TFT Genetics
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Part 1: Genetics 101 - Basic Principles of Genetics

Introduction

All of the anatomical and physiological features that I will be discussing in this and subsequent essys are either totally under genetic control, or can be influenced by genetic factors. Therefore, before discussing specific genetic features it would be useful to define some of the basic genetic terms that I will be using. These include some commonly used, but often misunderstood terms, such as **gene, dominant** and **recessive**, as well as some less common terms such as **autosomal**, **sex-linked**, **allele**, **homozygous**, **heterozygous**, **genotype**, and **phenotype**. In this article I will try to define these terms and give examples so that we can come to some clear understanding of what each term means. Possibly even more importantly, I will try to make clear what a term does not mean. This is particularly important for some of these terms because they are often misunderstood. In subsequent essays I will introduce other terms as may be necessary to understand the concepts being presented in that essay. However, the terms above are sufficient for now. What do these terms mean? Simply put **autosomal** means that there is no difference in inheritance patterns between males and females. Both genders inherit (or do not inherit) the characteristic being described with equal frequency. Most inherited characteristics are autosomal. However, a few are **sex-linked**, which means that there is a gender-based difference in inheritance patterns. In people, for example, certain types of color-blindness are sex-linked, being inherited more frequently in men than in women.

To fully comprehend the concepts of **recessive** and **dominant** characteristics we need to have a basic understanding of **genes**. It is usually easier for people to understand genes and other genetic principles if they are defined by example. I will use human eye color as my primary example because it is something we can all see and relate to and because basic eye color (blue vs. brown) is controlled by a single gene. Other colors (hazel, green, etc.) require the participation of other genes and the genetics of these colors can be quite complex. However, if we stick with the basic, single-gene system of blue vs. brown we can illustrate most of the important genetic principles in a way that is not too difficult to understand. To start our discussion, we know that within the nucleus of every cell in every living organism are structures called chromosomes that contain the **DNA** molecules on which the genes are located. We also know that we have two sets of chromosomes in each cell. One came from our mothers and one from our fathers. Each set contains genes for the various inherited characteristics such as eye color. One way to look at the situation is to think of the gene (also sometimes referred to as a **genetic locus**) as a location on a chromosome that contains information about a particular characteristic (in this case eye color). The term **allele**, then, refers to the specific information that resides in that location. In our example above then, we have a gene (location) for eye color but we have two possible alleles (specific pieces of information), one for brown color and one for blue color. For any autosomal characteristic, such as eye color, each individual inherits two alleles that control that characteristic. One allele is located on the set of chromosomes inherited from the male parent and one allele is on the set of chromosomes inherited from the female parent. If the two alleles are the same (either both brown or both blue) the individual is said to be **homozygous**. If the alleles are different (one brown and one blue) the individual is said to be **heterozygous**. The **phenotype** or outward visible appearance (in this case the color of the eyes) of the individual will depend on the **genotype** (i.e. what alleles an individual possesses) and, in heterozygous individuals, on the relationship between the alleles (i.e. which is dominant and which is recessive). In the case of human eye color, brown is dominant and blue is recessive. Individuals who are either homozygous for the dominant (brown) allele or who are heterozygous (having one brown allele and one blue allele) will exhibit the phenotype (brown eyes) associated with the dominant allele. Only individuals who are homozygous for the recessive (blue) allele will exhibit the phenotype (blue eyes) associated with that allele.

The Genetic Gamble

Now we come to the heart of genetics as it relates to breeders. How do we use these concepts to predict the outcome of specific matings? After all, as breeders that is what we are constantly trying to do. The operative word here is "try". All of genetics is based on probability, sometimes referred to as the "**genetic gamble".** We breed "**the best to the best and hope for the best**". We can't usually guarantee the outcome, but if we know something about genetic principles, we can tip the odds in our favor. How? Lets continue with our eye color example and lets pretend for the rest of our discussion that we can selectively mate individuals of our choosing (as we do with dogs). Before doing that however, we have to create some symbols so we can more easily see the possible outcomes. For eye color we can make symbols as follows:

B (upper case) = the **dominant allele** for brown eyes

b (lower case) = the **recessive allele** for blue eyes

BB = the **genotype** of individuals that are **homozygous** for the **dominant** allele; the **phenotype** of these individuals will be brown-eyed

