Allelic variation and pleiotropy of a single gene

Ch5.1

Pleiotropy of a single gene!!!!

Mutations in haplosufficient genes are recessive

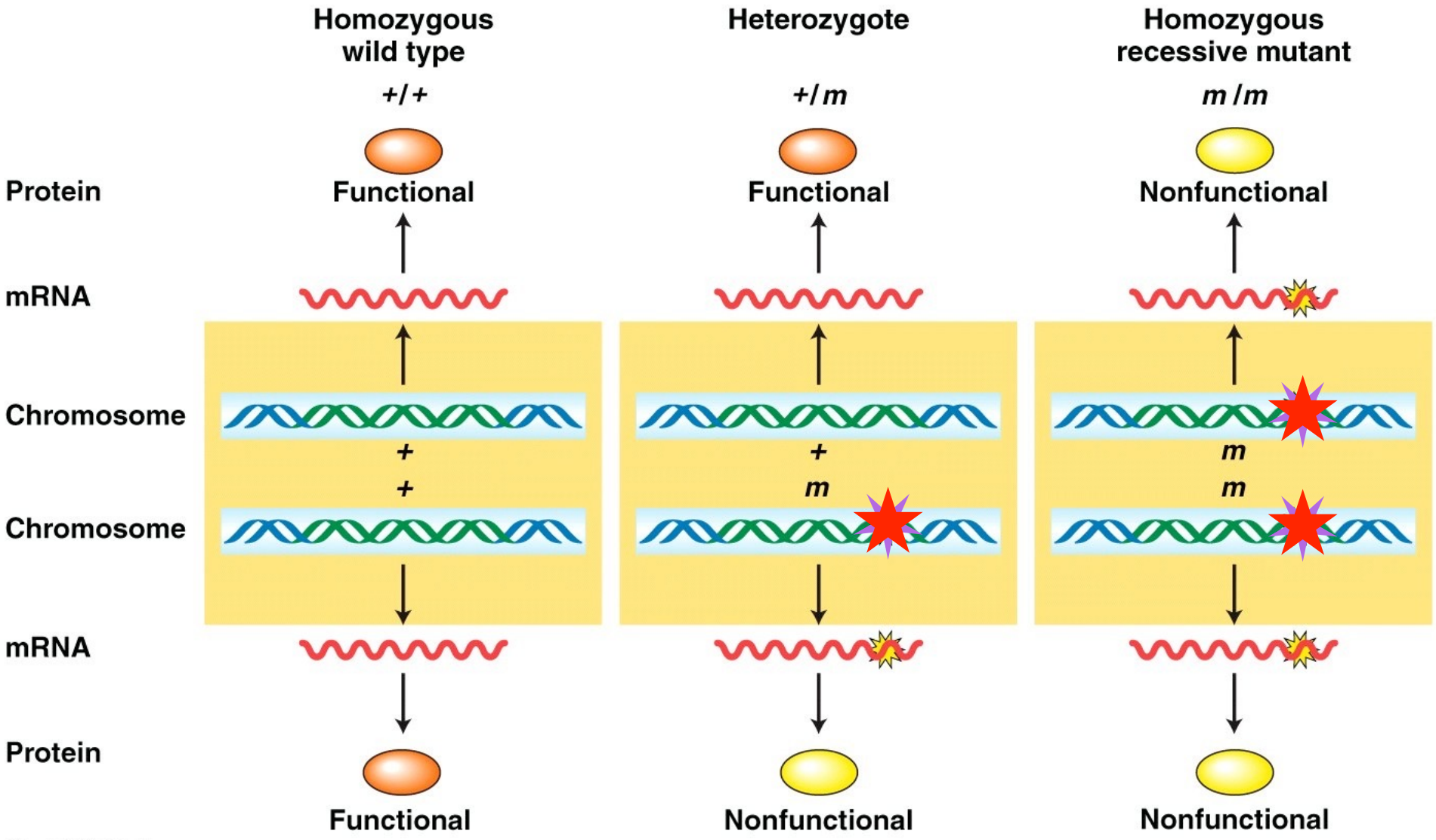
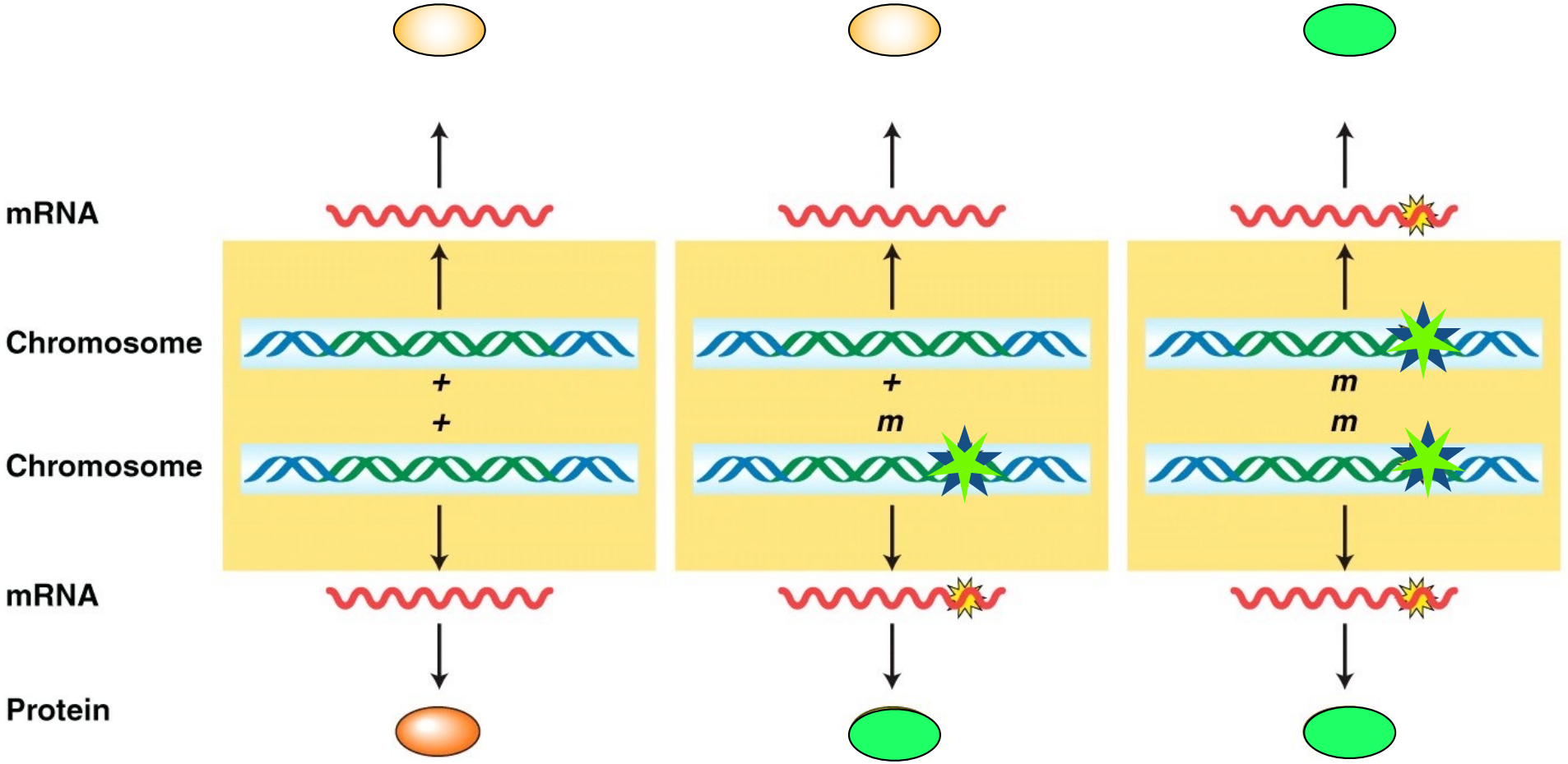


