Human Pedigrees

Bio207 Jan 9

http://www.erin.utoronto.ca/~w3bio/bio207/index.htm

Course Overview

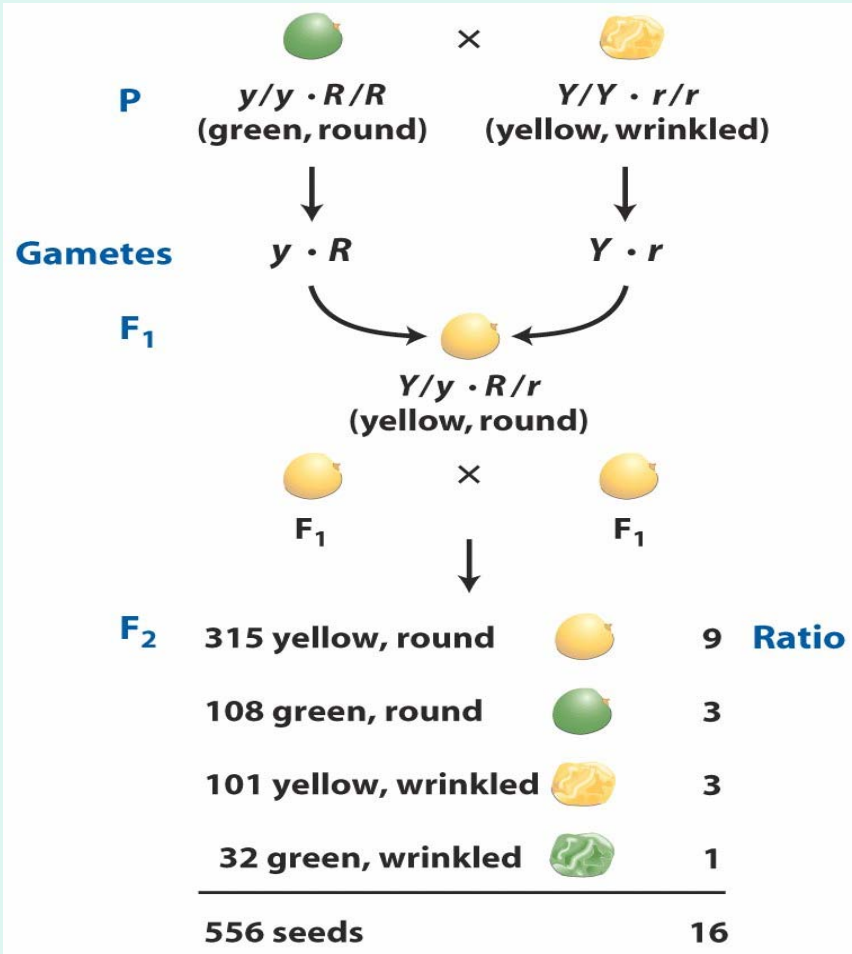
Outline Week	Topic	Chapter
1	Course objectives and Introduction to genetics	Ch. 1 & Ch. 2
2	Human Pedigrees	Ch. 2
3	Patterns of Inheritance: sex-linkage	Ch. 2
4	Chromosomal basis of inheritance	Ch. 3
5	Changes in chromosome number	Ch. 15
6	Gene Mapping	Ch. 4 (Ch. 16)
7	Gene to Phenotype	Ch. 6
8	Modified Mendelian ratios	Ch. 6
9	Model organisms and mutants	Ch. 6 (Ch. 16)
10	Genetics of Plant Development (Arabidopsis)	Ch. 18
11	Genetics of Animal Development (Drosophila)	Ch. 18
12	Behaviour Genetics/Quantitative genetics	Ch. 16 + papers

Introduction to genetic analysis

Griffiths, A., Wessler, S.R., Lewontin,R.C., Gelbart, W.M.,Suzuki, D.T. and Miller, J.H.
Eighth Edition, W.H. Freeman and Company NY

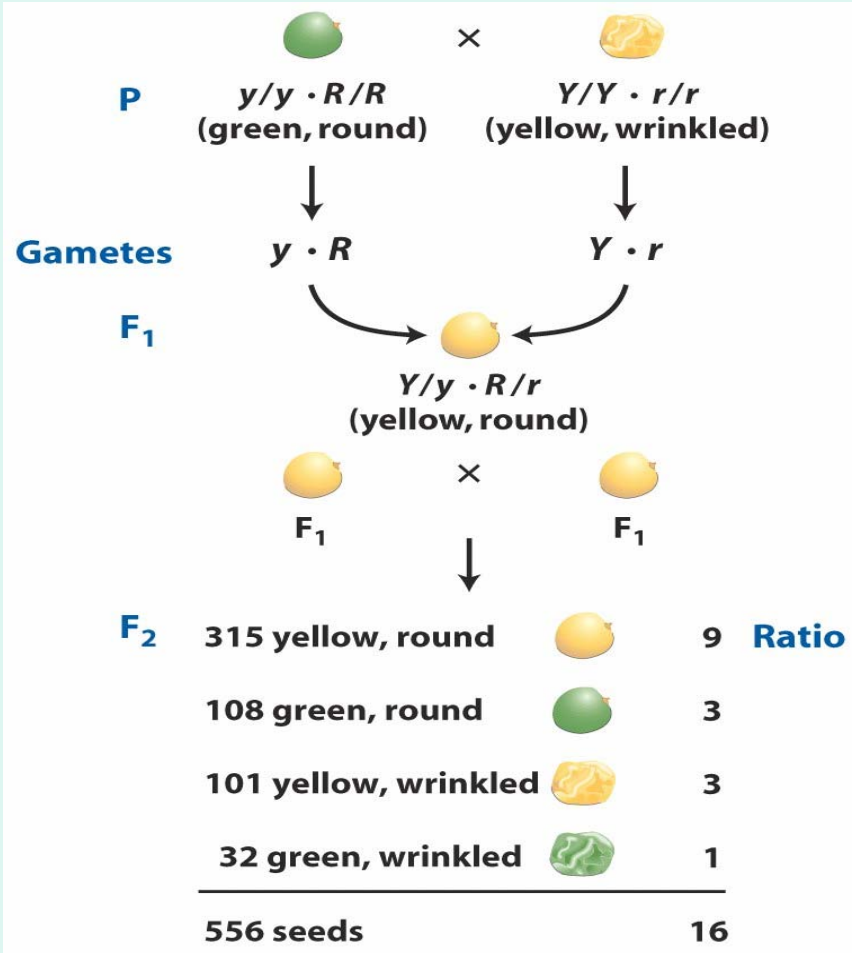
- Part I Transmission genetic analysis
- Chapter 1: all questions p. 24-26
- Chapter 2: all the questions p. 62-72

