CTNNB1

Name: Catenin Beta 1, aka Beta Catenin 1, β-catenin

Chromosomal Location: Chromosome 3, 3p22.1

Number of exons: 16

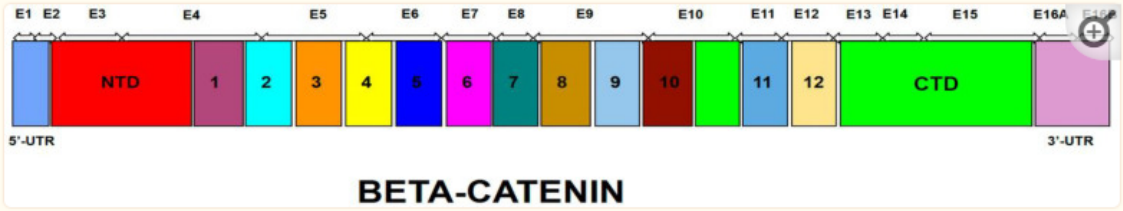
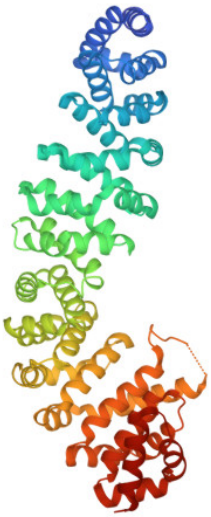


Figure 4

Schematic representation of the β catenin coding region; exon structure in correspondence to encoded protein domains.

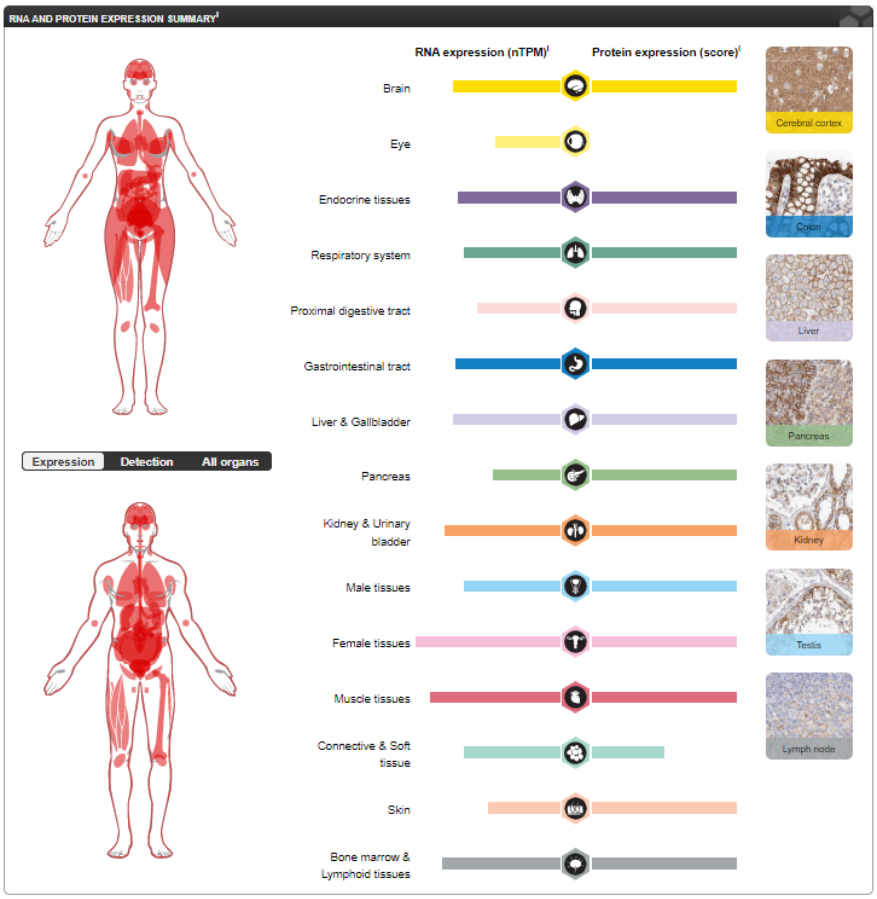
Source: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9604177/

