Sex linked inheritance, Sex influenced inheritance and Sex limited trait

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Humans

- 22 Autosomes
  - Chromosomal abnormalities very severe
  - Often fatal
- All have at least one X
  - Deletion of X chromosome is fatal
- Males = heterogametic sex
  - XY
- Females = homogametic sex
  - XX

- Some traits are carried on the sex chromosomes, X and Y.
- Most traits carried are present on the X-chromosome.
- The Y-chromosome is smaller, and so, very few genes are located on this chromosome.

- Sex traits can be categorized into three types of inheritance:

  (i)sex-linked (X-linked dominant and recessive traits e. g. color blindness and hemophilia),

  (ii)Sex influenced and

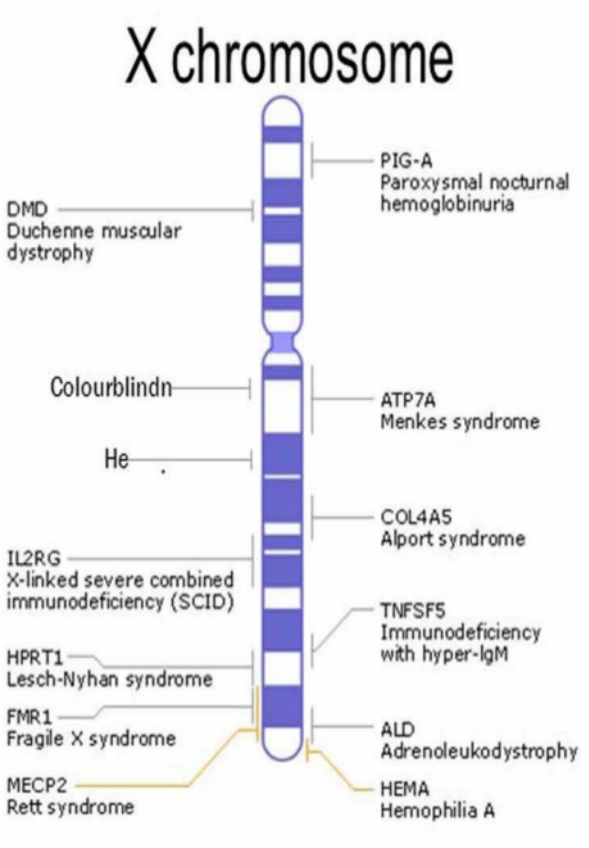
  (iii)sex-limited.

Sex-linked Genes

X chromosome:

•Contains ~1500 genes

- Characters for which genes are located on sex on X chromosomes are known as sex linked traits.
- Genes controlling these traits are called sex linked genes.
- Inheritance of such genes or characters is known as sex linked inheritance.
- Genes on the X chromosome are called “sex-linked”, because they expressed more often in males than in females.
- X-linked inherited diseases occur more frequently in males because they only have one X chromosome.
- In contrast, a mutant gene on an X chromosome in a female is usually covered up by the normal allele on the other X. Most mutations are recessive. So, most people with sex-linked genetic conditions are male.
- X linked inheritance may be X - linked dominant or X-linked recessive.
- Examples- Red Green Colour blindness, Hemophilia, Duchenne Muscular Dystrophy



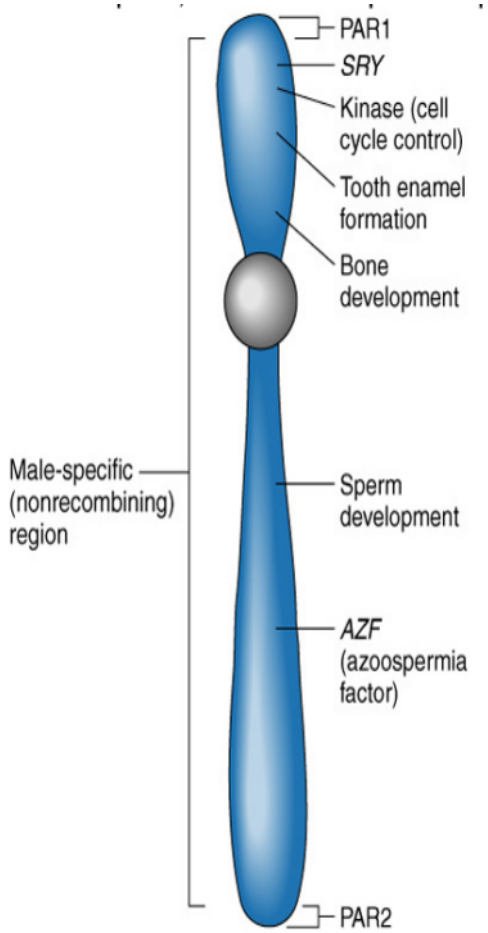
- The X chromosome contains over 153 million base pairs, the building blocks of DNA. In women, the X chromosome represents almost 5% of the total DNA and in men, who have only one X chromosome, it represents about 2.5% of the total DNA.
- Some genes on the X chromosome escape X-inactivation.
- Many of these genes are located at the ends of each arm of the X chromosome in areas known as the pseudoautosomal regions.
- Although many genes are unique to the X chromosome, genes in the pseudoautosomal regions are present on both sex chromosomes.
- As a result, men and women each have two functional copies of these genes.
- Many genes in the pseudoautosomal regions are essential for normal development.
- There are around 1500 genes located on the X chromosome and genetic research is focused on identifying these genes. These proteins perform a variety of different roles in the body.