Dihybrid cross



- The P gametes carry one allele of each gene pair
- Three of four F_2 are round *ie* 3:1 ratio for seed shape
- Three of four F_2 are yellow *ie* 3:1 ratio for seed colour

Dihybrid cross



- The P gametes carry one allele of each gene pair
- Three of four F_2 are round *ie* 3:1 ratio for seed shape
- Three of four F_2 are yellow *ie* 3:1 ratio for seed colour
- The two different 3:1 ratios combined at random gave the 9:3:3:1 ratio

Text ch. 2 p 37

Probability

Probability = the # of times an event happens/
the # of opportunities for an event to happen

- The probability of rolling a 3 on a die in one trial is:
  - P (of a 3) = 1/6

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- The second example shows the product rule:
  - The probability of two independent events occurring simultaneously is the product of each of their respective probabilities

Probability: Product rule

- The probability of two independent events occurring simultaneously is the product of each of their respective probabilities
  - Ie. RrYy x RrYy
    - What is the probability of getting rryy genotype ?
    - ¼ * ¼ = 1/16

Text p.39

R/r ; Y/y X R/r ; Y/y

*

¾ will be R_

¾ will be Y_ → ¾ * ¾ = 9/16 R_ ; Y_

¼ will be yy → ¾ * ¼ = 3/16 R_ ; yy

¼ will be rr

¾ will be Y_ → ¼ * ¾ = 3/16 rr ; Y_

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R phenotype

Y phenotype

*Note R_ represents RR and Rr ; similarly Y_ represents YY and Yy

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Probability question

- When many genes are considered you must use probabilities answer questions:
- Question: in the cross
  - AaBbCcDdEeFf x AaBbCcDdEeFf what proportion of the progeny will be AAbbCcDDeeFf ?

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    - P(AAbbCcDDeeFf) = (¼) x (¼) x (½) x (¼) x (¼) x (½) = 1/1024

Mendelian recessive alleles

- Many human conditions and diseases are determined by simple Mendelian recessive alleles.
- Quite often the recessive alleles of the same gene are revealed by cousin marriages / unions.
  - This is especially true of rare conditions where the chance mating of carriers is extremely rare

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  - This is especially true of rare conditions where the chance mating of carriers is extremely rare
  - For example ~20% of albinos are born of unions between cousins
  - And first cousin marriages account for ~40% of Tay-Sachs kids
  - Also true of disease-causing recessive alleles *eg*. cystic fibrosis and PK4 phenylketonuria

Methodologies used in genetics

- Isolation of mutations affecting the biological process under study.

Text ch. 1 p.11-12

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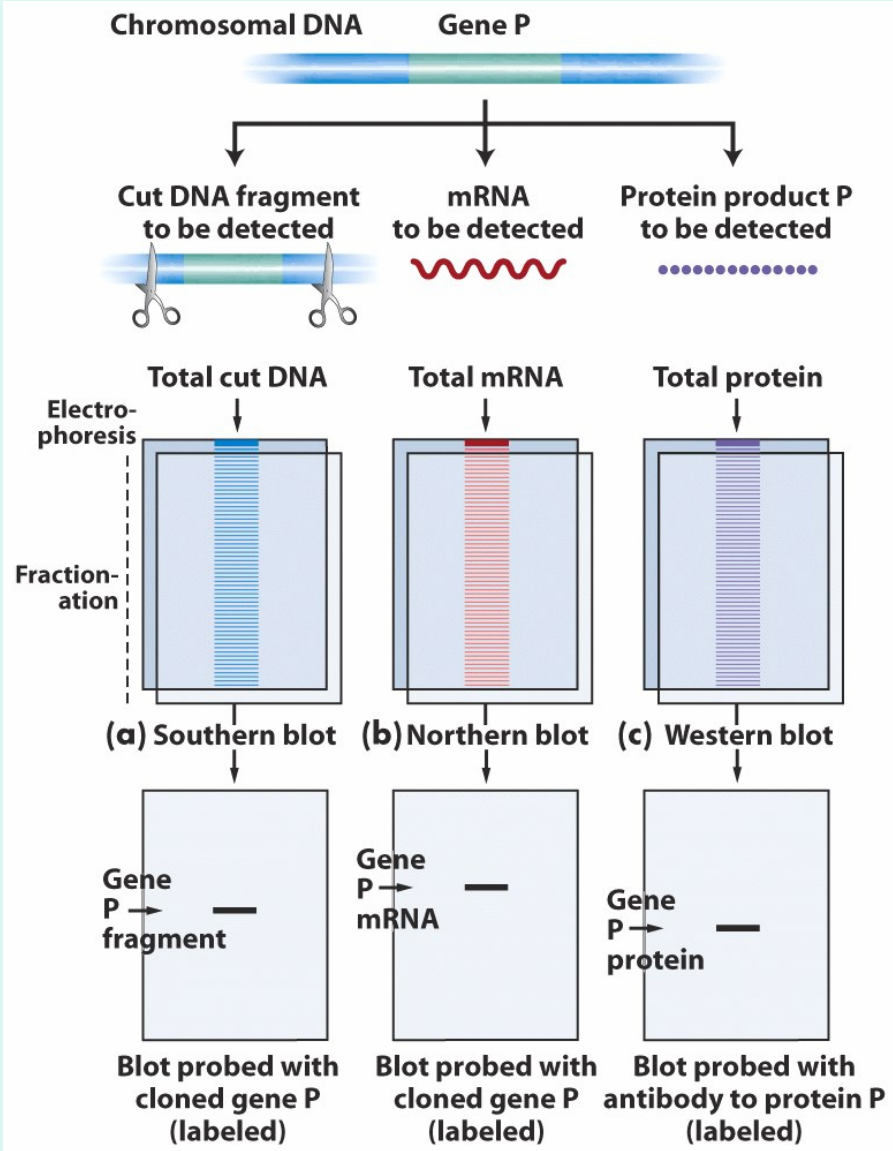
- Isolation of mutations affecting the biological process under study.
- Analysis of the progeny of controlled matings “crosses” if using model organisms (or pedigree analysis for humans)
- Genetic analysis of the biochemical process
- Microscopic analysis of the chromosome structure
- Direct analysis of the DNA

