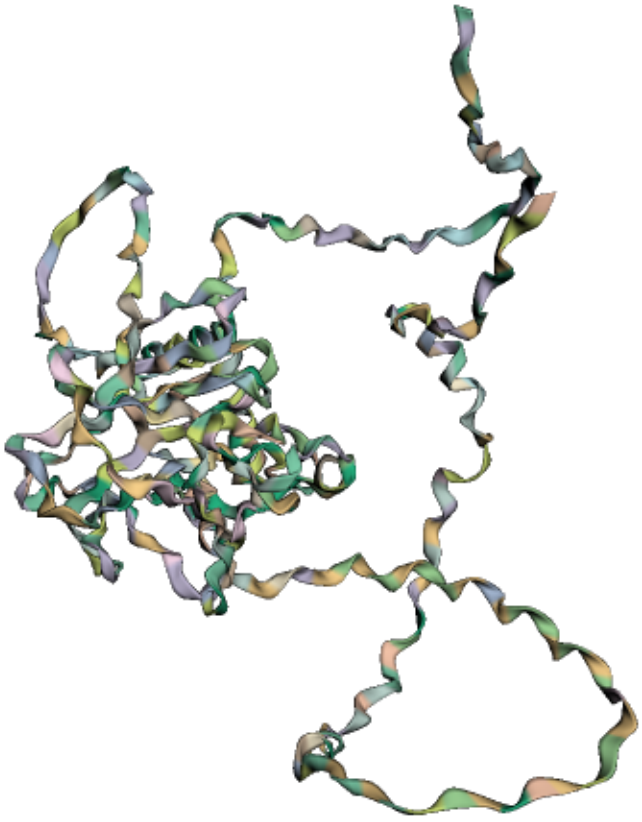
Protein Analysis Report

Cellular tumor antigen p53



Core Info

Protein Name: Cellular tumor antigen p53
Gene: TP53
Uniprot ID: P04637
Amino Acid length: 393
Cofactor(s): Zn(2+) - Binds 1 zinc ion per subunit.
Molecular Processes: Activator, DNA-binding, Repressor
Biological processes: Apoptosis, Biological rhythms, Cell cycle, Host-virus interaction, Necrosis, Transcription, Transcription regulation
Found on Chromosome 17

This gene encodes a tumor suppressor protein containing transcriptional activation, DNA binding, and oligomerization domains. The encoded protein responds to diverse cellular stresses to regulate expression of target genes, thereby inducing cell cycle arrest, apoptosis, senescence, DNA repair, or changes in metabolism. Mutations in this gene are associated with a variety of human cancers, including hereditary cancers such as Li-Fraumeni syndrome. Alternative splicing of this gene and the use of alternate promoters result in multiple transcript variants and isoforms. Additional isoforms have also been shown to result from the use of alternate translation initiation codons from identical transcript variants (PMIDs: 12032546, 20937277). [provided by RefSeq, Dec 2016]

