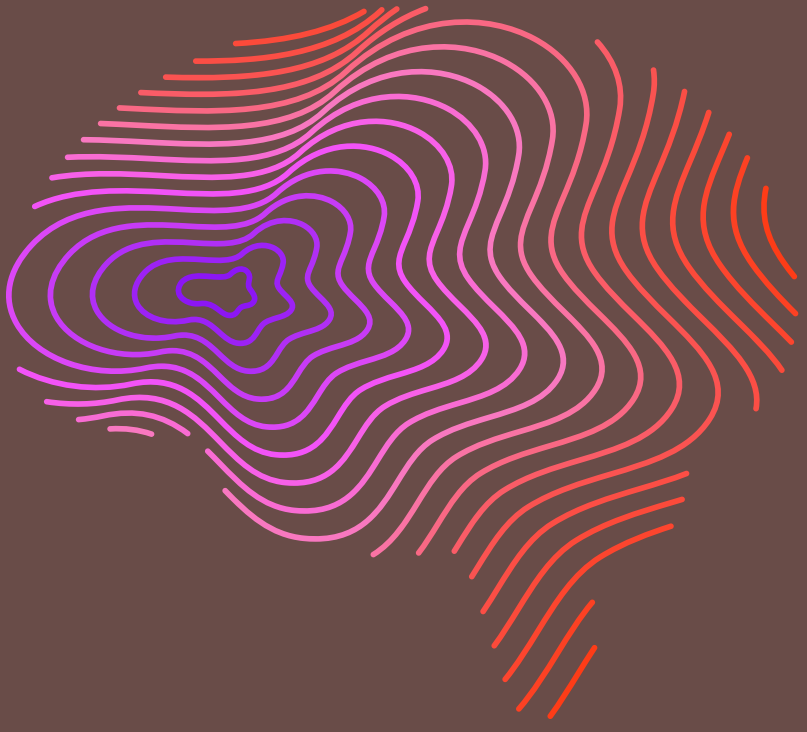
trublood®

the no risk biopsy



CNS

WHO Classification Compliant	Can Substitute Invasive Biopsy in Most Cases	Complete Diagnostic + Theranostic Work-up	Report in 7 Days

CLINICALLY VALIDATED

DATAR CANCER GENETICS

UNITED KINGDOM | GERMANY | INDIA

datarpgx.com

trublood® CNS

CAN SUBSTITUTE INVASIVE BIOPSIES IN MOST CASES

A NON-INVASIVE, BLOOD-BASED INVESTIGATION

- ✓ Symptomatic individuals who have been advised an invasive tissue biopsy to check for malignancy.
- ✓ Patients where an invasive biopsy has been inconclusive or inconsistent with clinical observations.
- ✓ Suspected cases of relapse.

A Space Occupying Lesion (SOL) in the brain is diagnosed by analysis of invasively accessed tumor tissue. If malignancy is confirmed, follow-through WHO molecular classification is imperative. However, there are looming risks of serious complications in tissue biopsies of the brain, including permanent morbidities or even death. Additionally, invasive biopsies can be inconclusive due to significant necrotic tissue in the tumors. These challenges are aggravated where disambiguation is required between a suspected metastatic relapse in the brain versus a new primary, cases of post treatment progression / pseudo progression and cases where a biopsy is considered too risky or impossible due to location of the lesion or due to comorbidities.

Trublood® CNS is a significant technical advancement that provides a viable alternative to invasive tumor biopsy in suspected CNS malignancies, mainly astrocytomas.

Trublood® CNS evaluates Circulating Tumor Cells (CTCs), cell free DNA and exosomal RNA using multiple platforms including ICC, NGS, FISH and functional interrogation for specific anticancer agents such as Temozolomide.

Trublood® CNS provides the treating clinician with the most relevant information for establishing diagnosis as per WHO classification, prognostication and stratification of patients for therapy selection and monitoring of disease progression – all without the need of an invasive biopsy.

EXECUTIVE SUMMARY

WHAT

Non-Invasive Diagnostic biopsy to substitute invasive tissue extraction.

FOR WHOM

Every Individual who has been advised a brain biopsy and desires a risk-free option.

WHY

Invasive biopsies are risky, inconvenient, painful and must be performed in a clinical setting. Trublood® CNS sample can be collected from patient's house or office.

HOW

Circulating Tumor Cells and Nucleic Acid are isolated from patient's blood sample and extensively analysed for diagnosis, prognosis and theranostics.

ANALYTES

Circulating Tumor Cells (CTCs), cell free DNA + RNA, Germline DNA.

TESTS

Immunocytochemistry (ICC) / Fluorescence Microscopy, Next Generation Sequencing (NGS), Droplet Digital Polymerase Chain Reaction (ddPCR), Fluorescence in Situ Hybridization (FISH), Live Cell Functional Interrogation.

