



ANALYSIS REPORT

Patient Information		Referral Information	
Name	-	Institution/Clinic	-
Date of Birth	-	Pathology Report No.	-
ID/Medical ID	-	Clinical Diagnosis	OLIGODENDROGLIOMA
Req. Physician	-		
Sample Details			
Type of sample #1	-	Date Received	-
Code of sample #1	-	Date of Report	-
Estimated TCC	60%	Sample QC	Pass
Macrodissection	Yes	Barcode	26xxxxxxGR

Molecular Analysis Results

Biomarker	Result	Comment
IDH1	Exon 4 c.395G>A, p.R132H (VAF 41.1%)	Table 1
CIC	Exon 20 c.4533_4535delCCGinsTCT, p.R1512L (VAF 75.7%)	Table 1
FUBP1	Exon 16 c.1519_1528del, p.P507Gfs*155 (VAF 73.2%)	Table 1
TERT	c.-146C>T, (C250T) (VAF 42.4%)	Table 1
MGMT promoter	Methylated	
Microsatellite Instability (MSI)	Stable (MSS)	
1p19q	1p19q co-deletion detected	Table 1



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Interpretation

Genetic Variation: **IDH1: c.395G>A (p.R132H)**

VAF*: 41.1%

OncoKB

Gene information

The IDH1 (isocitrate dehydrogenase 1) protein is an enzyme that catalyzes the oxidative decarboxylation of isocitrate to α -ketoglutarate (α -KG), a crucial step in the tricarboxylic acid (TCA) cycle. IDH1 utilizes NADP(+) as an electron acceptor and it is predominantly expressed in the cytosol and peroxisomes, playing a role in the cytoplasmic production of NADPH. Cancer-associated mutations in the catalytic site of IDH1 confer a gain-of-function of neomorphic enzymatic activity, allowing the mutant enzyme to convert α -KG to the "oncometabolite" D-2-hydroxyglutarate (2-HG) (PMID: [20171147](#)). 2-HG promotes tumor development by inhibiting a variety of enzymes that require α -KG as a substrate, including enzymes involved in DNA demethylation, histone demethylation, adaptation to hypoxia and collagen maturation. IDH1 mutations have been identified in glioma, cholangiocarcinoma and acute myeloid leukemia (AML) among others (PMID: [19657110](#), [23630074](#)) and may contribute to the progression of myeloproliferative neoplasms to bone marrow failure or AML (PMID: [29355841](#)).

Variant Information

The IDH1 R132H mutation is located in the catalytic site of the IDH1 protein. This mutation has been found in acute myeloid leukemia and gliomas, among others (PMID: [19935646](#), [29860938](#)). In vitro and in vivo studies have demonstrated that this mutation changes IDH1 enzymatic activity, allowing for the conversion of α -ketoglutarate (α -KG) to the "oncometabolite" D-2-hydroxyglutarate (2-HG), and leads to oncogenic activity, as evidenced by aberrant changes in DNA methylation, cytokine independence, dedifferentiation and in vivo increases in early hematopoietic progenitors compared to wildtype IDH1 (PMID: [19935646](#), [22763442](#), [23393090](#)). IDH1 mutations at the R132 residue, including the R132H mutation are central to WHO CNS5 classification of diffuse gliomas and this classification now has direct therapeutic weight, since the IDH1/2-targeted inhibitor vorasidenib is FDA-approved for the treatment of patients twelve years and older with astrocytoma or oligodendroglioma with a susceptible IDH1 mutation.

