Rover Redefined — Pet Genetics

Secrets of the Sequence Video Series on the Life Sciences • Grades 9 — 12
Teaching materials developed by VCU Life Sciences

V i r g i n i a   C o m m o n w e a l t h   U n i v e r s i t y

Classroom Tested Lesson

Video Description

"Secrets of the Sequence," Show 127, Episode 3
"Rover Redefined: Pet Genetics" – approximately 11 minutes viewing time

Mapping the genome has been much in the news. Researchers have charted the complete human genome, the cow genome, even the genome of the bubonic plague microbe. The latest animal to have its microscopic genetic code revealed is man's best friend – the dog. The resulting map will be of great value to dog's best friend – us. Because the canine genome is very similar to ours, it provides an unusually powerful research tool. Scientifically, dogs are useful because they have many litters of dozens and dozens of offspring and because dogs have been carefully bred for centuries by kennel owners who have kept accurate records.

Ward Television
Producer: Kelly Phipps
Featuring: Elain Ostrander: Clinical and Human Biology – Fred Hutchinson Cancer Research
     Center and Professor of Zoology and Genome Sciences – University of Washington, Kelly
     Frazer: Director of Genomics-Perlegen Science, Inc. Mali Eimen, Center for Narcolepsy
     Research, Narcoleptic Patient, Dr. Emmanuel Mignot: Psychiatry and Behavior Sciences –
     Stanford University
Lesson Authors; Reviewers: Liz Shabouk; Catherine Dahl and Dick Rezba
Trial Testing Teachers: Brooke Williams

National and State Science Standards of Learning

National Science Education Standards Connection
Content Standard A: Science as Inquiry
As a result of activities in grades 9-12, all students should develop:
- Abilities necessary to do scientific inquiry
- Understandings about scientific inquiry

Content Standard C: Life Science
As a result of their activities in grades 9-12, all students should develop understanding of:
- Molecular basis of heredity
- Biological evolution
- Interdependence of organisms

Content Standard E: Science and Technology
As a result of their activities in grades 9-12, all students should develop:
- Understanding about science and technology

Content Standard F: Science in Personal and Social Perspectives.
As a result of their activities in grades 9-12, all students should develop understanding of:

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- Personal and community health
- Science and technology in local, national, and global challenges

Content Standard G: History and the Nature of Science.

As a result of their activities in grades 9-12, all students should develop understanding of:

- Science as a human endeavor
- Nature of scientific knowledge

Selected State Science Standards Connections

Use http://www.eduhound.com (click on "Standards by State") or a search engine to access additional state science standards.

Delaware
Grades 9-12

By the end of the twelfth grade students should know that:

Science, Technology, and Society

1. The practice of science and technology is not a linear process. In many cases, the desire of scientists to find what is real in nature creates opportunities for technology development. At the same time, technology provides scientists with tools and techniques that allow expansion of their capabilities and effectiveness.

History and Context of Science

1. Science is an international activity in which significant inventions and innovations have come from around the world. Even though scientists live and work in different cultures and come from different backgrounds, many of their activities are part of international collaborative efforts, and the knowledge created is shared in order to maximize the benefits to society.

Heredity

1. Hereditary/genetic information in chromosomes is contained in molecules of DNA that consist of various combinations of four different subunits (nucleotides) that encode this information. Genes are sections of DNA that direct syntheses of specific proteins associated with traits in organisms.

Diversity

2. Similarities in DNA and protein structure are used to classify and determine degrees of kinship among organisms.

New Jersey
Grades 9-12
5.1 Scientific Process

A. Habits of Mind – Students will:
  3. Engage in collaboration, peer review, and accurate reporting of findings.
  4. Explore cases that demonstrate the interdisciplinary nature of the scientific enterprise.

B. Inquiry and Problem Solving – Students will:
  2. Show that experimental results can lead to new questions and further investigations.

5.2 Science and Society

A. Cultural Contributions – Students will:
  1. Recognize the role of the scientific community in responding to changing social and political conditions and how science and technological achievement affect historical events.

5.4 Nature and Process of Technology

A. Science and Technology – Students will:

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1. Know that scientific inquiry is driven by the desire to understand the natural world and seeks to answer questions that may or may not directly influence humans, while technology is driven by the need to meet human needs and solve human problems.
   B. Nature of Technology – Students will:
   1. Assess the impacts of introducing new technology in terms of alternative solutions, costs, tradeoffs, risk, benefits, and environmental impact.

5.5 Life Science
   C. Reproduction and Heredity – Students will:
   1. Describe how information is encoded and transmitted in genetic material.
   3. Assess the impact of current and emerging technologies on our understanding of inherited human characteristics.

