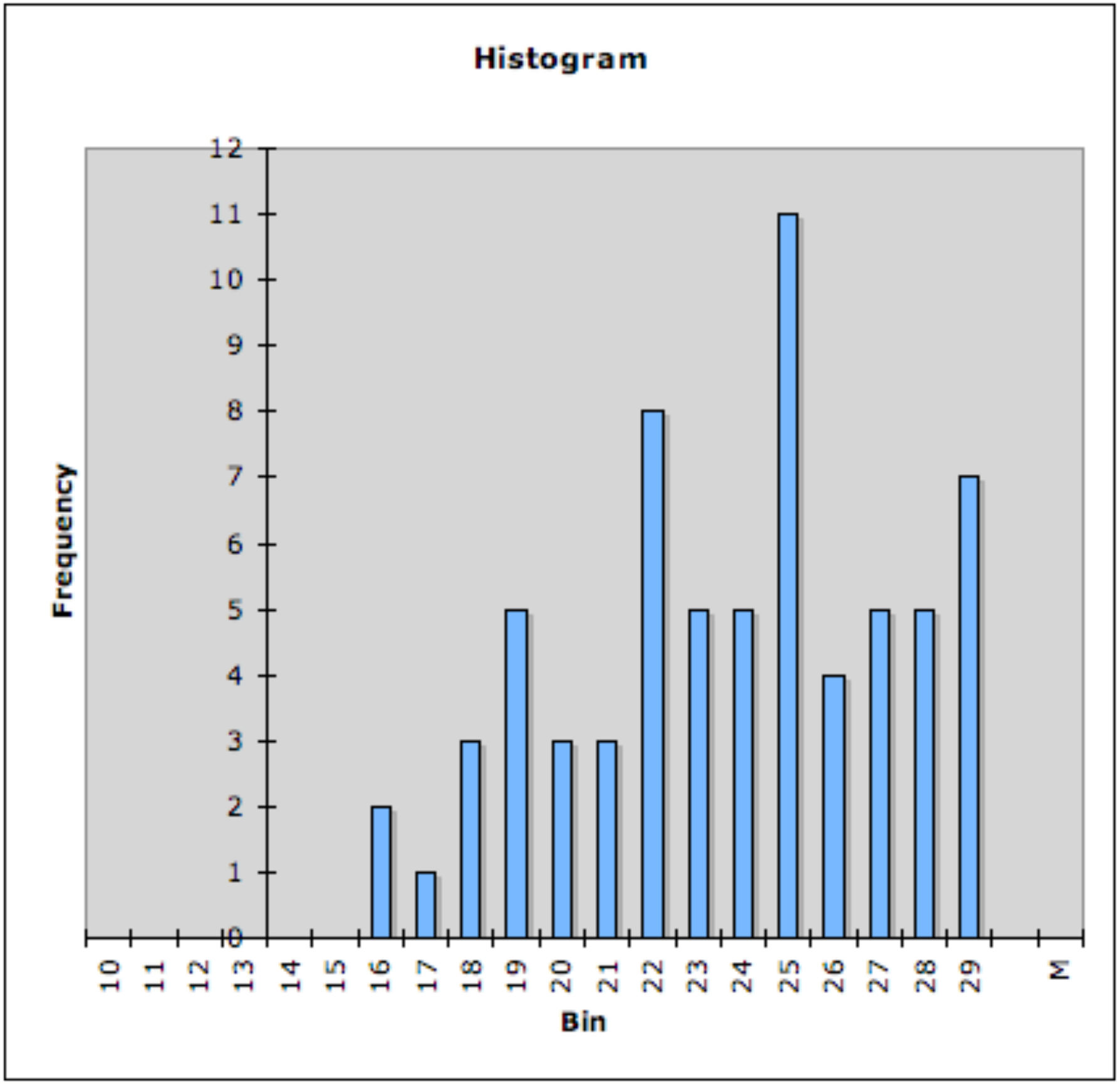
Histogram
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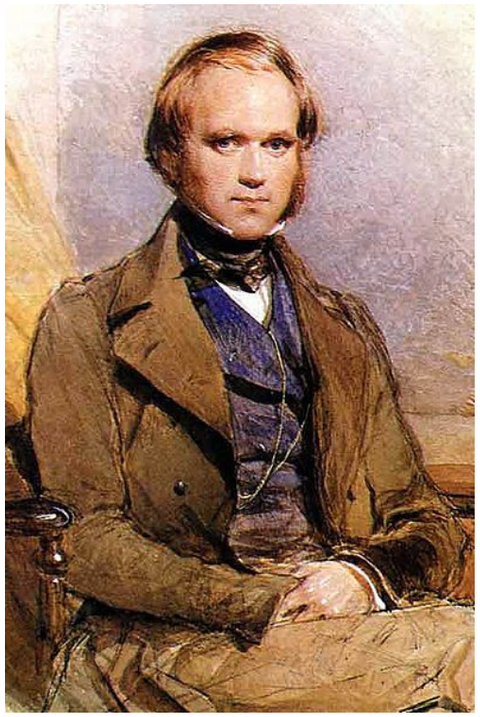
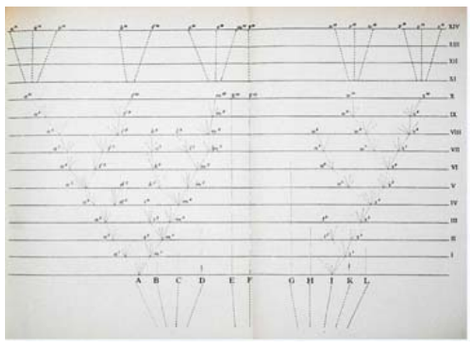
# Charles Darwin Film Series



Images from en.wikipedia.org



## *Evolution: Darwin's Dangerous Idea*

**Facilitator: Dr. Anya Plutynski**

Join the Marriott Library in celebrating Darwin's 200th birthday with the film *Evolution : Darwin's Dangerous Idea*. Evolutionary theory is featured in this film through the key moments in Darwin's life and current research utilizing dramatization and documentary sequences.

Dr. Anya Plutynski of the University of Utah's Philosophy Department will introduce the film and be available for questions and answers. Her research specialization is in the history and philosophy of science, particularly evolutionary biology in the early 20th century.

**Date: March 4, 2009**
**Time: 1:00 p.m.—3:00 p.m.**
**Place: Room 1120 Marriott Library**

Check **http://darwin2009.utah.edu** for more University of Utah and Marriott Library events.

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marie.paiva@utah.edu

J. Willard Marriott Library
THE UNIVERSITY OF UTAH

# Behavioral Genetics:

Phil/Biol 2510, Spring 2008

# Behavioral Genetics

The branch of genetics that studies the role of genetics in (complex) behavior, disentangling the relative contributions of genetics and environment in behavioral phenotypes.

Looks for genetic links for complex behaviors including personality traits, addiction, mental disease, intelligence, anti-social behavior, sexuality, and more. (Psychiatric genetics, developmental psychology, ethology, etc.

# Outline

- Nature v. Nurture (Heritability)
- Types of Studies
  - –Twin Studies
  - –Linkage Studies
  - –Association Studies
- Difficulties with Behavioral Genetics

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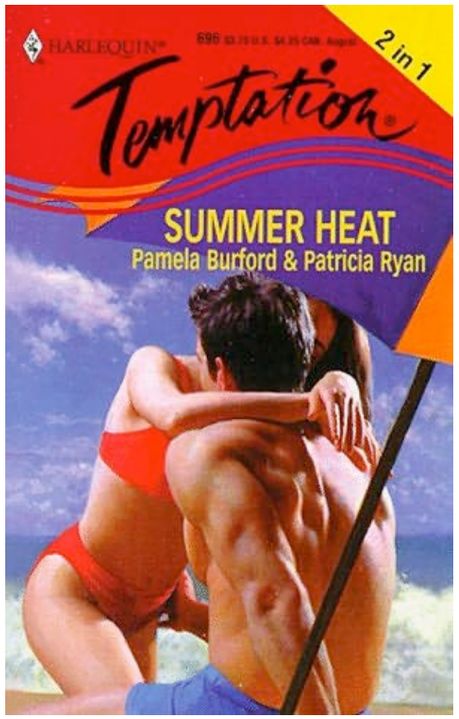
# Pamela Burford & Patricia Ryan




- Identical twins (1954):
  - from same fertilized egg that split in early development; share identical DNA.

- Similarities are striking
  - Physically similar: hair, eyes, height, looks, etc.
  - Both like to sew, art, cooking, same type of friends
  - Married two months apart, each has two children
  - Started new careers at same time: romance novelists

# What Accounts for these Similarities?

NATURE: Twins share identical DNA

or

NURTURE: Twins share similar environment, i.e., raised at same time and place by same parents

# Okay, but…

Doesn't it make sense to think that genes play a ***greater or lesser*** role in determining specific behavior?

This is what behavioral genetics is interested in…the genetic influence on complex traits, also known as **heritability**.

And, not just in individual pairings of twins, but whole **populations**…

# Heritability

- Heritability is measured by looking at variation within a group.

- Heritability is a number between 1 and 0.
  - H=1 means that all of the variation in a population is due to genetic factors
  - H=0 means that all of the variation is due to the environment

# Heritability

http://www.mvskokefood.org/cornstalk.JPG

# Heritability

Lets look at some corn plants

http://www.mvskokefood.org/cornstalk.JPG

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Lets look at some corn plants

In the field, some are tall, and some are short

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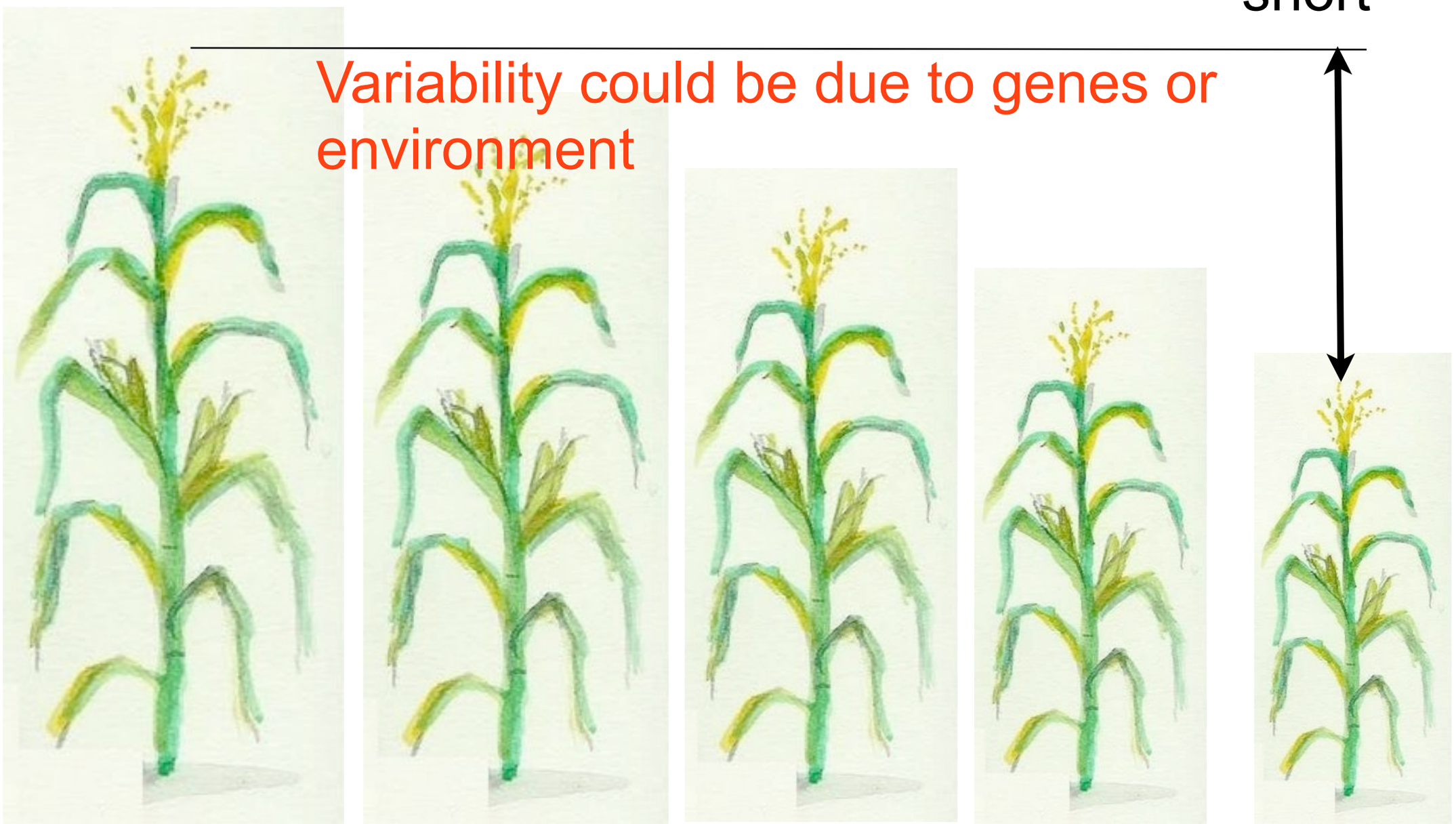
# Heritability

Lets look at some corn plants

In the field, some are tall, and some are short

Variability could be due to genes or environment



http://www.mvskokefood.org/cornstalk.JPG

# Heritability

Let’s grow a clone of one corn plant in the same field

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What will happen?

