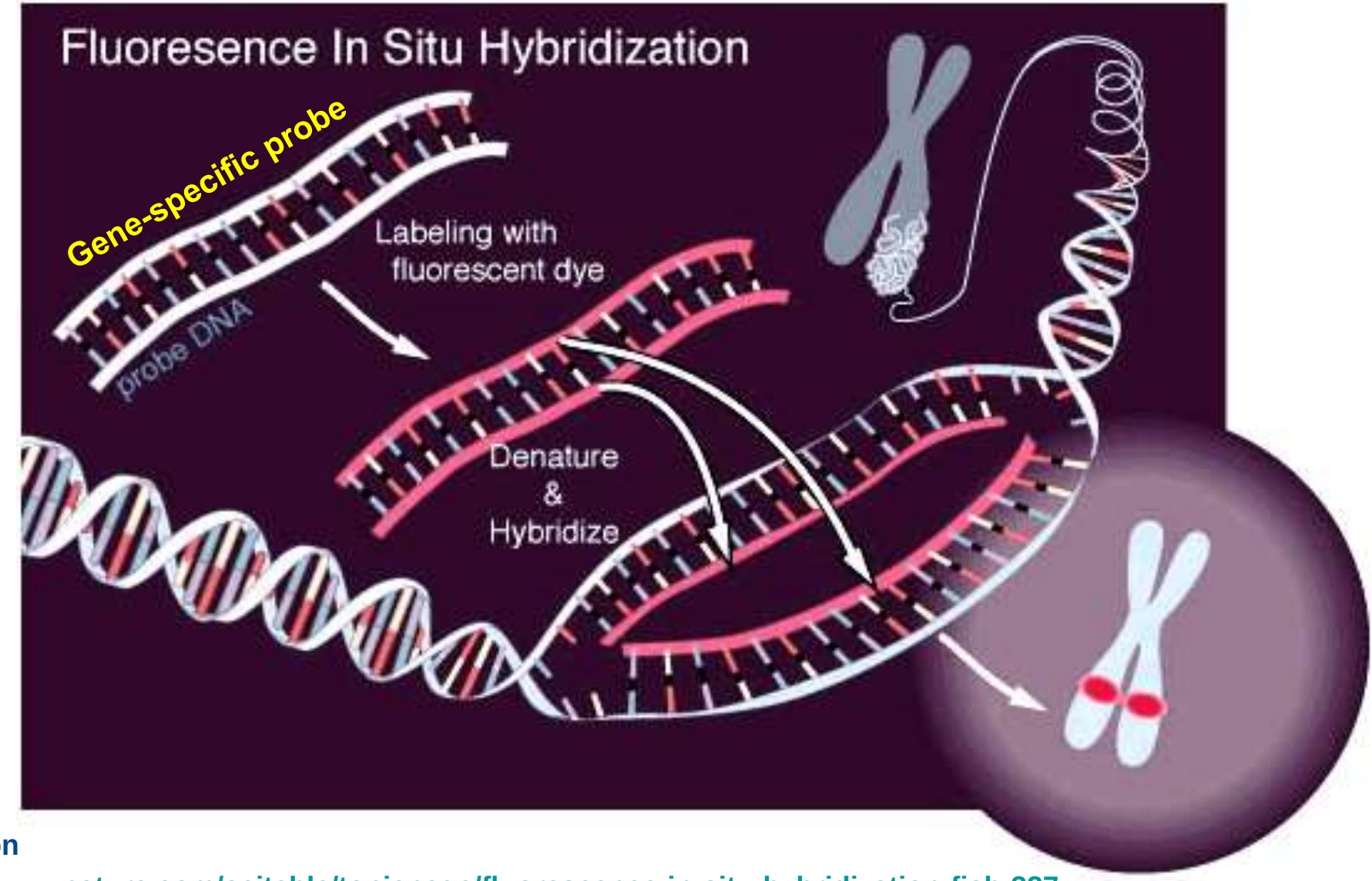


Figure 15.1

Enlarged image on next page

FISH: Fluorescence in situ hybridization



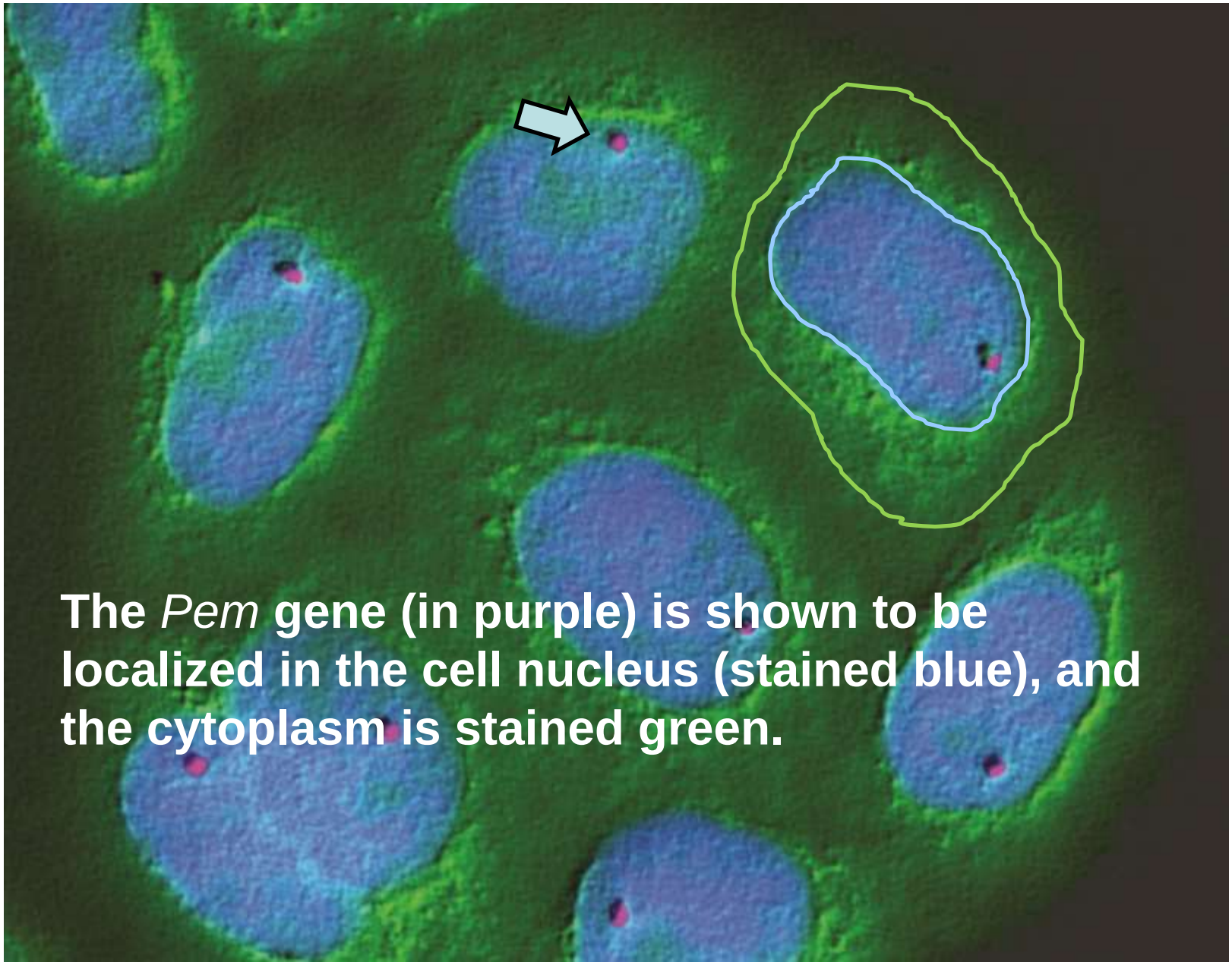
More on

http://www.nature.com/scitable/topicpage/fluorescence-in-situ-hybridization-fish-327

http://en.wikipedia.org/wiki/Fluorescence_in_situ_hybridization

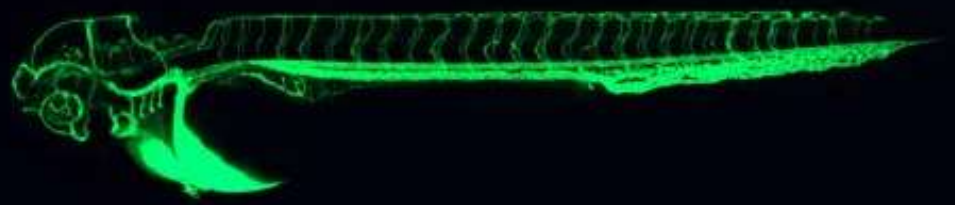
Figure 15.1

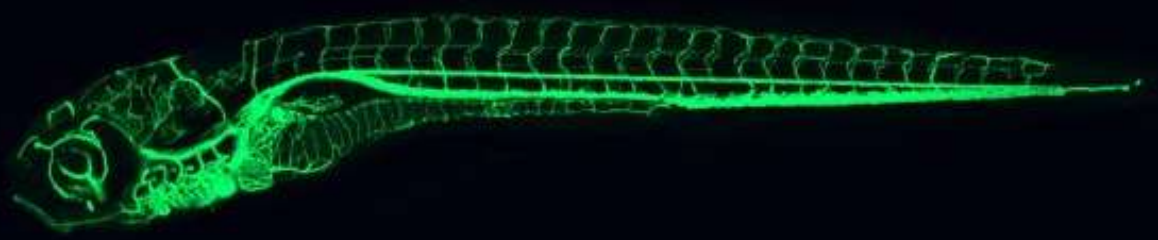
Gene, cell nucleus and the cytoplasm: Cell Multiple staining



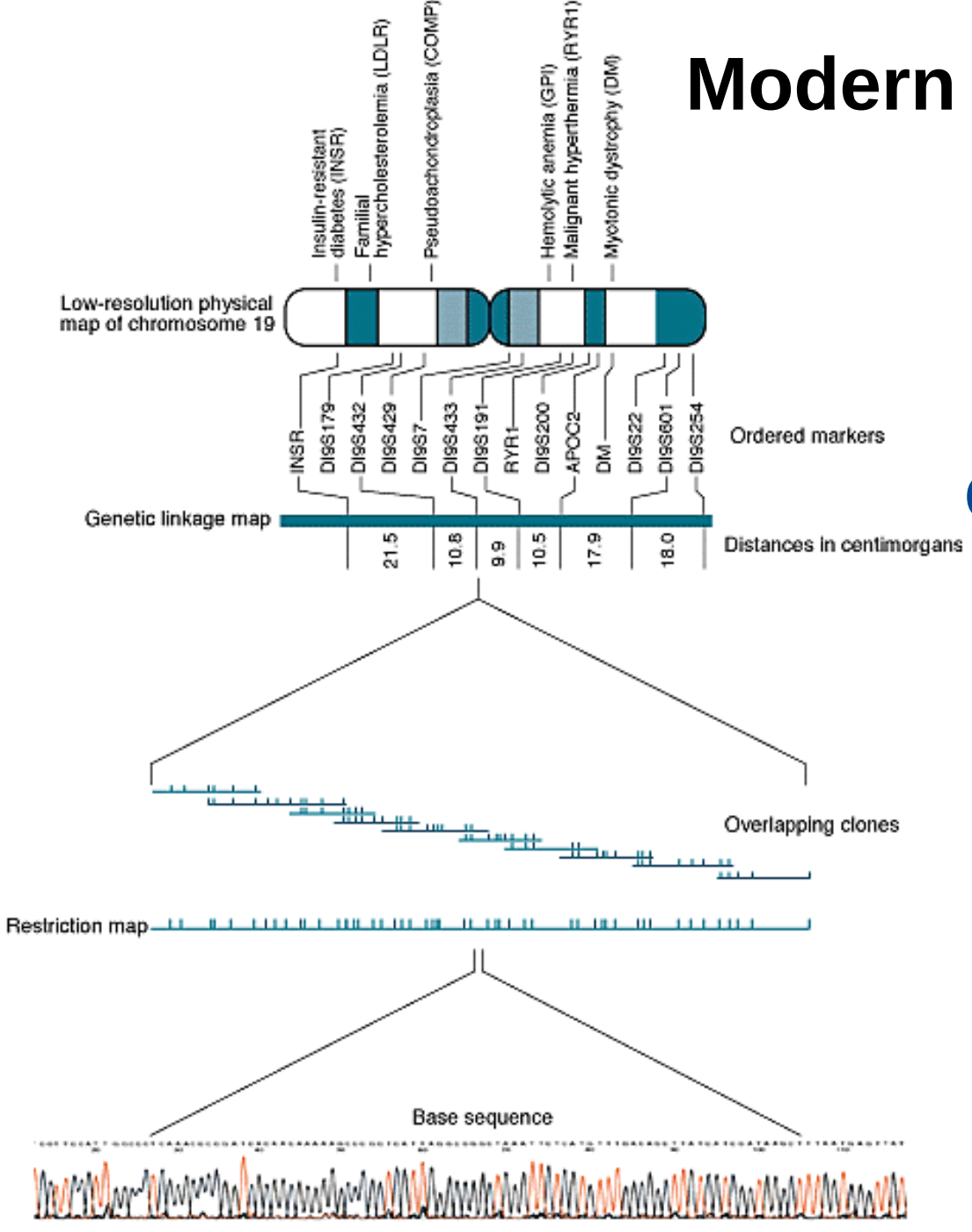
“Alzheimer” Zebrafish - stained for Tau (red), neurons (green), and pathologic Tau (blue).

Vasculature - the transparency of zebrafish larvae makes it possible to use high-resolution imaging to visualize in detail the entire system of blood vessels.





Modern Genome Project



Gene annotation

Genome mapping

Contig assembly

DNA Sequencing

(i.e. Next-Generation Sequencing, NGS)

Concept 15.1: Mendelian inheritance has its physical basis in the behavior of chromosomes

- **Mitosis and meiosis** were first described in the late 1800s (ch13)
- The **chromosome theory of inheritance** states:
  - Mendelian genes have **specific loci** (positions) on chromosomes
  - Chromosomes undergo segregation and independent assortment
- The behavior of chromosomes during meiosis was said to account for Mendel's laws of segregation and independent assortment

(進而解釋之前歸納出的規律)

Figure 15.2a

The chromosomal basis of Mendel's Laws

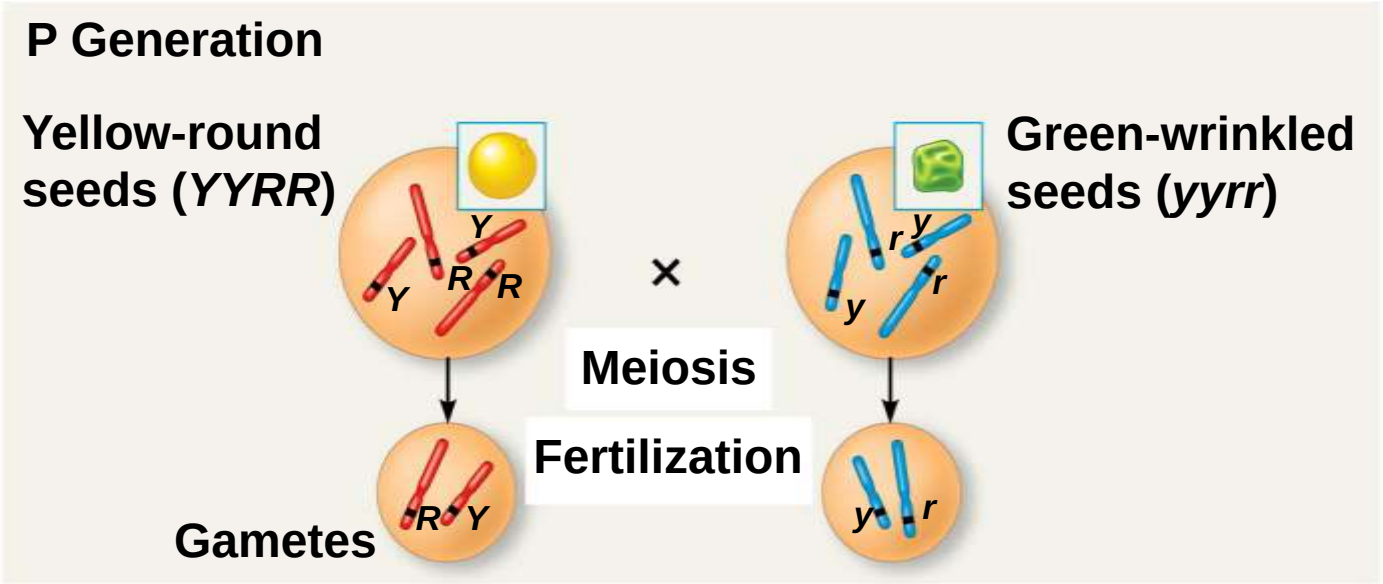


Figure 15.2b

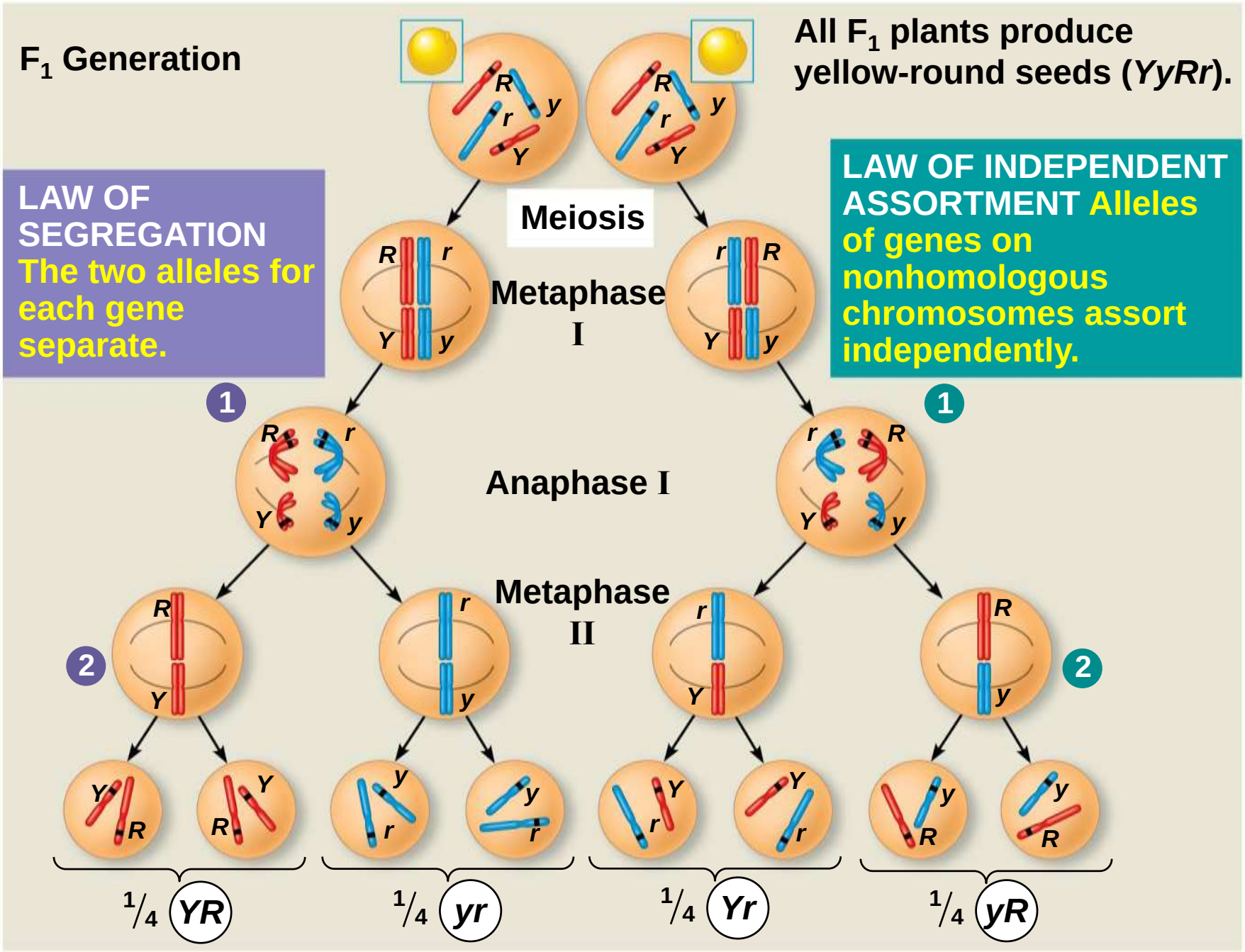
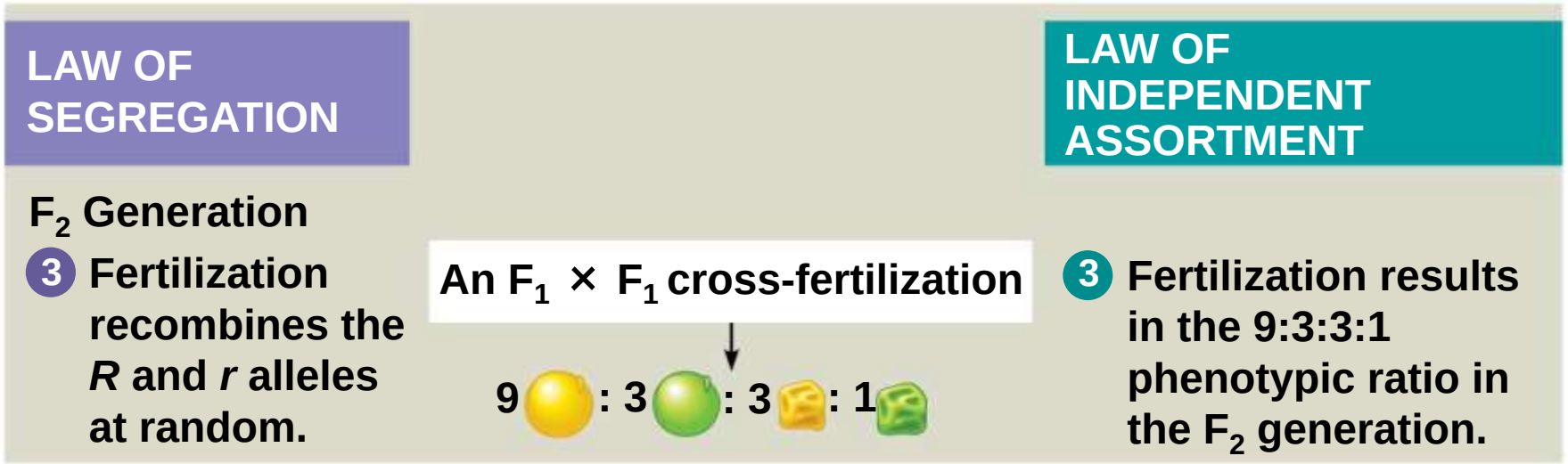


Figure 15.2c



EXTRA

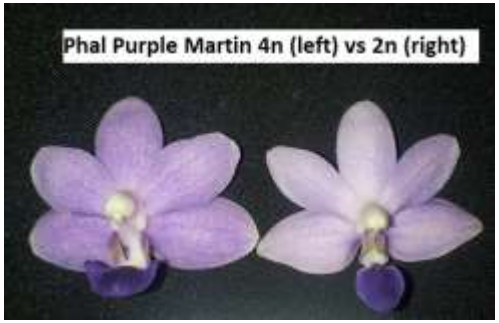
The Haploid Number of Chromosomes for a Variety of Organisms

Common Name	Scientific Name	Haploid Number	Common Name	Scientific Name	Haploid Number
Black bread mold	*Aspergillus nidulans*	8	House mouse	*Mus musculus*	20
Broad bean	*Vicia faba*	6	Human	*Homo sapiens*	23
Cat	*Felis domesticus*	19	Jimson weed	*Datura stramonium*	12
Cattle	*Bos taurus*	30	Mosquito	*Culex pipiens*	3
Chicken	*Gallus domesticus*	39	Mustard plant	*Arabidopsis thaliana*	5
Chimpanzee	*Pan troglodytes*	24	Pink bread mold	*Neurospora crassa*	7
Corn	*Zea mays*	10	Potato	*Solanum tuberosum*	24
Cotton	*Gossypium hirsutum*	26	Rhesus monkey	*Macaca mulatta*	21
Dog	*Canis familiaris*	39	Roundworm	*Caenorhabditis elegans*	6
Evening primrose	*Oenothera biennis*	7	Silkworm	*Bombyx mori*	28
Frog	*Rana pipiens*	13	Slime mold	*Dictyostelium discoidium*	7
Fruit fly	*Drosophila melanogaster*	4	Snapdragon	*Antirrhinum majus*	8
Garden onion	*Allium cepa*	8	Tobacco	*Nicotiana tabacum*	24
Garden pea	*Pisum sativum*	7	Tomato	*Lycopersicon esculentum*	12
Grasshopper	*Melanoplus differentialis*	12	Water fly	*Nymphaea alba*	80
Green alga	*Chlamydomonas reinhardi*	18	Wheat	*Triticum aestivum*	21
Horse	*Equus caballus*	32	Yeast	*Saccharomyces cerevisiae*	16
House fly	*Musca domestica*	6	Zebrafish	*Danio rerio*	25

