**What does a mutation do?**

Now that we understand how DNA works we want to understand at the molecular level what is happening with the genes in the Marcus, Reed, Summers and Medeiros families.

We have the pedigrees and we have sequences available for some members of the families. In groups we will work towards understanding what has happened in the genes underlying the health conditions in the different families. Each of you will analyze one sequence and report to the rest of the research group.

The first step is to translate the sequence into amino acids. Below you will find two tables with the codon assignment. Both tables have the same information, but the organization is different. Then you will analyze the sequences and **figure out** **what is happening with the protein**. After sharing your findings with your colleagues you should have a molecular explanation for the health conditions that afflict the different families.

|  |  |  |
| --- | --- | --- |
| **Health Condition:** | **Gene underlying health condition:** | **What is happening with the gene?**  **(What type of mutation did you find?)** |
| Osteogenesis Imperfecta |  |  |
| PKU |  |  |
| Achondroplasia |  |  |
| Duchenne’s Muscular Dystrophy |  |  |

Please describe some different types of mutations that can have an effect on a protein.

(Mutation is any change in a genetic sequence).

Can you identify mutations that have no effect on the protein? Why would this be possible?

**Genetic code**

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | **Second base** | | | | | | | |  |  |
|  |  | **T** | | **C** | | **A** | | **G** | |  |  |
| **First base** | **T** | **T T T** | Phenyl  Alanine (**F**) | **T C T** | Serine (**S**) | **T A T** | Tyrosine (**T**) | **T G T** | Cysteine (**C**) | **T** | **Third base** |
| **T T C** | **T C C** | **T A C** | **T G C** | **C** |
| **T T A** | Leucin | **T C A** | **T A A** | STOP | **T G A** | STOP | **A** |
| **T T G** | **T C G** | **T A G** | STOP | **T G G** | Tryptophan (**W**) | **G** |
| **C** | **C T T** | Leucin (**L**) | **C C T** | Proline (**P**) | **C A T** | Histidine (**H**) | **C G T** | Arginine (**R**) | **T** |
| **C T C** | **C C C** | **C A C** | **C G C** | **C** |
| **C T A** | **C C A** | **C A A** | Glutamine (**Q**) | **C G A** | **A** |
| **C T G** | **C C G** | **C A G** | **C G G** | **G** |
| **A** | **A T T** | Isoleucin (**I**) | **A C T** | Threonine (**T**) | **A A T** | Aspargine (**N**) | **A G T** | Serine (**S**) | **T** |
| **A T C** | **A C C** | **A A C** | **A G C** | **C** |
| **A T A** | **A C A** | **A A A** | Lysine (**K**) | **A G A** | Arginine (**R**) | **A** |
| **A T G** | Methionine (**M**) (START) | **A C G** | **A A G** | **A G G** | **G** |
| **G** | **G T T** | Valine (**V**) | **G C T** | Alanine (**A**) | **G A T** | Aspartic acid (**D**) | **G G T** | Glycine (**G**) | **T** |
| **G T C** | **G C C** | **G A C** | **G G C** | **C** |
| **G T A** | **G C A** | **G A A** | Glutamic acid (**E**) | **G G A** | **A** |
| **G T G** | **G C G** | **G A G** | **G G G** | **G** |

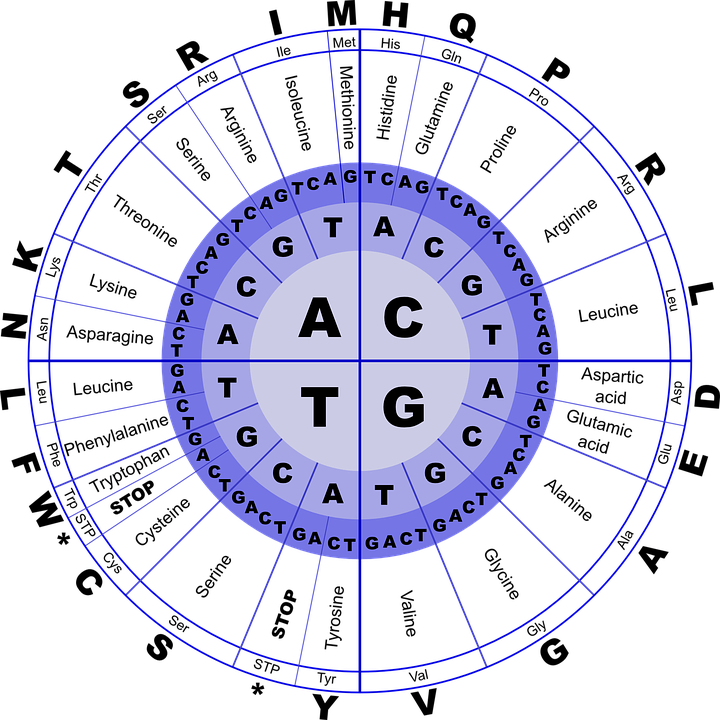


Image obtained from Pixabay: No attribution required.