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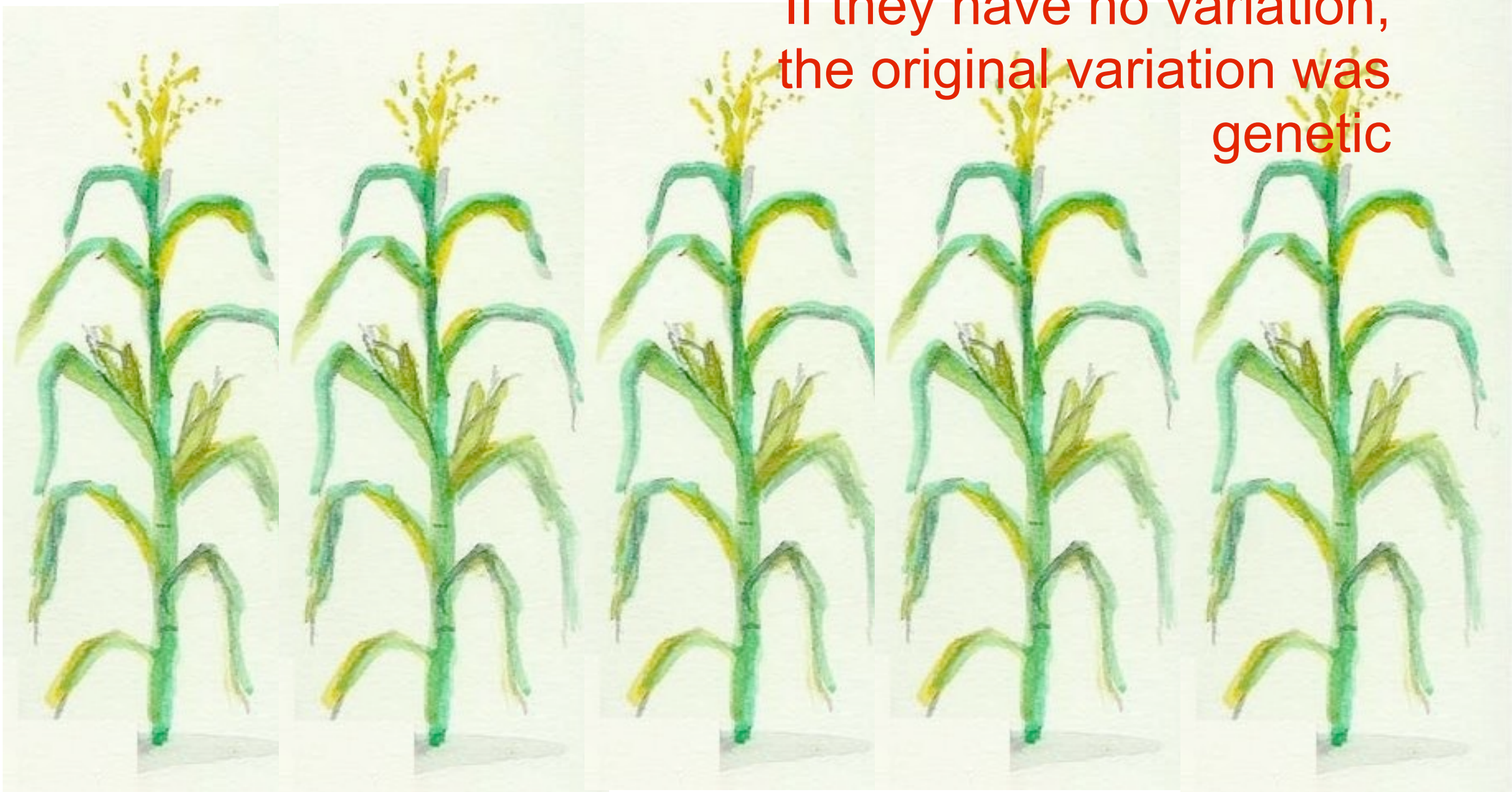
# Heritability

Let’s grow a clone of one corn plant in the same field

If they have no variation, the original variation was genetic



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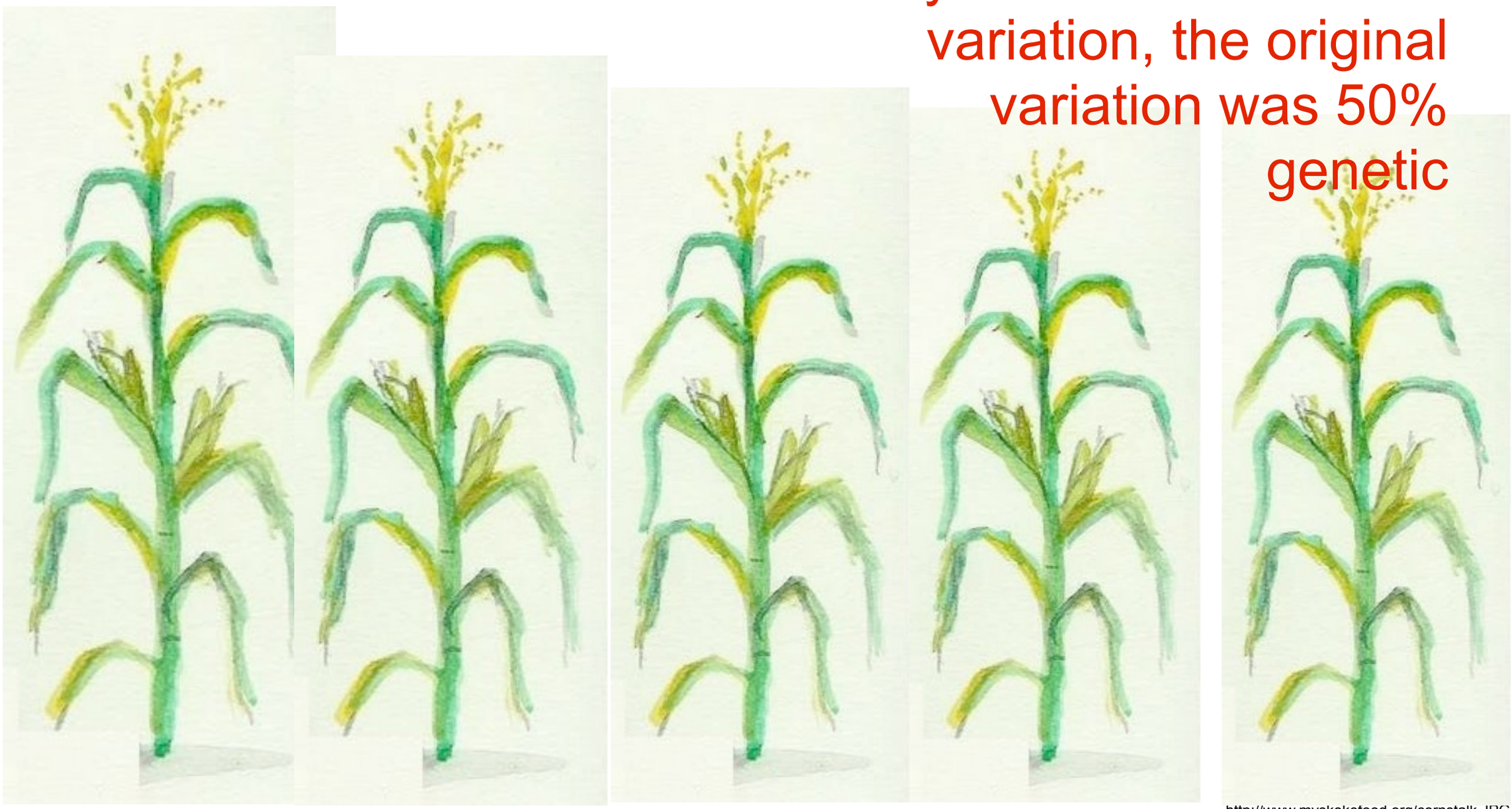
If they have 50% as much variation, the original variation was 50% genetic



http://www.mvskokefood.org/cornstalk.JPG

# Heritability

Let’s grow a batch of the original seeds in a greenhouse

http://www.mvskokefood.org/cornstalk.JPG

# Heritability

Let’s grow a batch of the original seeds in a greenhouse

What will happen?

http://www.mvskokefood.org/cornstalk.JPG

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If they have no variation, the original variation was due to environment

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# Heritability

$$H = \frac{\text{Variation due to genes}}{\text{Variation due to genes + environment}}$$

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- Heritability is a measure of variation of a phenotype in a particular population in a particular environment.
- For example: In a given population, for height, if H = 0.9, then 90% of the variation in height in that population can be explained by genetic variation.

- If the environment or genetics changes so that it contributes more or less variation, heritability will change

# Heritability

- Heritability of:
  - –economic risk attitude: 57%
  - –hedonic capacity: 46%
  - –stress perception: 44%
  - –alcohol misuse: 30-36%
  - –impaired balance in older people: 27%
  - –anorexia nervosa diagnosis: 22%

Twin Res Hum Genet. 2009 Feb;12(1):103-7.
Osteoporos Int. 2008 Sep 19.
Psychol Med. 2009 Feb;39(2):211-8. Epub 2008 May 28
Psychol Med. 2009 Mar;39(3):463-73.
Am J Drug Alcohol Abuse. 2002;28(3):557-84.

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# Strategy of Twin Studies

- Compares similarities and differences within a population; and between sub-groups within that population, e.g., MT, FT, and adopted individuals.

- Insofar as twins are more similar than the rest of the population with regard to a specified trait, then that difference between the twins and the rest of the population is explained by genetic elements.

# Two Assumptions

1. **Genetic Similarity**: Identical twins (MT) are 100% genetically identical and fraternal twins (FT) are on average only 50% genetically similar. (Caution: Not so clear that environment is similar between twins.)

2. **Similar Environment**: Environmental conditions for MTs raised in the same home are as similar as they are for FTs raised in the same home. (Caution: Even if raised apart, similar appearance results in similar treatment.)

**So**: If the environmental conditions for identical twins (MT) are as similar as they are for fraternal twins (FT), …then behavioral geneticists infer that a closer average correlation (similarity) of traits for identical twins is due to the genetic influence on those traits.

# Minnesota Twin Studies, 1988

# Minnesota Twin Studies, 1988

- Thomas Bouchard
  - Minnesota Study of Twins Reared Apart
  - **100s of twins separated at birth, raised apart**
  - Inventoried similarities & differences in batteries of tests.

- Surprising similarities discovered at reunion
  - **Oskar Stohr & Jack Yufe**
    - Stohr raised in Germany as Catholic; Yufe raised in Trinidad as Jew
    - Same type of clothes, glasses, identical mustache, both liked practical jokes in elevators
  - **Jim Lewis & Jim Springer**
    - Same height and weight, dog named ‘Toy’
    - Both married twice: 1st wife ‘Linda’, 2nd ‘Betty’
    - Named son ‘James Alan’ and ‘James Allen’
  - **Mark Newman & Gerald Levey**
    - Same type of mustache, glasses, each wore belt key on right side, and both volunteer firemen in New Jersey.

# Minnesota Twins' Personality

- Bouchard found that a host of personality traits were substantially affected by genes;

- > 50% (H = >.5) of variability observed in variety of traits (e.g., tendency to be religious) was typically explained by underlying variation in genes;

- Concluded that upbringing had surprisingly little effect upon personality traits…

Bouchard, T. (1990) Sources of human psychological differences: The Minnesota study of twins reared apart. *Science* 250; 223-28; see also Bouchard, T. (1994). Genes, environment, and personality. *Science* 264; 1700-1701.

# What DO Twin Studies Tell Us?

- That behaviors (phenotypes) are a combination of both genetic and environmental influences.
  - That some phenotypes have a **stronger** or **weaker** genetic influence (as calculated by H).

- Remember: heritability applies to a specific behavioral phenotype relative to a time, place, and environment
  - Change environment, different outcome.

# What DON’T Twin studies tell us?

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- NOT whether behavior is alterable
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- NOT which gene(s) responsible
  - That is, no gene(s) identified.

- NOT how the gene(s) affects behavior
  - That is, no causal pathway identified.

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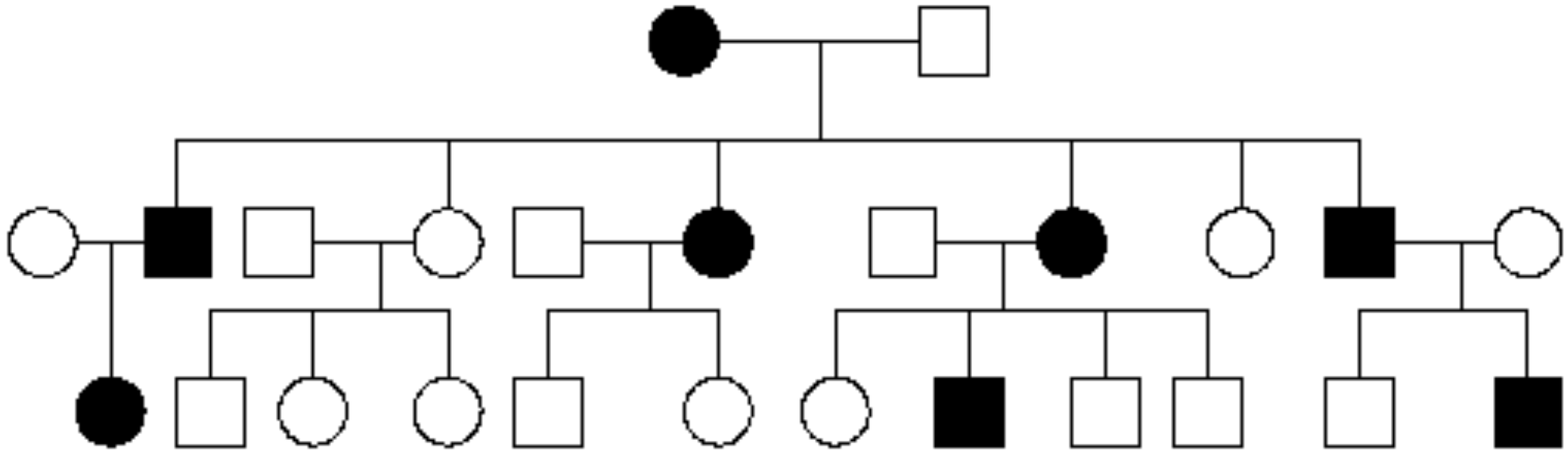
# Linkage Studies

- Looks for inheritance patterns of target behavior (phenotype) in a population (e.g., family tree) and then examines genetic similarities and differences within that population.
  - Looks for genetic similarities between those with similar target behavior; and
  - Looks for genetic differences between those with target behavior and those without target behavior.
  - Specifically looks for genetic markers associated with target behavior. (Classic Linkage Studies)

# We need family trees to locate genes

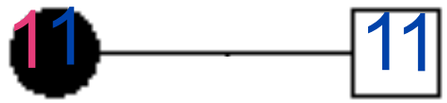


http://www.ucl.ac.uk/~ucbhjow/b241/mendel_1.html

# We need known DNA differences

- Remember there are several million common differences in the human population.
- We can track how those markers are inherited in a family.

# Tracking a phenotype in a family




Marker 1

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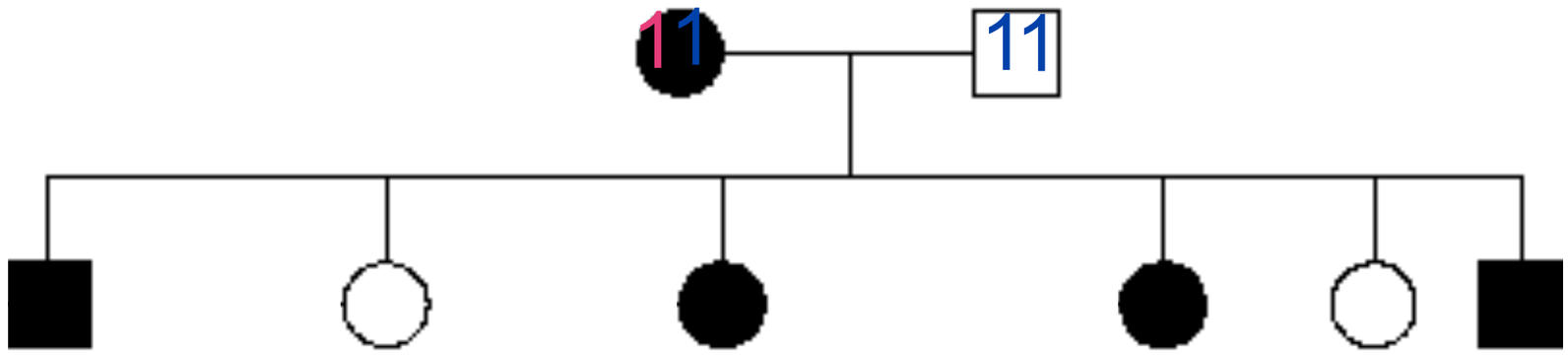