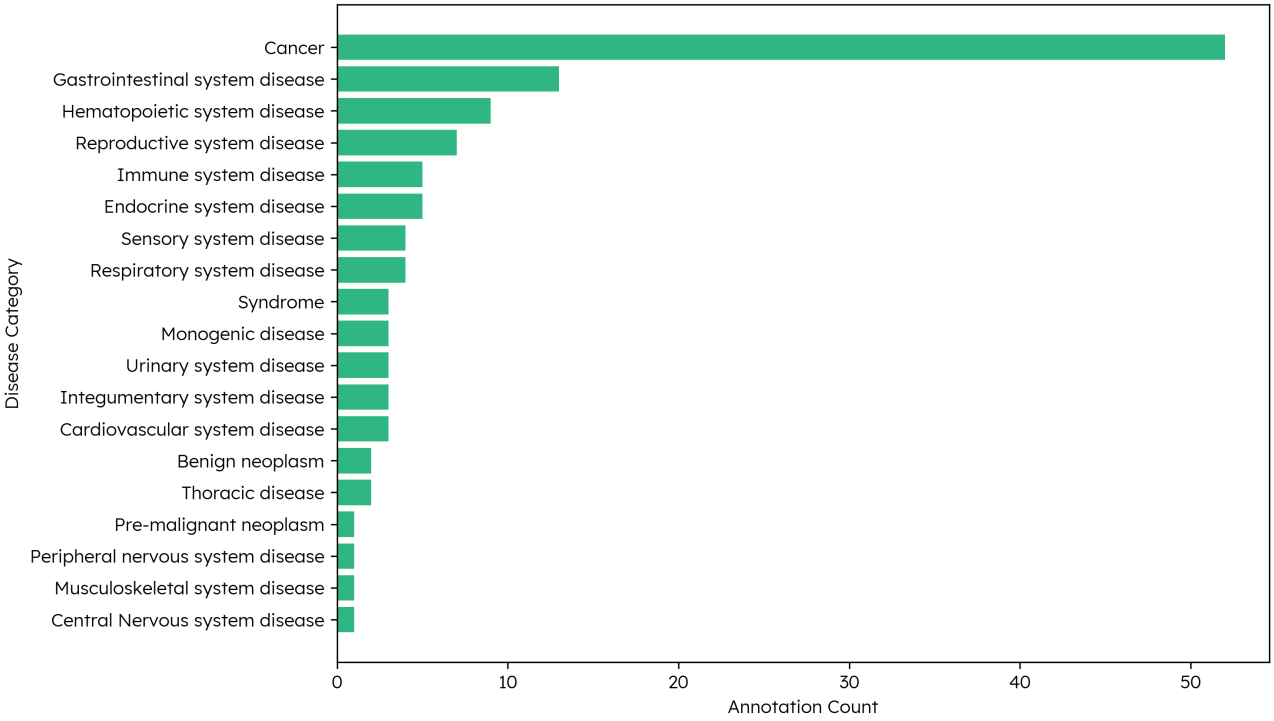
Protein Expression

Ubiquitous. Isoforms are expressed in a wide range of normal tissues but in a tissue-dependent manner. Isoform 2 is expressed in most normal tissues but is not detected in brain, lung, prostate, muscle, fetal brain, spinal cord and fetal liver. Isoform 3 is expressed in most normal tissues but is not detected in lung, spleen, testis, fetal brain, spinal cord and fetal liver. Isoform 7 is expressed in most normal tissues but is not detected in prostate, uterus, skeletal muscle and breast. Isoform 8 is detected only in colon, bone marrow, testis, fetal brain and intestine. Isoform 9 is expressed in most normal tissues but is not detected in brain, heart, lung, fetal liver, salivary gland, breast or intestine

Up-regulated in response to DNA damage. Isoform 2 is not induced in tumor cells in response to stress