**Marcus family**

Joy and Aaron Marcus have come to the Genetics Center because they are concerned about their newborn daughter, Janice. Because achondroplasia runs in Joy and Aaron’s family (see the family pedigree), the genetic counselor suggests Joy and Aaron to get genetic tested. With the test they will be able to identify if there are any changes in the *FGFR3* gene and confirm or rule out if this is the genetic condition afflicting Janice.

Joy and Aaron agreed to get tested, but they decided not to test Janice. Other members of the family, Carl, Ruth, Mat, Nat and Jack, also got tested (noted with an asterisk on the pedigree). Bellow you will find one of the many nucleotide sequences of the *FGFR3* gene that has been linked to achodroplasia. *FGFR3* gene is located on chromosome 4. Remember from previous models that individuals have two alleles (alternative forms) for each gene except for some of the genes that are on the sex chromosomes—males will have only one allele.

The top sequence is the reference sequence—the most common sequence present in individuals that do not present the medical condition. Dots indicate identical nucleotides. Bold letters indicate nucleotides that are different between alleles.

Ref. sequence: GGC ATC CT**C** AGC TAC **G**GG GTG GGC TTC TTC

Carl ... ... ... ... ... **G**.. ... ... ... ...

Carl ... ... ... ... ... **G**.. ... ... ... ...

Joy ... ... ... ... ... **C**.. ... ... ... ...

Joy ... ... ... ... ... **G**.. ... ... ... ...

Aaron ... ... ... ... ... **A**..... ... ... ...

Aaron ... ... ... ... ... **G**.. ... ... ... ...

Ruth ... ... ... ... ... **G**.. ... ... ... ...

Ruth ... ... ... ... ... **G**.. ... ... ... ...

Mat ... ... ..**G** ... ... **G**.. ... ... ... ...

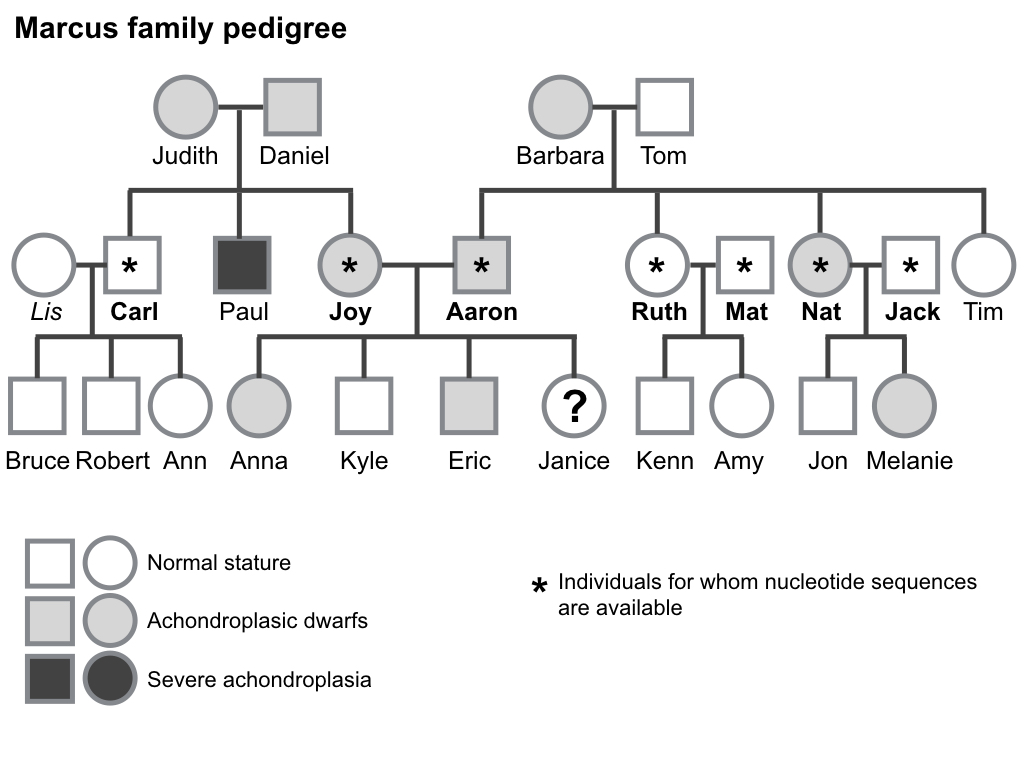
Mat ... ... ... ... ... **G**.. ... ... ... ...