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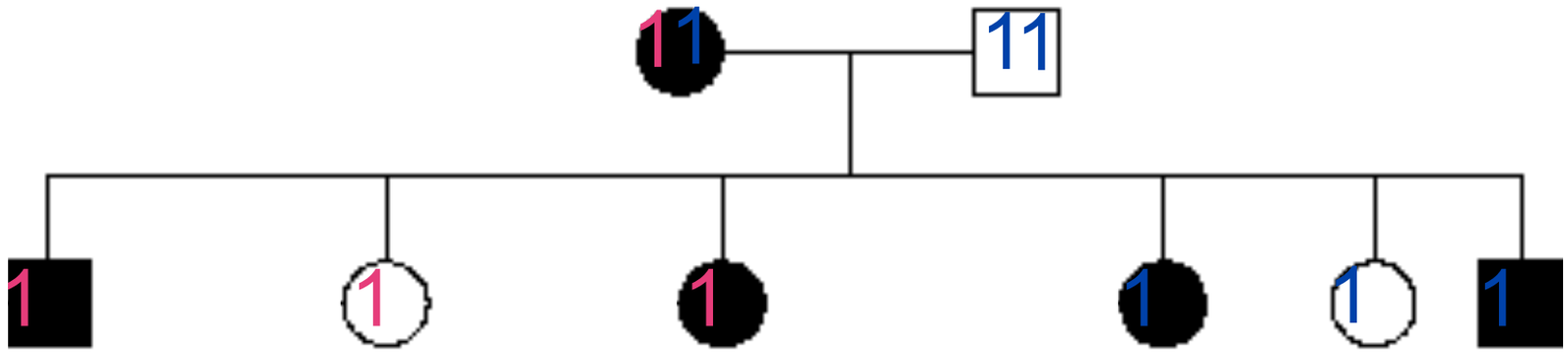


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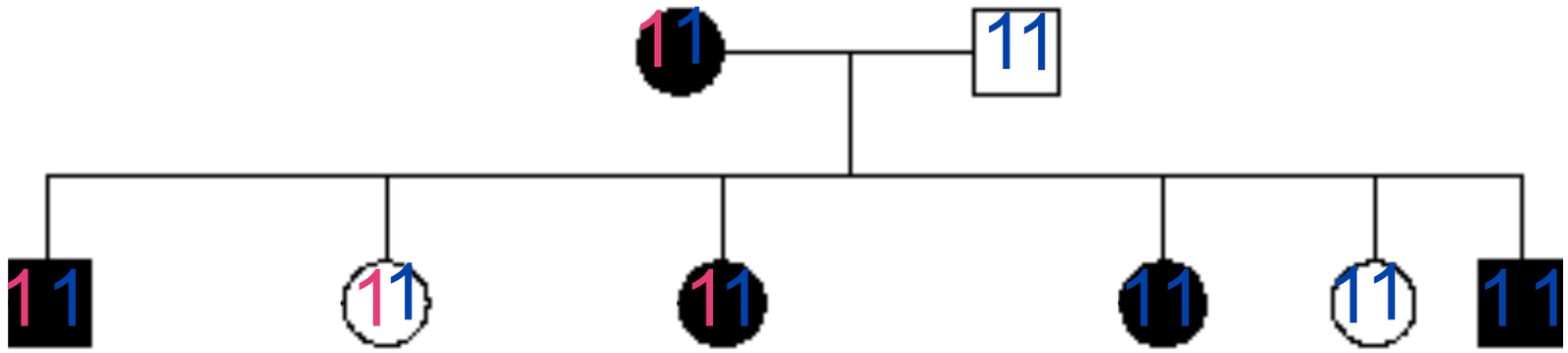


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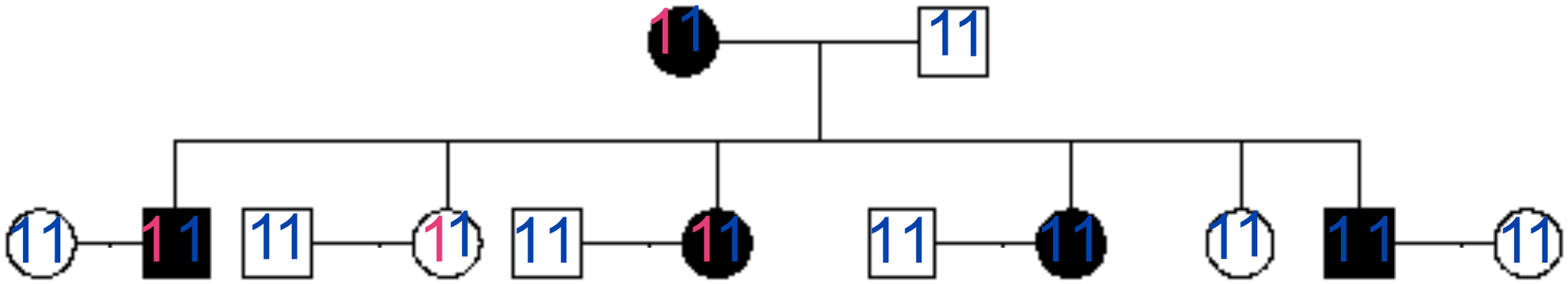


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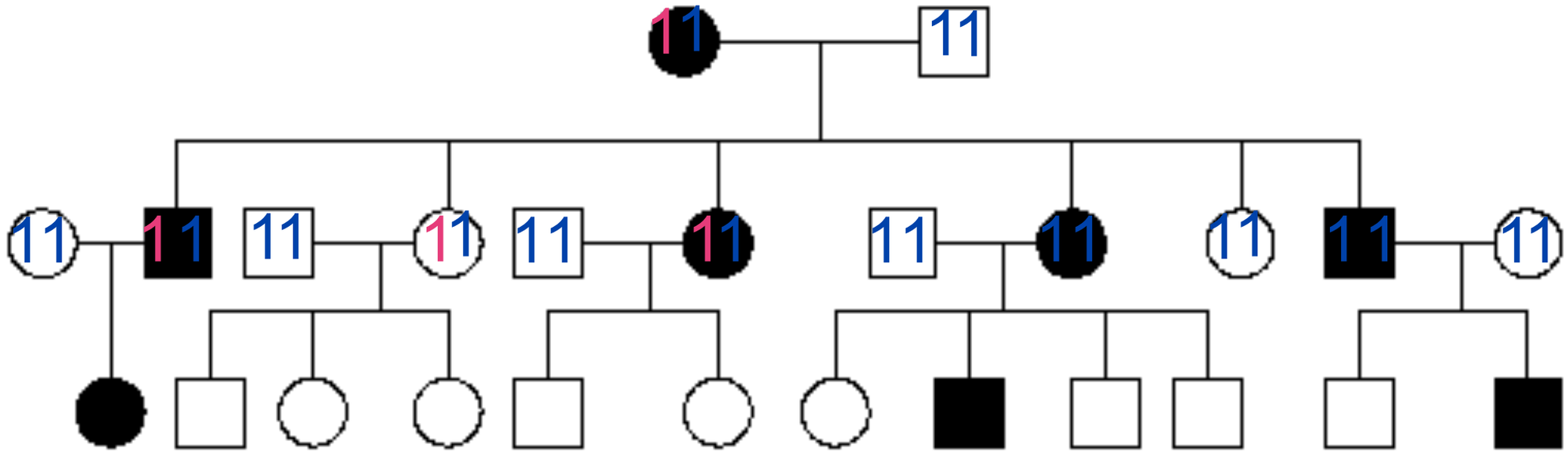


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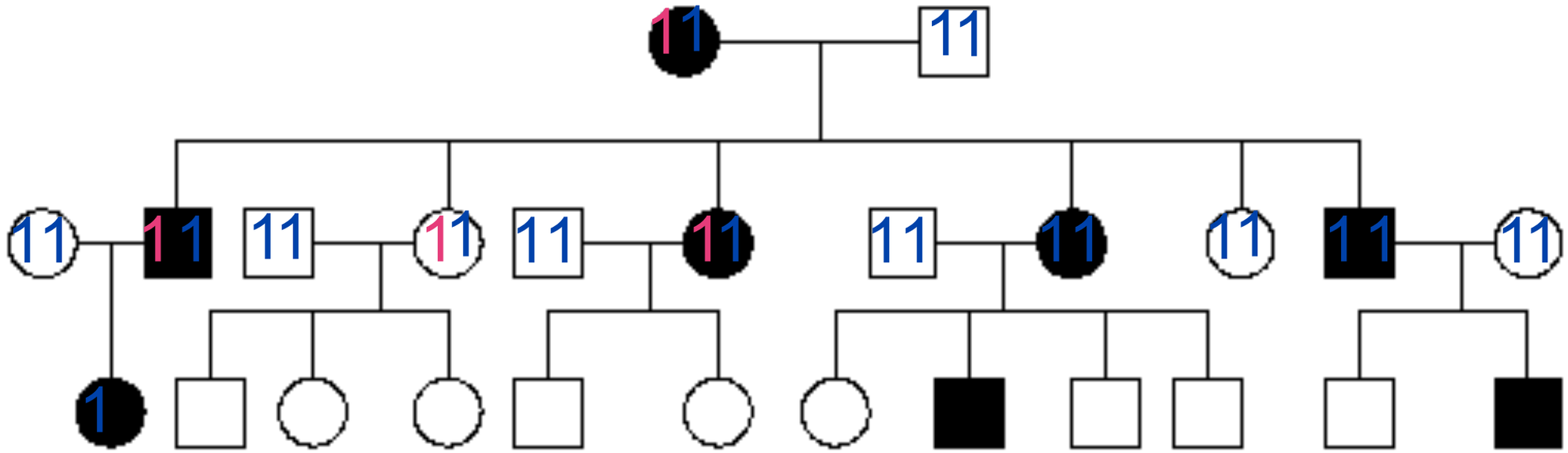


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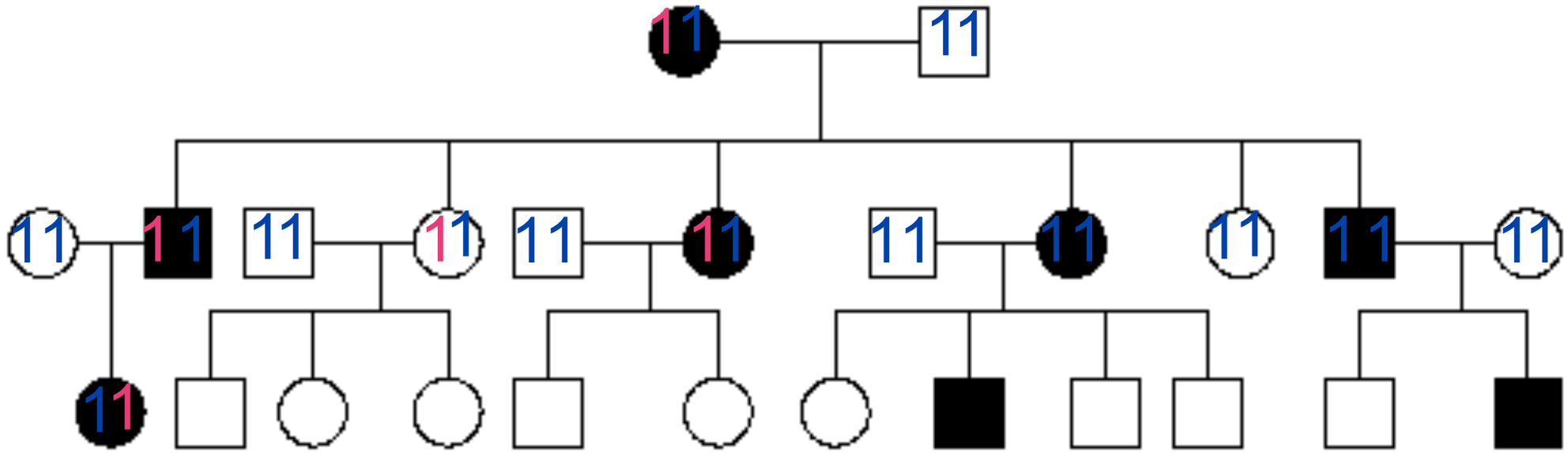


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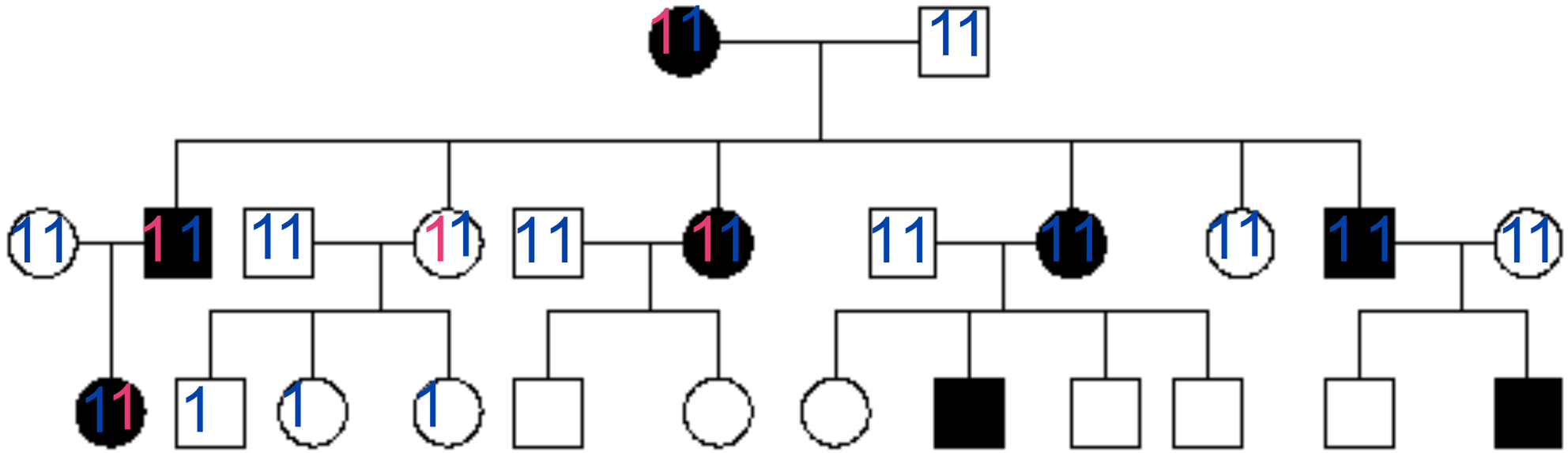


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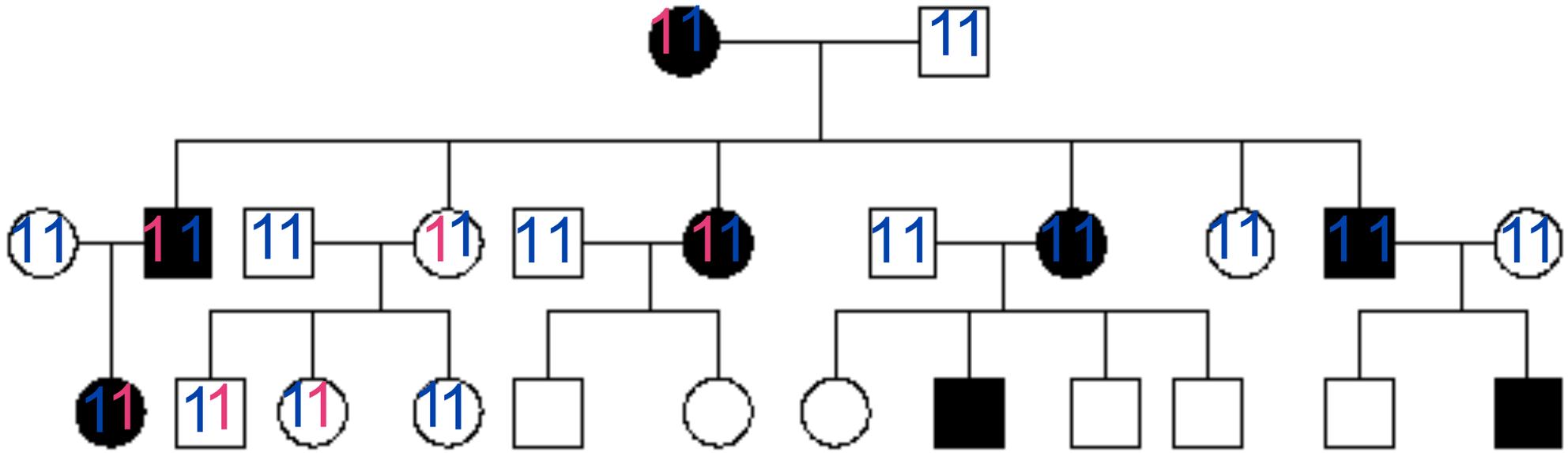