Disease Associations

Figure 1: Disease Annotation Level by Category



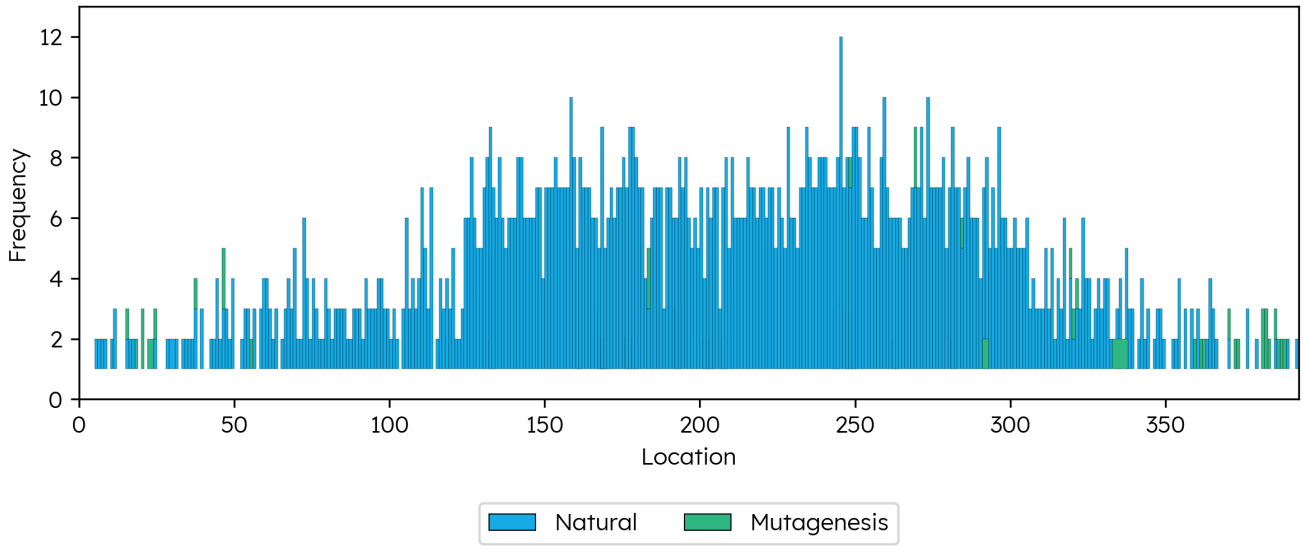
This gene is a marker for: acute myeloid leukemia, adenoid cystic carcinoma, basal cell carcinoma, cervical adenocarcinoma, cervical squamous cell carcinoma, cholesteatoma of middle ear, clear cell renal cell carcinoma, colorectal adenocarcinoma, colorectal cancer, ductal carcinoma in situ, endometrial adenocarcinoma, endometrial carcinoma, graft-versus-host disease, leukemia, lung non-small cell carcinoma, medulloblastoma, multiple myeloma, myelodysplastic syndrome, myelofibrosis, oral mucosa leukoplakia, oral submucous fibrosis, pterygium, renal cell carcinoma, serous cystadenocarcinoma, squamous cell carcinoma, T-cell non-Hodgkin lymphoma, transitional cell carcinoma, urinary bladder cancer

This gene is implicated in: acute myeloid leukemia, acute myeloid leukemia, B-lymphoblastic leukemia/lymphoma, basal cell carcinoma, breast cancer, choroid plexus papilloma, colorectal cancer, colorectal carcinoma, coronary artery disease, coronary restenosis, endometrial adenocarcinoma, esophagus squamous cell carcinoma, gastric adenocarcinoma, Graves' disease, hematologic cancer, hepatocellular carcinoma, high grade glioma, Leber hereditary optic neuropathy, Li-Fraumeni syndrome, Li-Fraumeni syndrome 1, low tension glaucoma, melanoma, mismatch repair cancer syndrome, multiple myeloma, multiple myeloma, myelodysplastic syndrome, myelodysplastic syndrome, nasal cavity cancer, nasopharynx carcinoma, oral squamous cell carcinoma, osteosarcoma, ovary serous adenocarcinoma, pancreatic cancer, pancreatic intraductal papillary-mucinous

neoplasm, paranasal sinus benign neoplasm, primary open angle glaucoma, prostate cancer, sarcoma, squamous cell carcinoma, stomach cancer, thyroid gland papillary carcinoma

Natural Variants & Mutagenesis

Figure 2: Mutagenesis and Natural Variations



Pathways

This list outlines various pathways involved in cellular processes like cell cycle regulation, apoptosis, senescence, and development. The pathways can be broadly categorized into several groups:

Regulation of TP53: These pathways focus on the tumor suppressor protein TP53, which plays a crucial role in cell cycle control and apoptosis. This category includes pathways like regulation of TP53 expression, activity through phosphorylation, acetylation, methylation, and association with co-factors. It also encompasses TP53-mediated regulation of gene transcription involved in cell cycle arrest (G1 and G2), DNA repair, cytochrome C release, and activation of caspases and death receptors.

Cell Cycle Regulation and DNA Damage Response: These pathways focus on maintaining proper cell cycle progression and responding to DNA damage. Key examples include the G1 and G2 checkpoints, DNA double-strand break repair, and the role of TP53 and other proteins like p21 in cell cycle arrest. The G2/M DNA damage checkpoint and the involvement of GTSE1 in G2/M progression after the checkpoint are also included.