Horse – 64 Chromosomes Fertile

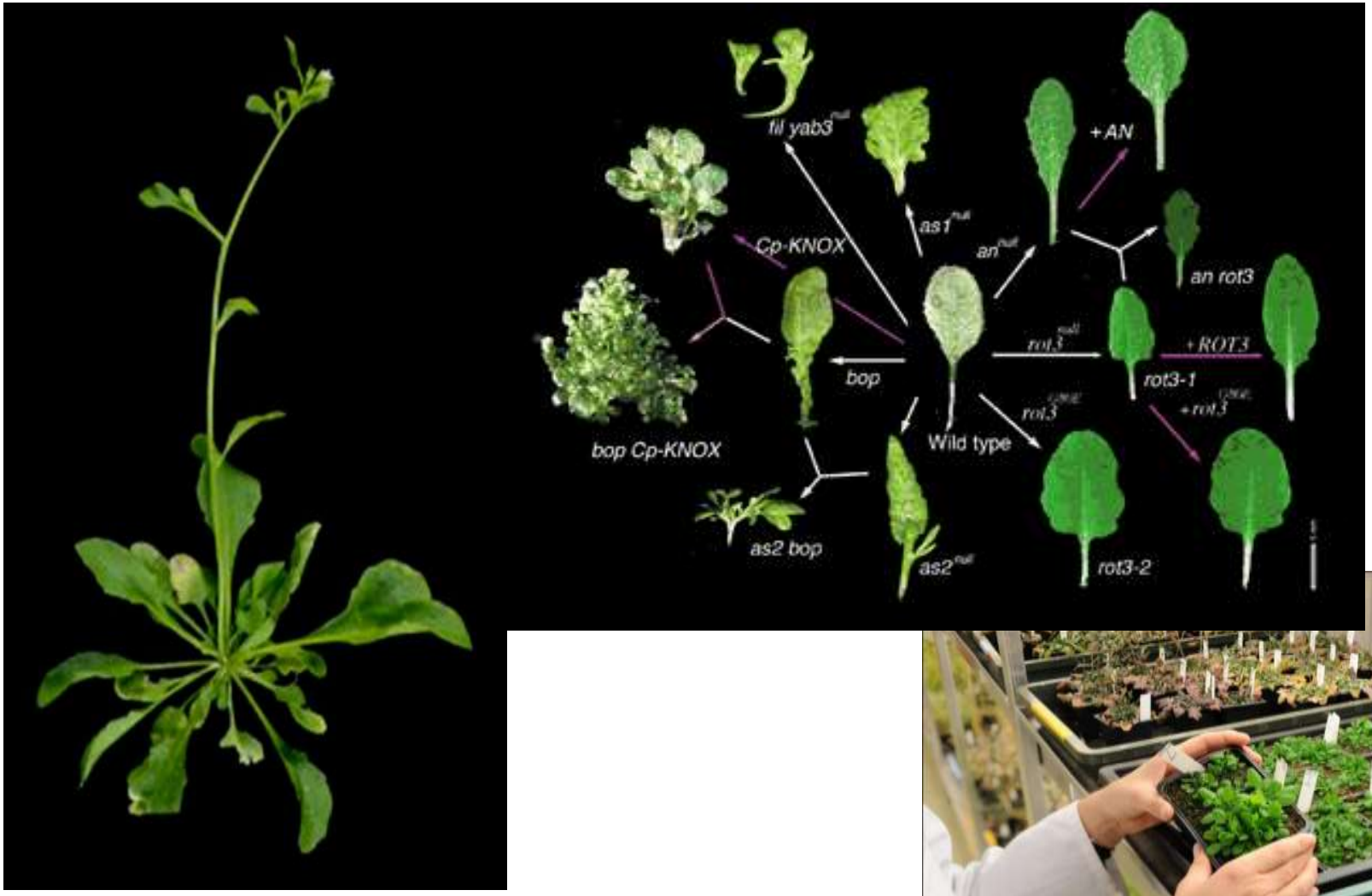
Donkey – 62 Chromosomes Fertile

Mule – 63 Chromosomes Infertile (Mostly)



Today, pea is replaced by

Arabidopsis (阿拉伯芥) as **the primary model plant**



Arabidopsis thaliana

Is there Money in Genetic Research ?

- **Genome Editing Technologies**
  - (i.e. CRISPR/Cas9)
- **Genetically modified organism** (GMO)

孟山都 Monsanto: 基改農業生技

http://en.wikipedia.org/wiki/Monsanto

2016 revenue: US$13.5B; Net income: US$1.3B

TSMC 2016 revenue: US$ 31.6B; Net income: US$11.1B

華大基因 BGI www.genomics.cn

Stock price: 2017/7/13 CNY 13.64

2017/11/8 CNY 210.50

Morgan's Experimental Evidence: *Scientific Inquiry*

Pea has its limitation….

Fruit Fly 果蠅 as the Model Organism for genetics

Thomas Hunt **Morgan (1866-1945)**

- Provided convincing evidence that chromosomes are the location of Mendel's heritable factors

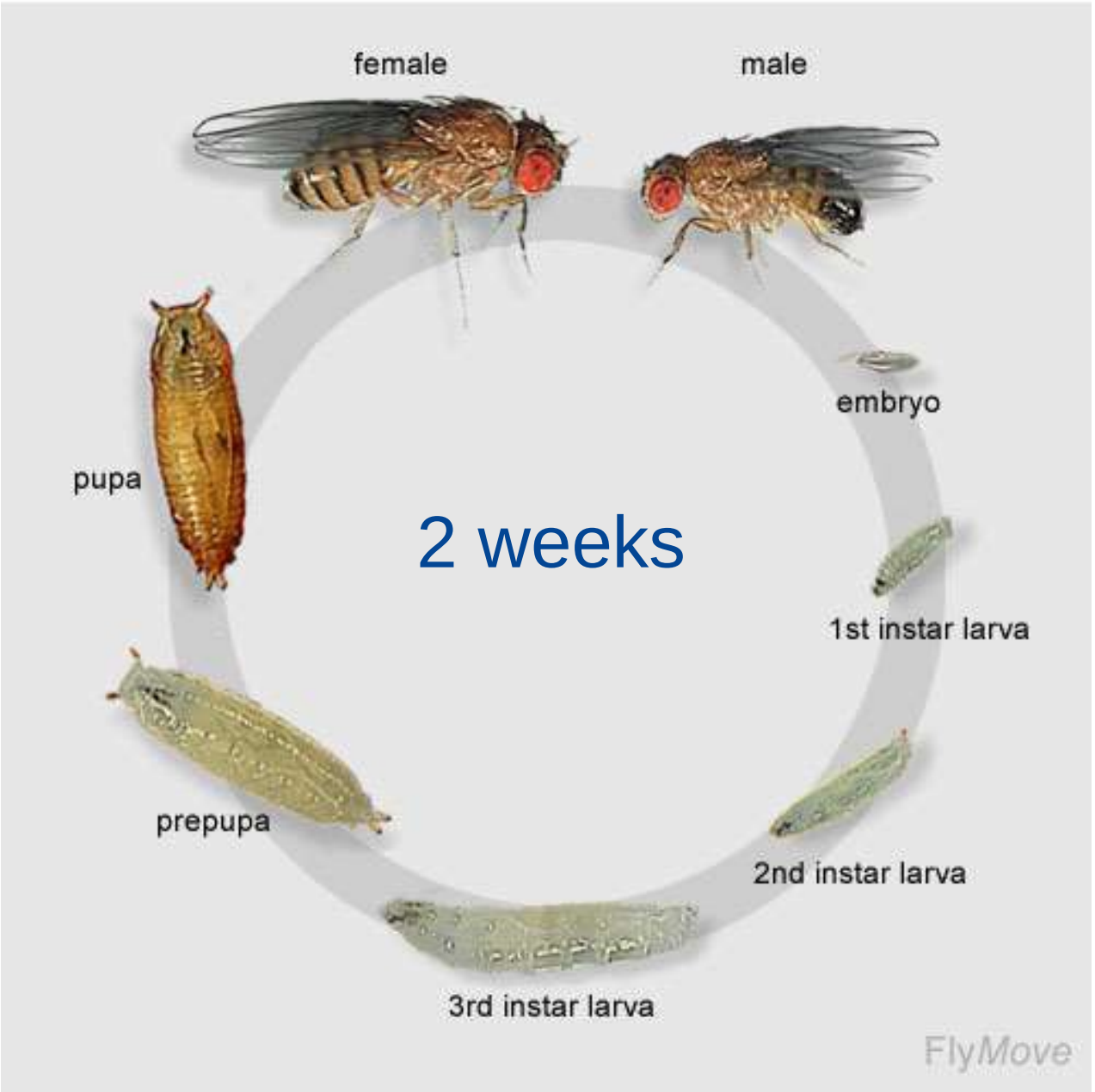
Morgan's Choice of **Experimental Organism**

實驗模式生物

Morgan worked with **fruit flies (Drosophila)**

- Because they breed at a high rate
- A new generation can be bred every two weeks
- They have only four pairs of chromosomes

The life cycle of *Drosophila melanogaster*



Wild type vs. Mutant phenotype

- Morgan noted **wild type**, or normal, phenotypes that were common in the fly populations
- Traits alternative to the wild type are called *mutant phenotypes*

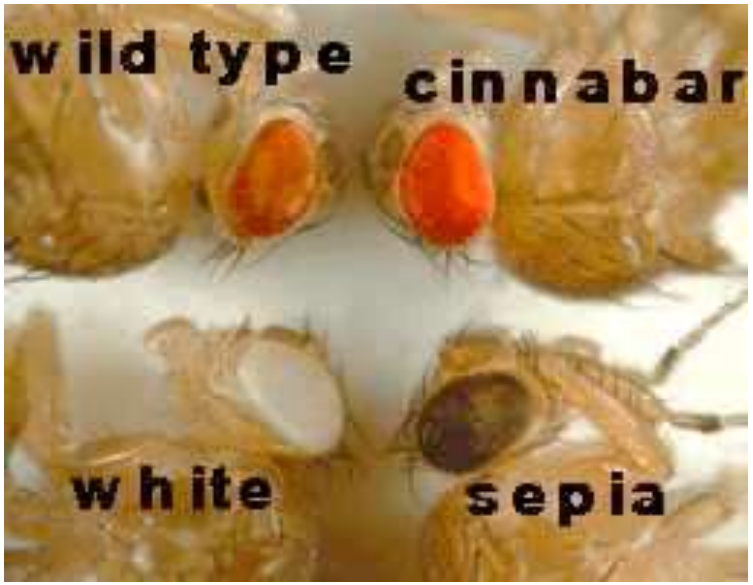
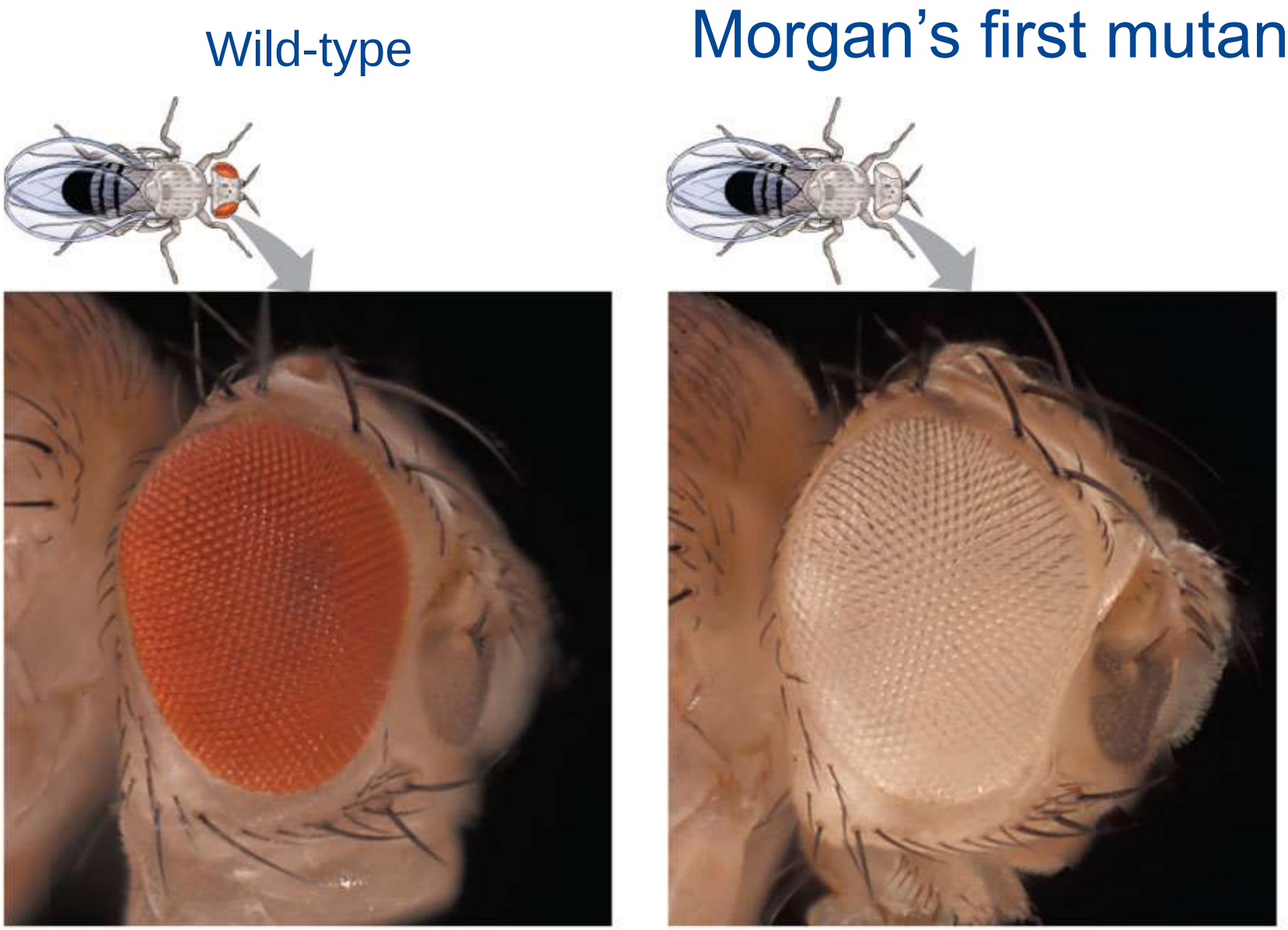


Fig. 15-3



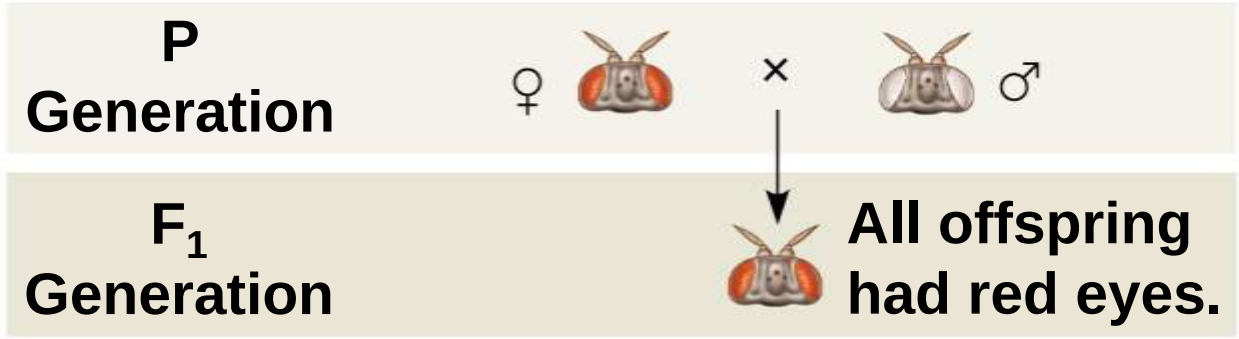
Correlating Behavior of a Gene's Alleles with Behavior of a Chromosome Pair

- In one experiment, Morgan mated male flies with **white eyes (mutant)** with female flies with **red eyes (wild type)**
  - The **F_1 generation** all had **red eyes**
  - The F_2 generation showed the **3:1 red:white eye ratio**, but only **males** had white eyes
- Morgan determined that the white-eyed mutant allele must be located on the X chromosome
- Morgan's finding supported the chromosome theory of inheritance

Figure 15.4a

Similar to Mendel's experimental design

Experiment



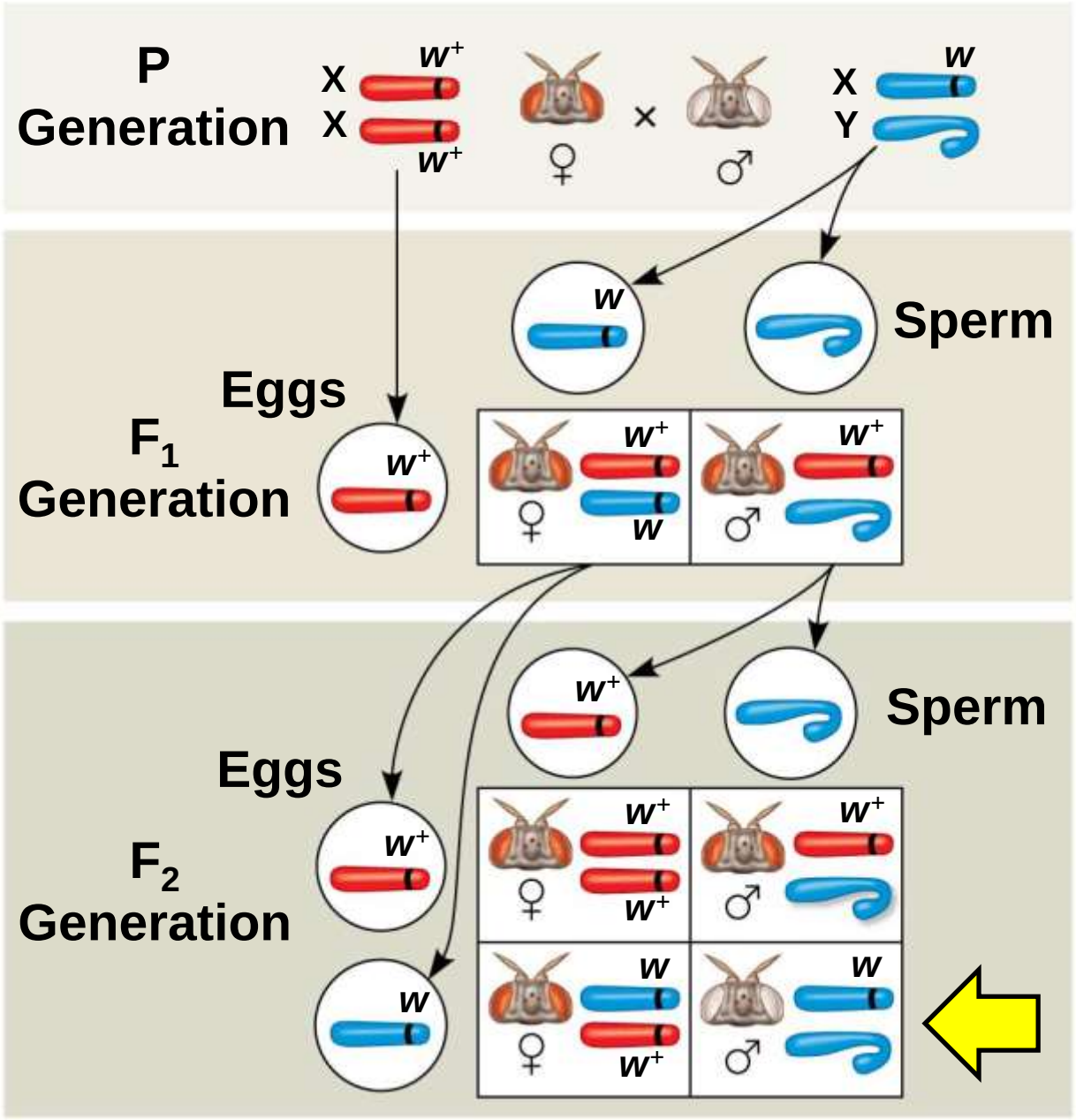
Results

3:1 ratio was observed.

But, why male only?

Figure 15.4b

Conclusion



Concept 15.2: Sex-linked genes exhibit unique patterns of inheritance

- In humans and some other animals, there is a chromosomal basis of sex determination

Hermaphrodite 雌雄同體

in Louvre

discovered in 1608

Sequential hermaphrodite

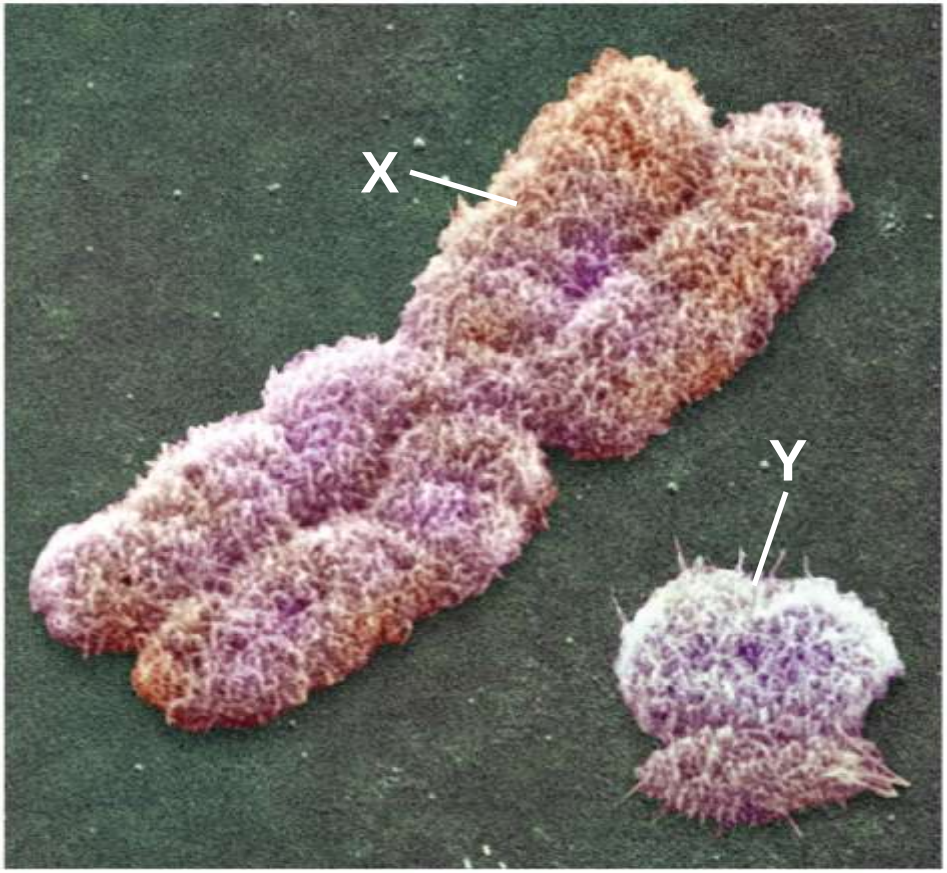
Simultaneous hermaphrodite

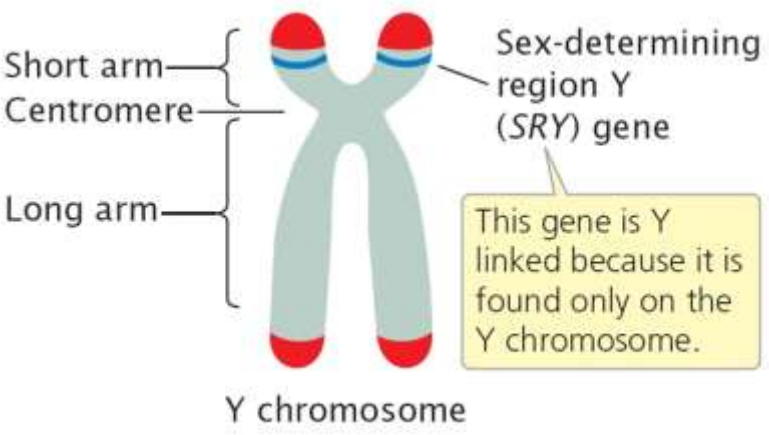
The Chromosomal Basis of Sex

- In humans and other mammals, there are two varieties of sex chromosomes: a larger X chromosome and a smaller Y chromosome
- Only the ends of the Y chromosome have regions that are homologous with the X chromosome
- **The *SRY* gene on the Y chromosome codes for the development of testes**

Fig. 15-5

Human sex chromosomes

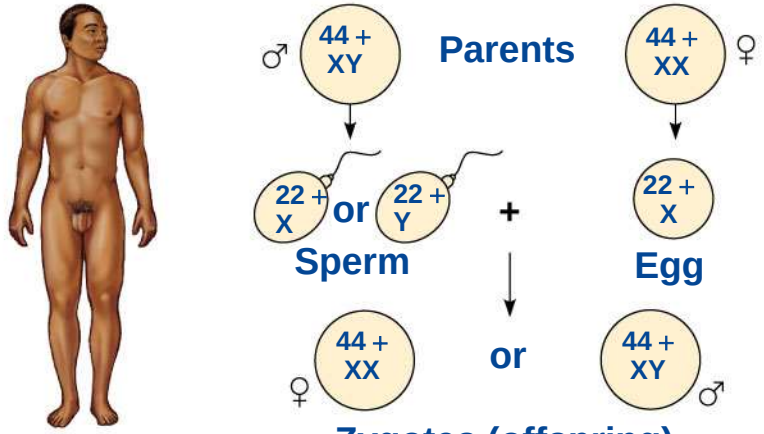




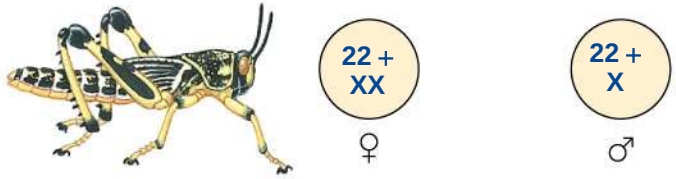
Question: can you think of any applications based on this knowledge of SRY gene?

