Lab #12
Human Genetics and Gene Expression

Section 1: Human Characters and Mendelian Inheritance

[2] Welcome to further investigation into the remarkable world of genetics! We have spent a great deal of time understanding the genetics of Mendel's pea plants, following inheritance in fruit flies and even enjoying guinea pigs! I said that we would go on to focus on humans, investigate Brooke's pregnancy risk and answer why only female cats are calico…so we better getwer why only female ca

[10] Evaluate your earlobes next. Are they attached or unattached? Some people have earlobes that curve up between the lowest point of the earlobe and the point where the ear joins the head and it would be thought that they had **un**attached earlobes inherited in a dominant manner and noted with U. Earlobes that blend in with the side of the head have been thought to be inherited in a recessive manner and are called attached noted with u. Note your presumed phenotype and genotype on the table. Make sure you clearly distinguish between upper and lower case U's!

[11] Thumb extensibility or "hitch-hiker's" thumb is a measurement of distal hyperextensibility of the thumb. A thumb that can bend back starting from at least a 50 degree angle to approaching 90 degrees was considered to be hitch-hiker's thumb and thought to be inherited in a homozygous recessive manner (hh). The inability to bend the thumb was considered to be a dominant trait (H-). Examine your thumb and note your presumed phenotype and genotype on the table.

[12] Go to the demonstration table and take out one piece of paper from a vial marked PTC. Place the PTC test paper on your tongue. PTC tasting is the measurement of the ability to taste phenylthiocarbamide, a harmless chemical referred to as PTC. People who are thought to carry the dominant allele find the taste of the paper very bitter and are referred to as a "taster". Those that have been traditionally thought to be homozygous recessive non-taster (tt) find the paper tasteless. Make note of your presumed phenotype and genotype on the table provided.

[13] Now, complete the remainder of the table in your lab book by evaluating your frontal hairline and the presence of mid-digital hair on your fingers. Remember, descriptions of each character are written in the lab book for your review. Once you complete the table, we will talk about the findings on YOU.

[14] The Mendelian inheritance of these characters certainly seems straight-forward enough…why the controversy over the teaching of this information? Because the more we learn about how genes work, the more we understand how complex inheritance can be.

[15] Are you one of the students that do not fit into either of the two categories being evaluated? Maybe the PTC paper tastes odd, but not necessarily bitter. Perhaps your thumb can bend at a 40 degree angle, but not quite 50. There are cases of parents with attached earlobe, autosomal recessive, that have an offspring with unattached earlobes. There are cases of identical twins with different tongue rolling abilities.

[16] Does this mean you were you given to the wrong parents at birth? Not likely….biology is the study of life, and our knowledge grows with more investigation. Let's examine some ideas that have built on Mendel's rules of inheritance.

[17] An important word in genetics is PENETRANCE. Penetrance is the likelihood that an individual with a given gene will express that phenotype. Let's consider what might influence a gene to express a phenotype. Write the definition for penetrance in your lab book.

[18] Environment can influence a gene. Siamese cats and Himalayan rabbits each have a gene that codes for dark fur to cover their entire body but the expression of that gene is affected by

temperature. Because the gene is heat sensitive, the cooler the area on their body the darker the fur color will be. In general, the face and paws will be dark, but in the winter months, you will see your Siamese cat get darker, especially if he goes outside. Human skin tone is also affected by the sun. Answer a question in your lab book about our Himalayan rabbit.

[19] Another important idea in genetics is polygenic inheritance. Polygenic inheritance describes inheriting a phenotypic character in which the expression depends on the effect of many genes. What if it took gene A **and** B to be a tongue roller? Each of your non-roller parents might have had one of those genes and then individually passed both of them on to you. Human eye color is one example of a character that is determined by the expression of multiple genes. Note the definition for polygenic inheritance in your lab book.

[20] All of this tells us – Mendel wasn't wrong, there is just so much to learn in this world. Mendelian inheritance has remained perfectly accurate in many of the characters and disorders we have identified. It may simply have been applied too quickly and without proper research to characters such as tongue rolling or earlobe attachment, characters that are inherited with greater variation than can be described by Mendelian inheritance.

