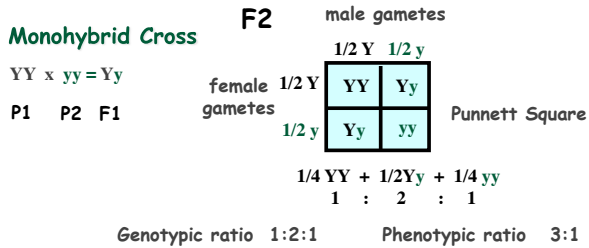


Review of Mendelian Genetics

- ☞ **Law of Equal Segregation.** The two alleles of each trait (Y and y) separate (segregate) during gamete formation, then unite at random, one from each parent, at fertilization.
- ☞ **Law of independent assortment.** Segregation of alleles of two different genes are independent of one another.



Terms

- ☞ **Genes** are what we now call the segregating units that Mendel discovered, and **alleles** are the differing forms of a gene that control traits.
- ☞ **Genotype** (the exact alleles present) vs **phenotype** (observable consequence) of an organism.
- ☞ **Homozygous** (homozygote) vs **heterozygous** (heterozygote).
- ☞ **Mutation** = sudden, heritable change in an allele. Most of the allele variation that we study in genetics arises from mutation.
- ☞ Standard allele = **wild type** = most common allele found in the wild.
- ☞ New allele/Variant allele/Mutant allele (depends on the organism).

Today

- ☞ Applying Probability, sampling and combinations (Product rule, sum rule) to mendelian genetics
- ☞ Extend these ideas to human genetics (pedigrees)

Probability = $\frac{\text{\# times event is expected to happen}}{\text{\# opportunities (trials)}}$

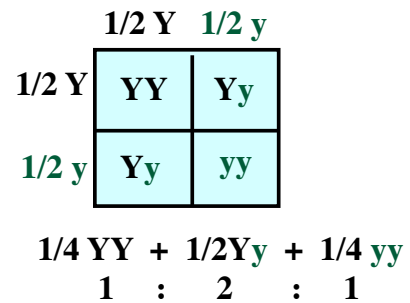
Product Rule (Law of the Product)

The probability of independent events occurring together is the product of the probabilities of the individual events

$$\text{prob(a and b)} = p(a)p(b)$$

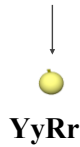
Example of tossing two coins.

Punnett Square is a way of depicting the Product Rule.



Dihybrid Cross: Two genes.

Consider the two genes: Y (yellow) and y (green) and R (round) and r (wrinkled).



















Dihybrid Cross:











↓
 All possible gametes: $RY \ Ry \ rY \ ry$

$$p(\text{RY gamete}) = \frac{1 \text{ gamete}}{4 \text{ gametes}} = \frac{1}{4}$$

		♂ gametes			
		$RY \frac{1}{4}$	$Ry \frac{1}{4}$	$rY \frac{1}{4}$	$ry \frac{1}{4}$
♀ gametes	$RY \frac{1}{4}$	$RRYY \frac{1}{16}$ 	$RRYy \frac{1}{16}$ 	$RrYY \frac{1}{16}$ 	$RrYy \frac{1}{16}$ 
	$Ry \frac{1}{4}$	$RRYy \frac{1}{16}$ 	$RRyy \frac{1}{16}$ 	$Rryy \frac{1}{16}$ 	$RrYy \frac{1}{16}$ 
	$rY \frac{1}{4}$	$RrYy \frac{1}{16}$ 	$Rryy \frac{1}{16}$ 	$rryy \frac{1}{16}$ 	$rrYy \frac{1}{16}$ 
	$ry \frac{1}{4}$	$RrYy \frac{1}{16}$ 	$Rryy \frac{1}{16}$ 	$rrYy \frac{1}{16}$ 	$rryy \frac{1}{16}$ 

Punnett Square of a Dihybrid Cross

 : 3
 : 3
 : 1
 : 1

 Round, yellow  Wrinkled, yellow
 Round, green  Wrinkled, green

From monohybrid crosses, chance of the offspring showing the dominant trait is 3/4 (i. e. 3:1). Using the product rule, the 9:3:3:1 ratio of a dihybrid cross can be predicted.

Monohybrid.

Yellow to green is $3/4$ to $1/4$ (3:1)
 Round to wrinkled is $3/4$ to $1/4$ (3:1).

Dihybrid

Yellow round =	$3/4 \times 3/4 = 9/16$	9
Yellow wrinkled =	$3/4 \times 1/4 = 3/16$	3
Green round =	$1/4 \times 3/4 = 3/16$	3
Green wrinkled =	$1/4 \times 1/4 = 1/16$	1

Shorthand way of doing this is $(3:1) \times (3:1) = 9:3:3:1$, helpful when considering several traits simultaneously.

What is the probability of finding a zygote of RRYy genotype in the cross RrYy x RrYy?