Genetic Variation: **CIC: c.4533_4535delCCGinsTCT (p.R1512L)**

VAF*: 75.7%

OncoKB

Gene information

CIC (also Capicua) is a transcriptional repressor that is a member of the high mobility (HMG)-box protein family (PMID: [32073140](#)). CIC is expressed in a variety of tissues and is a critical regulator of patterning, differentiation, and signaling (PMID: [10652276](#), [32073140](#)). Chromatin modifiers, such as the Sin/HDAC3 histone deacetylase complex, are recruited to sites bound by CIC to inhibit gene expression of target genes (PMID: [29844126](#)). CIC exists in diverse protein complexes including with ATXN1, which directly binds CIC and modulates its transcriptional repressor activity (PMID: [17190598](#)). The CIC-ATXN1 complex regulates the expression of several transcription factors, including members of the ETS protein family (PMID: [27869830](#)). Loss of CIC expression results in the derepression of ETS transcriptional regulators, such as ETV4, which can activate extracellular remodeling programs and metastasis (PMID: [27869830](#), [22014525](#)). In addition, CIC is a negative regulator of receptor tyrosine kinase (RTK) and MAPK signaling pathways and acts as a transcriptional repressor in the absence of RTK signaling (PMID: [11714680](#), [11861482](#), [29844126](#), [28178529](#)). CIC is recurrently mutated in oligodendrogliomas, including in 1p/19q-deleted cancers (PMID: [21817013](#), [22869205](#), [22588899](#)). Somatic mutations and deletions have also been found in various other cancer types, including in lung and gastric cancers (PMID: [25079317](#), [27869830](#)). Chromosomal translocations that produce chimeric CIC proteins fused to several partner proteins, including DUX4 or FOXO4, occur in aggressive round cell sarcomas and result in aberrant CIC-mediated transcriptional activation (PMID: [19837261](#), [25007147](#), [21813156](#)).

Variant Information

There is no available functional data about the CIC R1512L mutation (However, it has been identified as a statistically significant hotspot and is likely to be pathogenic).



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Genetic Variation:	FUBP1: c.1519_1528del (p.P507Gfs*155)	VAF*: 73.2%	OncoKB
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Gene information

The protein FUBP1, binds single-stranded DNA, including regulatory DNA elements upstream of genes. Among the motifs it binds is the far upstream element (FUSE), which is located upstream of the MYC oncogene (PMID: [22926519](#)). Regulation of MYC by FUBP1 is complex; while overexpression of FUBP1 can activate transcription of the MYC gene, it has also been reported that inactivating mutations of FUBP1 activate MYC expression (PMID: [20420426](#)). FUBP1 is also known to bind RNA (PMID: [23818605](#)), such as in order to regulate the splicing of MDM2, an important negative regulator of the tumor suppressor TP53 (PMID: [24798327](#)). FUBP1 was reported to be mutated at relatively low frequency (<8%) across a variety of cancers (cBioPortal, Nov 3, 2015). It is most frequently mutated in gliomas, which also show frequent deletion of 1p, where the FUBP1 gene is located (PMID: [22869205](#), [21817013](#)).

Variant Information

FUBP1 truncation mutations occur throughout the gene and are associated with decreased FUBP1 protein expression (PMID: [24117486](#)). Loss of FUBP1 on chromosome 1p is associated with IDH1 and CIC mutations on chromosome 19q in gliomas (PMID: [24117486](#), [22072542](#), [21817013](#)). In vitro studies with HEK293 cells expressing central DNA-binding domain truncated FUBP1 demonstrate that FUBP1 truncation mutations are inactivating as measured by reduced transcriptional activity compared to full-length FUBP1 (PMID: [30500954](#)). The FUBP1 P507Gfs*155 is a truncating mutation in a tumor suppressor gene, and therefore is likely pathogenic.

Genetic Variation:	TERT: c.-146C>T (C250T)	VAF*: 42.4%	OncoKB
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Gene information

The TERT gene encodes the catalytic subunit of telomerase, an enzyme that maintains telomere length and genomic integrity. TERT expression is low or absent in somatic cells; however, telomerase activity is upregulated in a vast majority of tumors and likely contributes to cancer cell immortality (PMID: [24657534](#), [9282118](#)). Sequencing of the TERT promoter identified activating mutations in a number of cancer types including melanoma, hepatocellular carcinoma, urothelial carcinoma, medulloblastoma and glioma (PMID: [23348506](#), [23530248](#)). Tumors with highly recurrent TERT promoter mutations tend to originate from tissues with lower rates of self-renewal (PMID: [23530248](#)). TERT promoter mutations, C228T and C250T, account for the majority of the somatic TERT promoter alterations and occur 124 and 146 base pairs upstream of the ATG start codon of TERT, respectively. Both promoter mutations create binding motifs for erythroblast transformation-specific (ETS)/ T-cell factor (TCF) transcription factors and enhance telomerase activity (PMID: [23348503](#), [23348506](#), [26194807](#)). In addition to promoter mutations, TERT, located on chromosome 5p, is amplified across many cancer types (PMID: [20164920](#)).

