Lecture 9: Mapping a gene defined by the mutation

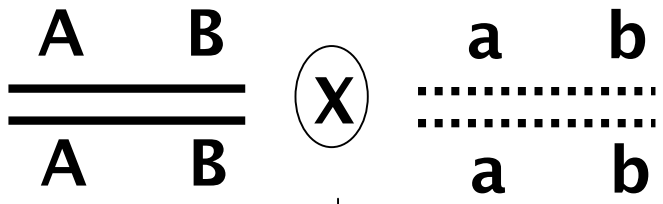
I. Classical mapping

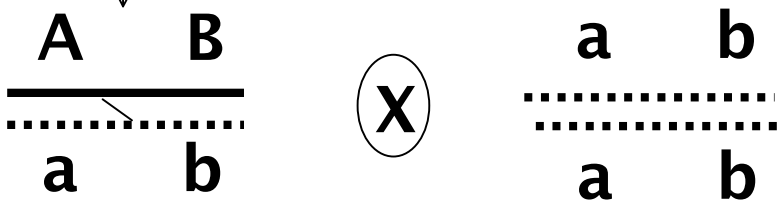
II. Molecular mapping

III. Positional cloning

Read 387-398
Fig. 11.17; 11.19; 11.20; 11.21; 11.22

Self-reviewing of classical genetics
Read: 114-117; 123-127
Fig. 5.2; 5.3; 5.4; 5.5; 5.10; 5.12





F2:

A B/a b		90
a b/a b		90
A b/a b		10
a B/a b		10

$$\frac{Ab + aB}{total} = \text{rec, freq.}$$

$$\frac{10 + 10}{200} = 0.1 = 10\%$$

Fig. 5.2

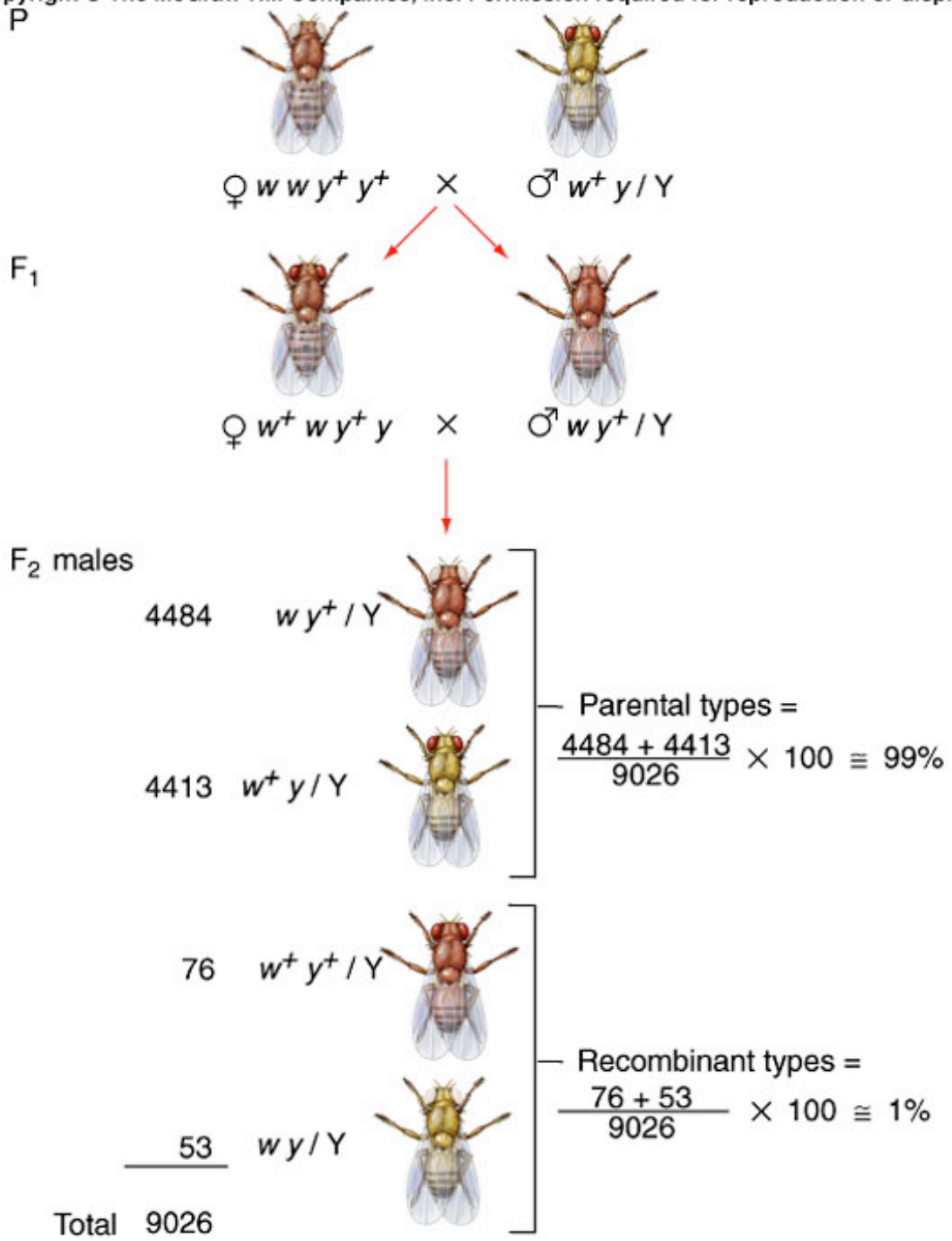


Fig. 5.4

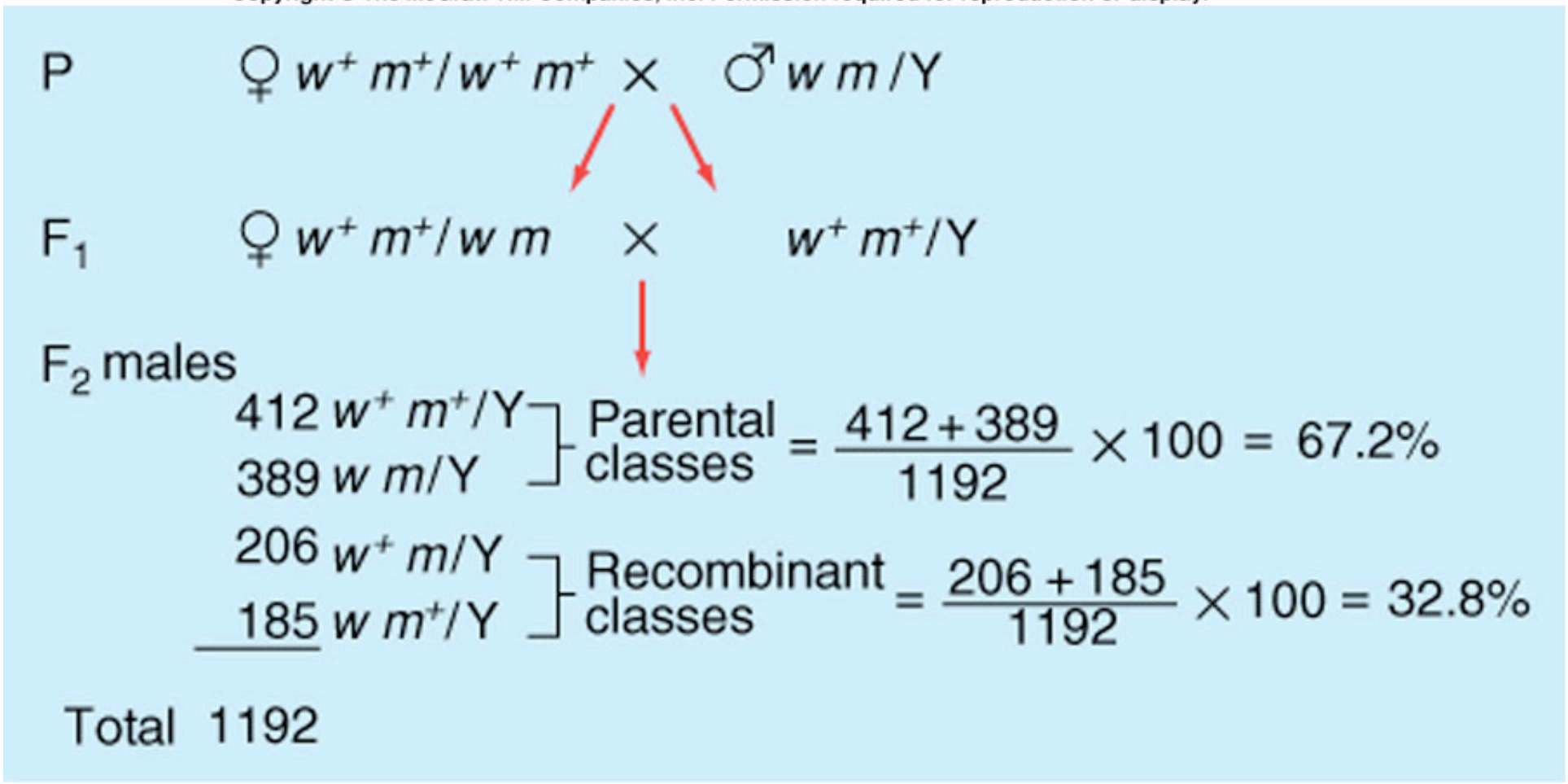
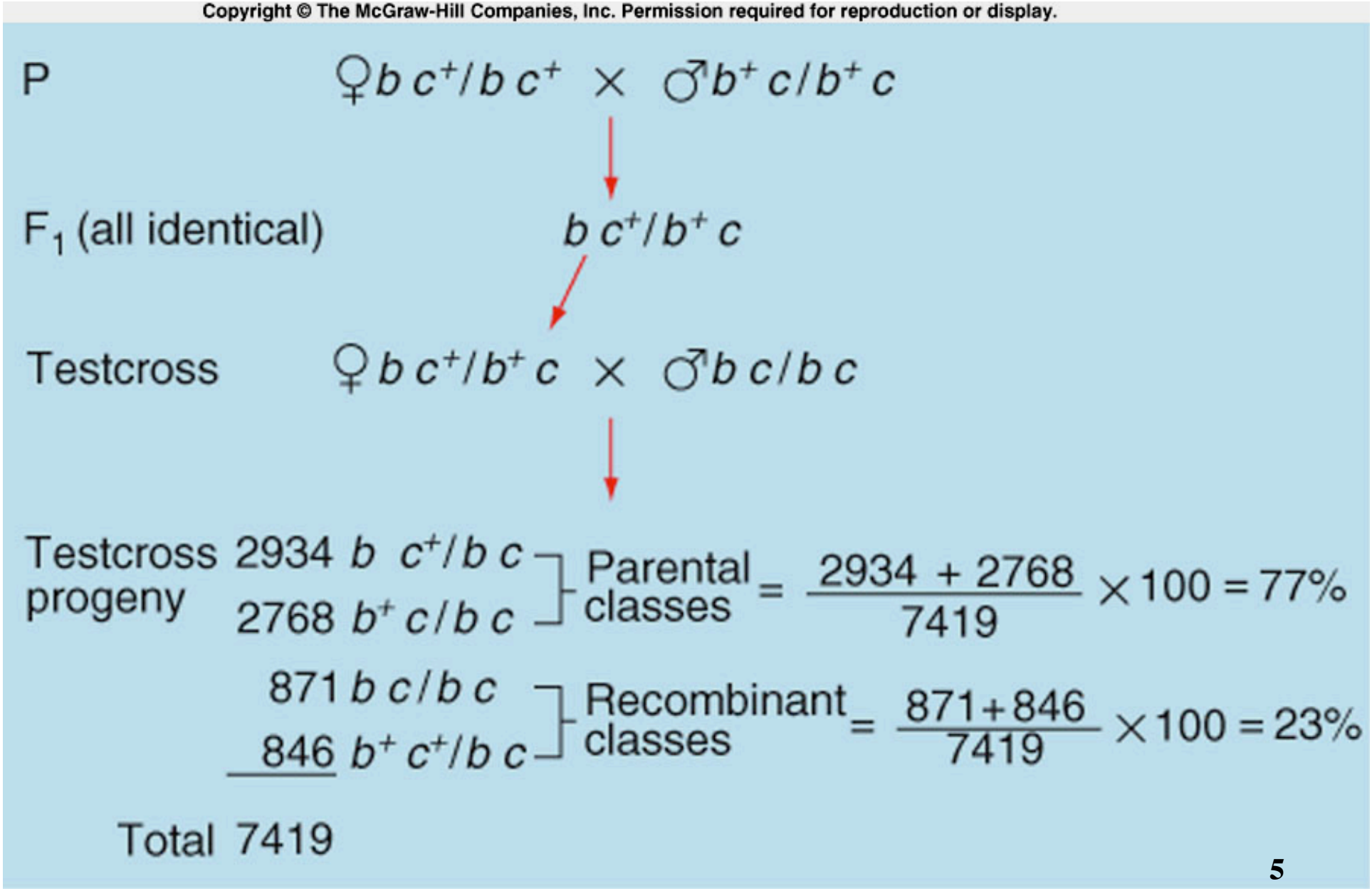
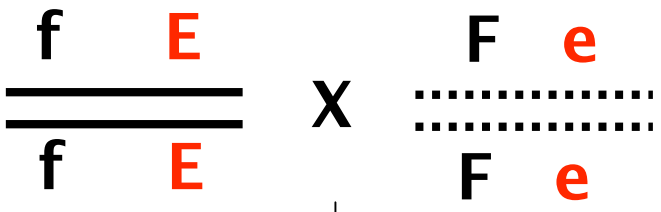
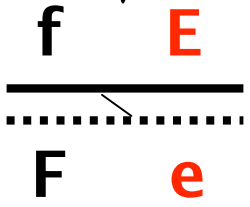