Overview

Although other videos in this *Secrets of the Sequence* series present information obtained from the mapping of the human genome, this video explains what "mapping the genome" means. It answers the question, "Why do we map a species and what information do we get from this map?" The map tells us which genes are on which chromosome and precisely where they lie on the chromosome. The video also answers the question, "Why is a dog's genome useful for studying the human genome?" A dog's genome makes it much easier to locate markers that can be used to map the human genome for multiple reasons. The primary reasons for using the dog's genome are that it has fewer variables and that dogs have similar diseases to humans.

Finding the exact area in the human genome to link to a specific disease has been difficult. Researchers have found it much easier to isolate gene sequences in the maps of simpler organisms, like dogs, and then use these "signs" to guide them through the human map.

Testing: A sample related multiple choice item from State Standardized Exams

The Human Genome Project was begun in 1988 by scientists from 13 nations as a worldwide effort to understand the sequencing of all of the DNA in the human body. "What is one potential benefit of this research?

A. It will help to explain human cultural differences.
B. It will create communication between research centers.
C. It will help find the genes responsible for many diseases. *
D. It helps to classify man most accurately in the animal kingdom.

Source: Virginia Standards of Learning Assessment, Spring 2003 Released Test

Video Preparation

Preview the video and make note of the locations at which you will need later to pause the video for discussion.

Before Viewing

1. Ask: "What do you think it means to map a genome?"
   To know which genes sit on which chromosome and where the genes lie on that chromosome.

2. Have students view the Human Gene Map at http://www.ncbi.nlm.nih.gov/SCIENCE96/
    Allow them to browse by chromosome to see actual maps, as well as observe specific
    genetic disease locations on those chromosomes.

3. Ask: What does the word homogeneity mean?
    Similar in nature – having characteristics in common within species and between species.
    Comes from the Greek words, homos meaning same and genesis meaning origin.

4. While watching the video, direct the students to:
    a) listen carefully to determine what homogeneity there is between species.
    b) list the reasons why researchers study the dog's genome to learn more about the
        human genome.

During Viewing

1. **START** the video.

2. **PAUSE** the video (8.58 minutes into the video) after the Dr. Mignot says "…finding the
    dog gene solved the human problem."

    Ask: "Why did the researcher have to "guess" where to look in the genome?"
    Because the genome had not yet been mapped

    Ask: "Why would the researcher look for the gene for narcolepsy in the dog and not
    directly in the human?"
    It took 10 years of guessing and a lot of persistence to find the gene for narcolepsy in the
    dog. If the researcher had been looking in the human genome - where there are so many
    more genes - it would have taken even longer. Because this disease affects one in every
    2000 people, it was an important research effort.

3. **RESUME** the video and play to the end.

After Viewing

1. The word "conserve" is used in this video. Explain to the students that this means the
    genetic sequence has remained the same over time. Discuss which sequences are more
    likely to be conserved.
    Sequences that are conserved over time are ones that have a specific function.

2. Discuss whether there is more homogeneity in dogs or in humans.

    Ask the following questions:

    a) ""Which do you think are more homogeneous - dogs or people?
        Dogs - Explain that the more homogeneous the species, the fewer variables there are
        in the species' genome.

    b)   "In which genome will it be easier to isolate a gene specific to a disease?
        The dog's genome

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c) "Can an aardvark be homogenous with a human?"
Yes

d) "Why is it important to compare the genomes from different species to look for homogeneity?"
The areas in which different species are homogenous are likely to be those that hint at where vital functions are coded.
Have students list some of these vital functions.

3. Have the students list their responses to question 4b) in "Before Viewing" where they were asked to list the reasons why researchers study the dog's genome to learn more about the human genome.

   - *Less variation in the dog genome than in the human genome due to controlled breeding of dogs over time*
   - *Multiple generations of a dog can be studied at the same time due to shorter life cycles of dogs. This leads to improved DNA statistical analysis over what is available for humans.*
   - *Dogs have large number of offspring in most litters and multiple litters for each breeding pair that also improves DNA statistical analysis over what is available for humans.*
   - *Dogs have similar diseases to humans.*

4. Conduct the student activities on pedigrees.

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Teacher Notes for the Student Activities:
Activity 1: Understanding Pedigrees
Activity 2: Human vs. Pooch Pedigrees

Materials
- 1 Copy for each student : Student Handout 1 – Understanding Pedigrees
- 1 Copy for each student: Student Handout 2 – Human vs. Pooch Pedigrees:
- Answer keys – See Appendix A: Case Studies
              See Appendix B:

Procedure

Activity I:
1. Distribute copies of the Student Handout 1: – Understanding Pedigrees.