Fig 5-1

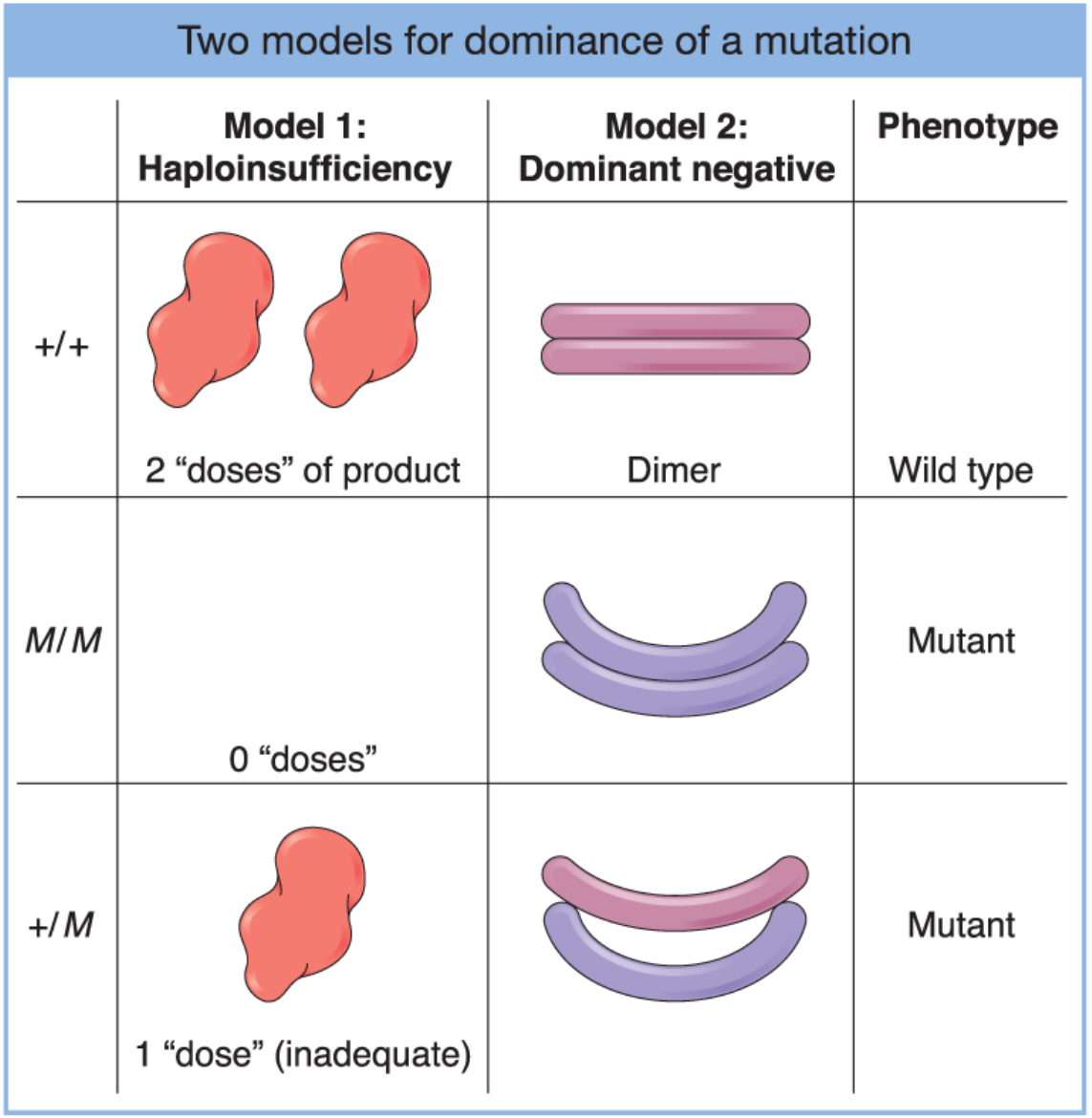
Dominant Mutations

Having a single copy of the mutation produces a phenotype (disease) despite having a wild-type copy of the gene.



Could loss-of-function mutations be dominant?

