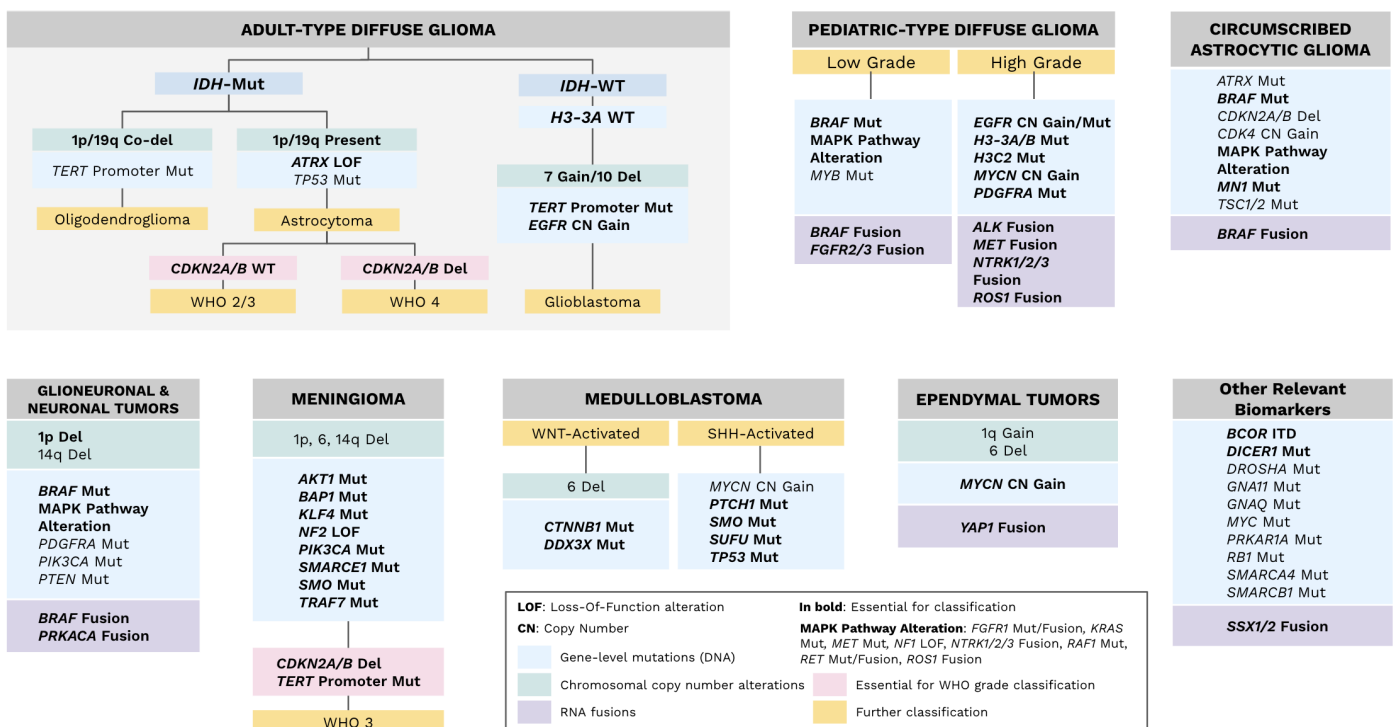# LUCENCE

Profiling Brain Tumors to Standard-of-Care

Supporting WHO Blue Book CNS Tumor Classification [1]

UNITED™ CNS is a next-generation sequencing (NGS) panel aiding in the classification of central nervous system (CNS) tumors.

The test runs simultaneous interrogation of molecular alterations essential for the classification of various CNS tumor subtypes and grades — supporting accurate diagnosis and treatment of both adult and pediatric CNS tumors.

WHO 2021 CNS Tumor Classification - Required Targets on UNITED™ CNS

ADULT-TYPE DIFFUSE GLIOMA

IDH-Mut

1p/19q Co-del
TERT Promoter Mut
Oligodendroglioma

1p/19q Present
ATRX LOF
TP53 Mut
Astrocytoma

CDKN2A/B WT → WHO 2/3
CDKN2A/B Del → WHO 4

IDH-WT
H3-3A WT

7 Gain/10 Del
TERT Promoter Mut
EGFR CN Gain
Glioblastoma

PEDIATRIC-TYPE DIFFUSE GLIOMA

Low Grade
BRAF Mut
MAPK Pathway
Alteration
MYB Mut

BRAF Fusion
FGFR2/3 Fusion

High Grade
EGFR CN Gain/Mut
H3-3A/B Mut
H3C2 Mut
MYCN CN Gain
PDGFRA Mut

ALK Fusion
MET Fusion
NTRK1/2/3 Fusion
ROS1 Fusion

CIRCUMSCRIBED ASTROCYTIC GLIOMA

ATRX Mut
BRAF Mut
CDKN2A/B Del
CDK4 CN Gain
MAPK Pathway
Alteration
MN1 Mut
TSC1/2 Mut

