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 get going.

[3] Does Mendelian inheritance apply to humans? Yes – you have already seen an example of that in your last lab when you evaluated a family and their chances of having children that are deaf.

[4] How about simple human characters you may have heard about like tongue rolling, ear attachment and hitchhikers thumb? These have been used traditionally to teach Mendelian inheritance of human traits, but as we learn more about genetics, this method of teaching has become controversial…let's look at why.

[5] First, let's consider some of the human characters that have been taught traditionally as inherited in a Mendelian manner. Let's investigate using you as our human subject, and keep track of the findings about you. Let's start with tongue rolling. Can you roll your tongue? There is a mirror available on the demonstration table if you are not sure. If you can, your tongue will look U-shaped, almost like a tube.

[6] The ability to roll the tongue has been thought to be inherited in a dominant manner, meaning you would have the genotype of either homozygous dominant RR or heterozygous Rr. The only way for us to know if you are homozygous dominant or heterozygous for this trait would be to perform a test-cross with you and a partner of a known recessive genotype. Read the start of Section 1, make note of the definition of testcross, and write down the first two genotypes for "rollers" in your lab book.

[7] A testcross is not feasible in lab today! Genetic experimentation with humans takes way too long to produce large numbers of offspring and is generally frowned upon by society, so we will have to designate your genotype as "capital R dash" (R-) if you can roll your tongue. This means we presume you have a dominant allele, but we are not sure what the other allele might be. Fill in the blank with this notation if you can roll your tongue, but your exact genotype is unknown.

[8] Now if you cannot roll your tongue, you would be considered a non-roller and have a recessive genotype of rr. Write the homozygous recessive genotype in your lab book.

[9] Now you will see in the lab manual a description of six different human characters. After you have read about each character and listened to the descriptions in the program, fill in the chart that follows starting with what you would consider to be your presumed phenotype and genotype for tongue rolling. This is where we will collect information about you, our human subject.

[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 known to be inherited in a Mendelian autosomal dominant manner. Remember autosomes are a chromosome not directly involved in determining the sex of an organism. Therefore, achondroplasia is inherited in a dominant manner on an autosome, specifically human chromosome number 4.

[22] Let's learn how to use an important tool in genetics while looking at achondroplasia. This is a pedigree. Pedigrees are diagrams depicting a family history that follows the inheritance of a genetic trait over a number of generations. Write this definition down in your lab book.

[23] In a pedigree, squares represent males, circles represent females. Lines horizontally between squares and circles represent a mating. Lines descending from the horizontal lines indicate offspring. The Roman numerals represent generations. Squares or circles that are shaded-in represent individuals with a particular trait or syndrome, in this case, dwarfism caused by achondroplasia.

[24] Examine this same pedigree with the genotype listed underneath each individual. This will help you recognize the pattern of a dominant disorder. It is fitting in a pedigree of an autosomal dominant disorder that every affected individual has at least one affected parent. There is also a high probability that we will see the disorder in every generation. Copy this information down in your lab book and answer some questions about genotypes in a family with achondroplasia.

[25] Now examine this pedigree of individuals with a form of deafness inherited in an autosomal recessive manner. Pedigrees of families with autosomal recessive disorders can be recognized because there are affected individuals with unaffected parents. Also, there can be generations without affected individuals. Unaffected parents of affected offspring must be heterozygotes. Why do you think that is? Put your answer in your lab book and record what genotypes you think belong to each individual.

[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 a pedigree notation for obligate carriers…these are individuals we can assume are carrying the gene because they have affected offspring.

[27] You are ready to work some problems on your own! You will be investigating the genetics of three different disorders. You will first consider sickle cell anemia; a disorder that causes red blood cells to become sickle shaped and block blood flow. You will review a case of albinism which is the absence of normal pigmentation in skin, hair and eyes. Also, you will do a problem involving brachydactylism, a genetic disorder that causes a reduction in finger and toe size. Return to the program when you are finished with problems 1 through 4 in Section 1!

Section 2: Genes That Have Multiple Alleles

[28] So far we have concentrated on characters or disorders that have just two different alleles for each gene. For some characters, such as ABO blood groups, there can be multiple alleles possible. Even when characters have multiple alleles available remember that any one individual can only possess two alleles, one from their mother and one from their father.

