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BioEd℠

Complex Traits

Genetic Testing and Designer Dogs

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Baylor College of Medicine

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SOURCES

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Page 4: Wayne, R., and Ostrander, E. Lessons learned from the dog genome. *TRENDS in Genetics*. 23 (2007): 557-567. Licensed for use March 2, 2016: Elsevier and Copyright Clearance Center: License Number 3820930088090. http://www.sciencedirect.com/science/article/pii/S0168952507003058#

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Page 33: Clark, L., Wahl, J., Rees, C., and Murphy, K. Retrotransposon insertion in SILV is responsible for merle patterning of the domestic dog. *Proceedings of the National Academy of Sciences*. 1376–1381, doi: 10.1073/pnas.0506940103. Open access. Used with permission. Fig. 1. http://www.pnas.org/content/103/5/1376.full

OVERVIEW

Students learn about three examples where genetic mutations are related both to desirable characteristics and to harmful effects in certain dog breeds. Students place themselves in the roles of different individuals involved with dog breeding, health and care, and report on the relevance of canine genetic testing for each of the roles.

Genetic Testing and Designer Dogs

More than 1,000 tests have been developed to look for desirable or harmful gene alleles in dogs. Once a researcher has found a particular gene mutation or biochemical marker for a mutation, university-based or commercial laboratories develop tests for different versions of the gene. In the case of coat color, breeders use genetic testing to produce offspring with certain coat colors or patterns of markings. Many canine genetic tests screen for alleles that cause diseases, either immediately or as a dog becomes older. In some cases, genetic tests identify alleles that convey increased risk of developing a disease—depending on diet and other environmental factors. Of course, these technologies and approaches are based on the growing range of genetic tests available for humans.

WHIPPET

In this activity, students learn about three mutations that can be harmful in dogs. The first mutation is found in whippets and other breeds of dogs. The mutation affects a muscle protein (myostatin), such that dogs with one copy of the mutated allele are able to run faster (genotype Bb). Dogs with two copies of the mutation (BB), however, have an unusual body shape, bulky muscles, an overbite, shorter legs and thicker tails. This is another example of a single gene influencing many physical traits—because of its roles in different body systems. Bully whippets are not valuable as racing or as show dogs. Thus, one copy of the mutated allele produces dogs with an advantage in racing. However, dogs with two copies are undesirable as racing or show dogs.

SHETLAND SHEEPDOG

The second example focuses on the dappled or mottled coat pattern called merle, which is present in many dog breeds, including Shetland Sheepdogs. The allele that produces the desirable merle color markings is a version of a gene important for development of several systems during growth of the embryo. One copy of the merle allele leads to the observable color pattern, but few negative effects. Two copies, however, cause a variety of health problems, including vision and hearing problems, because these sensory systems do not develop properly. This situation creates a dilemma for breeders. If two merle dogs (genotype Mm) are bred, approximately 25% of the offspring will have two versions of the merle allele (MM) and will have hearing or eye defects. For this reason, many breeders insist on breeding a dog with a Merle coat (Mm) only to dogs with solid coats (mm). In this case, only half of the offspring will have the desirable merle markings—but all of the puppies will be healthy.

DALMATION

The third example involves the popular Dalmatian. Because of inbreeding over

many generations to develop a uniform set of physical characteristics—a disease trait also was incorporated into 100% of the bloodlines. All Dalmatians are homozygous for a disease mutation that predisposes dogs to develop painful stones in their bladders or kidneys (similar to human diseases). The disease, which is related to uric acid metabolism, can be managed through diet or medications, but sometimes surgery is necessary to remove the stones. In other words, all Dalmatians have two copies of the kidney stone (hyperuricemia) allele, which is recessive and involves a single nucleotide substitution. A breeding program was created to introduce the normal allele back into the breed. However, this action has generated considerable controversy among breeders, owners and Kennel Clubs, which register purebred dogs, and many organizations do not recognize the disease-free line of dogs as "pure" Dalmatians.