BRAF Fusion

GLIONEURONAL & NEURONAL TUMORS

1p Del
14q Del

BRAF Mut
MAPK Pathway
Alteration
PDGFRA Mut
PIK3CA Mut
PTEN Mut

BRAF Fusion
PRKACA Fusion

MENINGIOMA

1p, 6, 14q Del

AKT1 Mut
BAP1 Mut
KLF4 Mut
NF2 LOF
PIK3CA Mut
SMARCE1 Mut
SMO Mut
TRAF7 Mut

CDKN2A/B Del
TERT Promoter Mut

WHO 3

MEDULLOBLASTOMA

WNT-Activated
6 Del
CTNNB1 Mut
DDX3X Mut

SHH-Activated
MYCN CN Gain
PTCH1 Mut
SMO Mut
SUFU Mut
TP53 Mut

EPENDYMAL TUMORS

1q Gain
6 Del

MYCN CN Gain

YAP1 Fusion

Other Relevant Biomarkers

BCOR ITD
DICER1 Mut
DROSHA Mut
GNA11 Mut
GNAQ Mut
MYC Mut
PRKAR1A Mut
RB1 Mut
SMARCA4 Mut
SMARCB1 Mut

SSX1/2 Fusion

LOF: Loss-Of-Function alteration
CN: Copy Number

In bold: Essential for classification
MAPK Pathway Alteration: *FGFR1* Mut/Fusion, *KRAS* Mut, *MET* Mut, *NF1* LOF, *NTRK1/2/3* Fusion, *RAF1* Mut, *RET* Mut/Fusion, *ROS1* Fusion

- Gene-level mutations (DNA)
- Chromosomal copy number alterations
- RNA fusions
- Essential for WHO grade classification
- Further classification

Test Specifications [2]

Methodology	Ultra-deep next-generation sequencing
Biomarkers analyzed	• SNVs, Indels, Fusions • Gene copy number variations, chromosomal copy number alterations • Microsatellite Instability (MSI) and Tumor Mutational Burden (TMB)
Sample type	FFPE tumor tissue
Turnaround time	2 weeks

	Sensitivity	Specificity
SNVs/Indels	98%	100%
Fusions	91.25%	100%
MSI-High	100%	100%

	R^2 Correlation to Whole Exome Sequencing
TMB	98.6%

- Results tested at the stated mutant allele frequencies using reference standards, FFPE cell line samples, and FFPE clinical samples.
- Sensitivity and specificity reported for SNVs and Indels are at 5% VAF.
- The limit of detection for chromosomal copy number alterations is 30% tumor fraction.

References [1] Gritsch, S. et al. Cancer 2022 128(1):47–58. [2] Ng, CC-Y. et al. Front. Mol. Biosci. 2022. 9:963243.

Gene List

The subset of genes relevant to CNS, targeted by UNITED™ CNS. Full gene list in UNITED™ brochure.

SNVs, Indels & CNVs

AKT1	*CDKN2A*	*FGFR1*	*H3C2*	*MYB*	*NTRK3*	*RB1*	*SSX1*
ALK	*CDKN2B*	*FGFR2*	*IDH1*	*MYC*	*PDGFRA*	*RET*	*SUFU*
ATRX	*CTNNB1*	*FGFR3*	*IDH2*	*MYCN*	*PIK3CA*	*ROS1*	*TERT*
BAP1	*DDX3X*	GNA11	KLF4	*NF1*	*PRKAR1A*	SMARCA4	*TP53*
BCOR	*DICER1*	GNAQ	*KRAS*	*NF2*	*PTCH1*	SMARCB1	TRAF7
BRAF	DROSHA	*H3-3A*	*MET*	NTRK1	PTEN	*SMARCE1*	TSC1
CDK4	*EGFR*	*H3-3B*	*MN1*	*NTRK2*	*RAF1*	*SMO*	TSC2

Genes in **bold** are essential for standard-of-care CNS classification.

RNA Fusions

ALK	FGFR1	*MET*	*NTRK2*	PDGFRA	RAF1	*ROS1*	*SSX2**
BRAF	*FGFR2*	*NTRK1*	*NTRK3*	*PRKACA**	RET	*SSX1*	*YAP1**
EGFR	*FGFR3*						

Genes in **bold** are essential for standard-of-care CNS classification.
**Genes tested in RNA panel only.

Chromosomal Copy Number Alterations

1p	1q	6	**7**	**10**	14q	19p	**19q**

Chromosome/chromosome arms in **bold** are essential for standard-of-care CNS classification.