

CHILDREN'S MERCY RESEARCH INSTITUTE

DNA Decoding Challenge

Presented by Illumina Corporate Foundation

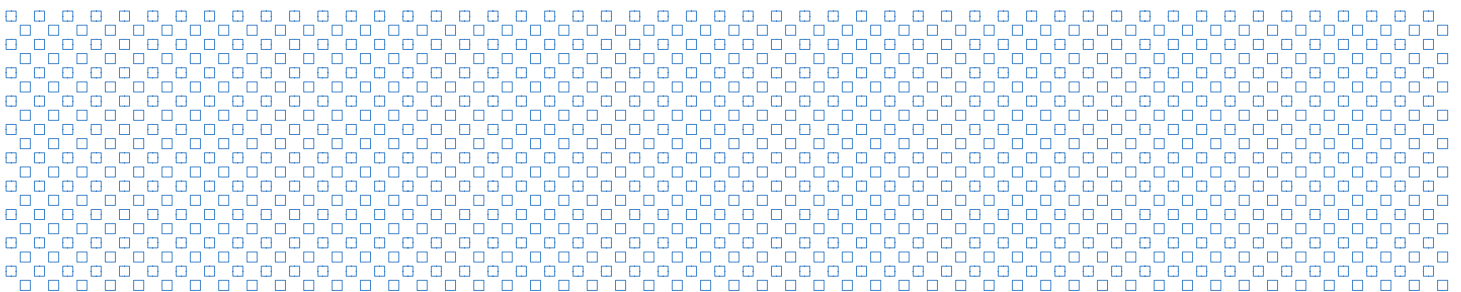


Children's Mercy has been providing care for children in our community since the hospital was founded by Drs. Katharine Berry Richardson and Alice Berry Graham in 1897. These two sisters believed that every child deserves access to quality health care and opportunities to reach their full potential, regardless of their station in life. They dreamed of one day building a research center focused solely on better understanding and treating the medical needs of children.

Today, that dream is a reality. At the Children's Mercy Research Institute (CMRI), scientists are embarking on a revolutionary journey to unlock discoveries that will allow speedy diagnoses, more precise treatments, cures, and prevention strategies for childhood illnesses. Using genetic information, the work happening inside the CMRI will elevate the level of pediatric care available to local families and influence the delivery of lifesaving care around the world.

To celebrate the opening of the CMRI, we have created an exciting opportunity for schools and learning centers to get involved. This real-world learning activity, designed for high school students, will challenge them to decode the DNA sequences displayed on the outside windows of the CMRI.

Students are invited to decipher the DNA sequences to determine what gene variants are represented. All these sequences and their respective variants were discovered in patients at Children's Mercy. The students can even take the investigation a step further by identifying the clinical implications of those variants.



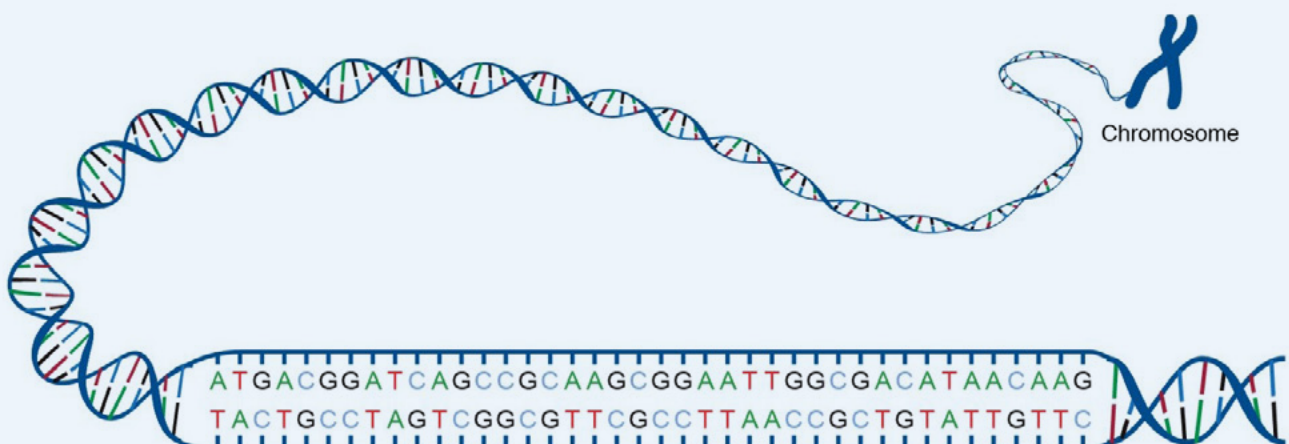
Help us solve these genetic cases!