Inheritance of Colorblindness

- A heterozygous female has normal color vision. Sons get their only X from their mother. So, ½ of the sons of a heterozygous mother are colorblind, and ½ are normal.
- A colorblind male will give his X to his daughters only. If the mother is homozygous normal, all of the children will be normal.
- However, the daughters will heterozygous carriers of the trait, and ½ of their sons will be colorblind.

Y chromosome

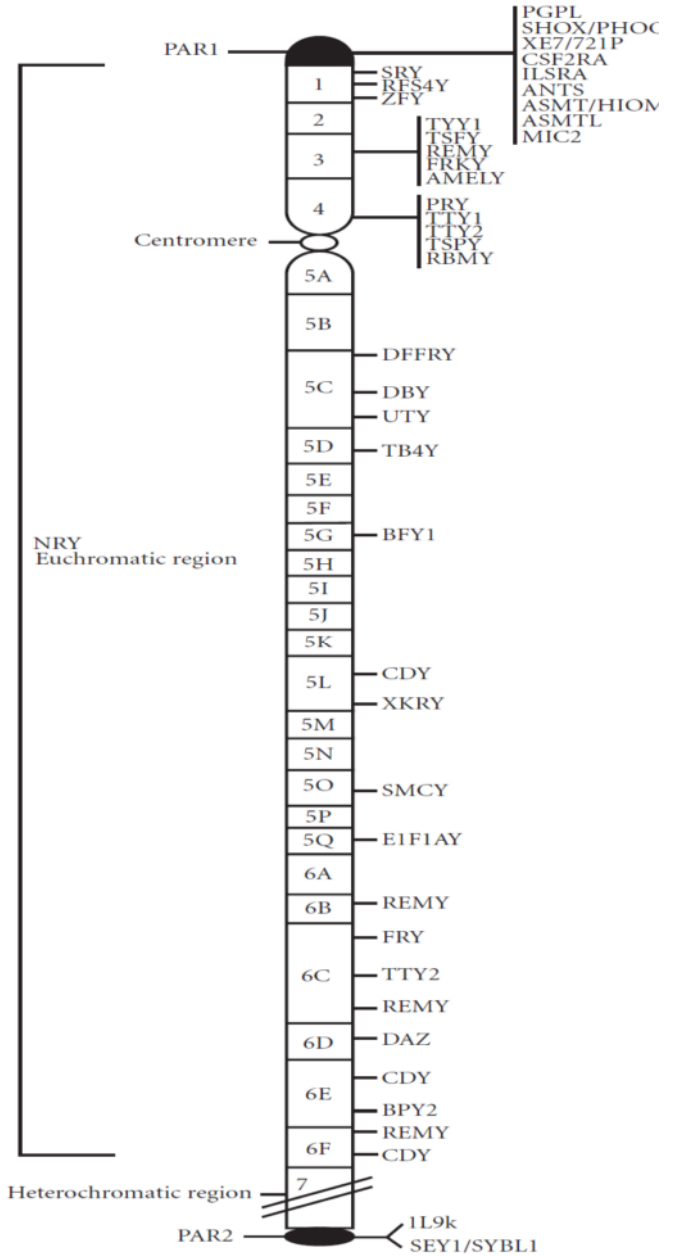
- Contains ~78 genes
- Majority of genes = Male Specific Region (MSR)
- SRY gene – determines “maleness”
- The Y chromosome is passed from father to son.
- SRY = **S**ex-determining **R**egion of **Y**
- A transcription factor (TF)
- TF’s are genes that control the expression of other genes (turn on/off)
- SRY turns on “male” genes
- “Male” genes activate male hormones
- Male hormones (testosterone) end up producing male structures
- Also, destroy female structures