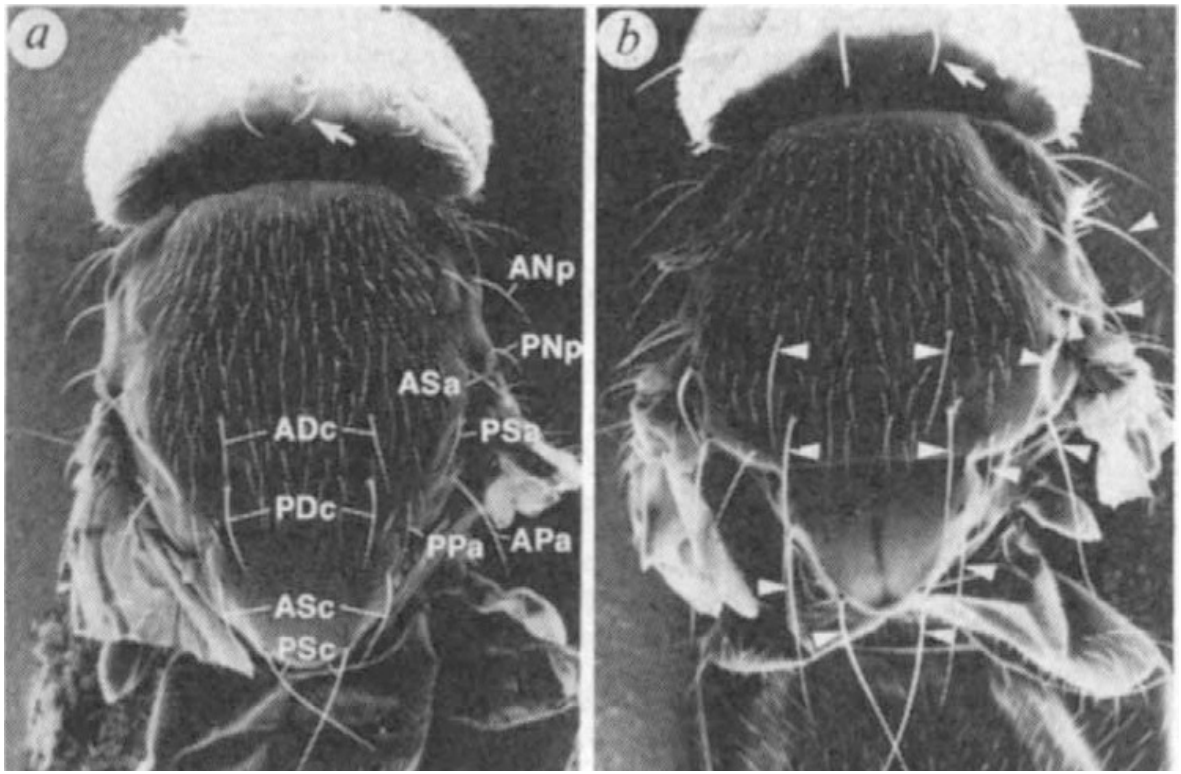
I. Dominant Mutations (Haploinsufficiency and Dom. Negatives)



Griffiths et al., *Introduction to Genetic Analysis*, 12e, © 2020 W. H. Freeman and Company

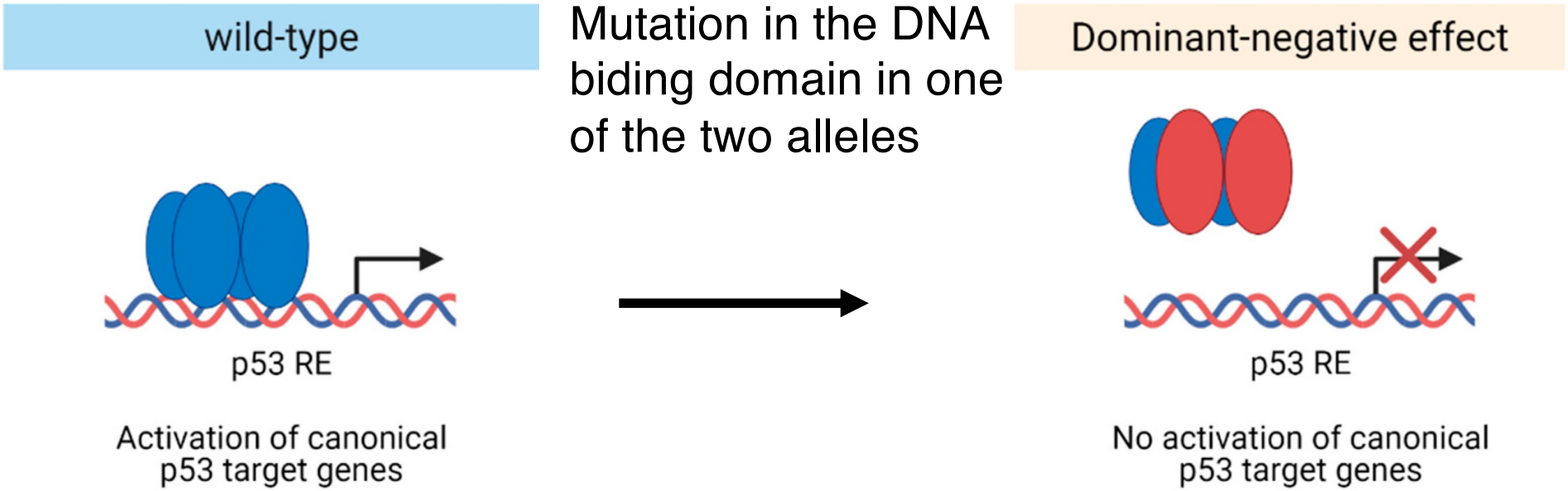
Fig 5-2

Mutations in genes coding ribosomal subunits in Drosophila are often dominant, haploinsufficiency



