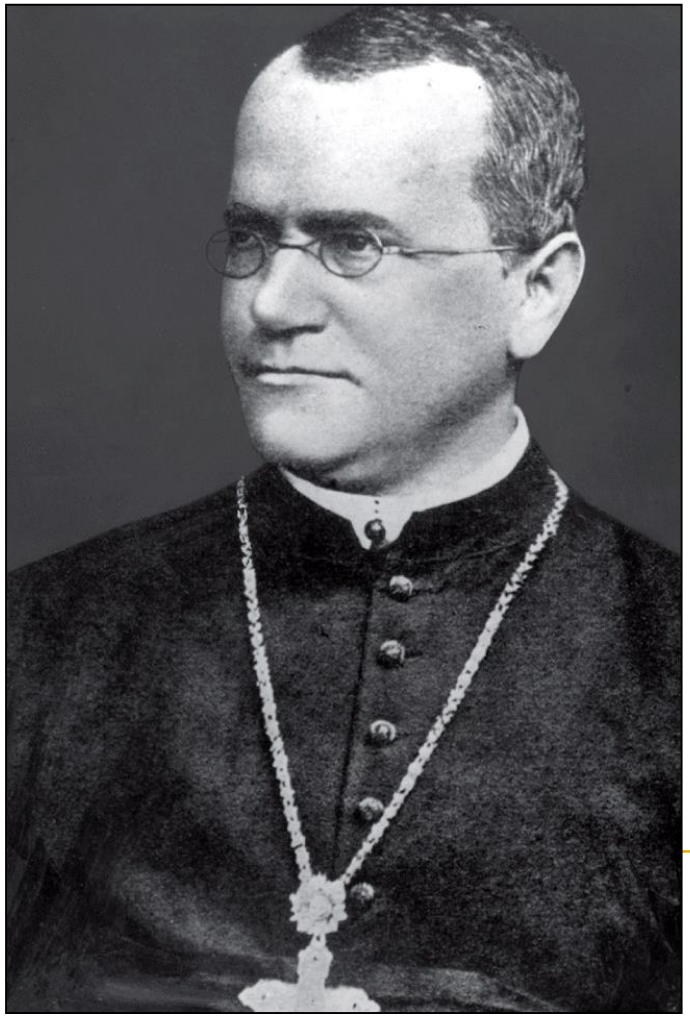
Mendelian Genetics II



Dr. Heng Chooi

Suggested Reading:
Pierce Genetics: A Conceptual Approach (4th edition 2012; 5th edition 2014)
Chapters 3, 6

Slides adapted from Assoc. Prof Martha Ludwig's lecture

Mendelian Genetics II - Learning Outcomes

Following this lecture you should:

- be able to describe a dihybrid.

- know how the 9:3:3:1 phenotypic ratio observed from a dihybrid self cross comes about.

- know and understand Mendel's Second Law.

- know how and why to apply a goodness of fit chi-square test.

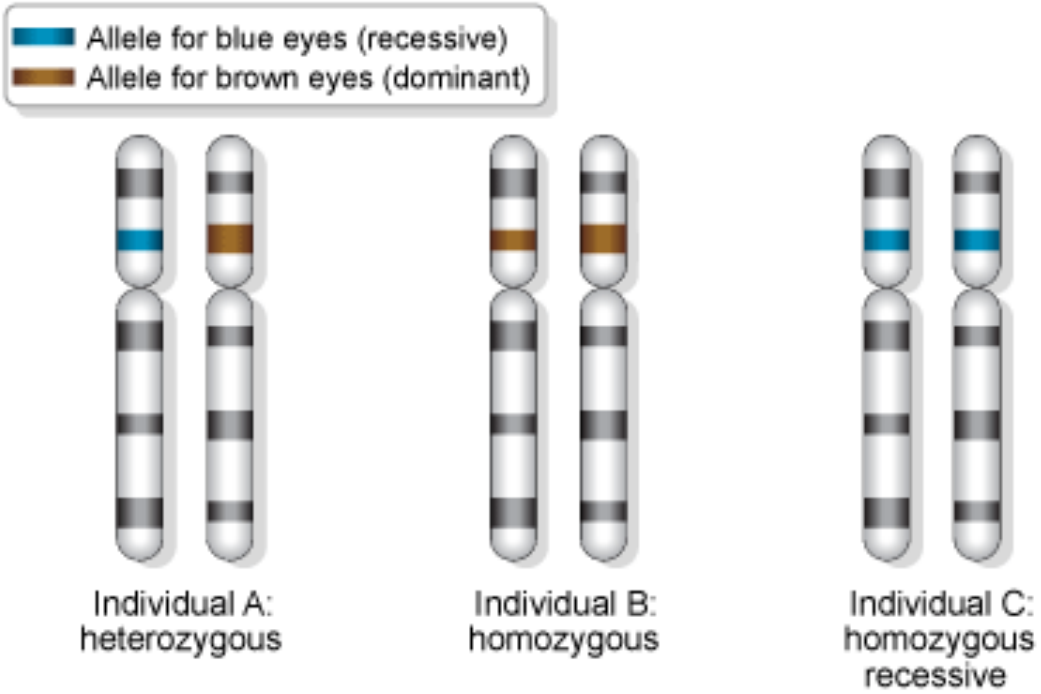
- be able to describe how Mendel's Laws and genetic crosses relate to chromosome behaviour at meiosis

- know the characteristics of autosomal recessive inheritance (e.g. in human pedigrees).

- know the characteristics of autosomal dominant inheritance (e.g. in human pedigrees).