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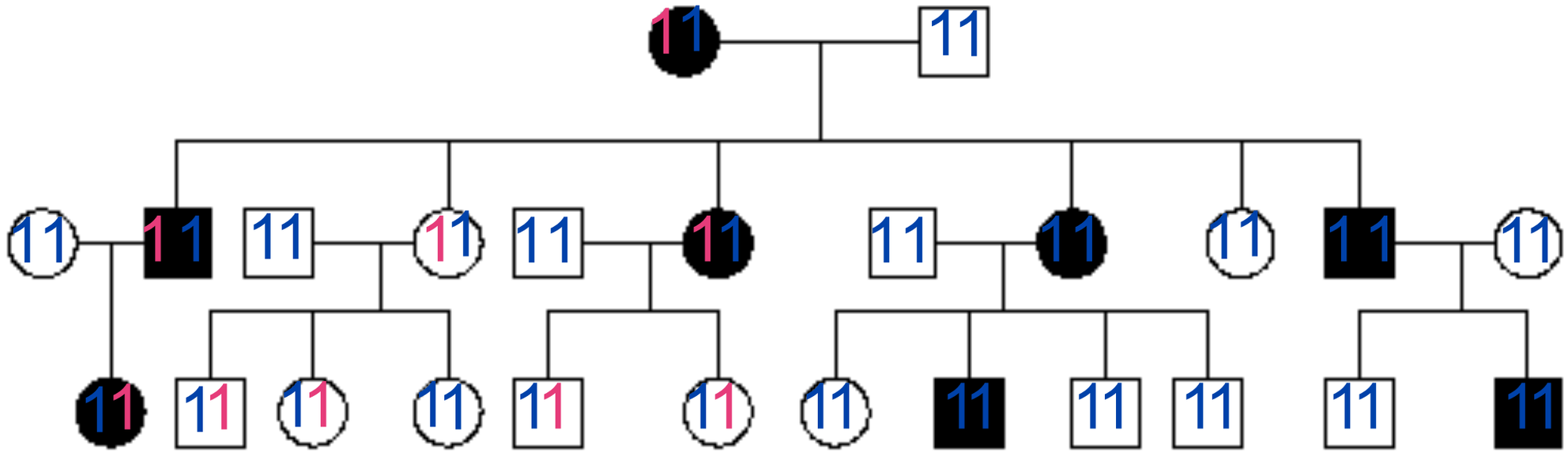


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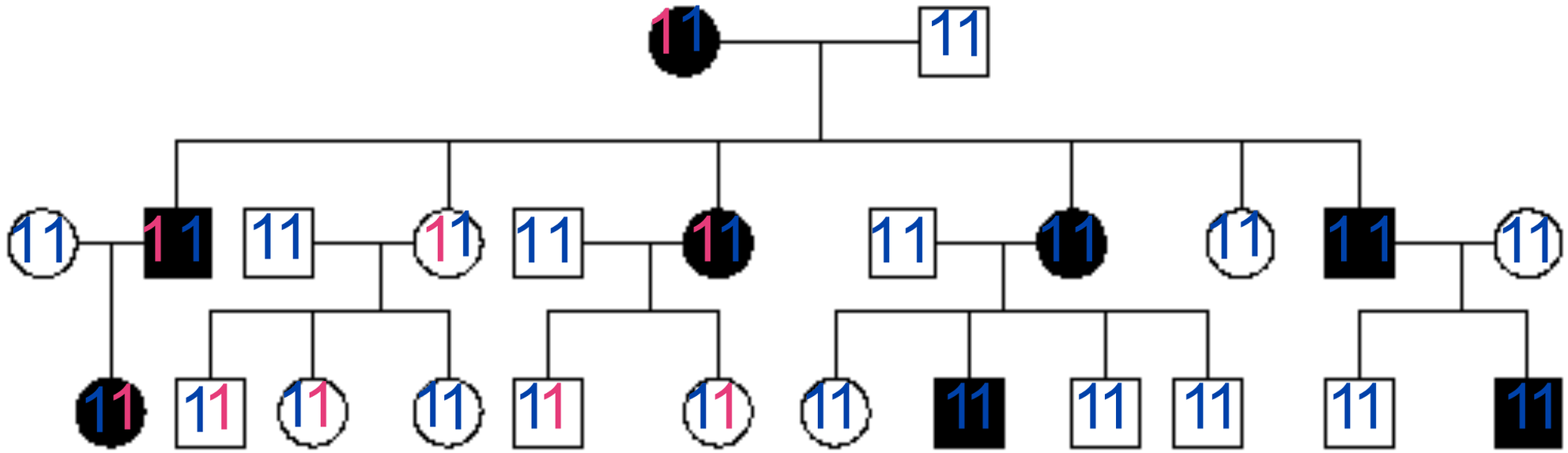


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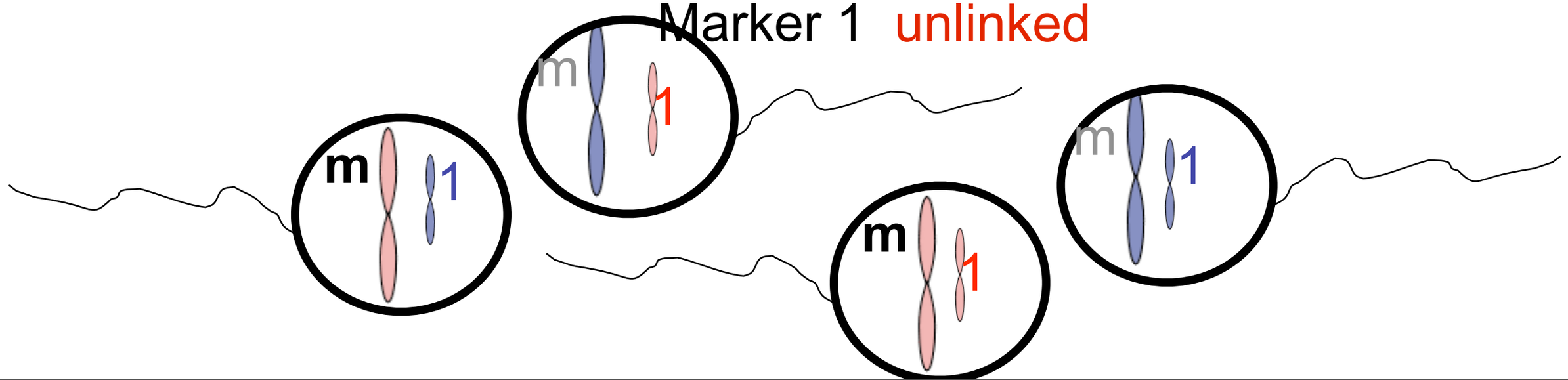

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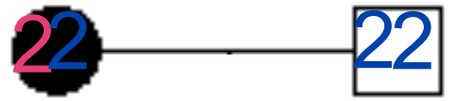


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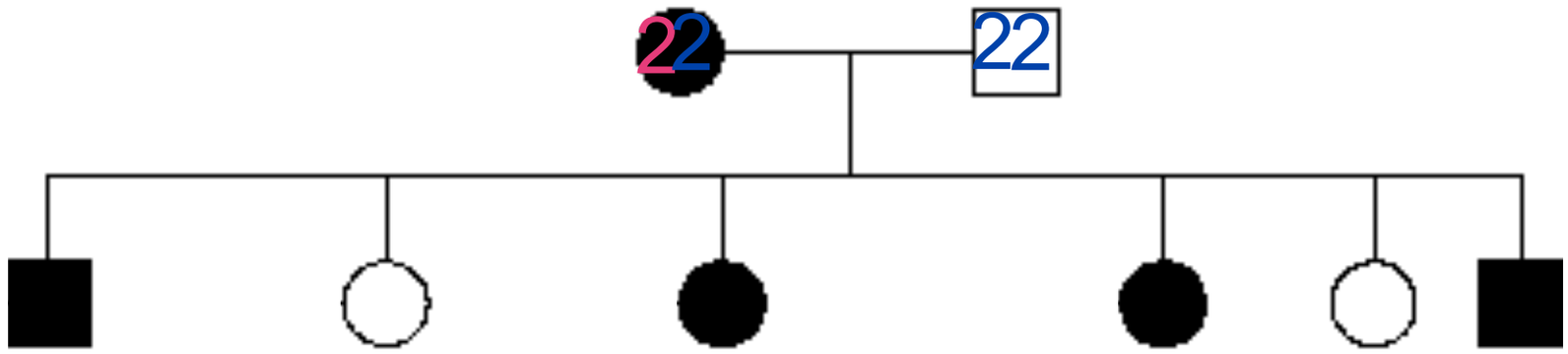
# Tracking a phenotype in a family

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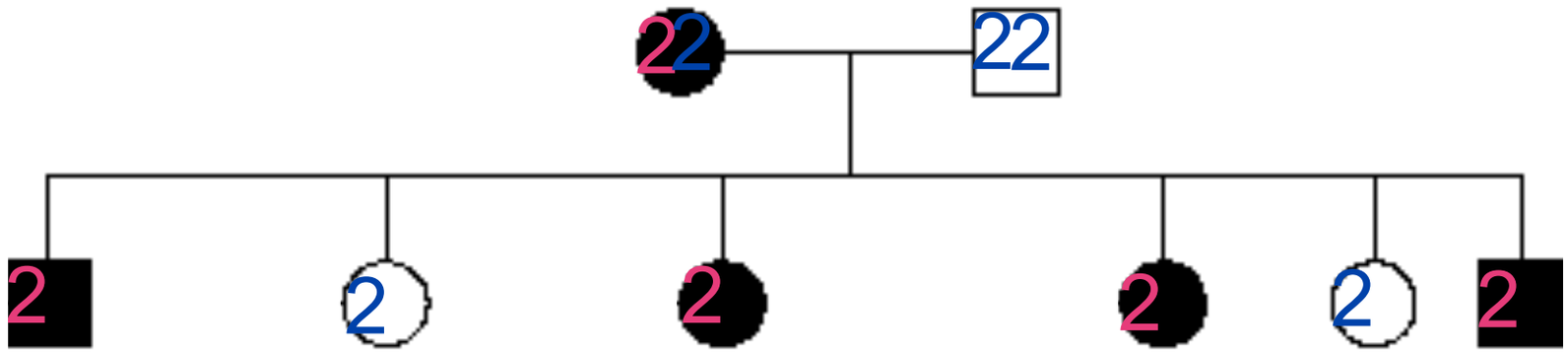


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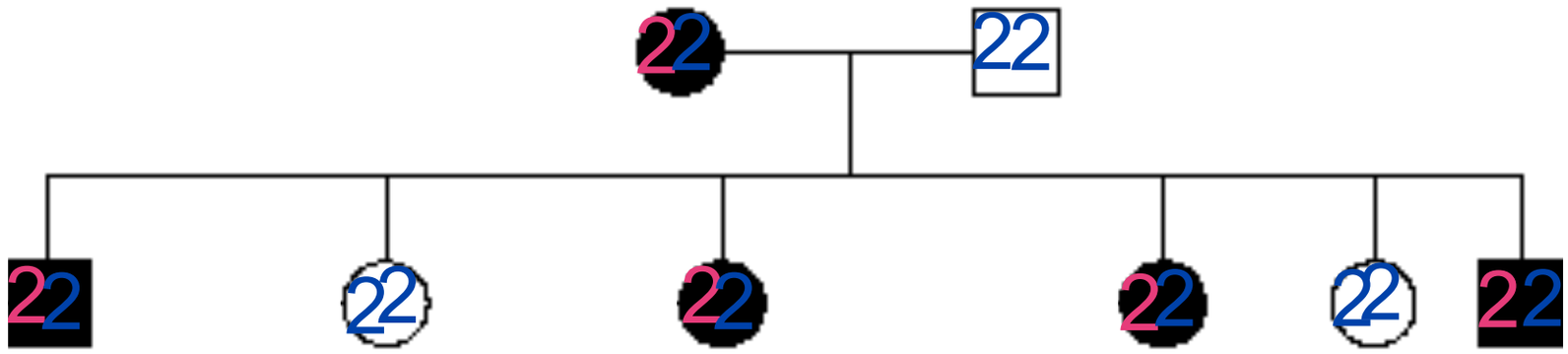


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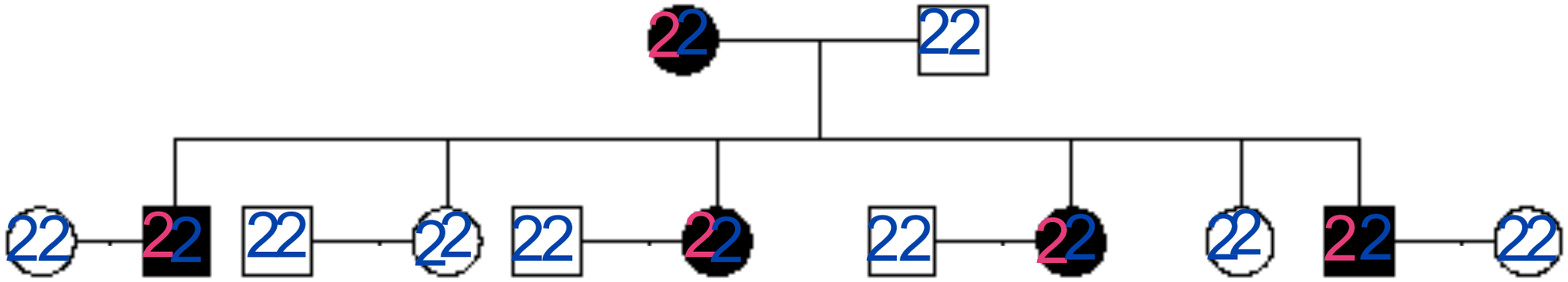


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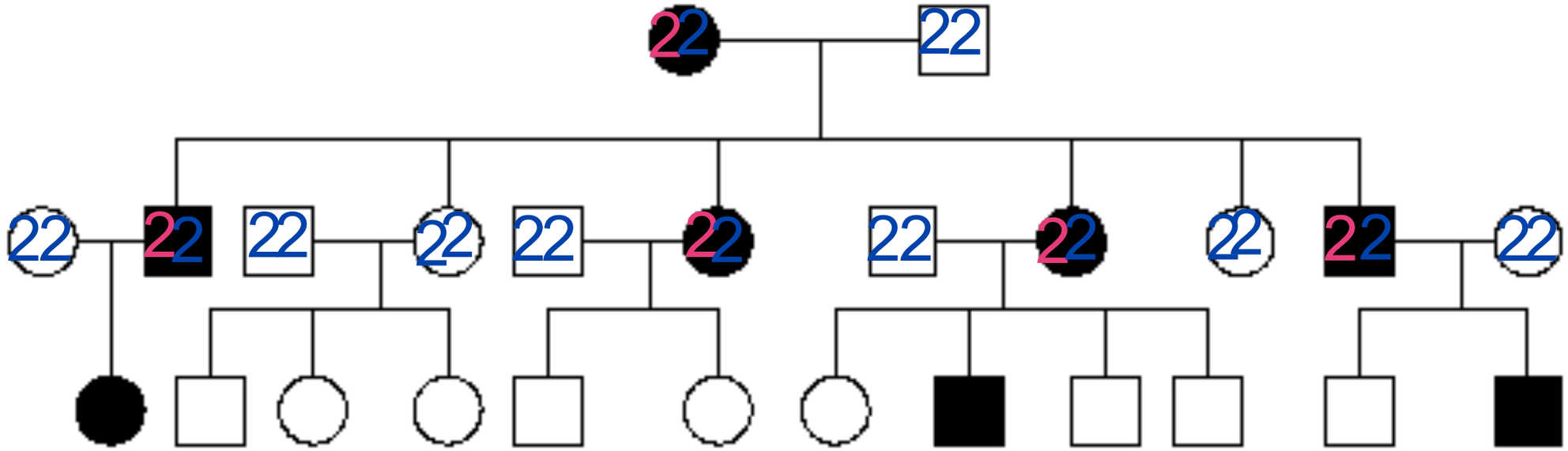