Genetic Variation:	MGMT promoter: Methylated	VAF*: N/A
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Gene information

O6-methylguanine-DNA methyltransferase (MGMT) is a DNA repair gene located on chromosome 10q26 that encodes a repair enzyme responsible for removing alkyl adducts from the O6 position of guanine. This enzyme plays a critical role in maintaining genomic integrity by reversing DNA damage induced by alkylating agents such as temozolomide (TMZ). The MGMT promoter methylation status is a well-established epigenetic biomarker in CNS tumors, particularly in glioblastoma (GBM) and lower-grade gliomas. Methylation of CpG islands within the MGMT promoter leads to transcriptional silencing of the gene, thereby reducing the tumor cells' capacity to repair alkylating agent-induced DNA damage — sensitizing the tumor to chemotherapy. MGMT promoter methylation is associated with a favorable prognostic and predictive outcome in patients with high-grade gliomas (PMID: [28266716](#), [36012105](#)). This result supports the likelihood of therapeutic benefit from alkylating agent-based regimens.

Genetic Variation:	1p19q: Co-deleted	VAF*: N/A
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Gene information

1p/19q codeletion refers to the combined whole-arm deletion of the short arm of chromosome 1 (1p) and the long arm of chromosome 19 (19q). This chromosomal alteration arises from an unbalanced translocation — $t(1;19)(q10;p10)$ — resulting in the simultaneous loss of genetic material from both arms. It is one of the most important molecular hallmarks in neuro-oncology and is considered a defining genetic event in the classification of diffuse gliomas ([PMID: 34185076](#)).

1p/19q codeletion carries significant prognostic and predictive value. Patients harboring this alteration have demonstrated markedly improved overall survival and progression-free survival compared to non-codeleted gliomas of equivalent histological grade. Furthermore, co-deleted tumors exhibit enhanced sensitivity to alkylating chemotherapy ([PMID: 28340142](#)). The detection of this codeletion supports a diagnosis within the oligodendroglial spectrum and is associated with a more favorable long-term clinical course ([PMID: 34185076](#)).

*VAF: Variant Allele Frequency



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Methodology

DNA based NGS analysis

DNA was extracted from the sample under investigation using the MagMax Total Nucleic Acid Isolation Kit (ThermoFisher). A capture based targeted next generation sequencing (NGS) analysis was performed, using the Oncology Multi-Gene Variant Assay (GenePlus) which is a qualitative in vitro diagnostic test. The analysis of 29 genes includes the entire exon regions and CNVs of 9 genes, partial exon regions of 20 genes and introns/promoters/fusion breakpoint regions of 10 genes. The test also reports on Microsatellite Instability (MSI) status. Sequencing was carried out on an MGI sequencing platform (DNBSEQ-T7).

Sequencing data are analyzed through bioinformatics pipeline for variant calling and interpretation using the Gene+Box data analysis and management system.

Sensitivity: Positive reference standards are tested with the assay, all corresponding mutation sites can be accurately detected, and the positive percent agreement (PPA) for all variants (SNVs, Indels, fusions and CNVs) assessed was 100%.

Specificity: Negative reference standards are tested with the assay, and the negative percent agreement (NPA) of SNVs, Indels, fusions and CNVs was 100%.

Limit of Detection (LoD): The limit of detection (LoD) of this assay is listed in the table below. The LoD is based on as low as 50 ng of gDNA input for library preparation. The assay can also be used to test microsatellite instability (MSI) with a tumor cell content as low as 10%.

Tumor Type	Limit of Detection
Single nucleotide variations (SNV)	Hotspot: VAF $\geq 2\%$; Non-hotspot: VAF $\geq 5\%$
Insertions/deletions (Indel)	Hotspot: VAF $\geq 2\%$; Non-hotspot: VAF $\geq 5\%$
Fusion (or rearrangement)	VAF $\geq 2\%$

MGMT promoter gene methylation

The CE-IVD geneMAP™ Methylation Analysis methylation-specific Realtime PCR (MSP) kit was used for the detection of MGMT promoter methylation in combination with the QuantStudio 3 Real Time PCR System (ThermoFisher) platform. Interpretation of results was conducted according to the manufactures instructions.