Apoptosis and Senescence: This category encompasses pathways leading to programmed cell death (apoptosis) and cellular senescence. Examples include the activation of NOXA and PUMA, translocation to mitochondria, TP53-mediated regulation of apoptosis genes, and the formation of senescence-associated heterochromatin foci (SAHF). Pathways involved in oxidative stress-induced senescence and oncogene-induced senescence are also included.

Development and Signaling: This group encompasses pathways involved in various developmental processes and signaling events. Examples include zygotic genome activation (ZGA), megakaryocyte development and platelet production, interleukin-4 and interleukin-13 signaling, and NF-kappa B signaling. The regulation of PTEN gene transcription and the involvement of RUNX3 in CDKN1A transcription are also included.

Other Pathways: This category encompasses various other pathways involved in protein regulation, like SUMOylation of transcription factors, autodegradation of COP1, and TriC/CCT association with target proteins. Pathways related to proteases, such as Ub-specific processing proteases and ovarian tumor domain proteases, are also included. The PKR-mediated signaling pathway and the impact of ALK fusions and mutations on signaling are also included in this category.

This list provides a glimpse into the complex network of pathways involved in crucial cellular functions, highlighting the intricate interplay between various signaling cascades and proteins that govern cellular life, death, and development.

Here is the full list of pathways (click for more info):

- Activation of NOXA and translocation to mitochondria
- Activation of PUMA and translocation to mitochondria
- Pre-NOTCH Transcription and Translation
- Oxidative Stress Induced Senescence
- Formation of Senescence-Associated Heterochromatin Foci (SAHF)
- Oncogene Induced Senescence
- DNA Damage/Telomere Stress Induced Senescence
- SUMOylation of transcription factors
- Autodegradation of the E3 ubiquitin ligase COP1
- Association of TriC/CCT with target proteins during biosynthesis
- Pyroptosis
- TP53 Regulates Metabolic Genes

- Ub-specific processing proteases
- Ovarian tumor domain proteases
- Recruitment and ATM-mediated phosphorylation of repair and signaling proteins at DNA double strand breaks
- Interleukin-4 and Interleukin-13 signaling
- TP53 Regulates Transcription of DNA Repair Genes
- TP53 Regulates Transcription of Genes Involved in Cytochrome C Release
- TP53 regulates transcription of several additional cell death genes whose specific roles in p53-dependent apoptosis remain uncertain
- TP53 Regulates Transcription of Caspase Activators and Caspases
- TP53 Regulates Transcription of Death Receptors and Ligands
- TP53 Regulates Transcription of Genes Involved in G2 Cell Cycle Arrest
- TP53 regulates transcription of additional cell cycle genes whose exact role in the p53 pathway remain uncertain
- TP53 Regulates Transcription of Genes Involved in G1 Cell Cycle Arrest
- Regulation of TP53 Expression
- Regulation of TP53 Activity through Phosphorylation
- Regulation of TP53 Degradation
- Regulation of TP53 Activity through Acetylation
- Regulation of TP53 Activity through Association with Co-factors
- Regulation of TP53 Activity through Methylation
- PI5P Regulates TP53 Acetylation
- G2/M DNA damage checkpoint
- G2/M Checkpoints
- Stabilization of p53
- Transcriptional activation of cell cycle inhibitor p21
- The role of GTSE1 in G2/M progression after G2 checkpoint
- Transcriptional Regulation by VENTX
- RUNX3 regulates CDKN1A transcription
- Regulation of PTEN gene transcription

- Loss of function of TP53 in cancer due to loss of tetramerization ability
- Signaling by ALK fusions and activated point mutants
- Regulation of NF-kappa B signaling
- Zygotic genome activation (ZGA)
- Factors involved in megakaryocyte development and platelet production
- PKR-mediated signaling

Citations

Uniprot: https://www.uniprot.org/uniprotkb/P04637

Protein Atlas: https://www.proteinatlas.org/search/P04637

AlphaFold: https://alphafold.ebi.ac.uk/entry/P04637

Alliance of Genome Resources: https://www.alliancegenome.org/gene/HGNC:11998