Text ch. 1 p.11-12

Probing DNA, RNA and Protein mixtures

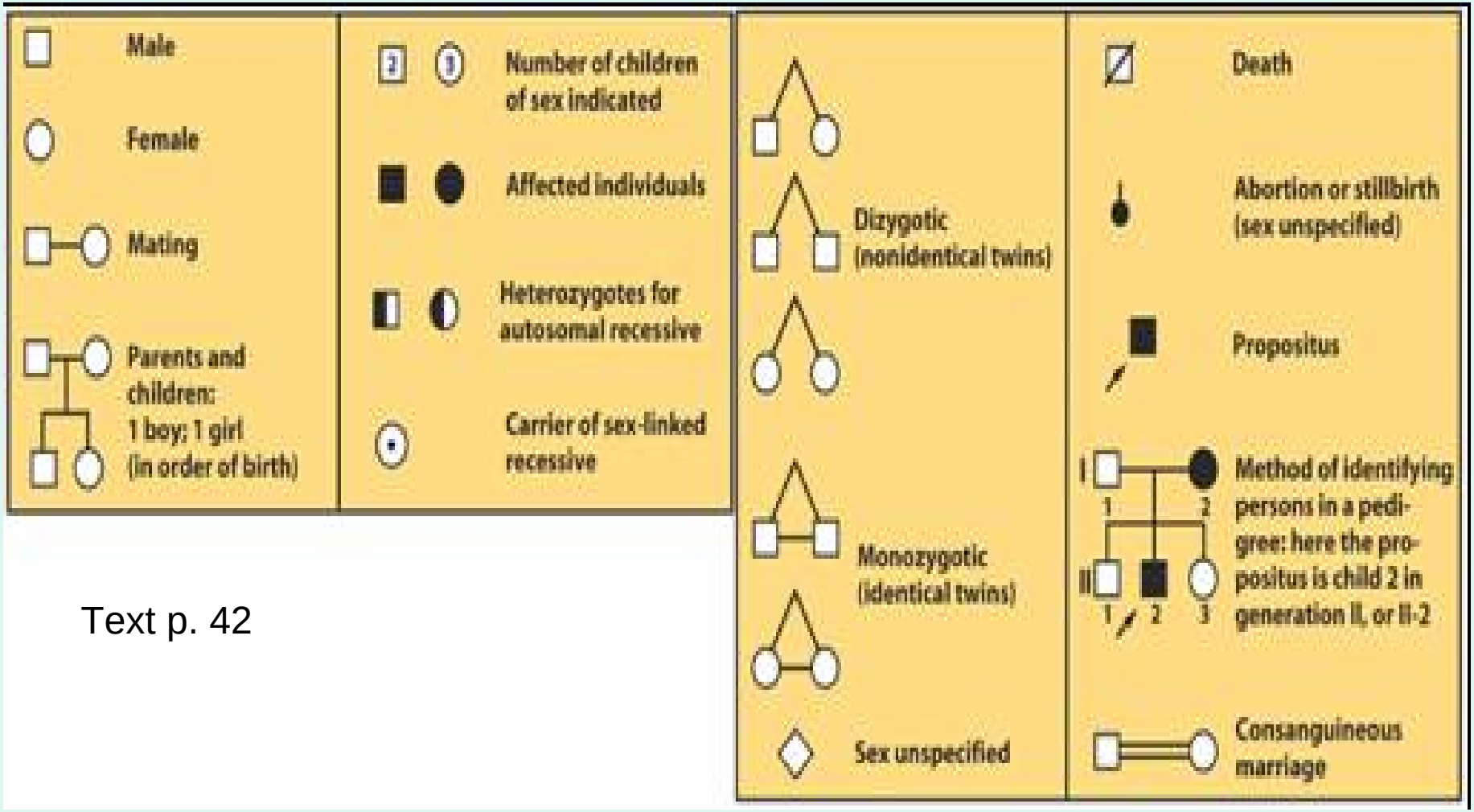


Text p. 3-7 & 12-13

Mendelian genetics:humans

- Mendelian genetics can be applied to human genetics
- The family tree or pedigree is constructed using symbols:

Human Pedigrees: symbols



Text p. 42

Autosomal recessive trait

Another example: albinism

In most people the cells in the skin can produce a pigment called melanin. Melanin can result in a range of skin pigments.

Rare mutations result in the complete lack of pigment: albinism.

Text ch.1 p 9-10

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The dominant allele A determines the ability to make pigment,
In albinos the synthesis of melanin is blocked.

A/A → Active enzyme → Pigmented

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a/a → Inactive enzyme → Albino

Text ch.1 p 9-10

Autosomal recessive

Albinism is caused by an allele that codes for a defective protein. The defective protein is insufficient for normal pigmentation only if the mutant allele is present in two copies, this situation is called haploinsufficiency.