[29] You have probably been informed by your doctor or your parents what your blood type is, for example type A, type B, type AB or type O. If not, this would be important information to be aware of. Before we discuss the genetics of the ABO blood groups, let's consider what the blood type you have tells us about your blood.

[30] In the ABO blood group system, your blood type designates what type of carbohydrates or lack thereof you have on the surface of your red blood cells. Matching compatible blood groups is critical for safe blood transfusions.

[31] Our immune system produces blood proteins called antibodies that recognize what carbohydrates we should have on the outside of our red blood cells. The carbohydrates are called antigens. Those antigens determine our blood type. The antibodies also recognize when antigens might be invaders to our body. If our antibodies find blood cells that do not belong to us, they attack those blood cells causing a severe clumping reaction to occur. The clumping can block blood vessels and cause death. This could happen with the wrong blood transfusion.

[32] If your phenotype is blood type A, you have A antigens on the outside of your red blood cells and you have antibodies in your blood plasma against the antigen B. Record this information as we go along in your lab book.

[33] If you have blood type B, you have B antigens on your red blood cells and you produce an antibody against antigen A.

[34] If you have blood type AB, you have both A and B antigens on your red blood cells and you do not produce antibodies against either A or B.

[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.

[36] You now recognize four phenotypes for blood type. The four phenotypes involve three different alleles that can produce six different genotypes. As we examine these different genotypes, we will revisit a familiar inheritance pattern and learn about a new one…codominance. Let's start by revisiting dominant - recessive inheritance patterns seen with allele I^A or I^B and their relationship to allele *i*.

[37] The capital letter "I" is used to represent blood group alleles that produce antigens and stands for isoagglutinogen, a term that means antigen. Capital I with a superscript A or B would represent alleles that produce antigens. An allele represented by lower case *"i"* produces no antigen.

[38] Therefore, I^A represents the allele that produces red blood cell antigen A. I^B would represent the allele that produces red blood cell antigen B. Both are dominant to lower case *i,* which represents the allele that does not produce any detectable amount of red blood cell antigen. These symbols represent the three alleles for this gene.

[39] Here are our six genotypes. The first two genotypes produce individuals with blood type A: $I^A I^A$ and $I^A i$. Remember, I^A is dominant over i, and therefore individuals with either of these two genotypes will have red blood cells with A antigens and will produce antibodies against B.

[40] Alleles $I^B I^B$ and $I^B i$ will produce individuals with blood type B. I^B is dominant over allele i and individuals with either of these two genotypes will have red blood cells with B antigens and will produce antibodies against A.

[41] Individuals with alleles $I^A I^B$ have blood type AB. These two alleles exhibit codominance as they both contribute a different antigen…they are ***both*** expressed in heterozygous individuals. Do not confuse this with what we learned previously about incomplete dominance, where the two different alleles express one intermediate phenotype. Write down the definition for codominance in your lab book.

[42] Allele *i* is recessive, and an individual with the genotype *ii* will not produce antigens A or B on their red blood cells but will produce antibodies against A and B. Complete the table of genotypes for each blood type in your lab book.

[43] Does your table look like this one? If not, get the instructor to help you. If so, you are ready to tackle a few genetics problems involving blood types in your lab book. Return here once you complete the work on problems 1 through 3 in Section 2.

[44] Take a look at these figures. Consider that the majority of individuals in the United States have type O blood. Did you think that those with *recessively* inherited type O had a blood type that was rare or undesirable like some disorders that we have seen? A recessive allele can be more abundant than a dominant allele, and sometimes represent the more normal or common

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 *RHD* 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. The consequences of this disease can be severe, even fatal, to the fetus.

[48] Thanks to dedicated scientists, women whose fetuses are at risk for this disorder receive an injection of Rh immune globulin to suppress their immune response at key points in pregnancy, after miscarriage or termination…a good reason to know if you are Rh positive or negative. The discovery of the Rh system and the prevention of hemolytic disease of the newborn have been major contributions of genetics to medicine. Complete a couple more questions in your lab book about the Rh factor.

Section 3: Sex Chromosomes, Gender, and Genetic Abnormalities

[49] Many organisms, including almost all mammals, have a pair of sex chromosomes. The sex chromosomes in general determine an individual's gender and are commonly designated with an X and a Y. You are already familiar with these human female and male karyotypes from previous labs. The term karyotype also refers to the standard chromosome set of an individual and is written as 46,XX for females and 46,XY for males. Human females have two X chromosomes and human males have an X and a Y chromosome in every diploid cell. Make note of this in your lab book at the start of Section 3.