Nat ... ... ... ... ... **A..** ... ... ... ...

Nat ... ... ... ... ... **G**.. ... ... ... ...

Jack ... ... ... ... ... **G**.. ... ... ... ...

Jack ... ... ... ... ... **G**.. ... ... ... ...

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**Reed Family**

Carolyn and John Reed brought their one year-old daughter Samantha to the Clinical Genetics Center because they are concerned that she might have Osteogenesis Imperfecta (OI).

Because OI runs in the Reed family (see the family pedigree), the genetic counselor suggested Carolyn and John to get genetic tested. The test to identify changes in *COL1A1* gene is available in clinical laboratories and will allow them to confirm or rule out if OI is the genetic condition that Samantha carries.

Because genetic tests can be expensive and are usually not covered by the insurance, Carolyn and John decided to ask just few members of the family to get tested. Below you will find a short nucleotide sequence for one of the many regions of the *COL1A1* gene that is linked with OI. (Family members that got tested are denoted with an asterisk on the pedigree). *COL1A1* gene is located on chromosome 17. Remember from previous models that individuals have two alleles (alternative forms) for each gene except for some of the genes that are on the sex chromosomes—males will have only one allele.

The top sequence is the reference sequence—the most common sequence present in individuals that do not present the medical condition. Dots indicate identical nucleotides. Bold letters indicate nucleotides that are different between alleles. Dash line (-) indicates absence of that nucleotide.

Ref. sequence: CC**T** GGT GC**T CCT GGT GC**C CCT GGC CCC GT**T**

Carolyn ... ... ... ... ... ... ... ... ... ...

Carolyn ..**C** ... ... ... ... ... ... ... ... ...

Frank ... ... ... ... ... ... ... ... ... ..**A**

Frank ... ... ..**- --- --- --**. ... ... ... ..**A**

John ... ... ..- --- --- --. ... ... ... ...

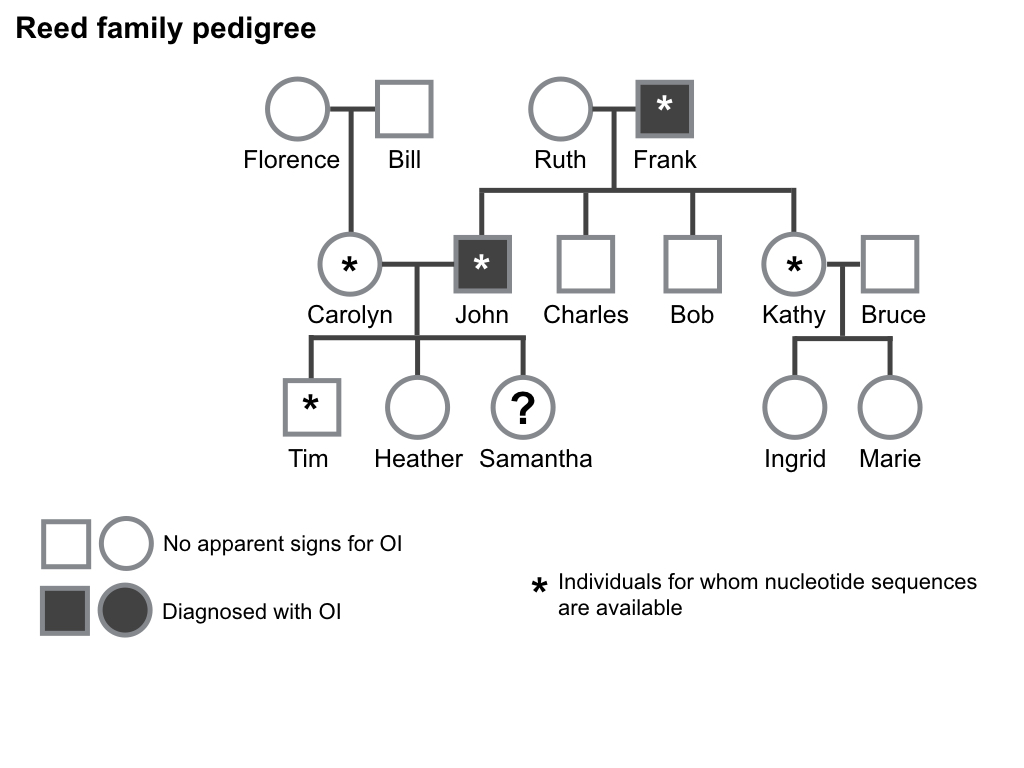
John ... ... ... ... ... ... ... ... ... ...