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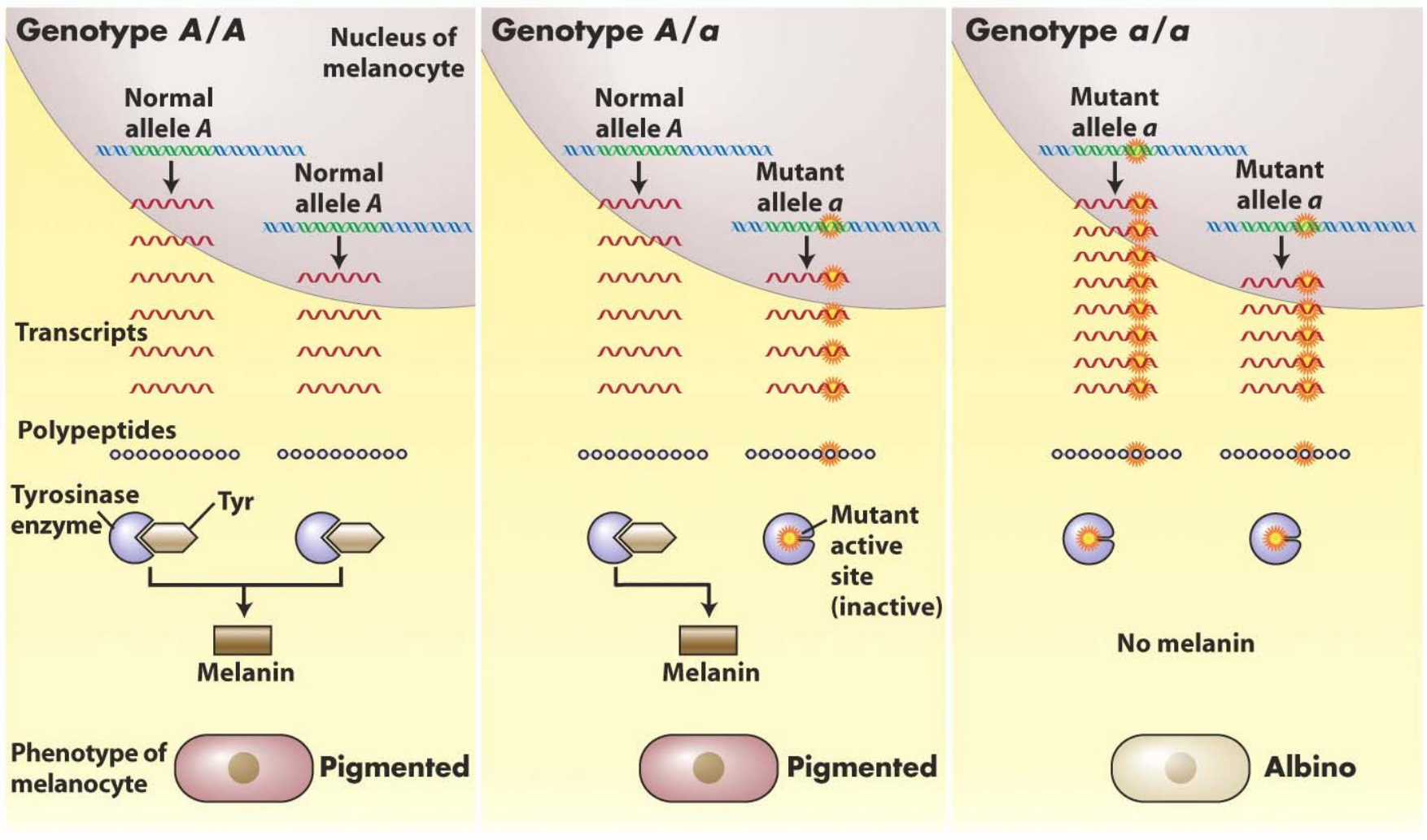
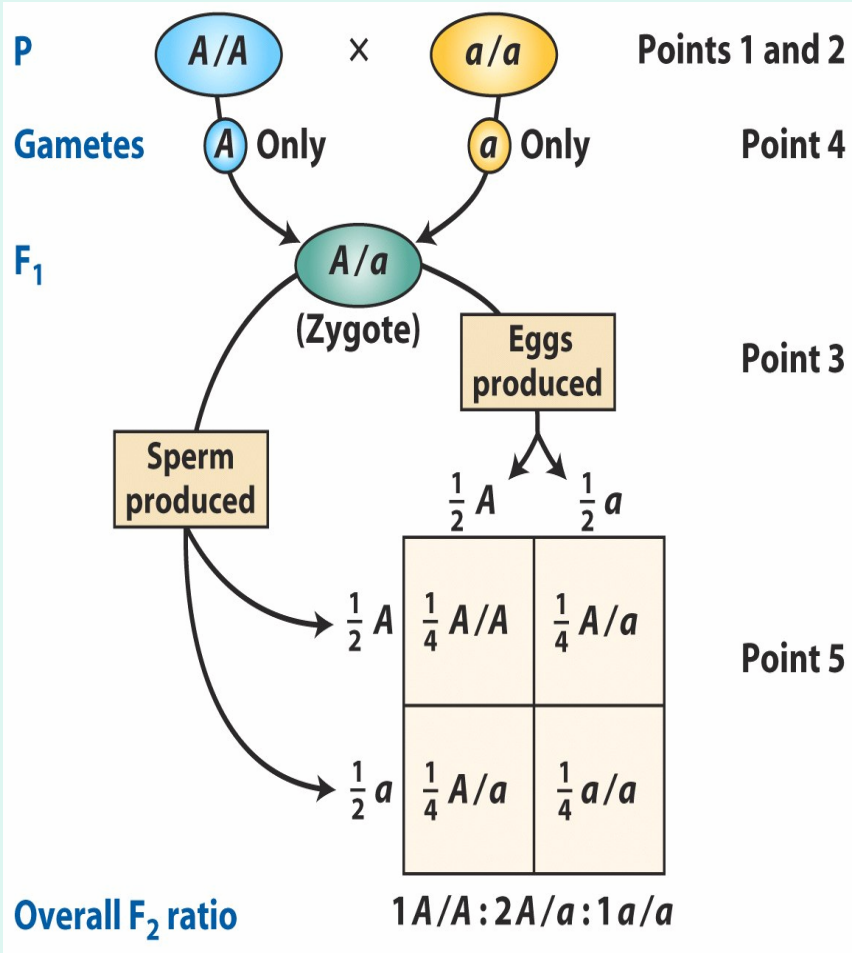
Text ch.1 p 9-10

Molecular basis of albinism



Text p.9-11

Explanation of 1:2:1 ratio



- The existence of genes and gene pairs

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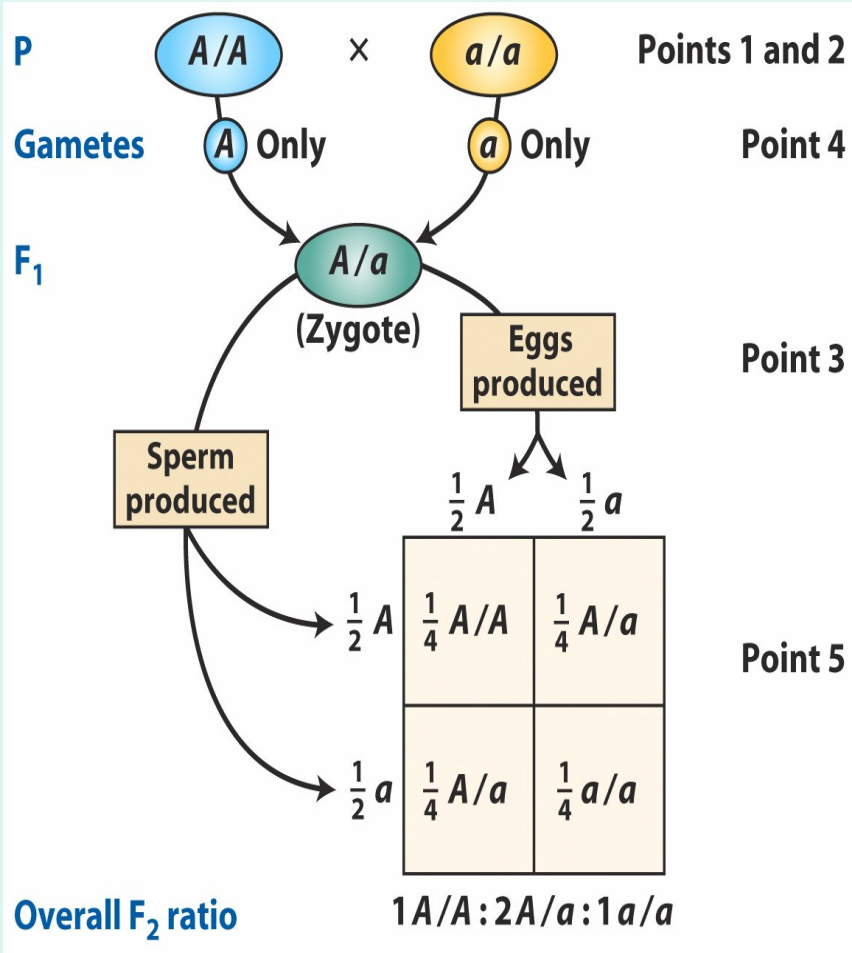