Many p53 mutant alleles in cancer function as a dominant negative

P53 is a transcription factor that binds DNA as a homotetramer

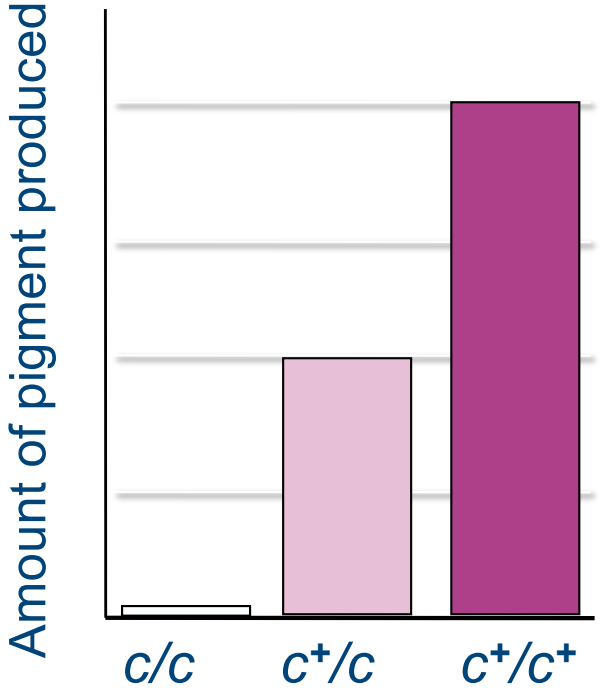


II. Incomplete or Partial Dominance (Dose-determinant)

Snapdragon flower color

c/c *c*⁺/*c*⁺ *c*⁺/*c*

John Kaprielian/Science Source



Eg. Enzymes that produce pigments

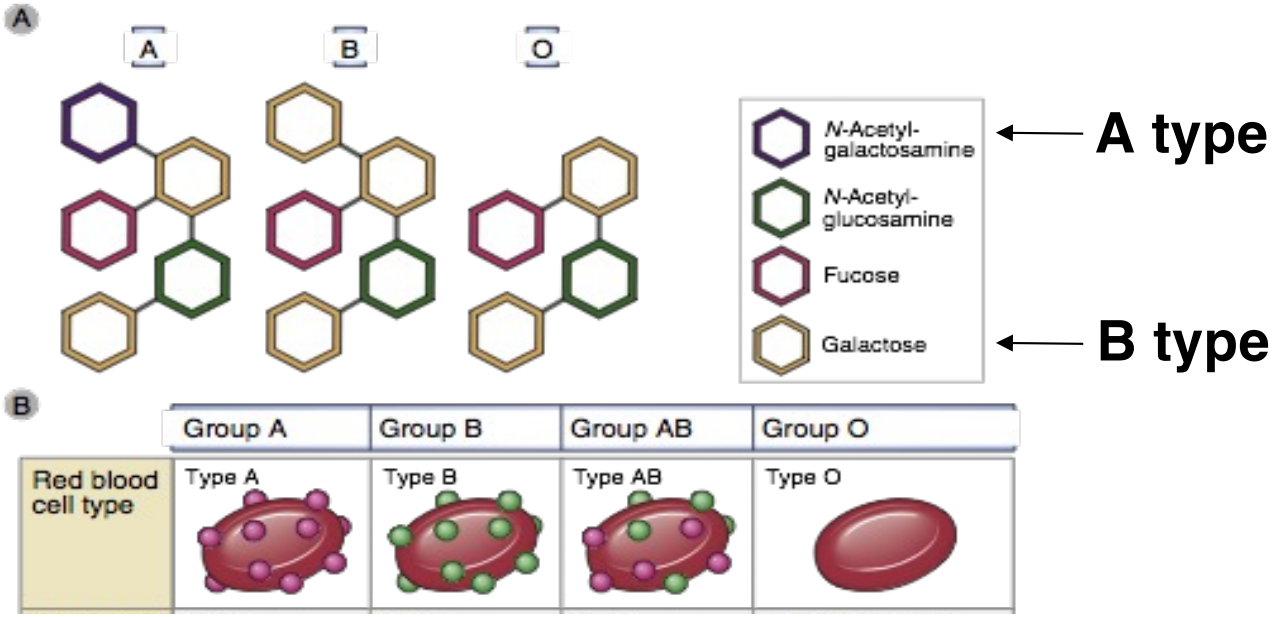
Fig 5-3

III. Codominance (both alleles are expressed/detected)

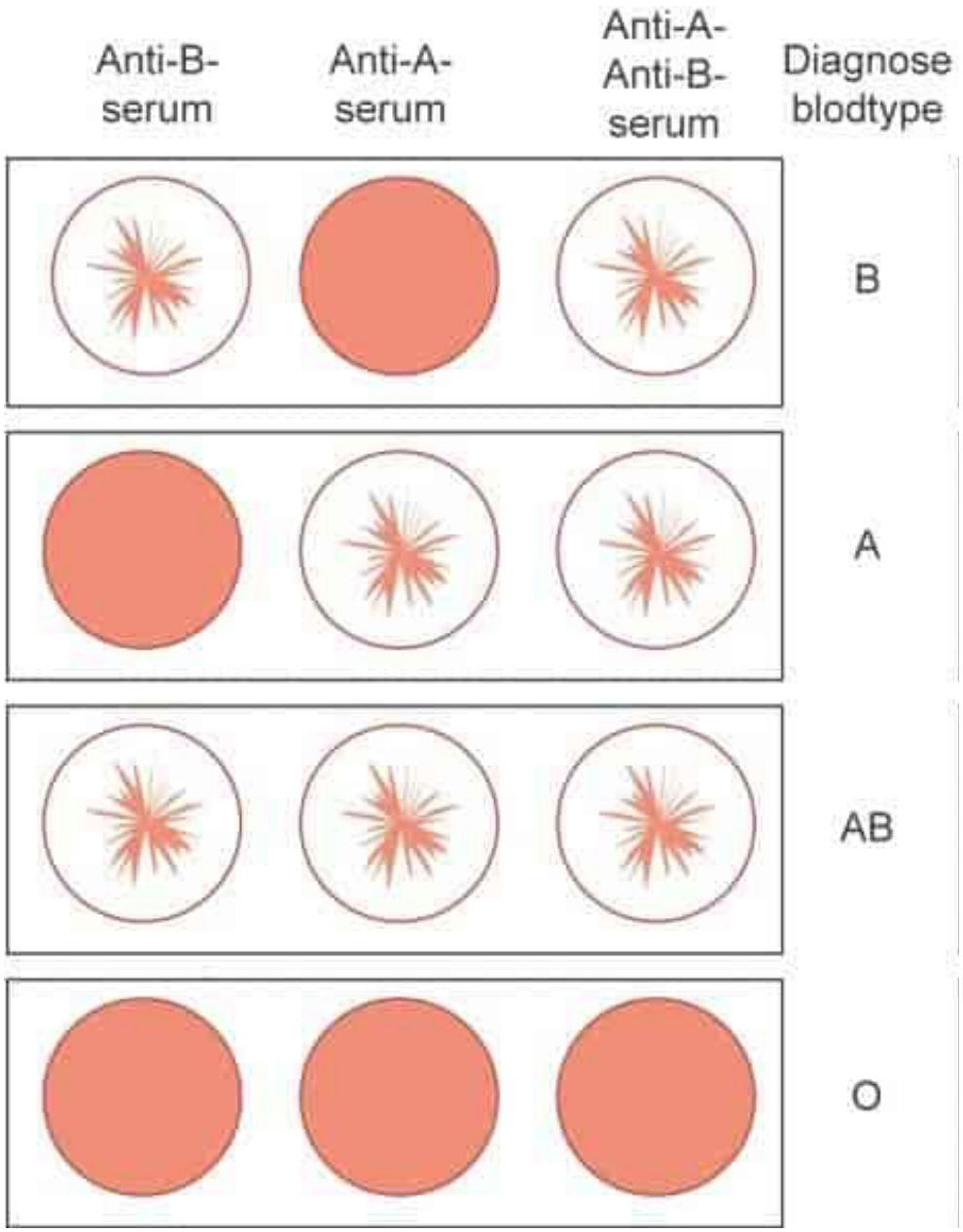
Three alleles determine the blood type: *i*, I^A & I^B