SAMPLE TYPE

Peripheral blood as per protocol.

TURN AROUND TIME

7 Days

VALIDATION

Trublood® CNS

Trublood® CNS non-invasive diagnostic biopsy for suspected brain malignancies has been developed by Datar Cancer Genetics based on the findings of two clinical trials registered with the CTRI (Registration No. CTRI/2019/02/017663).

Trublood® CNS has been extensively validated with data from more than 1,000 samples from asymptomatic individual donors as well as more than 200 samples from patients with various CNS malignancies and 27 patients with benign conditions totalling more than 1,250 evaluable samples till December, 2019.

SENSITIVITY	SPECIFICITY
73.1%	100%

Basis

- Circulating Tumor Cells (CTCs) are viable malignant cells that have been released by tumors into circulation.
- Non-tumorigenic cells in peripheral blood have functional apoptotic mechanism, but CTCs are resistant to apoptosis.
- An epigenetically active stabilizing process can eliminate normal cells and confer survival privilege on apoptosis - resistant CTCs.
- Sufficient CTCs can be enriched and harvested for Immunocytochemistry (ICC) profiling with markers used in immunohistochemistry (IHC) which aid in determination of histopathological subtypes of tumor tissue.
- CTCs in brain tumors are defined as cells in the peripheral blood that are CD45 (-) and positive for various brain tumor related markers (e.g. GFAP, S100, Nestin etc.) depending upon the tumor type.
- Antibody clones used in the Trublood® CNS assay for analysis of tumor antigens/ markers are internationally approved for IVD use.

Usual Tissue Biopsy	Trublood® CNS
Invasive, needs tissue and is ultimately expensive	Completely non invasive and is ultimately less expensive
Requires Hospitalization and Anesthesia / sedatives	No need for Hospitalization / Anesthesia
Risk of serious complications such as hemorrhage, cerebral, edema	No risk of complications
Risk of permanent morbidities	No risk of morbidities
Serial / sequential biopsies are impossible	Can be performed as often as necessary
Not viable if primary tumor is inaccessible	Viable even if primary / metastasis are undetectable

CENTRAL NERVOUS SYSTEM (BRAIN)

RISK FACTORS ASSOCIATED WITH CONVENTIONAL INVASIVE CNS BIOPSIES

- Intracranial hemorrhage
- Cerebral edema
- Infection
- Problems with sedation or anesthesia
- Permanent morbidity

RADIOLOGICAL SIGNS OF CNS MALIGNANCIES

- Heterogeneous poorly marginated mass
- Thick, irregular-enhancing margins and a central necrotic core or hemorrhagic component
- Multiple areas of enhancement connected to each other by abnormal white matter signal
- Mass with possible ring enhancement

LIMITATIONS

- May not differentiate between astrocytoma and oligodendroglioma.
- Identification of rare histological subtypes may not be possible.

Platform	Gene/Marker	SNV	CNAs	Expression	Functional Assay
IMMUNOCYTOCHEMISTRY	GFAP			•	
	S100			•	
	Nestin			•	
	PanCK			•	
	EMA			•	
	OLIG2			•	
	Transthyretin			•	
	Synaptophysin			•	
	Cam 5.2			•	
	CK7			•	
	CD45			•	
	IDH R132H			•	
NEXT GENERATION SEQUENCING	ATRX	•	•		
	BRAF	•			
	CDKN2A	•	•		
	CDKN2B	•	•		
	CIC	•	•		
	EGFR	•	•		
	FUBP1	•			
	H3F3A	•			
	HIST1H3B	•			
	HIST1H3C	•			
	IDH1	•			
	IDH2	•			
	PDGFRA	•	•		
	PTEN	•	•		
	TP53	•	•		
ddPCR[1]	EGFR vIII			•	
	TERT	•			
	IDH1 R132H	•			
FISH[2]	1p19q co-deletion		•		
	Chr.7 and Chr. 10		•		
	EGFR		•		
FM[3]	MGMT				•

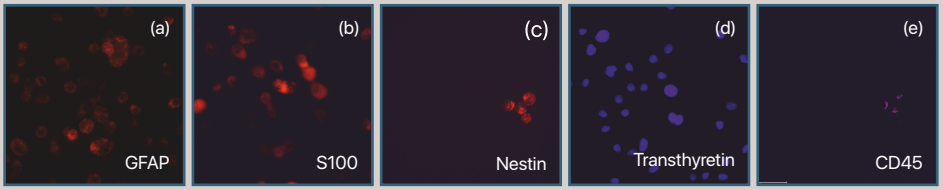
DIFFERENTIAL DIAGNOSIS

- ✓ Astrocytoma / Oligodendroglioma
- ✓ Anaplastic oligodendroglioma
- ✓ Anaplastic Astrocytoma
- ✓ Glioblastoma
- ✓ Medulloblastoma
- ✓ Diffuse Intrinsic Pontine Glioma (DIPG)
- ✓ Ependymoma
- ✓ Choroid Plexus Tumor