2. Have students read all the information and study the pedigree on the first page. Review the terms and ensure that students recall related concepts including dominant, recessive, heterozygous, and others.

3. Have students read the example under "Analyzing Case Studies" and discuss how the pedigree was constructed from the description.

4. There are three case studies for students to analyze. Assign one or more for students to complete as individuals or groups. One case study could be assigned for homework if desired.

5. Review students' answers to the case studies. Make a transparency of the answer key or provide students with copies.
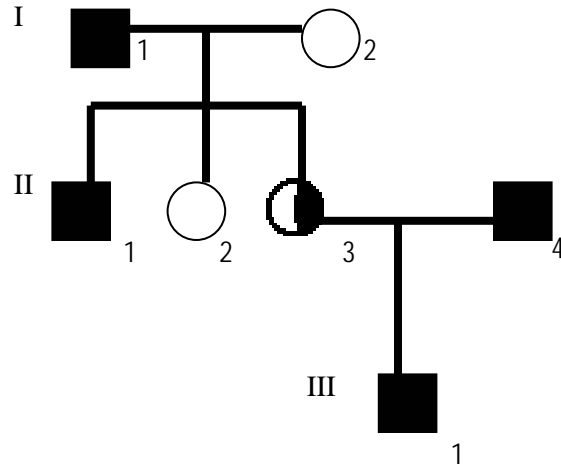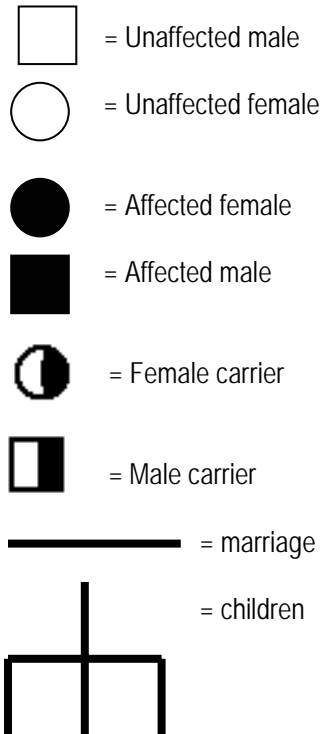
Activity 2:

6. Divide students into groups of 3-4 to work on Activity 2 – Human vs. Pooch Pedigrees. Distribute copies of the Student Handout 2.

7. Discuss the procedures for the activity found on the Student Handout.

8. After students have completed both pedigrees, provide them with the pedigree answer key and discuss their answers to the questions:
   - What is the type of genetic disease for canine cone degeneration and for achromatopsia?
       Autosomal recessive

   - About how many years would it take to produce 5 generations of dogs? Five generations of humans?
       Dogs: as little as 5 years; usually somewhat more.
       Humans: Approximately 20 years per generation, or 100 years for 5 generations.

   - What are some of the reasons scientists study the dog's genome to better understand the human genome?
       See Question 3 in the 'After Viewing' section

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Student Handout: Activity 1 – Understanding Pedigrees

In this activity you will learn to read, interpret, and create a genetic map called a pedigree by analyzing case studies of genetic diseases. A pedigree is a diagram of a family's genealogy that shows the family members' relationships to each other and how a particular trait or disease has been inherited.

Procedure

Study the diagram and the meaning of the symbols, connecting lines, and words below.

☐ = Unaffected male

○ = Unaffected female

● = Affected female

■ = Affected male

◖ = Female carrier

◧ = Male carrier

—— = marriage

⊥ = children

Roman Numerals denote generations
Arabic Numerals denote individuals in each generation
Example: **II-3** is a carrier for the trait

Analysis Models of a disease or trait
A = dominant allele
a = recessive allele

Autosomal recessive: is not a sex-linked disease (trait) and it will only show up in a person who has both recessive alleles (aa); a person who has a heterozygous genotype (Aa) is a carrier for the disease (trait).

Autosomal dominant: is not a sex-linked disease (trait) and will show up in a person who is either homozygous (AA) or heterozygous (Aa) for that gene. Many times this type of model is caused by a direct mutation to the DNA, rather than an inherited mutation, and a disorder will show up in families with no prior history.

X-linked recessive: the disease (trait) will show up in a male who has the gene on the X chromosome (X^aY) or a female who has the recessive allele on both X chromosomes (X^aX^a); a female with the gene on one X chromosome (X^AX^a) is a carrier for the disease (trait).

X-linked dominant: the disease (trait) will show up in males who have the gene on the X-chromosome (X^AY) and a female who has the allele on one (X^AX^a) or both X chromosomes (X^AX^A).