PAR1
SRY
Kinase (cell cycle control)
Tooth enamel formation
Bone development
Male-specific (nonrecombining) region
Sperm development
AZF (azoospermia factor)
PAR2

- The Y is one of the smallest chromosomes in the human genome (~ *60 Mb)and represent around 2%–3%* of a haploid genome.

- Cytogenetic observations based on chromosome-banding studies allowed different Y regions to be identified: the pseudoautosomal portion (divided into two regions: **PAR1 and PAR2**)and the euchromatic and heterochromatic regions.

- The Pseudoautosomal regions (PAR): PAR1 is located at the terminal region of the short arm (Yp), and the PAR2 at the tip of the long arm (Yq). PAR1 and PAR2 cover approximately 2600 and 320 kb of DNA, respectively.



Schematic representation of the Y chromosome. Genes in the two pseudoautosomal regions (PAR1 and PAR2)as well as in the nonrecombining Y region (NRY)ar e illustrated

Quintana-Murci and Fellous, 2001.Journal of Biomedicine and Biotechnology, 1:18–24

- The pseudoautosomal regions, and in particular PAR1, are where the Y chromosome pairs and exchanges genetic material with the pseudoautosomal region of the X chromosome during male meiosis.
- Consequently, genes located within the PAR are inherited in the same manner as autosomal genes. The euchromatic region is distal to the PAR1 and consists of the short arm paracentromeric region, the centromere and the long armparacentromericregion.
- Finally, the heterochromatic region comprises distal Yq corresponding to Yq12. This region is assumed to be genetically inert and polymorphic in length in different male populations, since it is composed mainly of two highly repetitive sequences families, DYZ1 and DYZ2, containing about 5000 and 2000 copies of each respectively.

Quintana-Murci and Fellous, 2001.Journal of Biomedicine and Biotechnology, 1:18 –24

Genes of the human Y chromosome PAR1, PAR2, and NRY.

Gene symbol	Location	Gene name	Associate pathology/function	X-homologs
CSFR2Rα	PAR1	GM-CSF receptor α subunit	unknown	+
SHOX	"	Short stature homebox-containing	short stature, Lerf-Weill syndrome	+
IL3RA	"	Interleukin-3 receptor α subunit	unknown	+
ANT3	"	Adenine nucleotide translocase	unknown	+
ASMTL	"	Acetylserotonine methyltransferase-like	unknown	+
ASMT	"	Acetylserotonine methyltrans-ferase	unknown	+
XE7	"	X-escapee	unknown	+
PGPL	"	Pseudoautosomal GTP-binding protein-like	unknown	+
MIC2	"		unknown	+
SRY*	Yp: 1A1A	Sex Reversal Y	Sex reversal	–
RPS4Y	Yp: 1A1B	Ribosomal protein S4, Y	Turner syndrome?	+
ZFY	Yp: 1A2	Zinc-finger Y	Turner syndrome?	+
PRKY	Yp: 3C-4A	protein kinase, Y	unknown	+
TTY1*	Yp: 4A	testis transcript, Y1	unknown	–
TSPY*	Yp: 3C+5	testis-specific protein, Y	gonadoblastoma?	–
AMELY	Yp: 4A	Amelogenin, Y	unknown	+
PRY*	Y: 4A, 6E	putative tyrosine phosphatase protein-related Y	infertility?	–
TTY2*	Y: 4A, 6C	testis transcript, Y2	unknown	–
USP9Y (or DFFRY)	Yq: 5C	ubiquitin-specific protease (or Drosophila fat-facets related, Y)	azoospermia?	+
DBY	Yq: 5C	DEAD box, Y	infertility?	+
UTY	Yq: 5C	Ubitiquitous TRY motif, Y	infertility	+
TB4Y	Yq: 5D	Thymosin ?4, Y isoform	infertility	+
BPY1*	Yq: 5G	basic protein, Y1	Turner?	+
CDY	Yq: 5L, 6F	chromodomain, Y	infertility?	–
XKRY*	Yq: 5L	XK-related, Y	infertility?	–
RBM*	Yp+q	RNA-binding motif, Y	infertility?	–
SMCY	Yq: 5P	Selected Mouse cDNA, Y	unknown	+
EIF1AY	Yq: 5Q	Translation initiation factor 1A, Y	infertility?	+
DAZ*	Yq: 6F	Deleted in azoospermia	infertility?	–
VCY2	Yq: 6A	variably charged protein, Y2	infertility	–
IL9R	PAR2	Interleukin 9 receptor	unknown	+
SYBL1	"	Synaptobrevin-like 1	unknown	+
HSPRY3	"	Human-sprouty 3	unknown	+
CXYorf1	"	CXYorf1	unknown	+