1p19q co-deletion

The CE-IVD ZytoLight® Glioma 1p/19q Probe Set (ZytoVision) was used for the qualitative detection of deletions involving the human chromosomal region 1p36.31 as well as deletions involving the human chromosomal region 19q13.32-q13.33 by fluorescence in situ hybridization (FISH). Interpretation of results was conducted according to the manufactures instructions.



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Quality Control Results

Quality Control Index		Result	Criteria
Sequencing Quality Assessment	Average effective sequencing depth ¹	760	≥ 500
	Fraction of target covered with ≥ 50x ²	100%	≥99%
	Fraction of base quality ≥ Q30 ³	99%	≥80%
Tumor cell content ⁴		60%	>20%
Overall Assessment ⁵		PASS	

Note:

1. Average effective sequencing depth: Average sequencing depth on target without duplicated reads.
2. Fraction of target covered with ≥ 50x: The proportion of bases that sequencing depth reach or above 50x on target, this index reflecting the coverage uniformity of sequencing.
3. Fraction of base quality ≥ Q30: The proportion of base quality in sequencing data that reach or above Q30, that is the probability of base recognition accuracy rate exceeds 99.9%.
4. An overall tumor cell content percentage of ≥ 20% is recommended for the efficient detection of somatic alterations in the sample analyzed.
5. Overall Assessment: The quality control overall assessment results are divided into two levels: "PASS" and "RISK". When the overall quality assessment result is "RISK", 94-96% of coverage was achieved in the genes analysed, hence there is a small range where clinical actionable variations could be undetected.

Disclaimer

1. This test is mainly used to assist clinical decision-making, and the result does not represent clinical decision.
2. The test should be interpreted by combining the actual patient context.
3. As evidence on variants and drugs evolves, previous classifications may later be modified. The interpretation of a variant is based on current available evidence.
4. Sequence variants were reported using Human Genome Variation Society (HGVS) nomenclature. Classification and interpretation of variants follow guidelines of American College of Medical Genetics and Genomics (ACMG), Association of Molecular Pathology (AMP), American Society of Clinical Oncology (ASCO) and College of American Pathologists (CAP).
5. Database and references used: Reference genome (GRCh37), annotation using A Locus Reference Genomic (LRG), database referencing 1000G (phaseIII-ucsc), EXAC (0.3.1), dbSNP (147), PolyPhen2/SIFT (ensdb v73), PhyloP (2013-12-06), Clinvar (2018-8) and Cosmic(V80).

Limitations

1. The test is limited to test genomic variations on DNA level and does not involve RNA level or protein level.
2. Scientific data show that not all patients carry genomic variations that are associated with targeted drug, therefore not all subjects can be matched with targeted therapies or clear resistance mechanism.
3. Genetic variation beyond the detection range of this test or some non-gene mutation related factors such as drug interactions may affect the clinical effects of drugs.
4. Fraction of base quality ≥ Q30: The proportion of base quality in sequencing data that reaches or exceeds Q30, indicating that the probability of base recognition accuracy rate exceeds 99.9%.

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5. Every molecular test has an internal 0.5-1% chance of failure. This is due to rare molecular events and factors related to the preparation and analysis of the samples.
6. Improper sample collection, transportation and storage may lead to compromised or invalid results.



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Genes Analyzed

29 gene alterations									
ATRX*	BRAF*	CDKN2A*	CDKN2B*	CIC*	CTNNB1*	EGFR*	ERBB2*	FUBP1*	H3F3A
HIST1H3B	HIST1H3C	IDH1	IDH2	MET	MYC	MYCN	MYD88	NF1	NF2
PTCH1	SMARCA4	SMARCB1	SMO	SUFU	TERT	TP53	TSC1	TSC2	
10 fusions									
ALK	BRAF	FGFR1	FGFR2	FGFR3	NTRK1	NTRK2	NTRK3	RET	ROS1
MGMT methylation									
1p19q co-deletion**									

*CNV (amplification/deletion) analysis is included for these genes

**1p19q is tested only when an IDH1/IDH2 mutation is detected.

Table 1.