[50] In this part of the lab we will concentrate on the sex chromosomes. This will answer the questions about Brooke's pregnancy risk for mental retardation and why only female cats are calicos. We will also look at other genetic abnormalities that center around these unique sex chromosomes.

[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 pattern for these genes was first studied by a man name Thomas Hunt Morgan in the early 1900's. He was studying our old friend *Drosophila melanogaster*, the fruit fly, and he discovered a male fly with white eyes instead of the normal red eyes.

[55] When Morgan crossed this unusual white eyed male with a normal, red-eyed female, all of the offspring had red eyes. This indicated to Morgan that the allele for mutant white eyes was recessive. Of course to be complete, Morgan went on to cross the F_1 generation offspring just as Mendel did with his sweet peas.

[56] Morgan expected a ratio of 3:1 red to white eyes following the F_1 cross and that is what he got…with an exception! Morgan found that in his F_2 generation no female had white eyes! All white eyed flies were male! Morgan certainly was not sleeping on the job…would you have thought to check for gender differences in the outcome?

[57] Morgan concluded that eye color was "sex-linked". Morgan deduced that the gene for eye color was located on the X chromosome and there was no corresponding gene on the Y chromosome. He recognized that a female has two alleles for eye color…one on each of her X-chromosomes. A male, however, has only one allele for eye color and will express whatever he has because it is on his only X chromosome. Since Morgan found eye color to be recessive, both X chromosomes would need to have the gene for white eye color before the female could express the unusual phenotype.

[58] What about humans? There is a gene on the human X chromosome that codes for proteins called opsins that are found in photoreceptor cells of the retina. A mutation, which is any permanent, heritable change in the nucleotide sequence of DNA, can lead to a lack of normal proteins. This deficit can cause insensitivity to light of red and green wavelengths. The end result can be colorblindness. This test chart helps to identify colorblindness. A person with normal

vision will see a “96”. If you have red-deficient vision, you will see only a “6”. If you have green-deficient vision, you will see only a “9”. Answer a question about red-green colorblindness and write down the definition of mutation in your lab book.

[59] Though the mutation for colorblindness would be considered “sex-linked”, this term has become obsolete because it fails to distinguish between the X and the Y chromosomes. It is more appropriate to say X-linked disorder or Y-linked character. Also, there are very few genes on the Y chromosome. The few genetic disorders that are actually attributed to the Y chromosome, like hairy ear rims, are referred to as Y-linked. Answer a couple more questions before we review a chart on X-linked recessive disorders.

[60] As would be predicted with an X-linked recessive disorder, more males than females are affected. In the United States about 7% of men are colorblind and only about 0.4% of females. Why a gender discrepancy? Men have only one X chromosome, and if that X-chromosome has the recessive allele, the man will be colorblind. A woman having two X chromosomes could be affected, could be a carrier (a heterozygote) or could be unaffected based on her alleles. Review the chart of X-linked recessive disorders and using the correct allele symbols answer questions 1 and 2 following the chart in your lab book.

[61] Hemophilia is an X-linked recessive disorder. It is also known as “bleeder’s disease” due to a mutation that prevents proper blood clotting. Interestingly, hemophilia was prominent in European royalty. The disorder has been traced back to Queen Victoria of England who passed the mutation on to the royal families of Spain, Germany and Russia. William and Harry, sons of the late Princess Diana, are not affected. Could they have been? For fun, follow the pedigree on the screen and click on your answer. Then, answer the hemophilia question on Princess Beatrice in your lab book.

[62] Let’s explore Brooke’s pregnancy risk. In the last lab, we read that Brooke and her husband had been referred to a genetic counselor because Brooke’s cousin John had undiagnosed mental retardation. Cousin John’s behavior seemed autistic to Brooke, but his appearance was generally normal. Cousin John’s family refused to talk about his condition.

[63] Brooke and her husband met with a genetic counselor to evaluate the risk to her fetus. After a family pedigree had been drawn, the genetic counselor expressed concern that Brooke’s cousin could have fragile X syndrome, the most common form of *inherited* mental retardation. The genetic counselor recommended drawing Brooke’s blood to run a simple, inexpensive genetic test for fragile X. This test is readily available to any concerned individual.