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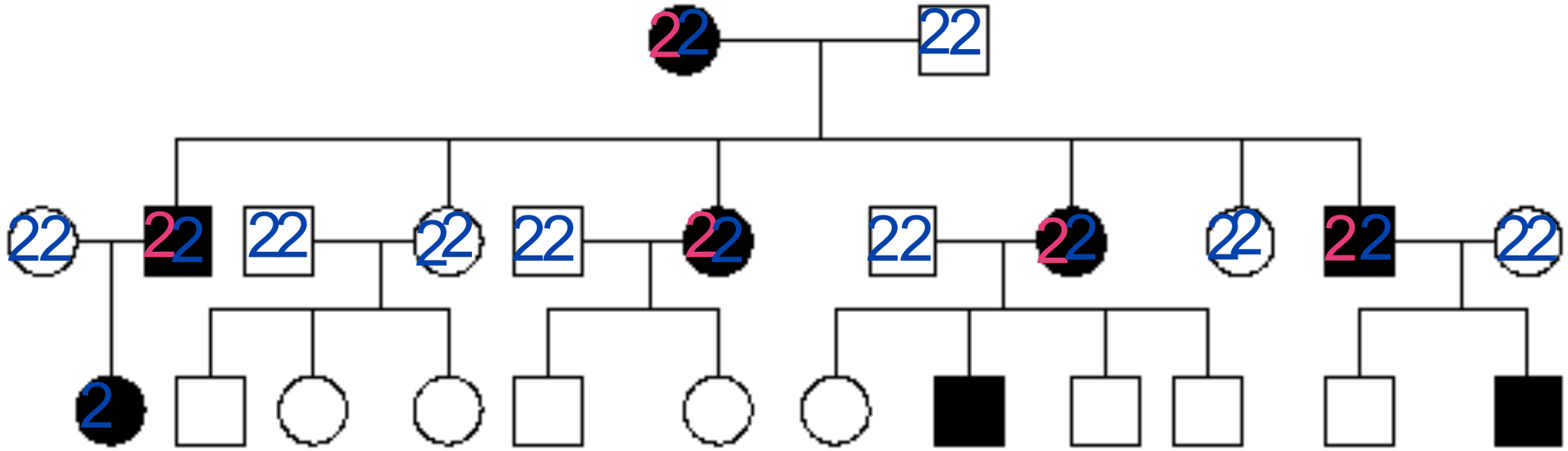


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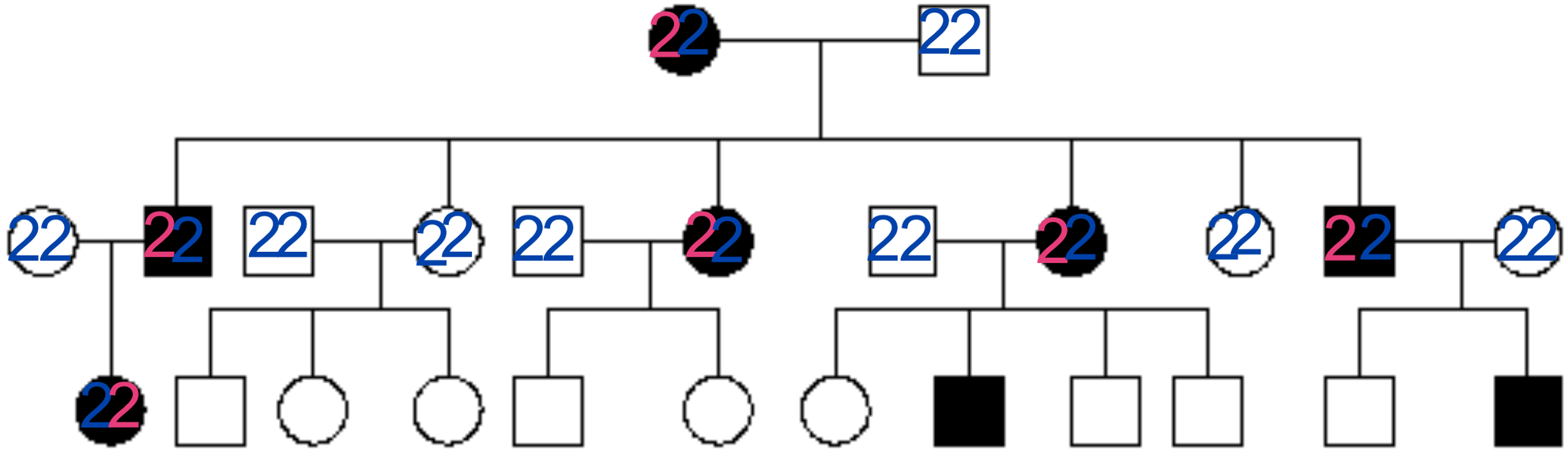


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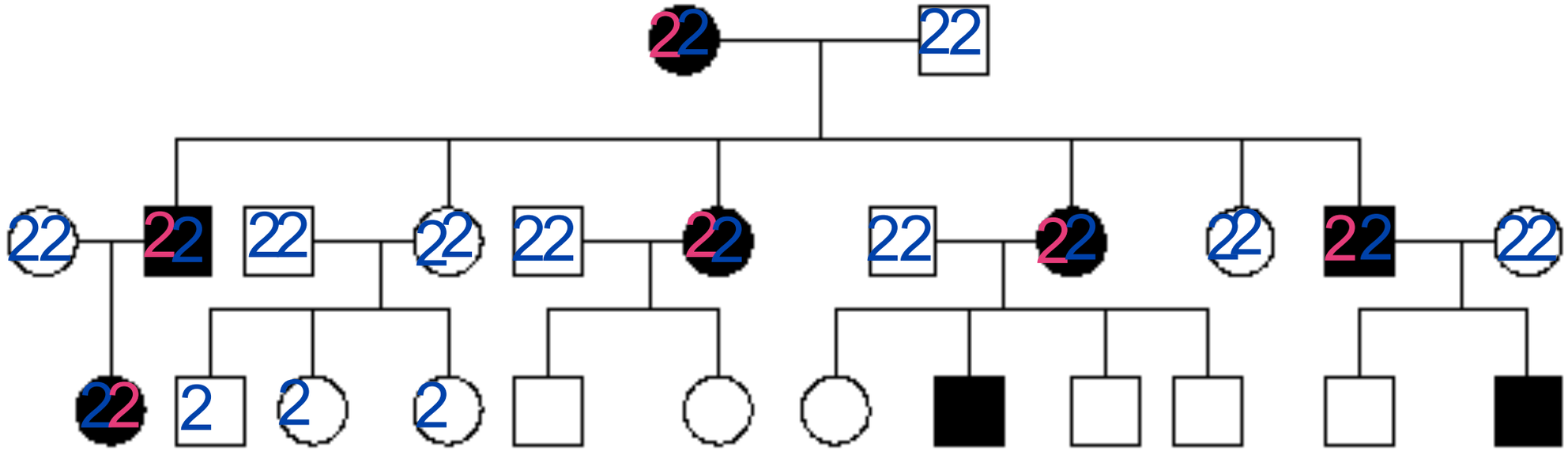


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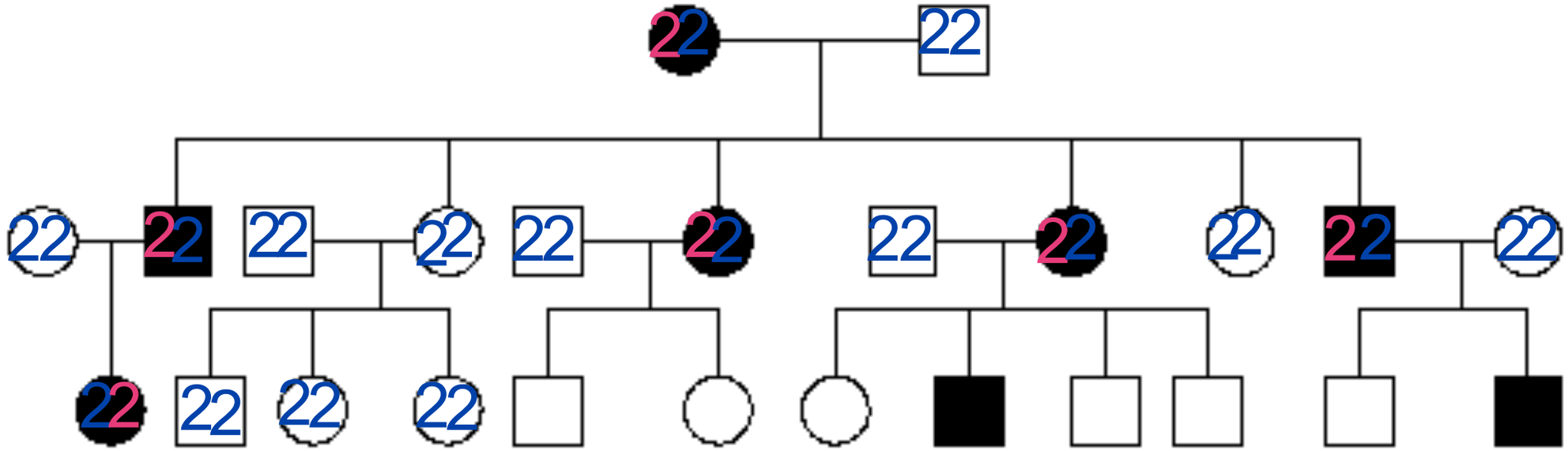


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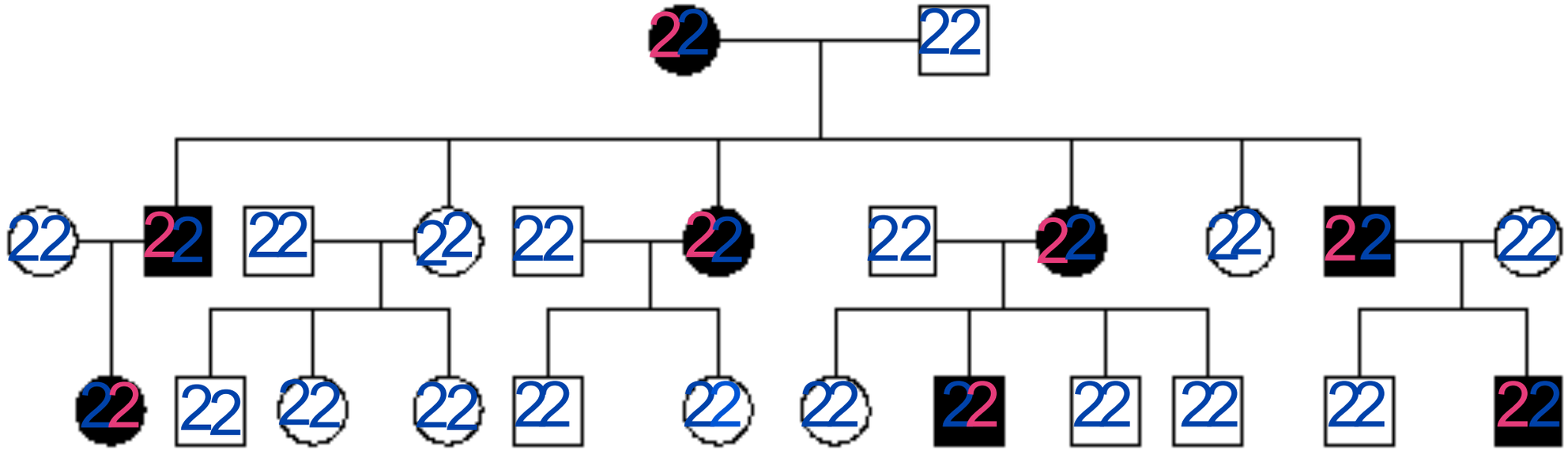


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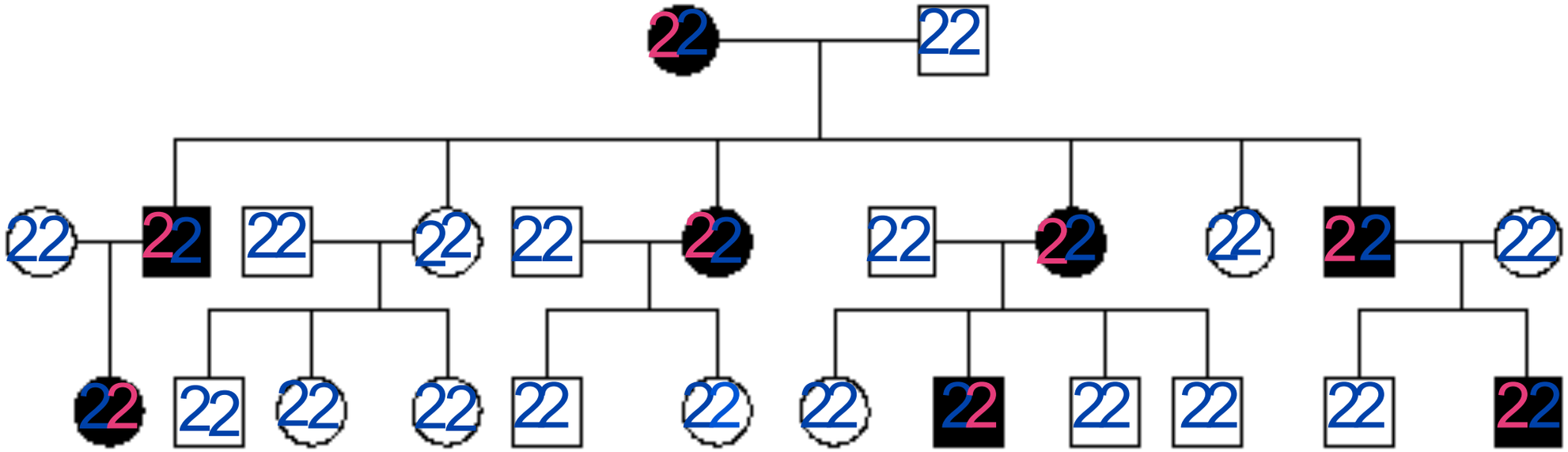
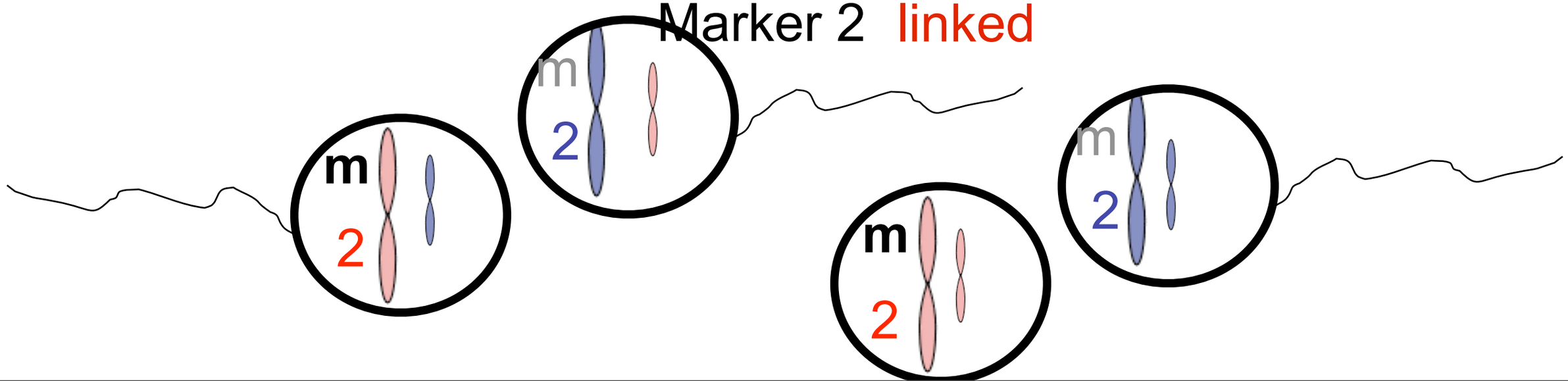



Marker 2 linked



# Linkage and Sexual Preference

- Genes determine sex (XX or XY). Do they determine sexual preference? In the 1990s Dean Hamer investigated the genetic basis for homosexual behavior.