Y-linked: the disease (trait) will only be found in males; no females will have the disease (trait) or carry the allele because they do not have a Y chromosome.

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Analyzing Case Studies

Procedure

1. Read the following case studies as assigned by your teacher.
2. For each assigned case study, draw a pedigree for that family.
3. Label the genotype for each individual.
4. Identify the type of genetic disease (e.g., Autosomal dominant)

Example
Disease

Cystic Fibrosis is caused by an error in the CFTR (Cystic Fibrosis Transmembrane Conductance Regulatory) gene, which is found on chromosome #7. This error creates a condition where glands that produce mucus, sweat, and intestinal secretions do not function properly. The disorder shortens the life span of an individual because many die from lung, heart, or liver complication, usually before the age of 30.

Family History

Ellen is a four year old girl who has been diagnosed with cystic fibrosis. She has an older brother and sister, who are unaffected by the disease. Neither one of her parents have been affected by the disease. How is it possible for Ellen to have cystic fibrosis?

Pedigree and Analysis

1

1Aa   2Aa

I

II

Ellen aa
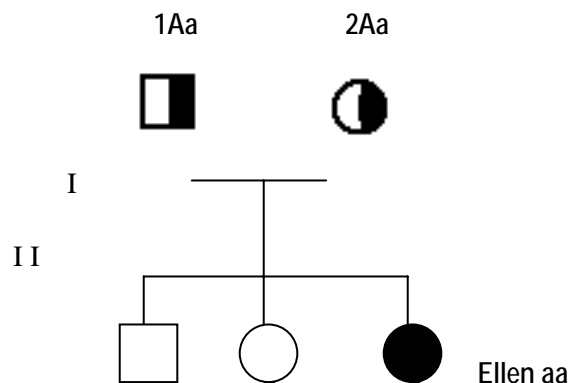
Autosomal recessive: Cystic Fibrosis is an autosomal disease because it is found on an autosomal chromosome (#7) and not on a sex chromosome (#23). It is also recessive because neither parent shows signs of the disease but their daughter Ellen does. This means that both parents must be carriers in order for Ellen to have the recessive genotype. It is not possible to tell if Ellen's siblings are homozygous (AA) or heterozygous (Aa) without a PCR DNA test.

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Case Study #1
Disease
Hemophilia is a bleeding disorder that slows down the clotting process. People with this condition often experience prolonged bleeding following injury or surgery, and in severe cases, spontaneous bleeding into joints and muscles. Though rare, this disorder can be fatal if not treated properly.

Family History
Every male on the maternal side of Sue Ann's family, except her younger brother Bill, has this genetic condition; Grandpa Joe and sons Steve (married to Joan who has it, but they have no children) and Brian (wife deceased but did not have it). Brian's three boys called Mo, Larry, and Curly all have the condition. Sue Ann's mom and grandmother do not have the condition, but Sue Ann's older brother Mike does. Sue Ann's father does not have the condition, and there is no record in his family history of anybody having this condition. Sue Ann has done some research on hemophilia, and has discovered it is in the group of genetic diseases that are sex-linked.

Pedigree and Analysis

Case Study #2
Disease
Hutchinson-Gilford progeria syndrome is a genetic condition characterized by the dramatic, rapid appearance of aging beginning in childhood. Affected children typically look normal at birth and in early infancy, but then grow more slowly than other children and develop a characteristic facial appearance, hair loss, aged-looking skin, and severe hardening of the arteries. Individuals diagnosed with this disorder do not live past the age of 13.

Family History
Mary has three living children, Beth, John, and Philip. Her oldest child, also Mary, (recently deceased) was diagnosed with Hutchinson-Gilford progeria syndrome. No one in either her or her husband's families has ever been diagnosed with this disease.

Pedigree and Analysis

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Case Study #3
Disease
Phenylketonuria (commonly known as PKU) is an inherited disorder that increases the amount of the amino acid phenylalanine to harmful levels in the blood. If PKU is not treated, excess phenylalanine can cause mental retardation and other serious health problems.

Family History
Peter and Yvonne's only child, Derek, has been diagnosed with a mild case of PKU. Because Yvonne was aware of the medical history in her family, her doctor was able to detect early on that Derek had the disorder. Yvonne's mother also had PKU, but neither Yvonne nor her unmarried sister Polly, have the disease. After Derek's diagnosis, Peter found out that his deceased paternal grandfather also had been diagnosed with PKU. Peter and his father are only children and are not affected by PKU.

Pedigree and Analysis

Student Handout: Activity 2- Human vs. Pooch Pedigrees

Purpose
In this activity you will construct and compare two pedigrees to understand why scientists are using a dog's genome to study the human genome.