1. What is the probability of RR in the F2?
2. What is the probability of Yy in the F2?

Thus, the probability of RRYy is

3. Alternatively, The probability of a gamete being RY is $1/2R \times 1/2Y = 1/4RY$. $1/4 \times 1/4 = 1/16$ RYRY.

Sum Rule (Law of the Sum)

The probability of either of two mutually exclusive events occurring is the sum of their individual probabilities

$$\text{prob}(a \text{ or } b) = p(a) + p(b)$$

- Sum of all the probabilities of all possible events = 1.
- Probability of something not happening is 1 minus the probability of it happening.

Punnett Square and the Sum Rule.

		male gametes	
		1/2 Y	1/2 y
female gametes	1/2 Y	YY	Yy
	1/2 y	Yy	yy

Chance of a Yy individual is the sum of the probabilities of getting the Y from the male and the y from the female ($1/2 \times 1/2 = 1/4$, product rule) and getting the Y from the female and the y from the male ($1/2 \times 1/2 = 1/4$, product rule).
Sum rule $1/4 + 1/4 = 1/2$.

What is the probability of obtaining a round, green seed from dihybrid (RrYy) cross?

Genotype can be either RRYy or Rryy

RR yy

$$1/4 RR \times 1/4 yy = 1/16 RRYy (\text{product rule})$$

Rr yy

$$1/2 Rr \times 1/4 yy = 1/8 Rryy (\text{product rule})$$

$$\text{Sum rule: } 1/8 + 1/16 = 3/16$$

Determine the probability that a plant of genotype CcWw will be produced from the following cross: CcWw x Ccww

Chance of being Cc =

	1/2 C	1/2 c
1/2 C	CC	Cc
1/2 c	Cc	cc

Chance of being Ww =

	1/2 W	1/2 w
1/2 w	Ww	ww
1/2 w	Ww	ww

Chance of being CcWw =

What fraction of the progeny from the following cross will have smooth and red fruit with purple stems?

PpRrAa x ppRRAa

P - smooth
p - peach
R - red
r - yellow
A - purple
a - green

Smooth =

Red =

Purple =

Smooth, Red, Purple =

What is the probability of randomly choosing three plants that do NOT have smooth and red fruit with purple stems?

3/8 probability of obtaining smooth, red, purple.

Choosing three in a row that are not smooth red purple =

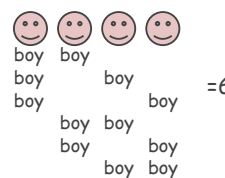
Binomial expansion

$$\frac{N!}{K!(N-K)!} = \text{number of possible ways that } K \text{ individuals can be selected from } N.$$

N = Total number of individuals, coins, etc.

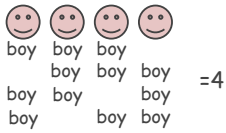
K = number of individuals with a specific character.

Example If you have 4 kids, how many ways are there of having 2 boys and two girls?



$$\frac{4!}{2!(4-2)!} = \frac{4!}{2!2!} = \frac{1 \times 2 \times 3 \times 4}{1 \times 2 \times 1 \times 2} = \frac{24}{4} = 6$$

Example If you have 4 kids, how many ways are there of having 3 boys and 1 girl?



$$\frac{4!}{3! (4-3)!} = \frac{4!}{3! 1!}$$

$$= \frac{4}{1} = 4$$



$$\frac{4!}{1! (4-1)!} = \frac{4!}{1! 3!}$$

$$= \frac{4}{1} = 4$$

Mendelian Analysis in Humans

Most traits are affected by more than one gene and cannot be analyzed using simple Mendelian genetics.

Many single gene traits that can be followed cause rare diseases, rather than common phenotypes.

Genetics is not straight forward:

No pure breeding humans;

Generation time is long;

No controlled matings;

Siblings rarely mate to generate F2.

Small family sizes

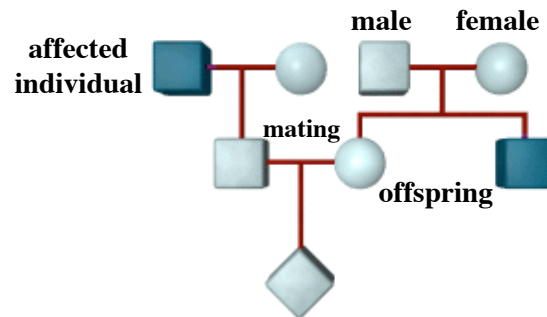
How can one study human genes, and map genes that cause human diseases?

•Geneticists make use of the variation that already exists in the population.

•Pedigree analysis. Rare traits can be studied by carefully analyzing families that are affected. In other words, the trait may be rare in the population but common in a particular family.

Important assumption: When a trait is rare, and there is a random mating, you can always assume the person is not a carrier (heterozygotes).