Fig. 5.5



Mapping with a CAPS marker

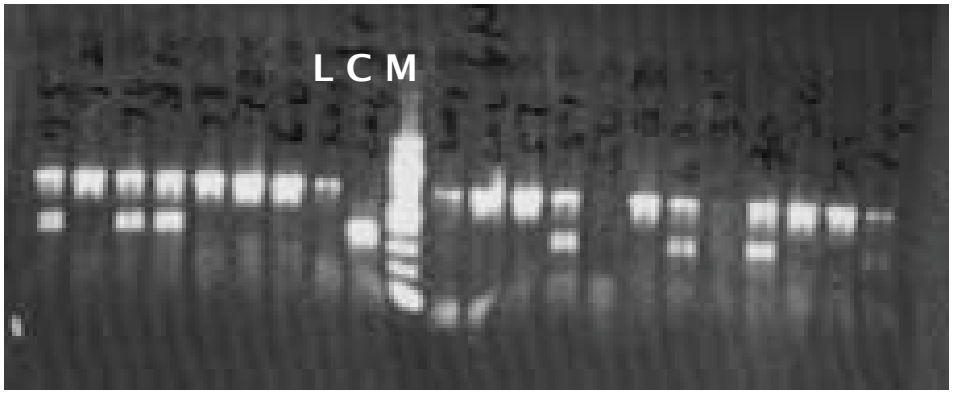




self

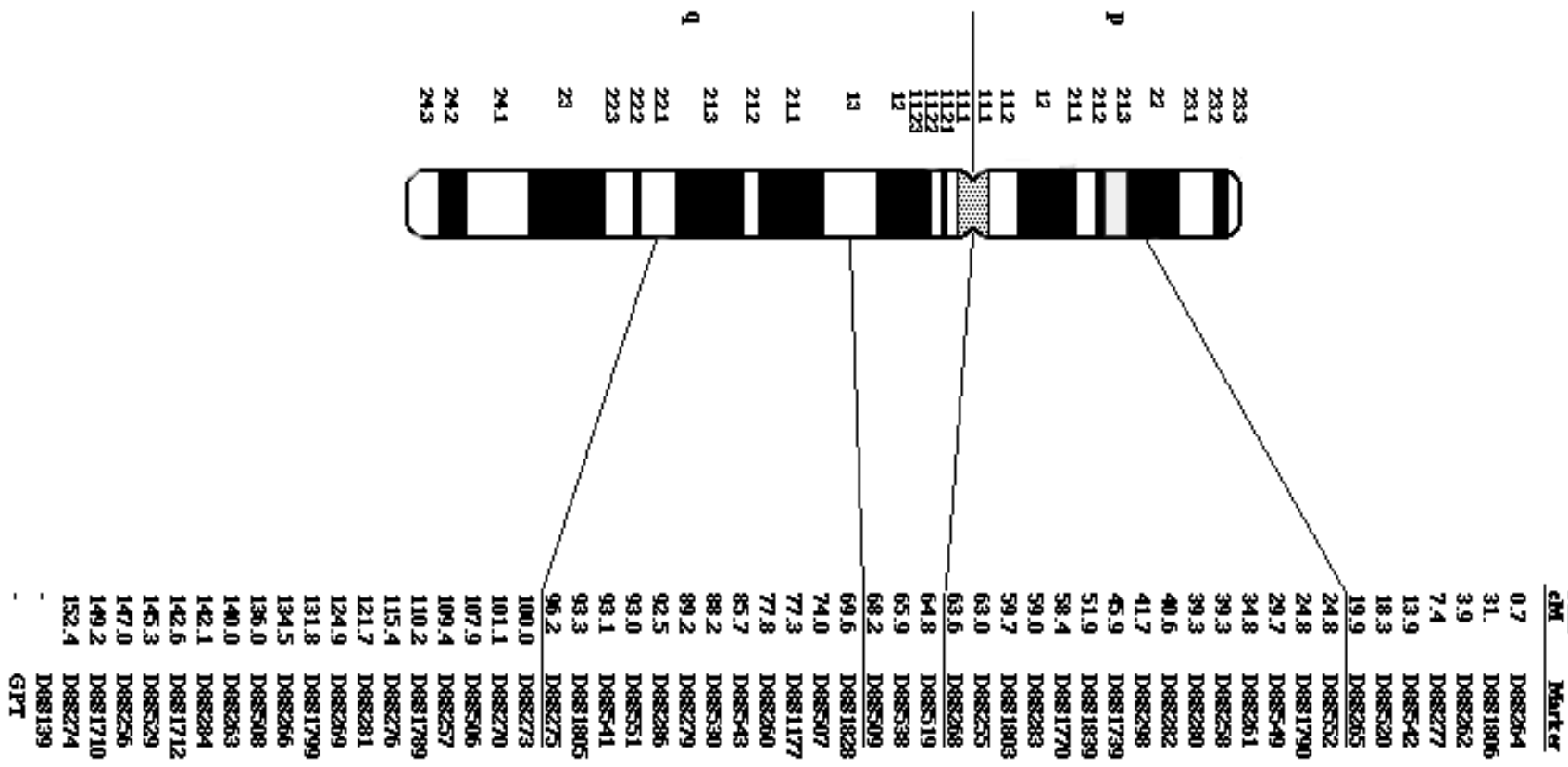
E/e: CAPS marker
F/f: a mutation causing abnormal flowers
Ler: solid line
Col: dotted line

No. of plants		No. of recombinant Chr.
11		0
6		1
0		2

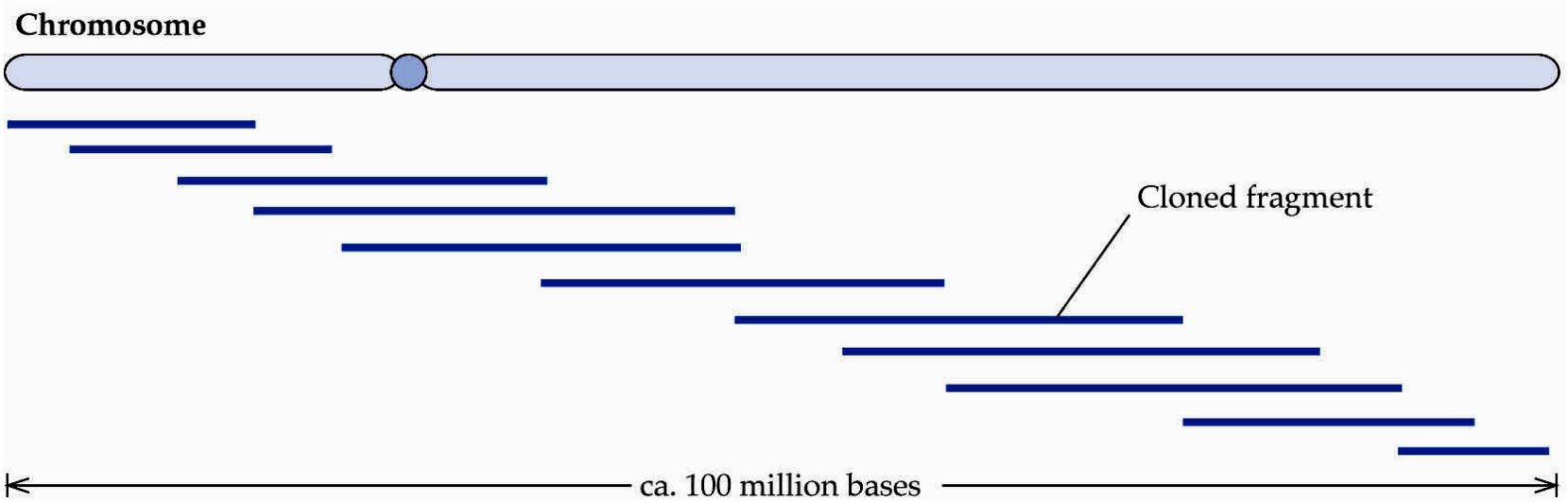


$$\frac{6}{17 \times 2} = 0.17$$

A genetic map of DNA markers



Physical map



In Arabidopsis: 1 cM = about 200 kb (50 genes)
In human 1cM = 1000 kb (~17 genes)

