

1 Mendelian Genetics

Chapter 14

2 Blending theory of heredity

- ✿ Pre-Mendelian theory of heredity proposing that hereditary material from each parent mixes in the offspring; once blended like two liquids in solution, the hereditary material is inseparable and the offspring's
- ✿ Individuals of a population should reach a uniform appearance after many generations
- ✿ Once traits blended, they cannot be separated out to appear again in later generations

3 Particulate Theory of Inheritance: Mendel's

- ✿ Parents transmit to their offspring discrete inheritable factors (now called genes) that remain as separate factors from one generation to the next

4 Gregor Mendel

- ✿ Augustinian monk
- ✿ Studied at University of Vienna from 1851-1853
- ✿ Studied w physicist, Doppler → QUANTITATIVE
- ✿ Studied w Unger, botanist → inheritance
- ✿ Mendel used a quantitative approach to his experimentation

5 Why Mendel was lucky

- ✿ Chose peas which were available in many varieties
- ✿ Strict control over pollination was possible due to structure of petals and pistil and stamens (used artist's brush to transfer pollen)
- ✿ Chose distinctive characters which happened to be either dominant or recessive and happened to be on different chromosomes

6 Characters chosen by Mendel

- ✿ Character: detectable inheritable feature of an organism; trait: variant of an inheritable character
- ✿ Flower color (purple or white), flower position (axial or terminal), seed color (green or yellow), seed shape (round or wrinkled), pod shape (inflated or constricted), pod color (green or yellow), stem length (tall or dwarf)

7 Crosses → Hybridization

- ✿ True breeding → always produced offspring w the same traits as the parents when parents self-fertilized
- ✿ Mendel crossed true breeding individuals (parents) and then their offspring (1st filial generation) to observe 2nd filial generation

8 generations

- ✿ P – parent
- ✿ F1 – first filial generation
- ✿ F2 – second filial generation results from crossing two F1 individuals

- 9 **Mendel's law of segregation**
- ✿ Allele pairs segregate during gamete formation (meiosis) and the paired condition is restored by the random fusion of gametes at fertilization
- 10 **Law of Independent Assortment**
- ✿ Each allele pair segregates independently of other gene pairs during gamete formation
- 11 **Mendel's Hypothesis**
- ✿ 1: alternative forms of genes are responsible for variations in inherited characters (alternative forms are now called alleles)
 - ✿ 2: for each character, an organism inherits 2 alleles, one from each parent
 - ✿ 3: if the two alleles differ, one is fully expressed (dominant allele) the other is completely masked (recessive allele)
 - ✿ 4: the two alleles for each character segregate during gamete production
- 12 **Genetic vocabulary**
- ✿ Homozygous: having 2 identical alleles for a trait
 - ✿ Heterozygous: have 2 different alleles for a trait
 - ✿ Phenotype: an organism's expressed traits
 - ✿ Genotype: an organism's genetic makeup
 - ✿ Testcross (backcross): breeding of organism w unknown genotype w homozygous recessive organism to determine whether the 1st organism was homozygous dominant or heterozygous dominant
 - ✿ Dihybrid cross: cross btwn parents that are heterozygous for 2 traits
- 13 **Dihybrid Cross Example**
- ✿ R is round seed, Y is yellow seed
 - ✿ r is wrinkled seed, y is green seed
 - ✿ RRYY x rryy → RrYy
 - ✿ Possible gametes of F1: RY, Ry, rY, ry (2^2 where 2 is number of alleles, and 2^2 is number of traits)
 - ✿ Cross yielded 315 round, yellow seeds,
108 round, green seeds,
101 wrinkled, yellow seeds,
32 wrinkled, green seeds
- 14 **Probability Rules**
- ✿ Rule of multiplication: the probability that independent events will occur simultaneously is the product of their individual probabilities
 - ✿ Rule of addition: the probability of an event that can occur in two or more independent ways is the sum of the separate probabilities of the different ways
 - ✿ Random events are independent of one another-not affected by the outcome of previous events
- 15 What is probability that a trihybrid cross btwn 2 heterozygous organisms will produce offspring aabbcc?

- ✿ Aa X Aa: probability of aa offspring = $\frac{1}{4}$
- ✿ Bb X Bb: probability of bb offspring = $\frac{1}{4}$
- ✿ Cc X Cc: probability of cc offspring = $\frac{1}{4}$
- ✿ aabbcc: probability = $\frac{1}{4} \times \frac{1}{4} \times \frac{1}{4} = \frac{1}{64}$

16 What is probability that a trihybrid cross btwn 2 heterozygous organisms will produce offspring that have at least 2 recessive phenotypes?

