CTNNB1

CONNECT AND CURE

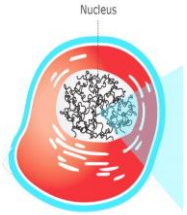
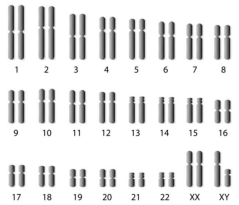
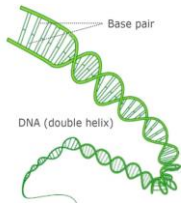
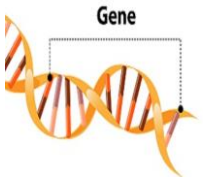
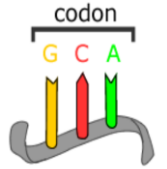
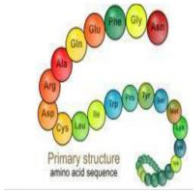
HOW TO READ

CTNNB1 GENETIC RESULTS

TONY KING

VERSION 1.0

GENES 101

A Library	Library Sections	Recipe Books	Chapters in the Recipe book	Specific Recipe	Words on the page	"The product"
						
Human Body	**Cell's Nucleus**	**Chromosomes**	**Sections of DNA**	**GENE (CTNNB1)**	**Codon (1 codon = 1 Amino Acid)**	**Protein (Beta Catenin)**
						

RIBOSOME READER

When a mutation occurs in a codon (word) it causes the wrong amino acid to be produced which causes Ribosomes (the reader) in a cell to translate the sentence (protein) incorrectly. Specific one letter changes can code for ending the synthesis ie an early termination. The protein is now shorter than normal and can be missing critical parts.

TYPES OF GENE MUTATIONS

Chromosomes are like encyclopedias; one set is from the mother, one is from the father

Genes are like pages of descriptions.

RED → RDD

THE CAR WAS RED → THE WAS RED

Mutations are like misspelled words or the disruption of a sentence

MISSENSE MUTATIONS change one word or letter

THE CAR WAS RED → THE CAR WAS HAT

THE CAR WAS RED → THE CAR WAS RDD

INSERTION MUTATIONS add one word or letter

THE CAR WAS RED → THE CAR HAT WAS RED

THE CAR WAS RED → THE CAR ESW ASR ED

NONSENSE MUTATIONS end the instructions too soon

THE CAR WAS RED → THE CAR

DELETION MUTATIONS

THE CAR WAS RED → THE WAS RED

THE CAR WAS RED → THE RWA SRE D

**Insertions and deletions can disrupt the three letters per codon rule causing a frameshift mutation. Ribosomes in a cell only read genes in groups of three bases. The shift alters all the downstream codons effectively disrupting the production of the protein – Beta Catenin in our case.*

TYPES OF MUTATIONS EXPLAINED

MISSENSE

- Change in letter changes single amino acid
- Protein made but may be incorrect since wrong amino acid

NONSENSE

- Change in letter leads to “stop” instruction codon
- No protein or a very shortened protein is made

FRAMESHIFT
Insertion/deletion

- Affects pattern of ‘3 letters= 1 codon’
- Change in letter affects multiple amino acids
- Protein may or not may not be made, possibly wrong shape

SPLICE SITE

- Changes part of gene that affects how gene is processed into instruction to make protein
- Without correct instruction, protein not made correctly or at all

Genetic Testing- How to read your child’s test results

AN EXAMPLE

Specimen Type:	**OraCollect Buccal**	**Date Specimen Received:**	**11/6/2018**
Submitters ID No:	**56270996**	**Date Test(s) Started:**	**11/7/2018**
Ordered By:	**DR. REBECCA AHRENS-NICKLAS**	**Date of Report:**	**2/5/2019**

Test(s) Requested: Diagnostic Testing / XomeDx / Whole Exome Sequence Analysis

Clinical Indication: Male with global developmental delay, speech disorder, spastic diplegia, abnormal muscle tone, and microcephaly

A sample from this individual's father (GeneDx #1910476) and mother (GeneDx #1910511) were also submitted for variant segregation analysis by whole exome sequencing.

1. Causative Variants in Disease Genes Associated with Reported Phenotype:

Gene	Disease	Mode of Inheritance	Variant	Coding DNA	Zygosity	Inherited From	Classification
CTNNB1	CTNNB1-Related Disorder	Autosomal Dominant	p.R587X	c.1759 C>T	Heterozygous	De Novo	Pathogenic Variant

ACMG Secondary Findings: None identified.

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Gene – CTNNB1

There are approximately 30,000 genes in the human genome, each of them have a specific name, and they each provide the instructions to make an average of 3 proteins. Each protein has a specific job to do in the body. CTNNB1 is one of these genes and it produces the protein Beta Catenin. Beta Catenin is responsible for cell to cell adhesion and gene transcription.