Yeast Artificial Chromosomes YAC

Vector	insert size	Host
YAC:	100-1000kb	yeast
BAC:	80-300kb	bacterium
Cosmid:	20-50 kb	bacterium
Lamda:	10-20kb	bacterium
Plasmid:	0.2-15kb	bacterium

A PHYSICAL MAP OF HUMAN CHROMOSOME 11

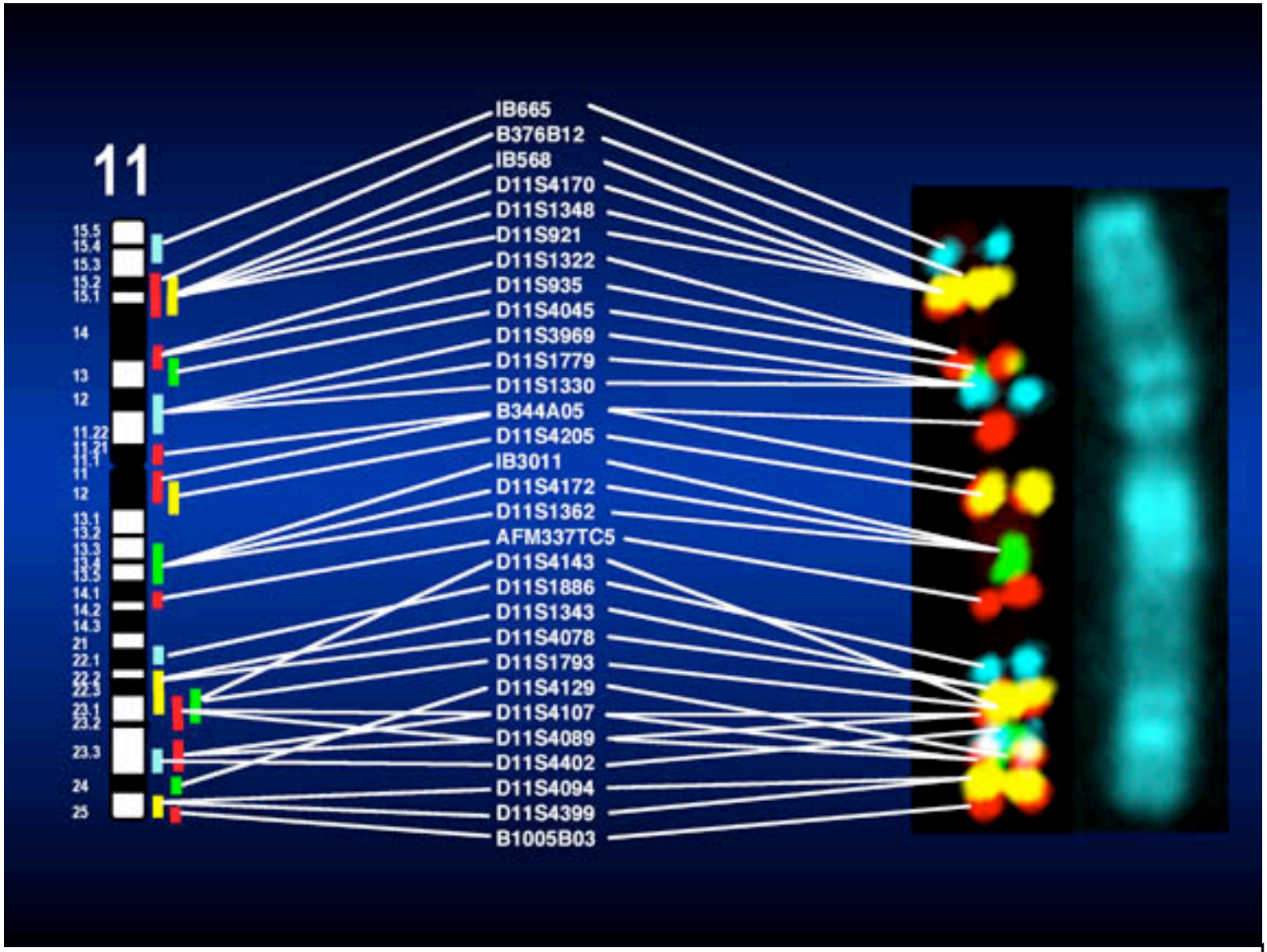
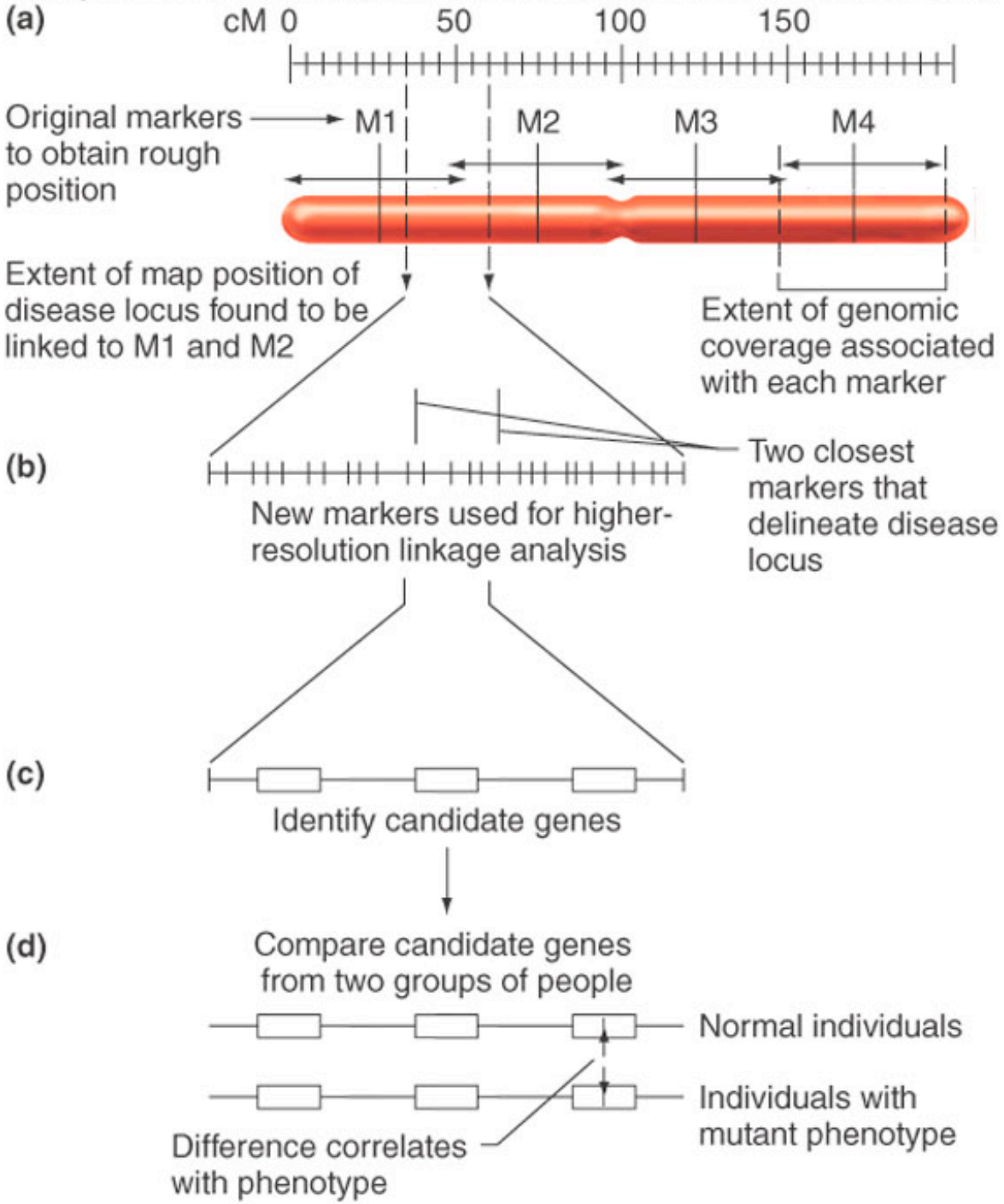