Allele = two alternative (or same) forms of a gene found at the same place on a chromosome (locus).

i.e. each gene in a diploid individual comes in pair (two copies), which we call each of these copies – alleles. One allele can have slight variation to the other.



http://www.bbc.co.uk/schools/gcsebitesize/science/ocr_gateway/understanding_organisms/variation_inheritancerev4.shtml

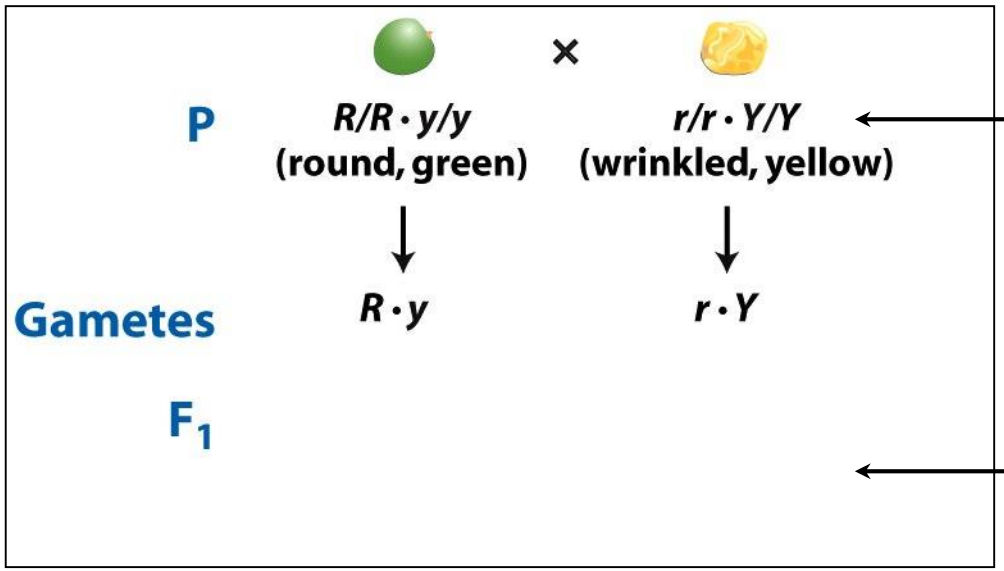
Dihybrid Crosses - The Experiments

[Remember: a monohybrid is a heterozygote for a single gene, e.g. A/a]

Dihybrid: double heterozygote (e.g. A/a, B/b)

- if the genes are on different chromosomes: A/a ; B/b
- if the genes are on the same chromosome: AB/ab
- if the location of the two genes is not known: A/a • B/b

Reminder:
A and a are two alleles (forms) of the same gene

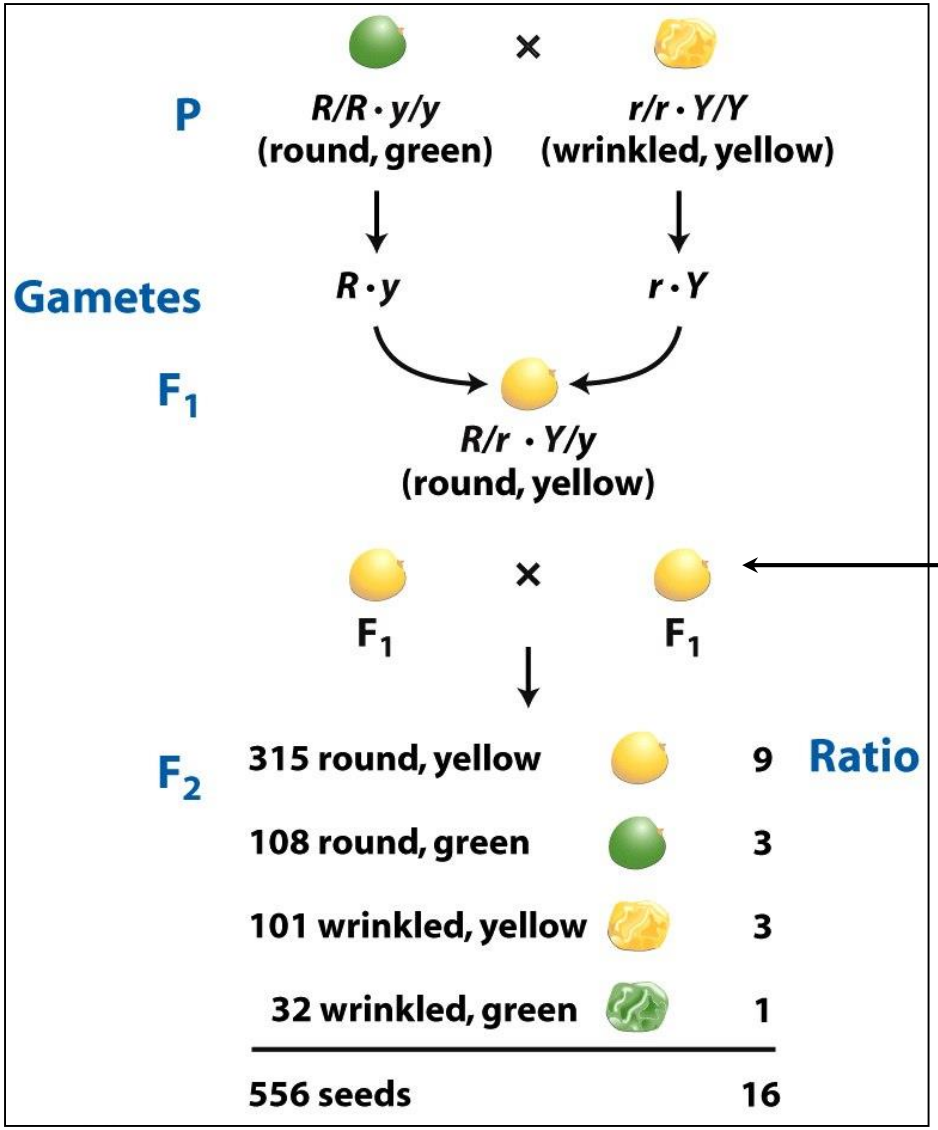


Mendel did not know the location of the units of inheritance

round and yellow are the dominant phenotypes, R and Y are the dominant genes

Griffiths *et al*. (2012) *Introduction to Genetic Analysis*, p 83

Dihybrid Crosses - The Experiments



What happened to the 3:1 ratio?