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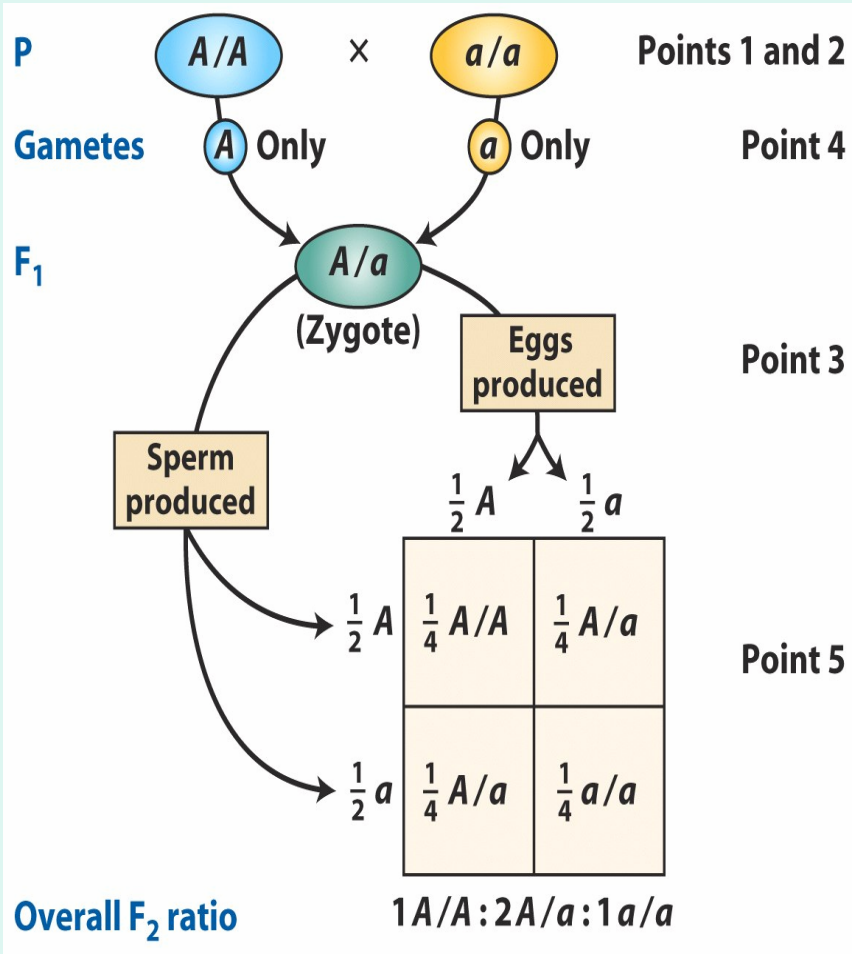
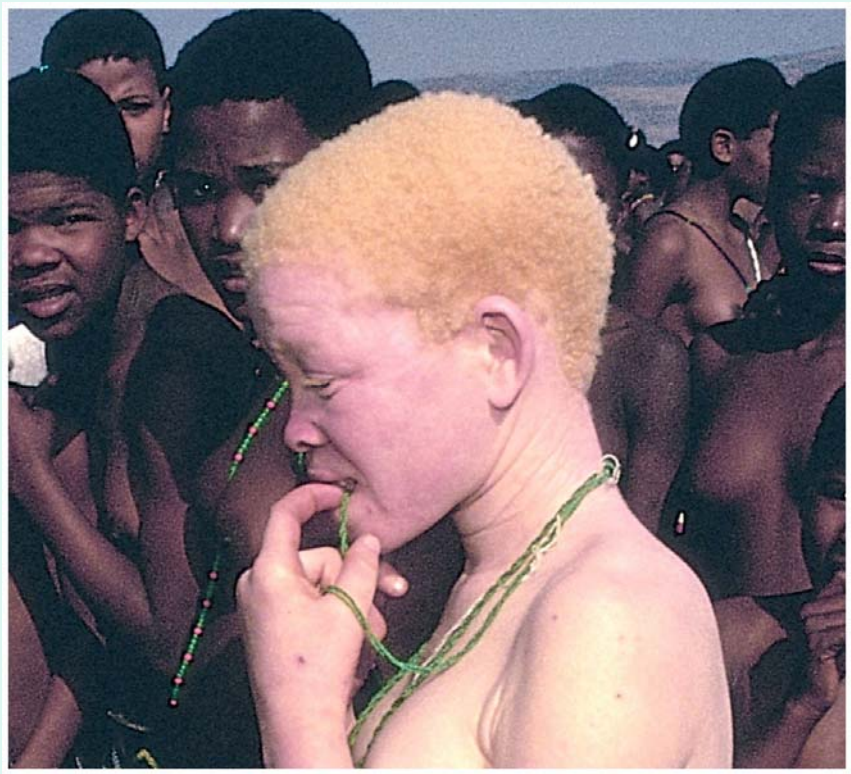
Explanation of 1:2:1 ratio

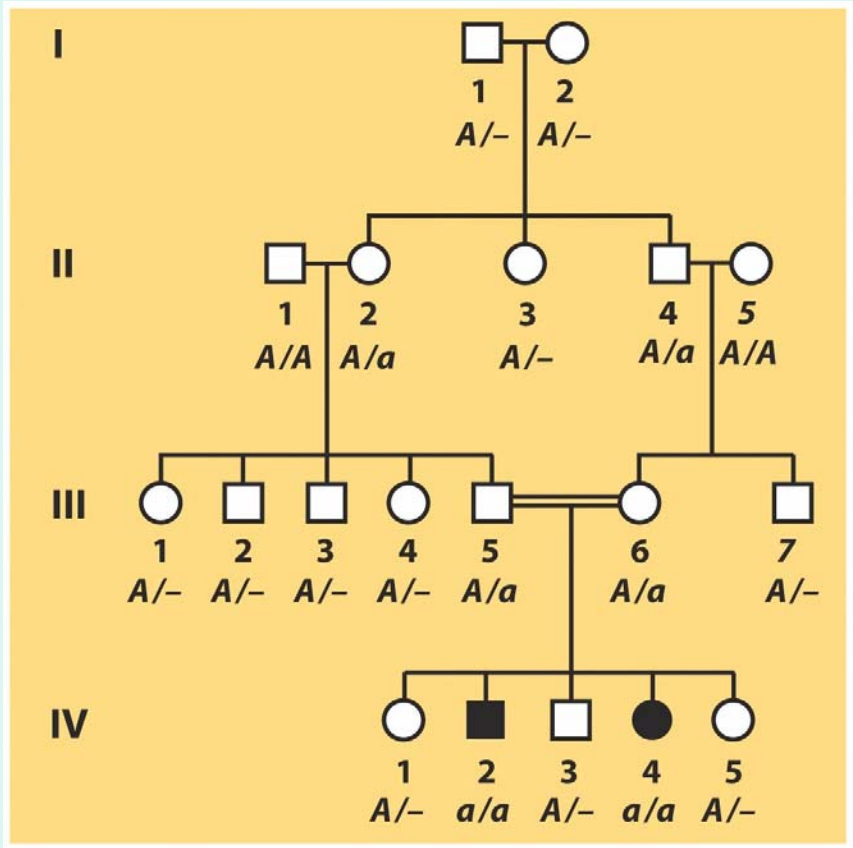


- The existence of genes and gene pairs
- The members of the gene pairs segregate equally
- Halving of gene pairs in gametes
- Random fertilization