Bb = the **genotype** of individuals that are **heterozygous**; the **phenotype** of these individuals will also be brown-eyed

bb = the **genotype** of individuals that are **homozygous** for the **recessive** allele; the **phenotype** of these individuals will be blue-eyed

We also need to understand what I refer to as the cardinal rule of genetics:

You cannot give to your offspring what you do not have

An individual who is homozygous for an allele such as the B (brown) allele (i.e. their genotype is BB) can only pass that allele to their offspring. They cannot pass the blue allele (b) because they do not have one. On the flip side, an individual who is homozygous for the b (blue) allele (i.e. their genotype is bb) can only pass that allele to their offspring. They cannot pass the brown allele (B) because they do not have one. Finally, an individual who is heterozygous (i.e. their genotype is Bb) can pass either allele to their offspring. In fact, the principles of probability suggest that approximately 50% of the offspring should get the recessive allele from a heterozygous parent while 50% should get the dominant allele. **Notice** that if a parent is **heterozygous** there is no difference in frequency of inheritance in their offspring between the dominant and recessive alleles. The dominant/recessive relationship **ONLY** affects the **phenotype** (outward physical appearance) of heterozygous individuals and has no bearing on either frequency of occurrence of the alleles in a population or frequency of inheritance of the alleles among offspring. This is a difficult concept to grasp and one that we will come back to in another essay. For now, however, please accept this as a fundamental principle of genetics and lets continue with our eye color example.

We can easily see that if we apply the cardinal rule of genetics (remember: you cannot give to your offspring what you do not have) then, when two blue-eyed individuals who are homozygous for the blue allele (bb) mate and produce children, all of those children will also be homozygous for the blue allele (bb) and all will be blue-eyed. We can represent this symbolically as:

bb x bb (parents) ➔ bb (all children)

Blue-eyed parents can never produce brown-eyed children. They simply do not have the dominant brown allele to give. If they did they would be brown-eyed not blue-eyed. **Think about it!**

What about the situation where one parent is blue-eyed and the other is brown-eyed. Can they produce blue-eyed children? It depends on the genotype of the brown-eyed parent. Remember the genotype of the blue-eyed parent has to be homozygous for the blue (b) allele → bb. However the brown-eyed parent can either be homozygous for the brown (B) allele (i.e. BB) or heterozygous (Bb). Let's look at each of these matings.

First, what about a homozygous brown-eyed parent mating with a blue-eyed parent (who must be homozygous or he/she would not be blue-eyed)? Symbolically, we represent this as:

BB x bb (parents) ➔ Bb (all children)

Notice that all children have the heterozygous genotype (one brown allele and one blue allele) and therefore all have the brown-eyed phenotype (no blue-eyed children here).

However what if the brown-eyed parent is heterozygous (Bb) instead of homozygous? Then we have:

Bb x bb (parents) ➔ Bb (1/2 of the children) + bb (1/2 of the children)

Approximately half the children should be heterozygous and have brown eyes while half should be homozygous for the blue allele and therefore have blue eyes. Notice that I say should. This is the "gamble" part of the genetic gamble. With this mating it is possible for all children to be brown-eyed or all to be blue-eyed. However, the more children involved the more likely it is that you will come close to the predicted value. It's like flipping a coin. If you flip it 10 times you should get 5 heads and 5 tails, but you could get 6 and 4 or 7 and 3, 8 and 2, 9 and 1, or even 10 and 0 for either heads or tails. However, if you flip it 1,000 times you are more likely to come close to the predicted value of 500 heads and 500 tails. Some deviation is possible but you probably would not ever get 1000 heads and 0 tails (unless the coin is weighted somehow).

But back to eye-color. The last two matings involved one brown-eyed and one blue-eyed parent. What about matings between two brown-eyed parents? There are three possible matings: 1) Both parents could be homozygous (BB); 2) One could be homozygous (BB) and the other heterozygous (Bb); or 3) Both could be heterozygous (Bb). Let's look at these one at a time:

1) Both parents are homozygous. We can represent the mating symbolically as:

BB x BB (parents) ➔ BB (all children)
No blue-eyed children here

2) One parent is homozygous (it does not matter which one) and the other is heterozygous. We can represent this mating symbolically as:

BB x Bb (parents) ➔ BB (1/2 of the children) + Bb (1/2 of the children)

In this mating approximately half the children will be homozygous brown-eyed (BB) and the other half will be heterozygous brown-eyed (Bb). No blue-eyed children from this mating either.