How has this more complex ratio come about?

selfed

9:3:3:1 phenotypic ratio

Griffiths *et al*. (2012) *Introduction to Genetic Analysis*, p 83

Dihybrid Crosses - The Explanation

The number of individuals for each trait:

Seed shape:

Round 315 + 108 = 423
Wrinkled 101 + 32 = 133

} 3:1

Seed colour:

Yellow 315 + 101 = 416
Green 108 + 32 = 140

} 3:1

The 9:3:3:1 ratio is made up of two different 3:1 ratios combined at random

3/4 of the F_2 are round

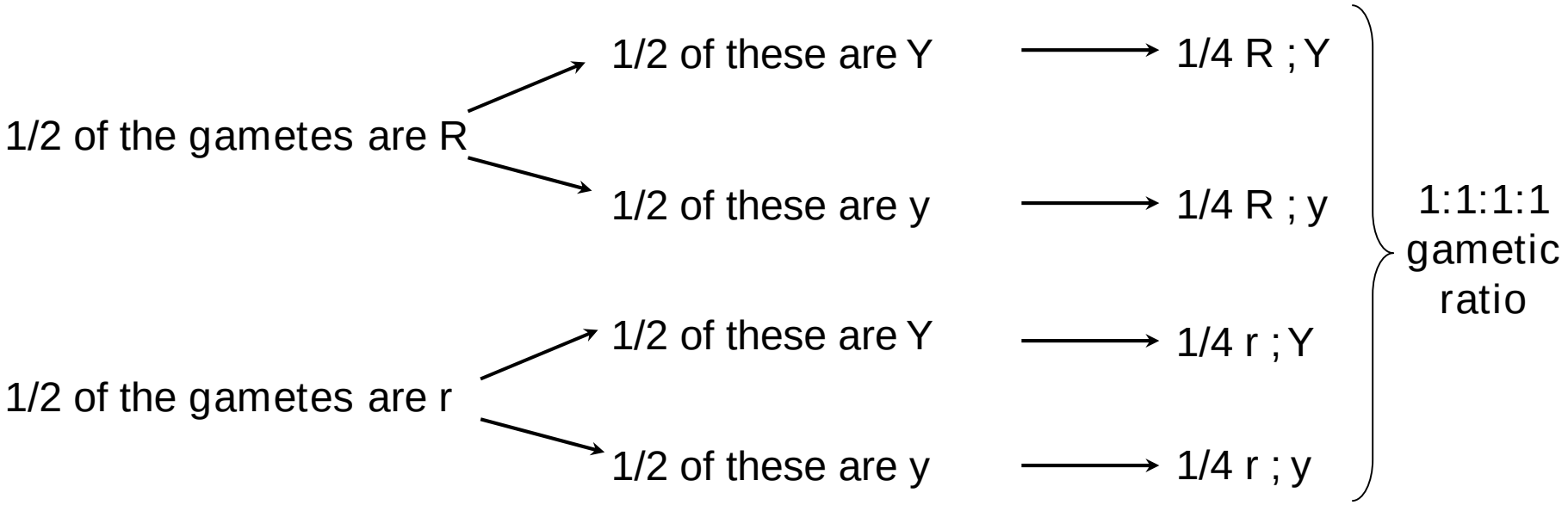
1/4 of the F_2 is wrinkled

Mendel's Second Law - The Law of Independent Assortment

"Gene pairs on different chromosome pairs assort independently at meiosis."