Text p. 33

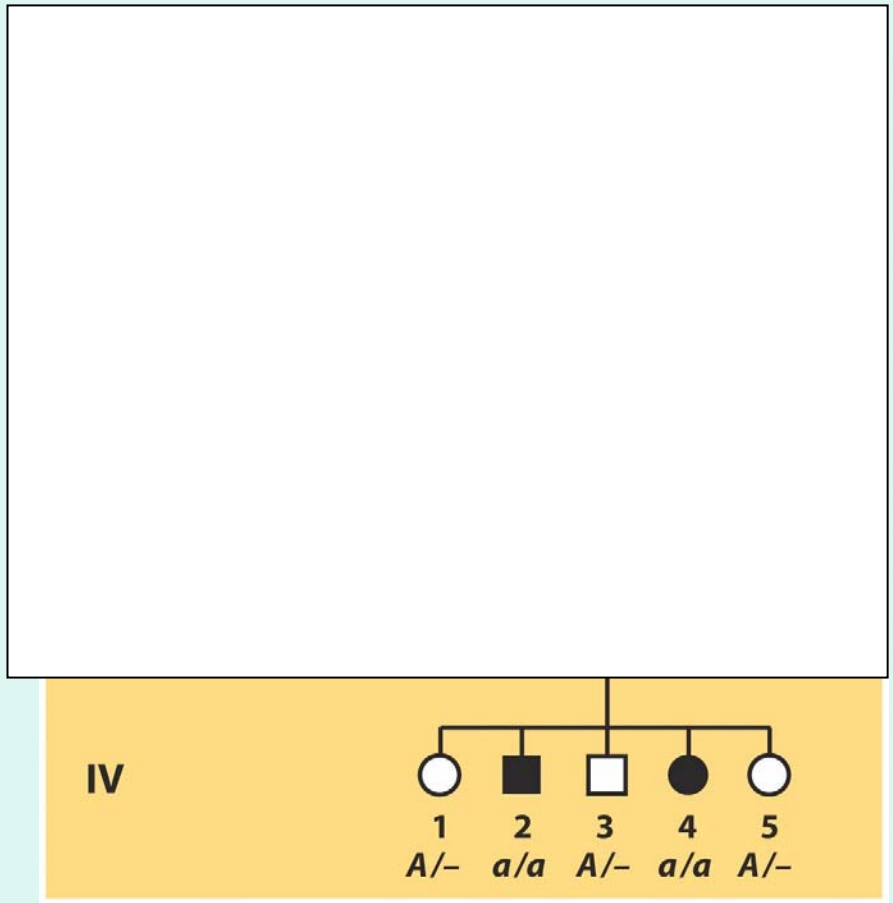
Pedigree example: albinism





Autosomal recessive *eg*: albinism

- IV-3 came to the genetic consult visit what is the probable genotype of his parents given that he's told you neither of them are albino?