[1] ddPCR - Droplet Digital Polymerase Chain Reaction
[2] FISH - Fluorescence in Situ Hybridization
[3] FM - Fluorescence Microscopy

Exosomal mRNA Sequencing (20,800 Genes)

ILLUSTRATIVE IMMUNOCYTOCHEMISTRY IMAGES



PHARMACOGENETICS

Pharmacogenetic Analysis is performed on germline DNA for those drugs which are relevant for the respective patient's cancer from the following table:

ONCOLOGY

- ✓ Carboplatin
- ✓ Cisplatin
- ✓ Cyclophosphamide
- ✓ Methotrexate
- ✓ Oxaliplatin
- ✓ Rituximab
- ✓ Vincristine

NEUROLOGY / PSYCHIATRY

- ✓ Amitriptyline
- ✓ Aripiprazole
- ✓ Atomoxetine
- ✓ Brexpiprazole
- ✓ Bupropion
- ✓ Citalopram
- ✓ Clobazam
- ✓ Clomipramine
- ✓ Clozapine
- ✓ Desipramine
- ✓ Dextroamphetamine
- ✓ Diazepam
- ✓ Doxepin
- ✓ Escitalopram
- ✓ Fluoxetine
- ✓ Galantamine
- ✓ Haloperidol
- ✓ Iloperidone
- ✓ Imipramine
- ✓ Midazolam
- ✓ Mirtazapine
- ✓ Nortriptyline
- ✓ Paroxetine
- ✓ Perphenazine
- ✓ Pimozide
- ✓ Sertraline
- ✓ Thioridazine
- ✓ Trimipramine
- ✓ Venlafaxine
- ✓ Zuclopenthixol

PAIN MANAGEMENT

- ✓ Alfentanil
- ✓ Buprenorphine
- ✓ Carisoprodol
- ✓ Codeine
- ✓ Fentanyl
- ✓ Hydrocodone
- ✓ Ibuprofen
- ✓ Morphine
- ✓ Oxycodone
- ✓ Tramadol

SAMPLE COLLECTION

Requirement : Total 5 Tubes containing 34 ml whole blood

FIRST DRAW	SECOND DRAW	THIRD DRAW
		
2 ml	8 ml, 8 ml	10 ml, 6 ml
SST Tube (Yellow Cap)	DCG Tube (Brown Cap)	EDTA Tube (Purple Cap)

Note:

- Sequence of draw should not be altered.
- Blood should be drawn only and only as per above method.
- Blood drawn should be performed only by qualified phlebotomist under medical supervision.
- Ship at 4 °C in the container provided by DCG.

Precautions

- The patient must not have received any form of cancer therapy (radiation / chemotherapy / surgery / endocrine etc.) at least 15 days prior to collection of sample.
- The patient must not have received oral or IV corticosteroids at least 15 days prior to collection of sample.
- Patient has no current febrile or any other acute inflammatory illness.
- Patient does not have acute exacerbation or flare-up of an inflammatory condition requiring escalation in medical therapy at least 5 days prior to collection of sample.
- Patient has not received blood transfusion / PET-CT / CT scan at least 5 days prior to collection of sample.

PUBLICATIONS

IJC International Journal of Cancer

- ✓ Circulating Ensembles of Tumor Associated Cells: A Redoubtable New Systemic Hallmark of Cancer.

OXFORD ACADEMIC Neuro-Oncology

- ✓ Diagnosis of Gliomas Using Circulating Glial Cells.
- ✓ Prospective, Blinded Plasma Based Analysis for Diagnosis of Newly Diagnosed Glioma.
- ✓ Algorithm Based Liquid Biopsy for the Diagnosis of Glioblastoma.
- ✓ Liquid Biopsy for Identification of Newly Diagnosed Glioma.

AACR American Association for Cancer Research

- ✓ A mRNA Signature that Accurately Discerns Gliomas from Healthy Individuals.

- Turn Around Time (TAT) for above report is 7 working days.

Intellectual Property

- Trublood® CNS comprises processes, technologies and trade-marks / copyrights which are proprietary to Datar Cancer Genetics and could be the subject matter of Intellectual Property rights under various jurisdictions.

Contact us:
response@datarpgx.com
datarpgx.com

CAP ACCREDITED | CLIA Accredited Laboratory No.: 99D2171983

DATAR CANCER GENETICS
UNITED KINGDOM | GERMANY | INDIA