TP53 gene mutation

TP53 gene mutations are important molecular markers in diffuse astrocytic tumors and medulloblastomas.

TP53 gene mutations are very common in human cancers and are the underlying cause of Li-Fraumeni syndrome. Testing for these is performed by polymerase chain reaction (PCR).

Whenever possible, appropriate molecular genetics should also be evaluated. Testing for IDH1 and/or IDH2 mutations should be done in all diffuse gliomas if possible. Other tests (e.g. 1p/19q co-deletion or TP53 gene mutations) are done as appropriate.

The combination of P53 and IDH1 as an immunohistochemical panel showed a specificity of 96% and sensitivity of 91% for differential diagnosis of reactive gliosis and low-grade astrocytoma. These 2 markers can be extremely helpful for this differential diagnosis [1)].

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see Medulloblastoma, SHH-activated, and TP53-mutant.

see Medulloblastoma, SHH-activated, and TP53-wildtype

Li-Fraumeni syndrome is usually caused by a germline mutation in the TP53 tumor suppressor gene on chromosome 17p13.

These mutations result in a p53 protein that is less able to control cell proliferation. Specifically, it is unable to trigger apoptosis in cells with mutated or damaged DNA.

TP53 mutations: 27% primary glioblastoma and in 81 % of secondary glioblastomas.

The TP53 gene encodes TP53 (tumor protein 53), which is a tumor suppressor that prevents cells from dividing and signals them to undergo apoptosis if they sustain irreparable DNA damage. TP53 gene mutations are very common in human cancers and are the underlying cause of Li-Fraumeni syndrome.

Testing for these is performed by polymerase chain reaction (PCR).

In general, ATRX & TP53 mutations are mutually exclusive of 1p/19q co-deletion, and as such may be used as confirmatory markers to distinguish astrocytomas from oligodendrogliomas.

Indications: ATRX is a confirmatory test along with IDH1 mutation. ATRX & TP53 can be detected by immunohistochemical (IHC) stains or by Fluorescence in situ hybridization (FISH) and may be done in

some hospitals or may be sent out to specialty labs; results typically take ≈ 2–3 days. The cost of IHC is on the order of $100–150 U.S., FISH is about $200–250 U.S.

Complete deletion of both the short arm of chromosome 1 (1p) and the long arm of chromosome 19 (19q) is pathognomonic for oligodendroglioma. It is strongly associated with IDH mutation and is mutually exclusive of ATRX & TP53 mutations.

TP53 point mutations are found in 50% of all cancers and seem to play an important role in cancer pathogenesis. Thus, Human-induced pluripotent stem cells (hiPSCs) overexpressing mutant TP53 are a valuable tool for the generation of in vitro models of cancer stem cells or for in vivo xenograft models.

TP53 mutations appear to be highly represented (> 80%) in all gemistocytic astrocytomas, and this is likely to be higher among gemistocytic astrocytoma IDH-mutant.

Uhlmann et al. from the University Hospital of Düsseldorf, described a protocol for the alteration of gene expression in hiPSCs via overexpression of a mutant form of the TP53 (R249S) gene using lentiviral transduction. A high amount of TP53 protein is detected 1 week after transduction and antibiotic selection. Differentiation of transduced hiPSCs gives insight into a better understanding of cancer formation in different tissues and may be a useful tool for genetic or pharmacologic screening assays.

Basic Protocol 1: Production and concentration of third-generation lentivirus Support Protocol 1: Cloning of gene of interest into modulation vector Support Protocol 2: Preparation of DMEM GlutaMAX™ with 10% fetal bovine serum and 1% penicillin-streptomycin Basic Protocol 2: Transduction of human-induced pluripotent stem cells and selection of positively transfected cells Support Protocol 3: Preparation of Matrigel® -coated plates Support Protocol 4: Preparation of mTeSR™1 medium [2].

Complete deletion of both the short arm of chromosome 1 (1p) and the long arm of chromosome 19 (19q) is pathognomonic for oligodendroglioma [3] [4] It is strongly associated with IDH mutation and is mutually exclusive of ATRX & TP53 mutations.

References

1)

Geramizadeh B, Kohandel-Shirazi M, Soltani A. A Simple Panel of IDH1 and P53 in Differential Diagnosis Between Low-Grade Astrocytoma and Reactive Gliosis. Clin Pathol. 2021 Feb 11;14:2632010×20986168. doi: 10.1177/2632010×20986168. PMID: 33634261; PMCID: PMC7887675.

2)

Uhlmann C, Kuhn LM, Tigges J, Fritsche E, Kahlert UD. Efficient Modulation of TP53 Expression in Human-induced pluripotent stem cells. Curr Protoc Stem Cell Biol. 2020 Mar;52(1):e102. doi: 10.1002/cpsc.102. PubMed PMID: 31883435.

3)

Louis DN, Perry A, Reifenberger G, et al. The 2016 World Health Organization Classification of Tumors of the Central Nervous System: a sum- mary. Acta Neuropathol. 2016; 131:803–820
4)
Stupp R, Brada M, van den Bent MJ, et al. High- grade glioma: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol. 2014; 25 Suppl 3:iii93–ii101