The lights of the Children's Mercy Research Institute aren't just another beautiful addition to the skyline of Kansas City. The lights represent the hidden genetic codes that the scientists inside had to crack. Often the best solutions to our most difficult problems come from many brains thinking in different ways, so we need your help! In these four cases, you will learn more about how understanding these genetic variations can help kids and their families live better lives. But first, let's review the basics of DNA and DNA Sequencing:

DNA Basics

- DNA, or deoxyribonucleic acid, is the hereditary material inside the cells of humans and almost all other organisms.
- DNA contains the instructions needed for an organism to develop, survive and reproduce. Genes are the part of our DNA that encode proteins, and proteins carry out these different functions in the body.
- DNA is made of chemical building blocks called nucleotides. These building blocks are made of three parts: a phosphate group, a sugar group, and one of four types of nitrogenous bases:
 - » Adenine (A), Guanine (G), Cytosine (C) Thymine (T)



DNA Sequencing:

- DNA sequencing determines the order of these bases, A G C T, similar to the way letters of the alphabet appear in a certain order to form words and sentences.
- The DNA sequence tells scientists the kind of genetic information that is carried in a particular DNA segment. Knowing the sequence can be helpful in a variety of ways, including:
 - » Determining which parts of DNA contain genes and which parts of DNA carry regulatory instructions.
 - » Highlighting changes in a gene that may cause a genetic disorder. A genetic disorder or genetic condition is a disruption in normal bodily functions caused in whole or in part by a change in the DNA sequence.
- You might hear other people refer to genetic changes as genetic mutations, but really, they are variations. Just because a change causes a difference, it doesn't mean that the outcome is necessarily harmful. Every human being has variants! Think about how brown and blue eyes are just variations in the genes that affect eye color.

How can DNA sequencing help determine if someone has a genetic disorder?

When scientists know the order of nucleotides, they can identify which change(s) contribute to or cause a condition.

- » A reference or reference sequence is the order of bases that scientists have generally agreed upon. A variant is a change that differs from this agreed upon sequence.
- » On the CMRI building, the **blue lights** represent bases that correspond with the reference sequence and the **red lights** represent bases that deviate from the reference (i.e. variants).

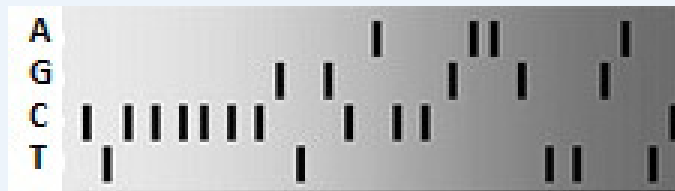
Here is a simplified example: Take a look at the example below. Notice that the variant DNA has a base change at the 2nd nucleotide. Scientists can now look at this variant to see if it could be the possible cause of a genetic disorder.

Reference DNA sequence	A-T-G-C-C-T-A-A-C
Variant DNA sequence	A- C -G-C-C-T-A-A-C

Sanger Sequencing:

- Sanger sequencing is one of the many methods scientists use to determine the nucleotide sequence of DNA.
- In short, four reactions are created, one tube for each nucleotide (A, G, C and T). The reaction ingredients combine inside the tube to form the bands we see on the gel, which represent the different positions of a nucleotide in a given sequence.
- The bands have different sizes depending on what nucleotide is present and how far into the sequence it is.
- However, all these different-sized bands are jumbled up in one reaction tube. They can be separated by adding the tube contents to a gel. When an electrical current is applied, the gel material acts like a mesh, separating out the different sized bands.
- Because each reaction tells us where that nucleotide is in a sequence, we can look at all the reactions together to form the full sequence.