XX vs. XY in human

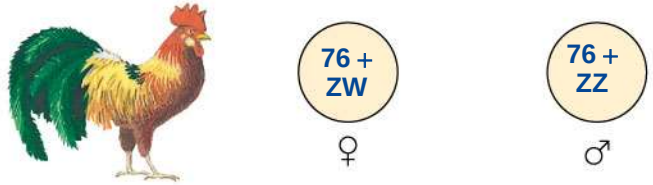
- Females are XX, and males are XY
- Each ovum contains an X chromosome, while a sperm may contain either an X or a Y chromosome – **X-Y system**
- Other animals have different methods of sex determination
  - X-0 system; Z-W system; Haplo-diploid system



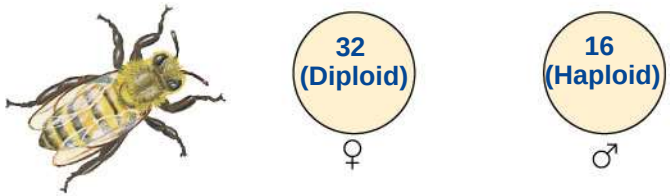
(a) The X-Y system



(b) The X-0 system



(c) The Z-W system



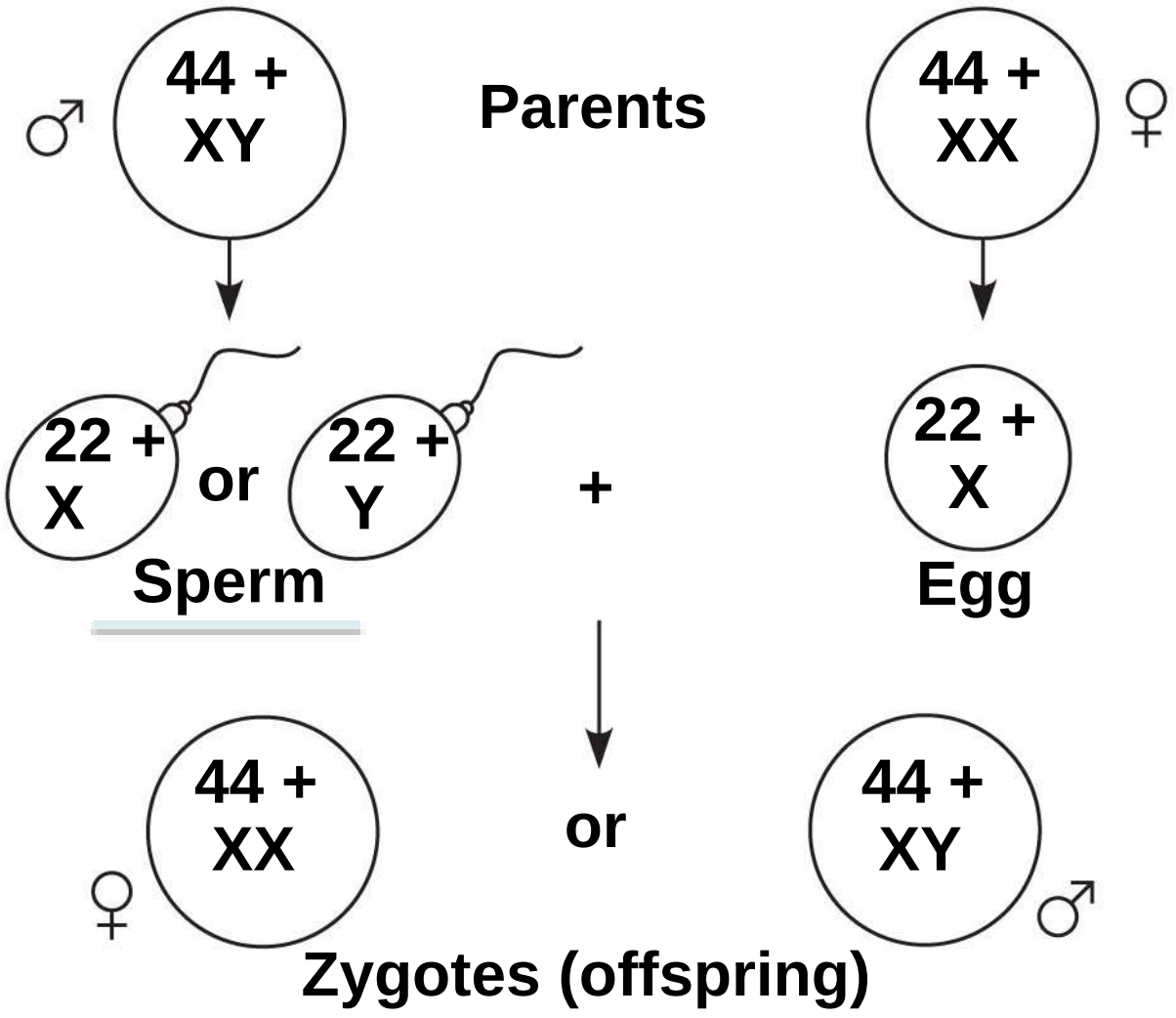
(d) The haplo-diploid system

Diversity of Life

Some chromosomal systems of sex determination

Figure 15.6

Fig. 15-6a

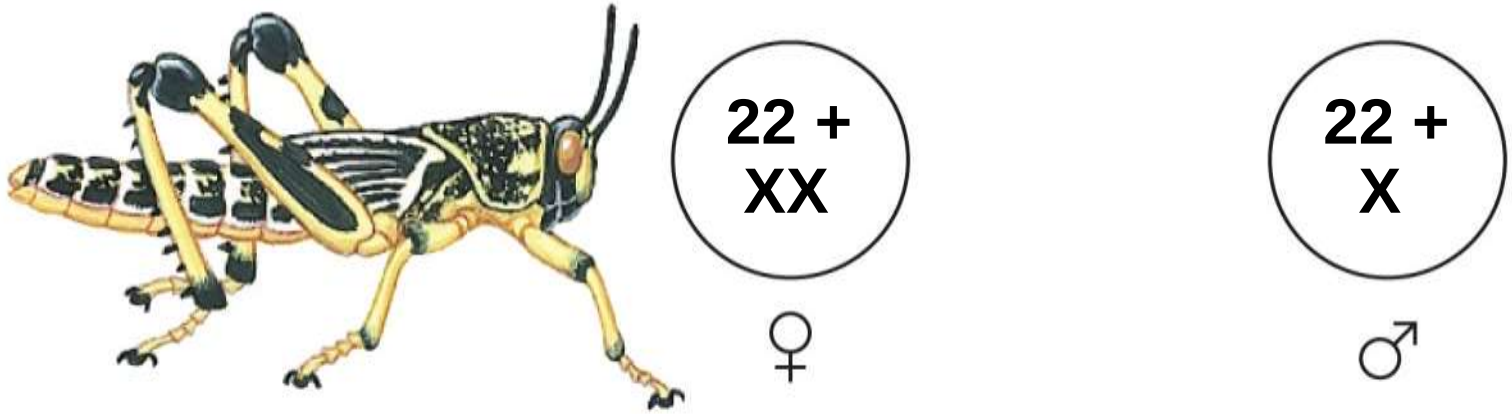


(a) The X-Y system

Whether X or Y in sperm

Fig. 15-6b

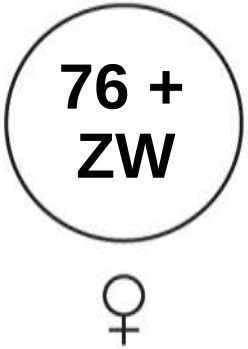
Sperm cell contains an X or no chromosome



(b) The X-0 system

Fig. 15-6c

Sex chromosome in the egg



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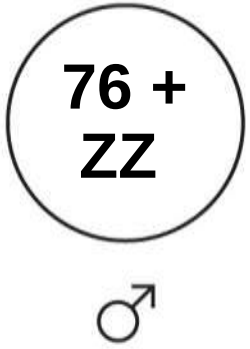


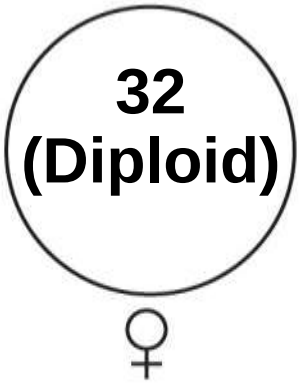
♂

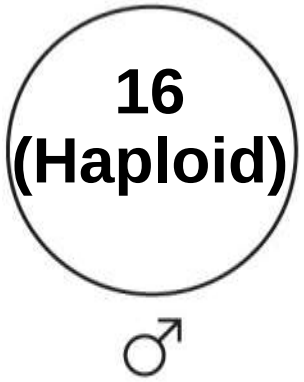
(c) The Z-W system

Fig. 15-6d

Fertilized egg → females

Unfertilized egg → males; no father





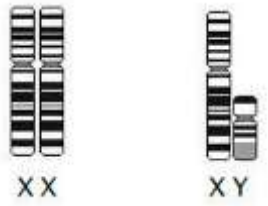
(d) The haplo-diploid system

Inheritance of Sex-Linked Genes

- The sex chromosomes have genes for many characters unrelated to sex
- A gene located on either sex chromosome is called a **sex-linked gene**
- In humans, sex-linked usually refers to a gene on the larger **X chromosome**

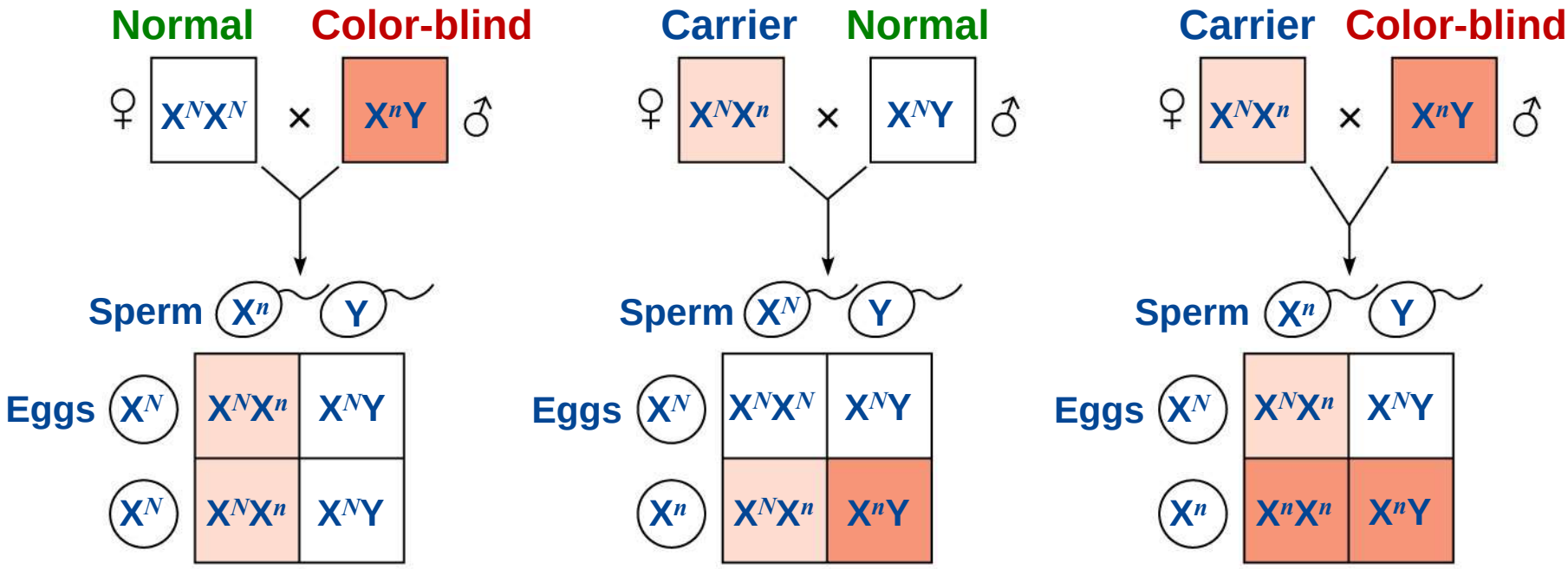
Sex-linked recessive disorders in males

- Sex-linked genes follow **specific patterns of inheritance**
- For a recessive sex-linked trait to be expressed
  - A female needs two copies of the allele
  - A male needs **only one copy** of the allele
- **Sex-linked recessive disorders** are much more common in **males** than in females



The transmission of sex-linked recessive traits

(using **color blindness** 色盲 as an example)



(a)

Color-blind father
Dominant homozygote mother
Carrier daughter
Unaffected son

(b)

Carrier mother
½ Carrier daughter
½ Affected son

(c)

Carrier mother
Color-blind father
½ Affected son
½ Carrier daughter
½ Affected daughter

Figure 15.7

Sex-linked recessive disorders in males

- **Defined**: Inherited conditions found on X chromosome
- Usually recessive
- Females: XX chromosomes
  - $X^H X^H$ = healthy
  - $X^H X^h$ = healthy carrier
  - $X^h X^h$ = disease
- Males: XY chromosomes
  - $X^H Y$ = healthy
  - $X^h Y$ = disease
- Rare in women (back-up X chromosome)
- Ex: Colorblindness, Hemophilia, Muscular dystrophy

$X^H X^H$

or

$X^H X^h$

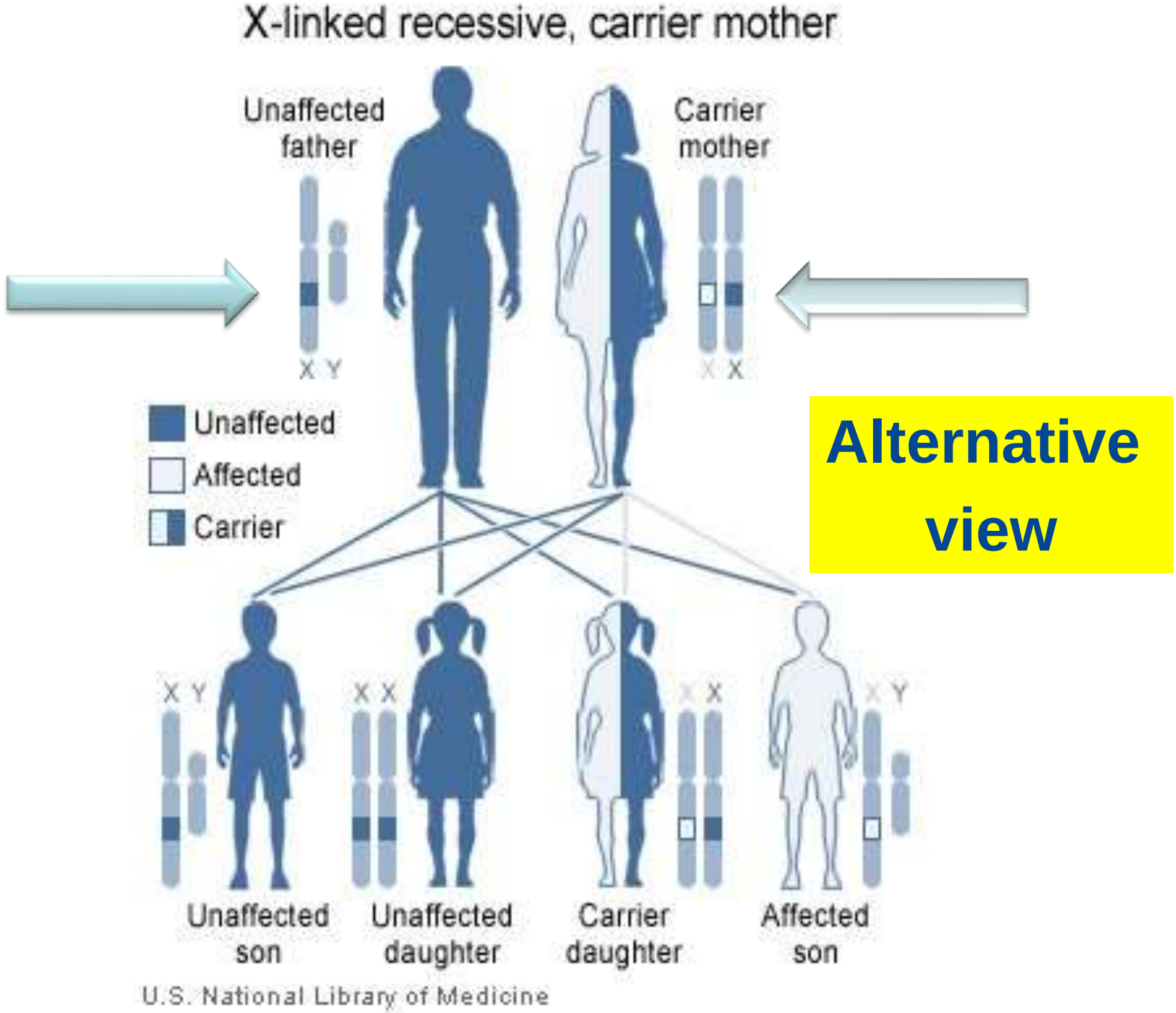
or

$X^h X^h$

$X^H Y$

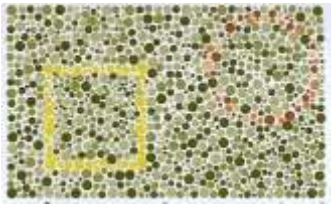
or

$X^h Y$

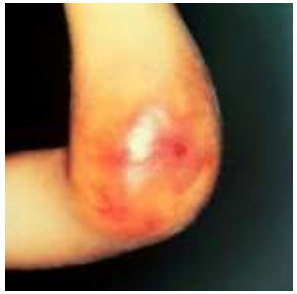

X-linked recessive, carrier mother
Unaffected father
Carrier mother
X Y
X X
Unaffected
Affected
Carrier
Alternative view
X Y
X X
X X
X Y
Unaffected son
Unaffected daughter
Carrier daughter
Affected son
U.S. National Library of Medicine

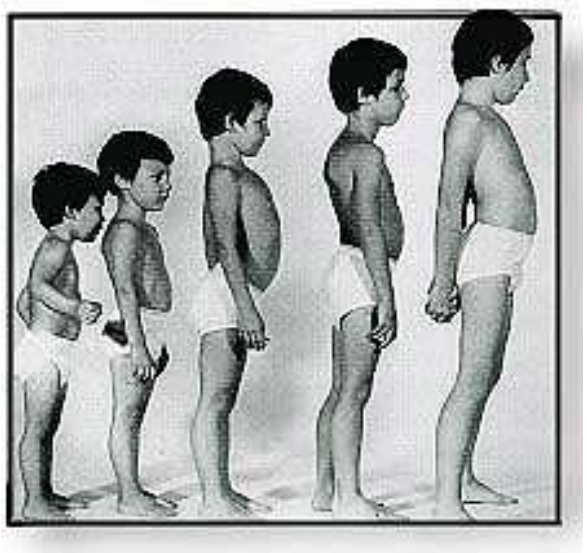
X chromosome diseases

- Some disorders caused by recessive alleles on the X chromosome in humans:
  - **Color blindness** (色盲)



  - **Duchenne muscular dystrophy (杜顯氏/裘馨氏肌肉萎縮症)**
  - **Hemophilia (血友病)**





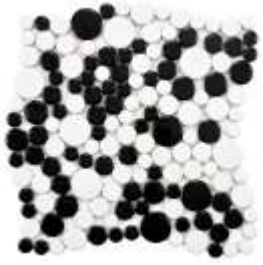
X Inactivation in Female Mammals

- In mammalian females, one of the two X chromosomes in each cell is randomly inactivated during embryonic development

To present over-expression!

- The inactive X condenses into a **Barr body**

- If a female is heterozygous for a particular gene located on the X chromosome, she will be a mosaic for that character



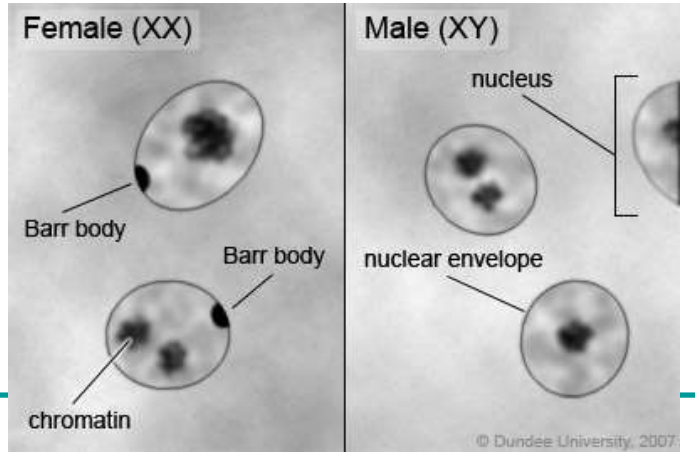
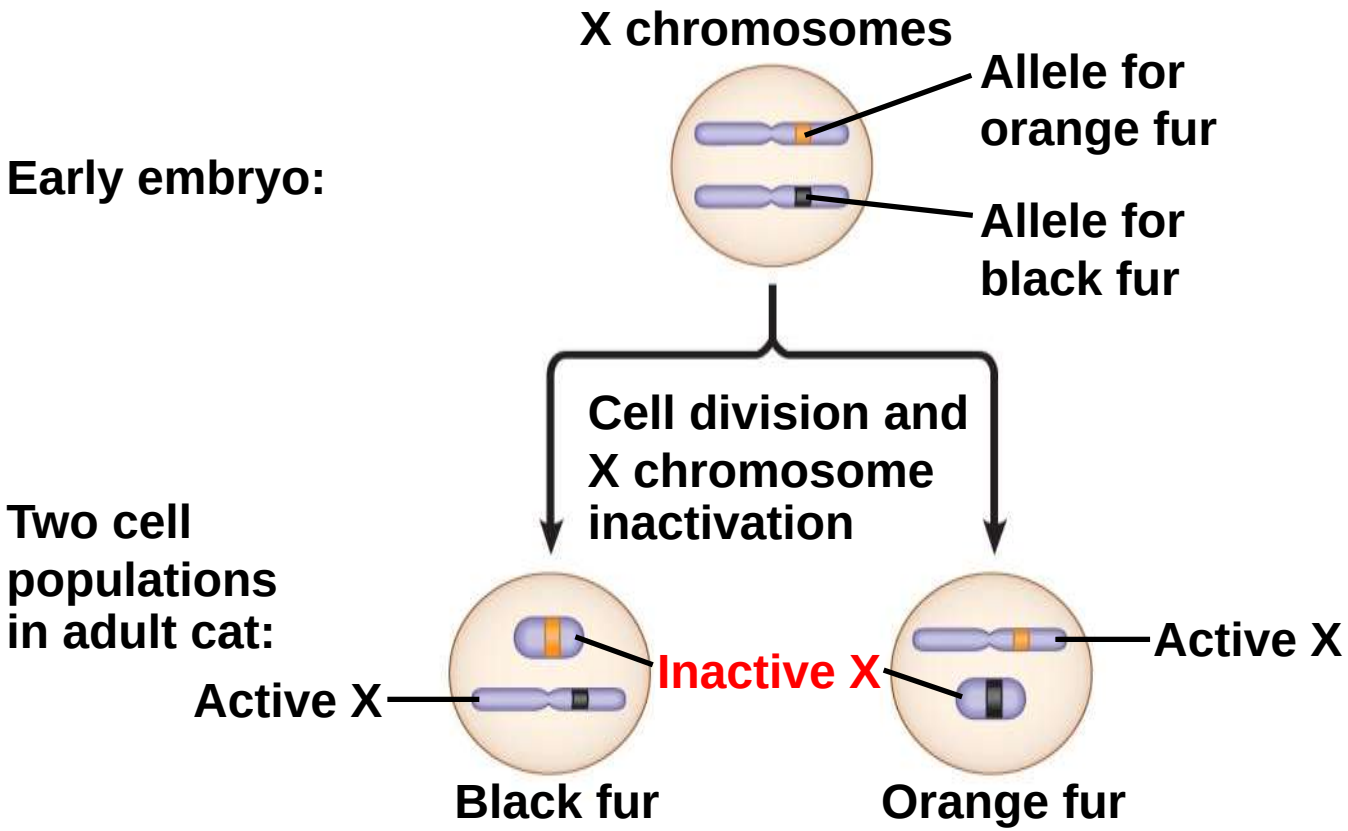
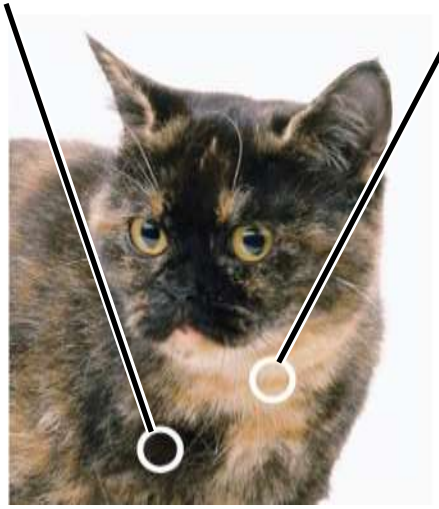


Fig. 15-8



X inactivation and the tortoiseshell cat



複製貓外觀難以相同!