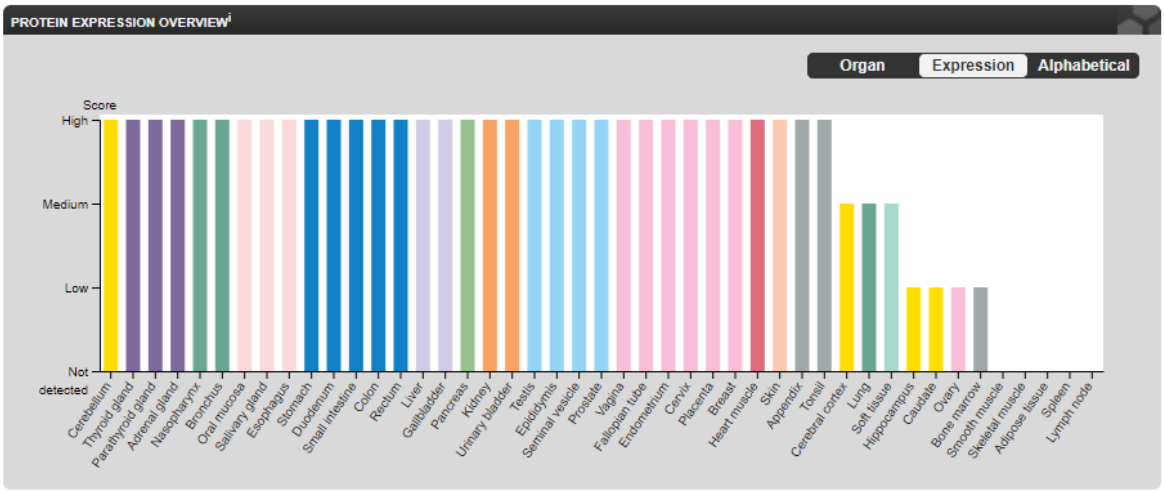
Protein/Enzyme: CTNNB1 encodes for a protein called Catenin (aka, Cadherin-Associated Protein), which is an 88kDa protein (avg. size of human proteins is 32kDa). This protein has several very characteristic repeats, called armadillo repeats each approximately 40 amino acids long.



Source: https://www.rcsb.org/structure/1v18

Tissue Expression: CNNTB1 protein is expressed in a large number of tissues within the body as well as during embryonic development.

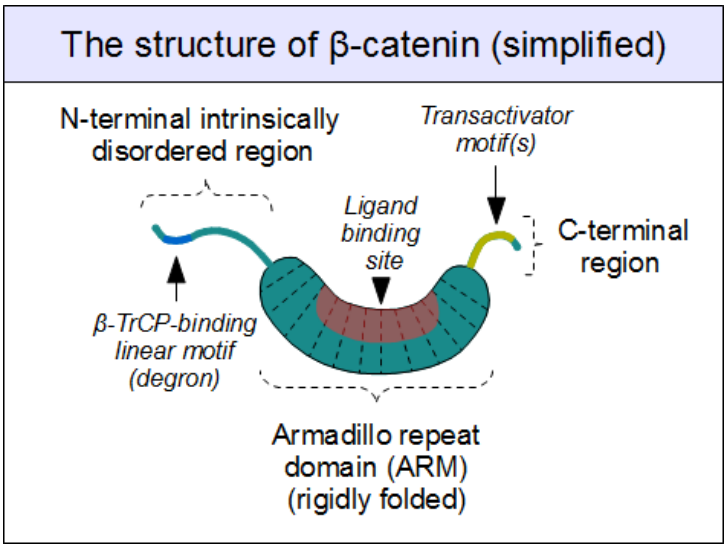




Source: https://www.proteinatlas.org/ENSG00000168036-CTNNB1/tissue

Protein Structure:

Beta-catenin protein consists of several very characteristic repeats, each approximately 40 amino acids long, called armadillo repeats. These repeats fold together into a single, rigid protein domain with an elongated shape – called armadillo (ARM) domain. Due to the complex shape of individual repeats, the whole ARM domain is not a straight rod: it possesses a slight curvature, so that an outer (convex) and an inner (concave) surface is formed. This inner surface serves as a binding site for the various interaction partners of the ARM domains.