Below is an example of a Sanger sequencing gel. The sequence of the DNA can be identified by reading the bases left to right in order of which the bands appear. The sequence below would be read as: CTCCCCCGTGCACCGAAGTTGATC.

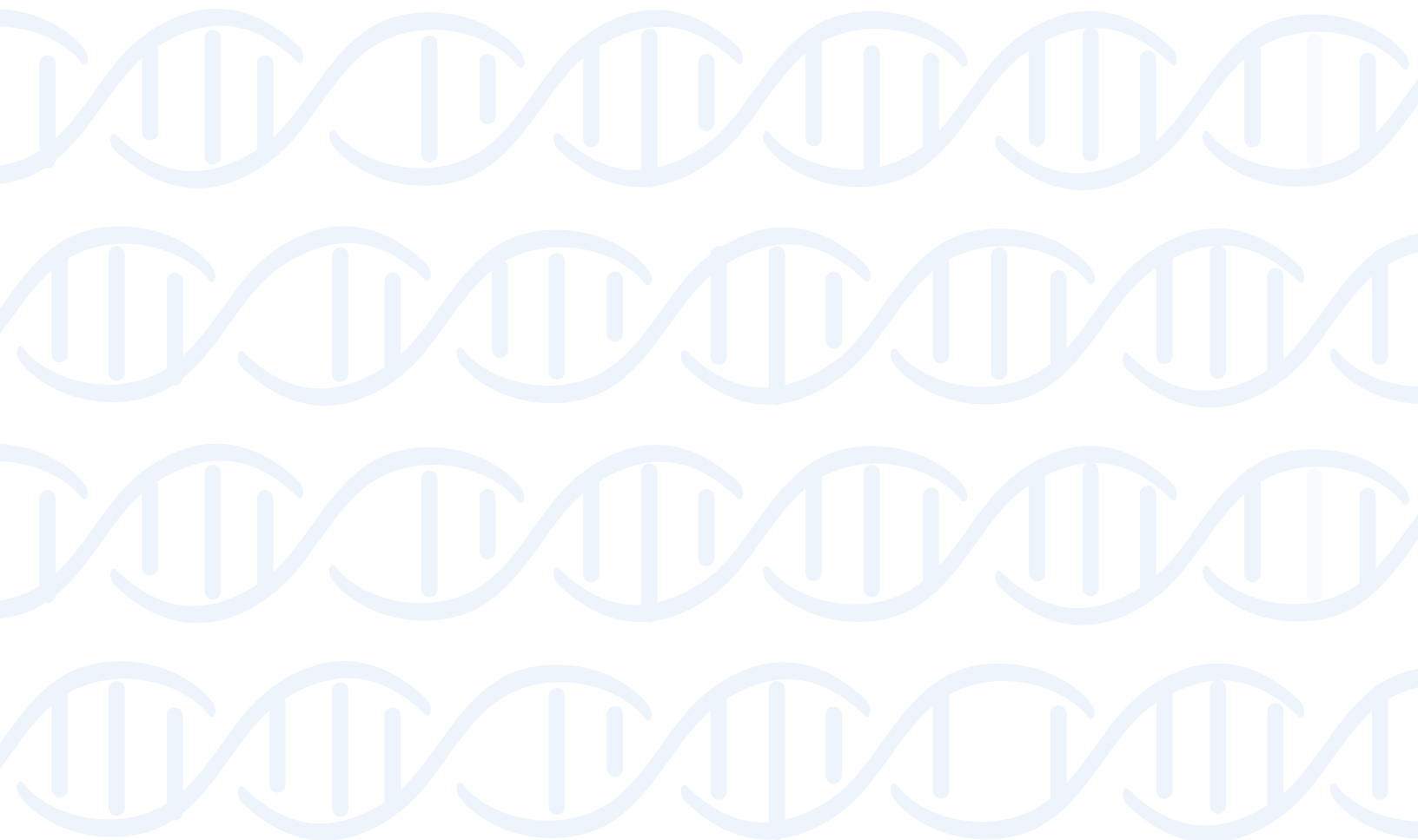


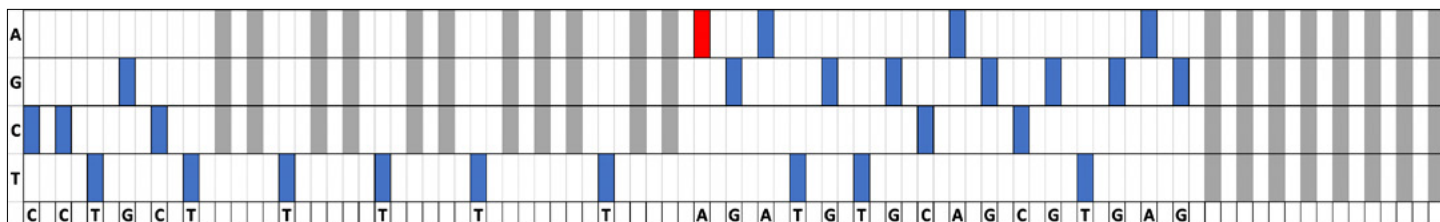
Want to learn more? Check out our Helpful Resources page at the end of this document!

A large, curved building facade at night, illuminated with blue and white lights. The building features a grid of windows, many of which are lit up. The "Children's Mercy" logo is visible in the top right corner of the image.

Case #1 Questions

1. What sequence did the scientists see, which is represented on the building?
 2. What gene are the scientists looking at?
 3. If genes are like the blueprints for cells to make proteins, what does the protein for this gene do?
 4. What genetic condition is associated with this protein when it isn't functioning properly?
- *Optional Challenge Question 1:* How do the specific variants (red bands) in the gene sequence change the function of the protein?
 - *Optional Challenge Question 2:* What sort of treatments could the doctor prescribe to help Shameika?





