Genetics overview notes

Science, Genetics

* Proteins were originally thought to be the molecule of heredity because they were more complex than DNA, were very present, and DNA was only found on chromosomes * * S type â†’ dead mouse * R type â†’ healthy mouse * S type (heat killed) â†’ healthy mouseâ†’ no S cells isolated from mouse * S type (heat killed) plus R â†’ dead mouse * S type â†’ dead mouse * R type â†’ healthy mouse * S type (heat killed) â†’ healthy mouseâ†’ no S cells isolated from mouse * S type (heat killed) plus R â†’ dead mouse Three key genetic experiments: 1. Griffith (1928) — streptococcus and mice * Conclusion: something in dead S cells forced R cells to transform, but transformative substance (DNA) was not discovered until much later 2. Avery, McLeod, & McCarthy (1944) — discovered that DNA was responsible for heredity * Treated heat-killed S type with: 1. RNAase for RNA â†’ R + S colonies (transformation) 2. Proteinase for protein â†’ R + S colonies (transformation) 3. DNAase for DNA â†’ R but no S (no transformation) 3. Hershey-Chase (1952) — radioactively labeled DNA and proteins separately in E. coli * Attached phosphorus to DNA and sulfur to proteins (of phages) * Resulting offspring had phosphorus but no sulfur * Thus supporting the hypothesis that DNA was responsible for heredity * * Strands are anti-parallel (pair in opposite directions) * Strands are anti-parallel (pair in opposite directions) Watson, Crick (1953), Wilkens, & Franklin — responsible for discovery of double helix (sugar backbone & paired nucleotides A/T and C/G) * DNA has directionality from polarity * Starts at 5’ end with phosphate * Ends at 3’ end with hydroxyl * Discovery showed that nucleotide sequence could: 1. Be copied. 2. Code for information. 3. Result in errors as a result of base changes (mutations). * Remember: genes code for specific proteins,

which is how genes exert effect on organisms indirectly * Prof. Garrod (1908) proposed that hereditary disease was due to inborn errors of metabolism * Linked defective enzyme to Alkaptonuria (black urine disease) * This disease results from oxidation of homogentisic acid * Beadle and Tatum (1941) — One-Gene-One-Enzyme Hypothesis * Looked at bread molds and mutated spores (fungi) * Found that mutant asexual spores can grow in complete medium but not in minimal medium * Un-mutated spores grow in both medium * Gregor Mendel — disproved the theory of blending inheritance * Mendel’s Genetic Hypothesis: factors remain unchanged as they are passed through generations and each parent contributes distinct elements of heredity down, known as factors (or genes) * Chose to use true breeding garden pea plants because: 1. They have many observable, uniform traits. 2. They self-fertilize, but can be artificially fertilized. * Reciprocal cross — a cross between different true-breeding pea varieties in both directions * Mendel’s reciprocal crosses resulted in all F1 progeny showing only 1 parent trait (round v. wrinkled) * Principle of Segregation: genes randomly separate into reproductive cells * Gametes: reproductive cells that contain only 1 copy of the gene, & unite randomly when fertilized * Transposable element: DNA sequence capable of transposing from one location to another * Includes molecular basis of insertion of wrinkled (w) mutation in SBEI, or starch-branching enzyme * Both forms of SBEI gene (W and w) can be seen on gel if gene is co-dominant * Testcross: cross between dominant phenotype of unknown genotype + known homozygous recessive genotype * Used to confirm that F1’s are heterozygotes through observation of different gametes in the progeny generation * Di-hybrid cross: the inheritance of two