Instructions
1. Read the background information below and study the data in the tables.
2. Construct a 5 generation human family pedigree for achromatopsia.
3. Construct a 5 generation canine family pedigree for cone degeneration.
4. Answer the following questions:
   - What is the type of genetic disease for canine cone degeneration and for achromatopsia?

   - About how many years would it take to produce 5 generations of dogs? Five generations of humans?

   - What are some of the reasons scientists study the dog's genome to better understand the human genome?

Background Information
Cone degeneration is a canine disease and is phenotypically similar to human achromatopsia. Both the canine disease and the human counterpart are characterized by day-blindness and retinal cone function in adults. Humans have 23 paired chromosomes and dogs have 39 paired chromosomes. However, mapping disease genes in canine pedigrees is made easier by the ability to control mating, obtain large numbers of siblings, and use the shorter generation time as compared with human families. Therefore it is simpler and faster to identify the gene location on the canine genome, and then use that location to help determine the location on the human genome.

a) Human Family
Use the following information to construct a pedigree for this family afflicted with achromatopsia. Note: There will be 3 individuals in this family for whom you will not be able to determine a distinctive genotype.

	NAME	RELATIONSHIP	STATUS
Generation V			
	Luis	Son of Zelda and Ramon	afflicted
Generation IV			
	Ramon	Son of Ricardo and Lydia	healthy
	Zelda	Married to Ramon	healthy
	Filipe	Son of Ricardo and Lydia	healthy
	Juan	Son of Miguel and Letty	afflicted
	Cira	Daughter of Miguel and Letty	healthy
	Roberto	Son of Miguel and Letty	healthy
	Nora	Daughter of Jesus and Margarita	healthy
	Alejandro	Son of Pedro and Beatriz	afflicted
	Delia	Daughter of Dano and Andrea	afflicted

|			
	Tio	Son of Dano and Andrea	afflicted
	Maria	Daughter of David and Guadelupe	afflicted
	Nariza	Daughter of David and Guadelupe	afflicted
Generation III			
	Lydia	Daughter of Carlos and Imelda	healthy
	Ricardo	Married to Lydia	healthy
	Helga	Daughter of Carlos and Imelda	afflicted
	Letty	Daughter of Carlos and Imelda	healthy
	Miguel	Married to Letty	healthy
	Margarita	Daughter of Carlos and Imelda	afflicted
	Jesus	Married to Margarita	healthy
	Beatriz	Daughter of Carlos and Imelda	healthy
	Pedro	Married to Beatriz	healthy
	Juanita	Daughter of Javier and Bonita	afflicted
	Benito	Son of Javier and Bonita	healthy
	Dano	Son of Chito and Chelita	afflicted
	Andrea	Married to Dano	healthy
	Davod	Son of Chito and Chelita	afflicted
	Guadelupe	Married to David	healthy
	Horatio	Son of Chito and Chilita	healthy
	Lucio	Son of Chito and Chelita	health
Generation II			
	Imelda	Daughter of Rigo and Esmerelda	healthy
	Carlos	Married to Imelda	healthy
	Javier	Son of Rigo and Esmerelda	afflicted
	Bonita	Married to Javier	healthy
	Chito	Son of Rigo and Esmerelda	healthy
	Chelita	Married to Chito	afflicted
Generation I			
	Rigo	Married to Esmerelda	afflicted
	Esmerelda	Married to Rigo	healthy

b) Canine Family

Use the following information to map out the pedigree of this canine family afflicted with cone degeneration. Because the location of the gene for this disease has been located in the canine genome, it can be determined through DNA analysis if a dog is a carrier or not and this is indicated in the list below. Sire indicates the father and dame indicates the mother; M is male and F is female.

	NAME	SIRE	DAM	STATUS
Generation V				
	M1	Generation IV, M8	Generation III, F16	afflicted
	M2	Generation IV, M8	Generation III, F16	afflicted
	M3	Generation IV, M8	Generation III, F16	afflicted
	F4	Generation IV, M8	Generation III, F16	afflicted
	F5	Generation IV, M8	Generation III, F16	afflicted
	F6	Generation IV, M8	Generation III, F16	afflicted