Fig. 11.17



Steps in identifying the gene in a chromosome region

Step1: Categorize genes in the region

Step2: Determine mRNA expression pattern

- EST
- Northern hybridization

Step3: Determine changes between wt and mut

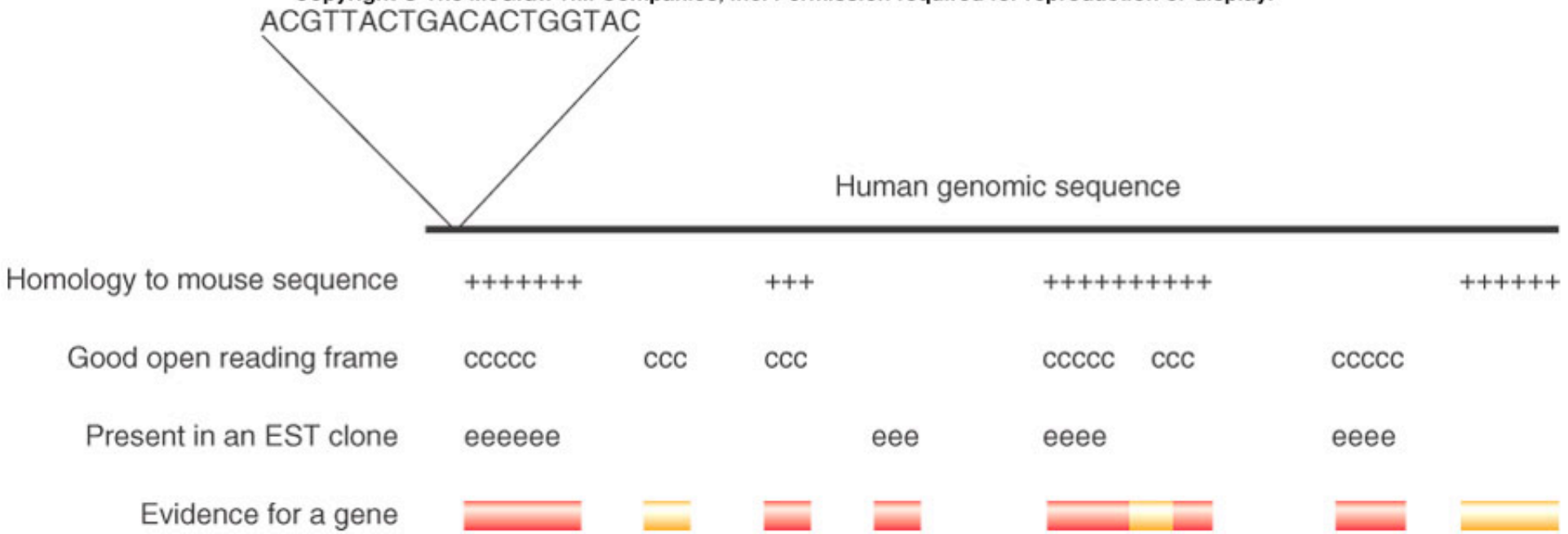
- Expression pattern
- DNA sequence

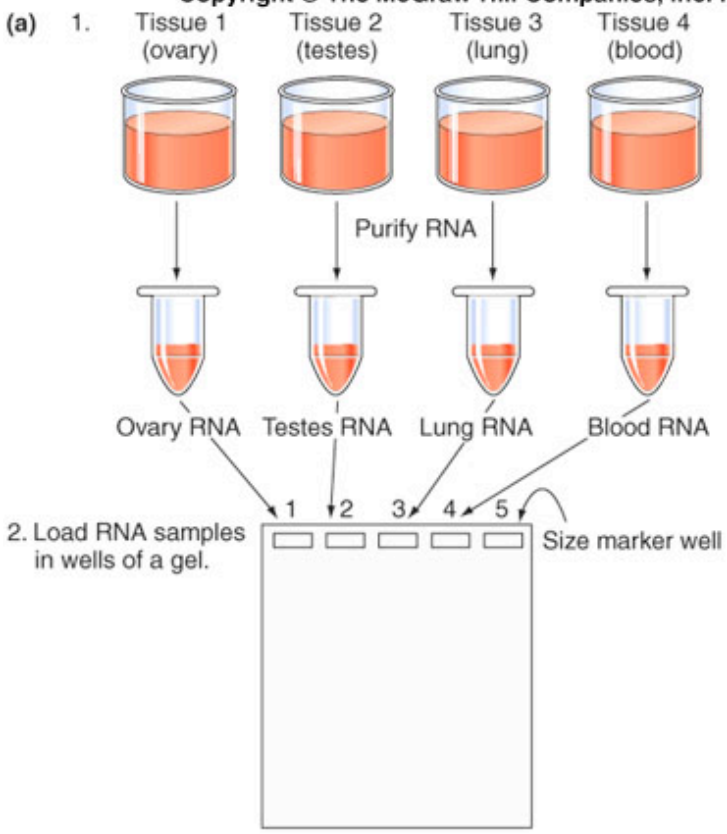
Step4: Transgenic studies (SRY example)