traits on the same cross; allowed for Mendel’s 9: 3: 3: 1 discovery * Caused by Principle of Independent Assortment, or the independent segregation/separation of alleles among genes * Autosomal dominant inheritance: includes Huntington’s Disease * Caused by a tri-nucleotide repeat expansion in the gene coding for Huntington’s, one of several polyglutamine diseases * Autosomal recessive inheritance: includes albinism * Dominance: depends on phenotype of trait in question * Incomplete dominance: often seen when genotype is quantitative, rather than discrete * Co-dominance: more often seen in molecular traits than morphological * Multiple alleles: presence in a population of more than 2 alleles of a gene * Blood type is determined by polysaccharides (polymers of sugars) on the surface of red blood cells that are added by transferase enzyme with alleles IA and IB * Antibodies — proteins made by immune system in response to antigens * Clumping of blood is a result of the reaction between matching antibodies and antigens * Variable expressivity: genes showing to different degrees in different individuals * Penetrance: proportion of individuals with matching genotypes & phenotypes (100% = always expressed) * Gene interaction: when multiple loci (genes) determine a single phenotype * Epistasis: when gene interaction results in one gene masking the effect of another * Principle of Complementation — if two recessive mutations are on alleles of different genes, then phenotype of individual containing only 1 copy of each mutation will show wildtype phenotype * Failure to complement — if two mutations occur on the same gene, then the phenotype of an organism that contains one copy of each mutation is mutant * Mutant Screen — a large-scale systematic experiment to isolate multiple new mutations

affecting a particular trait * Complementation test — cross between mutant strains aimed at finding whether mutations are on different genes, or the same gene * Complementation group — group of mutations that fails to complement one another (i. e. on same gene) * Somatic cell: cell of the body, containing a fixed number of chromosomes * Are diploid (2n), with 2 copies of each chromosome * Germ cells (gametes) are haploid, and are joined in fertilization to produce the diploid somatic cell * Chromosome compliment — the complete set of chromosomes * Interphase: the process in which cell is duplicated prior to mitosis, lasting about 23 hours * G1 — pre-DNA synthesis + checkpoint * S — DNA synthesis in which DNA replicates and chromosomes are duplicated * G2 — post-DNA synthesis + checkpoint * Mitosis: the process of chromosomal segregation and cell division resulting in two identical daughter cells * Consists of four stages following interphase: 1. Prophase: each chromosome condenses, and nuclear envelope disintegrates 2. Metaphase: mitotic spindle forms and attaches to centromere at kinetochore while chromosomes line up in the center of the cell at the metaphase plate 3. Anaphase: the 2 sister chromatids of each chromosome separate & move towards opposite spindles 4. Telophase: nuclear envelope forms around each compact group of chromosomes and spindle disappears as nucleoli form * Meiosis: results in 4 genetically different daughter cells with only 1 copy of each chromosome pair * Chiasma(ta) — results from physical exchange of DNA between chromatids of homologous chromosomes during crossing over. Functions: * Sticks homologous chromosomes together so that they can align correctly in metaphase I * Exchange genetic information between homologs to increase genetic diversity Chiasma(ta) —

results from physical exchange of DNA between chromatids of homologous chromosomes during crossing over. Functions: * Sticks homologous chromosomes together so that they can align correctly in metaphase I * Exchange genetic information between homologs to increase genetic diversity Takes much longer than mitosis (days or weeks) and occurs in meiocytes * Consists of two stages of division but only 1 of replication * Meiosis I: 4 stages resulting in reductional division (chromosome # is halved) a) Prophase I: homologous chromosomes condense, crossing over occurs i. Leptotene (thin thread) — condensation of chromosome threads in which chromosomes condense and become visible ii. Zygotene (paired thread) — first part of chromosome pairing (synapsis) iii. Pachytene — chromosomes are completely paired, and recombination/crossing over occurs iv. Diplotene — synapsed chromosomes shorten and repel one another v. Diakinesis — chromosomes repel one another, but are held together by chiasmata b) Metaphase I: bivalents (paired homologs and their chromatids) line up randomly on the metaphase plate, allowing for independent assortment c) Anaphase I: homologous chromosomes separate and move to poles, which is the cellular basis for allele segregation d) Telophase I: spindle breaks down, and 2 nuclei are formed (each with a haploid set of duplex chromosomes); cells prepare for meiosis II * Meiosis II: equational division (chromosome number stays the same), resembles mitosis without the DNA replication * 2 haploid cells become 4 haploid cells, each of which contains the equivalent of a single sister chromatid from each pair of homologous chromosomes * The 2 sister chromosomes (now separate cells) aren’t identical due to crossing over in Prophase I * In humans, meiosis occurs in meiocytes