Diagnosis-Related gene alterations, included in the panel based on 2021 WHO classification of CNS tumors	
Tumor Type	Genes Altered
Astrocytoma, IDH-mutant	IDH1, IDH2, ATRX, TP53, CDKN2A/B
Oligodendroglioma, IDH-mutant, and 1p/19q-codeleted	IDH1, IDH2, 1p/19q, TERT promoter, CIC, FUBP1
Glioblastoma, IDH-wildtype	IDH-wildtype, TERT promoter, EGFR
Polymorphous low-grade neuroepithelial tumor of the young	BRAF, FGFR family
Diffuse low-grade glioma, MAPK pathway-altered	FGFR1, BRAF
Diffuse midline glioma, H3 K27-altered	H3 K27, TP53, PDGFRA
Diffuse hemispheric glioma, H3 G34-mutant	H3 G34, TP53, ATRX
Diffuse pediatric-type high-grade glioma, H3-wildtype, and IDH-wildtype	IDH-wildtype, H3-wildtype, PDGFRA, MYCN, EGFR
Infant-type hemispheric glioma	NTRK family, ALK, ROS, MET
Pilocytic astrocytoma	KIAA1549-BRAF, BRAF, NF1
High-grade astrocytoma with piloid features	BRAF, NF1, ATRX
Pleomorphic xanthoastrocytoma	BRAF, CDKN2A/B
Subependymal giant cell astrocytoma	TSC1, TSC2
Ganglion cell tumors	BRAF
Dysembryoplastic neuroepithelial tumor	FGFR1
Rosette-forming glioneuronal tumor	FGFR1, PIK3CA, NF1
Diffuse leptomeningeal glioneuronal tumor	KIAA1549-BRAF fusion
Dysplastic cerebellar gangliocytoma (Lhermitte-Duclos disease)	PTEN
Extraventricular neurocytoma	FGFR (FGFR1-TACC1 fusion), IDH-wildtype
Spinal ependymomas	NF2, MYCN
Medulloblastoma, WNT-activated	CTNNB1
Medulloblastoma, SHH-activated	TP53, PTCH1, SUFU, SMO, MYCN
Medulloblastoma, non-WNT/non-SHH	MYC, MYCN
Atypical teratoid/rhabdoid tumor	SMARCB1, SMARCA4
Desmoplastic myxoid tumor of the pineal region, SMARCB1-mutant	SMARCB1
Meningiomas	SMO, H3K27, TERT promoter, CDKN2A/B
Adamantinomatous craniopharyngioma	CTNNB1
Papillary craniopharyngioma	BRAF