The gene responsible for the blood type encodes a glycosyltransferase

Genotype	Blood Type
I^A/I^A, I^A/i	A
I^B/I^B, I^B/i	B
I^A/I^B	AB
i/i	O



A and B are dominant over O, but codominant wit h each other in conventional assay



How we classify dominance is often determined by the phenotype we characterize, (methods of detection/observation)

Hb gene encodes beta-globin, which is a subunit of hemoglobin

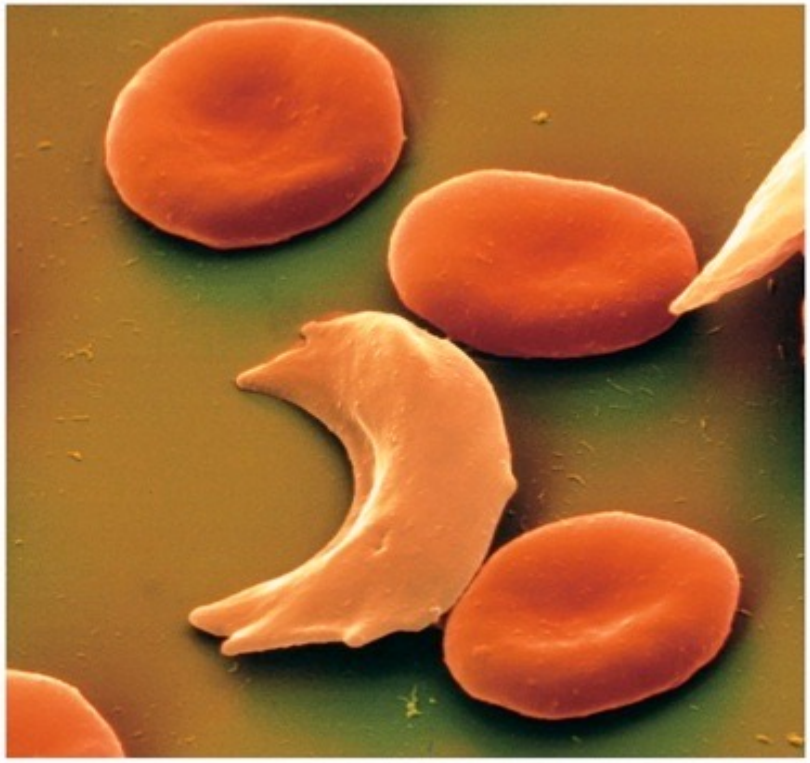


Fig 5-4 The sickle-shaped cell is caused by a single mutation in the gene for hemoglobin

Phenotype: anemia

Hb^A/Hb^A No anemia
Hb^S/Hb^S anemia
Hb^A/Hb^S No anemal

Hb^A is **dominant** to Hb^S

Phenotype: Blood cell shape

Hb^A/Hb^A a normal shape
Hb^S/Hb^S a sickle shape
Hb^A/Hb^S a slight sickle shape

Hb^S is **incomplete dominant** to Hb^A

Phenotype: presence of Hb^A and Hb^S at the protein level.

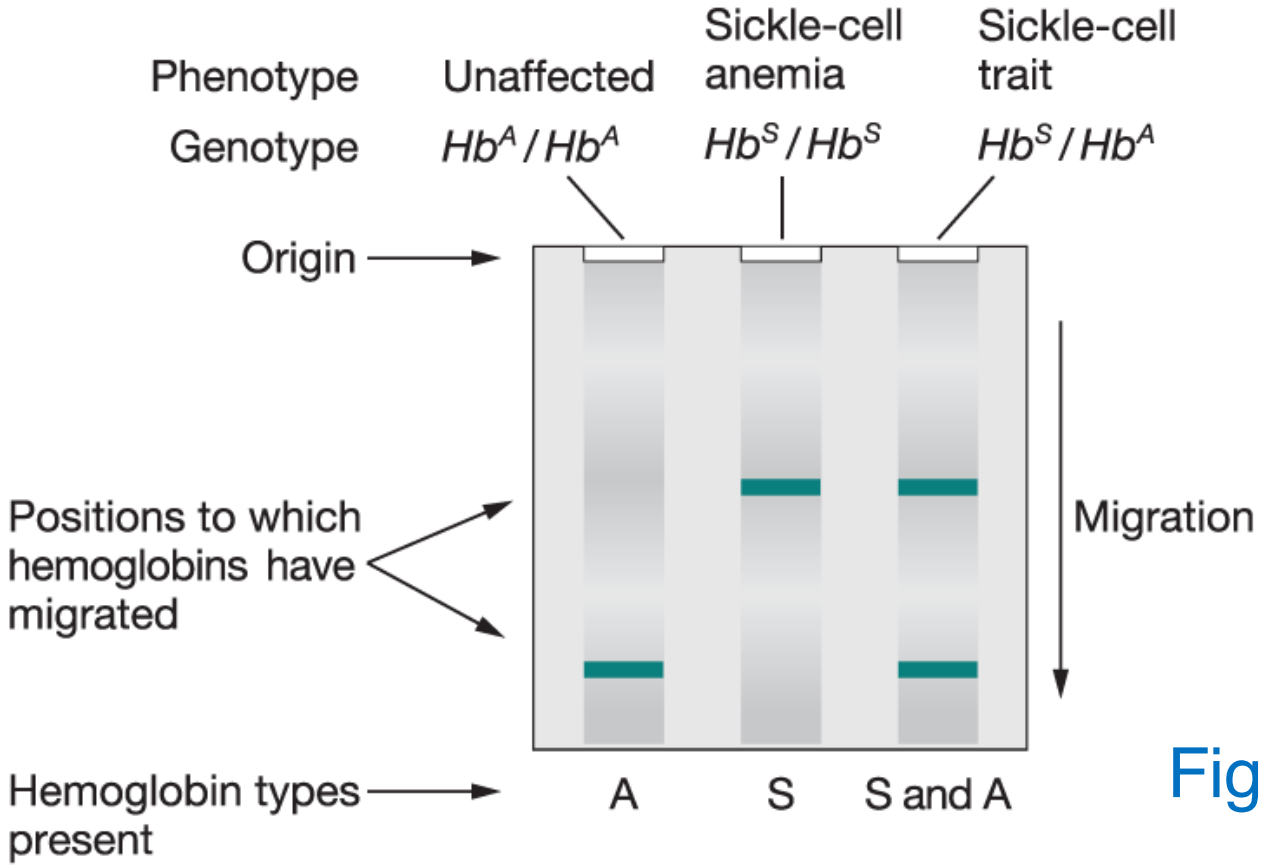


Fig 5-5

Hb^A and Hb^S are **codominant** **because both allele can be clearly discerned at the protein level**