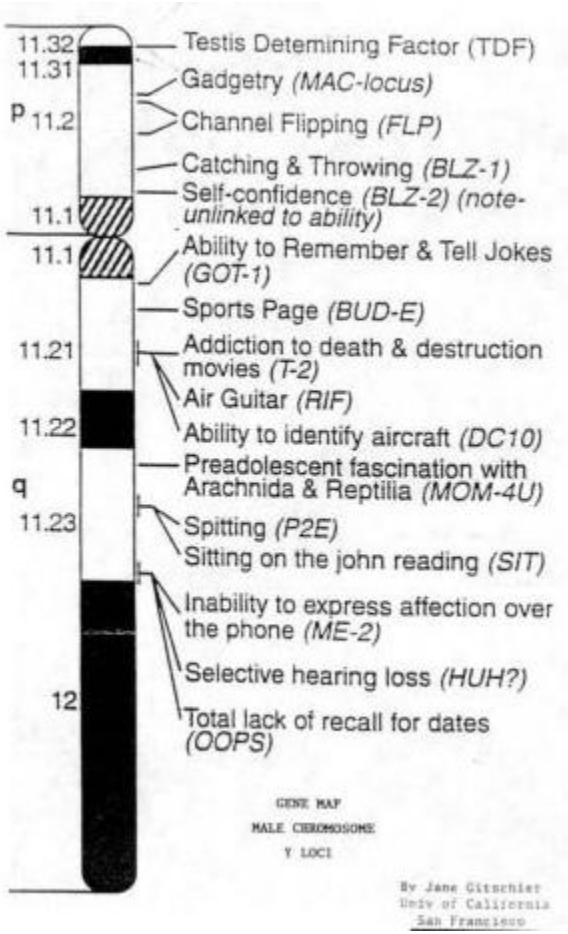
*Testis-specific genes or families.

Note: All genes expressed specifically in the testis are present in multiple copies dispersed throughout the euchromatic portion of the Y chromosome. Exceptional is SRY, which is expressed specifically in the testis but present in single copy.

Quintana-Murci and Fellous, 2001. Journal of Biomedicine and Biotechnology, 1:18-24

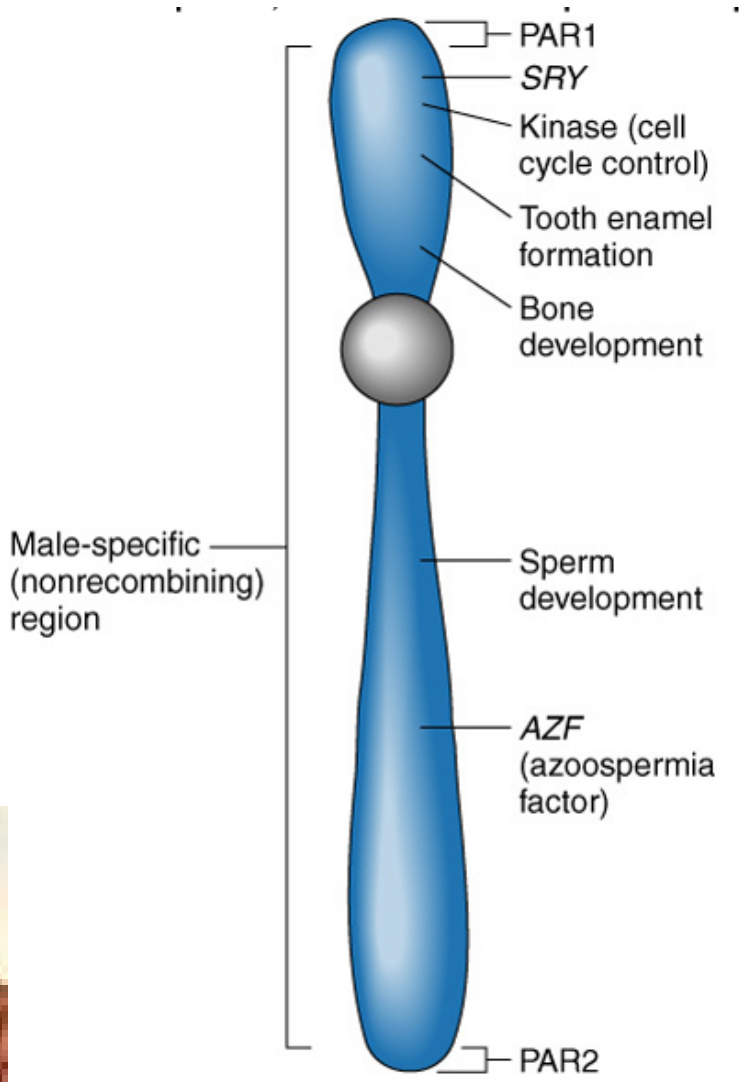
The term hemizygous is used for X linked gene in males as they carry only one allele with regard to sex linked trait.