Case #2 Questions

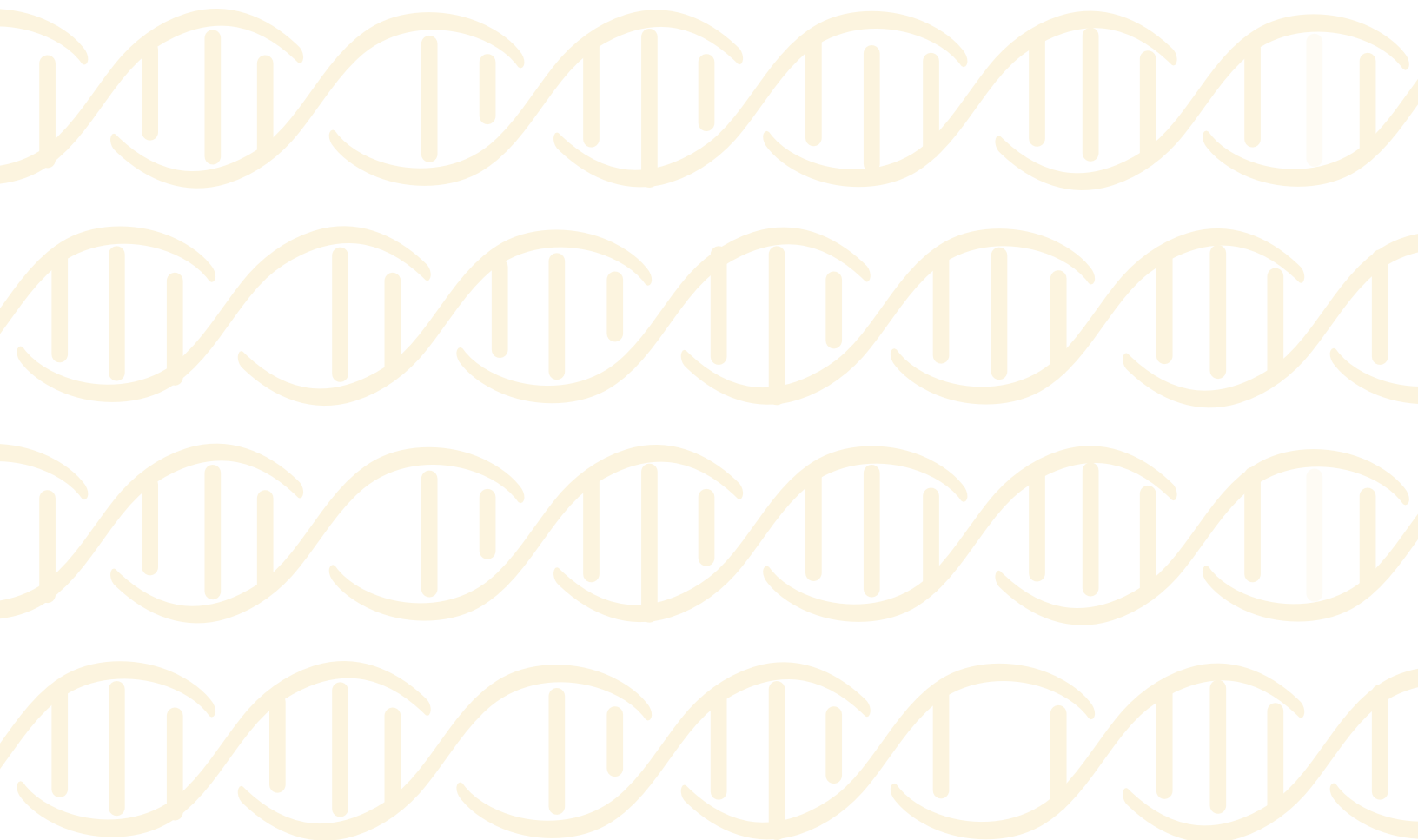
1. What is the sequence the scientists looked at?
 2. What is the gene that matches the sequence?
- *Optional Challenge Question 1:* What is Ben's specific rare variant?
 - *Optional Challenge Question 2:* How does Ben's specific variant affect the way he would metabolize atomoxetine?
 - *Optional Challenge Question 3:* Based on the effect of this variant, how might Ben be dosed compared to someone with another variant that does not cause a change in the function of the protein? (Assume the other copy of his gene produces a non-functional protein.)

A large, modern building at night, illuminated with blue light. The building features a prominent blue neon outline of a stylized figure holding a heart, with the text "Children's Mercy" next to it. The building's facade is composed of many small, rectangular windows, some of which are lit up.

[illegible]

Case #3 Questions

1. A rare variant was found in Dorian's DNA sequence, which is displayed on the CMRI windows. What is the decoded sequence?
2. What is the gene that corresponds to the sequence?
 - *Optional Challenge Question 1:* What is the rare variant?
 - *Optional Challenge Question 2:* Knowing the gene and the variant helped surgeons target the specific part of the pancreas that was causing the problem and remove it. After the surgery, Dorian's blood sugar level then stabilized, and the baby made a full recovery. Based on symptoms, laboratory and genetics results, what is the diagnosis of Dorian's condition?
 - *Optional Challenge Question 3:* If Dorian's condition is considered autosomal dominant in this case, why is it that both biological parents are healthy and have never shown any similar pattern of symptoms?



An aerial night photograph of the Children's Mercy hospital complex. The image is framed by a glowing blue light trail that forms a large, irregular rectangle. The hospital building is illuminated with numerous small, vertical blue light trails, creating a grid-like pattern. The surrounding area is dark, with some city lights visible in the background. The text "Children's Mercy" is visible in the top right corner of the image.