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References

1. Louis DN, et al. **The 2021 WHO Classification of Tumors of the Central Nervous System: a summary.** Neuro Oncol. 2021 Aug 2;23(8):1231-1251. PMID: [34185076](#). PMCID: PMC8328013, DOI: 10.1093/neuonc/noab106
2. Binabaj MM, et al. **The prognostic value of MGMT promoter methylation in glioblastoma: A meta-analysis of clinical trials.** J Cell Physiol. 2018 Jan;233(1):378-386. PMID: [28266716](#) DOI: 10.1002/jcp.25896
3. Sareen H, et al. **Molecular Biomarkers in Glioblastoma: A Systematic Review and Meta-Analysis.** Int J Mol Sci. 2022 Aug 9;23(16):8835. PMID: [36012105](#) PMCID: PMC9408540, DOI: 10.3390/ijms23168835
4. Jacob AG, et al. **The splicing factor FUBP1 is required for the efficient splicing of oncogene MDM2 pre-mRNA.** J Biol Chem. 2014; 289:17350-64. doi: 10.1074/jbc.M114.554717 (PMID: [24798327](#))
5. Hsiao HH, et al. **Quantitative characterization of the interactions among c-myc transcriptional regulators FUSE, FBP, and FIR.** Biochemistry. 2010; 49:4620-34. doi: 10.1021/bi9021445 (PMID: [20420426](#))
6. Bettgowda C, et al. **Mutations in CIC and FUBP1 contribute to human oligodendroglioma.** Science. 2011; 333:1453-5. doi: 10.1126/science.1210557 (PMID: [21817013](#))
7. Lam YC, et al. **ATAXIN-1 interacts with the repressor Capicua in its native complex to cause SCA1 neuropathology.** Cell. 2006; 127:1335-47. doi: 10.1016/j.cell.2006.11.038 (PMID: [17190598](#))
8. Jiao Y, et al. **Frequent ATRX, CIC, FUBP1 and IDH1 mutations refine the classification of malignant gliomas.** Oncotarget. 2012; 3:709-22. doi: 10.18632/oncotarget.588 (PMID: [22869205](#))
9. Debaize L, et al. **Interplay between transcription regulators RUNX1 and FUBP1 activates an enhancer of the oncogene c-KIT and amplifies cell proliferation.** Nucleic Acids Res. 2018; 46:11214-11228. doi: 10.1093/nar/gky756 (PMID: [30500954](#))
10. Yip S, et al. **Concurrent CIC mutations, IDH mutations, and 1p/19q loss distinguish oligodendrogliomas from other cancers.** J Pathol. 2012; 226:7-16. doi: 10.1002/path.2995 (PMID: [22072542](#))
11. Goff DJ, et al. **Establishment of dorsal-ventral polarity of the Drosophila egg requires capicua action in ovarian follicle cells.** Development. 2001; 128:4553-62. doi: 10.1242/dev.128.22.4553 (PMID: [11714680](#))
12. Okimoto RA, et al. **Inactivation of Capicua drives cancer metastasis.** Nat Genet. 2017; 49:87-96. doi: 10.1038/ng.3728 (PMID: [27869830](#))
13. Mardis ER, et al. **Recurring mutations found by sequencing an acute myeloid leukemia genome.** N Engl J Med. 2009; 361:1058-66. doi: 10.1056/NEJMoa0903840 (PMID: [19657110](#))
14. Dang L, et al. **Cancer-associated IDH1 mutations produce 2-hydroxyglutarate.** Nature. 2009; 462:739-44. doi: 10.1038/nature08617 (PMID: [19935646](#))
15. Horn S, et al. **TERT promoter mutations in familial and sporadic melanoma.** Science. 2013; 339:959-61. doi: 10.1126/science.1230062 (PMID: [23348503](#))
16. Wang B, et al. **ATXN1L, CIC, and ETS Transcription Factors Modulate Sensitivity to MAPK Pathway Inhibition.** Cell Rep. 2017; 18:1543-1557. doi: 10.1016/j.celrep.2017.01.031 (PMID: [28178529](#))
17. Beroukhi R, et al. **The landscape of somatic copy-number alteration across human cancers.** Nature. 2010; 463:899-905. doi: 10.1038/nature08822 (PMID: [20164920](#))
18. Killela PJ, et al. **TERT promoter mutations occur frequently in gliomas and a subset of tumors derived from cells with low rates of self-renewal.** Proc Natl Acad Sci U S A. 2013; 110:6021-6. doi: 10.1073/pnas.1303607110 (PMID: [23530248](#))
19. Popovici-Muller J, et al. **Discovery of AG-120 (Ivosidenib): A First-in-Class Mutant IDH1 Inhibitor for the Treatment of IDH1 Mutant Cancers.** ACS Med Chem Lett. 2018; 9:300-305. doi: 10.1021/acsmchemlett.7b00421 (PMID: [29670690](#))
20. Zhang J and Chen QM. **Far upstream element binding protein 1: a commander of transcription, translation and beyond.** Oncogene. 2013; 32:2907-16. doi: 10.1038/ncr.2012.350 (PMID: [22926519](#))
21. Graham C, et al. **The CIC-DUX4 fusion transcript is present in a subgroup of pediatric primitive round cell sarcomas.** Hum Pathol. 2012; 43:180-9. doi: 10.1016/j.humpath.2011.04.023 (PMID: [21813156](#))
22. Roch F, et al. **EGFR signalling inhibits Capicua-dependent repression during specification of Drosophila wing veins.** Development. 2002; 129:993-1002. doi: 10.1242/dev.129.4.993 (PMID: [11861482](#))
23. Heidenreich B, et al. **TERT promoter mutations in cancer development.** Curr Opin Genet Dev. 2014; 24:30-7. doi: 10.1016/j.gde.2013.11.005 (PMID: [24657534](#))