[21] Achondroplasia, the most common form of human dwarfism is v0 0 0Tm *F*1.0 1 Tf (nheritance has remaw0

[26] Are these the genotypes you recorded for autosomal recessive deafness in your lab book? The squares and circles with a dot in the middle represent

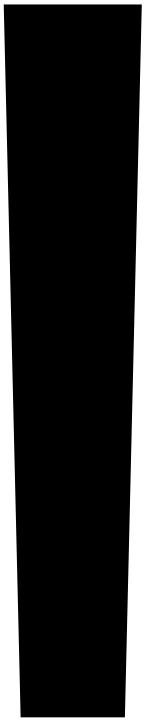
[35] Individuals who have type O blood do not have antigens A or B on their red blood cells, and produce antibodies that will attack either A or B antigens. Make sure you have completed the table on blood group phenotypes before we move on to discuss blood group genotypes.

expression of a character. Also, note the column titled Rh type. What does it means to be Rh positive or Rh negative?

[45] When working with blood types, this question always arises. What does it mean for example, when you are O positive or perhaps B negative? The terms positive or negative listed after your ABO blood type refer to the Rh factor, a different blood antigen. It is called Rh factor because it was an antigen first identified in the blood of rhesus monkeys. The Rh blood antigen can be found in approximately 85% of people. Take a moment to answer the first two questions about Rh factor.

[46] Let's make simple a very complex inheritance. The human population is divided into two groups. The first group includes Rh positive individuals who express the antigen Rh D on their red blood cells through some variation of three closely linked genes. These individuals have the genotypes homozygous Rh+Rh+ or heterozygous Rh+Rh-. The other group is made up of Rh negative individuals who do not express this antigen and have the homozygous Rh-Rh- genotype. The Rh negative phenotype usually originates from being homozygous for a non-functional allele of the gene. Make note of these three genotypes in your lab book.

[47] Concerns over the Rh factor arise due to pregnancy and a very serious disorder called hemolytic disease of the newborn. Suppose a woman is Rh negative and she is pregnant. If her fetus is Rh positive due to the genotype of her partner, her body will form search and destroy antibodies that will attack the baby as if it was a germ or an invader.



[51] Lets review. Here you see two haploid genomes: one from a male sperm and one from a female egg. Let's take note of the difference…though they ***each*** have 22 autosomes, chromosomes that are not responsible for determining gender, the sperm has an X ***or a*** Y sex chromosome and the egg has an X sex chromosome only.

[52] The gender of an offspring is determined by which sex chromosome the father passes on, X or Y, to fertilize the female egg which can only have an X. Therefore, there is a 50% chance in each pregnancy that it will be male or female. The sex of offspring is determined at the moment of conception. Answer a couple more questions in your lab book.

[53]Your physical gender is genetically controlled, as many other aspects of you are determined. Does this mean having a Y chromosome will guarantee that you will love football? Two X chromosomes means you like to shop? That is not what it means to be male or female! Being male or female is a wonderful spectrum of characteristics brought about by vast combinations of genes and differing environments. Take a look at the prepared slide of human chromosomes on the demonstration table, compare it to the image on the screen, and complete the Punnett square activity for sex chromosomes in your lab book.

[54] Genes carried on the sex chromosomes have been called sex-linked genes. The inheritance

[65] Brooke's blood test results showed that she was in fact a carrier for fragile X with 105 "CGG repeats" on one X chromosome and a normal number of "CGG repeats" on the other. This meant there was a risk for the gene on the one of Brooke's X chromosomes to increase in repeat number to a full 200 repeats. An ultrasound revealed that Brooke was carrying a male fetus, and she underwent an amniocentesis. An amniocentesis utilizes a needle to collect fetal-DNA-containing fluid from around the fetus.

[66] Since Brooke was a carrier, what is the chance her male fetus would inherit the increased "CGG repeats" from one of her X chromosomes? If you answered 50%, you are correct. Brooke's amniocentesis results showed that the fetus inherited her normal X chromosome. A happy ending for this couple. Is it always? No. That is why information, testing and assistance are available for all couples when they reproduce so that they can make informed decisions for their lives.

[67] Answer a question about Brooke's pregnancy risk in your lab book and then answer some "thinking questions" before we move on. Do not be afraid to be wrong. There is an instructor available who will consider each fascinating question with you if you get stuck.

Section 4 – Chromosome Abnormalities and Nondisjunction

[68] Mutations in genes are not the only abnormalities that can arise in the sex chromosomes. Abnormalities can occur due to the complete loss or gain of an entire sex chromosome. Occasionally homologous chromosomes or a pair of sister chromatids fail to separate at anaphase. This error is called non-disjunction. This illustrates normal disjunction of the male sex chromosomes and non-disjunction of the female sex chromosomes. Write down the definition of non-disjunction.