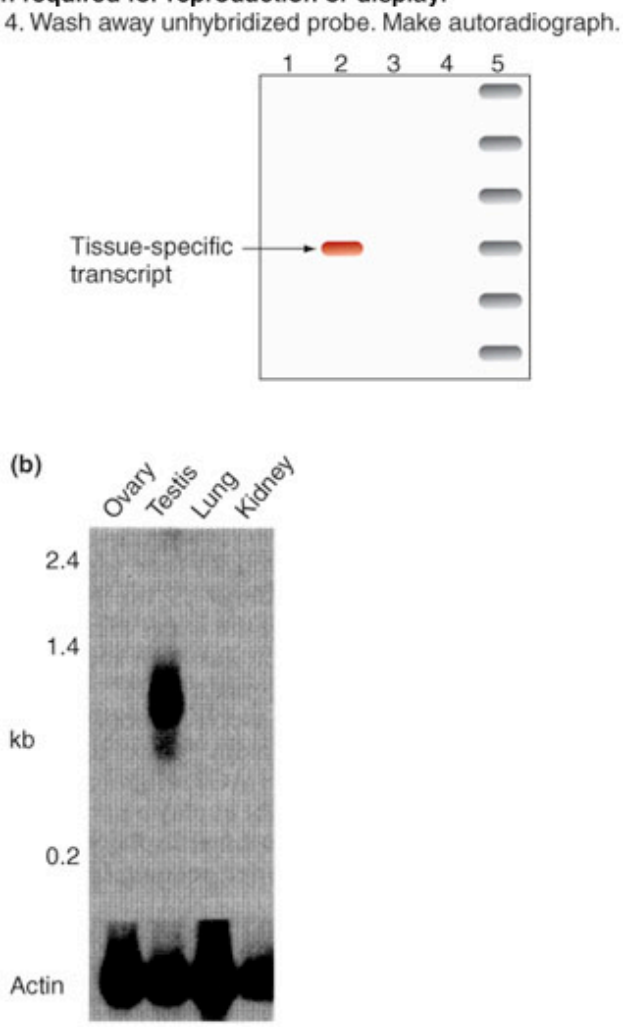
Case study: Cystic fibrosis

CFTR (Cystic fibrosis transmembrane conductance regulator)

Fig. 11.19



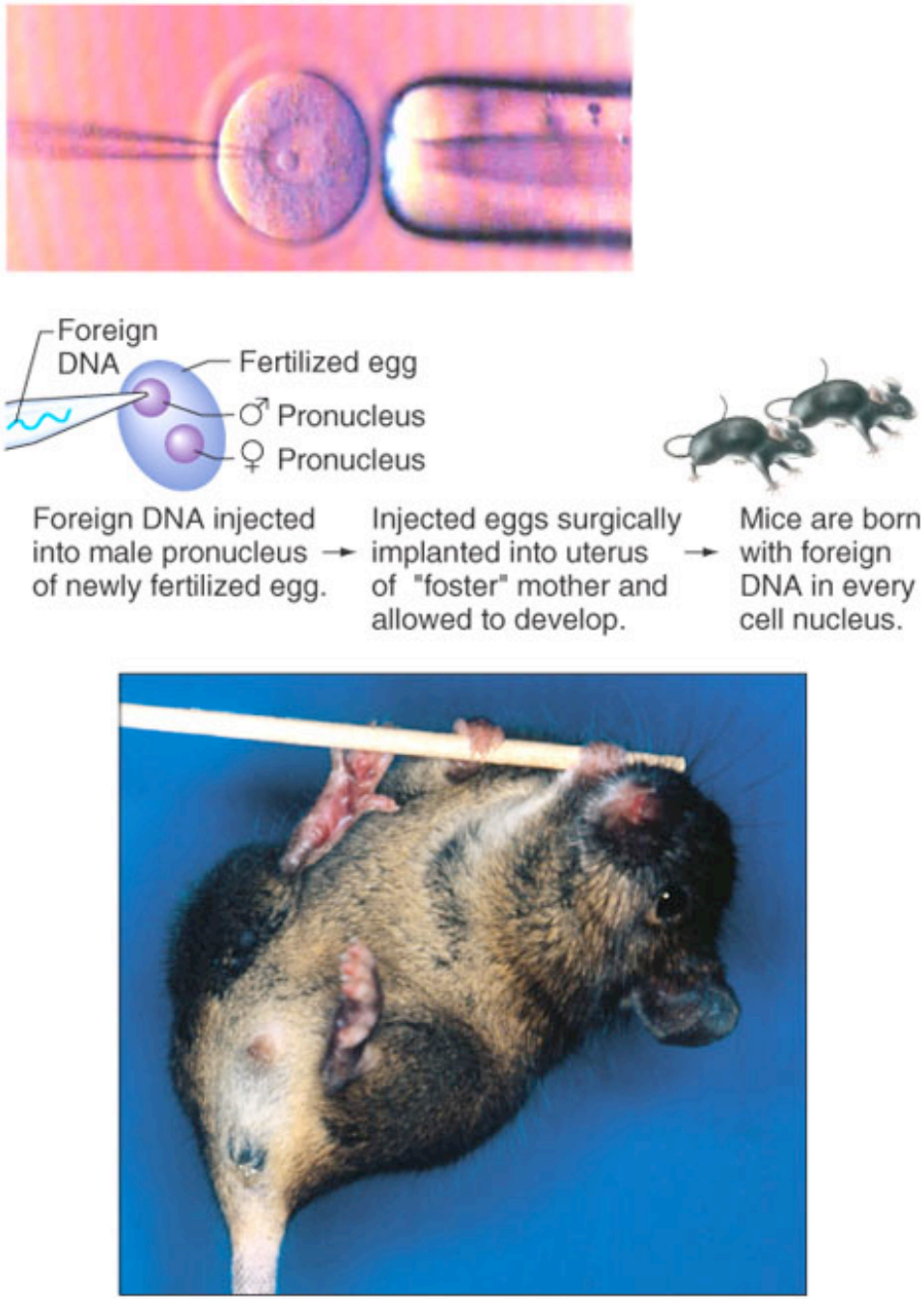




Testes-determining factor (TDF)