(oocytes form egg cells and spermatocytes form sperm cells) * In plants, plants, products of meiosis form spores which then undergo one or more mitotic divisions to produce a haploid gametophyte organism * Chromosome: a single molecule of DNA that can be circular or linear, and can contain anywhere from tens of kilo-base pairs to hundreds of mega-base pairs * Eukaryotic cells tend to have bigger linear chromosomes * Prokaryotic cells have smaller circular chromosomes * Chromatin: complex aggregation of DNA and protein that makes up structure of eukaryotic chromosomes a) Determines structure b) Regulates function of the chromosomes * Nucleosomes: the bead-like units of chromatin which DNA is wrapped around * Histones: the structural unit of the nucleosome “ bead" with 5 major types: * 5 major types — H1, H2A, H2B, H3, and H4 * Positively charged, allowing them to bind to the negatively charged DNA molecules * Chromatin fibers form discrete chromosome territories in the cell nucleus * Structure includes: a) Heterochromatin — compact/heavily stained regions of chromatin, made primarily of non-coding DNA sequences or satellite DNA * Found in chromosome tips (telomeres) & center (centromere) b) Euchromatin — much more gene-dense, only becomes visible after chromosome condensation in mitosis or meiosis * Metaphase chromosomes are highly coiled and tightly condensed, which allows for the movement of genetic material during nuclear division * The centromere is necessary for chromosome segregation and is part of the kinetochore * Kinetochore — the complex of DNA & proteins that the spindle fibers attach to and use to more the chromosomes in both mitosis and meiosis (site of attachment) * Chromosome Theory of Heredity — genes are located in chromosomes * After Mendel, genes were

assumed to be physically located on chromosomes based in the mechanisms of segregation and independent assortment seen in Meiosis * First evidence came from tracking pattern of transmission in sex chromosomes * Morgan's fruit fly experiments — one of 1st to find evidence that genes are on chromosomes * Found that genes like Red vs. White eye color didn't segregate in a typical Mendelian (autosomal) manner, resulting in discovery of X-linked inheritance * X-linked inheritance — includes hemophilia and red/green colorblindness * For rare traits, affected individuals are almost all males who have normal sons * Calvin Bridges (student of T. Morgan) showed that exceptional behavior of chromosomes is precisely paralleled by exceptional inheritance of genes * Looked at rare discrepancies in cross of a rare white eyed female & red-eyed male, found that male offspring were missing their Y chromosome, an example of nondisjunction * Nondisjunction: the failure of chromosomes to separate and move to opposite poles, resulting in loss or gain of a chromosome * a * b * a * b * Locus: the well-defined physical location of a gene on a chromosome * Alleles: homologous chromosome pairs that often contain alternative forms of a given gene * Segregate during Meiosis 1 through independent assortment * Genes & their alleles can be linked (inherited together) if located in close proximity on same chromosome * Not affected by configuration * Recombination: when gene combinations produce different allele combinations rather than the parental types, due to crossing over between genes * Linkage: the tendency of genes to stay together * Linkage group (map): the genetic map of all known genes in a chromosome * Frequency of

recombination: * a * b * a a * b * a * b * a * b * a * b * a * b * a * b * a * b * a * b * a * b * a * b * a * b * a * b * * b * a * b * a * b * a * b * a * b * a * b * a * b * a * b * a * b * a * b * a * b * a * b * a * b END OF REVIEW — START NEW MATERIAL * Molecular evolution: the comparative study of molecular genetic variation within and among species * Molecules are DNA, RNA, & protein * Population genetics (within populations) — population histories, subdivision, and adaptation * Molecular systematics (between species +): relationships between species and higher taxa * Systematics: the classification of life * Carl Linneaus' Systema Naturae (1735) — hierarchical taxonomic classification system * Kingdom Phylum Class Order Family Genus Species * Used binomial nomenclature — e. g. homo sapiens * Darwin's Origin of Species (1859) — turned systematics around by proposing the correct idea that all organisms are descendants of a common ancestor * Relationships among organisms can be depicted on tree of life (i. e. a phylogenetic tree) * Haeckel's Tree of Life (1866) — cnidarians (i. e. corals and their relatives) * Lineage splitting is called cladogenesis * Evolution of characters is called anagenesis * Phylogenetic (or evolutionary) trees depict relationships between organisms * Pre-molecules: morphological characteristics were used, as with today * Now: both molecular systematics and phylogenetics together is the gold standard * Uses DNA (mitochondrial, nuclear, whole genomes), RNA, and proteins * Both methods are searching for homologous characters, or characters that originated once and have been inherited from a common ancestor * Cladograms are phylogenies that indicate the order of