IV Recessive lethal

Homozygous mutations causing lethality in the animal, either recessive or dominant mutations

Normal mice have dark pigmentation,

“yellow mice” have lighter coats

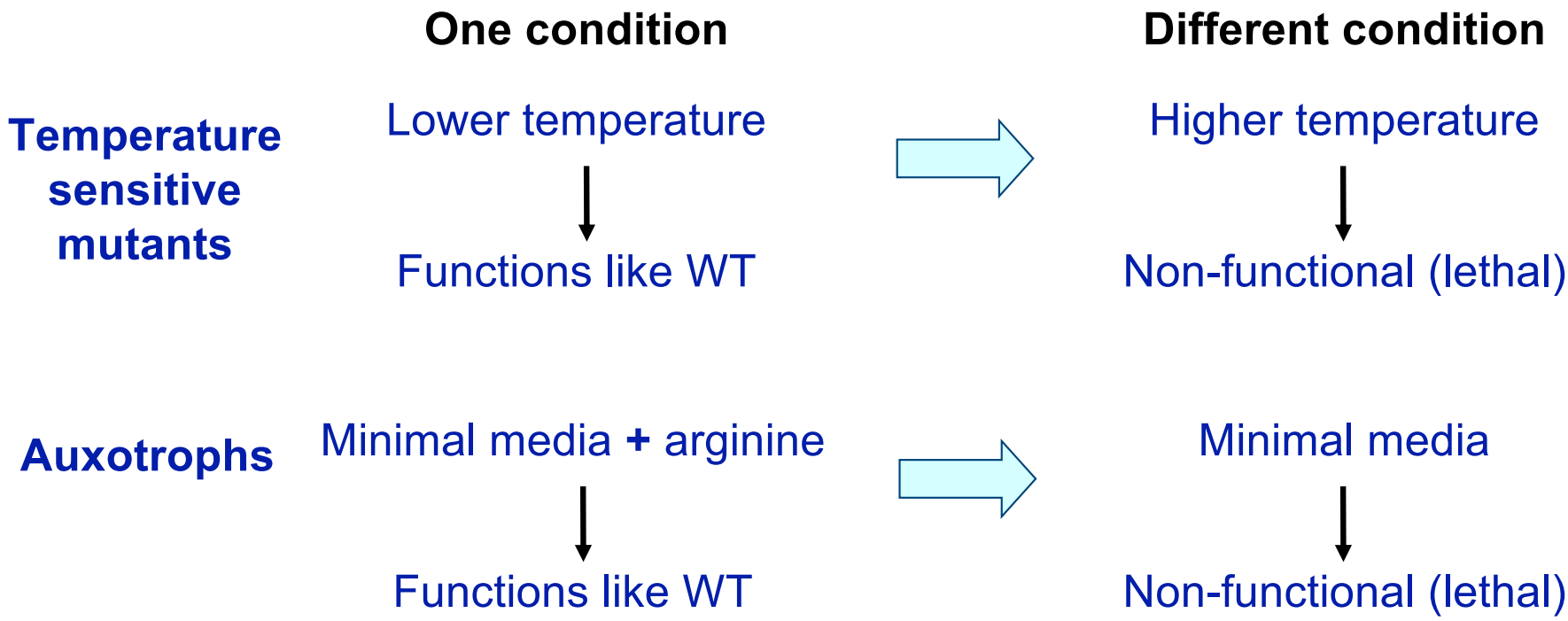
Yellow x Normal → 1:1 Yellow :Normal

Yellow x Yellow → 2:1 Yellow :Normal

Fig 5-7

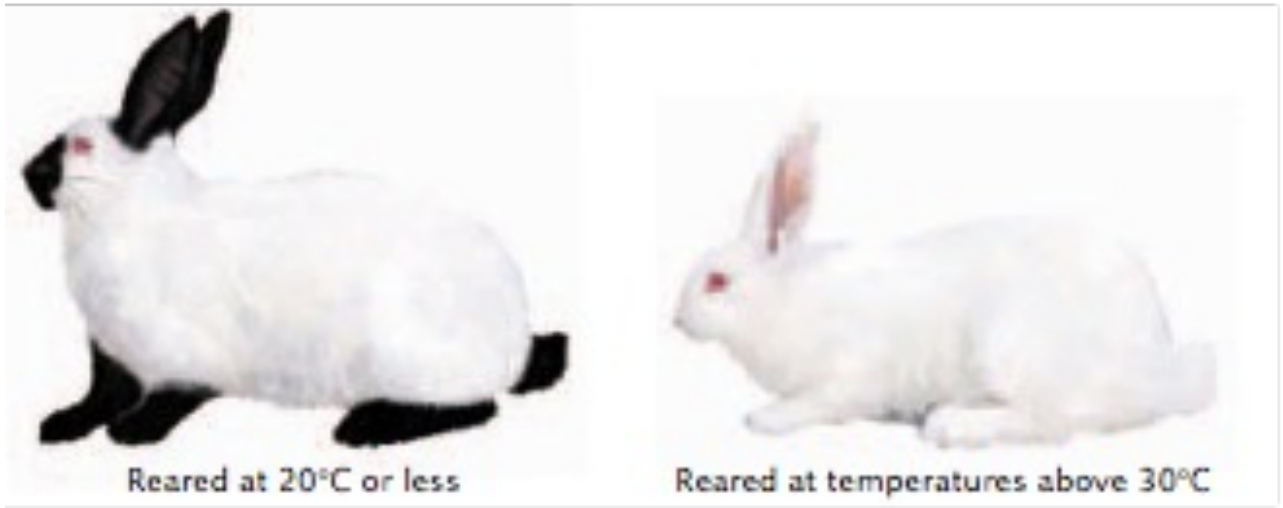
The yellow allele is dominant over dark pigmentation, but recessive lethal, two copies of the dominant allele causing lethality

IV Conditional alleles



Auxotrophs: organisms that lost the ability to synthesize certain substances required for their growth.