Pedigree Analysis



Fetus or unspecified progeny

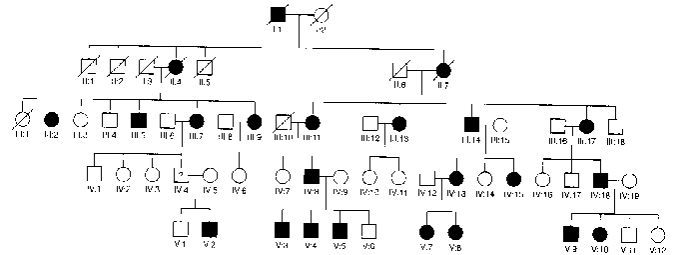
Filled, means affected, open means unaffected (normal).

Dominant (rare) Traits

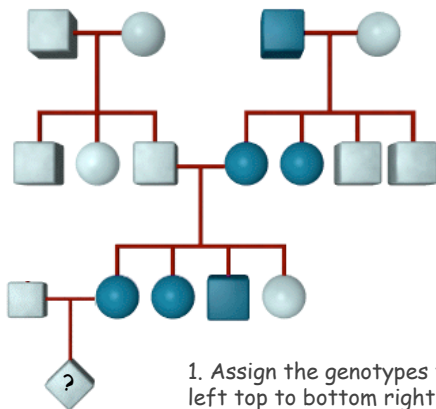
How can one look at a pedigree and tell that the disease is caused by a dominant gene.

- Affected individual always has an affected parent.
- Usually, Affected individuals appear in every generation.
- Two affected parents may have unaffected progeny.

(brachydactyly, 1906).



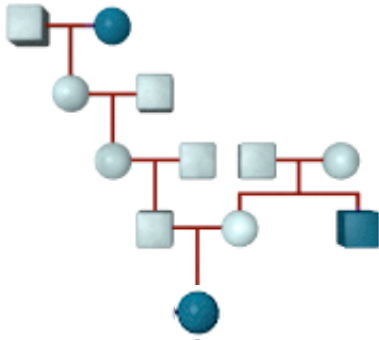
- Dominant single gene inheritance.
- Heterozygotes (carriers) show phenotype.



1. Assign the genotypes to all individuals, left top to bottom right, with Aa, etc.
2. Probability that diamond is affected?

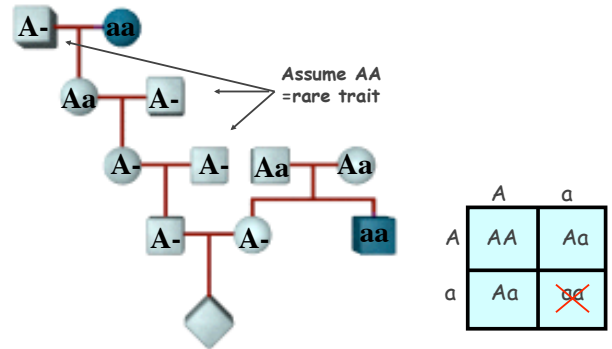
Recessive (rare) Traits

- appear in progeny of unaffected parents
- frequently show up in consanguineous matings (partners are blood related)
- all progeny from two affected individuals are affected



Fill in the genotypes, left to right, top to bottom, with Aa etc.

What is the chance the child will be affected by this rare disease?



Tips for pedigree analysis

- For an individual to be affected (homozygous), both parents need to be carriers (heterozygous). Therefore, to calculate the chance that an unknown individual will be affected, calculate the chances that the parents will be heterozygous, then multiply these by the chance that the offspring will get both the mutant alleles.

- For rare traits, make the simplifying assumption that unrelated, unaffected individuals are not carriers.

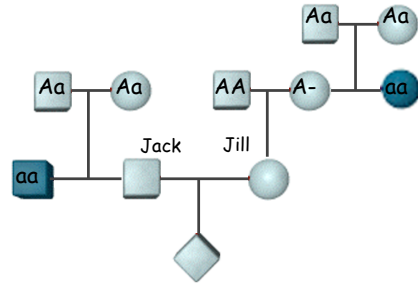
Cystic fibrosis is a rare recessive disorder. Jack whose brother has the disease marries Jill whose aunt has the disease.

- If they have one child, what is the probability that the child will have cystic fibrosis?
- If their first child has cystic fibrosis, what is the probability that their second child will have cystic fibrosis?
- If their second child has cystic fibrosis, what is the probability that their third child will have cystic fibrosis?
- If their first child has cystic fibrosis, what is the probability that of their next three children, two will be carriers and the other affected?

Cystic fibrosis is a rare recessive disorder. Jack whose brother has the disease marries Jill whose aunt has the disease.

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b) If their first child has cystic fibrosis, what is the probability that their second child will have cystic fibrosis?



c) If their second child has cystic fibrosis, what is the probability that their third child will have cystic fibrosis?

d) If their first child has cystic fibrosis, what is the probability that of their next three children, two will be carriers and the other affected?