[64] Fragile X is caused by a recessive mutation in the FMR1 gene on the X chromosome. The mutation can cause more than the normal amount of DNA to be copied when being passed on to offspring. Specifically, a full mutation has a large number of repetitions of DNA called a “CGG repeat”. If a male inherits 200 or more “CGG repeats” on his only X chromosome, the disabled FMR1 gene will not produce a protein required for normal brain function. This individual will have fragile X syndrome.

[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 is formed by unique sequences of bases along the strand of nucleotides of the DNA molecule you already know to be called genes.

[84] DNA's chemical alphabet produces a message that codes for amino acids and the building of a polypeptide chain. You recall that amino acids are the building blocks of polypeptides, and polypeptides form proteins. Therefore, DNA codes for proteins.

[85] There are 20 different amino acids that DNA can code for, and the unique arrangement of the amino acids in the polypeptide chain determines what protein is produced.

[86] The term codon is used to describe a three-nucleotide sequence that specifies a particular amino acid. A triplet of DNA nucleotides will provide the information necessary for the coding of a particular amino acid which in turn builds a polypeptide. The information will be sent

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 of a single-stranded RNA molecule using DNA as a template. This is possible through complementary base-pairing.

[93] In transcription, one strand of DNA nucleotides attracts free RNA nucleotides and copying of a gene begins. A DNA nucleotide with cytosine will base pair with an RNA nucleotide that has guanine. A DNA thymine will base pair with an RNA adenine. An important exception exists whenever there is adenine in DNA. RNA nucleotides do not have thymine. RNA will use uracil in place of thymine every time it base pairs with the DNA nucleotide adenine.

[94] Complete transcription of an mRNA molecule by dragging the correct RNA nucleotide to base pair with the DNA template. Once you have correctly transcribed a single stranded mRNA molecule record it in your lab book.

[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.

[99] Here is a diagram of the flow of information in the cell. You can see that DNA synthesizes RNA in the nucleus during transcription. RNA leaves the nucleus to locate a ribosome in the cytoplasm. The mRNA is translated into a protein on a ribosome using a tRNA during translation. Amazing! DNA to RNA to protein…and proteins produce your characteristics! Have an instructor initial your page when it is complete.

[100] This information begs the question…how do we know which amino acid is being added? The genetic code was deciphered in the 1960's by dedicated scientists. The genetic code is a table that shows which mRNA codons code for which amino acids. It was written and must be read in the language of **mRNA nucleotides**…do not try to decipher using tRNA anticodons! You will get the wrong amino acids! Copy down the definition for genetic code and answer a couple of questions.

[101] Here is your chance to interpret the genetic code. Proceed from left to right on the mRNA strand to identify each 3 base codon. The anticodons have already base paired, so they are not included. Use the genetic code and match each of the mRNA bases on the screen to their correct amino acid and then drag the name to the tRNA. Locate the first base from the mRNA strand on the left hand side of the genetic code table. Locate the second base of codon 1 on top of the table, and follow down that column until you arrive at the full triplet sequence of your first codon. There will be your amino acid! Continue until you have completed the polypeptide chain. Record this information in your lab book. Have an instructor initial this page before going on to Section 7. You are almost done!

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 who might be affected.

[103] Now let's look at a DNA mutation in terms of its effect on a protein. Recall your work in Section 1 on the recessive disorder sickle cell anemia. It causes red blood cells to become deformed…blocking blood flow and creating other life-threatening problems. The mutation that causes sickle cell anemia is a single substitution of one nucleotide base in the gene. Bases determine codons and codons dictate which amino acid is placed in the polypeptide chain.

[104] Red blood cells are primarily composed of the protein hemoglobin. Hemoglobin is formed using two different polypeptide chains. Individuals with sickle cell anemia form one abnormal chain in their hemoglobin which results in incorrect folding of the protein. This causes the red blood cells to sickle. The abnormal chain is the direct result of the placement of an incorrect amino acid due to the wrong instructions encoded in the mRNA. Complete section 7 by identifying the incorrect amino acid.

[105] Did you use the genetic code to identify the incorrect amino acid? That is the end of our lab on human genetics and gene expression. You did great work.