3) Both parents are heterozygous. Symbolically this mating and its probable outcome can be represented as:

Bb x Bb (parents) ➔ BB (1/4 of the children) + Bb (1/2 of the children) + bb (1/4 of the children)

Those of you who are blue-eyed (or have blue-eyed siblings), and who have two brown-eyed parents, can now breathe a sigh of relief (unless you'd rather not claim your siblings). By the principles of probability, approximately ¾ of the children from this mating (the quarter that are BB plus the half that are Bb) should be brown-eyed. However, about ¼ of the offspring should be bb (homozygous for the recessive allele) and therefore have the recessive phenotype (blue eyes). What was that? Your parents are both brown-eyed and all three of their children are blue-eyed. How is this possible? Remember our coin-flip example. While that is not the most probable outcome, it is possible, especially when dealing with small samples. The point is, two brown-eyed parents can indeed have blue-eyed children if, and only if, both parents are heterozygous, and are therefore carrying the recessive allele, which they do not express (they have brown eyes), but which they can pass to their children. Children who get the recessive allele from one parent but the dominant from the other will have the dominant phenotype, as will children who get the dominant allele from both parents. But, children who get the recessive allele from both parents will have blue eyes.

Therefore, if we examine all 6 of the above matings, we can see that blue-eyed children can only be produced if both parents have the recessive allele to give either because they are both blue-eyed themselves and are, therefore, homozygous for the recessive allele (bb x bb); or because one is a brown-eyed heterozygous carrier of the recessive allele while the other is blue-eyed (Bb x bb); or because both are brown-eyed heterozygous carriers of the recessive allele (Bb). If even one parent is homozygous for the dominant (brown-eyed) allele (BB), then that parent can never produce blue-eyed children no matter what the other parent is (BB, Bb, or bb). Two blue-eyed parents however, can never produce a brown-eyed child because only those who are homozygous (bb) are blue-eyed and by the cardinal rule of genetics you cannot give to your offspring what you do not have. Since blue-eyed people do not have the dominant (B) allele for brown-eyes (if they did they would be brown-eyed not blue-eyed) they cannot pass what they do not have to their children and all of the children from two blue-eyed parents will also be homozygous for the recessive allele and therefore blue-eyed.

But, you say, eye color is not an issue in dogs so what does all this have to do with breeding toy fox terriers? Only everything, that's all, as we will see in later articles. The principles associated with dominant/recessive relationships among alleles are the same in any species. For example, my next essay will focus on a recently identified genetic disorder in TFTs called Congenital Hypothyroidism with Goiter (CHG). This is a serious, but fortunately uncommon, disorder that is specific to TFTs and possibly a few other breeds. It is caused by an autosomal recessive mutation in a single gene. So its inheritance pattern is analogous to the pattern associated with blue eyes in the example we just looked at. There has been much discussion in the last few years about this disorder, primarily centering around the development, by Dr. John C. Fyfe of Michigan State University, of a simple DNA test that can distinguish between homozygous normal individuals and those that are clinically normal heterozygous carriers (no disorder themselves but can pass the allele for it to their offspring). The questions that have been raised in these discussions are:

1) How accurate is the test?
2) Should you test all your TFTs (at $40 per dog)?
3) Should you test any?
4) If you test all or some of your dogs and they test positive as heterozygous carriers, what should you do about it?

For what it is worth, I will give you my opinion in the next installment in this series. Subsequent essays in the series will discuss other genetic disorders, which can be either simple or complex, depending on the particular disorder. We will also look at structural features, which are very complex because they are influenced by multiple genes and by environmental influences as well.

At some point we will apply these principles to coat color in the TFT. Coat color seems simple but is deceptively more complex than it seems.

In conclusion, if you understand the concepts that I have presented here, plus a few others that I will introduce as we go along, then you can increase your probability of successfully breeding for desirable characteristics and breeding out undesirable ones. That is, you can tip the odds of the genetic gamble in your favor.