Dihybrid Crosses - The Explanation

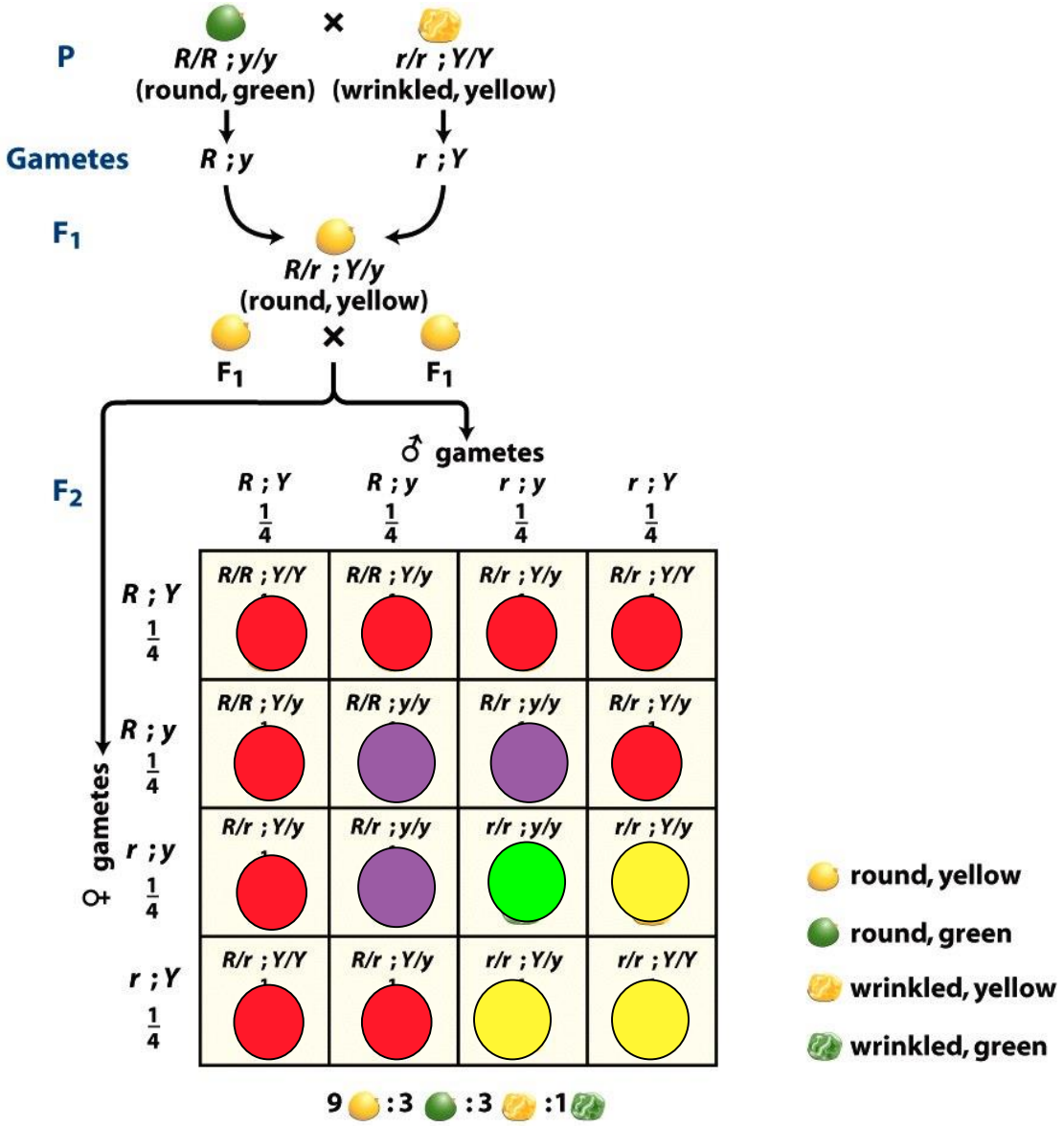
For the F_1 dihybrid R/r ; Y/y



In a F_1 x F_1 self cross - male and female gametes will be in the same proportions and the four female gametes will be fertilised randomly by the four male gametes

Mendel's two laws of equal segregation and independent assortment

Punnett Square - Illustrating the Genotypes of the F_2 Generation Resulting from a Dihybrid Cross



Griffiths *et al*. (2012), p 85; Crew (67) Biographical Memoirs of Fellows of the Royal Society *13*: 309

Using a Testcross to Verify the 1:1:1:1 Gametic Ratio Produced from a Dihybrid

R/r ; Y/y	x	r/r ; y/y	
1/4 R ; Y 1/4 R ; y 1/4 r ; Y 1/4 r ; y		all r ; y	1/4 R/r ; Y/y 1/4 R/r ; y/y 1/4 r/r ; Y/y 1/4 r/r ; y/y
gametes		gametes	progeny

Proportions of progeny correspond to proportions of gametes produced by the dihybrid

Remember: The tester (r/r ; y/y) contributes only recessive alleles - allows gametes produced by individual of unknown genotype to be determined from the progeny resulting from the cross

Determining the Probability that the Difference Between Observed and Expected Values are Due to Chance

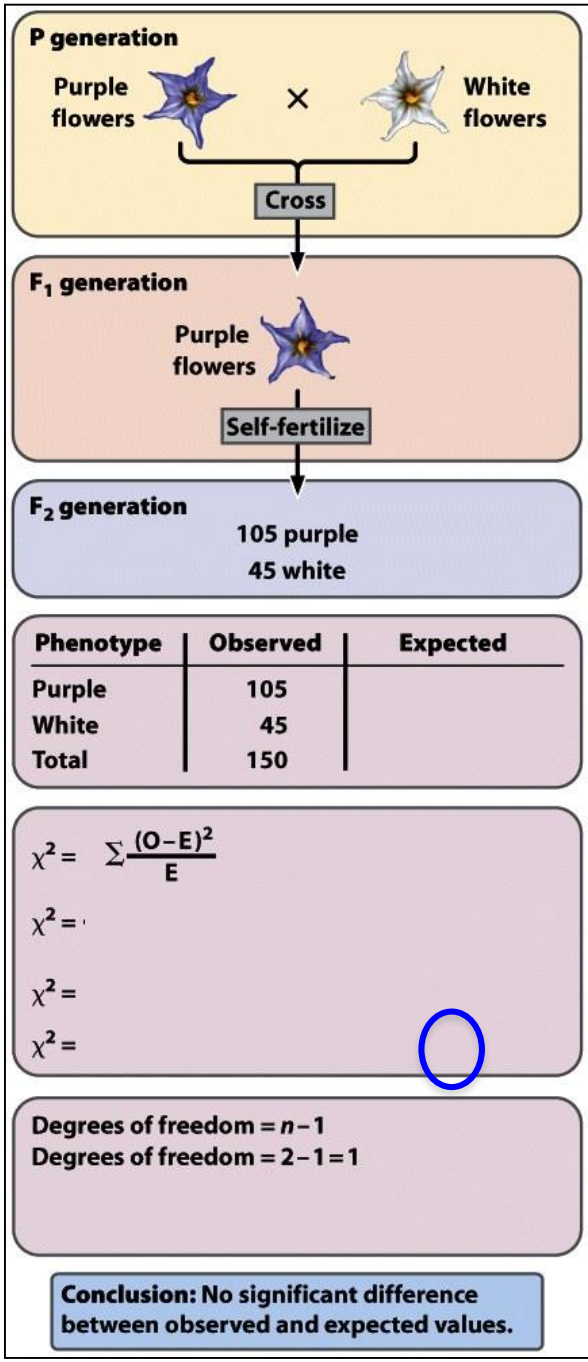
Goodness of Fit Chi-Square (χ^2) Test

Looks like a 3:1 ratio. Is it just by chance that these numbers deviate from a true 3:1 ratio?

When using the chi-square test, be sure to work with numbers of individuals, not proportions or percentages

Calculated chi-square value is compared with theoretical values with the same degrees of freedom (df; see Table, next slide)

- for a goodness of fit chi-square test, df = n – 1, where n is the expected number of phenotypes