Kathy ... ... ... ... ... ... ... ... ... ..**A**

Kathy ... ... ... ... ... ... ... ... ... ...

Tim ... ... ... ... ... ... ... ... ... ..**A**

Tim ..**C** ... ... ... ... ... ... ... ... ...

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**Medeiros family**

Juan and Cecelia Medeiros brought their son, Manuel, to the Genetics Counseling Clinic because he was beginning to show symptoms similar to those of his cousin David who has Duchenne’s Muscular Dystrophy (DMD). They are very concerned because David, age 18, is now confined to a wheel chair and he is not expected to live much past his twentieth birthday.

Because of the inheritance pattern of DMD, the genetic counselor suggested Juan and Cecilia to get their son genetic tested. The test to identify changes in *Dystrophin* gene is available in clinical laboratories and will allow them to confirm or rule out if Manuel is afflicted by DMD.

Cecilia was able to convince here sister Linda to get tested. Below you will find a short nucleotide sequences for one of the many regions of *Dystrophin* gene that has been linked to DMD. (Individuals with available sequences are denoted with an asterisk on the pedigree). *Dystrophin* gene is located on chromosome X. Males will have one allele (alternative form), while females will have two alleles.

The top sequence is the reference sequence—the most common sequence present in individuals that do not present the medical condition. Dots indicate identical nucleotides. Bold letters indicate nucleotides that are different between alleles. Dash line (-) indicates absence of that nucleotide

Ref. sequence: C A G G C **C** A A A T G T A A **- - - -** C A T C T G

Linda . . . . . . . . . . . . . . - - - - . . . . . .

Linda . . . . . . . . . . . . . . G T A A . . . . . .

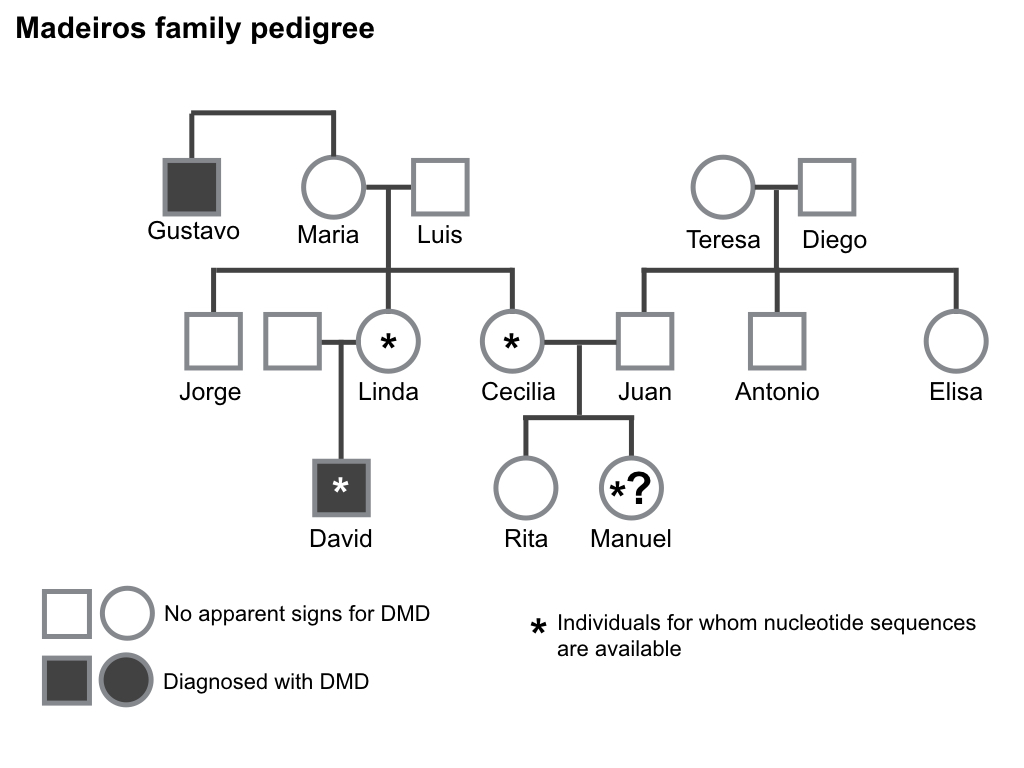
Cecilia . . . . . . . . . . . . . . - - - - . . . . . .