divergence * Synapomorphies: share derived characteristics * Autapomorphies: derived characters in 1 taxa * The problem: morphological similarity does not always indicate the evolutionary relationship between two organisms * Closely related organisms do not always resemble one another in appearance * Small genetic changes can lead to big morphological differences * Similar morphological characters (i. e. fins) can evolve multiple times * This independent origin of traits is called convergent evolution * These traits are homoplasies, and are bad for morphological phylogenies * Molecular phylogenies: based on genetic similarities in DNA, RNA, & protein and are more efficient * Reflect actual inheritance of genetic information via mutations * Allow us to look at the behavior of many genes (if not the whole genome) in order to examine genealogical relationships among individuals and between species * Used to study: i. The origins and relationships among species ii. The timing of their origins through the use of molecular clocks iii. The evolution of morphological characters (incl. the convergent evolution of traits) * The construction of molecular phylogenies starts with the molecular variations in DNA, RNA, & protein * i. e. amino acid differences in beta-globin between vertebrates * Molecular phylogenies are based on comparing similarities in sequences (DNA, RNA, or proteins) a. Each entry in the distance matrix equals the number of amino acid differences between the two sequences * This distance matrix allows the “ nearest neighbors" to be identified b. Nearest neighbors are then grouped together — statistical significance of each match is determined by a method known as “ bootstrapping" * The UPGMA gene tree has horizontal branch lengths scaled to the distances between the nodes * Bootstrapping indicates that the

branching order in shaded area of the tree cannot be resolved * Segregating mutation — a type of mutation that appears as a new mutation in just one individual, and can be passed on to progeny * Divides population into two groups: those who carry the mutation, and those who don’t * Fixed mutation — a mutation that has become widely spread and eventually found in every gene in a population * The fixed mutation is then considered to be the normal or wild type allele * Molecular clocks — provide a method for attaching a time scale on the tree, and estimating the time since the most recent common ancestor (TMRCA) of two species * Different regions of DNA have very different rates of molecular evolution * Terminology for relationships among genes: Homologs | Evolutionarily related gene sequences — can be within one or between two species | Orthologs | Genes in different species derived from a common ancestral gene — retain similar functions in the two species | Paralogs | Genes produced by duplication within a genome (i. e. species) — usually have new functions, even if related to the original | * For phylogenetics, you want to compare orthologs * Gene duplications (i. e. the paralogs) are important sources of new genes * Mitochondrial DNA sequences can be used to trace human evolution * Mitochondria are transmitted only along female lineage (rarely contributed by sperm) * Mitochondria have their own haploid genomes, independent from the human “ host" * Mitochondrial genome accumulates mutations (about 1 change per 3, 800 years) * Mitochondrial “ Eve" — the most recent matrilineal common ancestor of all living humans * Mitochondrial DNA (mtDNA) does not undergo recombination — thus, mutations and other differences do not get mixed between haplotypes via recombination * Mixing

— Clan of the Cave Bear Hypothesis * Ancient DNA comparisons of Neanderthal mtDNA with modern humans indicates no interbreeding * Whole genome sequencing using 454 bead sequencing suggests no mixing as well * Population genetics: the branch of genetics studying the make-up of groups of individuals, and how the genetic make-up of the groups changes over time * Mendelian population: a group of interbreeding, sexually reproducing individuals with a common set of genes (i. e. the gene pool) * Populations evolve through changes in their gene pools, meaning that population genetics is essentially a study of evolution * There are 4 major evolutionary forces: 1. Mutation 2. Migration 3. Inbreeding/genetic drift 4. Selection * Describing population genetic variation: * Genotype frequencies — [N = total samples] f(AA) = # AA/N f(Aa) = # Aa/N f(aa) = # aa/N * Allele frequencies — [p + q = 1] if [f(allele) = # copies of allele/total # copies of all alleles] p = f(A) = (2nAA + nAa)/2nq = f(a) = (2naa + nAa)/2n | OR | p = f(A) = f(AA) + ½ f(Aa)q = f(a) = f(aa) + ½ f(Aa) | * Example of population genetic variation: Allele associated with AIDS resistance is CCR5Î” 32 * Chemokines are signaling molecules used by the immune system * CCR5 is a chemokine receptor, and is used by HIV to attach to CD4+ T cells and invade them * Most human populations contain a CCR5 allele known as a Î” 32 (a deletion mutant) * Deletion creates a frameshift following codon 184 which results in 31 incorrect amino acids, rendering protein non-functional * Hardy-Weinberg Principle: models the effect of Mendelian principles and random mating on genotypic and allele frequencies * Based on the assumptions of: 1. Large population and random mating 2. No mutation, migration, or natural selection * Predictions: 1. Allelic frequencies remain constant from