There are many perspectives on how genetic information should be used to manage disease risk, breed "better" dogs for competition or as companions, or even to generate a profit. This activity enables students to explore these questions as they place themselves in different roles related to dog health, breeding and care.

MATERIALS

- Complex Traits slide set (slides 42–45), available at http://www.bioedonline.org/slides/classroom-slides1/genetics-and-inheritance/complex-traits/
- Computer and projector, or interactive whiteboard
- Set of "Job or Hobby Role Cards" copied onto cardstock (see p. 34; one card per student group)
- Copies of the student sheets (one set per student)
- Access to the Internet

PROCEDURE

1. Present Slide 42 and begin a class discussion about healthy and unhealthy mutations that can occur naturally in dogs, but some of which are caused by breeding practices.

2. Display Slide 43, which shows a purebred whippet dog, a genetically modified whippet, and a "bully" whippet. Explain to students that bully whippets have a mutation in the gene for a muscle protein (myostatin). Dogs with one copy of the mutation run faster. Dogs with two copies of the mutation have an unusual body shape, bulky muscles, an overbite, shorter legs and thicker tails. These dogs are not valuable as racing or as show dogs. Thus, one copy of the mutated allele produces dogs with an advantage in racing. However, dogs with two copies are undesirable as racing or show dogs.

3. Follow with Slide 44, which illustrates the merle pattern of color distribution that is typical of Shetland sheepdogs and several other dog breeds. Explain that the allele that produces desirable merle color markings is a version of a gene important for development of several systems during growth of the embryo. One copy of the merle allele leads to the observable color pattern, but few negative effects. Two copies, however, cause a variety of health problems, including vision and hearing problems.

4. Display Slide 45, which describes a disease mutation in Dalmatians and other breeds, such as Bulldogs. The mutation predisposes dogs to developing painful stones in their bladders or kidneys, and is related to similar human diseases. The disease can be managed through diet or medications, but sometimes surgery is necessary to remove the stones. Because of selective breeding for desirable characteristics, the disease trait also was incorporated into 100% of Dalmatians. In other words, all Dalmatians have two copies (homozygous) of the kidney stone (hyperurcosuria) allele, which is recessive. A breeding program was created to introduce the normal allele back into the breed. However, this action has generated considerable controversy among breeders, owners and kennel clubs, which register purebred dogs, and many organizations do not recognize the dogs without

the disease allele as "pure" Dalmatians.

5. Students may have many questions about the implications of the genetic conditions shown in the slides. Tell students, *Gene mutations are common in all living organisms. Most of these mutations do not affect the health or appearance of the individual. In some cases, however, mutations confer a benefit—in other cases, they cause a deformity or increase the likelihood that the individual will develop an illness.*

6. Next, explain to students that they are going to learn more about how genome science is advancing the understanding of diseases, but also is creating new kinds of questions. More than 1,000 genetic tests are available for use with dogs—these tests identify gene alleles related to color, size, and disease traits, among many others, including the traits we have just seen. The availability of genetic testing provides opportunities to improve health, but also raises many ethical questions. We will examine these questions from different points of view.

7. Project Slide 46. Students will work in teams to investigate and play the roles of different people involved with dog care, health and breeding. These different kinds of roles are described on the Role cards. Each group of students should receive one card, which will refer to a specific role (see student sheet).

8. Each group will consider two questions related to the assigned role.

    a) What does a person with this kind of job or hobby do?
    b) What would be my viewpoint about possible uses of canine genetic testing information? OR, How would I use genetic testing information?

    Students should consider different aspects of each person's role. For example, does he or she need to earn money from the dog activities? Does profit overrule the importance of producing healthy dogs? Is it important to keep breeds genetically "pure?"

9. Have students conduct their own research to answer the questions. Be sure to have Internet-safe browsing software available for students if they will be working in class. Some places to begin include the following Web sites.