Source: https://en.wikipedia.org/wiki/Catenin_beta-1

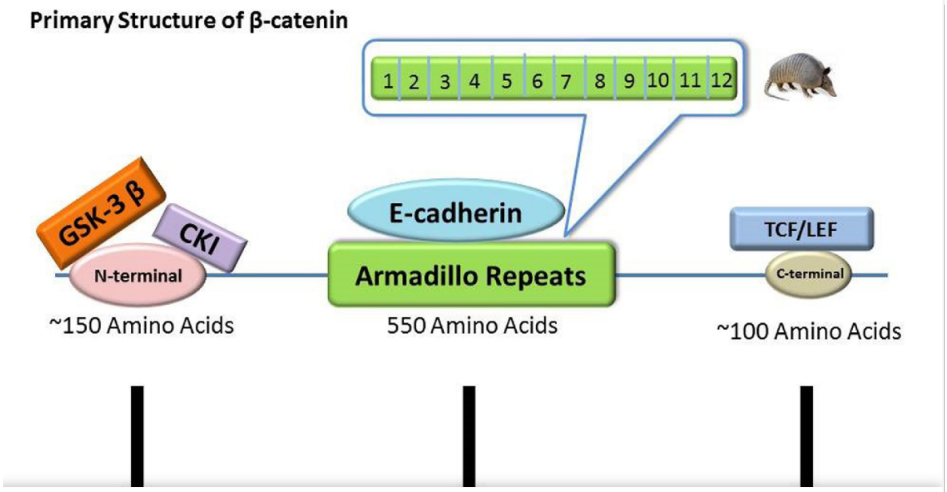


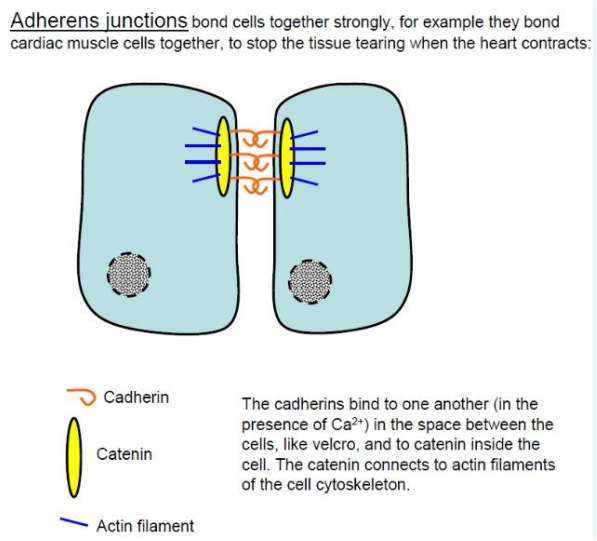
Figure 2: The primary structure of β-catenin and its relevant binding sites. β-catenin has three domains: a 550-amino-acid central repeat domain, an approximately 150-amino-acid N-terminal domain, and an approximately 100-amino-acid C-terminal domain. They are binding sites for E-cadherin, GSK-3β/CK-1, and TCF/LEF, respectively, and exert different roles.

Source: https://pubmed.ncbi.nlm.nih.gov/29435196/

Function:

Catenin is part of a complex of proteins that make up the adherens junctions (AJs).

Adherens junctions (or zonula adherens, intermediate junction, or belt desmosome) are protein complexes that occur at the junction between cells. They can appear as either bands encircling the cell (zonula adherens) or as focal areas of attachment to the extracellular matrix (focal adhesion). AJs are cell-cell adhesion complexes that bind cells together and are critical for the establishment and maintenance of epithelial cell layers, such as those lining organ surfaces.



Source: https://cronodon.com/BioTech/cells_junctions.html

Function of AJs:

- AJs mediate adhesion between cells. They are continuously assembled and disassembled, allowing cells within a tissue to respond to forces, biochemical signals and structural changes in their microenvironment.
- AJs communicate signals that neighboring cells are present around them. Once neighboring cells start touching each other tightly, AJs signal the cell to stop dividing, a process called contact inhibition.
- AJs anchor the actin cytoskeleton within the cell that acts as a scaffold for the cell to keep it's structural integrity.

Role of Catenin:

CTNNB1 plays a dual role in the cell.

- It is a core component of the WNT/CTNNB1 pathway, which is crucial for embryonic development and tissue morphogenesis (the process by which cell, tissue or organism develop their shape) and maintenance throughout the lifespan of all multicellular animals. In this capacity, it to activate certain target genes involved in these processes.

- It also has a key function at cell–cell junctions, where it is required to anchor cadherin proteins to the cytoskeleton, forming the essence of cell adhesion.