generation to generation 2. Genotypic frequencies stabilize (will not change) after one generation in the proportions HWE = AA: p2 Aa: 2pq aa: q2 * In Mendelian segregation — gametes are in equal ratios * In random mating — gametes unite at random * Implications of HWE: with rare alleles, there are many more heterozygotes than homozygotes for the rare allele * When one allele frequency is high, most individuals are homozygous * For autosomal recessive traits (incl. recessive diseases), most of the defective alleles are found in heterozygotes * Rare allele example: for a rare allele, the frequency in heterozygotes is greater than the frequency in homozygotes * HWE is useful for calculating frequency of carriers in populations (i. e. for cystic fibrosis), and can be useful for calculating the risk of having children with a recessive disease in known characters * Extending Hardy Weinberg to multiple alleles: * Frequency of any homozygous genotype = square of the allele frequency * Frequency of any heterozygous genotype = 2x product of the allele frequencies * For X linked genes, the genotype frequencies in males and females are different * For an X-linked gene with two alleles H and h, genotype frequencies are: Females: | Males: | HH = p2Hh = 2pqHh = q2 | H = pH = q | * The rarer the X-linked recessive allele, the more likely an affected individual will be male * The frequency of affected males can be used to calculate the frequency of the recessive alleles * i. e. Color blindness affects 1 out of every 20 Caucasian males q = 1/20 = 0. 05 Therefore, the expected frequency of colorblind females is: q2 = (0. 05)2 = 0. 0025, or about 1 out of every 400 * The processes that violate the assumptions of HWE and change the allele frequencies from generation to generation are: 1. Inbreeding — mating among relatives as an example of non-random mating

* Results in a reduction in heterozygosity (loss of heterozygotes) and thus an excess of homozygotes * This increases the frequency of deleterious homozygous recessive mutants within populations * Clearly shown in an example of self-breeding plants, in which the frequency of heterozygous genotypes is reduced by half in each successive generation with repeated self-fertilization * Effect of inbreeding is usually estimated based on reduction in heterozygosity * HI = the observed frequency of heterozygotes * Inbreeding coefficient (F) = measured in the reduction in the expected heterozygosity * Most importantly: with inbreeding, the proportion of heterozygotes decreases by 2Fpq, and half of this value is added to each homozygous genotype f (AA) = p2 + Fpq f (Aa) = 2pq - 2Fpq f (aa) = q2 + Fpq * In humans, inbreeding increases the risk of recessive homozygous diseases * Evolution is based on changes in allele frequencies present in the gene pool of a population, and are driven by mutation, migration, natural selection, and random genetic drift: 2. Mutation — the formation of new alleles 3. Migration — movement of individuals that can bring new alleles into a population 4. Selection - process by which populations become progressively better adapted to their environments * Darwin’s (1859) theory of natural selection is based on the following central tenets: i. In all organisms, more offspring are produced than survive and reproduce. ii. Organisms differ in their ability to survive and reproduce — some of these differences are due to genotypes. iii. More fit genotypes will survive better and reproduce more offspring — thus, alleles that enhance survival and reproduction increase in frequency from generation to generation * The effect of natural selection on a gene pool depends on the fitness of the