Conditional alleles temperature controlled phenotype



5.20 **The expression of some genotypes depends on specific environments.** The expression of a temperature-sensitive allele, *himalayan*, is shown in rabbits reared at different temperatures.

Tyrosine kinase that is active at a lower temperature

Penetrance and expressivity contrasted

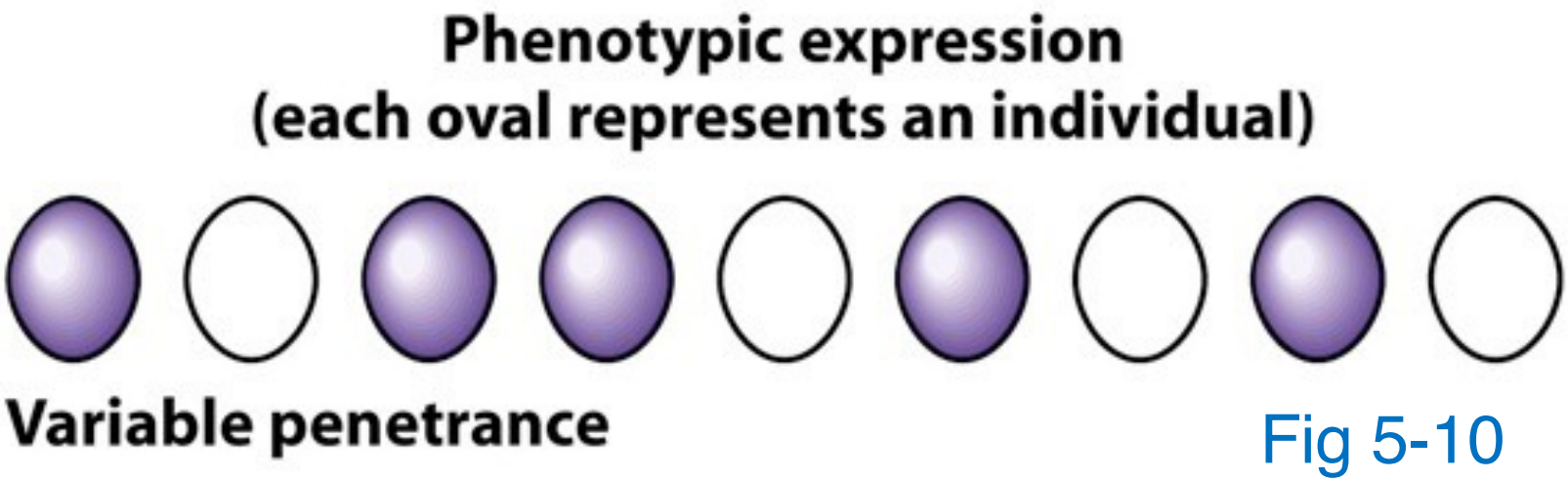


Fig 5-10

Penetrance: the percentage of individuals with a given allele who exhibit the phenotype of that allele

e.g. BRCA2 mutations predispose to breast, ovarian and pancreatic cancers

Why?

- Environment
- Interacting genes
- Subtlety of mutant phenotype - difficult to diagnose (psychiatric disorder)