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| Generation IV				
	F1	Generation III, M3	Generation III, F5	carrier
	F2	Generation III, M3	Generation III, F5	healthy
	M3	Generation III, M3	Generation III, F5	afflicted
	M4	Generation III, M3	Generation III, F5	afflicted
	M6	Generation III, M11	Generation III, F7	afflicted
	F7	Generation III, M11	Generation III, F7	afflicted
	M8	Generation III, M11	Generation III, F7	carrier
	F9	Generation III, M11	Generation III, F7	carrier
	F10	Generation III, M11	Generation III, F7	carrier
	M11	Generation III, M11	Generation III, F16	afflicted
	M12	Generation III, M11	Generation III, F16	afflicted
	M13	Generation III, M11	Generation III, F16	afflicted
	F14	Generation III, M11	Generation III, F16	afflicted
Generation III				
	M1	Generation II, M2	Generation II, F1	afflicted
	M2	Generation II, M2	Generation II, F1	carrier
	M3	Generation II, M2	Generation II, F1	carrier
	F4	Generation II, M2	Generation II, F1	afflicted
	F5	Generation II, M2	Generation II, F1	carrier
	F6	Generation II, M2	Generation II, F1	carrier
	F7	Generation II, M2	Generation II, F1	carrier
	F8	Generation II, M2	Generation II, F1	carrier
	M9	Generation II, M2	Generation II, F1	afflicted
	M10	Generation II, M2	Generation II, F1	carrier
	M11	Generation II, M2	Generation II, F1	afflicted
	M12	Generation II, M2	Generation II, F1	carrier
	F13	Generation II, M2	Generation II, F1	afflicted
	F14	Generation II, M2	Generation II, F1	carrier
	F15	Generation II, M2	Generation II, F1	carrier
	F16	Generation II, M2	Generation II, F1	afflicted
Generation II				
	F1	Generation I, M2	Generation I, F1	carrier
	M2	Generation I, M3	Generation 1I, F1	afflicted
Generation I				
	F1			healthy
	M2			afflicted
	M3			carrier

Appendix A: Answer Key for Activity A: Case Studies

Case Study # 1 – X-linked recessive model
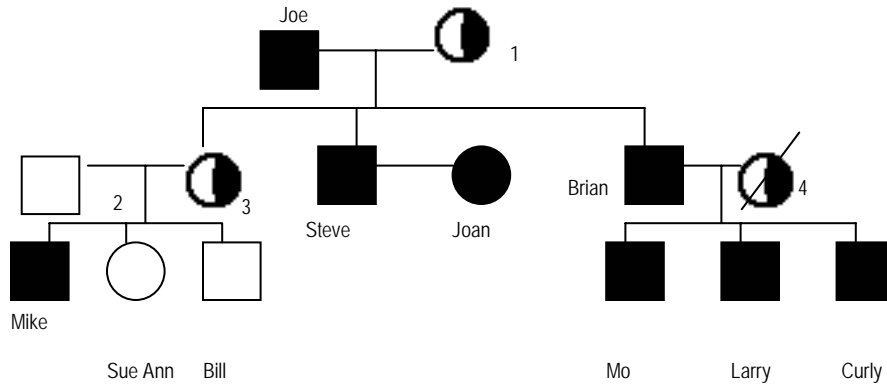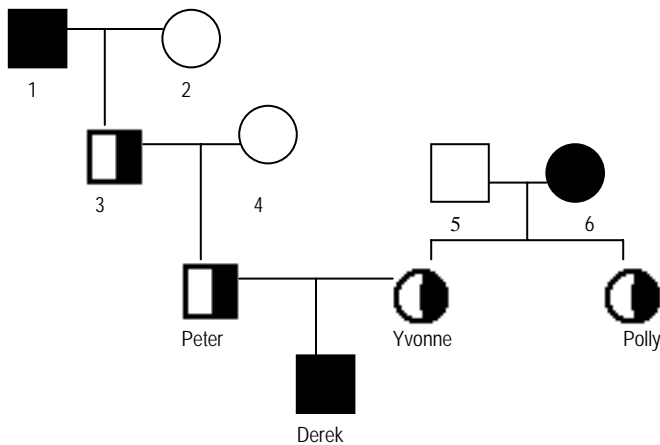

Joe – X^aY
1 – X^AX^a
Brian – X^aY
4 – X^AX^a
Mo – X^aY
Larry – X^aY
Curly – X^aY
Steve – X^aY
Joan – X^aX^a
2 – X^AY
3 – X^AX^a
Mike – X^aY
Sue – $X^AX^?$ (cannot be determined from info given)
Bill – X^AY

Case Study # 2 – Autosomal dominant due to direct mutation of DNA
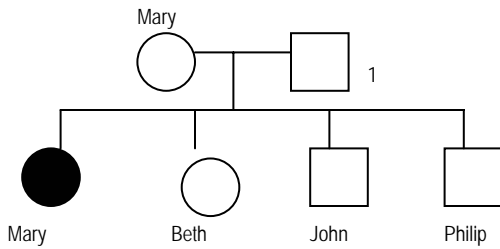
1 – aa
Mary (mother) – aa
Mary (daughter) – AA or Aa (either DNA mutation will causes the disease)
Beth – aa
John – aa
Philip - aa