genotypes in the population * Fitness — the relative reproductive success of one genotype compared to the others in the population * Fitness (W) values range from 0 — 1 * Types of natural selection include: * Directional selection: i. e. DDT resistance in mosquitos (R with DDT AND + without DDT) * Selection in diploids: when the favored allele is dominant, recessive allele in heterozygotes is not exposed to natural selection * Favored dominant alleles change slowly when common * Favored recessive alleles change slowly if rare * Rare alleles are found mostly in heterozygotes * Directional selection for or against very rare recessive alleles is inefficient because it is not exposed to selection in heterozygotes * The largest reservoir or harmful recessive alleles is in the genomes of heterozygous carriers, who are phenotypically normal * Heterozygote Superiority (aka overdominance): when the fitness of the heterozygote is greater than that of both homozygotes AA: Aa: aa W11 < W12 > W22 1 — s : 1 : 1 — t * Alleles reach a stable equilibrium when p/q = t/s * Best example is sickle cell anemia (also includes malaria as a classic example) * Selection can be balanced by new mutations: * New mutations generate harmful alleles and prevent their elimination by natural selection * Eventually, populations attain equilibrium in which the new mutations balance the selective elimination * Mutation-selection balance: recessive q^ = square root of mutation/selection (âˆšμ/s) dominant q^ = mutation/selection (μ/s) * e. g. Anchondroplasia (dominant human dwarfism) in which fitness (W) = 0. 74 s = 1 — 0. 74 = 0. 26 mutation at ca. 3 x 10-5 q-hat = 0. 00003/0. 26 = 0. 0001153 5. Genetic drift — random, undirected changes in allele frequency * Causes differences in allele frequencies among subpopulations * Eventually, populations will

become fixed for either the A or the a allele — this is why small, isolated populations tend to lose genetic diversity * Buri (1956) demonstrated genetic drift in Drosophila * If genetic drift were the only force shaping genetic variation, all alleles would eventually become fixed or lost over time * However, there are opposing factors such as large populations sizes, mutation/migration, and selection (het superiority) * An example of reduced polymorphism due to genetic drift is the hunting of the elephant seal off the Pacific coast to only 20 survivors * Though the population has since grown to over 100k, all are homozygous for every gene tested * Cheetahs also show a lack in genetic variability to the point where all can accept skin grafts from one another, and 52/52 genes tested showed no polymorphisms Genetic Basis of Complex Inheritance * Most traits are influenced by multiple genes and environmental factors * These multifactorial or complex traits do not show a simple correspondence between genotype and phenotype (i. e. Mendelian inheritance in the round and wrinkled pea) * Types of multifactorial traits: * Continuous traits: quantitative traits that vary continuously from one phenotypic extreme to the other (i. e. height, blood pressure, corn yield) * Categorical traits: traits in which the phenotype falls into a discrete category (i. e. # of eggs laid) * Threshold traits: traits with only two phenotypic categories, but whose inheritance is determined by effects of multiple genes and environmental factors (i. e. likelihood of having twins) * Most quantitative traits cannot be studied by the usual pedigree methods because: 1. Effects of one gene can be concealed by effects of other genes — and these genes will probably segregate independently 2. Environmental effects can cause individuals with identical genotypes to have

different phenotypes * Inbred lines — can be used to eliminate/reduce genetic variation in experimental animals and plants, but are still influenced by environmental and chance events (also can’t be used to study human traits) * Genetic effects on quantitative traits can be assessed by comparing the phenotypes of relatives that have a certain proportion of genes in common * The distribution of a trait in a population is a description of the population in terms of the proportion of individuals that have each of a phenotypes * Provides no info about the relative importance of genotype and environment * The two main quantities that describe a distribution are mean and variance * The mean is the peak of the distribution * The variance is a measure of the spread of the distribution Ïƒ2= | Î£ (x — xi)2N - 1 | The greater the variance in the population, the broader the spectrum * Standard deviation is square root of variance * Phenotypic variation: Ïƒp2 = Ïƒg2 + Ïƒe2 * Variation in a trait can be separated into genetic and environmental components * Genotypic variance Ïƒg2 = variation in phenotype caused by differences in genotype * Environmental variance Ïƒe2 = variation in phenotype caused by environment * Total phenotypic variance Ïƒg2 = genotype + environmental variance * When genetic and environmental effects contribute independently to the phenotype, the total variance in the population equals sum of genotype and environmental variance (as seen in equation) * Genotype and environment can interact, or they can be associated * Genotype-by-sex interaction: same genotype produces different phenotypes in males and females (for example, the distribution of height among women and men) * In the simplest case, environmental effects on individual phenotypes affect all genotypes equally * When this is untrue, the