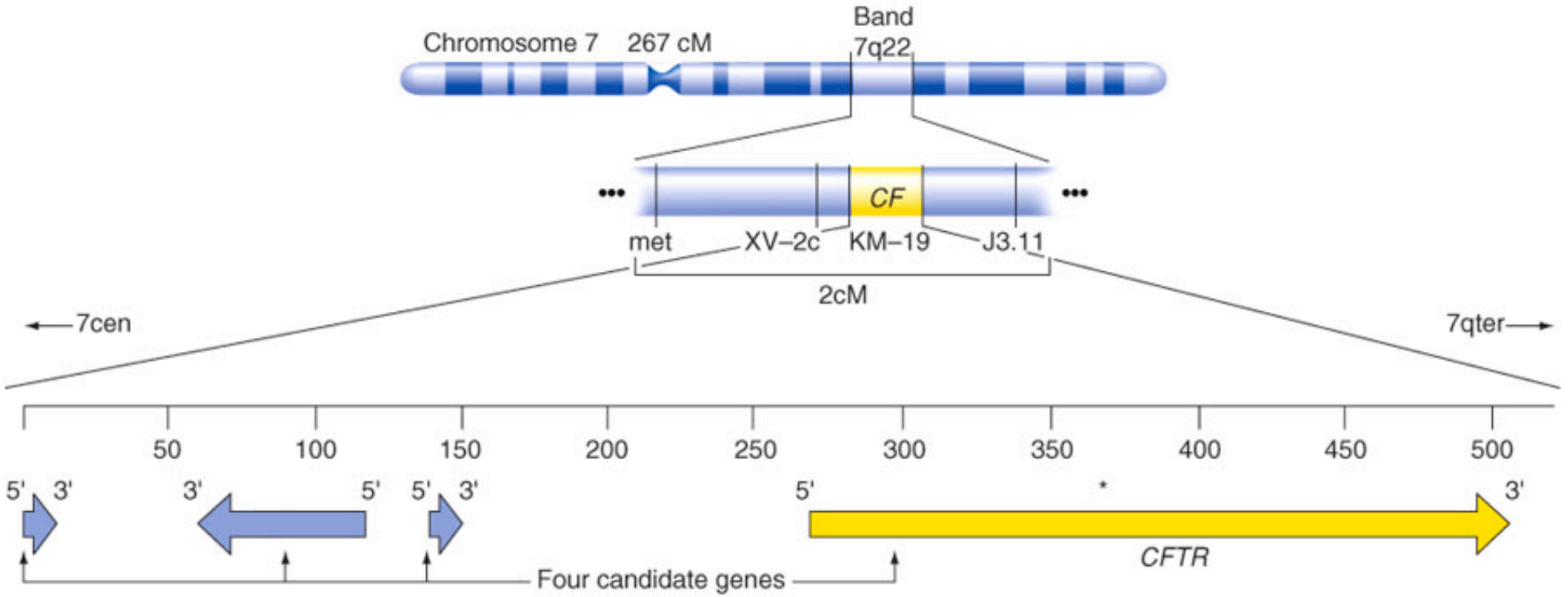
Fig. 11.20

Fig. 11.21



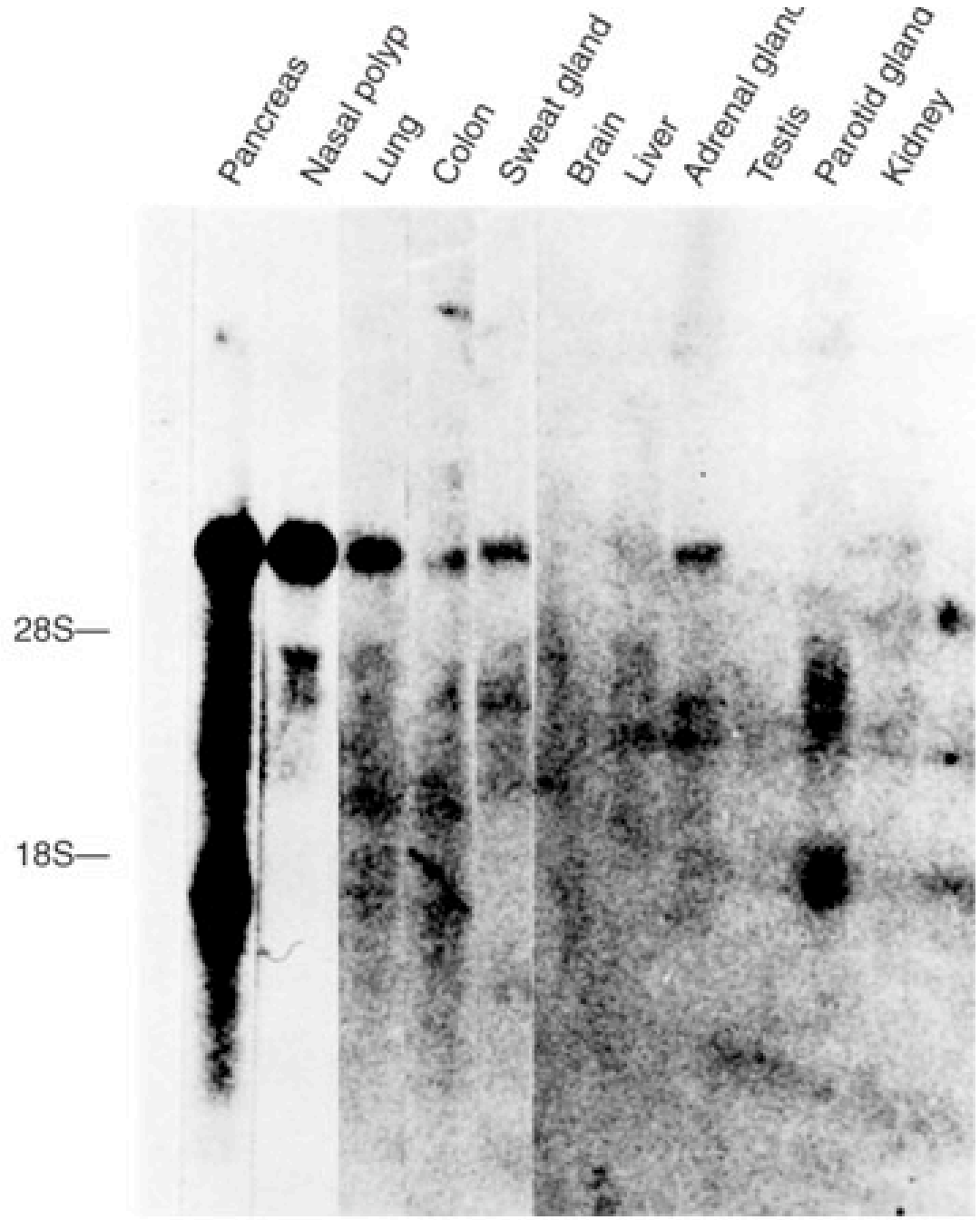
Cloning cystic fibrosis transmembrane conductance regulator (CFTR)