Thinking Question: how to perform gender test?

- Past and current **Gender testing** at the Olympics games

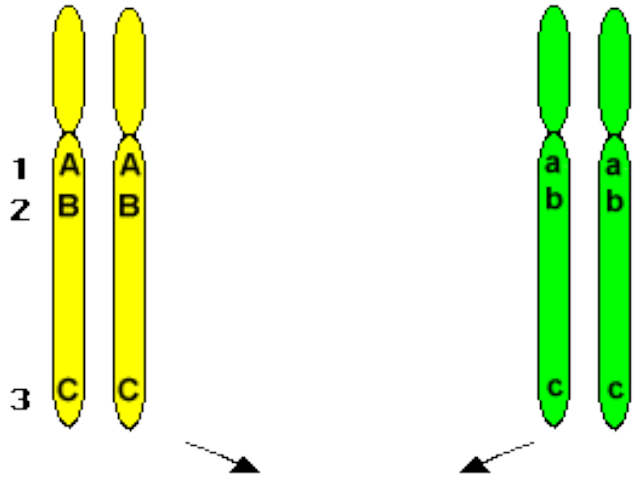
1. Female/male body parts
2. X/Y chromosome
3. SRY gene on Y chromosome
4. Barr Body
5. Testosterone levels (200-1200 ng/dl blood for males; 15-80 ng/dl blood for females)

Caster Semenya (1991-)

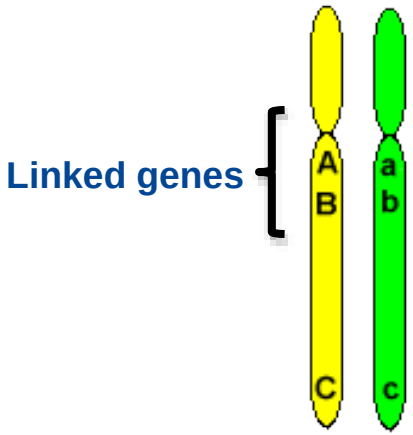
She is a South African middle-distance runner and 2016 Olympic gold medallist. (女子800M)

Concept 15.3: Linked genes tend to be inherited together because they are located near each other on the same chromosome

- Each chromosome has hundreds or thousands of genes



- Genes located on the same chromosome that *tend to be* **inherited together** are called **linked genes**



http://digilander.libero.it/avifauna/articoli_ornicoltura/PHTright7.html

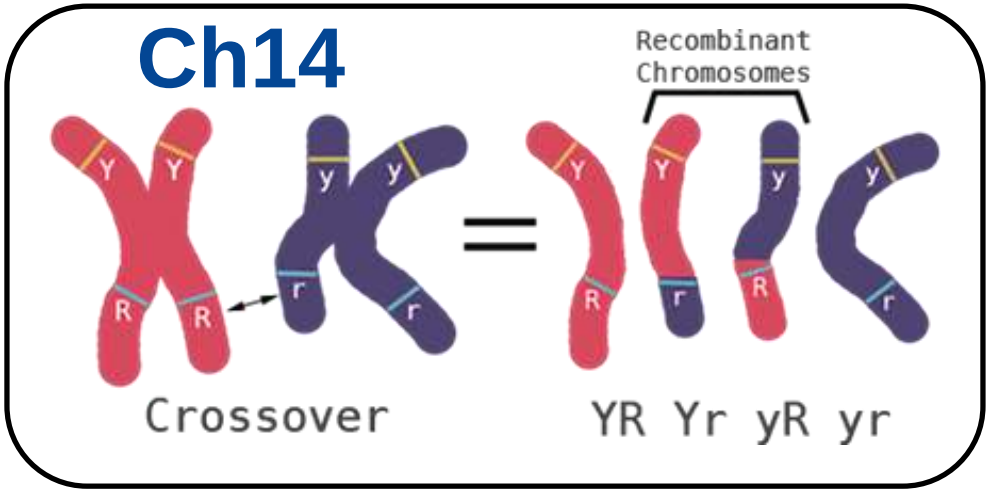
How Linkage Affects Inheritance

- Morgan did other experiments with fruit flies to see how linkage affects inheritance of two characters
  - Morgan crossed flies that differed in traits of **body color** (gray vs. black) and **wing size** (normal vs. vestigial 殘跡、退化)

    Gray body: *b*+ Black body: *b*

    Normal wings: *vg*+ Vestigial wings: *vg*

Figure 15.9a



Experiment

P Generation (homozygous)
Wild type (gray body, normal wings)
***b*⁺ *b*⁺ *vg*⁺ *vg*⁺**

Double mutant (black body, vestigial wings)
b b vg vg

F_1 dihybrid testcross
Wild-type F_1 dihybrid (gray body, normal wings)
b*⁺ *b vg*⁺ *vg

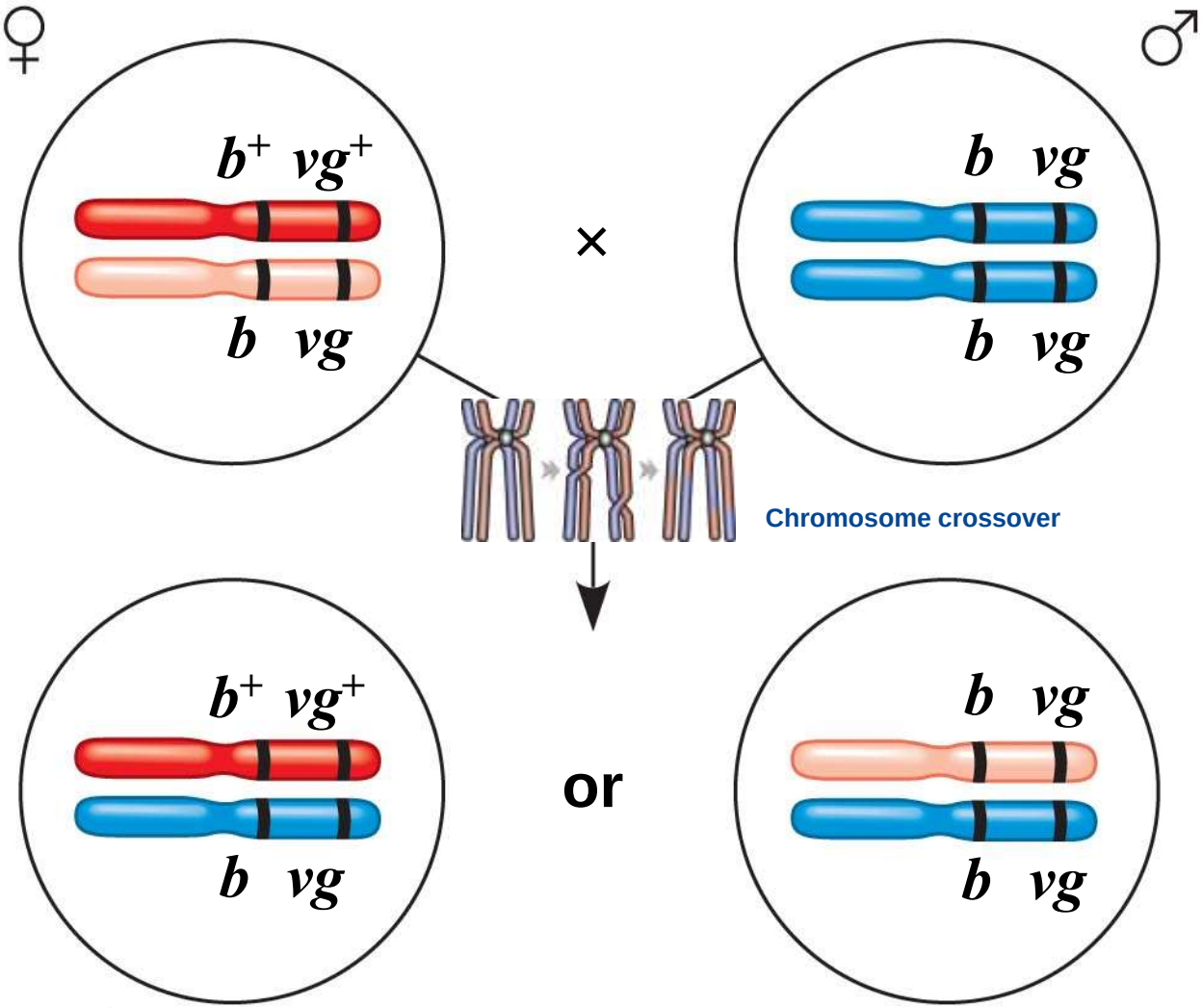
Homozygous recessive (black body, vestigial wings)
b b vg vg

How does linkage between two genes affect inheritance of characters?

Parents in testcross

Dihybrid female

Homozygous recessive male



Most offspring

Figure 15.9b

Experiment

Testcross offspring

Eggs: $b^+\ vg^+$ | $b\ vg$ | $b^+\ vg$ | $b\ vg^+$

Sperm: $b\ vg$

Wild type (gray-normal)	Black-vestigial	Gray-vestigial	Black-normal
			
$b^+\ b\ vg^+\ vg$	$b\ b\ vg\ vg$	$b^+\ b\ vg\ vg$	$b\ b\ vg^+\ vg$

PREDICTED RATIOS

Genes on different chromosomes:	1	:	1	:	1	:	1
Genes on the same chromosome:	1	:	1	:	0	:	0
Results	965	:	944	:	206	:	185

??

Note: Statistical analysis: Chi-Square (X^2) Test on Page 358

Parental phenotypes inherited together

- New findings:
  - Morgan found that body color and wing size are usually inherited together in specific combinations (parental phenotypes)
  - He noted that these genes do not assort independently, and reasoned that they were on the **same** chromosome

Genetic recombination

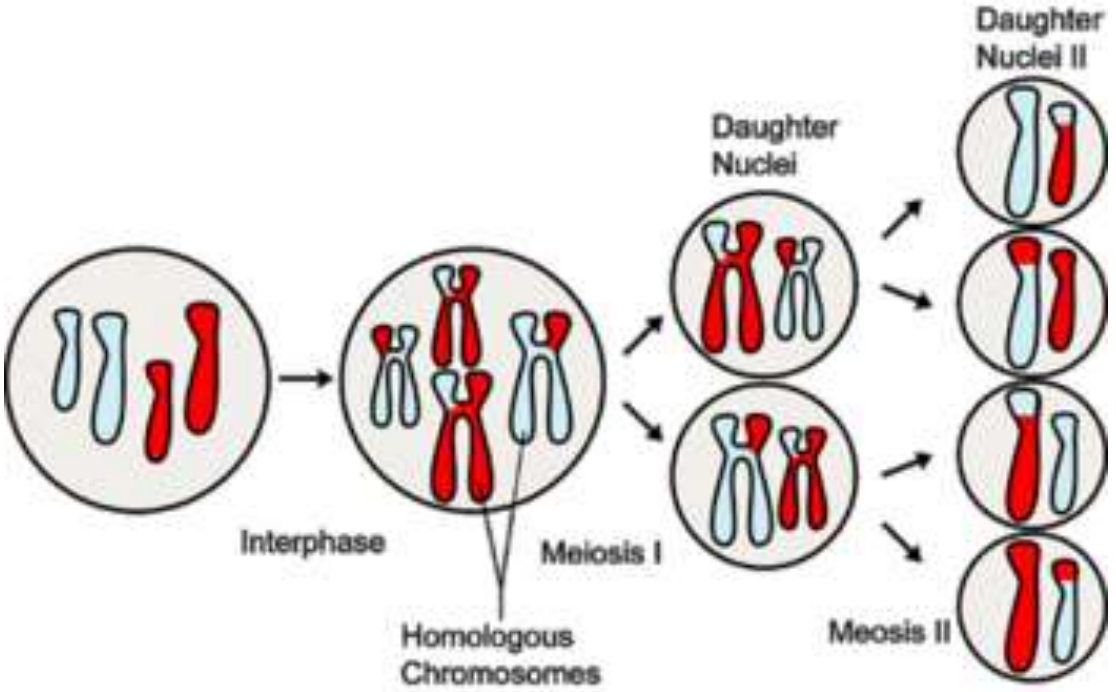
解釋之前實驗發現

- However, non-parental phenotypes (the production of offspring with combinations of traits differing from either parent) were also produced!
- Understanding this result involves exploring **genetic recombination** 遺傳重組

新知識拓展了既有知識

Genetic Recombination and Linkage

- The genetic findings of Mendel and Morgan relate to the **chromosomal basis of recombination**



Review Ch13

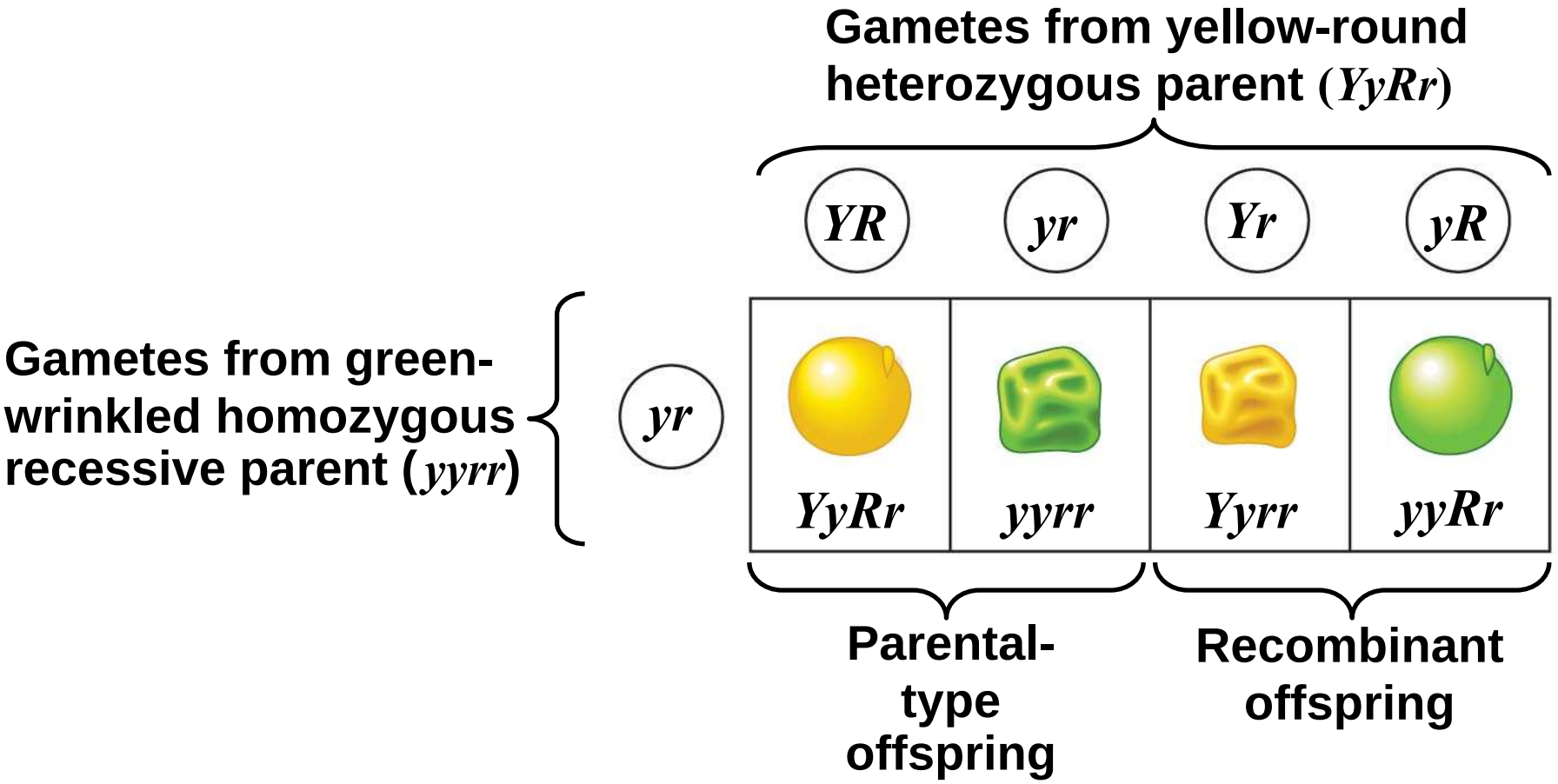
http://creationwiki.org/Genetic_recombination

Recombination of Unlinked Genes: Independent Assortment of Chromosomes

- Offspring with a phenotype matching one of the parental phenotypes are called **parental types**
- Offspring with nonparental phenotypes (new combinations of traits) are called **recombinant types**, or **recombinants**
- A 50% frequency of recombination is observed for any two genes on different chromosomes

Mendel has reported “recombinants” without knowledge of chromosome & genetic linkage:

Independent Assortment of Chromosomes



Recombination of Linked Genes: Crossing Over

- Morgan discovered that genes can be linked, but the **linkage was incomplete**, as evident from recombinant phenotypes
- Morgan proposed that *some process must sometimes break the physical connection between genes on the same chromosome*
- That mechanism was the **crossing over** of homologous chromosomes