environmental effects on phenotype differ according to genotype. This is known as genotype-by-environment interaction * Genotype-environment (G-E) interaction: environmental effects on phenotype differ by genotype * i. e. in poor environmental conditions, maize with genotype A performs better while maize with genotype B performs better in rich environmental conditions * Broad-Sense Heritability (H2) — ratio of genetic variation to phenotypic variation * Ratio of genetic variation to phenotypic variation H2 = Ïƒg2 / Ïƒp2 = Ïƒg2 / Ïƒg2 + Ïƒe2 So H2 = 1 (all genetic) H2 = 0 (all environment) * Knowledge of heritability is useful in plant and animal breeding because it can be used to predict the magnitude and speed of population improvement * Heritability in humans uses twin studies, to assess genetic variation * Identical— splitting of single fertilized egg, genetically identical * Fraternal — from two fertilized eggs, only half of the genes are identical * Twin studies tend to overestimate the genetic contribution to variance because environment experienced by twins is usually very similar * Plant and animal breeding often employs artificial selection, or “ managed evolution" * Select groups of individuals from a population to become parents of next generation * Truncation point: cut-off breeders * Broad-sense heritability (H2) gives idea of how well trait will respond to selection * Narrow-sense heritability (h2): measure of effectiveness * Measures how similar offspring are to parents, and the proportion of phenotypic variance transmissible from parents to offspring * Estimated using means of traits: M = mean phenotype of populationM* = mean phenotype of individuals selected as parents for the next generation (i. e. above truncation point)M’ = mean phenotype of progeny of selected parents | M’ = M + h2 (M* - M) | * Can be used to predict

changes in population mean with individual selection h2 = (M’ — M) / (M* - M) * Generally, h2 (narrow sense heritability) is less than (<) H2 (broad sense heritability) * H2 and h2 are equal only when alleles affecting the trait are additive in their effects are equal to the heterozygous phenotype that is exactly intermediate between homozygous dominant & recessive * There are limits to the improvement that can be achieved by artificial selection * Selection limit at which successive generations show no further improvement can be reached, because natural selection counteracts artificial selection * This is due to indirect harmful effects of selected traits (i. e. weight at birth vs. viability) * Correlated response: the effect of selection for one trait on a non-selected trait (i. e. the number of eggs and their size) * Inbreeding can have harmful effects: * Inbreeding depression: decrease in fitness due to harmful recessive alleles becoming homozygous * Heterosis - hybrid vigor refers to superior fitness of heterozygote (often used in crop production) * Pedigree studies of genetic polymorphisms are used to map loci for multifactorial quantitative traits * Quantitative trait locus (QTL) — a gene that affects a multifactorial quantitative trait * These traits are mapped genetically by checking for DNA polymorphisms that are closely linked to the trait of interest * Simple sequence repeats (SSRs) are often used — as many SSRs as possible are monitored to see which segregate with the trait throughout generations * QTL affects the multifactorial traits of fruit weight, acidity, and soluble solids mapped in tomato * QTL can sometimes be identified using a candidate gene approach * Researchers make an educated guess that genetic variation in a certain gene, known as the candidate gene, might affect a certain trait * A QTL affecting depression was identified using

the candidate gene approach * Serotonin signaling and depression: 1. Serotonin is released from the transmitting neuron 2. Serotonin transporters remove serotonin from the synapse 3. Serotonin is detected when it binds to receptors on the receiving neuron * Anti-depressants like Prozac block serotonin uptake from the synapse * Researchers discovered that with a polymorphism in the enhancer region of the human serotonin transporter, the long form expressed more transporter in human cells (16 verses 13 tandem repeats) * After finding the polymorphism, the researchers genotyped 845 people for the polymorphism * The SS (32%) and SL (49%) genotypes are much more likely than LL (19%) genotypes to develop severe depression in response to multiple stressful life events. * Genotypes SS and SL also have a greater risk of depression resulting from use of Ecstasy