Pierce (2012) *Genetics: A Conceptual Approach*, p 63

df = *n* – 1
= 2 – 1
= 1

Table 3.4 Critical values of the χ^2 distribution

	P							
df	**0.995**	**0.975**	**0.9**	**0.5**	**0.1**	**0.05**	**0.025**	**0.01**	**0.005**
1	0.000	0.000	0.016	0.455	2.706	3.841	5.024	6.635	7.879
2	0.010	0.051	0.211	1.386	4.605	5.991	7.378	9.210	10.597
3	0.072	0.216	0.584			7.815	9.348	11.345	12.838
4	0.207	0.484	1.064	3.357	7.779	9.488	11.143	13.277	14.860
5	0.412	0.831	1.610	4.351	9.236	11.070	12.832	15.086	16.750
6	0.676	1.237	2.204	5.348	10.645	12.592	14.449	16.812	18.548
7	0.989	1.690	2.833	6.346	12.017	14.067	16.013	18.475	20.278
8	1.344	2.180	3.490	7.344	13.362	15.507	17.535	20.090	21.955
9	1.735	2.700	4.168	8.343	14.684	16.919	19.023	21.666	23.589
10	2.156	3.247	4.865	9.342	15.987	18.307	20.483	23.209	25.188
11	2.603	3.816	5.578	10.341	17.275	19.675	21.920	24.725	26.757
12	3.074	4.404	6.304	11.340	18.549	21.026	23.337	26.217	28.300
13	3.565	5.009	7.042	12.340	19.812	22.362	24.736	27.688	29.819
14	4.075	5.629	7.790	13.339	21.064	23.685	26.119	29.141	31.319
15	4.601	6.262	8.547	14.339	22.307	24.996	27.488	30.578	32.801

$0.1 < P < 0.5$

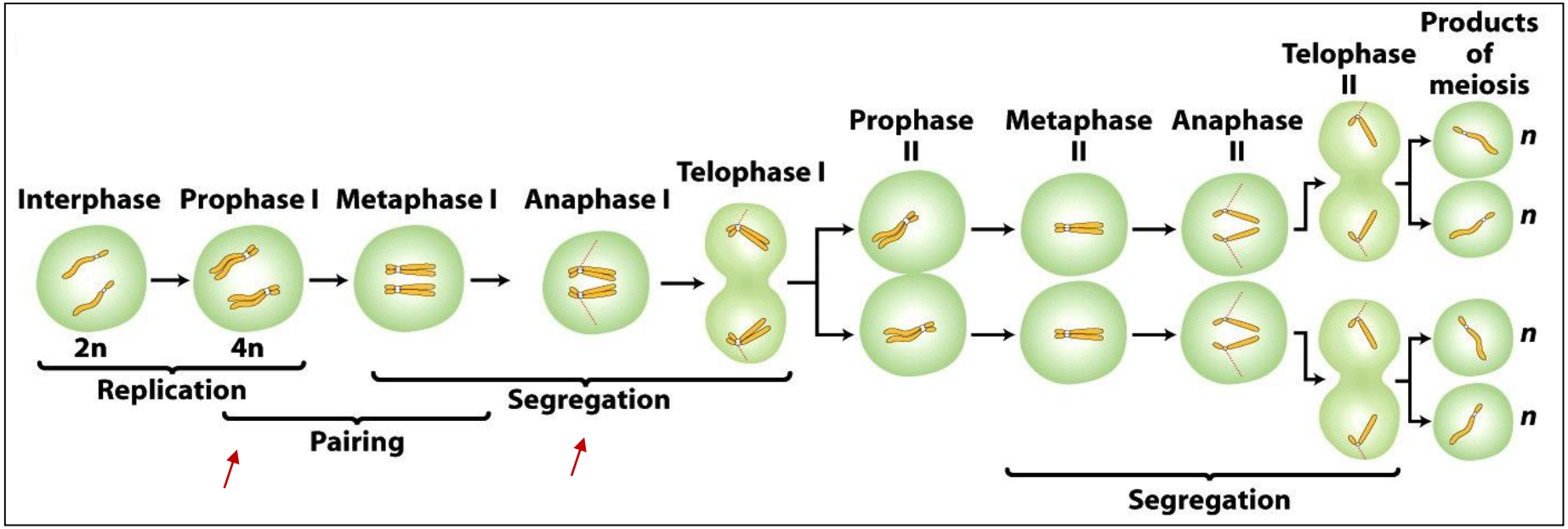
P, probability; df, degrees of freedom. *High probability deviation due to chance, hypothesis supported!*

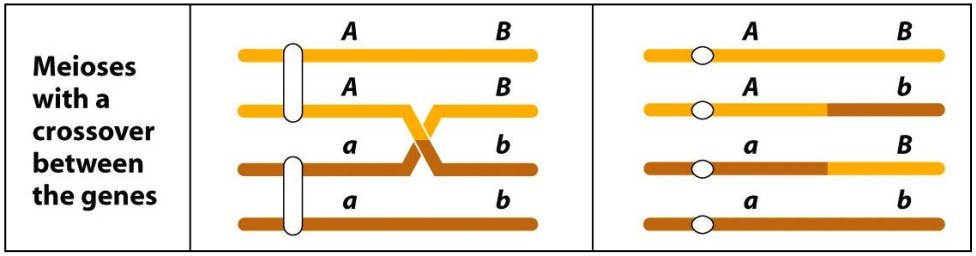
A 0.05 probability (P) level is the typically accepted cutoff value

- P > 0.05 suggest chance is responsible for the deviation seen between expected and observed values.
- P < 0.05 suggest that chance is not responsible, and a significant difference exists between the expected and observed values.