Pseudo-dominance is phenomenon in which a single copy of recessive allele is phenotypically expressed because a second copy of the gene is absent. This pseudo dominance found in male in humans.



SRY Gene

- SRY = **S**ex-determining **R**egion of **Y**
- A transcription factor (TF)
  - TF's are genes that control the expression of other genes (turn on/off)
- SRY turns on "male" genes
- "Male" genes activate male hormones
- Male hormones (testosterone) end up producing male structures
- Also, destroy female structures
- Example -Hairy Ears



Sex-influenced Character/ Sex-controlled character

- Sex-controlled character, also called Sex-influenced Character, a genetically controlled feature that may appear in organisms of both sexes but is expressed to a different degree in each.
- **Sex-influenced traits are autosomal traits that are influenced by sex.**
- **The character seems to act as a dominant in one sex and a recessive in the other**

What is a sex-influenced trait?

•Sex-influenced traits are **autosomal traits that are influenced by sex**. If a male has one recessive allele, he will show that trait, but it will take two recessive for the female to show that same trait.

•**Sex-Influenced Traits: expressed in both sexes, but they are expressed differently (Pattern Baldness)**

•A sex-influenced trait is a trait controlled by a pair of alleles found on the autosomal chromosomes (pairs 1 through 22) but it's phenotypic expression is influenced by the presence of certain hormones. Sex-influenced traits can be seen in BOTH sexes, but will vary in frequency between the sexes, or in the degree of the phenotypic expression.

•An allele is dominant in one sex but recessive in the other sex.

•May be X-linked or autosomal

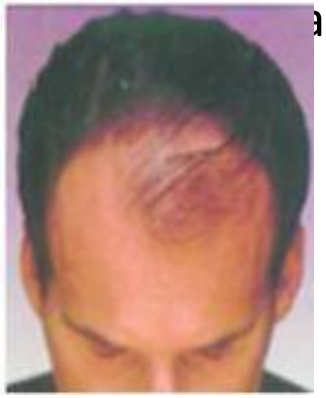
Sex-Influenced Traits

Some traits appear to be specific to one sex, but are not sex-linked: their genes are not on the X chromosome.

Such a trait is called sex-influenced. More specifically, a trait that is dominant in one sex but recessive in the other is a sex-influenced trait.

The best human example is male pattern baldness.

Baldness is dominant in males: heterozygotes and homozygotes both become bald. In females, baldness is recessive: only homozygotes (which are relatively rare) become bald. Also, females tend to lose hair more evenly than men, giving a sparse hair pat an completely baldness



	BB	Bb	bb
male	bald	bald	hair
female	bald	hair	hair

Pattern Baldness

- Pattern Baldness can occur in both males and females, however it is much more common in males.
- The combination of alleles for pattern baldness will lead to different phenotypic expressions depending on the sex of the individual.

Why is this?

Because the pattern baldness trait is influenced by the hormone testosterone.