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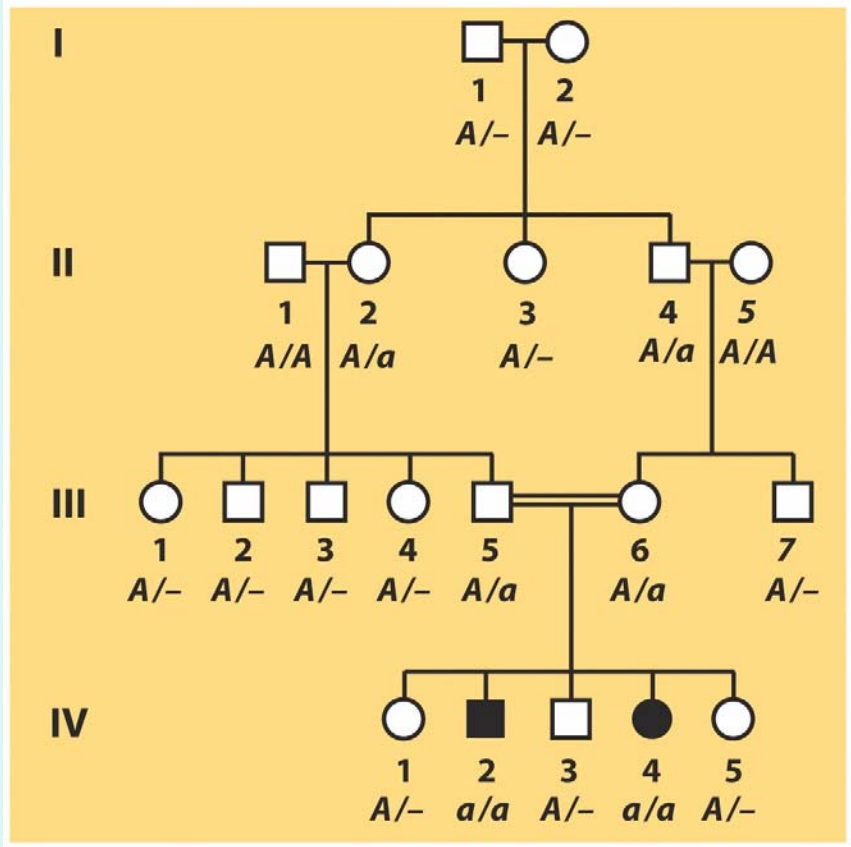
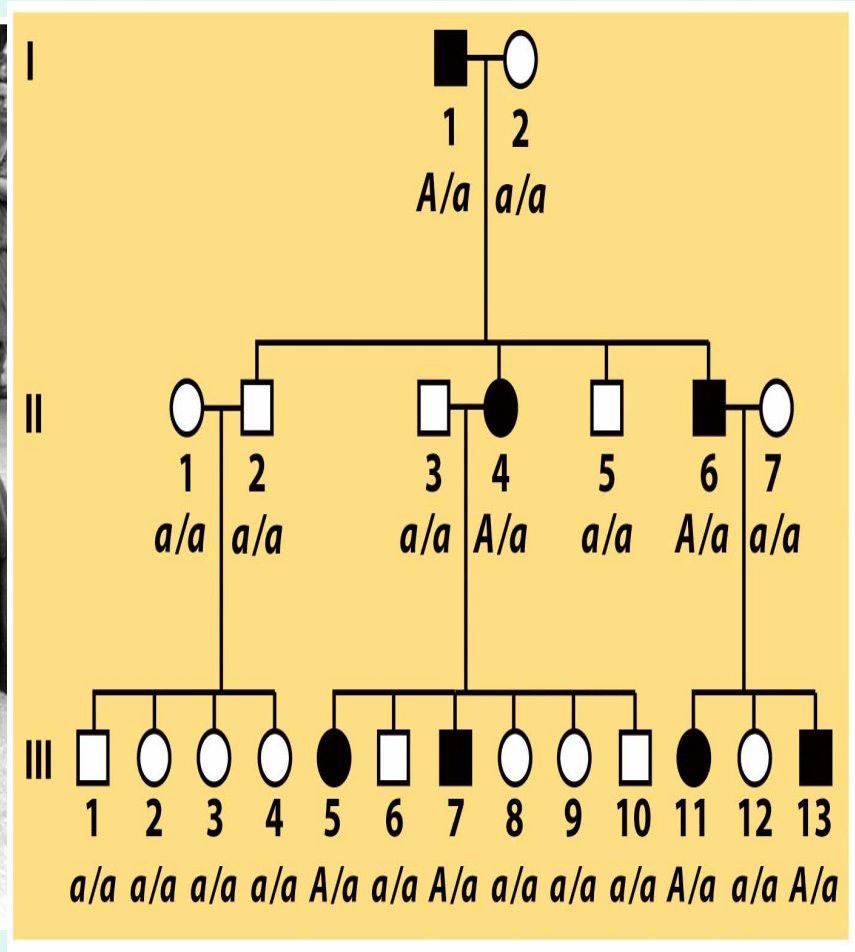
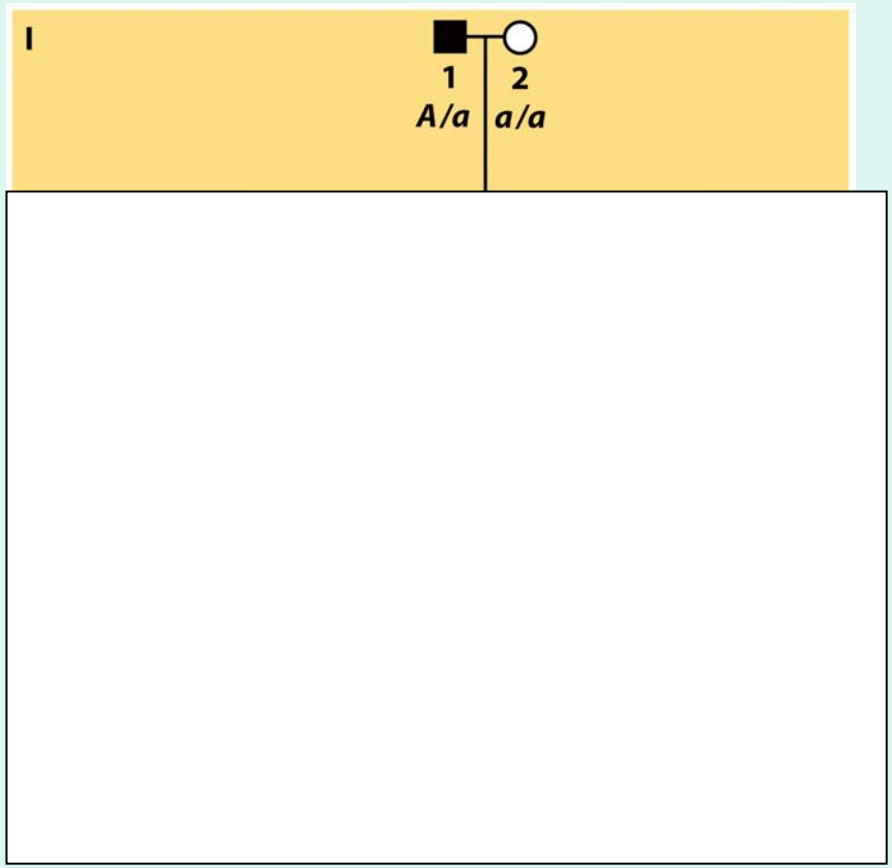


Autosomal dominant



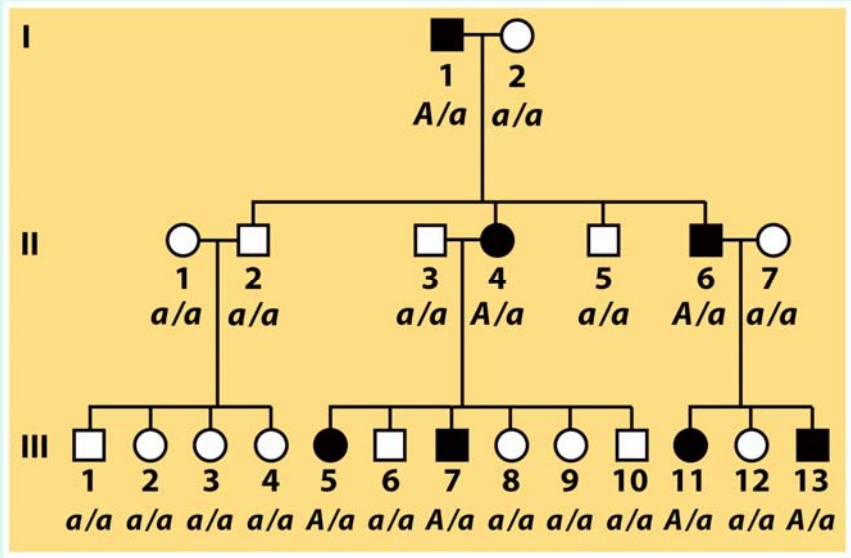
Autosomal…..

- I-1 and I-2 are having a child, what is the probability of the child having the pseudoacondroplasia phenotype?



Autosomal dominant

- I-1 and I-2 are having a child, what is the probability of the child having the pseudoacondroplasia phenotype?
- P(A_)= ½ * 1= ½
- Note the affected males and females in each generation, characteristic of a Mendelian autosomal dominant disorder.