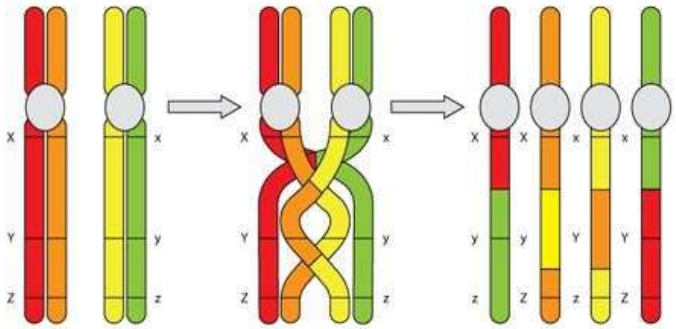


Figure 15.10a

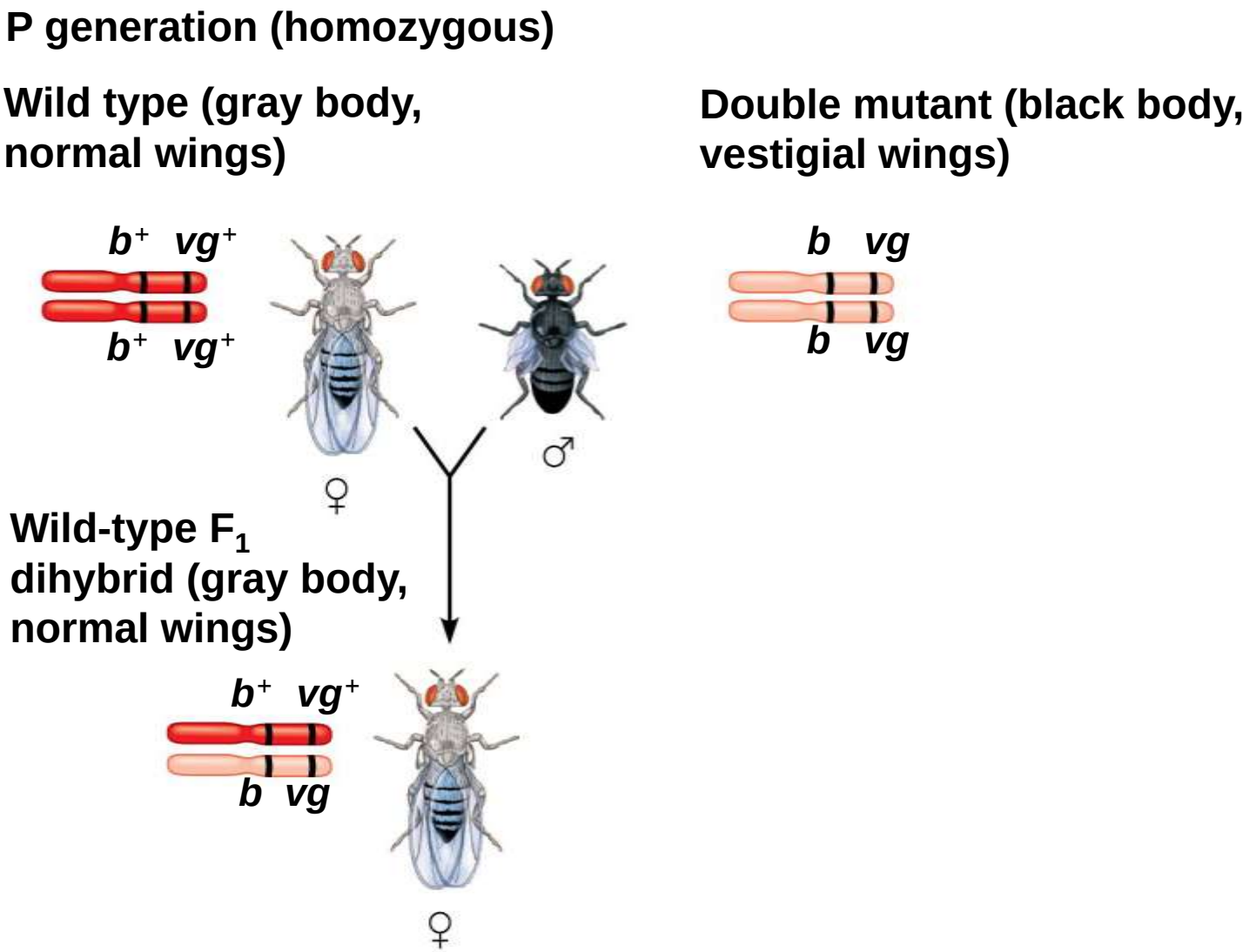


Figure 15.10b

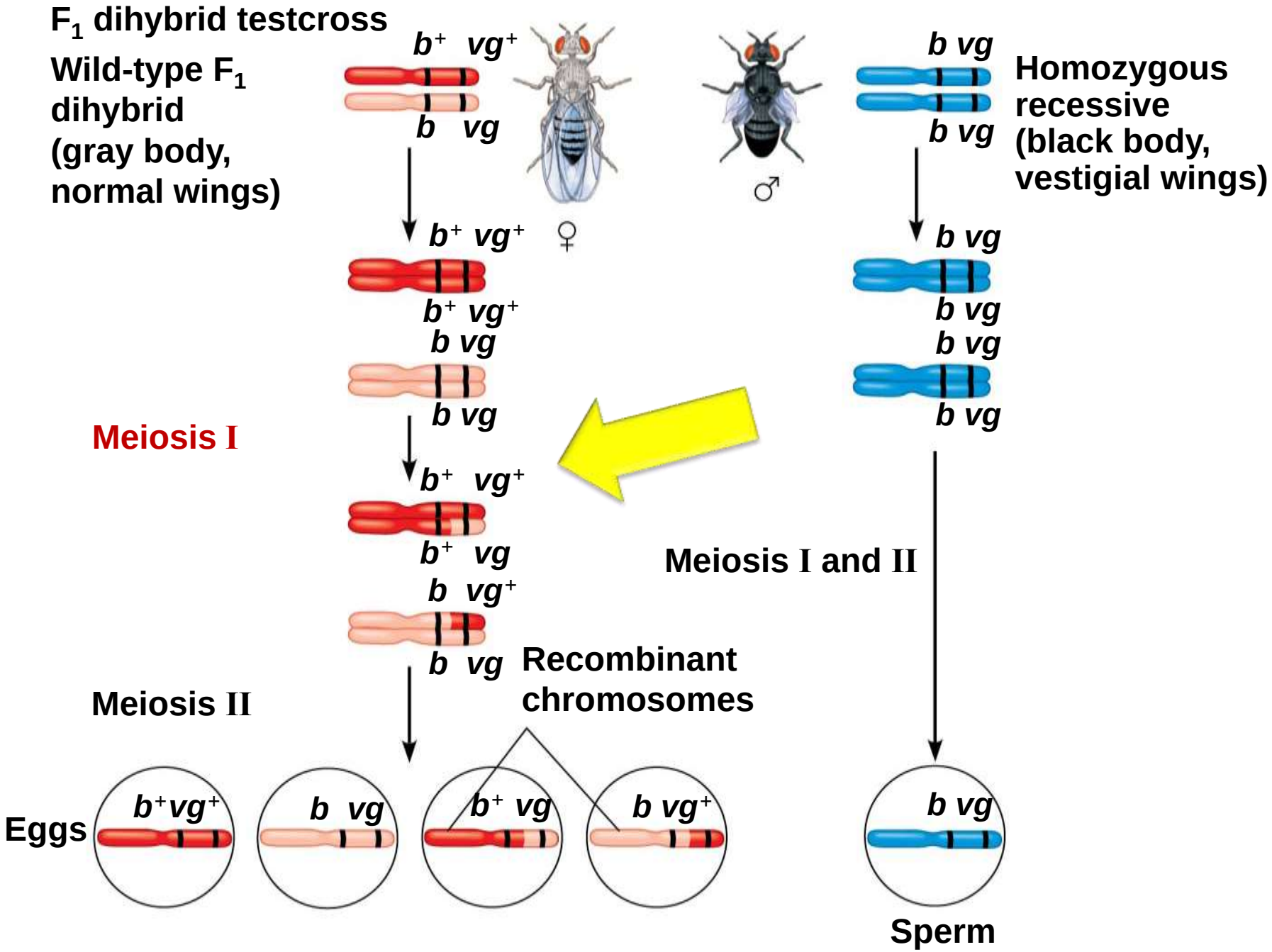
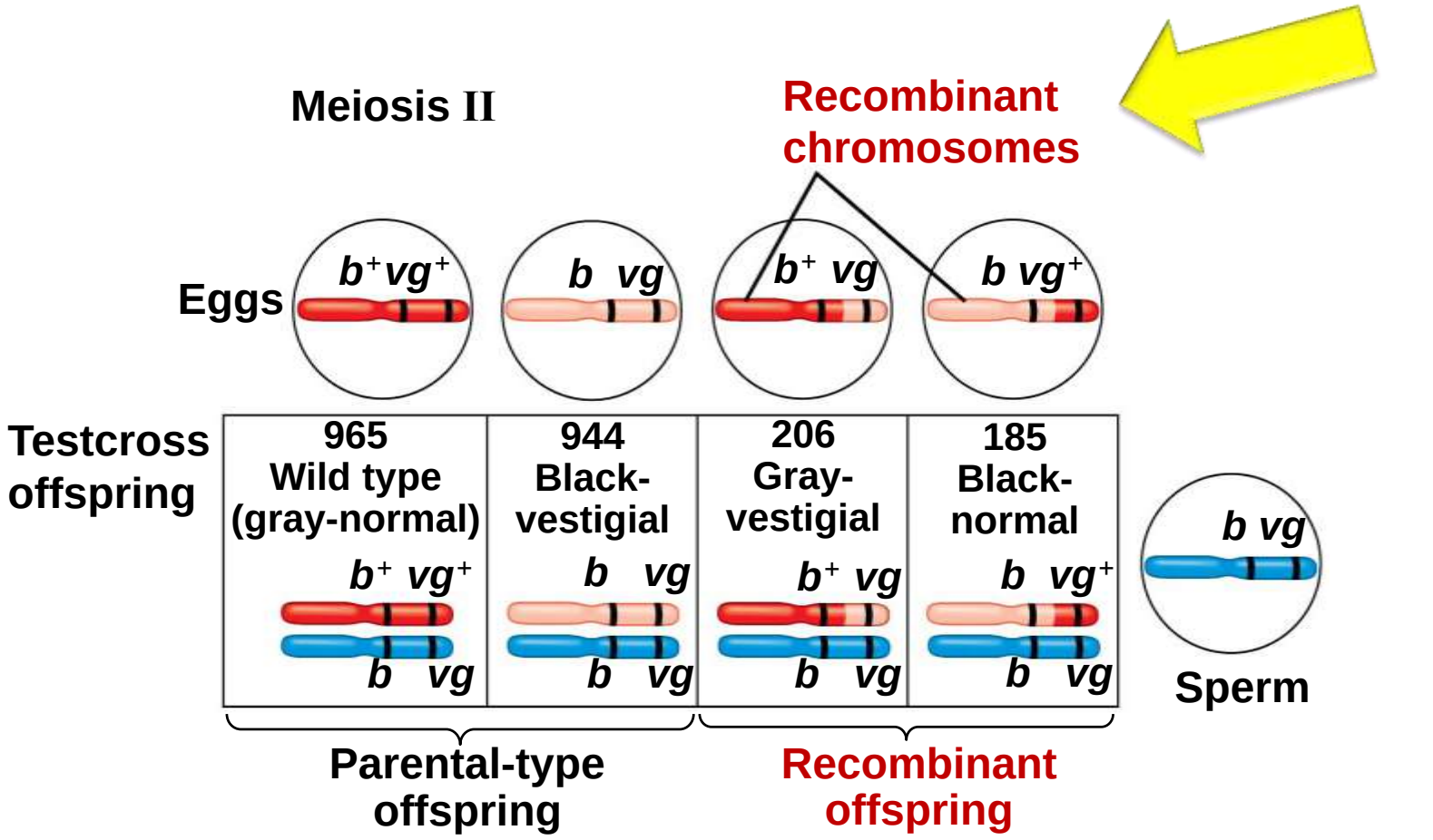


Figure 15.10c

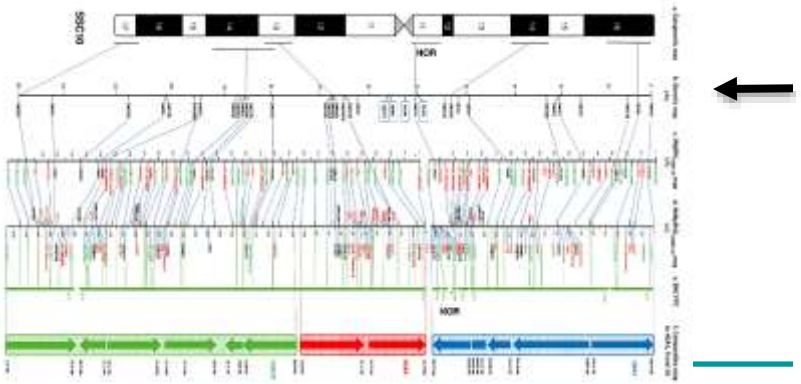


$$\text{Recombination frequency} = \frac{\text{391 recombinants}}{\text{2,300 total offspring}} \times 100 = 17\%$$

Mapping the Distance Between Genes Using Recombination Data: *Scientific Inquiry*

- Alfred Sturtevant, one of Morgan's students, constructed a **genetic map**, an ordered list of the genetic loci along a particular chromosome

- Sturtevant predicted that *the farther apart two genes are, the higher the probability that a crossover will occur between them and therefore the higher the recombination frequency*

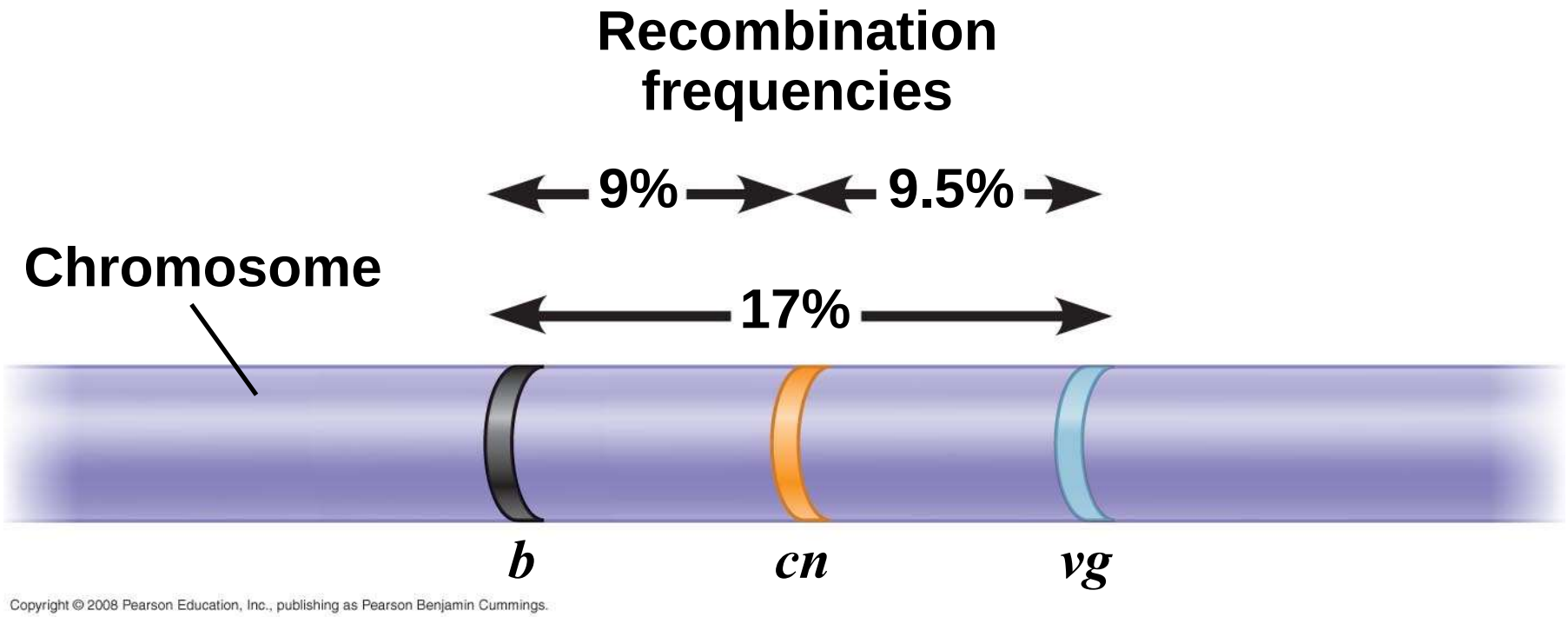


Constructing a Linkage Map

- A **linkage map** is a genetic map of a chromosome based on recombination frequencies
- Distances between genes can be expressed as **map units**; one map unit, or **centimorgan**, represents a 1% recombination frequency
- Map units indicate relative distance and order, not precise locations of genes

Fig. 15-11

Construction of a linkage map



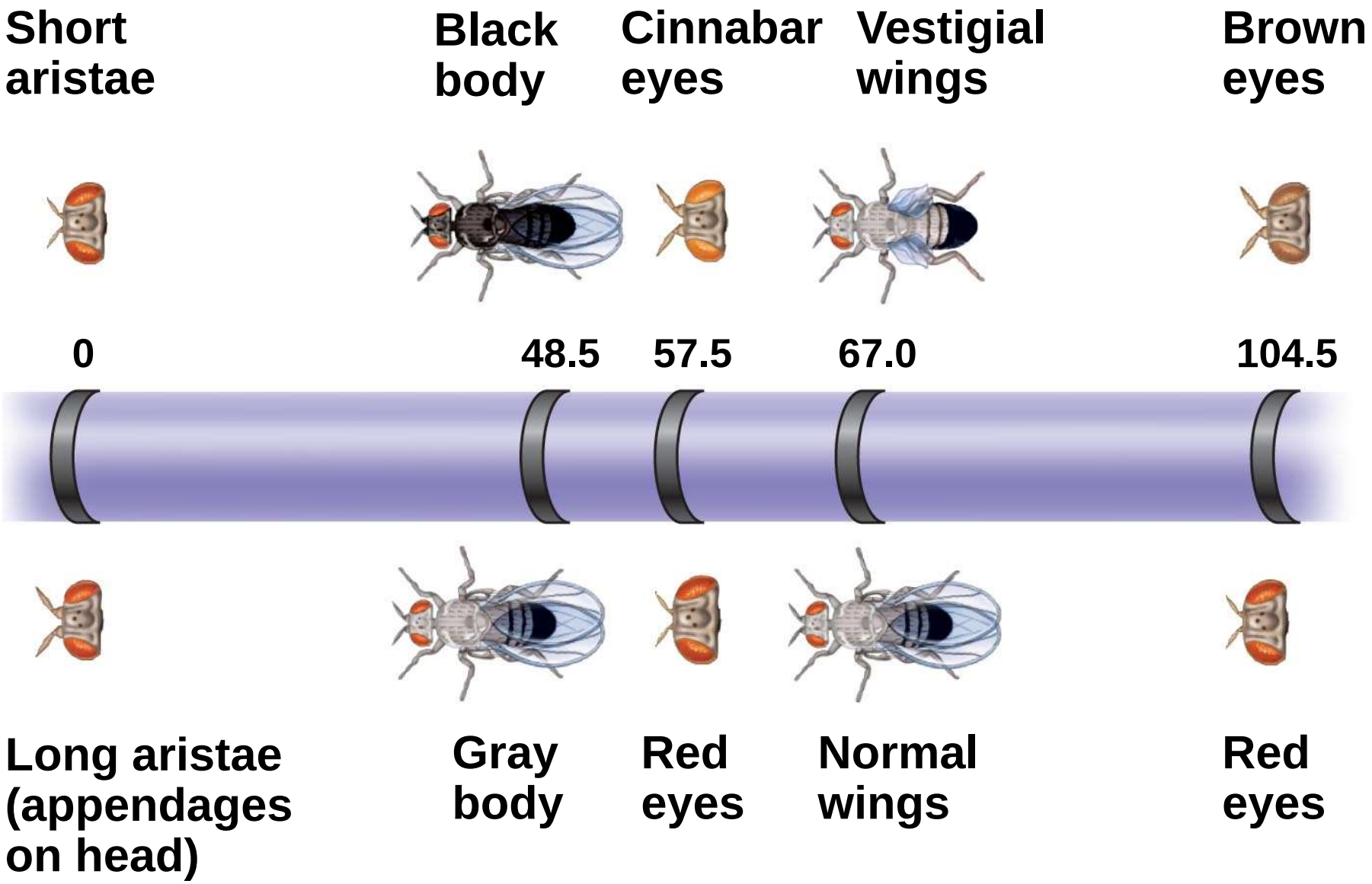
Physically linked may be genetically unlinked

- Genes that are far apart on the same chromosome can have a recombination frequency near 50%
  - Such genes are physically linked, but genetically unlinked, and behave as if found on different chromosomes

- Sturtevant used recombination frequencies to make linkage maps of fruit fly genes
- Using methods like chromosomal banding, geneticists can develop **cytogenetic maps** of chromosomes
- **Cytogenetic maps** indicate the positions of genes with respect to chromosomal features

Fig. 15-12

Mutant phenotypes

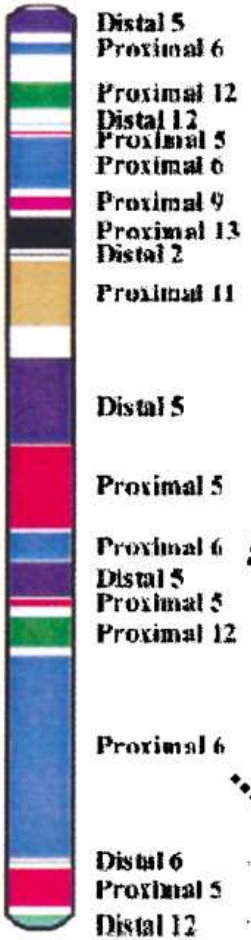


Wild-type phenotypes

Cytogenetic Map

of

Human chromosome 7



Conserved Synteny

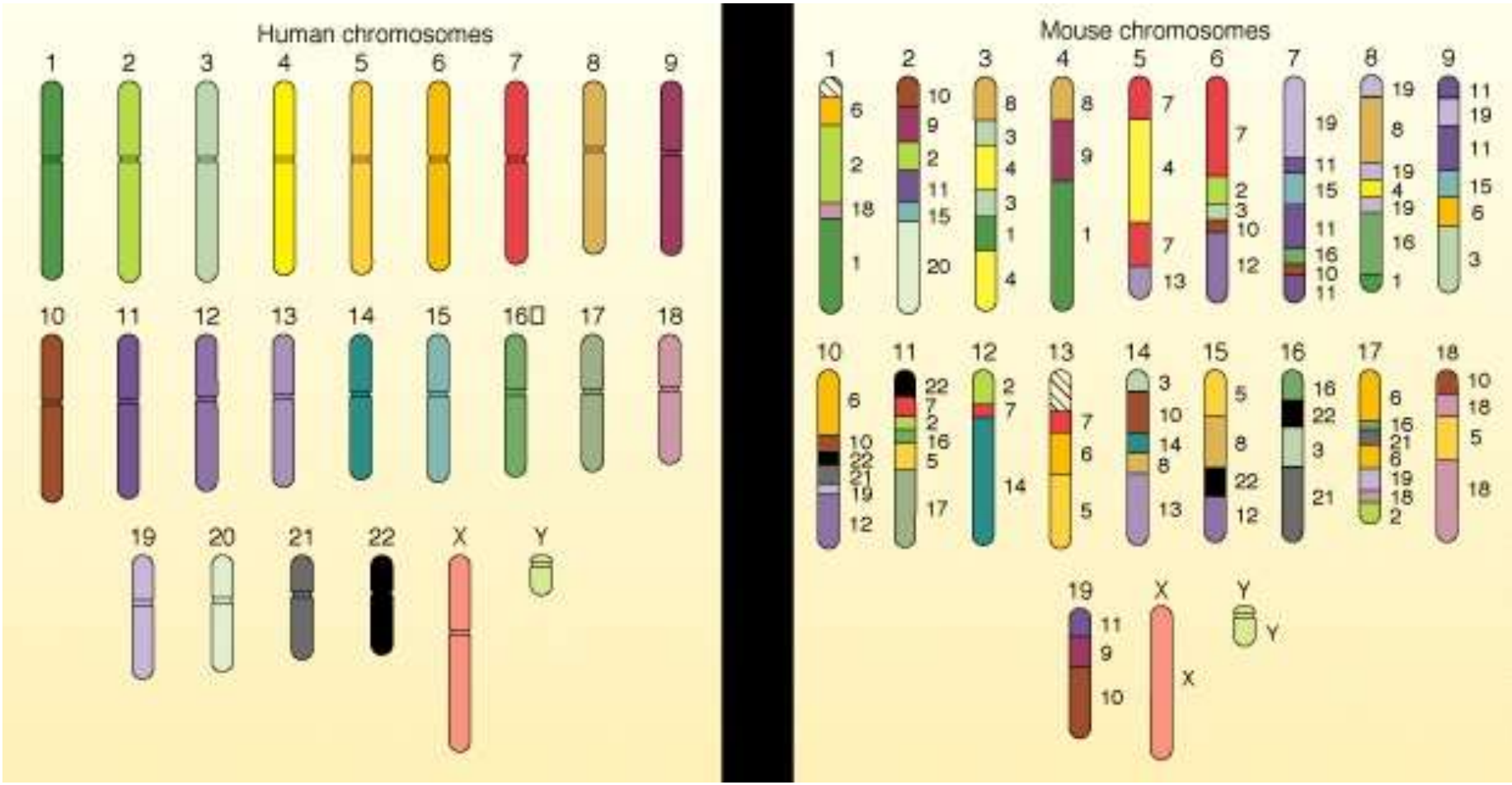
Conserved Segment

Human			Mouse		
STS links	cytogenetic position	gene symbol	chr	gene symbol	genetic positionX
	7q31	IPLA2(GAMMA)		1200006O19Rik	
	7q31.1-q31.2	NRCAM	12	Nrcam	22
	7q22	LAMB1	12	Lamb1-1	20
	7q31-q32	DLD	12	Dld	15.1
	7q31	SLC26A3	12	Slc26a3	11
	7q31	SLC26A4	12	Slc26a4	
	7q22.2	BAP29	12	Bcap29	17
	7pter-7cen	PP35	12	2310069P03Rik	
	7q31.1	HBP1	12	1700058O05Rik	
	7q22-q31.1	PRKAR2B	12	Prkar2b	
	7q22-q31.1	PRKAR2B	12	Prkar2b	
	7q22.3	PIK3CG	12	Pik3cg	
	7q22.3	LRRN3	12	Lrrn3	
	7q31.1	TFEC	2	Tefec	
	7q31.2	TES	6	Tes	1.5
	7q31.1	CAV2	6	Cav2	
	7q31.1	CAV1	6	Cav	
	7q31	MET	6	Met	4
	7q31.2-q31.3	CAPZA2	6	Capza2	3.05
	7q31.1-q31.3	ST7	6	St7	
	7q31	WNT2	6	Wnt2	4.2
	7q31.2	CFTR	6	Cftr	3.1
	7q31-q32	KCND2	6	Kcnd2	7.2
	7q31	ING3	6	Ing3	
	7q31.3	PTPRZ1	6	Ptprz	
	7q31.3	AASS	6	Lorsdh	4.5
	7q31-q32	SLC13A1	6	Slc13a1	4.7
	7q31.3	WASL	6	3110031I02Rik	
	7q31.3	HYALP1	6	4932701A20Rik	
	7q31.3	HYAL4	6	4632428M18Rik	
	7q31	GPR37	6	Gpr37	7.2
	7q31.32	FLJ13576	6	8430437G11Rik	
	7q31	GPR85	6	Gpr85	
	7q31.33	PPP1R3A	6	Ppp1r3a	
	7q31	*IMMP2L* *		Immp2l-pending	
	7q31	*MET* *	6	Met	4
	7q31	*SPAM1* *	6	Spam	7.2

http://genome.cshlp.org/content/13/1/1/F2.large.jpg

Human vs. Mouse genome

Pay attention to the distribution of color segments



http://fig.cox.miami.edu/Faculty/Dana/synteny.jpg

Concept 15.4: Alterations of chromosome number or structure cause some genetic disorders

- **Large-scale chromosomal alterations**
  - often lead to spontaneous abortions (miscarriages) or cause a variety of developmental disorders

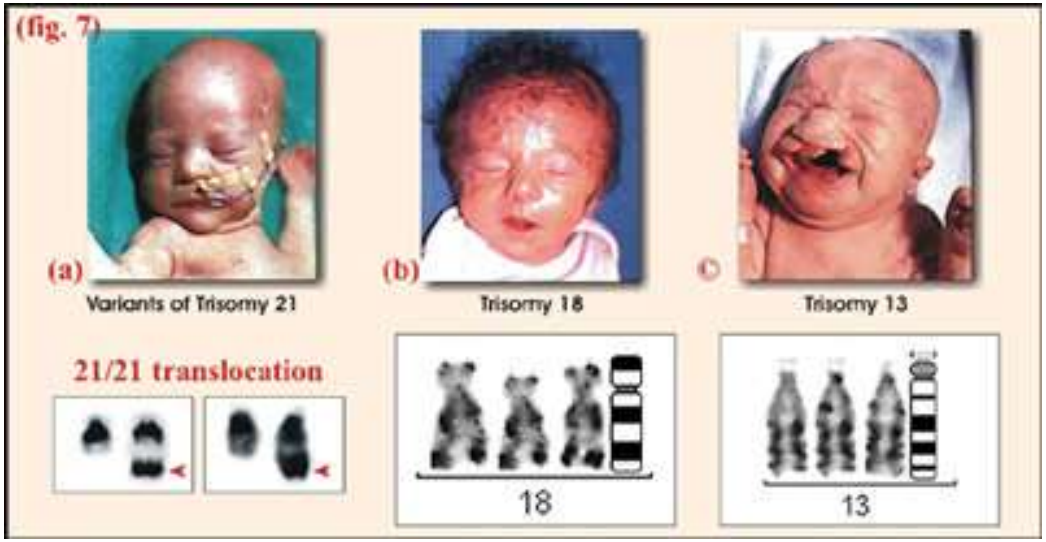


Image from: http://mattressessale.eu/tag/chromosomal-abnormalities

Abnormal Chromosome Number

- In **nondisjunction**, pairs of homologous chromosomes do not separate normally during meiosis
- As a result, one gamete receives two of the same type of chromosome, and another gamete receives no copy