For example:

B-represent the non-bald allele

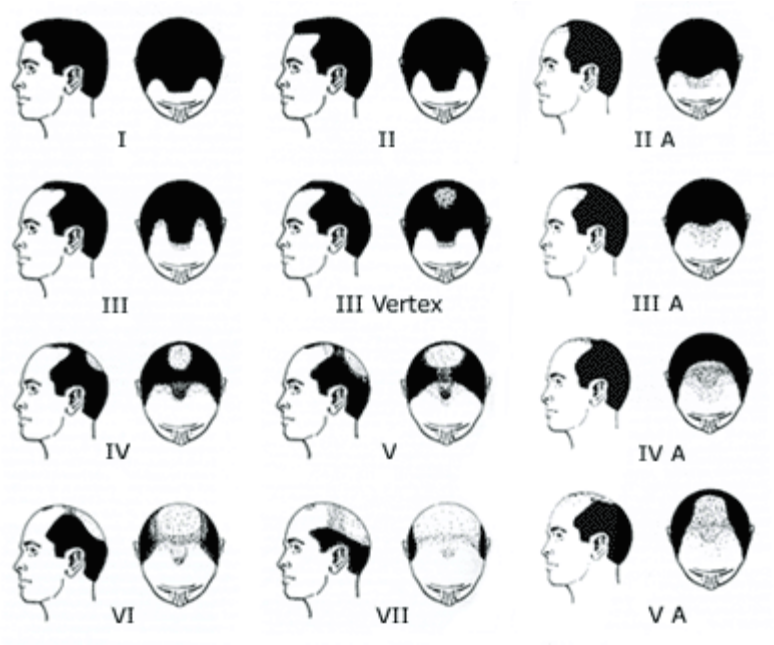
BB genotype: non-bald in both sexes

bb genotype: bald in both sexes

Bb genotype: bald in men; non-bald in females

Pattern Baldness

The “B” allele acts as a dominant allele in the heterozygous genotype in females, but acts as a recessive allele in the heterozygous genotype of the male.



Rheumatoid arthritis

- **Rheumatoid arthritis (RR) occurs more often in females than males due to the presence of estrogen.**
- A heterozygous woman marries a heterozygous male.
- RR would cause the condition in both sexes.
- A homozygous recessive, rr, genotype would prevent the disorder in both sexes

Sex Limited Traits

- Sex-limited traits are traits that are visible only within one sex.
- Genes are inherited from both parents
- **Either autosomal or X chromosome**
- Yet, affect a structure that is only present in one sex, therefore **phenotype shows a sex "difference"**
- A trait that affects a structure or function of the body that is present in only one of the sexes.

Sex Limited Traits

- Sex limited traits are those characters that are expressed physically in one sex of a species. These traits are controlled by sex limited genes or autosomal genes that are expressed only in one sex.
- These genes are present in both sexes of sexually reproducing species.
- Although they are present in both the sexes they are expressed in only one sex while in the other they remain “turned off”, which means that the trait has zero penetrance in the other sex.
- Despite having the same genotype, both the sexes show different traits or phenotypes for these genes.
- These genes are responsible for sexual dimorphism in a given species.
- Sex hormone and other physiological differences between male and female affect the expression of these genes.

Sex Limited Traits

•These genes enable both the sexes to settle down to their optimal phenotypes by avoiding the intralocus sexual conflict. This resolves the “push and pull” between the sexes over the trait.

•The differences in both the sexes can be displayed in size, color, and morphology.