- Advertised in gay publications for people to participate in a study. Collected information from over 100 families. Asked participants if they had gay siblings or cousins, aunts, uncles, or grandparents. Concluded homosexuality ran in many of these families.

- Discovered patterns in the distribution of gay relatives – most of the gay relatives were on the mother's side of the family.


Dean Hamer, 1995

# Genes and Sexual Preference

- Hamer reasoned that if homosexual behavior has a strong genetic basis, then it would be passed on the X chromosome. But not sure where…so, performed linkage study.

- Looked at 22 loci; a total of 40 pairs of brothers.

- He concentrated on families with brothers that were both gay, and excluded families that had gays on the father's side of the family (X linkage).

# *Xq28*

Found Marker on X Chromosome (*Xq28*):

- Of the 40 pairs, 33 had five markers that were the same.

- Concluded that a gene or genes that might influence sexual preference might be near these markers – classic linkage inference.

- July 1993, *Science*: Hamer et al., “A linkage between DNA markers on the X chromosome and male sexual orientation.”

# “Gay Gene”

Study received much attention*, both pro and con.

– Newspapers reported on discovery of “Gay Gene”

– 1995 study of 200 families with gay brothers (G. Ebers and G. Rice) found gay relatives on maternal side, but didn’t yield same result as Hamer (1993) – no linkage at Xq28. Hamer responded, in his book *Living with Our Genes*, that the Ebers and Rice study was conducted differently (and with bias), so their findings don’t dispute his own.

– Controversy continues…research continues…

*Published near the time that LeVay published on hypothalamic differences between homo- and heterosexual men. See Debate posted online.

# What does Hamer's study tell us?

- Not really a "gene" but a region of a chromosome.

- No identified causal pathway from gene(s) to behavior

- Complex behavior is, well, …complex
  - What is "homosexuality"? (time, place, environment)
  - Self-report and second-hand reports in study
  - Sexual behavior involves more than sex (See *The Real Story on Gay Genes*)

# Outline

- Nature v. Nurture (Heritability)
- Types of Studies
  - –Twin Studies
  - –Linkage Studies
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# Association Studies
(with Animals)

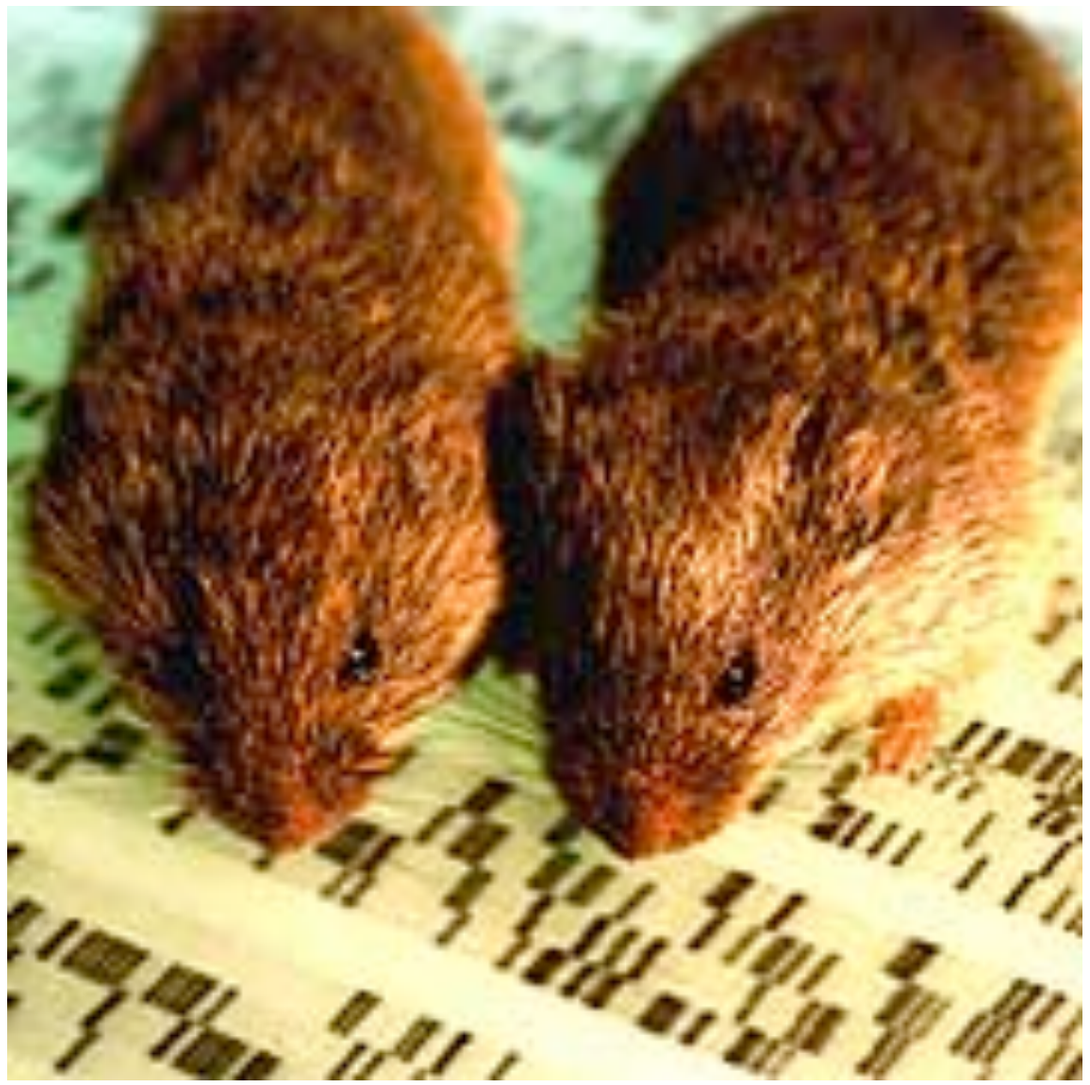
- Basic Strategy: Find gene of interest, and manipulate it to determine effect on behavior phenotype.

  – Use knock-out (and -in) technology or selective breeding to produce lines of organisms with and without gene of interest;

  – Then, observe behavioral differences.

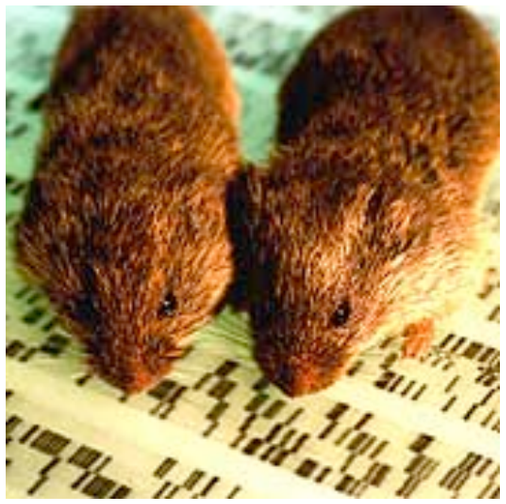
# Romantic Voles

- *Science* 10 June 2005. Study on variations in a gene promoter sequence that predict social behavior in voles – in particular parental care and monogamous mating.



See also Nicholas Wade, A Gene for romance? So it seems (Ask the vole). *New York Times*, July 19, 2005

# Romantic Voles

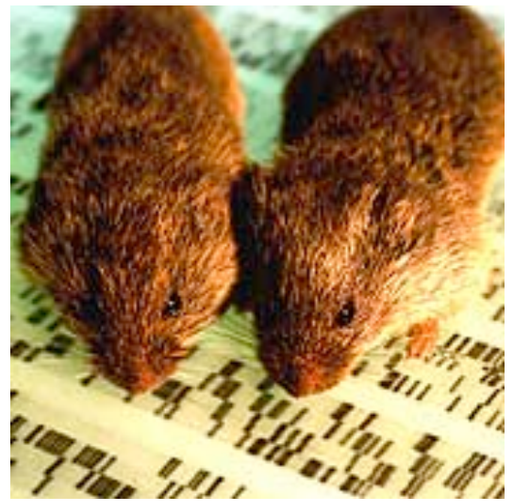


- Differences in promoter sequences in a particular gene drastically affects complex social behaviors.

- The difference in sequence length directly affects how, when and where the protein receptor for the hormone **vasopressin** presents itself in the brain – that is, it effects gene expression.

- Key: Vasopressin is linked to social learning.

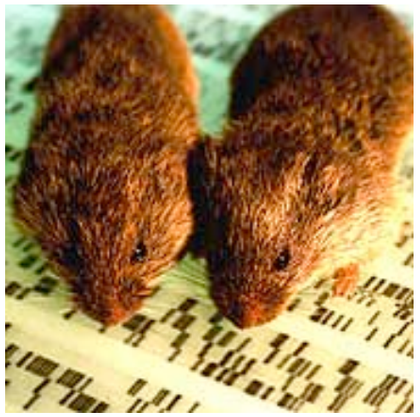
# Romantic Voles



- Researchers transferred a single gene from male **prairie voles** (which are monogamous) to male **meadow voles** (which are promiscuous).

- The result was a monogamous meadow vole!

# Romantic Mechanism?

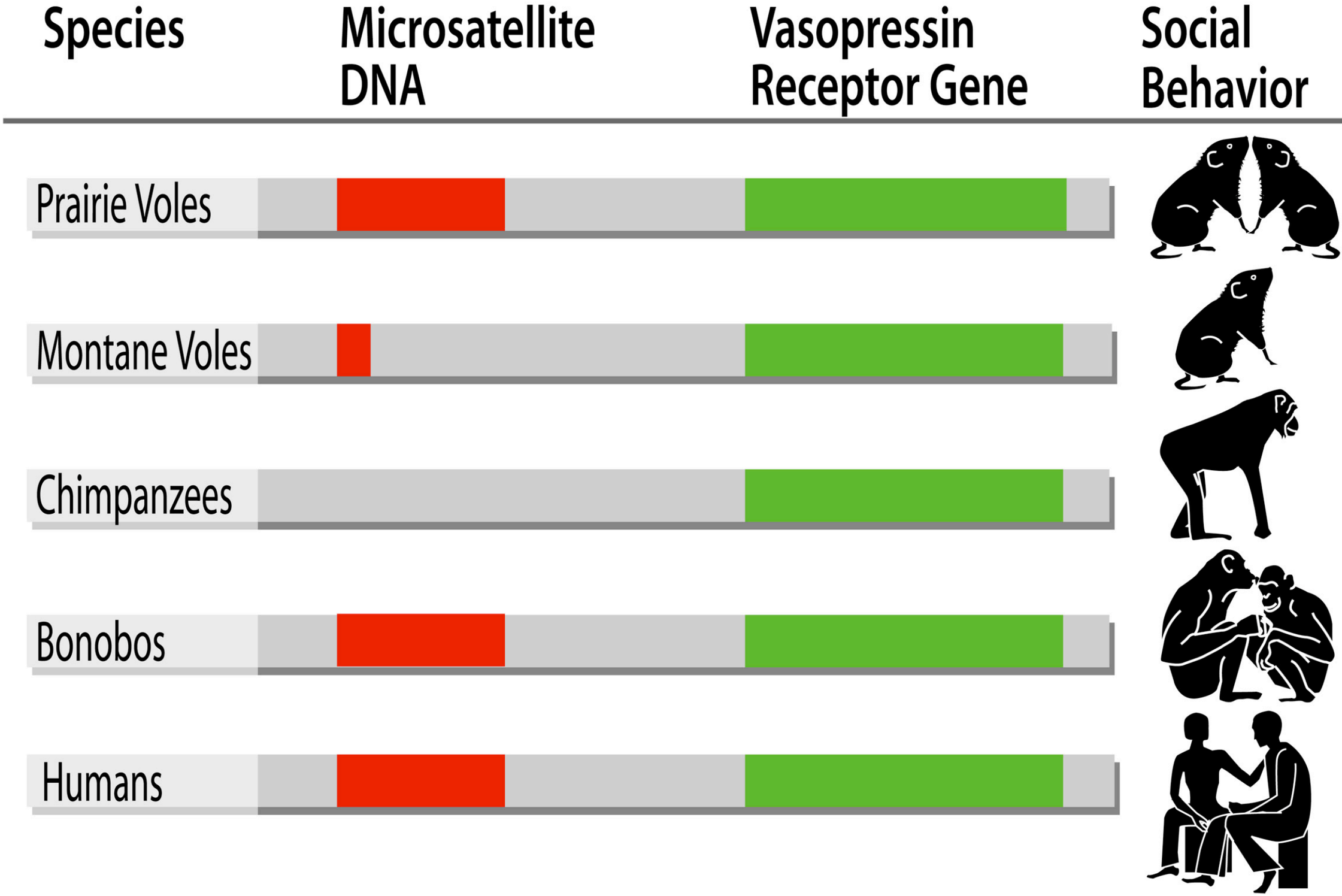


- Mating releases dopamine in the brain, dopamine receptors are located in the brain's pleasure center.

- In prairie voles (monogamous) the vasopressin receptors (social learning) **are also** located in the same pleasure centers. In meadow voles (promiscuous), the vasopressin receptors **are not** located in the same brain regions.

- Explanation: when mating prairie voles learn to associate the pleasure with a particular female, meadow voles do not. Thus pair-bonds are formed in prairie voles and not meadow voles.