Figure 15.13-1

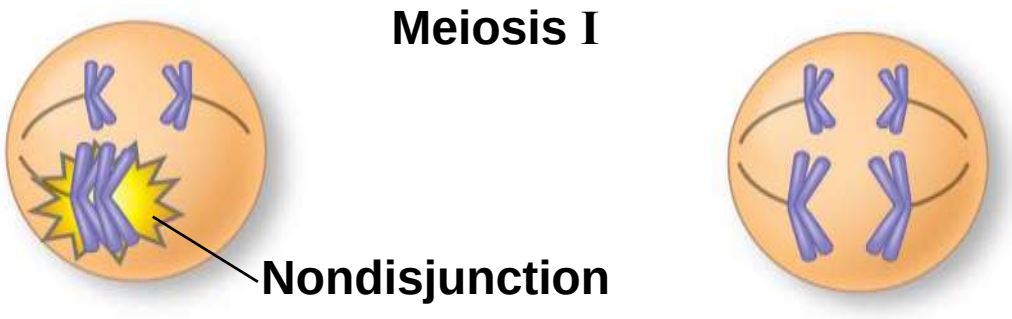


Figure 15.13-2

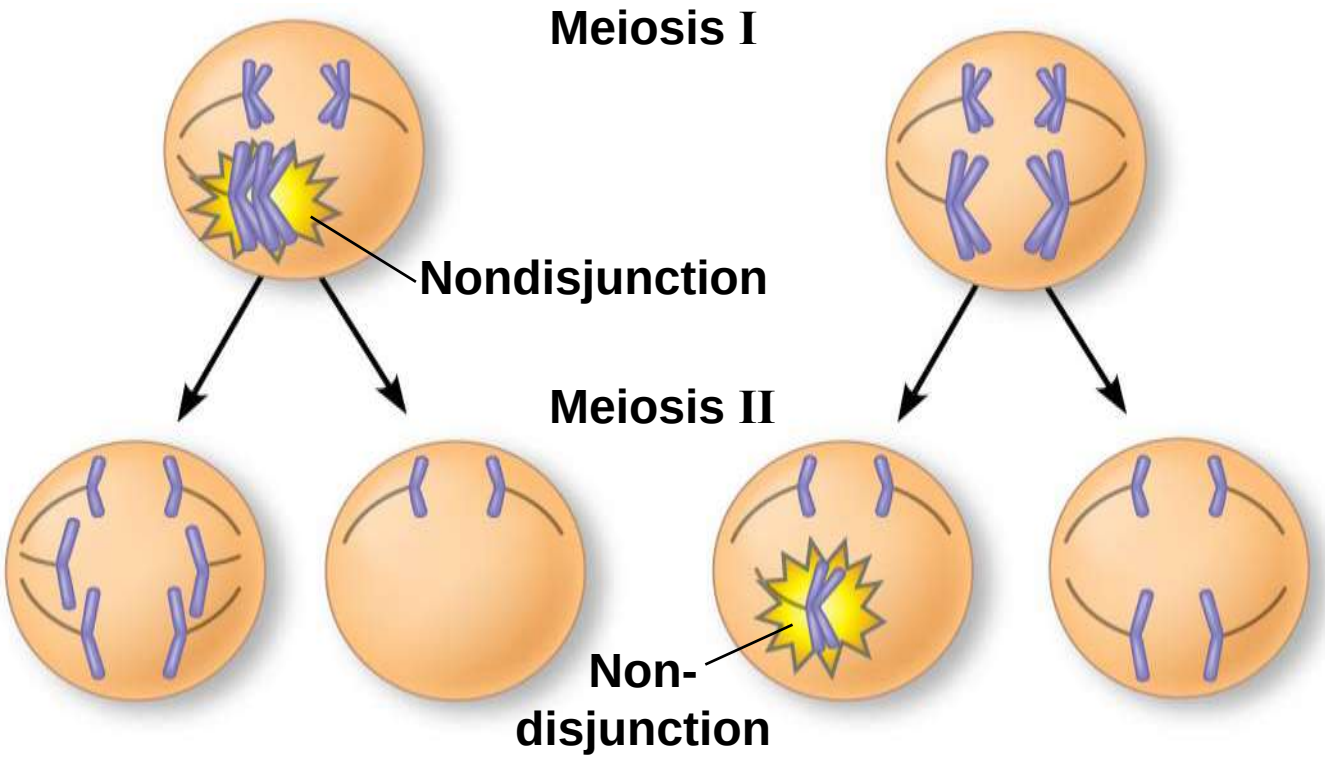
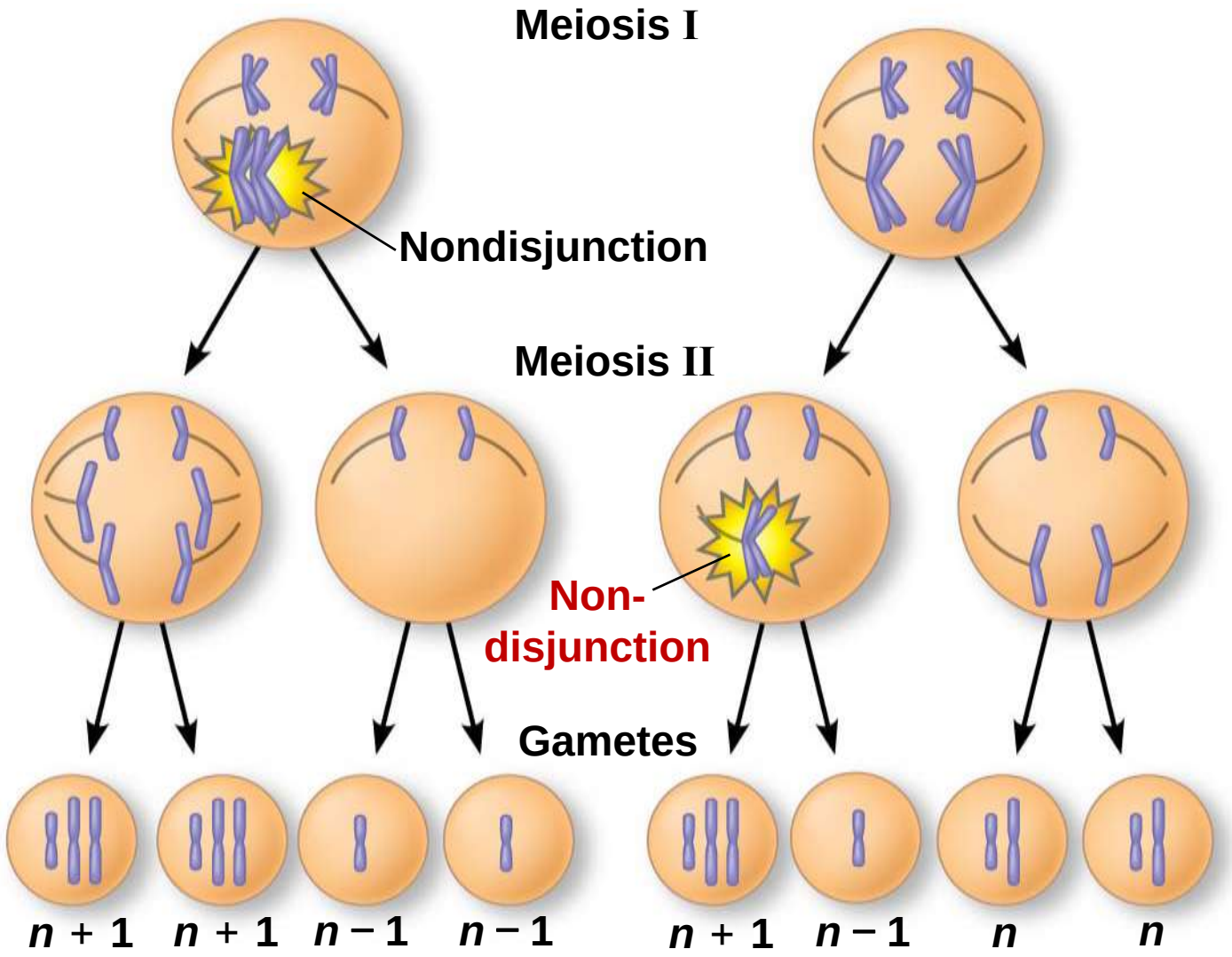


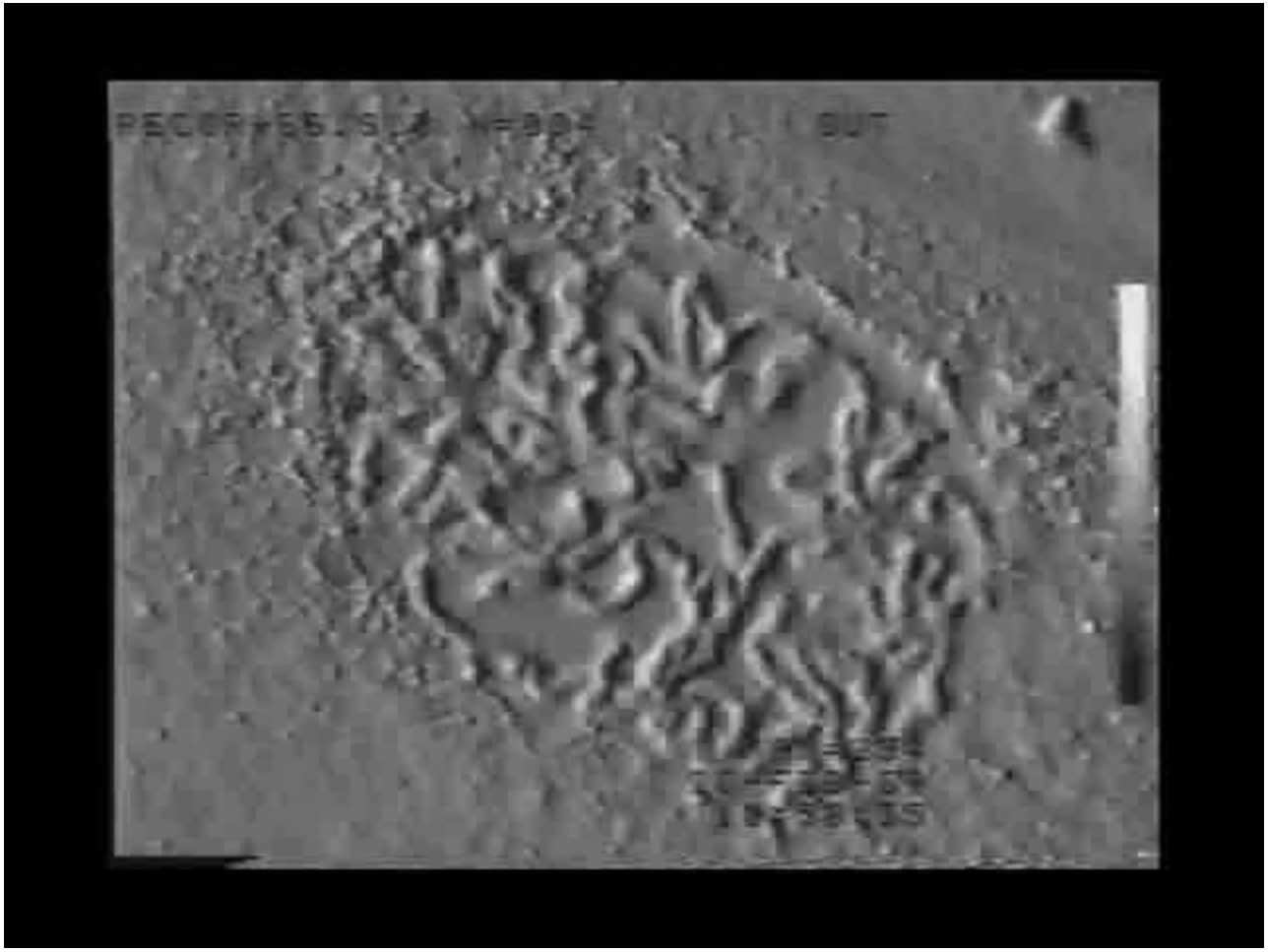
Figure 15.13-3



(a) Nondisjunction of homologous chromosomes in meiosis I

(b) Nondisjunction of sister chromatids in meiosis II

Video: Nondisjunction in Mitosis

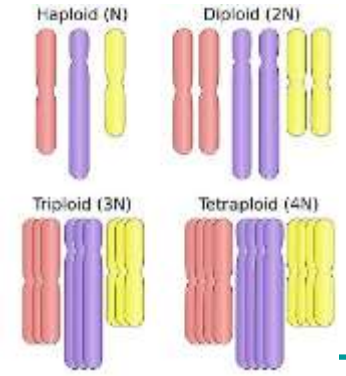


Abnormal chromosome number

- **Aneuploidy**非整倍體 results from the fertilization of gametes in which nondisjunction occurred
- Offspring with this condition have an abnormal number of a particular chromosome
    - A **monosomic** zygote has only one copy of a particular chromosome
    - A **trisomic** zygote has three copies of a particular chromosome

Abnormal chromosome number

- **Polyploidy** is a condition in which an organism has more than two complete sets of chromosomes
  - Triploidy (3*n*) is three sets of chromosomes
  - Tetraploidy (4*n*) is four sets of chromosomes
- Polyploidy is common in plants, but not animals
- Polyploids are more normal in appearance than aneuploids



Orchid!

Alterations of Chromosome Structure

- Breakage of a chromosome can lead to four types of changes in chromosome structure:
  - **Deletion** removes a chromosomal segment
  - **Duplication** repeats a segment
  - **Inversion** reverses a segment within a chromosome
  - **Translocation** moves a segment from one chromosome to another

See Figure next

Figure 15.14a

Alternations of chromosome structure

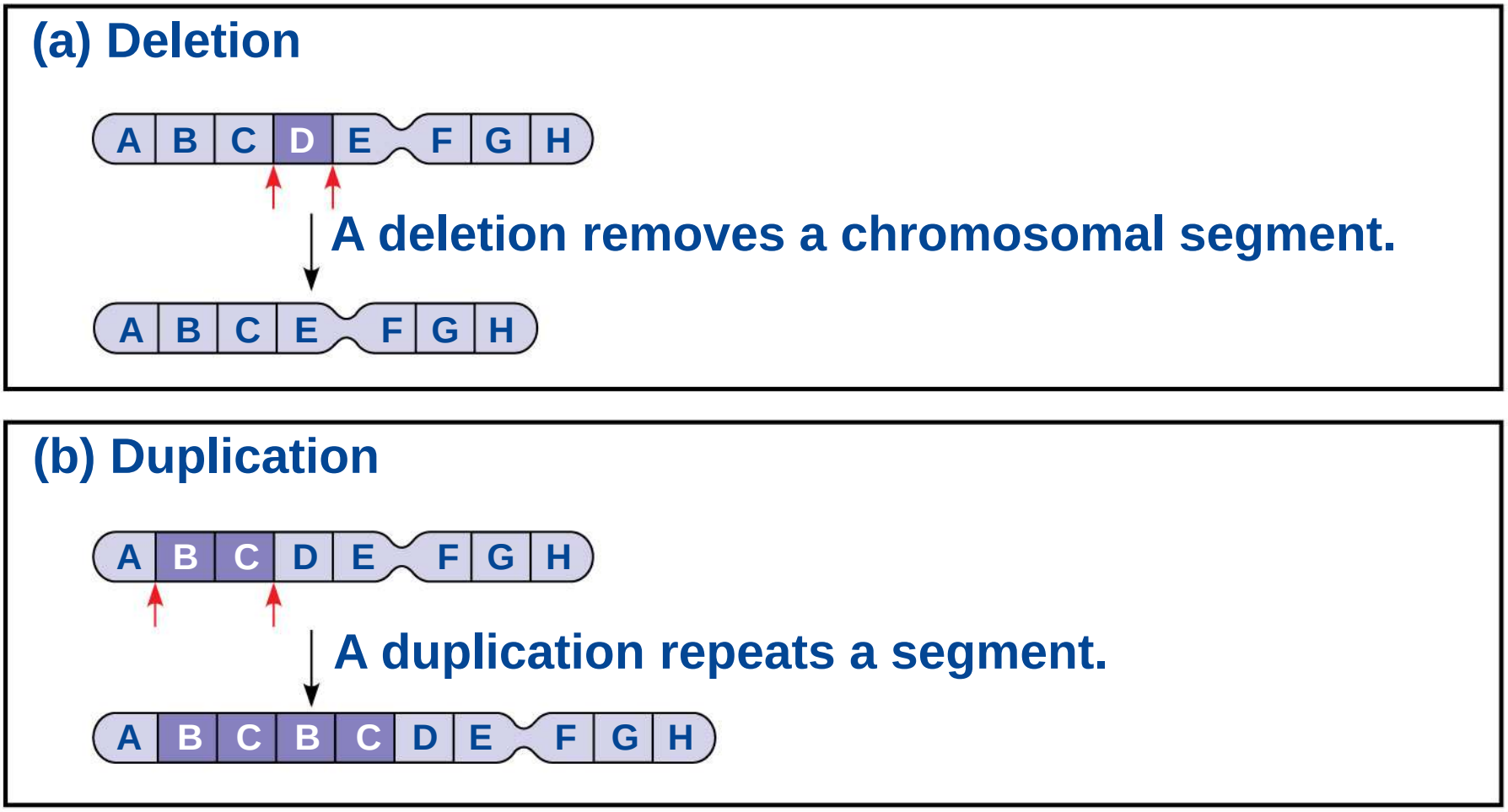
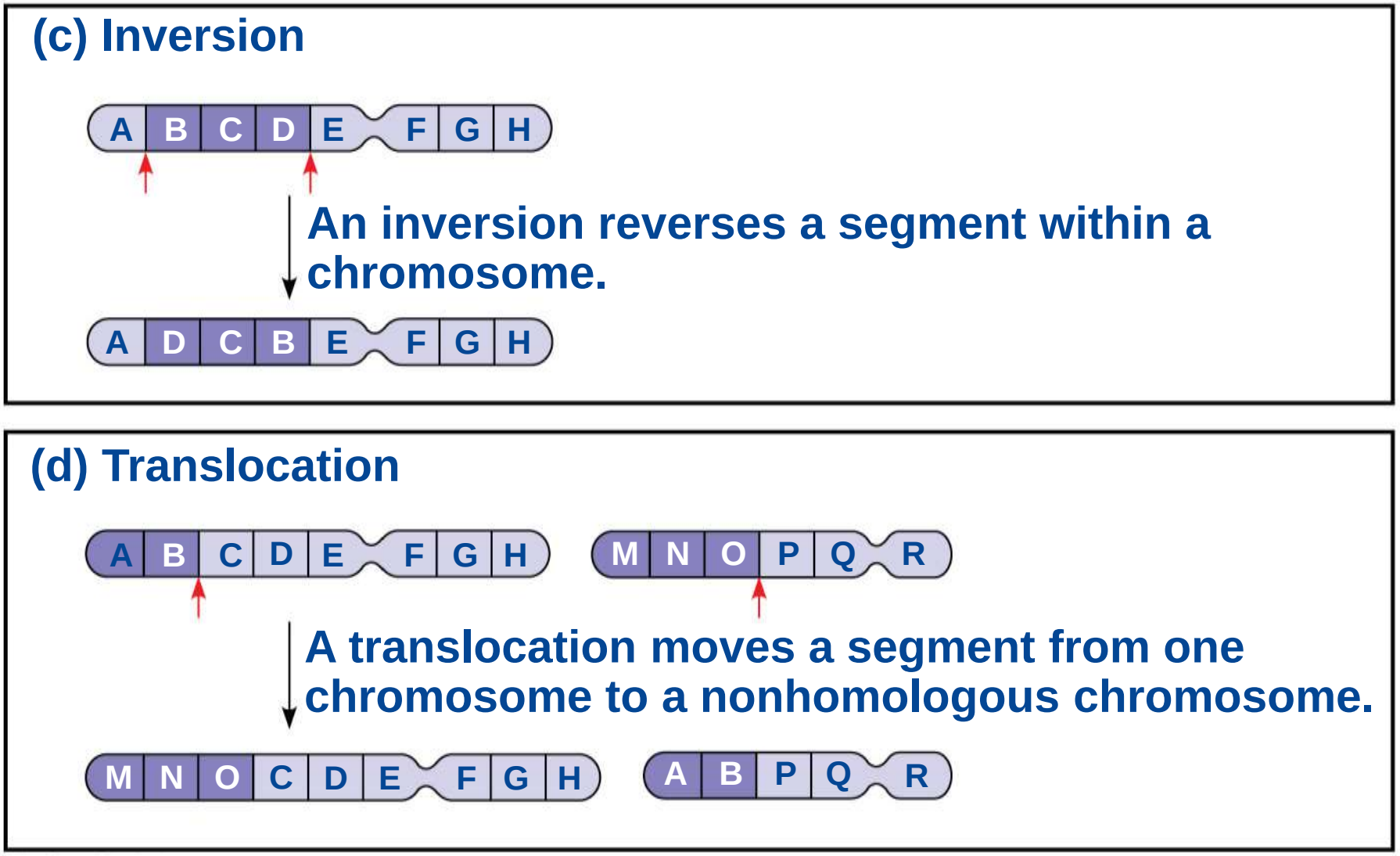


Figure 15.14b

Alternations of chromosome structure



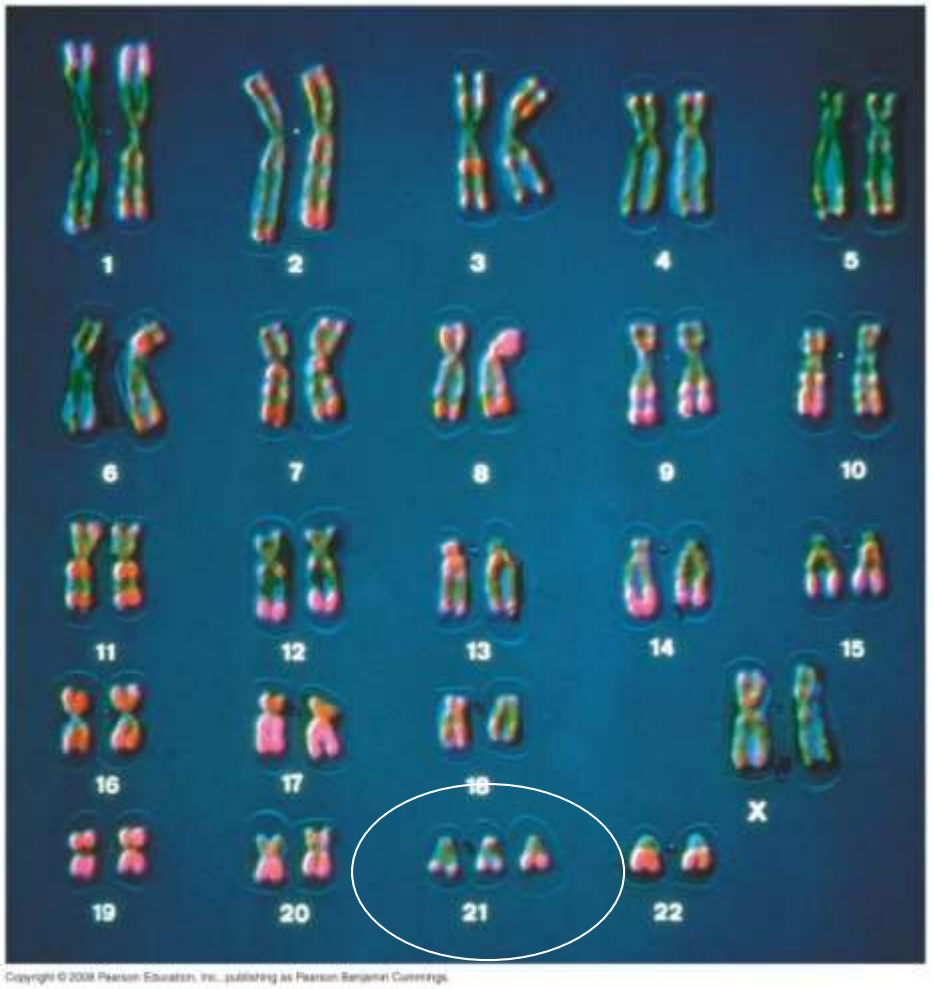
Human Disorders Due to Chromosomal Alterations

- Alterations of chromosome number and structure are associated with some serious disorders
  - Some types of aneuploidy appear to upset the genetic balance less than others, resulting in individuals surviving to birth and beyond
  - These surviving individuals have a set of symptoms, or **syndrome**, characteristic of the type of aneuploidy

Down Syndrome (Trisomy 21) 唐氏症症候群

- **Down syndrome** is an aneuploid condition that results from three copies of chromosome 21 (which results in overexpression of the genes on the aneuploid chromosome).
- It affects about one out of every 700 children born in the United States
- The frequency of Down syndrome *increases with the age of the mother*, a correlation that has not been fully explained

Fig. 15-15



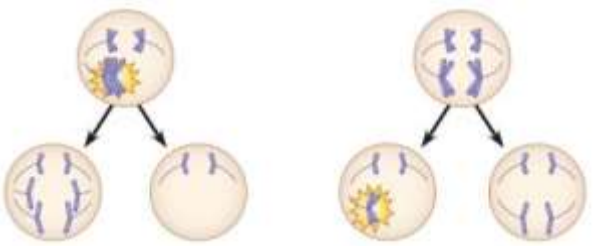
思考題:

高齡產婦為何較可能生下唐氏兒?