Incomplete penetrance and pedigrees

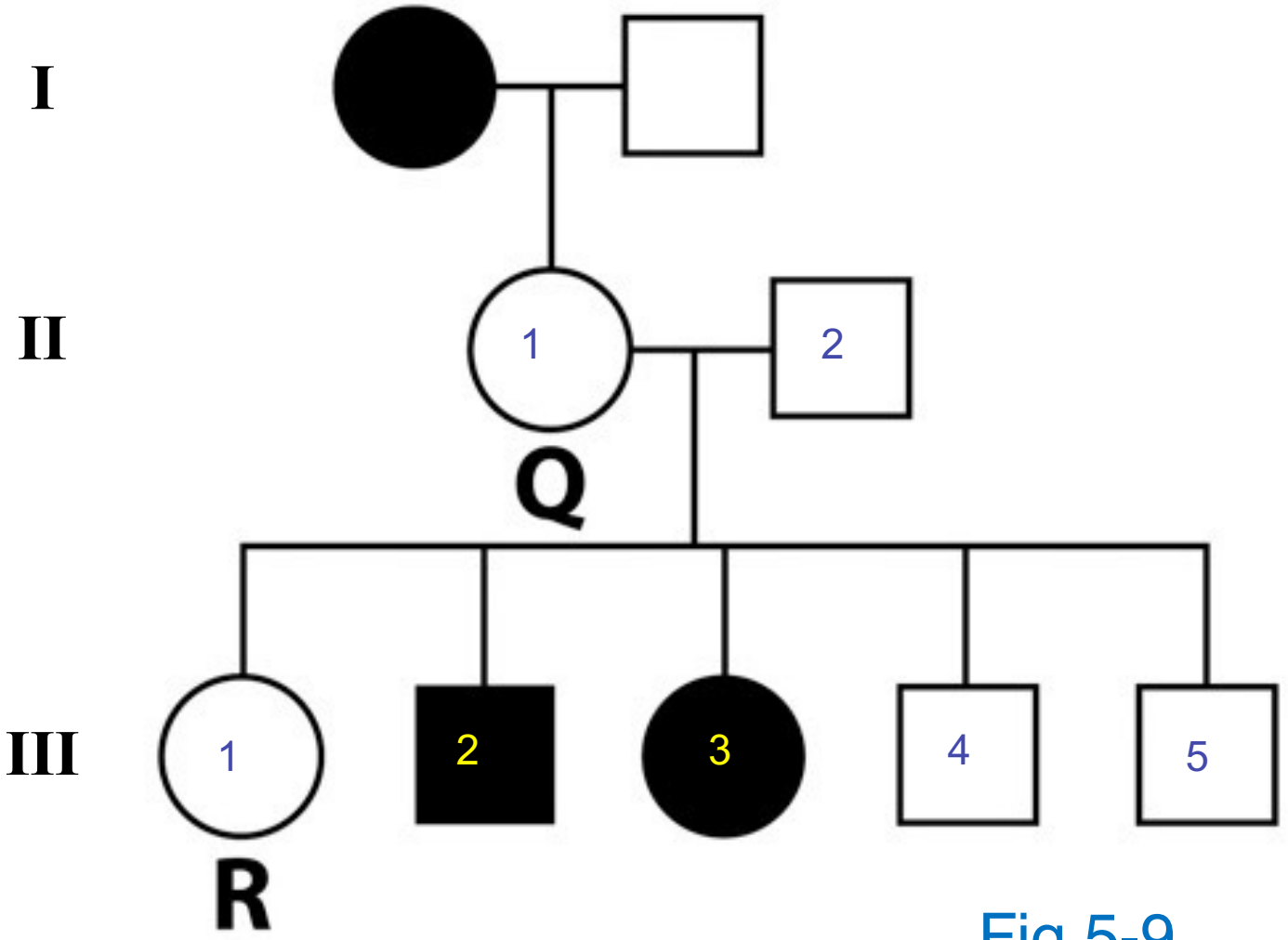


Fig 5-9

Penetrance and expressivity contrasted

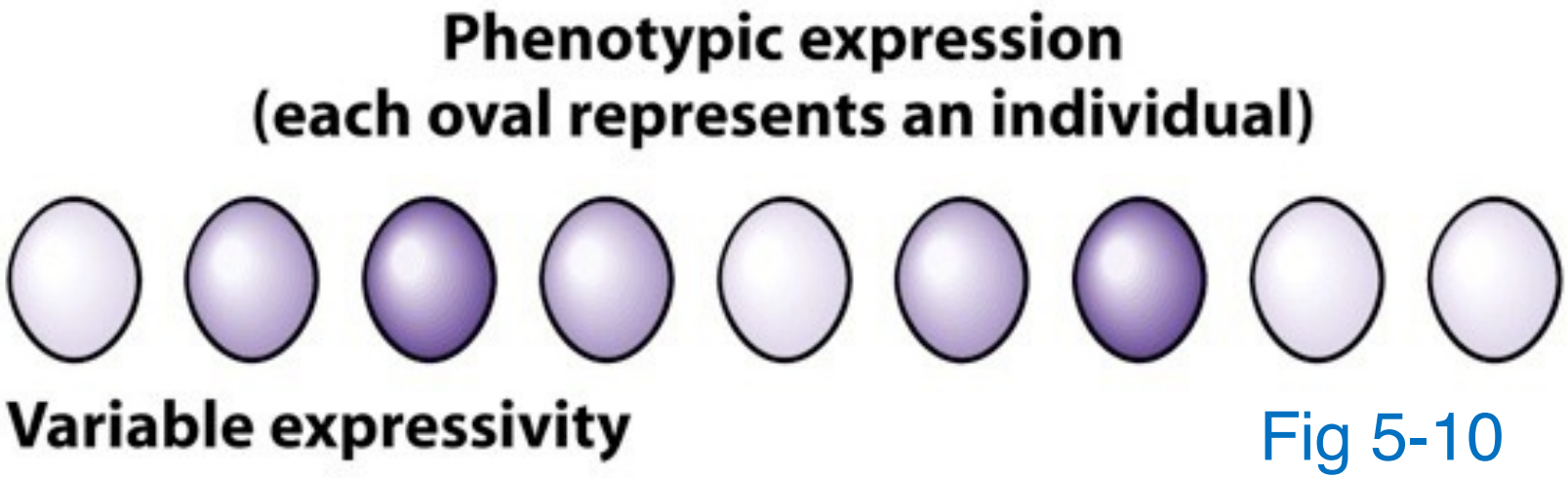
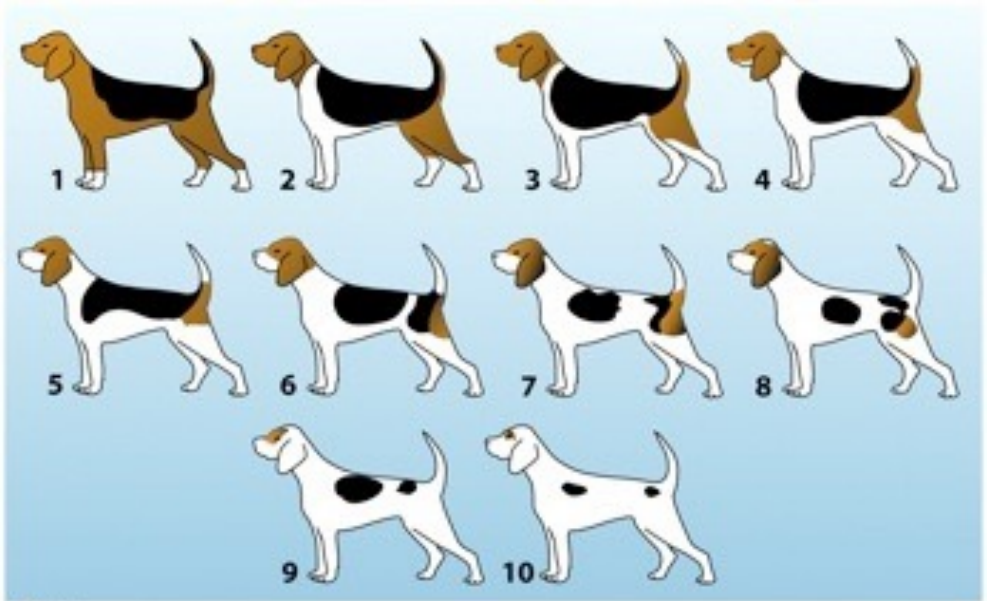


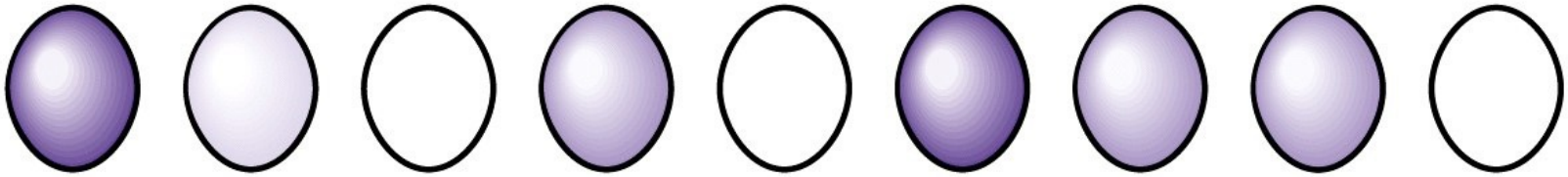
Fig 5-10

Expressivity: the degree to which a given allele is expressed at the phenotypic level, the intensity of the phenotype.



Penetrance and expressivity contrasted

Phenotypic expression
(each oval represents an individual)



Variable penetrance and expressivity

Neurofibromatosis type 1