- ✿ aabbcc = $\frac{1}{4} \times \frac{1}{4} \times \frac{1}{4} = \frac{1}{64}$
- ✿ aabbCc = $\frac{1}{4} \times \frac{1}{4} \times \frac{1}{2} = \frac{1}{32}$
- ✿ aabbCC = $\frac{1}{4} \times \frac{1}{4} \times \frac{1}{4} = \frac{1}{64}$
- ✿ aaBbcc = $\frac{1}{32}$
- ✿ aaBBcc = $\frac{1}{64}$
- ✿ Aabbcc = $\frac{1}{32}$
- ✿ AAbbcc = $\frac{1}{64}$
- ✿ $\frac{1}{64} + \frac{1}{64} + \frac{1}{64} + \frac{1}{64} + \frac{1}{32} + \frac{1}{32} + \frac{1}{32}$
- ✿ = $\frac{4}{64} + \frac{3}{32} = \frac{10}{64} = \frac{5}{32}$ will have 2 rec trait

17 **dominance**

- ✿ Complete dominance: dominant allele expressed, recessive not expressed
- ✿ Incomplete dominance: dominant and recessive alleles both expressed by blending, result is new phenotype which is intermediate between homozygous phenotypes
- ✿ Codominance: dominant and recessive alleles both expressed but don't blend, result is new phenotype which has both homozygous phenotypes present

18 **Tay-Sachs disease**

- ✿ Recessively inherited disease in humans; only children who are homozygous have disease
- ✿ Brain cells lack ability to metabolize lipids which accumulate in brain and lead to death
- ✿ Organismal level – heterozygotes symptom free
- ✿ Biochemical level- incomplete dominance, there is intermediate phenotype; have enzyme activity level between homozygous phenotypes
- ✿ Molecular level- heterozygotes produce equal numbers of normal and dysfunctional enzymes
- ✿ Half the normal amount of enzymes is sufficient to prevent lipid accumulation in brain

19 **Multiple Alleles**

- ✿ Gene has more than two alternative forms
- ✿ ABO blood alleles example
- ✿ 4 phenotypes: A, B, O, AB
- ✿ I^A , I^B , and i are alleles
- ✿ Alleles I^A and I^B are codominant both are expressed
- ✿ I^A produces anti B antibodies
- ✿ No antibodies are produced by i , which also has no antigens

20 **Antigens + antibodies**

- ✿ A person produces antibodies against foreign blood antigens (those not possessed by the individual). These antibodies react with the foreign antigens causing the blood cells to clump or agglutinate, which may be lethal
- ✿ For a blood transfusion to be successful, the red blood cell antigens of the donor must be compatible with the antibodies of the recipient.

21 **pleiotropy**

- ✿ Ability of a single gene to have multiple phenotypic effects
- ✿ Sickle-cell anemia: one gene causes many symptoms
- ✿ In tigers and Siamese cats, the gene for fur pigmentation also influences the connections between a cat's eyes and the brain; a defective gene causes both abnormal pigmentation and
- ✿ Cross-eye condition

22 **epistasis**

- ✿ Different genes interact to control the phenotypic expression of a single trait: the gene at one locus alters the phenotypic expression of a second gene that occurs after that locus

23 **Polygenic Inheritance**

- ✿ Quantitative characters vary in a continuum within a population
- ✿ Mode of inheritance in which the additive effect of two or more genes determines a single phenotypic character
- ✿ Leads to a continuum of phenotypes

24 **Environmental Impact on Phenotype**

- ✿ Norm of reaction: env conditions can influence the phenotypic expression of a gene, so that a single genotype may produce a range of phenotypes
- ✿ Limited (blood type)
- ✿ Range number of red:white blood cells
- ✿ Multifactorial: many traits are both polygenic and affected by env factors w a variety of possible expressions

25 **Pedigrees**

- ✿ Family tree that diagrams the relationships among parents and children across generations and that shows the inheritance of a pattern of a particular phenotypic character
- ✿ Squares symbolize males; circles – females
- ✿ Horizontal line connecting male & female-mating
- ✿ Offspring listed below in birth order, left to right
- ✿ Shaded symbols indicated individuals showing the trait being traced

26 **Pedigree analysis**

- ✿ Can be used to trace dominant, recessive traits
- ✿ Deduce whether a trait is determined by a dominant or recessive allele
- ✿ Predict the occurrence of a trait in future generations (can calculate probabilities)

27 **Recessively Inherited Disorders**

- ✿ Recessive alleles that cause human disorders are usually defective versions of normal alleles
- ✿ Defective alleles code for either a malfunctional protein or no protein at all
- ✿ Heterozygotes can be phenotypically normal, if one copy of the normal allele is all that is needed to produce sufficient quantities of the specific protein
- ✿ Phenotypes are express only in homozygotes
- ✿ Heterozygotes act as carriers