[69] Non-disjunction can result in an abnormal number of chromosomes first in gametes and then in offspring. Because one gamete gets two X's and the other gamete gets no sex chromosome, the resulting offspring have abnormal karyotypes and outcomes. See what happens if each type of abnormal egg is fertilized by a normal sperm.

[70] What if non-disjunction occurred with the male sex chromosomes? To consider this scenario, you must recognize that male X and Y chromosomes behave like homologous chromosomes during meiosis. Click on the correct answer and fill in your lab book when you have it.

[71] Turner syndrome is one outcome of nondisjunction of the sex chromosomes and results in a female with only one X chromosome. Note her karyotype is **45**,X because she is missing one chromosome. She is infertile, has delayed sexual maturation and slightly reduced intelligence. On the screen you can note her short stature, barrel chest, poor breast development, widely spaced nipples, and webbing of the neck. Approximately 99% of Turner syndrome fetuses are miscarried or stillborn. Match each syndrome name in your lab book as you hear the description in the program.

[72] A nondisjunction event that occurs during egg or sperm production results in an XXY male, a condition called Klinefelter syndrome, karyotype **47**,XXY. Individual's with Klinefelter syndrome are generally tall and have long arms and legs. The gonads are undeveloped and fail to produce sperm, therefore these individuals are infertile. Slight enlargement of the breasts is common as well as wide hips. Reduced intelligence is often observed.

[73] The nondisjunction event that leads to XYY males or trisomy X females result in tall individuals with normal sexual development. There is a high but not constant correlation between the extra Y chromosome in XYY males and behavioral problems. These findings are controversial. Females with trisomy X can have learning difficulties but the syndrome is highly variable in expression.

[74] Have you matched each syndrome to the correct description? Take a moment to check your answers against the table on the screen before we discuss nondisjunction in autosomes.

[75] Nondisjunction can also occur in any of the 22 pairs of human autosomes. Nondisjunction of an autosome during meiosis is the most common cause of trisomy 21 (meaning three chromosome 21's), better known as Down syndrome. Varying degrees of physical, psychomotor, and mental development is retarded in all children with Down syndrome. They are prone to respiratory disease, heart malformations, leukemia and they have a shortened life expectancy.

[76] Down syndrome is the most common genetic cause of mental retardation but not the most common cause of inherited mental retardation (that would be fragile X). Nondisjunction of any chromosome is a random accident or error that can occur in maternal or paternal meiosis and therefore does not cause a heritable syndrome. Failure of paired homologs to disjoin during anaphase I or failure of chromatids to disjoin during anaphase II can result in male or female gametes with an extra chromosome 21. Complete the last two questions of Section 4 before going on.

Section 5 – Barr Bodies and X Chromosome Inactivation

[77] It is possible to detect gender or sex chromosome abnormalities by examining an individual's cells with a microscope. This is possible because only one X chromosome in any cell is active. If there are additional X chromosomes in the cell they are inactive and will form a densely stained mass in the nucleus called a Barr body. The number of Barr bodies in a cell is equal to the total number of X chromosomes minus one. Write down the definition for Barr body in your lab book.

[78] A normal female has two X chromosomes, and therefore, would have one Barr body. Remember, only one X remains active in any cell. What about a woman with trisomy X? What about a male who has Klinefelter syndrome? Write down the number of Barr bodies in your lab book for a few individuals before we discuss X chromosome inactivation.

[79] X chromosome inactivation shuts-down the majority of genes on all but one X chromosome in a cell. In general, this applies to a normal female with two X chromosomes. X-inactivation

occurs early in embryonic development and guarantees that males and females receive the same dose of proteins produced by genes on the X chromosome. X chromosome inactivation also creates the unique black and orange or tortoiseshell pattern of fur in calico cats. Write down the definition for X-chromosome inactivation in your lab book.

[80] Two X chromosomes are required to have both black and orange fur. A gene for fur color is present on the X chromosome and can have either a black fur allele or an orange fur allele. To express both colors, a cat should be female and have two X chromosomes, each having a different color allele. The pattern of orange and black fur is created by which of the two X chromosomes are inactivated in any given cell. The white fur of the calico cat is produced by a different gene. Answer one last question before going on to Section 6.