A

G

C

T

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 41 42 43 44 45 46 47 48 49 50 51 52 53 54 55 56 57 58 59 60

G

Case #4 Questions

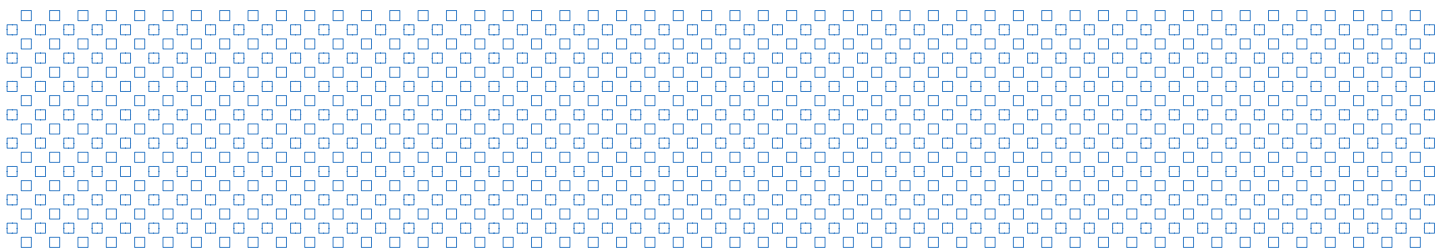
1. What is the decoded DNA sequence from the family members?
2. What gene does this sequence belong to?
3. How might knowing this variant and its effects help others with Tourette syndrome? (Maximum 200 words)

How to Submit Your Answers



Please submit your answers using this form: cmkc.link/decodeCMRiform

Or Scan this QR Code:



Helpful Resources



BACKGROUND INFORMATION

- Genetics
 - » DNA → RNA → Protein
 - › Khan Academy: <https://www.khanacademy.org/science/high-school-biology/hs-molecular-genetics>
 - » YouTube – CrashCourse
 - › DNA structure and replication: <https://www.youtube.com/watch?v=8kK2zwjRV0M>
 - › DNA transcription and translation: <https://www.youtube.com/watch?v=8kK2zwjRV0M>
 - › Cold Spring Harbor Laboratory, DNA Learning Center: <https://dnlc.cshl.edu/resources/animations/>
- Sanger Sequencing
 - » Khan Academy: <https://www.khanacademy.org/science/high-school-biology/hs-molecular-genetics/hs-biotechnology/a/dna-sequencing>
 - » YouTube – Frank Lectures: https://www.youtube.com/watch?v=-QIMkQ4E_wE
 - » YouTube – My2Sense: <https://www.youtube.com/watch?v=FvHRio1yyhQ>

Decoding the Sequence

- Hint: From top to bottom, the bases are in order of adenine (A), guanine (G), cytosine (C), and then thymine (T).
- Hint: Each case has 1 additional random nucleotide change that is not the variant shown in red. These variants do not cause a functional change to the resulting protein.

Find the Gene

- NCBI BLAST: <https://blast.ncbi.nlm.nih.gov/Blast.cgi>
 - » Hint: BLAST with the human genome.
 - » Hint: The more sequence that is decoded, the better the results will be.
 - » Hint: Try different optimization options under “Program Selection”.