Autosomal polymorphisms

- Polymorphism: the existence of two or more common phenotypes of a character in a population
- Often inherited in a standard Mendelian manner
- Human polymorphism examples include: widow's peak vs none; attached vs free earlobes

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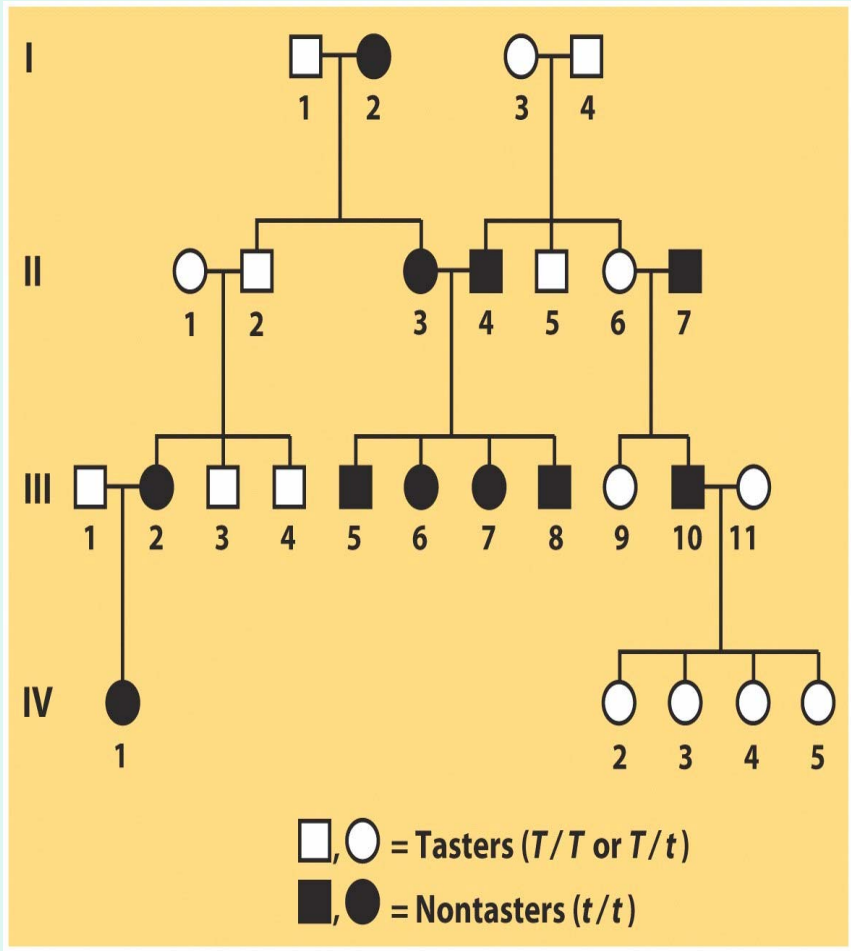
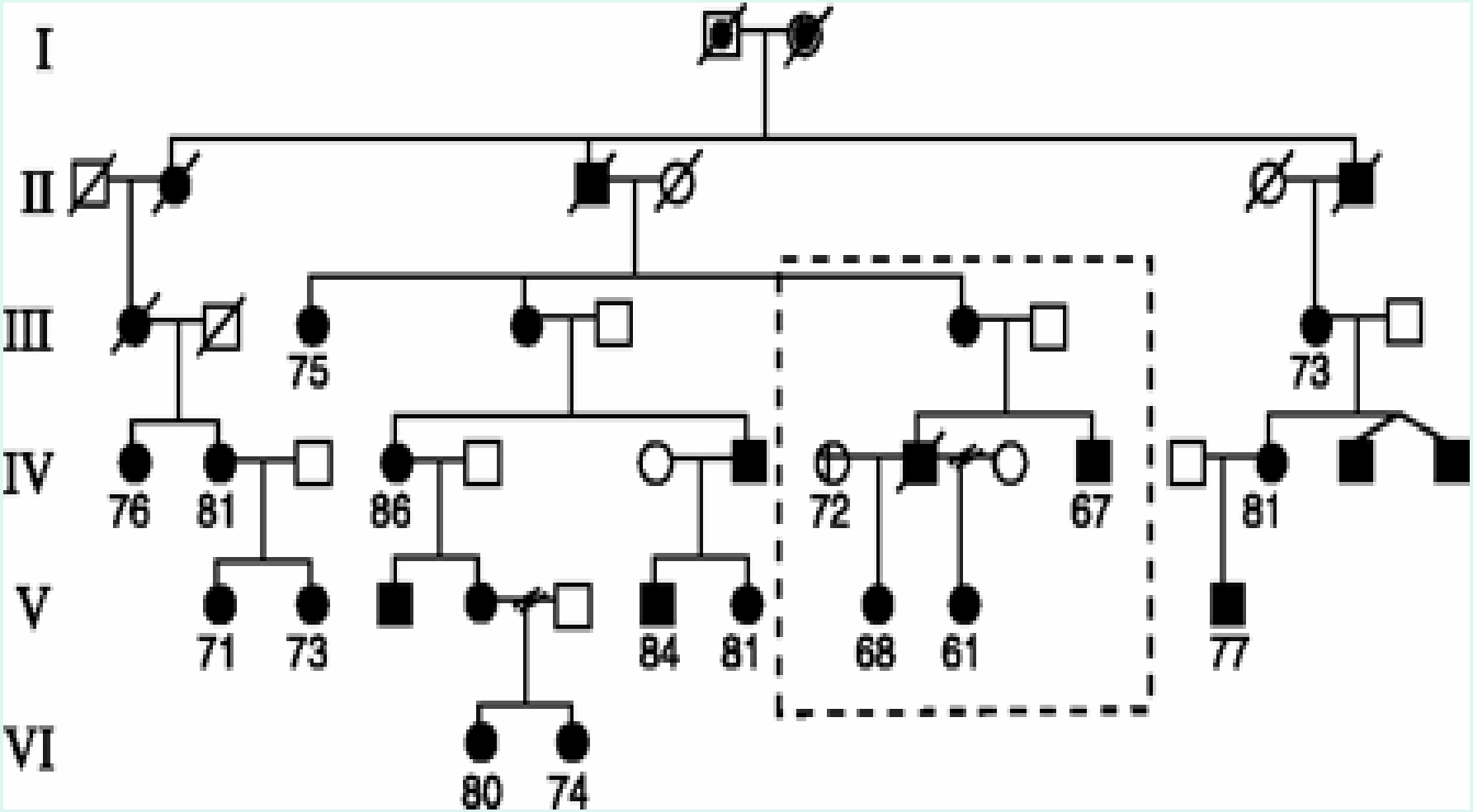
Autosomal polymorphism

- Human populations are dimorphic for the ability to taste a bitter chemical: phenylthiocarbamide (PTC)
- Is the allele that confers the ability to taste PTC dominant or recessive?



Advanced Sleep Phase Syndrome



Toh, et al.(2001) Science 5506:1040-3
http://www.sciencemag.org/cgi/content/full/291/5506/1040

FASPS

- Familial Advanced Sleep Phase Syndrome
- Autosomal dominant circadian rhythm variant

FASPS

- Familial Advanced Sleep Phase Syndrome
- Autosomal dominant circadian rhythm variant
- Affected individuals are “morning larks”
  - They go to sleep at about 7:30 pm and awaken about 4:30 am
  - 4 hour sleep temperature and melatonin rhythm advance
- Attributed to h*Per* a homolog of *period* gene in *Drosophila melanogaster*

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