Section 6 – DNA to RNA to Protein

[81] How does the information found in DNA determine an individual's characteristics? You have learned that DNA is the molecule of heredity; you know its structure and its ability to replicate. You know that it copies itself and divides to produce new cells through mitosis as well as gametes for reproduction through meiosis. How are the instructions in DNA translated into characteristics? DNA is the chemical code for protein synthesis.

[82] Let's review. DNA is composed of units called nucleotides. Each consists of the sugar deoxyribose, a phosphate group and a base. There are four bases: adenine, guanine, thymine and cytosine. We abbreviate the bases as A, G, T, and C. DNA molecules are composed of two strands of nucleotides held together by weak hydrogen bonds between the bases. One strand can predict what will be found on the other strand by following strict complementary base-pairing rules, A bonds with T, C bonds with G. Take a moment to complete the review in your lab book.

[83] DNA's chemical code is made up of the 4 bases we have just reviewed much like the English language is made up of 26 letters or binary code is made up of two symbols. The bases A, T, C and G are the letters of DNA's chemical alphabet that produce a message and relay information just as the English language uses 26 letters to communicate. The complete message

through a chemical messenger that we will discuss in a moment. Write down the definition of codon in your lab book and answer the first question about DNA triplets.

[87] Recall that a gene is a segment of DNA located along the length of a chromosome that will code for a particular polypeptide and therefore a particular character in an organism. The relationship between genes and polypeptides was established in the 1940's by two scientists, Beadle and Tatum. Their experiments with defective enzymes and mutant bread mold led to our current understanding that "the function of a gene is to dictate the production of a polypeptide". Make note of this in your lab book.

[88] Because our DNA never leaves the nucleus and protein synthesis occurs in the cytoplasm, a chemical messenger called messenger RNA or abbreviated mRNA, is necessary to perform this task. mRNA will carry DNA's information to the ribosome where protein synthesis will occur. Answer a couple more questions before we compare the molecular structures of RNA and DNA.

[89] Let's consider the structure of ribonucleic acid or RNA. It is a nucleic acid like DNA and is also composed of nucleotides. RNA has a sugar phosphate backbone like DNA, but RNA's backbone is made of phosphate and the sugar ***ribose***. Fill in the comparison table as we continue.

[90] You see listed on our comparison table the four nitrogenous bases of DNA. RNA contains the bases adenine, guanine and cytosine just like DNA, but the fourth base in RNA is not thymine. RNA contains the base uracil. Messenger RNA is a single-stranded molecule unlike DNA, which is double-stranded. Complete the table and summarize three specific ways DNA differs from RNA.

[91] Let's put this all together. We know that DNA contains the coded message to dictate protein synthesis and we know that mRNA carries the information to a ribosome for translation of the coded message into a protein. This flow of genetic information in a cell from DNA to RNA to protein is an important central concept in biology, and has two main stages that we term transcription and translation.

[92] Let's begin by considering transcription. The assembly of messenger RNA is accomplished by DNA in the nucleus. The DNA molecule unwinds just as it does in replication. The process of transcription is simply the production

[95] The mRNA strand that has been transcribed from the DNA template leaves the nucleus with the coded message to go to the cytoplasm and attach to a ribosome. Remember that ribosomes are the organelles that make polypeptides. Complete this step of information flow in your lab book.

[96] Another type of RNA molecule becomes involved as we enter the second stage of genetic information flow in the cell, translation. It is called transfer RNA and is abbreviated tRNA. Each tRNA serves as a translator between mRNA and amino acids. The tRNA carries one amino acid and has a triplet of nucleotides called an anticodon. tRNA's anticodon will be complementary to an mRNA's codon only if the tRNA is carrying the correct amino acid to be added next in the growing polypeptide chain.

[97]. Translation from the language of nucleotides to the language of amino acids occurs only if the correct tRNA anticodon base pairs to the mRNA's codon. Drag the tRNA to base pair with the correct mRNA codon on the screen then circle it in your lab book.

[98] To summarize, translation is the assembly of a unique sequence of amino acids to produce the required polypeptide chain, forming a protein, as directed by mRNA. Here in the program, you will complete translation by dragging the tRNA and its amino acid to its correct base pairing position on the mRNA. Record this information in your lab book.

Section 7 – The Effect of DNA Mutations on Proteins

[102] In this lab, we first considered DNA mutations when we discussed the cause of red-green colorblindness. We defined a mutation as any permanent, heritable change in the nucleotide sequence of DNA and we followed the inheritance pattern to see wj ETed the inheritance pattTed r.p the inherita

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