Case Study # 3 – Autosomal recessive

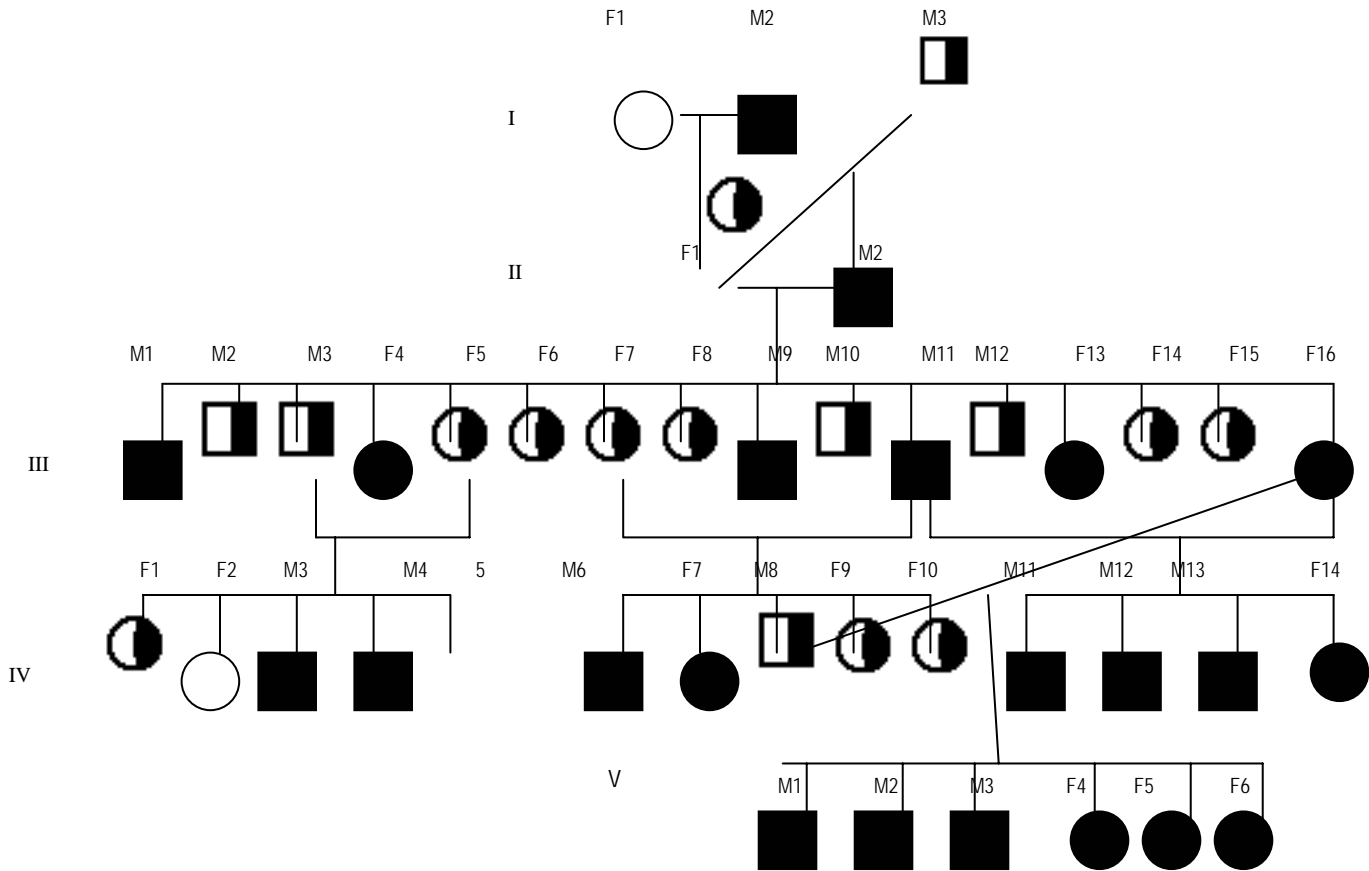1 – aa
2 – AA
3 – Aa
4 – AA
5 – AA
6 – aa
Peter – Aa
Yvonne – Aa
Polly – Aa
Derek - aa