# Same genes are in operation in humans and other mammals



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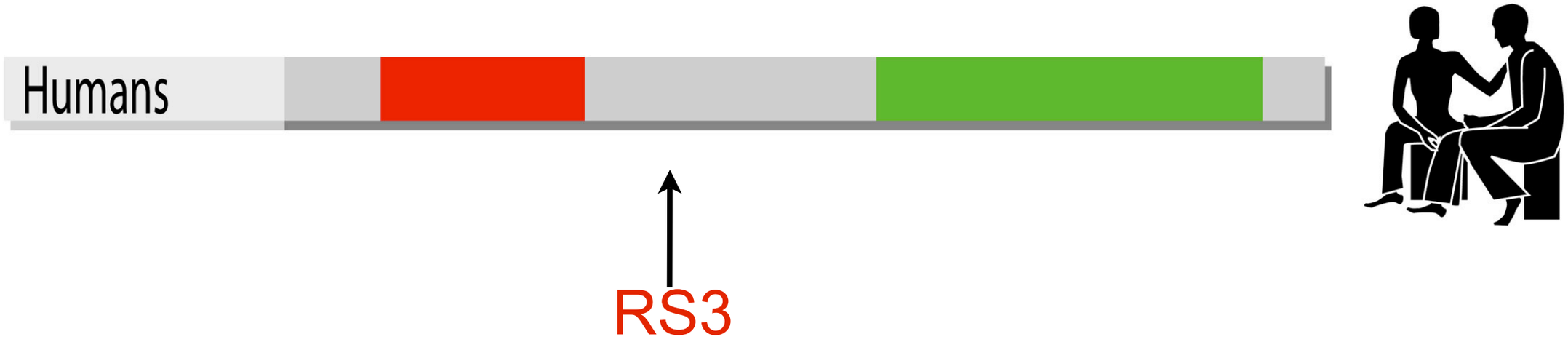



- September 2008, Walum *et al.*
- Not the same repeat as in prairie voles, but there are variations in the promoter region that are different between people (RS3)

# Vasopressin in Humans

- People were characterized on a Partner Bonding Scale to determine how happy their marriages were.

| | solitary alleles | | |
|---|---|---|---|
| | 0 | 1 | 2 |
| bonding score | 48 | 46 | 45 |

# Vasopressin in Humans

| Threatened divorce in the last year | | | |
|---|---|---|---|
| | solitary alleles | | |
| | 0 | 1 | 2 |
| No | 85% | 84% | 66% |
| Yes | 15% | 16% | 34% |

| Married? | | | |
|---|---|---|---|
| | solitary alleles | | |
| | 0 | 1 | 2 |
| Cohabitating | 17% | 16% | 32% |
| Married | 83% | 84% | 68% |

# Love and *Fos-B*

In early 1995, an M.D-Ph.D student, Jennifer Brown, was breeding mice with an inactivated form of the gene *FosB*. With the inactivation of the gene, healthy pups from the mutated mice died quickly. Observing this occurrence, Brown found that the mother mice ignored her offspring. From this discovery, Brown proposed that the inactivation of the gene *FosB* causes a defect in the nurturing behaviors of female mice. To prove this, Brown bred a series of knockout mice with the inactivated *FosB* gene. She then observed the nurturing behaviors of the knockout mice and compared them to those of the normal mice.

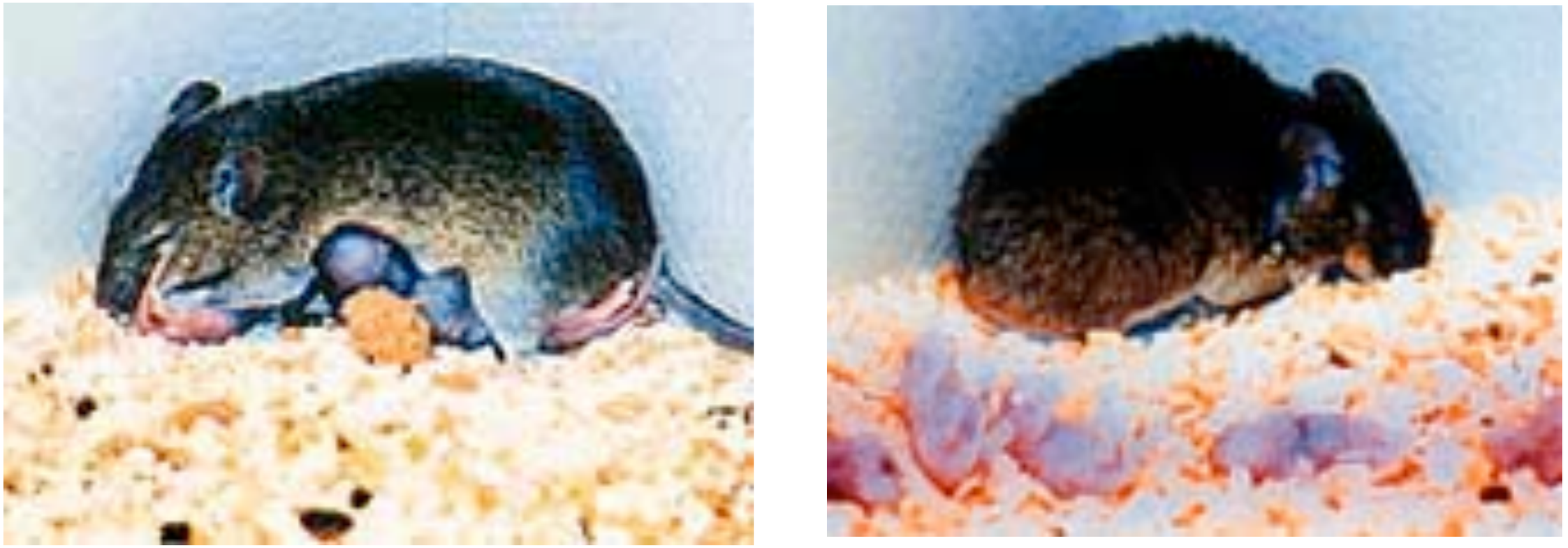
# *Fos-B* and nurturing behavior

Twenty-four to forty-eight hours after delivery, the mortality rate of the pups was in excess of fifty percent.

After birth, it was immediately noted that mutant mothers failed to exhibit normal nurturing behavior: creating a nest, cleaning the pups, retrieving them to the nest, and crouching over them for warmth and nursing.

The mutant mothers, rather, sat in a corner and ignored the pups that were scattered around the cage

# With and without *Fos-B*



Images: http://www.med.harvard.edu/publications/On_The_Brain/Volume06/Number2/synaphshot.html

Summary of this research available at http://student.biology.arizona.edu/honors96/group3/default.html

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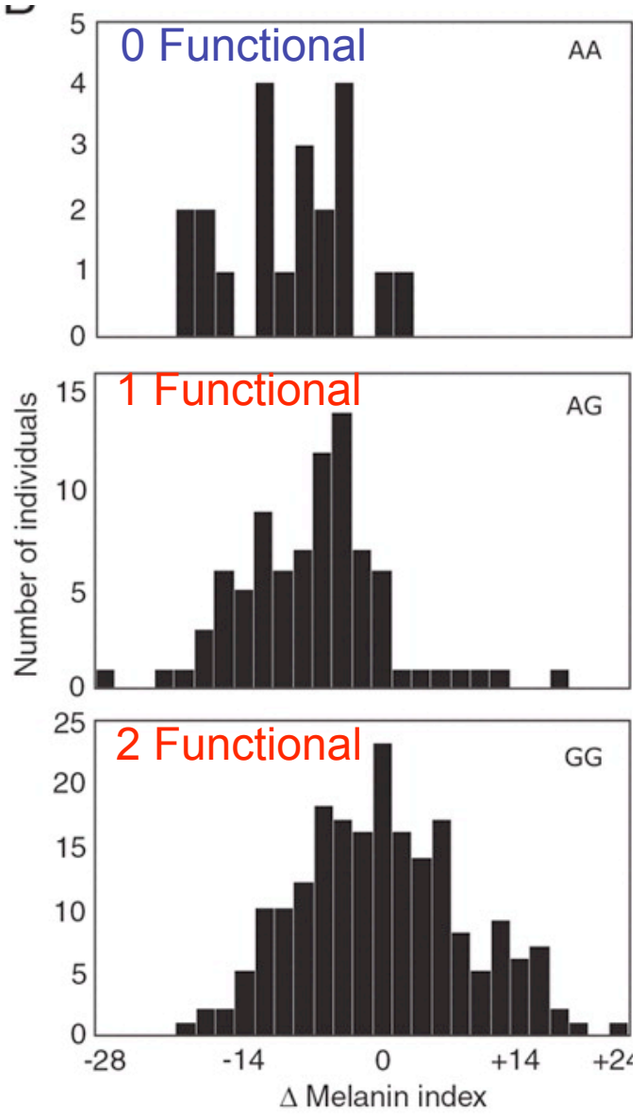
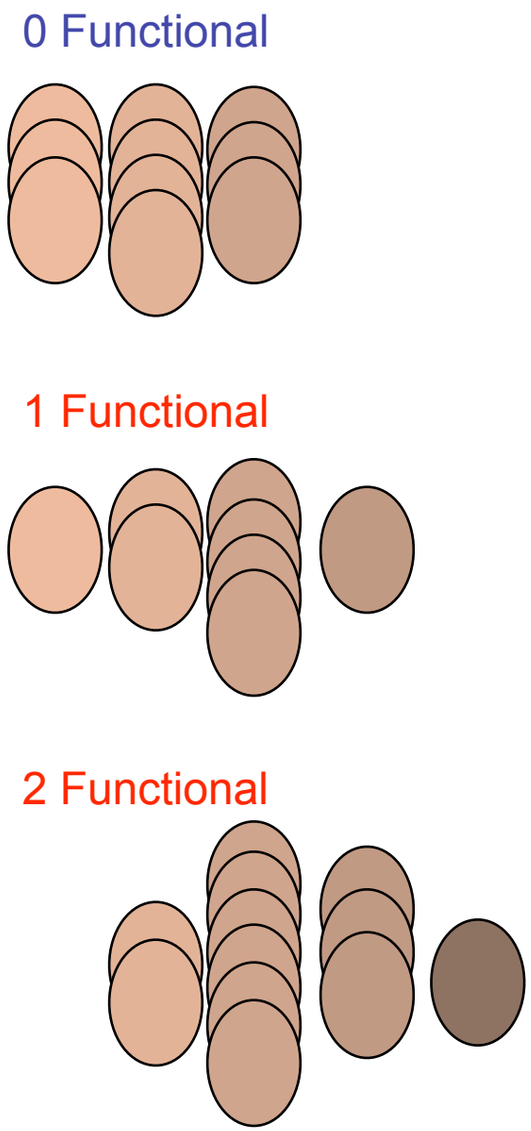
# So, what about sexuality?

- Sexual behavior is complex
  - We looked at several sexual behaviors: sexual orientation, mating patterns, and nurturing of young.
  - What is sexuality? What is the normal range of behavior?

- Defining a behavior can be very difficult

# Single genes generally have small effects



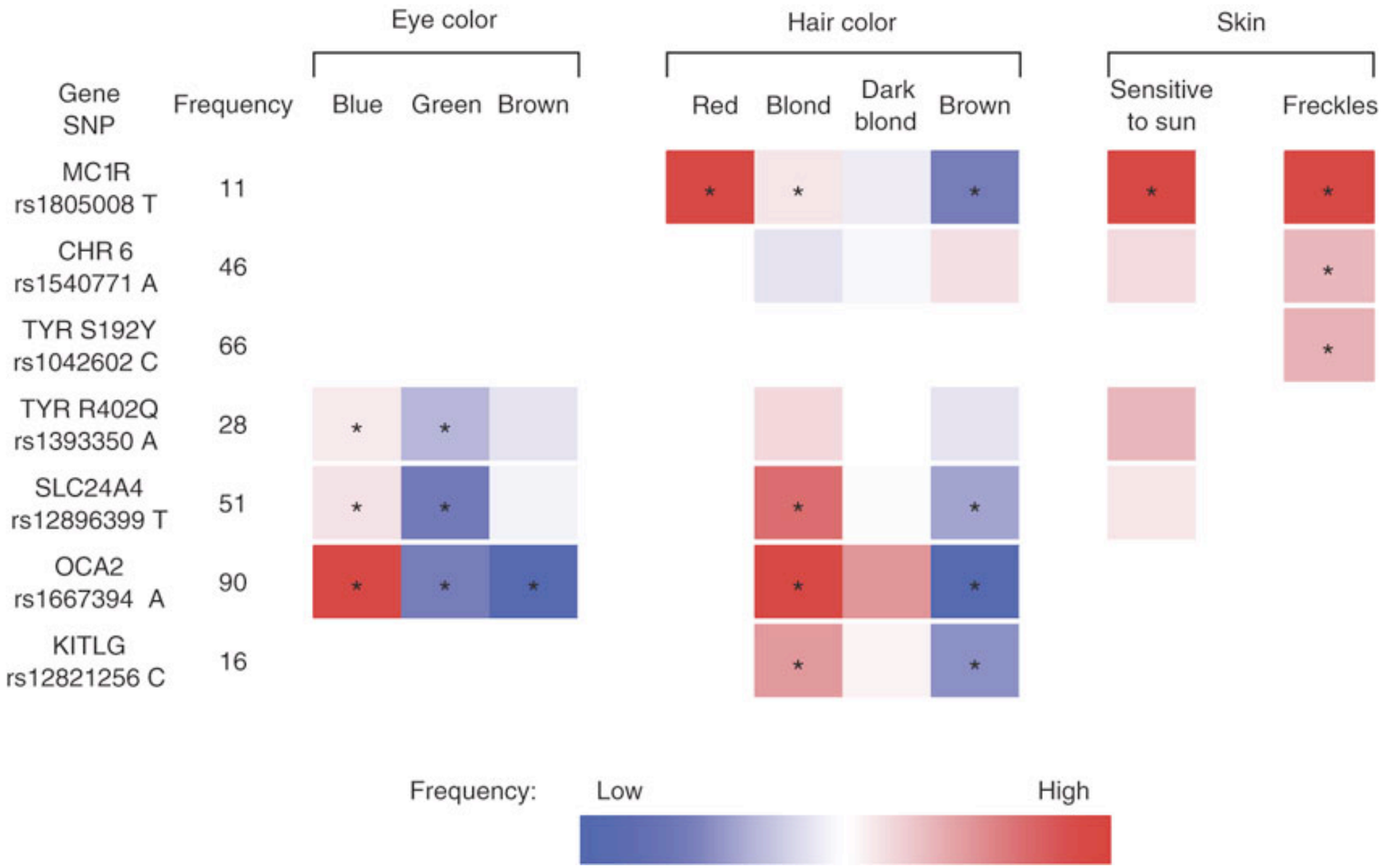




In African-American and African-Caribbean populations there is a mixture of African and European forms.

On average, people with the functional form have darker skin, but there are other genes involved.

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=16357253

# Many genes affect multiple phenotypes

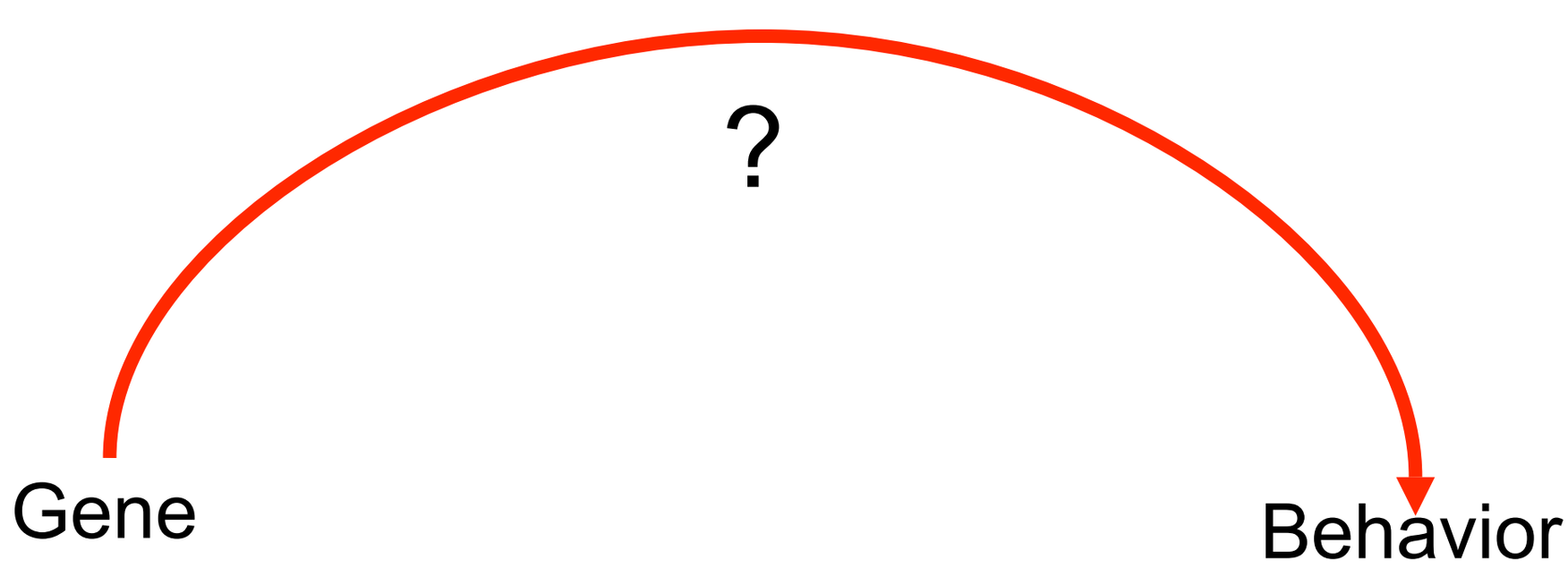



Carried out a genome-wide association scan for variants associated with hair and eye pigmentation, skin sensitivity to sun and freckling among 2,986 Icelanders.