Cecilia . . . . . . . . . . . . . . G T A A . . . . . .

Juan . . . . . **G** . . . . . . . . G T A A . . . . . .

Manuel . . . . . . . . . . . . . . - - - - . . . . . .

**Medeiros family pedigree**

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**Summers family**

Joe and Angie, recently had their second child, Jane, who was diagnosed with phenylketonuria (PKU) at the time of her birth. To learn more about their daughter’s disease Joe and Angie decided to get their family genetic tested for the gene that codes for the enzyme Phenylalanine hydroxylase(PHA).

Bellow you will find a short nucleotide sequence for the *PHA* gene for Joe, Angie, Josh, Jane and Tom. *PHA* gene is located on chromosome 12. Remember from previous models that individuals have two alleles (alternative forms) for each gene except for some of the genes that are on the sex chromosome—males will have only one allele.

The top sequence is the reference sequence—the most common sequence present in individuals that do not present the medical condition. Dots indicate identical nucleotides. Bold letters indicate nucleotides that are different between alleles.

Ref. sequence: GCT GCC AC**A** ATA CCT **C**GG CCC TTC TCA GTT

Angie ... ... ..**T** ... ... **.**.. ... ... ... ...

Angie ... ... ..**T** ... ... **T**.. ... ... ... ...

Josh ... ... ..**T** ... ... ... ... ... ... ...

Josh ... ... ... ... ... ... ... ... ... ..**.**

Joe ... ... ... ... ... **T**.. ... ... ... ...

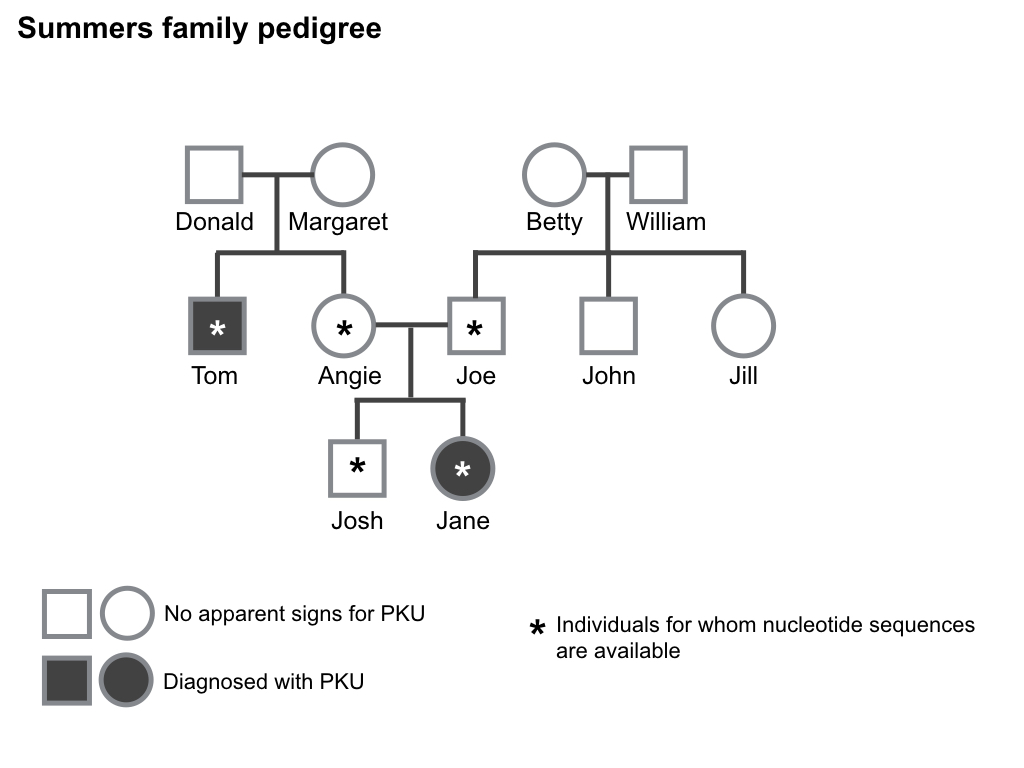
Joe ... ... ... ... ... ... ... ... ... ..**.**

Jane ... ... ..**T** ... ... **T**.. ... ... ... ...

Jane ... ... ... ... ... **T**.. ... ... ... ...

Tom ... ... ..**T** ... ... **T**.. ... ... ... ...

Tom ... ... ... ... ... **T**.. ... ... ... ...

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