APPENDIX B: Answer Key For Activity 2: Human vs. Pooch Pedigrees

Human family pedigree
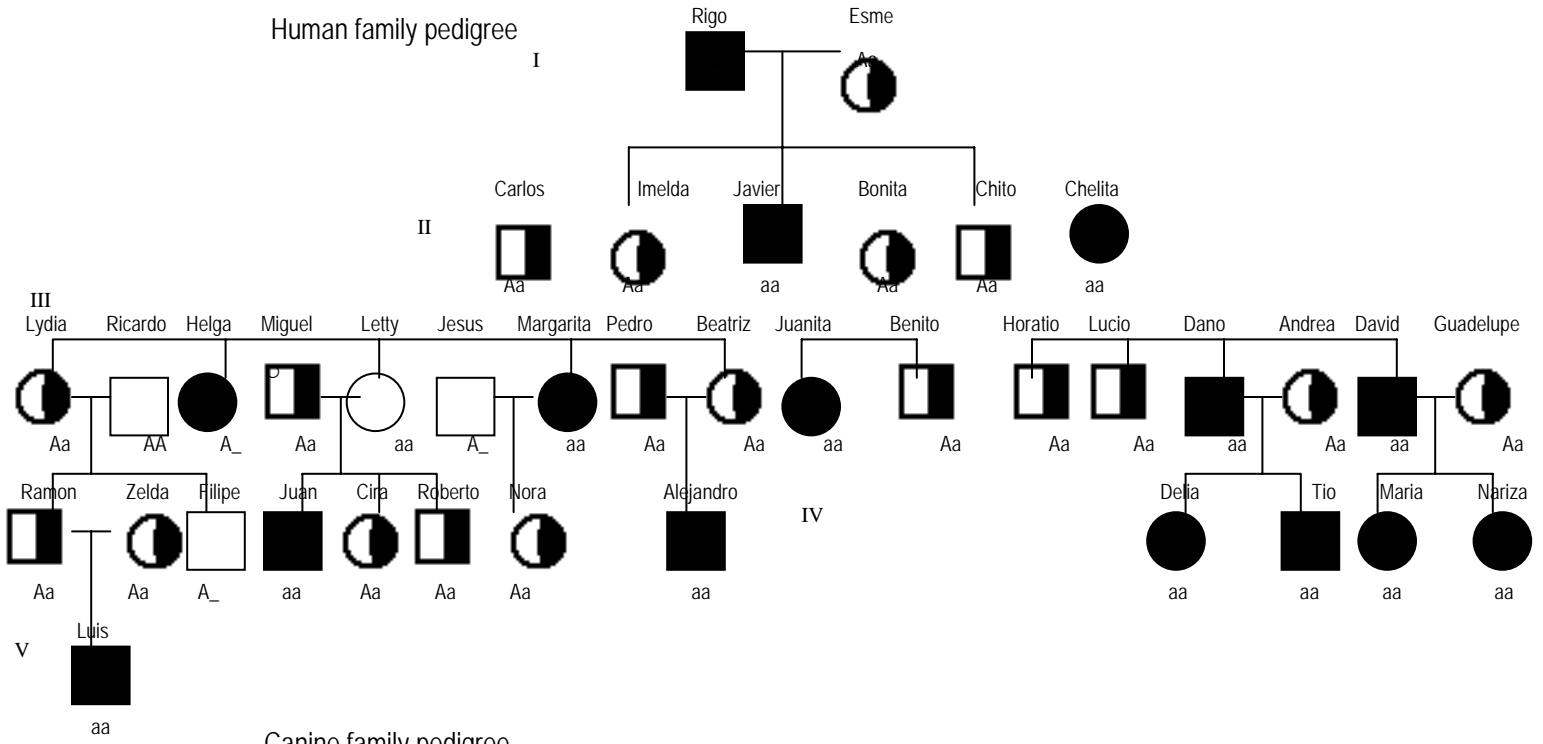
Canine family pedigree

Additional Resources

Because Web sites frequently change, some of these resources may no longer be available. Use a search engine and related key words to locate new Web sites.

Information on Dog Breeds
www.glenroseffa.org/dogbreeds.ppt
http://www.akc.org/breeds/recbreeds/breeds_a.cfm
http://www.dogbreedinfo.com

Information on Pedigrees
http://web.mit.edu/esgbio/www/mg/pedigrees.html
http://www.people.virginia.edu/~rjh9u/pedsymb.html
http://www.genesoc.com/nutrition/pedigree.htm

Information on Genetic Diseases
http://ghr.nlm.nih.gov/ghr/
http://www.ornl.gov/sci/techresources/Human_Genome/home.shtml
http://www.kumc.edu/gec/support/
http://medlineplus.gov/

Genomic Revolution
http://www.ornl.gov/sci/techresources/Human_Genome/education/education.shtmL
This Web site of the government-funded Human Genome Project has links about genomics, the history of the project, and more.

Secrets of the Sequence Videos and Lessons
This video and 49 others with their accompanying lessons are available *at no charge* from
www.vcu.edu/lifesci/sosq

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