Sulem P et. al Nat Genet. Dec. 2007

# What about sex?

- Causal pathway is crucial
  - How do we get from gene to behavior?



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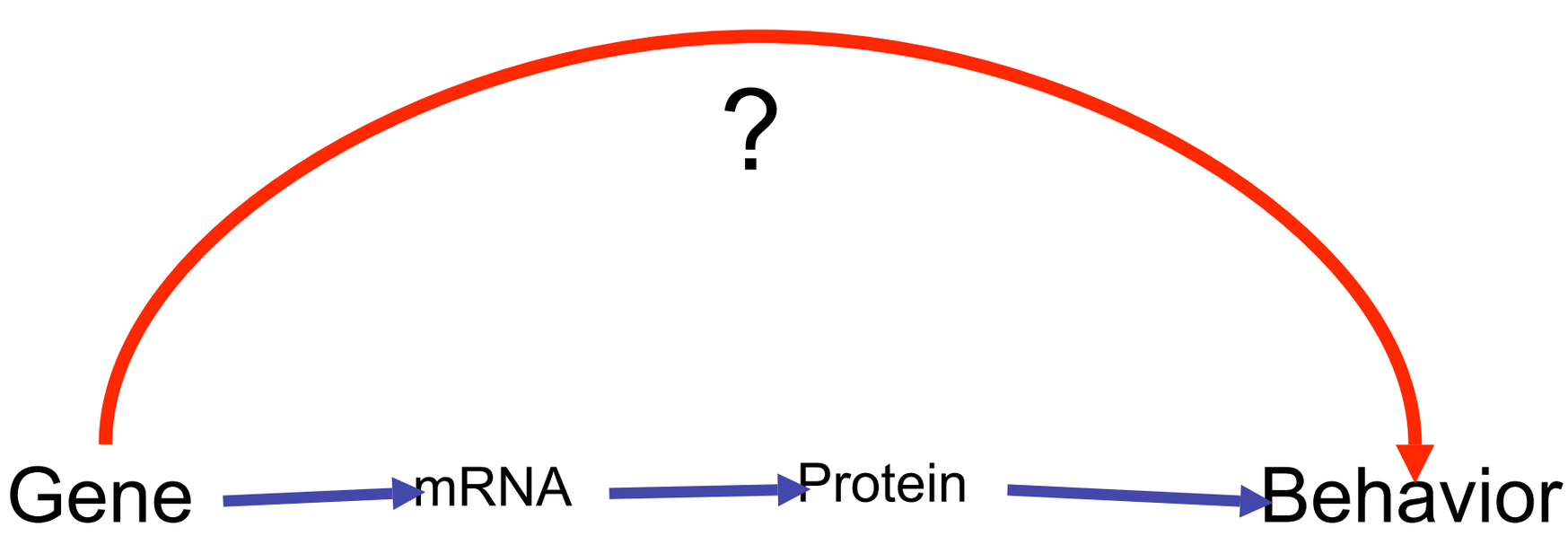

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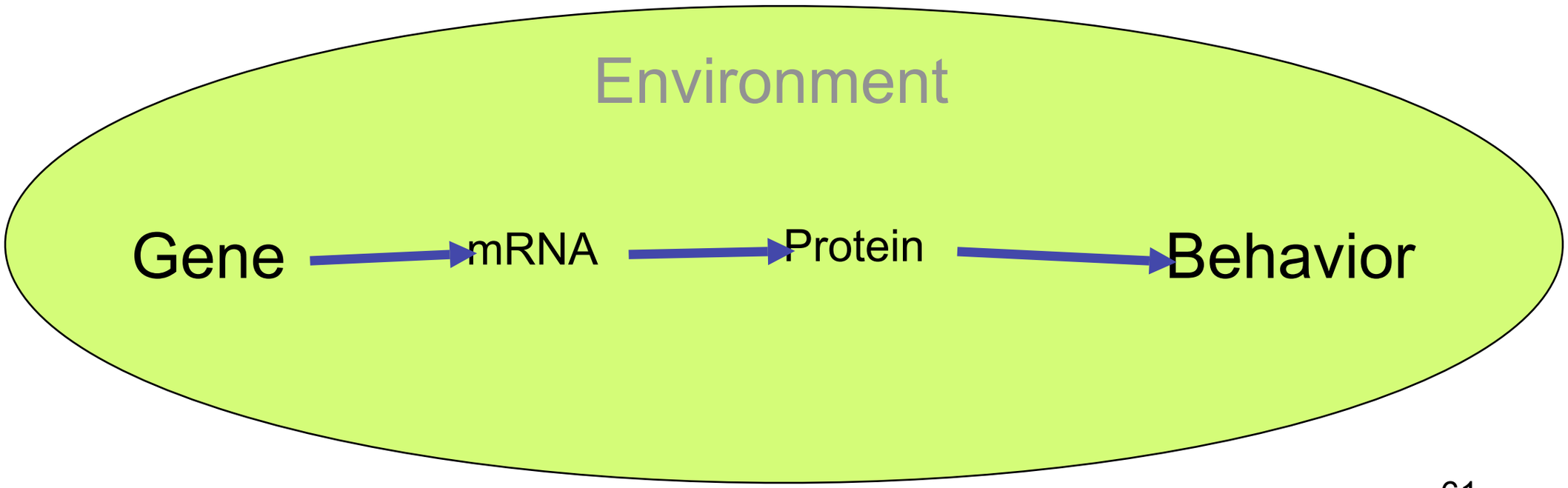


# Implications:
# Why study homosexuality?

- Curiosity about genetics of sexuality

- Evolutionary puzzle
  - If homosexuals defeat reproductive aims, why still present in population?

- More problematic reasons… “medicalization” and politics

# "Medicalization" of Behavior?

When normal behavior is increasingly viewed as a disorder. Due to increasing commercial and social pressures to use medical interventions, what was once within a normal range is now considered dysfunctional, or abnormal – leading to reduced tolerance of different behaviors.

- Consider *Viagra* and *Prozac*
- Consider ADD/H and depression

# “Leave gay sheep alone.”

- Researchers in Oregon propose studies on sheep regarding sexual partner selection, hormones and brain function.

- Responding on behalf of PETA to sex research in sheep, Martina Navratilova writes a letter to the universities in Oregon:


•Sexual partner preference, hypothalamic morphology and aromatase in rams.Roselli CE, Larkin K, Schrunk JM, Stormshak F. Physiol Behav. 2004 Nov 15;83(2):233-45

•Brokeback Mutton: Gay sheep and human destiny.By William Saletan. http://www.slate.com/id/2158877/ *Also see* See: http://www.slate.com/id/2159262/

•Blog.bioethics.net/2007/01/martina-navratilova-leave-gay-sheep.html

# “Leave gay sheep alone.”

“How can it be that, in the year 2006, a major university would host such homophobic and cruel experiments? … I respectfully ask that you pull the plug on this appalling and misguided research. Surely you can find a way to redirect the millions of public tax dollars that are being wasted on these experiments to a more fruitful venture – perhaps by funding a gay and lesbian community center to foster dialogue and acceptance for people of all sexual preferences?” She also accused researchers of trying to find a “prenatal treatment for various sexual conditions.”

# 4 Difficulties with Behavioral Genetics

1. Defining and measuring behavior

2. No (single) “gene for X”:
   - polygenetic influence

3. Predicting how behavior develops:
   - complexity of gene-environment interactions (nature/nurture)
   - pathways (effects of single gene are minimal)

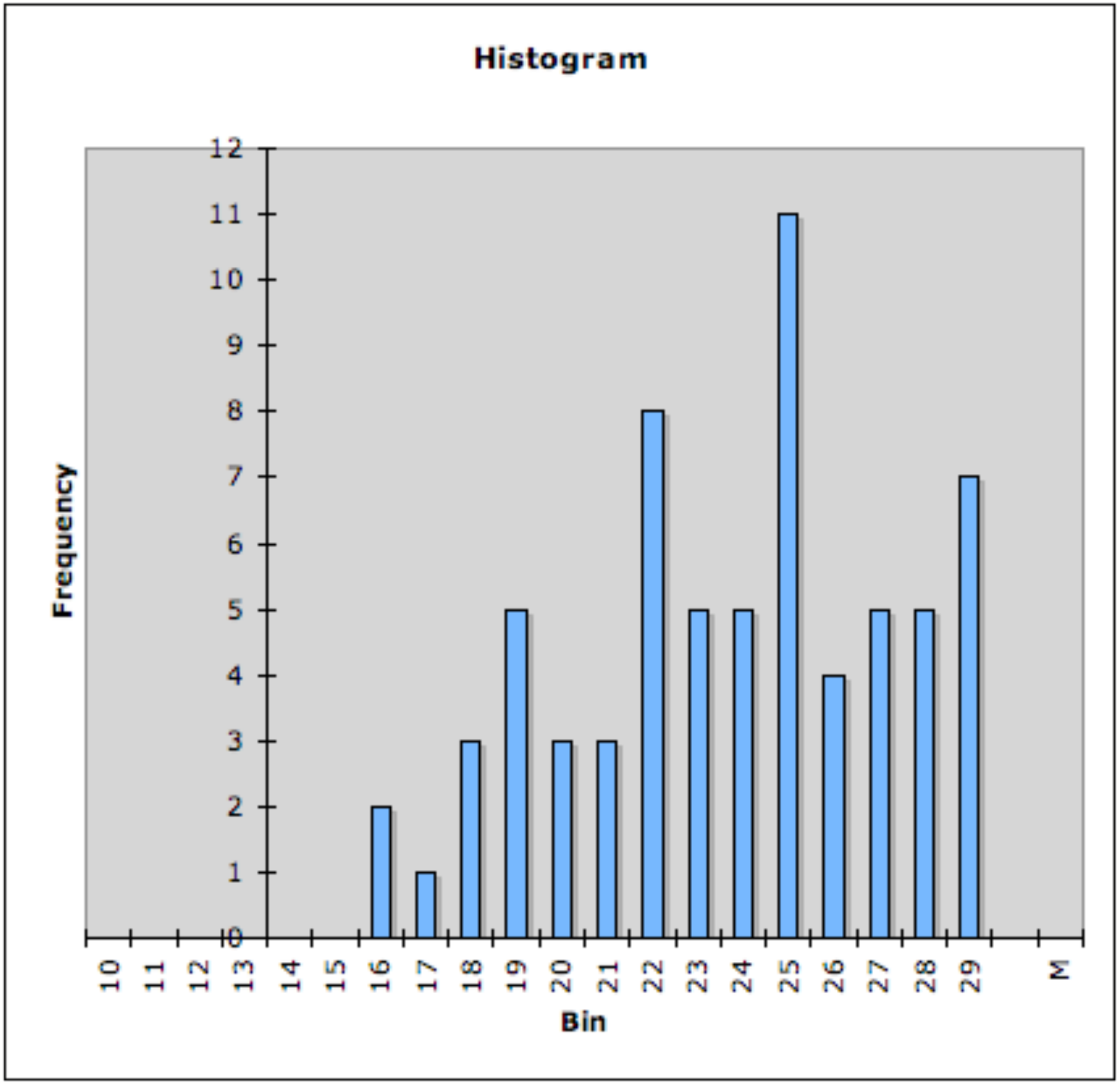
4. Potential for misinterpretation and misapplication
   - “Medicalization” and politicization of normal behaviors

# Summary

- Tools of the Trade
  - Twin, linkage, and association studies
  - Heritability Estimates (nature v. nurture)
  - Genes and causal pathways

- Specific studies
  - Minnesota, Hamer, voles, and mice
  - Types of inferences and limits of inference

- 4 Difficulties of Behavioral Genetics


Histogram
Frequency
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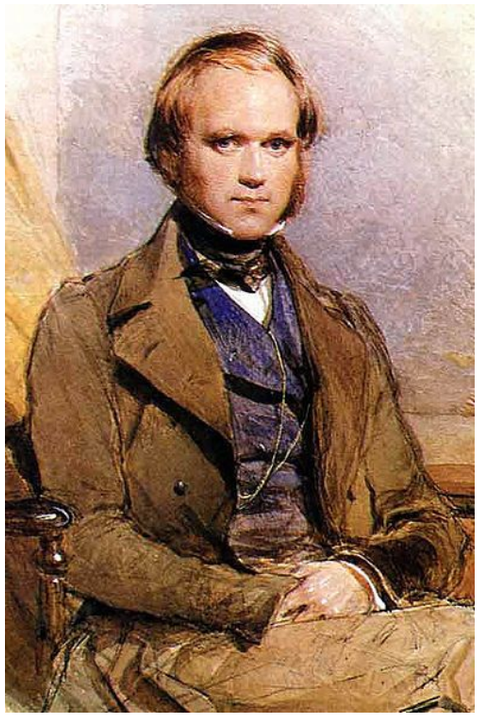
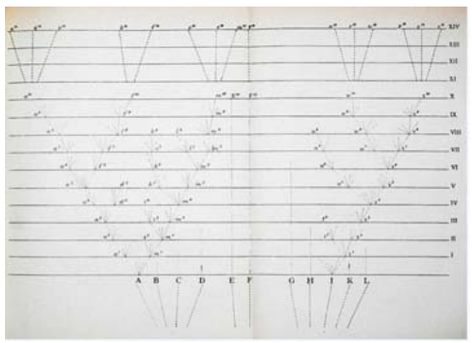
# Charles Darwin Film Series



Images from en.wikipedia.org



## *Evolution: Darwin's Dangerous Idea*

**Facilitator: Dr. Anya Plutynski**

Join the Marriott Library in celebrating Darwin's 200th birthday with the film *Evolution : Darwin's Dangerous Idea*. Evolutionary theory is featured in this film through the key moments in Darwin's life and current research utilizing dramatization and documentary sequences.

Dr. Anya Plutynski of the University of Utah's Philosophy Department will introduce the film and be available for questions and answers. Her research specialization is in the history and philosophy of science, particularly evolutionary biology in the early 20th century.

**Date: March 4, 2009**
**Time: 1:00 p.m.—3:00 p.m.**
**Place: Room 1120 Marriott Library**

Check **http://darwin2009.utah.edu** for more University of Utah and Marriott Library events.

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