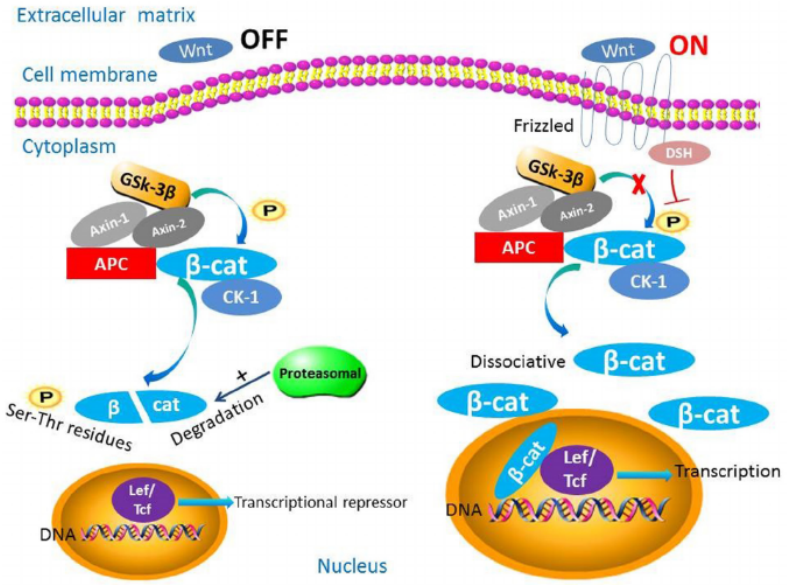


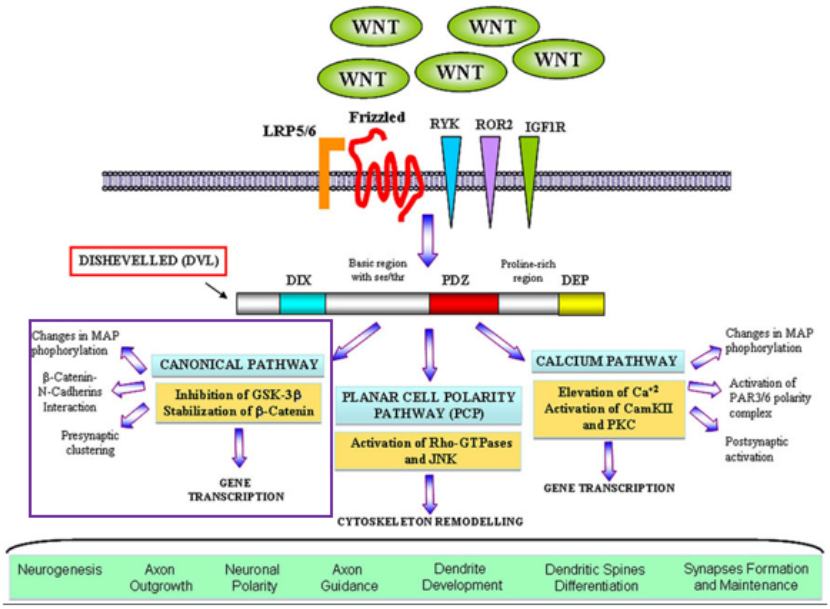
Figure 1: The biological roles of β-catenin in the Wnt/β-catenin signaling pathway. This pathway has two states dependent upon the presence or absence of Wnt ligands. When Wnt ligands are absent, β-catenin is phosphorylated by the destruction complex and degraded. When Wnt ligands are present, β-catenin is not degraded and translocates to the nucleus and functions as a transcription factor

Source: https://www.researchgate.net/publication/322080621_Exon_3_mutations_of_CTNNB1_drive_tumorigenesis_A_Review

Role in Neurodevelopment:

The Wnt signaling pathway plays a pivotal role in:

- Development of the central nervous system and regulation of the structure and function of the adult nervous system.
- Regulating developmental processes, including embryonic patterning, cell specification, and cell polarity.
- Regulating the formation and function of neuronal circuits by controlling neuronal differentiation, axon outgrowth and guidance, dendrite development, synaptic function, and neuronal plasticity.
- In the nervous system, the expression of Wnt proteins is a highly controlled process and one of the cascades that Wnt factors can signal through is the canonical or β-catenin pathway