Fig. 11.22a



Northern blots help eliminate other 3 candidate genes

Fig. 11.22b



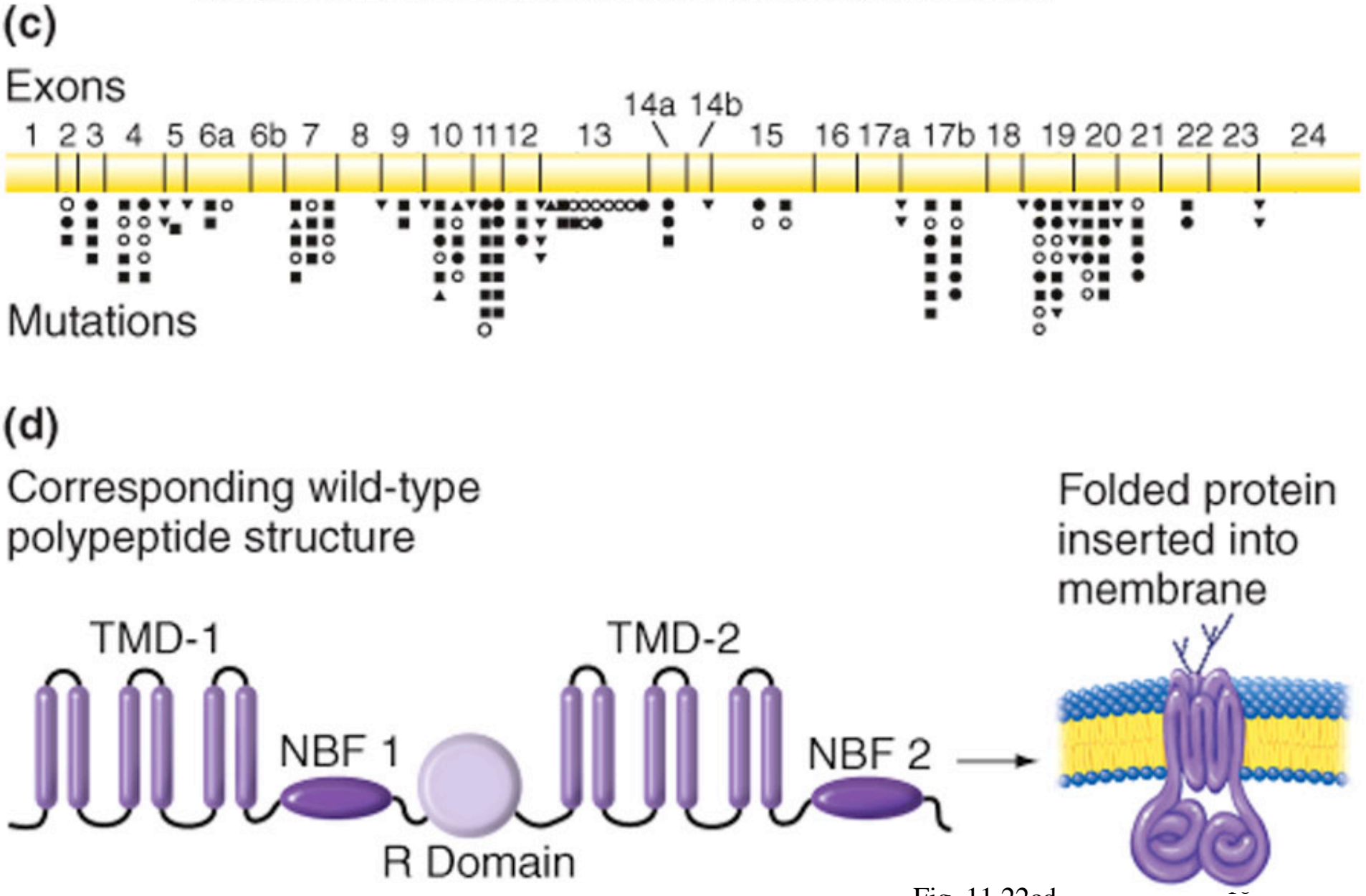
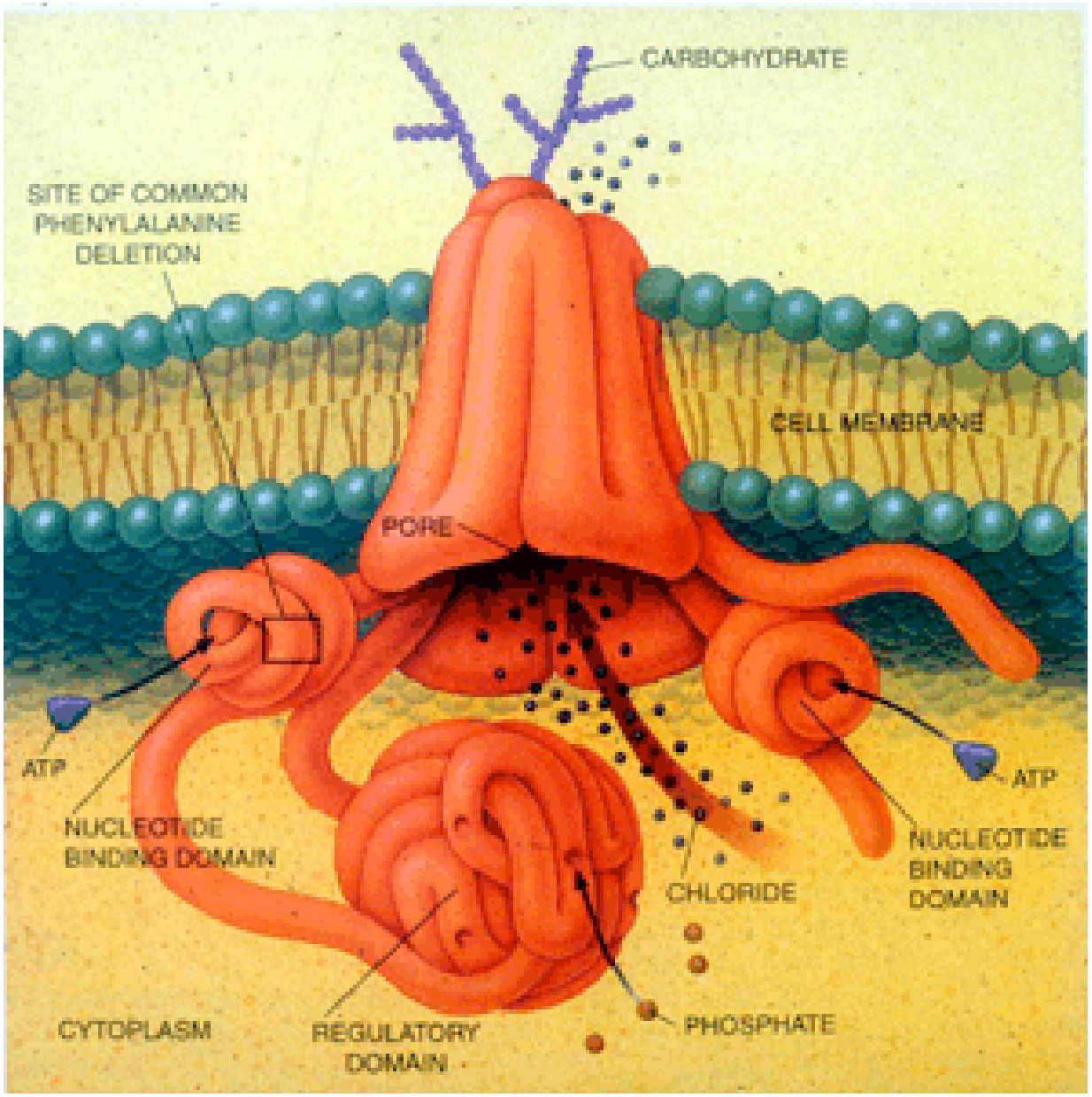


Fig. 11.22cd

CFTR


CARBOHYDRATE
SITE OF COMMON PHENYLALANINE DELETION
CELL MEMBRANE
PORE
ATP
NUCLEOTIDE BINDING DOMAIN
ATP
NUCLEOTIDE BINDING DOMAIN
CHLORIDE
CYTOPLASM
REGULATORY DOMAIN
PHOSPHATE