Pierce (2012) *Genetics: A Conceptual Approach*, p 62

Relating Genetic Crosses and Mendel's Laws with Chromosome Behaviour in Meiosis



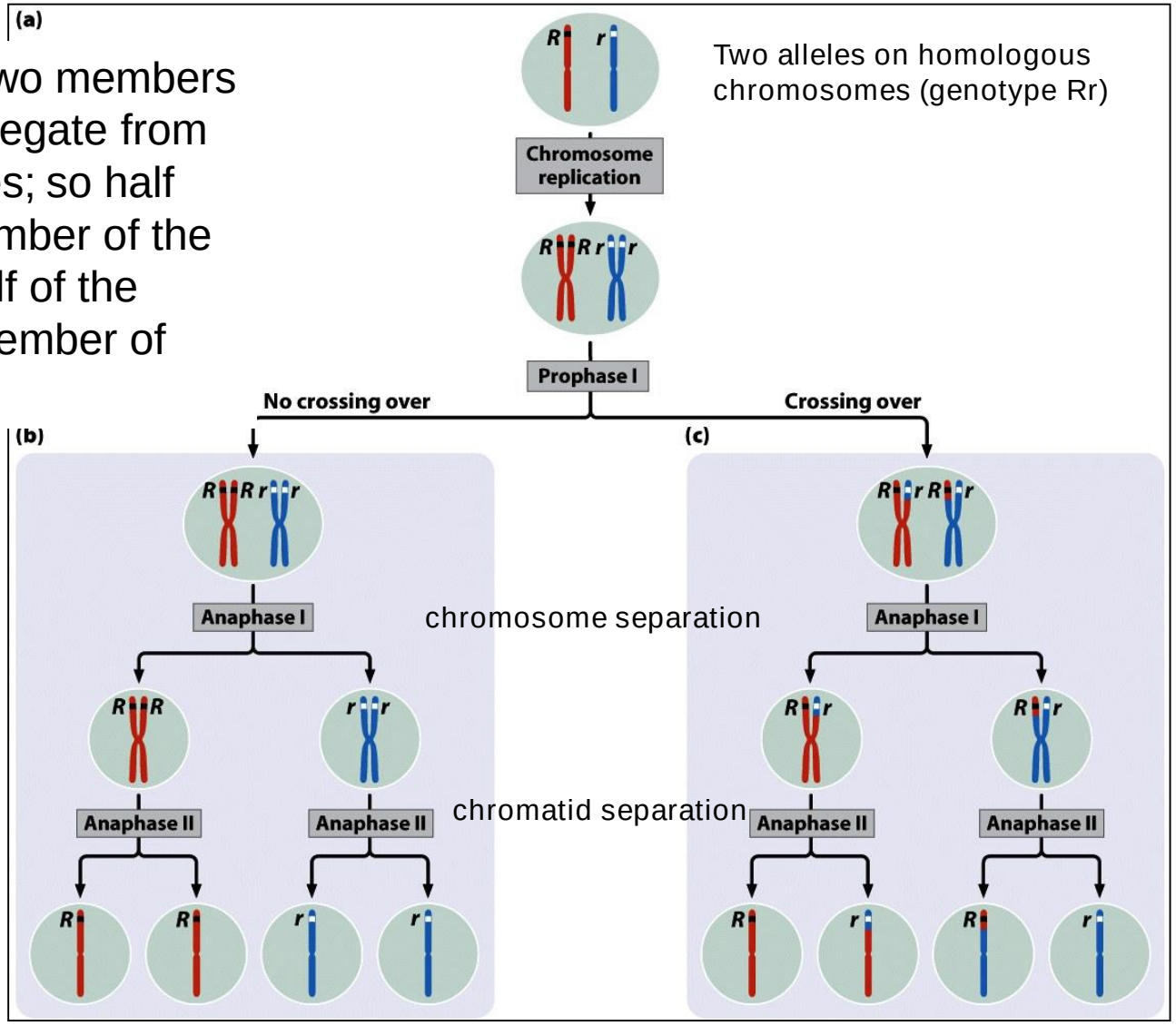


Crossing over occurs in Prophase I (if it occurs)

Griffiths *et al*. (2012) *Introduction to Genetic Analysis*, pp 36, 129

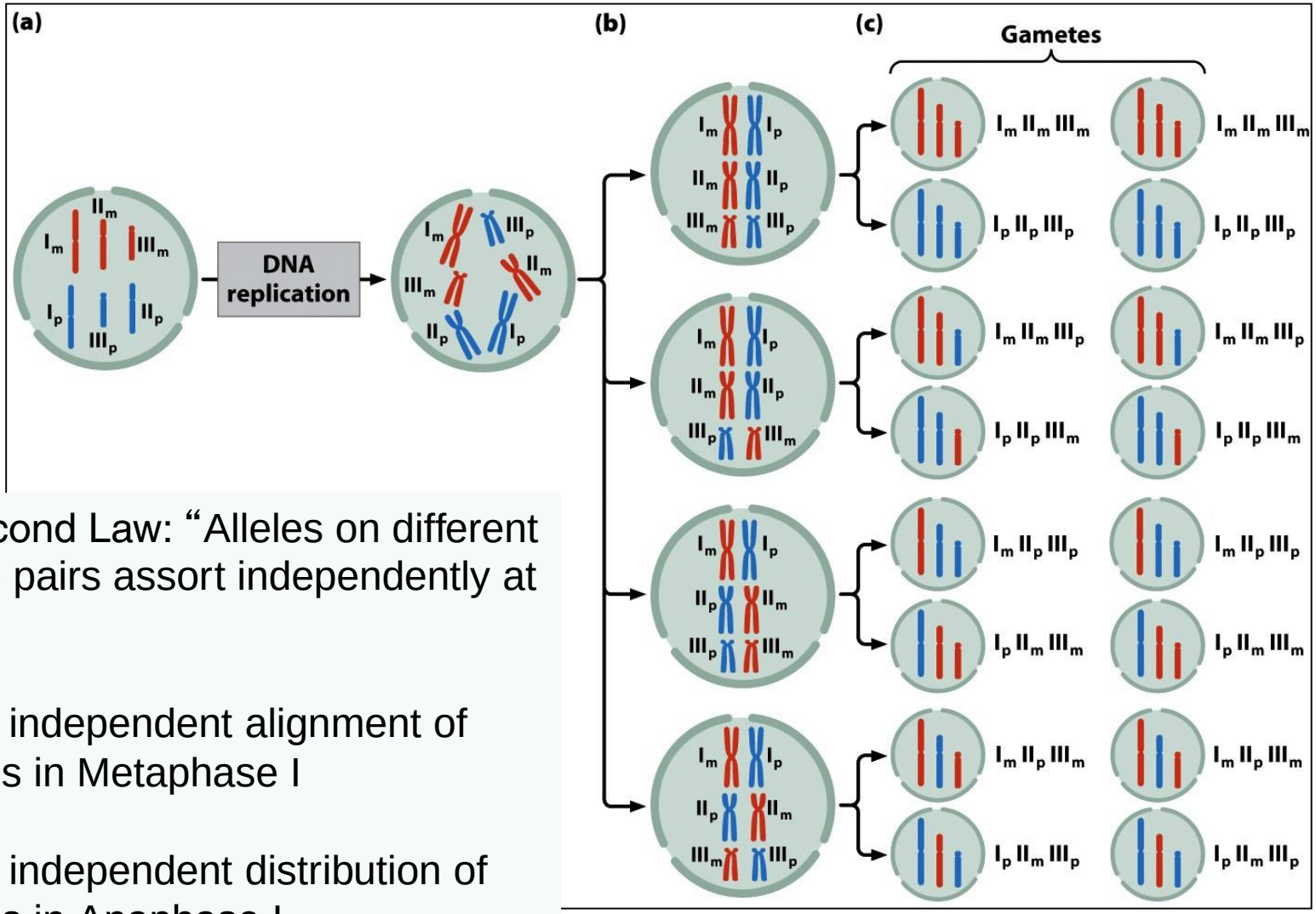
Relating Genetic Crosses and Mendel's Laws with Chromosome Behaviour in Meiosis