Helpful Resources



Find the Variant

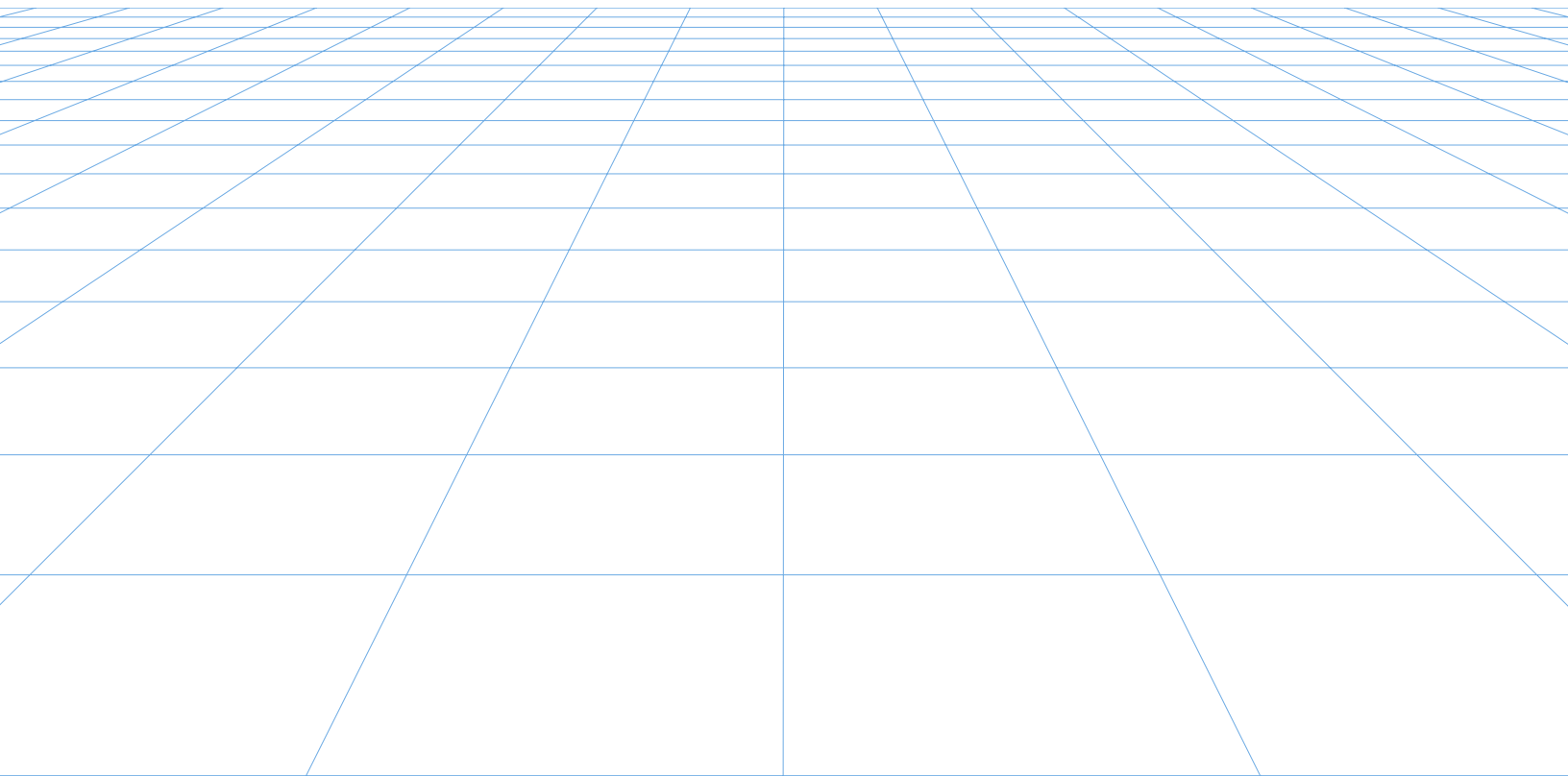
- NCBI dbSNP: <https://www.ncbi.nlm.nih.gov/snp/>
 - » Hint: Start by typing the gene name into the search bar.
 - » Hint: When in a specific reference SNP report, the sequence can be put into the “find” box on the interactive sequence viewer display.
 - » Hint: “rs#” or reference SNP (single nucleotide polymorphism a.k.a nucleotide variant) number. It is an identification number that is unique to every published variant.

Find the Function of the Variant

- NCBI ClinVar: <https://www.ncbi.nlm.nih.gov/clinvar/>
 - » Hint: rs#'s can be cross-referenced to ClinVar
- Pharmacogene Variation Consortium: <https://www.pharmvar.org/>
 - » Hint: Useful for examining genes involved in drug metabolism

Gene Function/ Associated conditions

- NCBI Gene: <https://www.ncbi.nlm.nih.gov/gene/>
- NCBI OMIM: <https://www.ncbi.nlm.nih.gov/omim/>





Children's Mercy Research Institute

KANSAS CITY

Contact us

DecodeCMRI@cmh.edu

childrensmercy.org/research