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24. Lee Y, et al. ATXN1 protein family and CIC regulate extracellular matrix remodeling and lung alveolarization. Dev Cell. 2011; 21:746-57. doi: 10.1016/j.devcel.2011.08.017 (PMID: 22014525) 25. Jiménez G, et al. Relief of gene repression by torso RTK signaling: role of capicua in Drosophila terminal and dorsoventral patterning. Genes Dev. 2000; 14:224-31. (PMID: 10652276) 26. McKenney AS, et al. JAK2/IDH-mutant-driven myeloproliferative neoplasm is sensitive to combined targeted inhibition. J Clin Invest. 2018; 128:789-804. doi: 10.1172/JCI94516 (PMID: 29355841) 27. DiNardo CD, et al. Durable Remissions with Ivosidenib in IDH1-Mutated Relapsed or Refractory AML. N Engl J Med. 2018; 378:2386-2398. doi: 10.1056/NEJMoa1716984 (PMID: 29860938) 28. Ward PS, et al. The common feature of leukemia-associated IDH1 and IDH2 mutations is a neomorphic enzyme activity converting alpha-ketoglutarate to 2-hydroxyglutarate. Cancer Cell. 2010; 17:225-34. doi: 10.1016/j.ccr.2010.01.020 (PMID: 20171147) 29. Sahm F, et al. CIC and FUBP1 mutations in oligodendrogliomas, oligoastrocytomas and astrocytomas. Acta Neuropathol. 2012; 123:853-60. doi: 10.1007/s00401-012-0993-5 (PMID: 22588899) 30. Sasaki M, et al. IDH1(R132H) mutation increases murine haematopoietic progenitors and alters epigenetics. Nature. 2012; 488:656-9. doi: 10.1038/nature11323 (PMID: 22763442) 31. Wong D and Yip S. Making heads or tails - the emergence of capicua (CIC) as an important multifunctional tumour suppressor. J Pathol. 2020; 250:532-540. doi: 10.1002/path.5400 (PMID: 32073140) 32. Weissmann S, et al. The Tumor Suppressor CIC Directly Regulates MAPK Pathway Genes via Histone Deacetylation. Cancer Res. 2018; 78:4114-4125. doi: 10.1158/0008-5472.CAN-18-0342 (PMID: 29844126) 33. Yoshimoto M, et al. Detailed cytogenetic and array analysis of pediatric primitive sarcomas reveals a recurrent CIC-DUX4 fusion gene event. Cancer Genet Cytogenet. 2009; 195:1-11. doi: 10.1016/j.cancergencyto.2009.06.015 (PMID: 19837261) 34. Sugita S, et al. A novel CIC-FOXO4 gene fusion in undifferentiated small round cell sarcoma: a genetically distinct variant of Ewing-like sarcoma. Am J Surg Pathol. 2014; 38:1571-6. doi: 10.1097/PAS.0000000000000286 (PMID: 25007147) 35. Huang FW, et al. Highly recurrent TERT promoter mutations in human melanoma. Science. 2013; 339:957-9. doi: 10.1126/science.1229259 (PMID: 23348506) 36. Losman JA and Kaelin WG. What a difference a hydroxyl makes: mutant IDH, (R)-2-hydroxyglutarate, and cancer. Genes Dev. 2013; 27:836-52. doi: 10.1101/gad.217406.113 (PMID: 23630074) 37. Losman JA, et al. (R)-2-hydroxyglutarate is sufficient to promote leukemogenesis and its effects are reversible. Science. 2013; 339:1621-5. doi: 10.1126/science.1231677 (PMID: 23393090) 38. Li H, et al. Far upstream element-binding protein 1 and RNA secondary structure both mediate second-step splicing repression. Proc Natl Acad Sci U S A. 2013; 110:E2687-95. doi: 10.1073/pnas.1310607110 (PMID: 23818605) 39. Chiba K, et al. Cancer-associated TERT promoter mutations abrogate telomerase silencing. Elife. 2015; 4:(unknown pages). doi: 10.7554/eLife.07918 (PMID: 26194807) 40. Shay JW and Bacchetti S. A survey of telomerase activity in human cancer. Eur J Cancer. 1997; 33:787-91. doi: 10.1016/S0959-8049(97)00062-2 (PMID: 9282118) 41. Cancer Genome Atlas Research Network. Comprehensive molecular characterization of gastric adenocarcinoma. Nature. 2014; 513:202-9. doi: 10.1038/nature13480 (PMID: 25079317) 42. Baumgarten P, et al. Loss of FUBP1 expression in gliomas predicts FUBP1 mutation and is associated with oligodendroglial differentiation, IDH1 mutation and 1p/19q loss of heterozygosity. Neuropathol Appl Neurobiol. 2014; 40:205-16. doi: 10.1111/nan.12088 (PMID: 24117486)			