    American Kennel Club Breeder
    http://www.akc.org/enewsletter/akc_breeder/2011/summer/genetics.cfm

    American Canine Association
    http://acacanines.com/

    University of California Davis Veterinary Genetics Laboratory
    http://www.vgl.ucdavis.edu/index.php

    American Kennel Club Canine Health Foundation. Gene for Merle Color Pattern Discovered
    http://www.akcchf.org/research/success-stories/gene-for-merle-color-pattern.html

    As Breeders Test DNA, Dogs Become Guinea Pigs
    http://www.nytimes.com/2007/06/12/science/12dog.html?pagewanted=all&_r=0

10. Have each group present its findings as a poster, oral presentation or slide show. After each group has made its presentation, allow the rest the class to ask questions. Students will discover that access to genetic information raises new ethical and moral questions, which do not have simple answers. Encourage students to discuss different viewpoints.

Designer Dogs: Bully Whippets









PUREBRED WHIPPET (bb) | **MIXED ALLELES (Bb)** | **BULLY WHIPPET (BB)**

"Bully" whippets have two copies of a gene mutation (BB) that causes bulky muscles and other changes in appearance. The mutation affects a muscle protein (myostatin), such that dogs with only one copy of the mutation (Bb) have greater muscle mass are able to run faster than other whippets. Thus, one copy of the mutated allele produces dogs with an advantage in dog racing.

However, dogs with two copies of the mutation (BB), have significantly more muscle mass and are stronger than normal, with an unusual body shape, an overbite, shorter legs and thicker tails. Bully whippets are undesirable as racing or show dogs, and can have severe health problems.

Mosher, D., Quignon, P, Bustamante, C., Sutter, N., Mellersh, C., Parker, H., et al. (2007) A Mutation in the Myostatin Gene Increases Muscle Mass and Enhances Racing Performance in Heterozygote Dogs. *PLoS Genet* 3(5): e79. doi:10.1371/journal.pgen.0030079 Public domain. http://journals.plos.org/plosgenetics/article?id=info:doi/10.1371/journal.pgen.0030079

Designer Dogs: A Merle Coat

PUREBRED SHETLAND SHEEPDOG (mm)

MIXED ALLELES RESULT IN MERLE PATTERN (Mm)

TWO MUTATIONS WITH MAJOR HEALTH ISSUES (MM)

A dappled or merle coat is considered desirable in many dog breeds. Merle coat pattern is controlled by an allele that also is important for normal eye and ear development.

The Shetland sheepdog shown at the top left is purebred, with no mutations (mm). The dog shown above has mixed alleles (Mm) which results in a desired merle pattern, with few negative health effects.

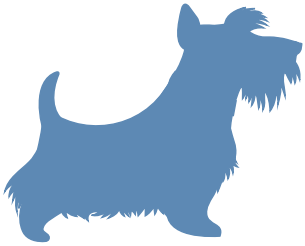
However, the sheepdog shown at the bottom left has two mutations of the merle allele (MM). Dogs with this mutation may be blind, deaf, or both, or have other health issues.

Clark, L., Wahl, J., Rees, C., and Murphy, K. Retrotransposon insertion in SILV is responsible for merle patterning of the domestic dog. *Proceedings of the National Academy of Sciences*. 1376–1381. doi: 10.1073/pnas.0506940103. Fig. 1. http://www.pnas.org/content/103/5/1376.full. Open access. Used with permission.

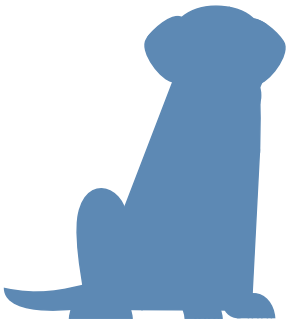
Job or Hobby Role Cards

Breeder of Racing Dogs

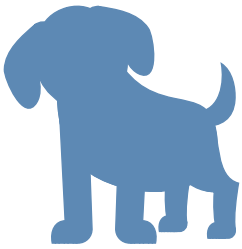
Breeder of Show Dogs



Canine Genetics Testing Lab Owner



Kennel Club Representative



Pet Owner

Researcher of Canine Genetics

Veterinarian