Source: https://www.researchgate.net/publication/248706369_CWNT_signaling_in_neuronal_maturation_and_synaptogenesis

Disease Association:

Disruption of CTNNB1 is known to been associated with:

- Cancers
- CTNNB1 Syndrome
- Neural tube defects
- Autism Spectrum Disorder
- Alzheimer's
- Bone diseases
- Vascular conditions such as exudative vitreoretinopathy

Mutation types:

There is substantial variability in the types of mutations detected in patients with CTNNB1 Syndrome and its correlation with symptoms. Mutations associated with CTNNB1 Syndrome are scattered throughout the gene, with the exception of the first coding exon (exon 2), although one cannot exclude the possibility that pathological mutations also occur in this exon and have just not been detected yet.

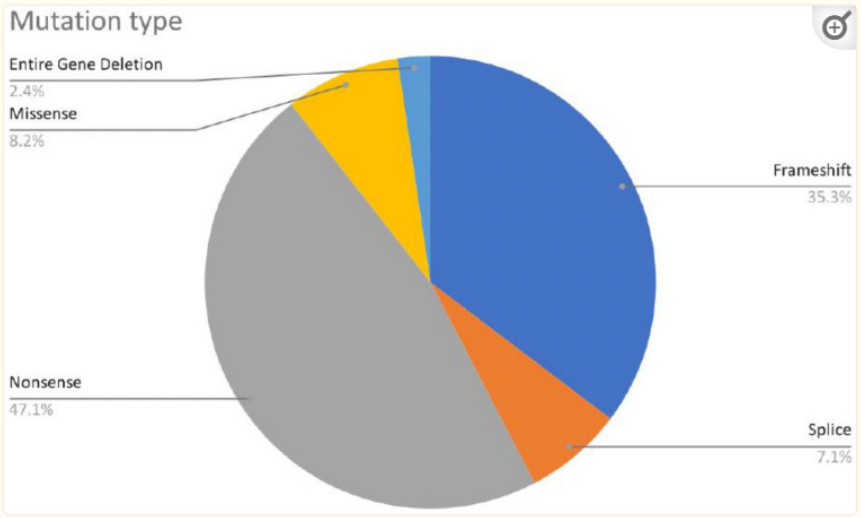


Figure 7

Distribution of CTNNB1 mutation types.

Source: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9604177/

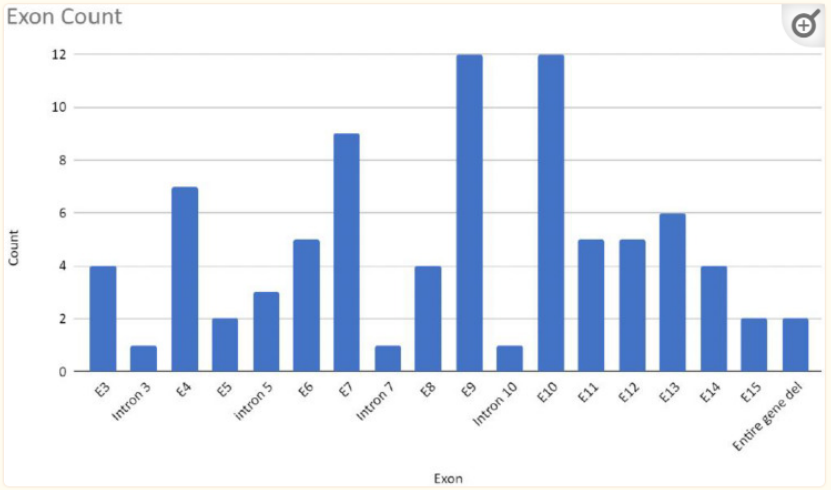


Figure 8

Number of mutations detected in individual intron or exon regions or whole gene deletions of analyzed samples in this study (n = 84).

Source: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9604177/

Genetic Testing:

There are several commercial genetic diagnostic companies that offer CTNNB1 sequencing, for example:

- Blueprint Genetics

- Fulgent Genetics
- Prevention Genetics
- Invitae

If one is interested in genetic testing for CTNNB1, it is crucial to speak to a genetic counselor to understand if testing is appropriate, understand what information testing can and cannot provide and how to go about getting tested, including ways to pay for it. The National Society of Genetic Counselors directory lists over 3,300 genetic counselors in the US and Canada.