What is the origin of the maternal age effect in Trisomy 21?

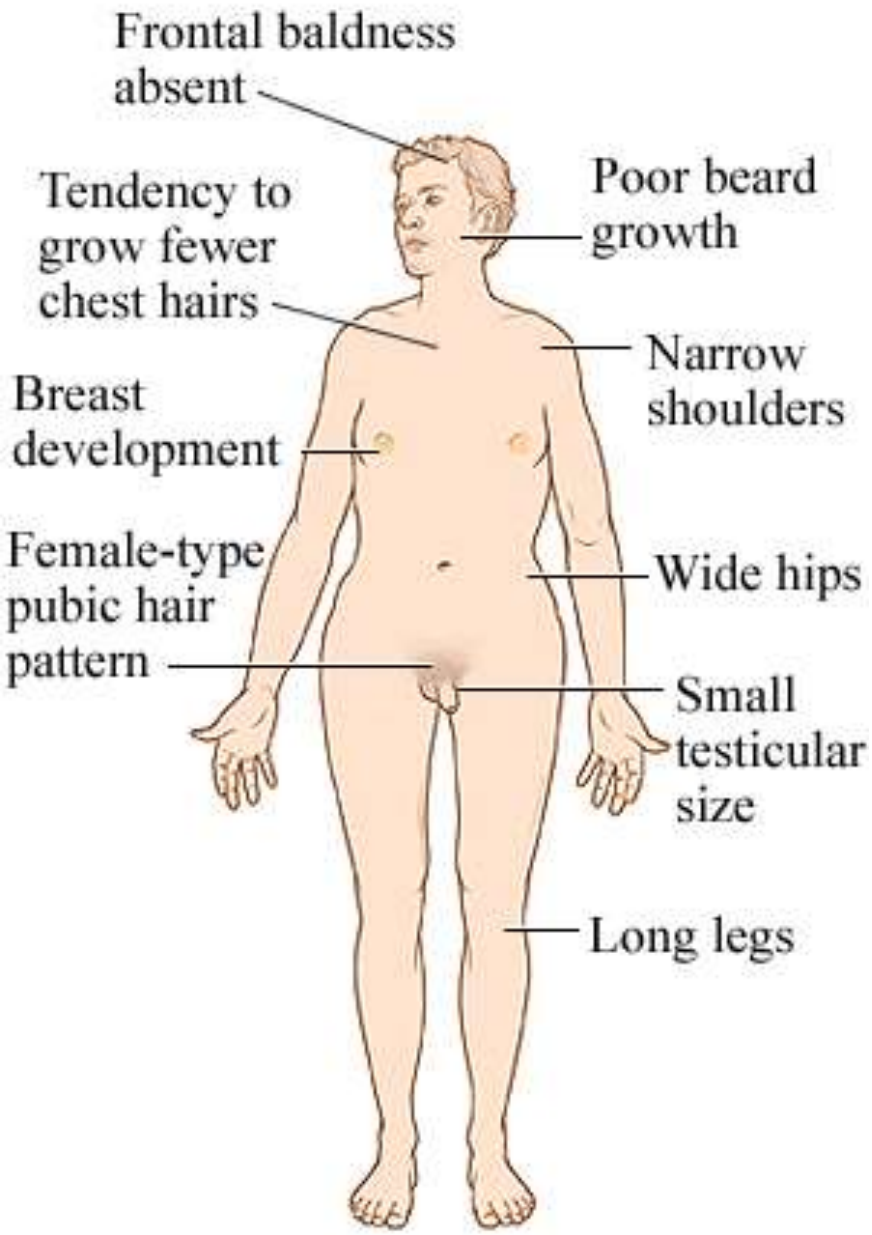
Aneuploidy 非整數倍體 *of Sex Chromosomes*

- **Nondisjunction** of sex chromosomes produces a variety of aneuploid conditions

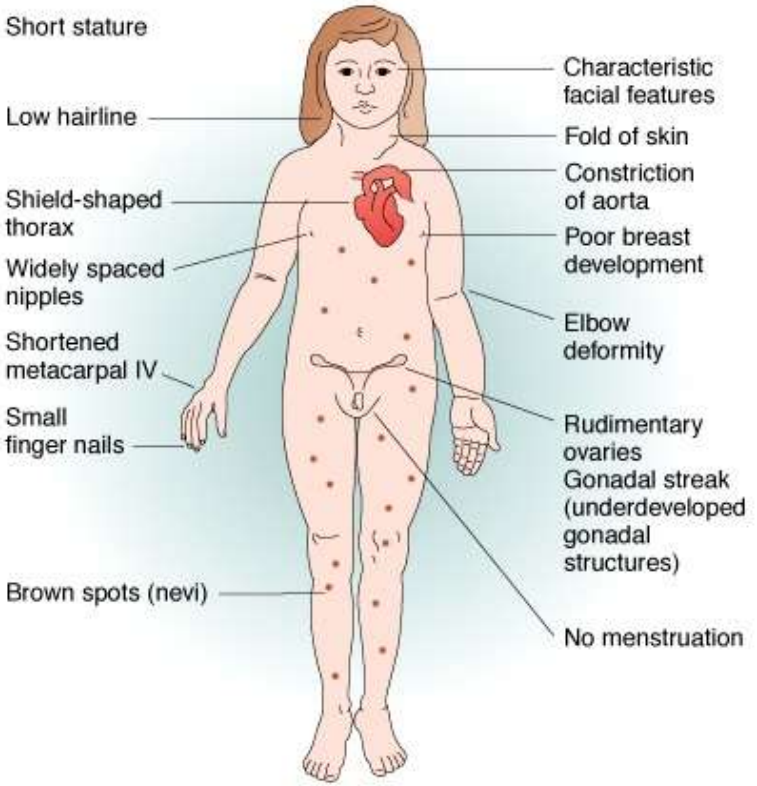


  - ***Klinefelter syndrome*** is the result of an extra chromosome in a male, producing **XXY** individuals
  - **Monosomy X**, called ***Turner syndrome***, produces **X0** females, who are sterile; it is the only known viable monosomy in humans

Klinefelter Syndrome



Turner Syndrome



Disorders Caused by Structurally Altered Chromosomes

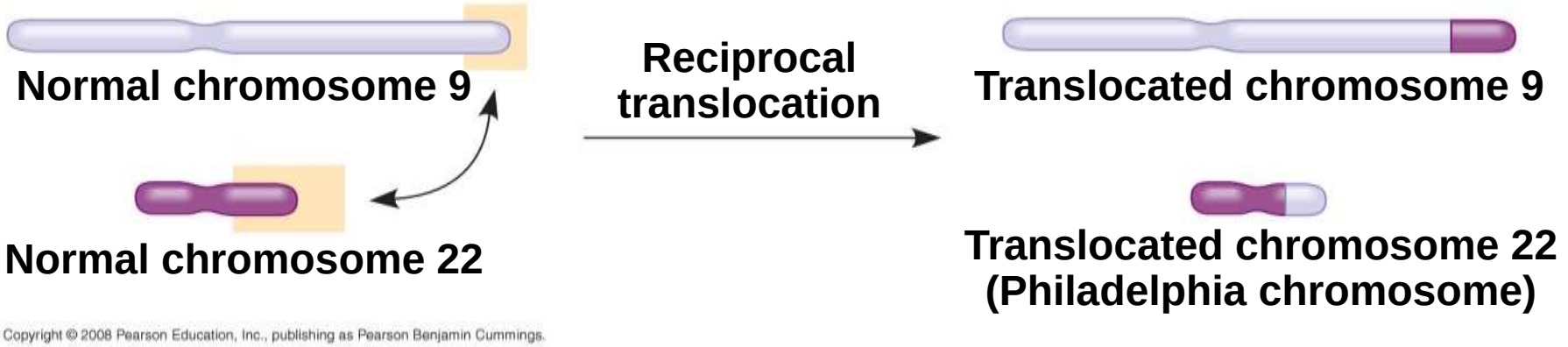
- The syndrome ***cri du chat*** ("cry of the cat"), results from a specific deletion in chromosome 5
  - A child born with this syndrome is mentally retarded and has a catlike cry (貓哭症); individuals usually die in infancy or early childhood

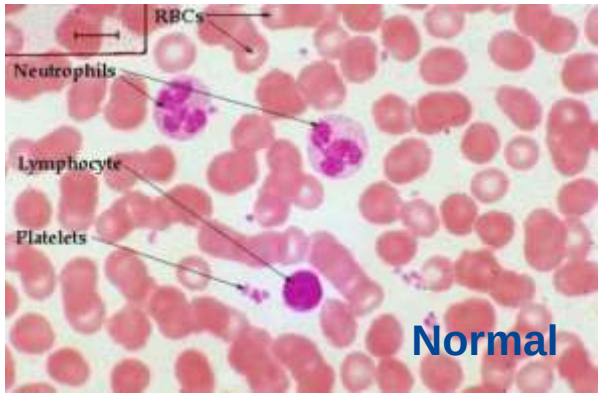
Disorders Caused by Structurally Altered Chromosomes

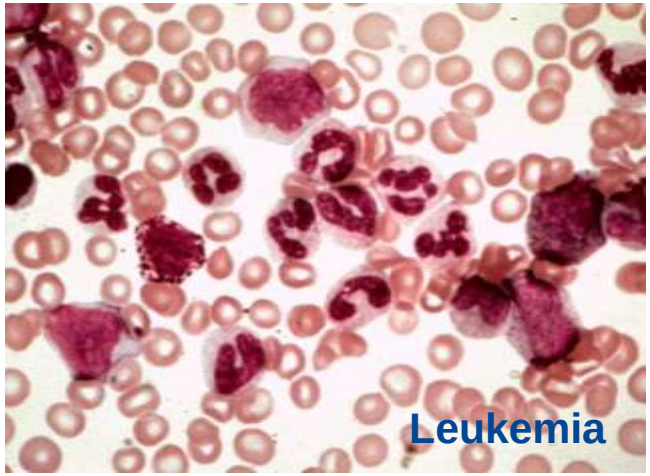
- Certain cancers, including *chronic myelogenous leukemia* (CML), are caused by translocations of chromosomes
- ***Chronic myelogenous leukemia*** (CML / 慢性骨髓性白血病), are caused by translocations of chromosomes (chromosome 9 and 22)
- The resulting shortened chromosome 22 is called the *Philadelphia chromosome*.

Fig. 15-16

Translocation associated with chronic myelogenous leukemia (CML) 慢性骨髓性白血病







Concept 15.5: Some inheritance patterns are exceptions to the standard chromosome theory

- There are two normal exceptions to Mendelian genetics
  - One exception involves genes located **in** the nucleus – **genomic imprinting**
  - The other exception involves genes located **outside** the nucleus – **organelle genes**

Genomic Imprinting (基因印記)

- For a few mammalian traits, the phenotype depends on which parent passed along the alleles for those traits
- Such variation in phenotype is called **genomic imprinting**
- Genomic imprinting involves the **silencing of certain genes** that are “stamped” with an imprint during gamete production (sperm or eggs)

Figure 15.17a

得自父親的

Paternal chromosome

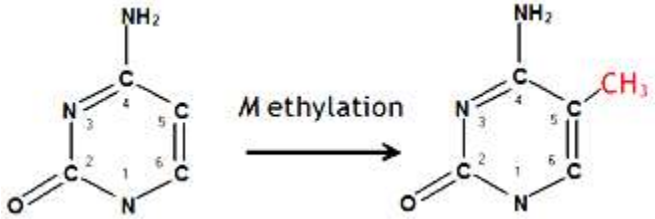
Maternal chromosome

Normal *Igf2* allele is expressed.

Normal *Igf2* allele is not expressed.

Normal-sized mouse (wild type)

(a) Homozygote



Chemical Changes on DNA!

Figure 15.17b

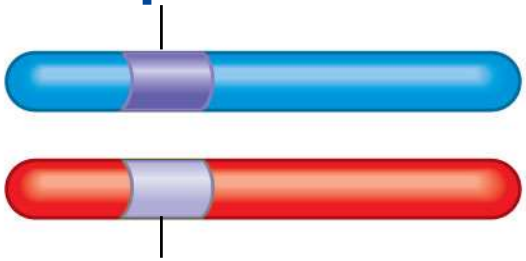
Mutant *Igf2* allele inherited from mother

Normal-sized mouse (wild type)

Mutant *Igf2* allele inherited from father

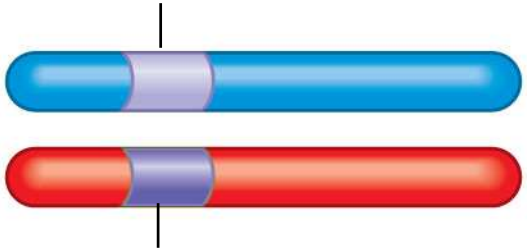
Dwarf mouse (mutant)

Normal *Igf2* allele is expressed.



Mutant *Igf2* allele is not expressed.

Mutant *Igf2* allele is expressed.



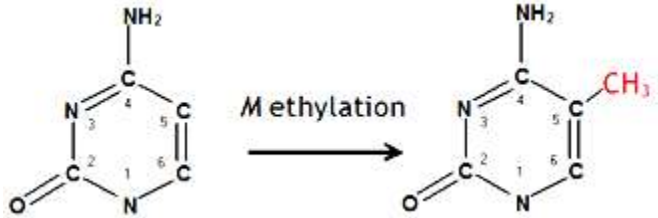
Normal *Igf2* allele is not expressed.

(b) Heterozygotes

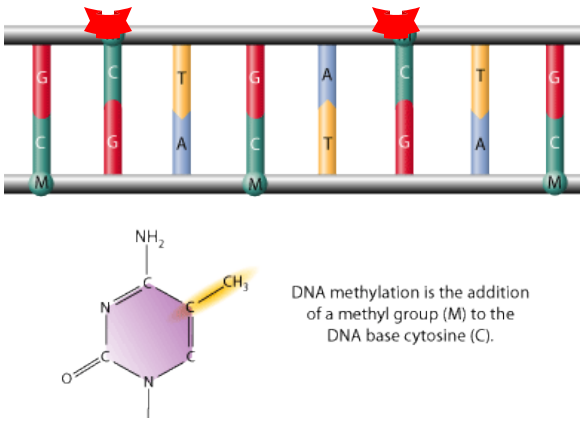
Mutant phenotype is seen only when **the father** contributed the mutant allele

Summary on **genomic Imprinting**

- It appears that imprinting is the result of the methylation (addition of $-CH_3$) of cysteine nucleotides



Chemical Changes on DNA!



- Genomic imprinting is thought to affect only a small fraction of mammalian genes
- Most imprinted genes are critical for embryonic development

Inheritance of Organelle Genes (胞器基因)

- Extranuclear genes (or cytoplasmic genes) are found in organelles in the cytoplasm
- Mitochondria, chloroplasts, and other plant plastids (植物色質體) carry small circular DNA molecules
- Extranuclear genes are inherited maternally because the zygote's受精卵 cytoplasm comes from the egg
- The first evidence of extranuclear genes came from studies on the inheritance of yellow or white patches on leaves of an otherwise green plant

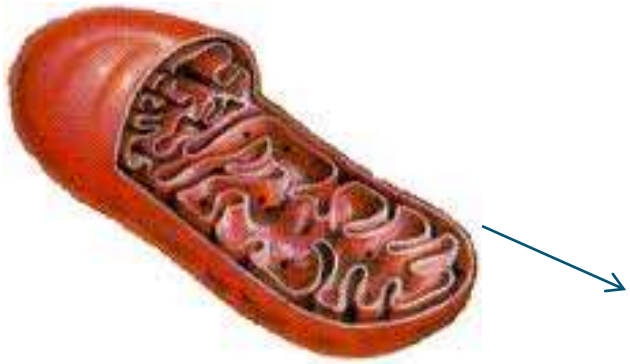
Variegated (striped or spotted) leaves from *English Holly* (冬青; *Ilex aquifolium*)– mutations in pigment genes located in plastids

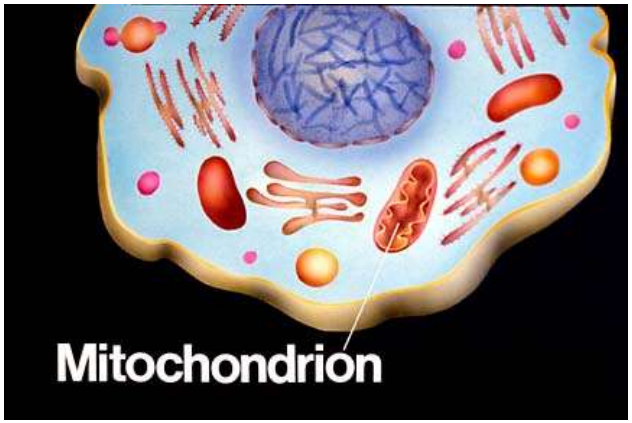
Popular X’mas decoration

Do you know “Mistletoe/槲寄生“?

Mitochondria diseases

- Some defects in mitochondrial genes prevent cells from making enough ATP and result in diseases that affect the muscular and nervous systems
  - For example, **mitochondrial myopathy** (線粒體肌病) and **Leber's hereditary optic neuropathy** (雷伯氏遺傳性視神經萎縮症)



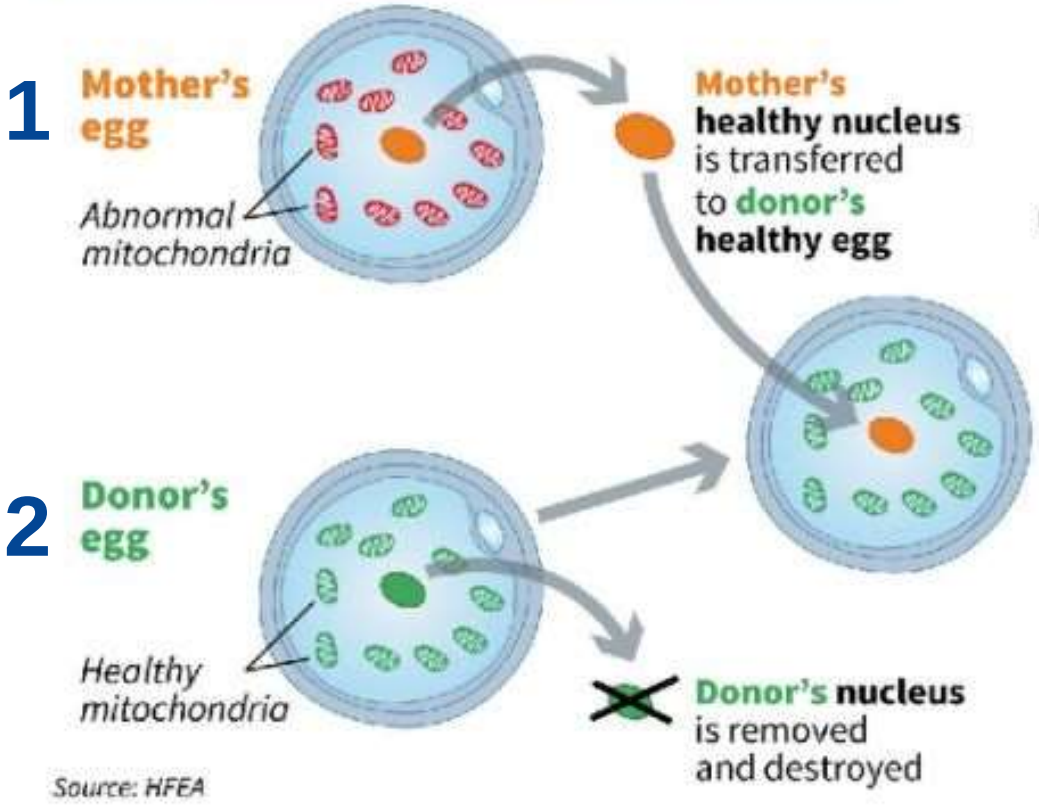


Preventing mitochondrial diseases

Three-parent babies

Treatment using DNA from 3 people, designed to enable women carrying hereditary diseases to have healthy, genetically-related children

In-vitro fertilisation (IVF) using mitochondrial DNA



Source: HFEA

Mitochondrion

Energy-generating "powerhouse" within cell. **Mutations in mitochondrial DNA can cause serious diseases**

Potential treatment risk

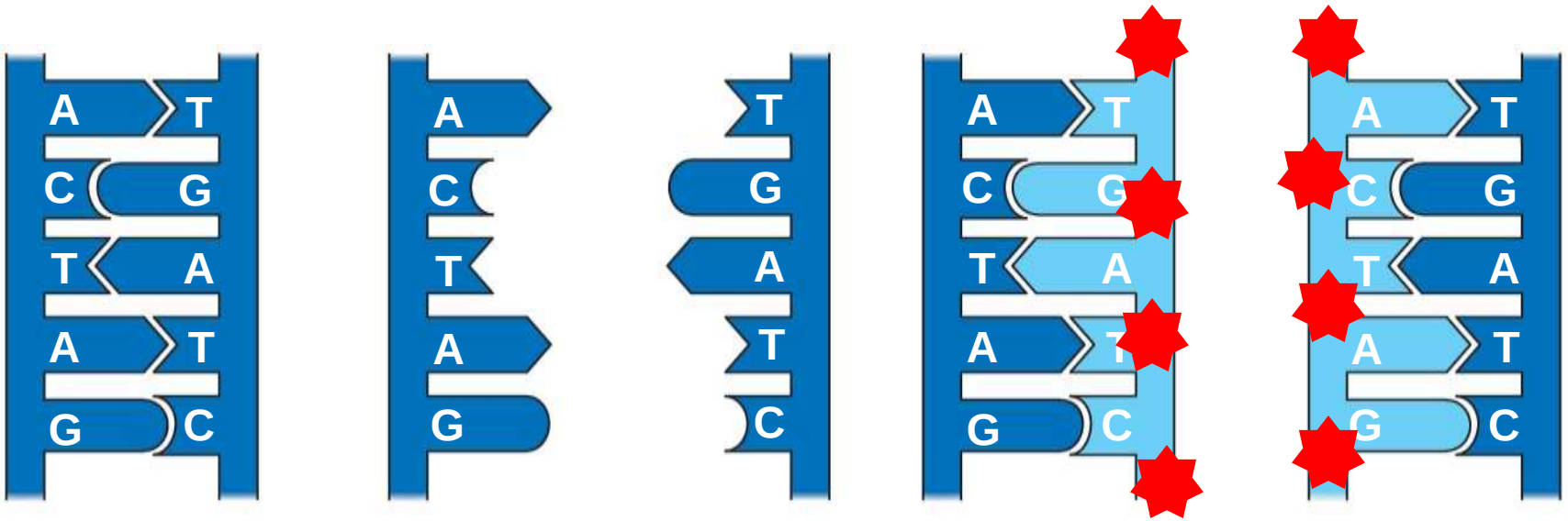
Uncertainties remain over the interaction between the mother's nuclear DNA and the donor's mitochondrial DNA

You should now be able to:

1. Explain the chromosomal theory of inheritance and its discovery
2. Explain why sex-linked diseases are more common in human males than females
3. Distinguish between sex-linked genes and linked genes
4. Explain how meiosis accounts for recombinant phenotypes
5. Explain how linkage maps are constructed

6. Explain how nondisjunction can lead to aneuploidy
7. Define trisomy, triploidy, and polyploidy
8. Distinguish among deletions, duplications, inversions, and translocations
9. Explain genomic imprinting
10. Explain why extranuclear genes are not inherited in a Mendelian fashion

DNA : the basic concept



(a) Parent molecule

(b) Separation of strands

(c) "Daughter" DNA molecules, each consisting of one parental strand and one new strand

Fig. 16-9-3

主流的模式生物

酵母菌 (*Saccharomyces cerevisiae* 與 *Schizosaccharomyces pombe*)
線蟲 (*Caenorhabditis elegans*)
果蠅 (*Drosophila melanogaster*)
斑馬魚 (*Denio rerio*)
小鼠 (*Mus musculus*)
阿拉伯芥/擬南芥 (*Arabidopsis thaliana*)