Mendel's First Law: "The two members of a gene pair (alleles)segregate from each other into the gametes; so half the gametes carry one member of the gene pair and the other half of the gametes carry the other member of the gene pair."



Pierce (2012) *Genetics: A Conceptual Approach*, p 50

Relating Genetic Crosses and Mendel's Laws with Chromosome Behaviour in Meiosis



Mendel's Second Law: "Alleles on different chromosome pairs assort independently at meiosis."

•random and independent alignment of chromosomes in Metaphase I

•random and independent distribution of chromosomes in Anaphase I

Pierce (08) *Genetics: A Conceptual Approach*, p 31

Recognising Equal Segregation and Independent Assortment

Use Mendel's Laws to predict;

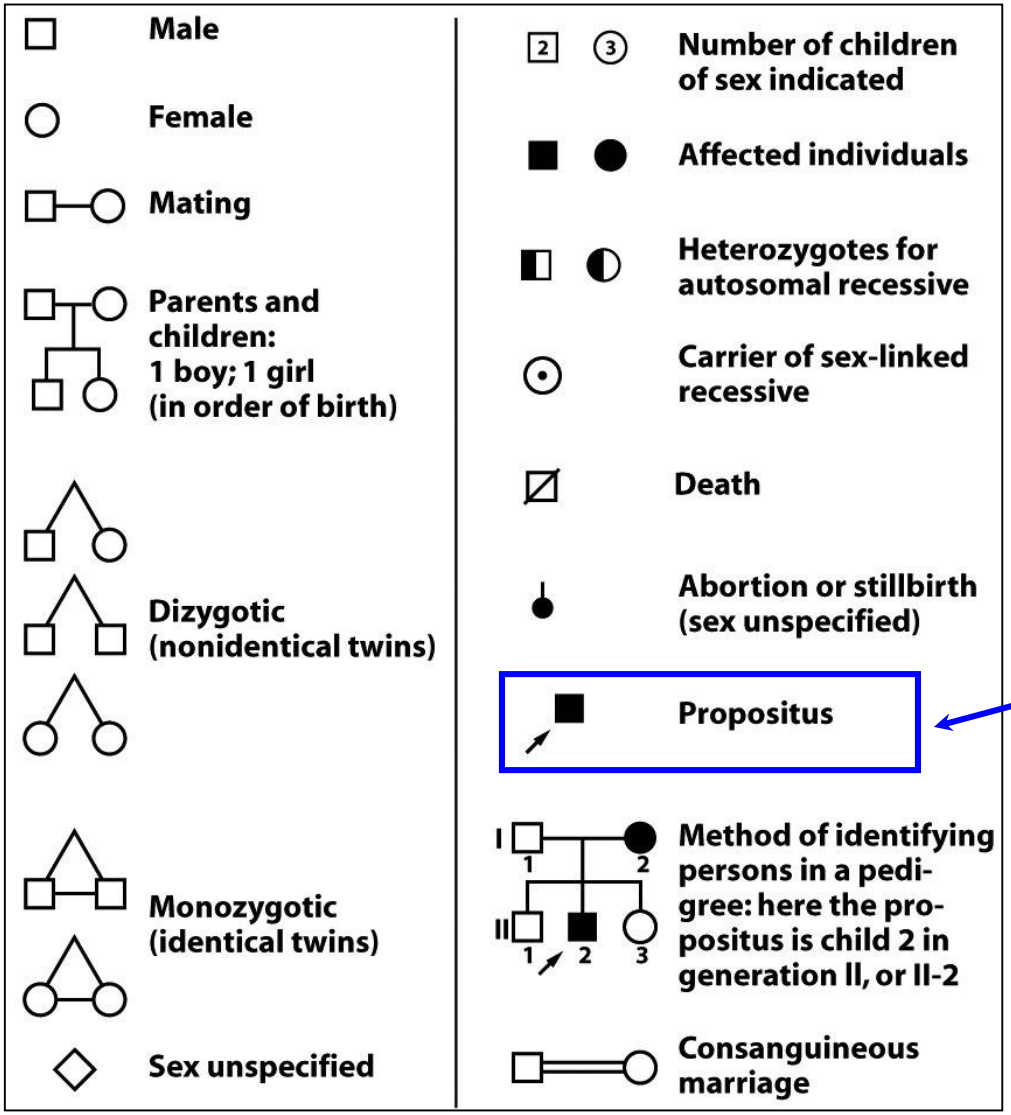
- progeny from known parental genotypes
  - establish stocks for plant and animal breeding or basic research
  - likelihood of inheriting a medical condition or disorder caused by a single gene

- parental genotypes from progeny phenotypes
  - inheritance patterns of particular traits (e.g. dominant, recessive)

Have a look at this interactive site:
http://www.sumanasinc.com/webcontent/animations/content/mendel/mendel.html
http://www.sumanasinc.com/webcontent/animations/content/mendelindassort.html

(*need Adobe Flash plugin)

