NATIONAL **FRAGILE X** FOUNDATION

GENETICS OF FRAGILE X

WHAT ARE CHROMOSOMES AND GENES?

Our bodies are made of 60 trillion cells.

Each cell has 23 pairs of **chromosomes** – one copy in each pair comes from our biological mom and the other copy comes from our biological dad. The chromosomes are numbered 1 to 22. The 23rd pair is called **sex chromosomes**.

For sex chromosomes, females typically have two X chromosomes; males typically have one X and one Y chromosome. Each chromosome is broken up into thousands of smaller regions called **genes**.

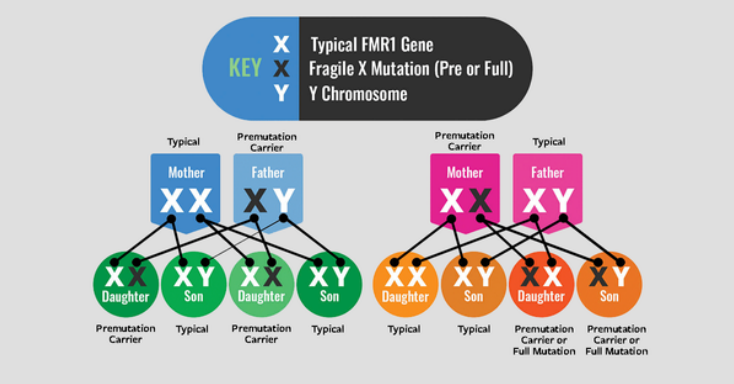
We can think of genes as "sentences" made up of a string of "words." **CGG** is an important "word" in the ***FMR1*** "sentence." If there is a spelling mistake and CGG is repeated too often in *FMR1*, it can cause *FMR1* to not work properly.

Everyone has the gene for Fragile X, called *FMR1*, on each of their X chromosomes. If the gene has an atypical expansion (a repeat of the CGG sequence), it can increase the risk for Fragile X-associated conditions.

Want to know more?

- fragilex.org
- contact@fragilex.org

WHAT IS X-LINKED INHERITANCE & WHAT DOES IT MEAN FOR FRAGILE X?



Each parent passes along one copy from each of the 23 pairs of chromosomes to their child.

A **daughter** will inherit one X chromosome from her mother and one X chromosome from her father. She will have two copies of the *FMR1* gene – one from each parent.

A **son** will inherit one X chromosome from his mother and the Y chromosome from his father. He will have one copy of the *FMR1* gene because it is on the X chromosome, which he only receives from his mother.

If a **mother** has one typical *FMR1* gene on one X chromosome and an expanded *FMR1* gene on the other, she can pass either gene to her sons and daughters. If a **father** has one *FMR1* copy of expanded length on his X chromosome, he can only pass this along to his daughters.

Females have two copies of the *FMR1* gene. The severity of Fragile X syndrome in females depends on if the typical or expanded X chromosome is inactivated in each cell. This process, called X-inactivation, occurs when each cell randomly "turns off" one of its X chromosomes.

Males have only one copy of the *FMR1* gene, so if that copy is expanded to a full mutation, there is no second copy to compensate. This is why males with *FMR1* full mutation expansions tend to be more severely impacted than females.

WHAT ARE EXPANSION RANGES?

Ranges refer to the number of CGG copies that are in the *FMR1* gene. The range can tell us which Fragile X-associated condition someone is at risk for.

TYPICAL: < 45 CGG Repeats – this *FMR1* copy will work properly.

INTERMEDIATE/GRAY ZONE: 45-54 CGG Repeats – This *FMR1* copy will work properly, but it can expand and may add additional CGG copies if it is passed on to the next generation. Anticipation is the name for expansion when passed to the next generation.

PREMUTATION: 55-200 CGG Repeats - Individuals with premutation ranges may have Fragile X-associated conditions like Fragile X-associated tremor/ataxia syndrome (FXTAS) or Fragile X-associated primary ovarian insufficiency (FXPOI). *FMR1* genes with this range can expand when passed down to the next generation. The more CGG repeats a mother has in her premutation, the higher the chance that it will expand to the full expansion range if it is passed down.

FULL MUTATION: >200 CGG Repeats – A full expansion of the *FMR1* gene causes Fragile X syndrome.