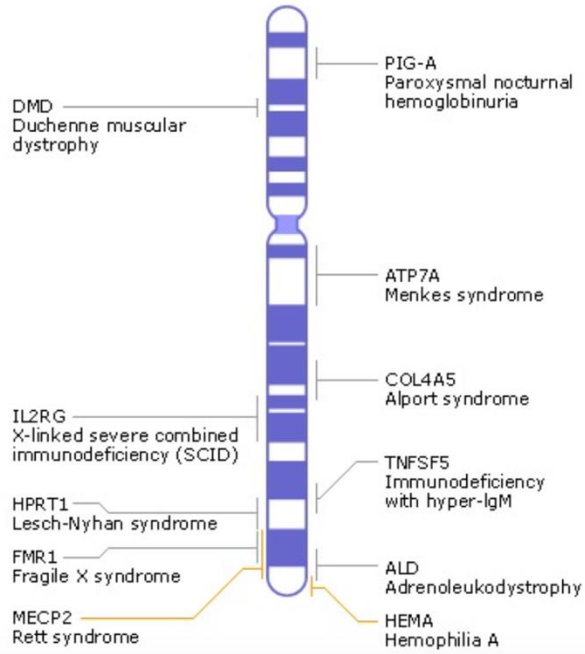
Sex-linkage and Human Disease

Below is a screen shot of from the book 'Genes and Disease'. Specifically, the image identifies some of the genes associated with X-linked human diseases.

Chromosome X Go to:

- Contains over 1400 genes
- Contains over 150 million base pairs, of which approximately 95% have been determined
- See the diseases associated with chromosome X in the NCBI Genome Data Viewer.



With your group research three of the genes/disease identified in the figure to the left and complete the table below.

Disease	Associated X-linked gene	Inheritance pattern	Disease Symptoms

Select one disease that is *inherited* to continue to investigate through the rest of this activity.

Answer the following questions:
What is the name of the disease/disorder that you selected?

What gene is mutated in this disease/disorder?

What is the inheritance pattern of this disease/disorder?

In humans, which is the hemizygous sex?

X/Y Chromosomal inheritance

Using construction paper create:
9 X-chromosomes (strips of construction paper)
3 Y- chromosomes (shorter & different colored strips of construction paper)

Randomly assign the mutated (disease carrying) or non-mutated (non-disease carrying) allele to each X-chromosome (write a designation on the paper, use a colored sticker… Whatever makes sense to your group).

Randomly put 6 X-chromosomes in one pile
Put the remaining 3 chromosomes in a different pile with the 3 Y chromosomes

Why does one pile have only Xs and the other pile has both Xs and Ys?

Draw 1 chromosome from pile #1

- Enter its type (X or Y) into the first cell in the table below
- Enter its genotype (mutant/disease carrying or non-mutant) in the second cell in the table below

Draw 1 chromosome from pile #2

- Enter its type (X or Y) into the first cell in the table below
- Enter its genotype (mutant/disease carrying or non-mutant) in the second cell in the table below

Based on the two chromosomes drawn and the disorder/disease's inheritance pattern determine the Offspring sex, Offspring Genotype, and Offspring Phenotype

Repeat until you have created 6 offspring

Chrom1 (X or Y)	Chrom 1 genotype	Chrom 2 (X or Y)	Chrom 2 genotype	Offspring Sex	Offspring Genotype	Offspring Phenotype

Do you see any patterns in the offspring genotypes and phenotypes?

Is one sex more likely to have the disease phenotype than the other?
Why?

*****Discuss the disease/disorder you choose with the class******

X-inactivation

🧬 **What is X-Inactivation?**

X-inactivation is a process that occurs in **mammals with more than one X-chromosome** to balance the expression of **X-linked genes** between XY and XX individuals. In individuals with two X chromosomes, one of them is **randomly inactivated** in each cell during early embryonic development. The inactivated X chromosome condenses into a structure called a **Barr body** and is largely **transcriptionally silent**.

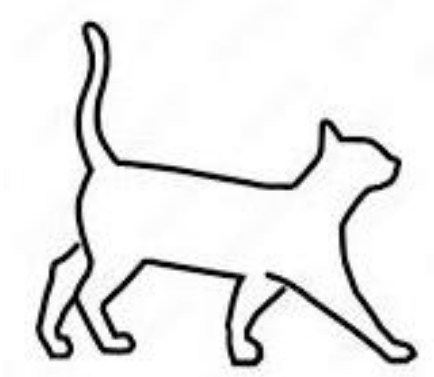
This means that in heterozygous XX(+) individuals—those with two different alleles for an X-linked gene—some cells express one allele, and some express the other. Which expresses which is determined very early, when the embryo is a blastula. Once the pattern is set all cells descended from the cells present in the blastula (via mitosis) maintain the same silenced X. This is called a **mosaic pattern of gene expression.**

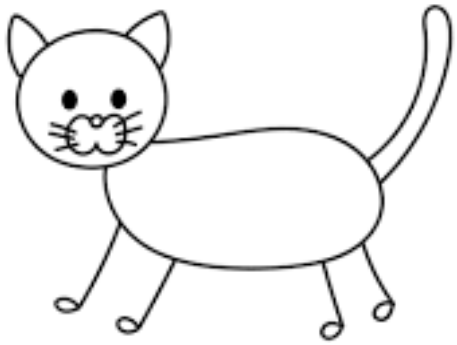
In cats
A gene for coat color called 'orange'
Has two alleles (O = orange, o = black/brown)
This gene is carried on the X-chromosome

What is the sex _____ and genotype _____ of a cat who is heterozygous for the 'orange' gene?

Using the paper provided, create a large outline of a cat.
This cat is heterozygous.

Using the construction paper provided, create a visual representation of what this heterozygous cat's coat should look like. Label the alleles expressed.





Could a cat with male-typical phenotype (testicles, a penis) have the pattern you've created on your cat outline?

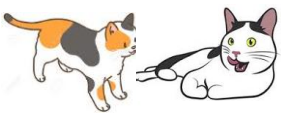
Was your cat completely black and orange like this?

So, how do we get this??

A **second gene** is involved in the coat color of calico cats (the ones with white fur).
This second gene is autosomal.

What does 'autosomal' mean?

The KIT gene is the primary gene involved in the white patches of calico cats. It has three alleles with the following dominance pattern.
$W^D > w^s > w$

Allele	Phenotype	
W^D	dominant white	
w^s	white patches	
w	no white	

What is it called when the expression of one gene masks or modifies the effect of another gene at a different locus?

Alter your cat's coat color to the expected phenotype in each of the following genotypes:

Oo W^Dw^s

Oo ww

Oo w^sw

What is this interaction between two genes to produce a series of different phenotypes called?