應用於這六種模式生物的遺傳學技術與細胞分子生物技術都已臻於完備，所以是最為普遍的模式生物。

這些生物因為具備了幾項條件而受到研究者的青睞：

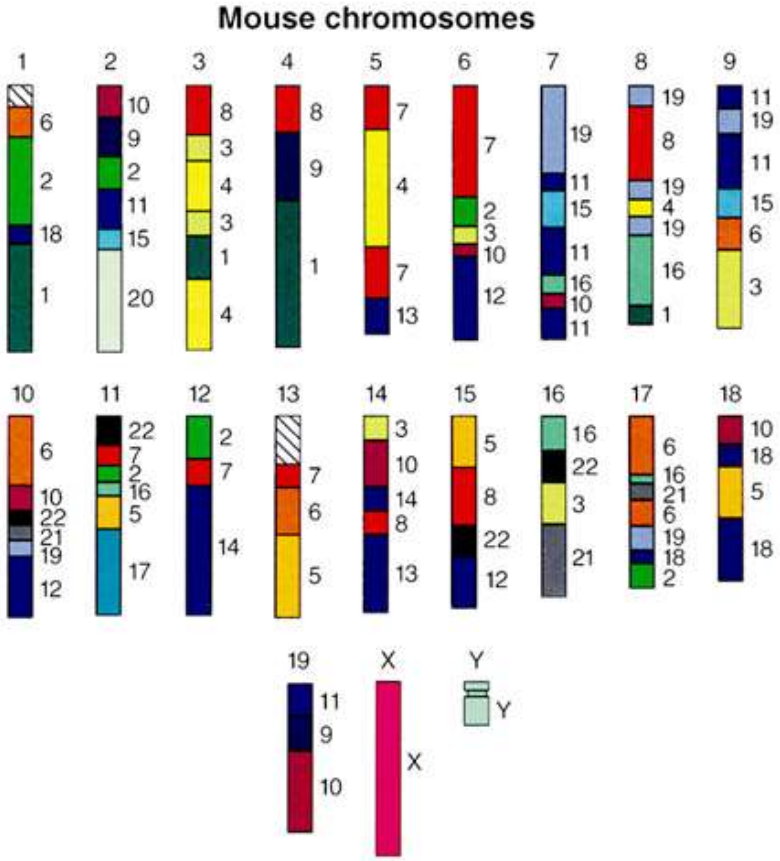
- 這些生物都是體積不大，易於繁殖，所以有利於在實驗室中培養保存與操作。
- 模式生物都有一些其他生物所不能媲美的特質，例如：酵母菌是單細胞的真核生物，組成不複雜，基因體的規模也很小，有利於把十分複雜的生命現象化約到可供進行實驗操控的研究。此外，分子遺傳學家也找到許多可供篩選或鑑識的基因產物標記(marker)，所以要進行各種實驗都十分方便。

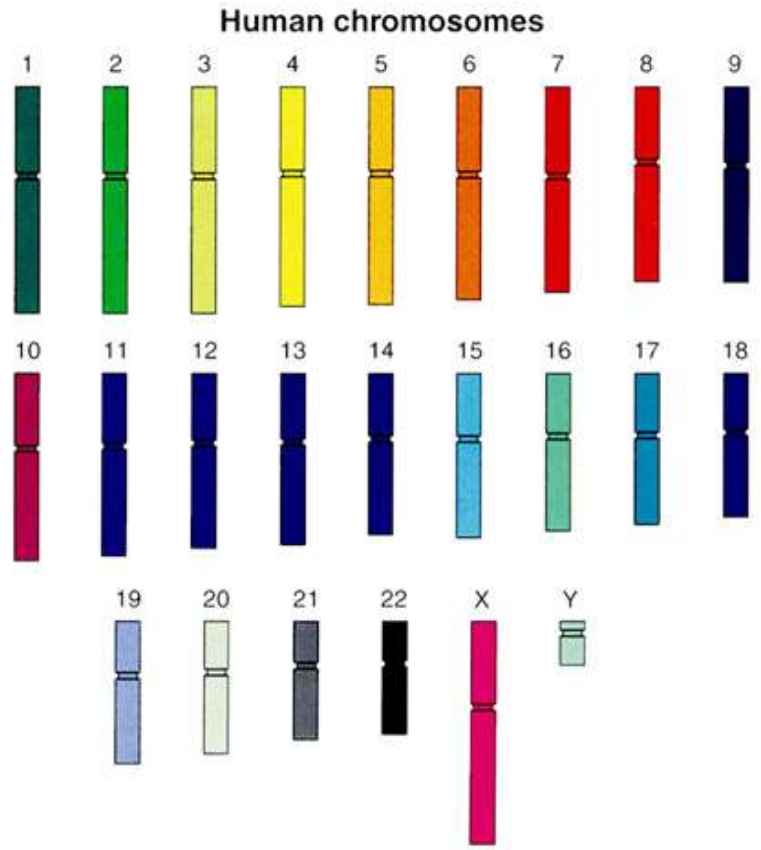
至於線蟲細胞發育的過程與每個細胞的命運已經久為人知，所以是研究發育生物學的一項利器。果蠅更是傳統遺傳學使用的材料，而且果蠅的性狀特徵繁多，有許多突變種，從型態上的複眼顏色到行為上的趨光反應都能觀察與篩選，不論是研究基因調控或體制形成(pattern formation)，或是學習行為與趨化反應的分子基礎，都能以果蠅為對象。擬南芥被譽之為"植物的果蠅"，是研究植物發育遺傳與生裡的好材料；老鼠就更不必提了，這是最類似人類的模式生物，長得快又生得多，也有許許多多不同的突變品系，但是因為老鼠已演化到十分高階的複雜度，實驗技術操縱就複雜困難多了，因此有人倡議用斑馬魚來彌補小鼠的缺陷, 因為斑馬魚體積更小子代更多生活週期更短，且同為脊椎動物，對於研究所得的結果更有機會可以類推適用於人類醫學上。

其實模式生物的選定除了經過前人有目的的選擇倡議之外，更有一種自發的正向回饋機轉。**當某種模式生物研究的人愈多，發展出適合該生物特性的種種實驗方法與工具就愈多，就更有利於研究探索出新知識，然後吸引更多人利用該模式生物來探討種種生命現象**，如此循環最後便造成幾種生物一枝獨秀，寡占大多數研究人員的關愛眼神。

Original text from: http://seacity2.blogspot.tw/2001/03/blog-post.html

Mouse and Human Genetic Similarities



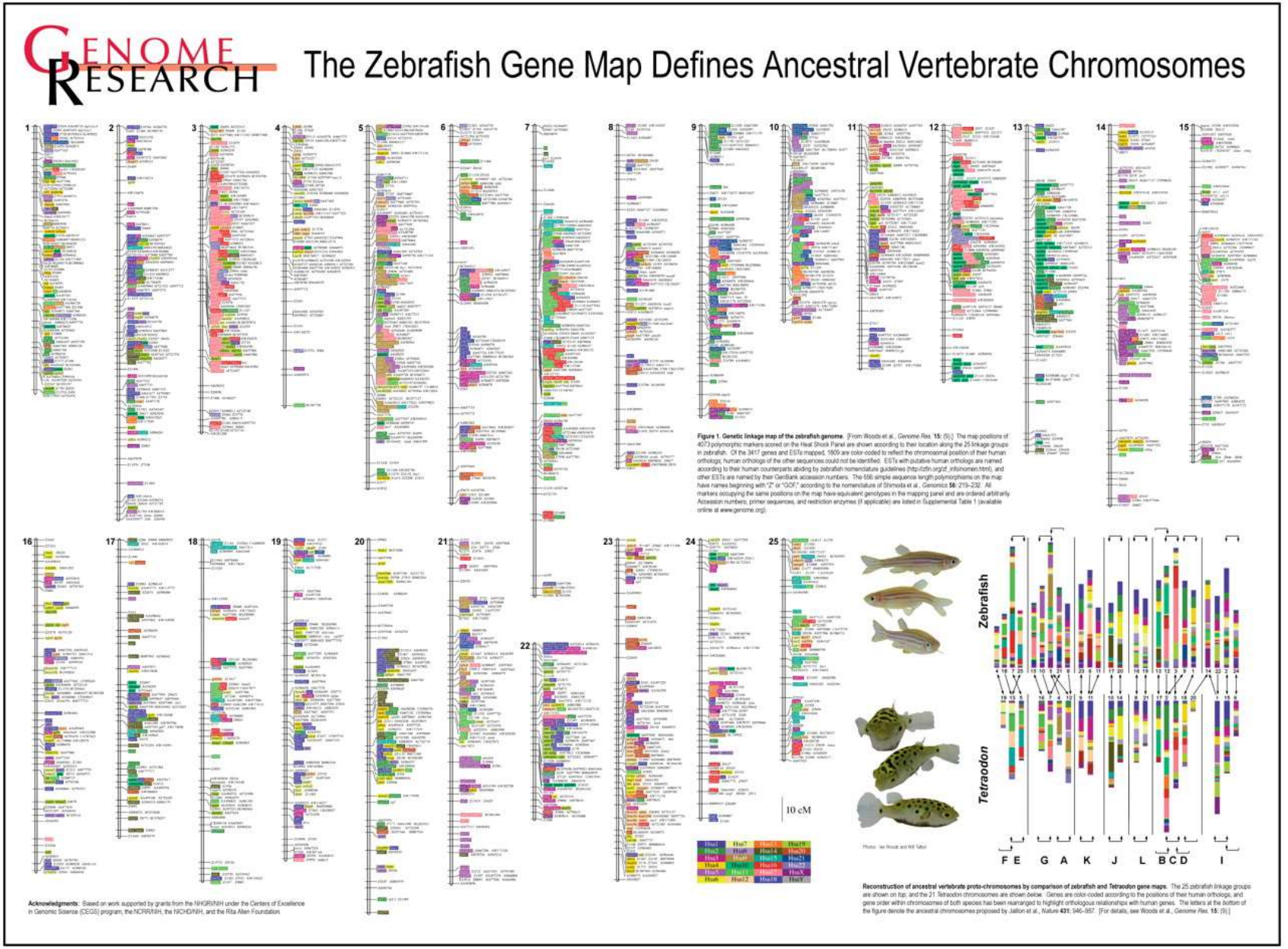


Courtesy Lisa Stubbs
Oak Ridge National Laboratory

YGA 98-075R2

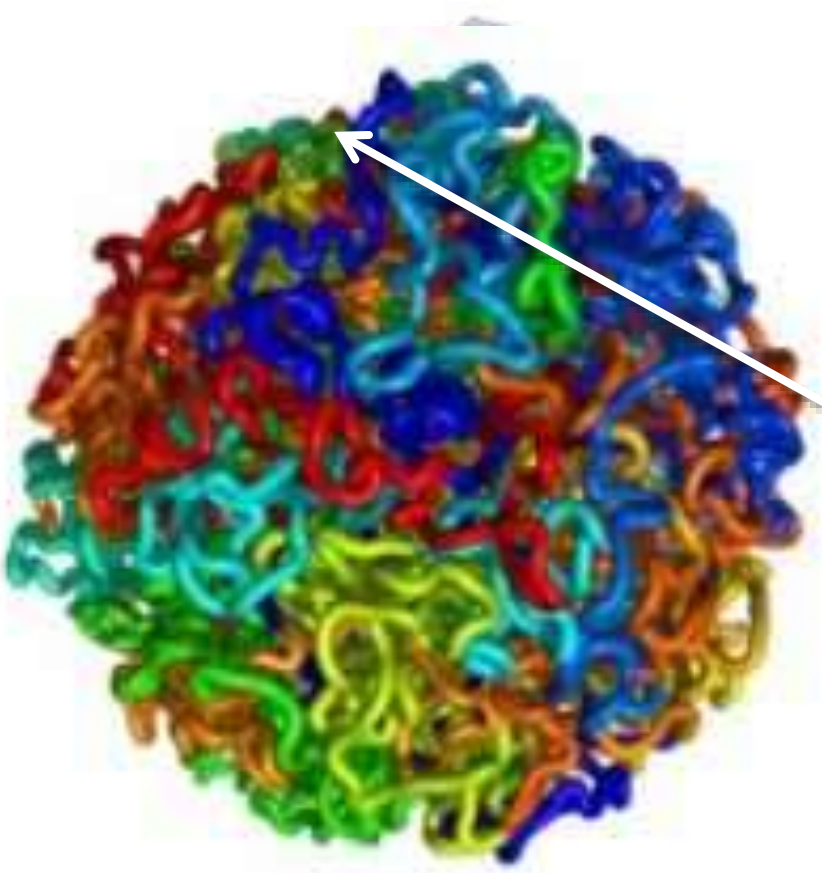
http://genomics.energy.gov/gallery/basic_genomics/view.np/view-35.html

The Zebrafish Gene Map Defines Ancestral Vertebrate Chromosomes.



Woods I G et al. Genome Res. 2005;15:1307-1314

Presenting the human genome: Now in 3D!



Y

The completion of the human genome sequence in 2001
ıs, to me, the most important accomplishment in biology.
ıce then, we have journeyed to the next frontier through
ınificant improvements in our ability to analyze and map
ne expression and transcription factor–binding sites in
e human genome. We now understand that the genome
far more complex than linear information could explain.
erefore, to fully appreciate the rules by which the
nome operates on an organismal level, we have to
mprehend higher-order chromosomal organization. To
ach that pinnacle, we need first to understand how the
nome is spatially organized and how that organization
ects basic nuclear and cellular processes. We also need
learn how transcriptional dynamics and epigenomic
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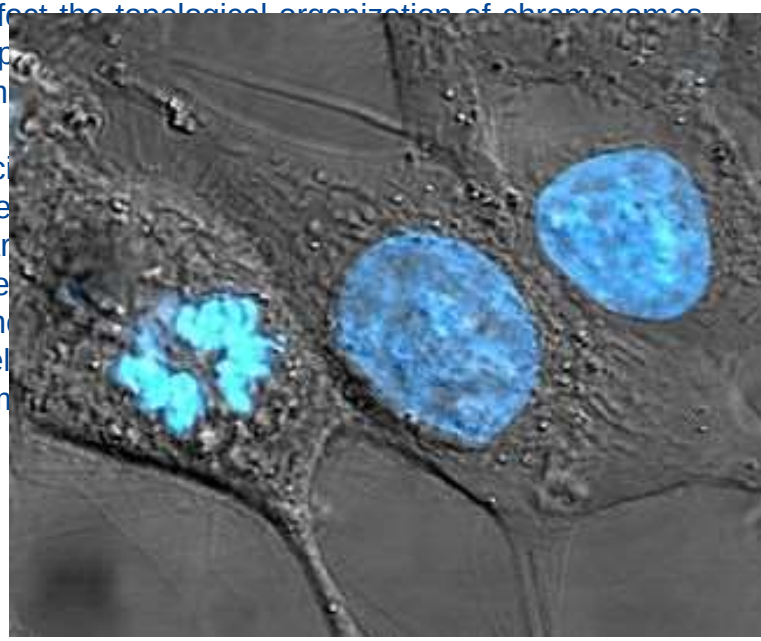
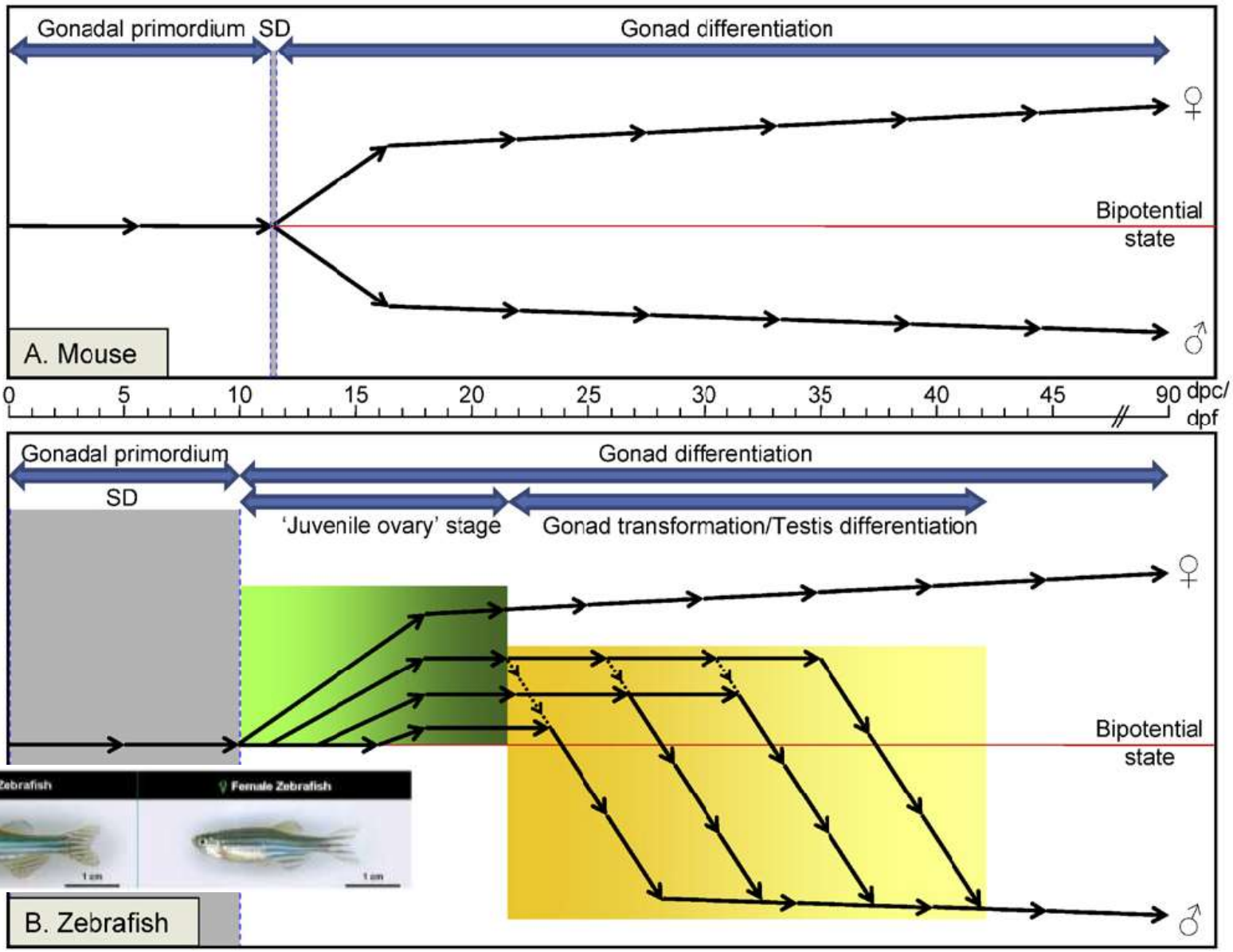
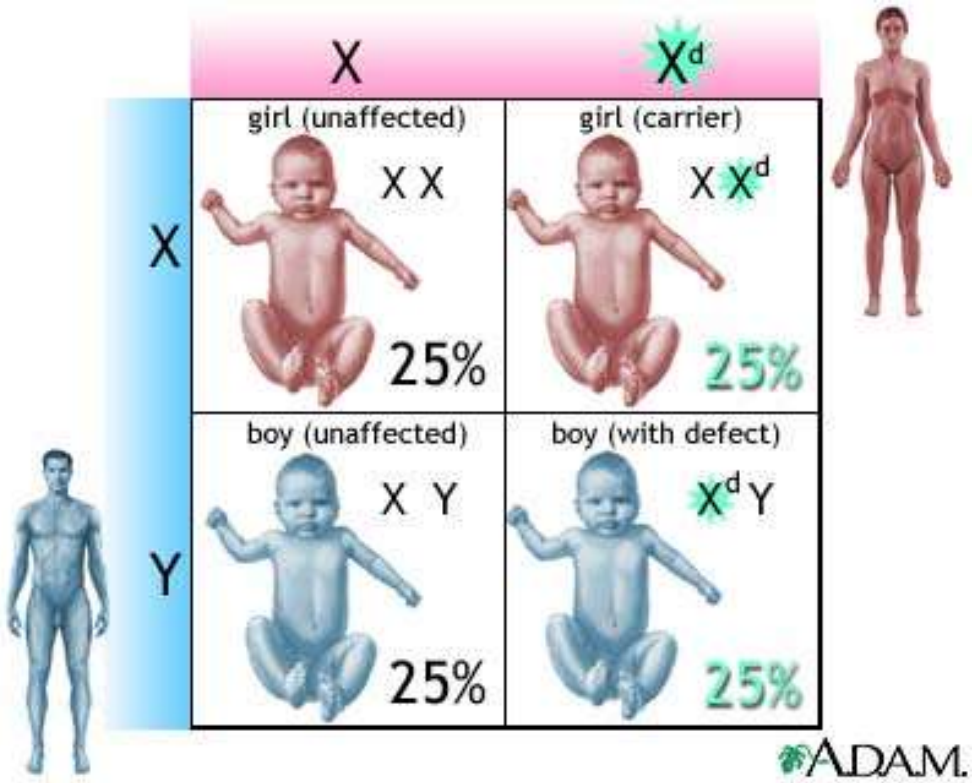


Comparison of Gonad differentiation between mouse and zebrafish

L. Orban et al. / Molecular and Cellular Endocrinology 312 (2009) 35–41



X-linked recessive genetic defects

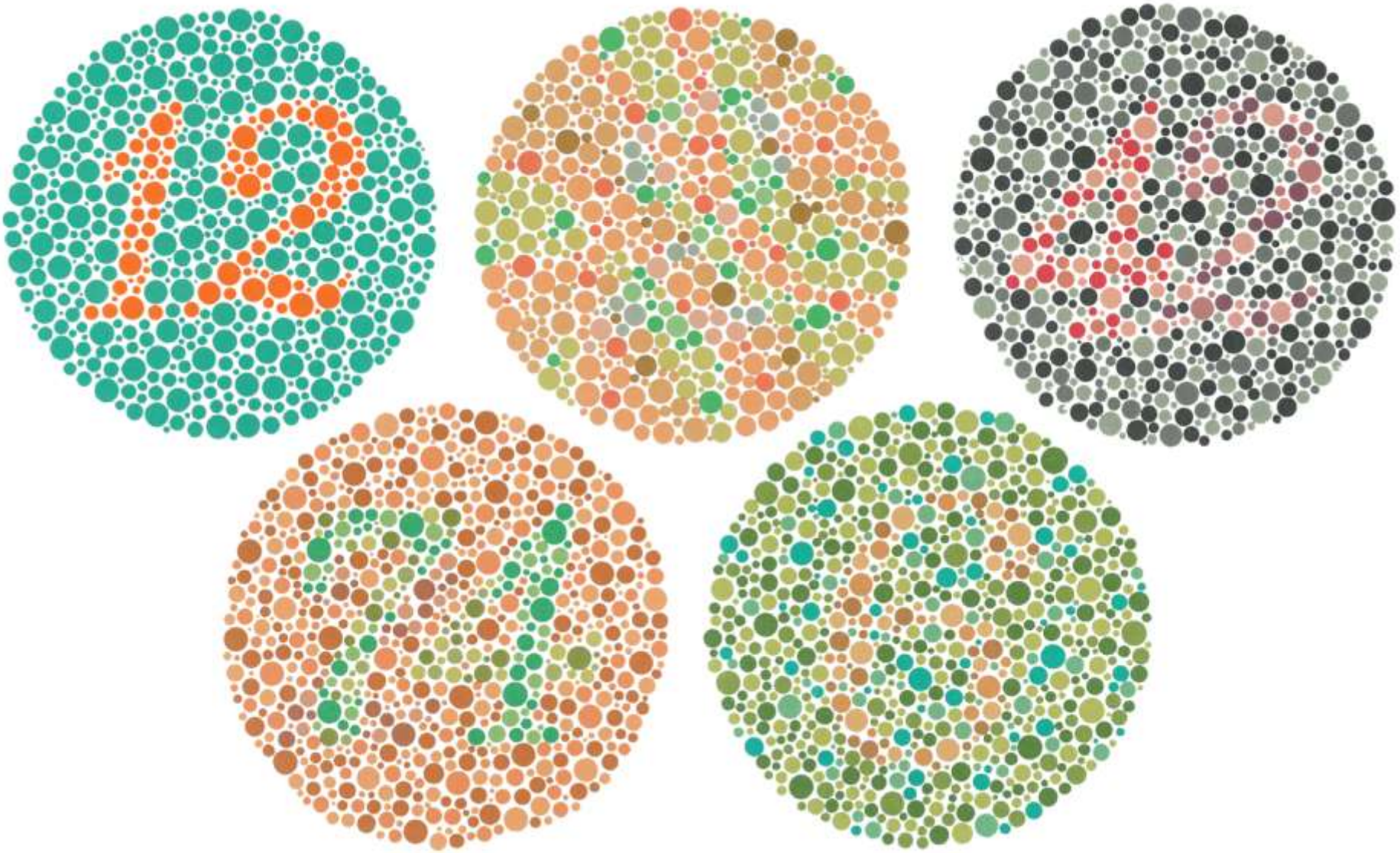


One X will randomly condensed into Barr body. Will the girl carrier display the symptom?

Hemophilia A – clotting factor VIII deficiency

(this factor is expressed in liver)

: *normal range* 0.45-1.58 iu/ml



2015 ranking of the global top 10 biotech and pharmaceutical companies based on revenue (in billion U.S. dollars)