•Examples

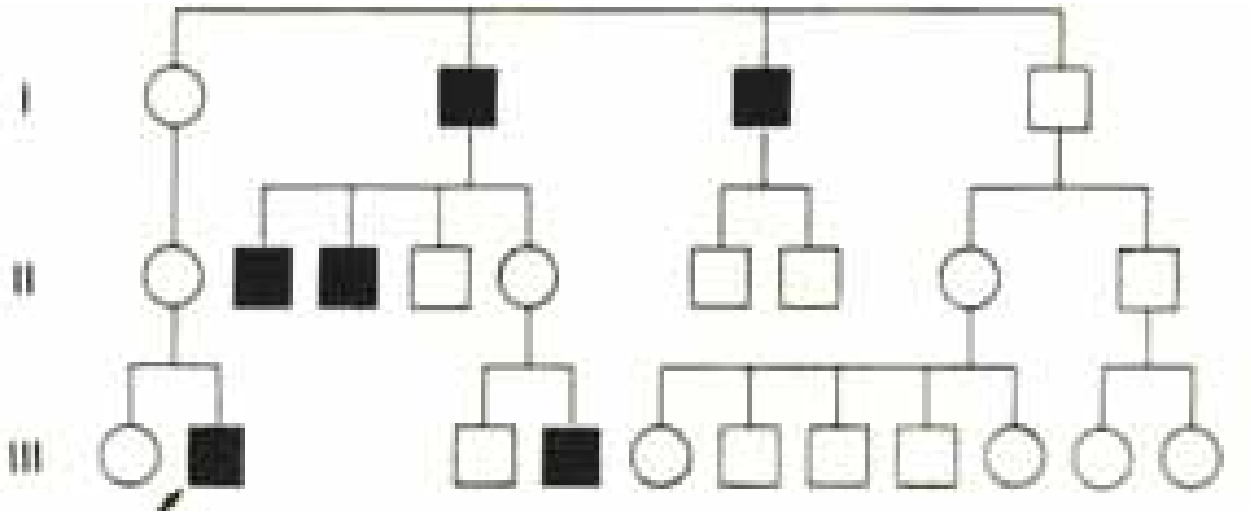
(i)Horns in cattes

(ii)Milk production

Another example is the **milk secretion in cattle**. Although both sexes carry the milk controlling genes, only the female cattle secrete milk. The genes that control milk yield and quality in dairy cattle, for example, are present in both bulls and cows, but their effects are expressed only in the female cattle.

Pedigree Analysis in real life: complications

Sex-limited expression
=> trait only found in males OR females



Sex-limited traits

•Sex-limited traits are traits that are visible only within one sex.

•In birds, sex mechanism is ZZ/ZW type (**ZZ-male,ZW-female)**.

•For instance, **barred coloring in chickens** normally is visible only in the roosters (A **rooster**, also known as a **cockerel** or **cock**, is an adult male chicken(*Gallus gallus domesticus*).

•**Sex-linked barring** is a **plumage pattern** on individual feathers in chickens, which is characterized by alternating pigmented and a pigmented bars.

•The pigmented bar can either contain red pigment (pheomelanin) or black pigment (eumelanin) whereas

Hackle feathers

Sex-Limited Traits: autosomal traits expressed in only one sex (Lion’s mane)

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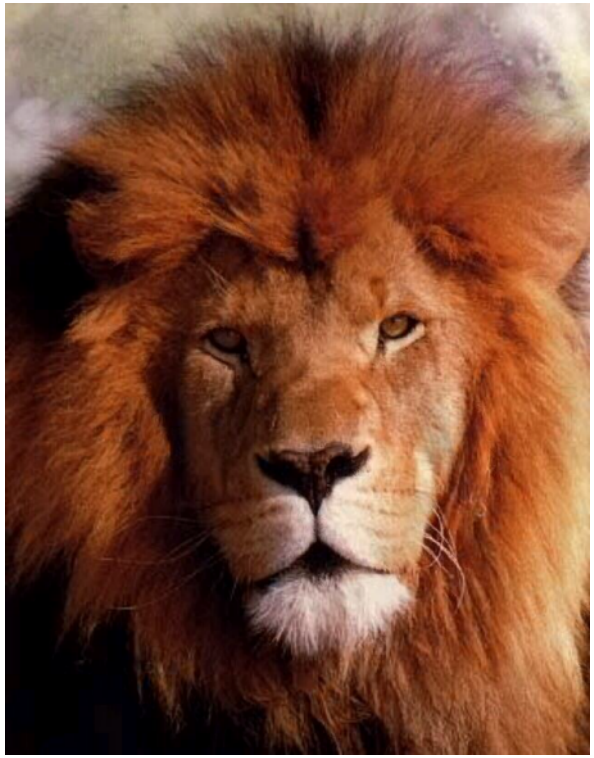

Suggested Reading

1. Human Molecular Genetics – Tom Stratchen & Andrew P. Read. Pub: John Wiley & Sons.
2. An introduction to Genetic Analysis– Griffith, Miller, Suzuki, Lewontin, Gelbard. Pub: W.H. Freeman & Co.
3. Genomes 2 – T.A. Brown, Pub: Wiley-Liss. John W. & Sons.
4. Emery's Elements of Medical Genetics– R.F. Mueller, I.D. Young, Pub: Churchill
5. An Introduction to Human Molecular Genetics– J.J. Pasternak, Pub: Fitzgerald Science