Single Gene Inheritance - Human Genetics



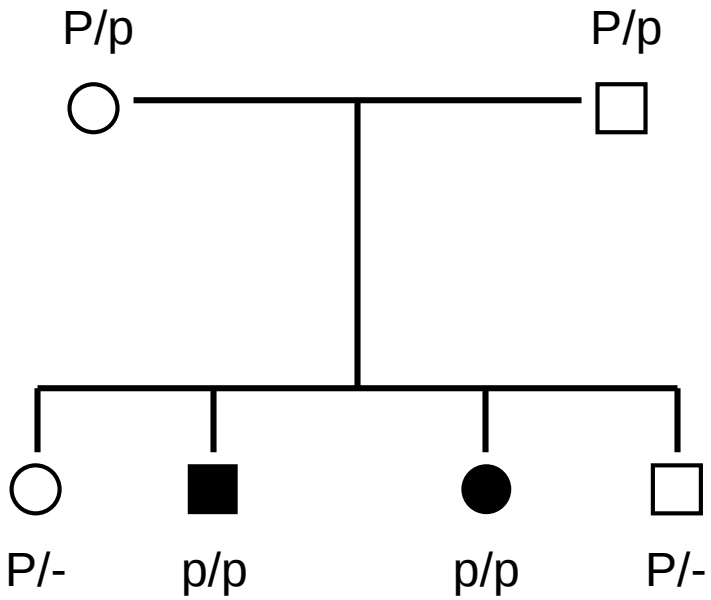
Cannot do controlled crosses with humans

Use pedigree analysis (family tree) to infer single gene inheritance

family member with distinct phenotype

Griffiths *et al*. (2012) *Introduction to Genetic Analysis*, p 54

Human Mendelian Genetics - Autosomal Recessive Traits



P = normal condition
p = disorder

■ , ● affected

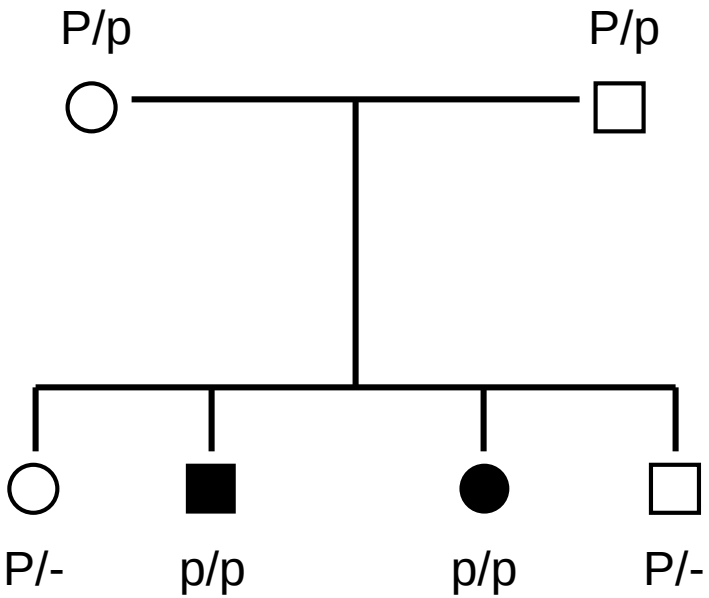
Autosomal recessive inheritance is characterised by:

- both parents being heterozygotes
- appearance in progeny of unaffected individuals
- both male and female progeny affected
- may skip generations

e.g. Phenylketonuria (PKU)

- defective gene encoding the enzyme phenylalanine hydrolase
  - converts phenylalanine to tyrosine
- phenylpyruvic acid is synthesised from phenylalanine instead
  - neurological damage, mental retardation

Human Mendelian Genetics - Autosomal Recessive Traits



Expected a 3:1 ratio, not a 1:1 ratio...

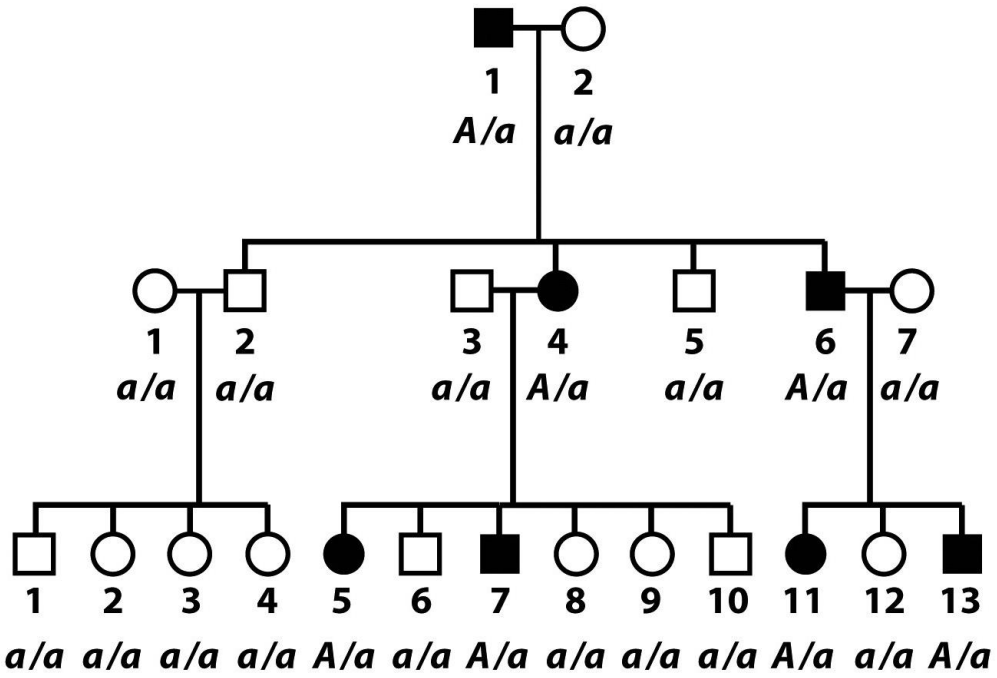
HOWEVER: sample size is small

To see a 3:1 ratio, would need around 20 progeny(!)

P = normal condition
p = disorder

■ , ● affected

Human Mendelian Genetics - Autosomal Dominant Traits



Autosomal dominant inheritance is characterised by:

- appearance in every generation
- both male and female progeny affected
- affected parent has a 50% chance of passing allele to each child
- e.g. Huntington disease

Griffiths *et al*. (2012) *Introduction to Genetic Analysis*, p 57