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Disease– CTNNB1 Related Disorder

Aka CTNNB1 Syndrome is a rare and generally non-inherited genetic neurological disorder. Some genes are associated with more than one disorder or set of symptoms. An individual's specific symptoms or disorder often depends on the type of mutation you have and where your mutation falls within your gene. (aka did it occur in the beginning, middle, or end).

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Mode of Inheritance– Autosomal Dominant

Autosomal just means the genetic disease is located on one of the numbered, or non-sex, chromosomes. Dominant simply means a single copy of the disease mutation is enough to cause a disease. In contrast, a Recessive disorder means two copies of the mutation are needed to cause disease.

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Coding DNA – c.1759 C>T

Precisely where in the DNA the mutation occurred.

Simply Denotes we are talking about DNA Coding level ← **c. 1759 C>T** → The letter should be a **C** but mutated to a **T**

1759th letter in the DNA base pair sequence.

The 1759th letter of the CTNNB1 gene should be a C but was mutated to a T.

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Variant – p.R587x- aka Gene Mutation.

So, because of the previously mentioned mutation (C>T) the 587th codon was supposed to code for Arginine but instead read as a stop codon, which tells the body to the stop making the CTNNB1 protein at that position. This caused one copy of Tony’s CTNNB1 gene to not properly produce Beta Catenin leading to either an absent or shortened version of the CTNNB1 protein

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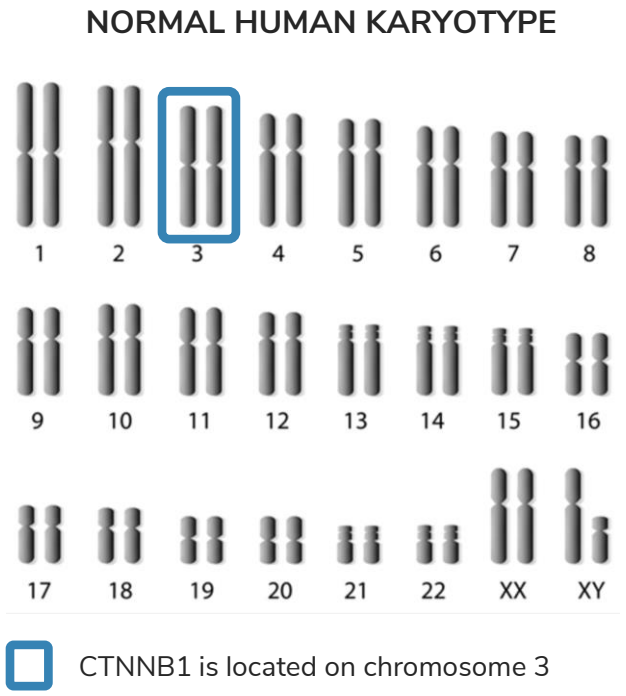
Zygosity
The degree to which both copies of a chromosome or gene have the same genetic sequence

Heterozygous
The Genetic change is only found on one of the two copies of the gene.

Hemizygous
The Genetic change is found on the X chromosome in a male. Males only have one X chromosome so the term is –hemi versus –hetero



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Inherited from– De Novo

Literal translation is “New” De Novo mutations are not inherited from Mom or Dad. It is a Spontaneous Mutation that occurs during embryonic development. No one is at “fault”.

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Everyone has mutations or spelling differences resulting in thousands of genetic changes, but most don't cause medical issues or disease. When a mutation is identified, the lab needs to figure out whether the particular change found is disease causing (pathogenic) or not (benign). The lab will label or a classify a change on how certain they are that this change is disease causing. The following is the different types of classification:

- **Pathogenic:** The variant is responsible for causing disease. There is ample scientific research to support an association between the disease and the gene variant. These variants are often referred to as mutations.
- **Likely pathogenic**: The variant is probably responsible for causing disease, but there is not enough scientific research to be certain.
- **Variant of uncertain significance (VUS or VOUS)**: The variant cannot be confirmed to play a role in the development of disease. There may not be enough scientific research to confirm or refute a disease association or the research may be conflicting.
- **Likely benign**: The variant is probably not responsible for causing disease, but there is not enough scientific research to be certain.
- **Benign**: The variant is not responsible for causing disease. There is ample scientific research to disprove an association between the disease and the gene variant.

*** This change was reported as pathogenic meaning the lab was very certain that this change caused disease. Contributing factors includes the fact that this mutation had been reported in another patient with CTNNB1 related disorder, and the type of change (nonsense mutation).*

CTNNB1
CONNECT CURE

CONTACT US

Tony King –Bear, Delaware USA

tony.king@ctnnb1.org

www.curectnnb1.org