28 Examples of Recessively Inherited Diseases

- ✿ Human genetic disorders are not usually evenly distributed among all racial and cultural groups due to the different genetic histories of the world's people
- ✿ Cystic fibrosis, most common lethal genetic disease in the US, 1:2,500 Caucasians, rarer in other races
- ✿ 4% of Cauc are carriers
- ✿ Dominant allele codes for membrane protein that controls Cl⁻ traffic across the cell membrane
- ✿ Cl⁻ channels are defective or absent in CF individuals
- ✿ Disease symptoms result from thick mucus in pancreas and lungs

29 Tay-Sachs

- ✿ 1:3,600 births; incidence is 100x higher in Ashkenazic (central European Jews) than among Sephardic (Mediterranean Jews) and nonJews
- ✿ Brain cells of babies w this disease are unable to metabolize gangliosides because enzyme doesn't function properly
- ✿ As lipids accumulate in brain, infant has seizures, blindness, degeneration of motor and mental performance
- ✿ Life expectancy is a few years

30 Sickle-Cell Disease

- ✿ 1:400 African-Americans born in US
- ✿ Caused by a single amino acid substitution in hemoglobin
- ✿ Abnormal hemoglobin molecules tend to link together and crystallize, especially when blood oxygen content is lower than normal
- ✿ Red blood cell deform from the normal disk to sickle shape
- ✿ Sickled cells clog tiny blood vessels, causing pain and fever

31 Sickle Cell Trait

- ✿ 1:10 African-Americans are heterozygous for the sickle-cell allele and are said to have sickle cell trait
- ✿ Usually healthy, some suffer symptoms after an extended period of low blood oxygen levels
- ✿ Alleles are codominant
- ✿ High incidence of heterozygotes is related to fact that in tropical Africa where malaria is endemic heterozygotes have enhanced resistance to malaria compared to normal homozygotes

32 Consanguinity

- ✿ Genetic relationship results from shared ancestry
- ✿ Parents w recently shared ancestry are more likely to inherit the same recessive alleles than unrelated persons
- ✿ Because some embryos are aborted prior to birth, it is difficult to assess extent to which consanguinity increases the incidence of inherited diseases
- ✿ Most cultures forbid marriage between closely related adults

- 33 **Dominantly Inherited Disorders**
- ✂ Achondroplasia dwarfs (one type of dwarfism) affects 1:10,000 people who are heterozygous for this gene
 - ✂ Homozygous dominant condition results in spontaneous abortion of the fetus, homozygous recessive are of normal phenotype 99.9% of population
- 34 **Lethal Dominant Disorders**
- ✂ Are always expressed; result from new genetic mutations that occur in gametes and later kill the developing embryo
 - ✂ Can be retained in population if late acting
- 35 **Huntington's Disease**
- ✂ Woody Guthrie's disease
 - ✂ Degenerative disease of the nervous system cause by late acting lethal dominant allele
 - ✂ Phenotypic effects appear around 35-40 years of age; it is irreversible and lethal once the deterioration of the nervous system begins
 - ✂ Located near tip of #4 chromosome
 - ✂ There is a test to detect Huntington's allele prior to symptoms appearing
- 36 **Multifactorial Disorders**
- ✂ Disease that have both genetic and environmental influences
 - ✂ Heart disease, diabetes, cancer, alcoholism, some forms of mental illness
 - ✂ Hereditary is often polygenic and poorly understood
 - ✂ Best strategy is to educate people about the role of env and behavioral factors that influence development of these diseases
- 37 **Genetic Testing and Counseling**
- ✂ Preventative approach to assess the risks
 - ✂ Carrier recognition of prospective parents
 - ✂ Fetal testing: amniocentesis and chorionic villus sampling
 - ✂ Amniocentesis extracts 10cc amniotic fluid; presence of chemical in fluid indicate some genetic disorders, some test are done on cells grown in culture from fetal cells which are karyotyped to id chromosomal defects
- 38 **CVS**
- ✂ Chorionic villus sampling
 - ✂ Physician suctions off a sm amount of fetal tissue from the chorionic vili of the placenta
 - ✂ These embryonic cells are rapidly dividing and can be karyotyped immediately, usually providing results in 24 hours
 - ✂ Can be performed at only 8 to 10 weeks of pregnancy
- 39 **Other fetal testing methods**
- ✂ Ultrasound
 - ✂ Fetoscopy: thin fiber-optic scope into uterus
 - ✂ Amniocentesis and fetoscopy have a 1% risk of complication such as maternal bleeding or fetal

death, so they are used only when risk of genetic disorder or birth defect is relatively high

40 Newborn Screening

- ✿ Some are routine test performed at birth
- ✿ Can detect disorders like PKU, phenylketonuria
- ✿ Recessively inherited, 1:15,000 births in US
- ✿ Annot properly break down the amino acid phenylalanine
- ✿ Phenylalanine and its byproduct (phenylpyruvic acid) can accumulate in the blood to toxic levels, causing mental retardation
- ✿ If infant placed on diet that is low in phenylalanine, effects of disorder are reduced