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Selective Phenotypic and Genotypic Evaluation of Circulating Glial Cells for Improved Diagnosis of Glial Malignancies

DATAR CANCER GENETICS
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S. Limaye[1], F. Massoudi[2], N. Rohatgi[3], D. Akolkar[4], R. Datar[4], T. Crook[5], S. Schuster[6], V. Datta[4], P. Shejwalkar[4], S. Patel[4], K. O'Neill[7], D. S. Patil[4], N. Syed[8]

[1]Medical Oncology, Sir H. N. Reliance Foundation Hospital, Mumbai, India, [2]Neurosurgery, Orange Coast Medical Center – Memorial Care, Fountain Valley, CA, USA, [3]Medical Oncology, Fortis Memorial Research Institute, Gurugram, Delhi, India, [4]Molecular Oncology, Datar Cancer Genetics, Nashik, India, [5]Oncology department, Cromwell Hospital, London, UK, [6]Molecular Oncology, Datar Cancer Genetics Europe GmbH, Eckersdorf, Germany, [7]Neurosurgery, Charing Cross Hospital – Imperial College Healthcare NHS Trust, London, UK, [8]Brain Sciences, Imperial College London-Hammersmith Campus, London, UK

INTRODUCTION

- The diagnosis of glial malignancies (GLI-M) in individuals presenting with radiologically evident intracranial space-occupying lesions (ICSOL) is based on histopathological examination (HPE) of tumor tissue obtained via surgical resection or via a biopsy in cases where the tumor cannot be surgically resected.
- Surgical resection may not be viable due to the proximity of the lesion to regions associated with vital functions or comorbidities; up to 40% of cases with high-grade brain cancers have been reported to be unresectable.
- Further, brain biopsies have been reported to be unviable, inconclusive, or non-diagnostic in up to 20% of cases.
- Finally, about 70% of all brain tumors are eventually diagnosed as non-malignant (benign).
- Accurate diagnosis plays a critical role in the effective management of glial malignancies.
- However, obtaining tissue specimens for histopathologic investigation carries inherent procedural risks.

CONTACT

Dr. Sewanti Limaye, MD,
Sir H. N. Reliance Foundation Hospital, Mumbai, India
sewanti@yahoo.com

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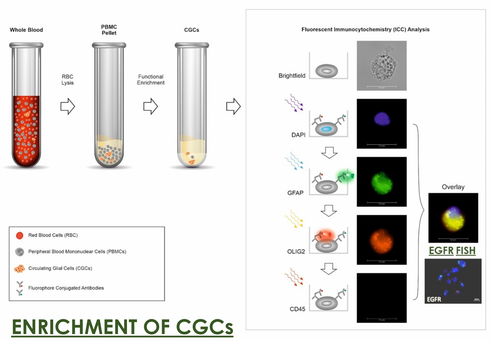
OBJECTIVES

- We present profiling of circulating glial cells (CGCs) by analysing cell lineage-specific markers using immunocytochemistry (ICC) to aid in the non-invasive diagnosis of glial malignancies. We demonstrate the feasibility of EGFR fluorescence in situ hybridization (FISH) on the circulating glial cells.

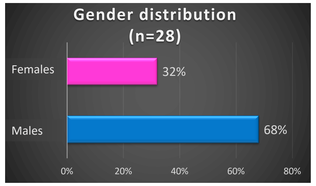
METHODS

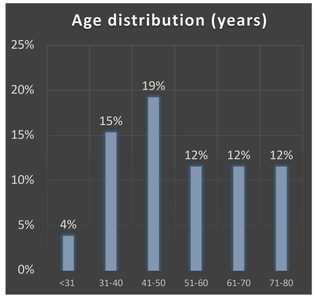
- In a prospective blinded study, blood specimens from patients suspected of intracranial space-occupying lesions (ICSOL) (n=28) were collected before the invasive biopsy.
- CGCs were enriched with the proprietary label-free, size-independent, non-mechanical method and were profiled using the TriNetra™ Glio assay that detects CGCs using ICC profiling of cell lineage-specific markers (GFAP and OLIG2).
- CGCs were also used for EGFR copy number gain analysis using FISH.
- In a separate cohort comprising matched tissue and blood specimens from 44 cases (22 benign and malignant cases each), CGC profiling with ICC and EGFR FISH was performed to evaluate the concordance of profiled biomarkers on the circulating glial cell population.

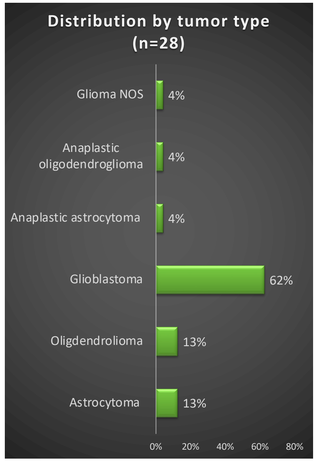


ENRICHMENT OF CGCs

STUDY POPULATION



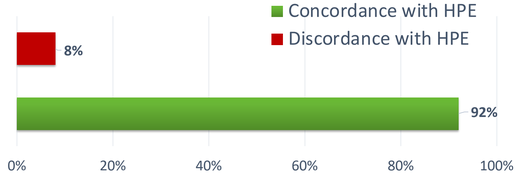




RESULTS

- TriNetra™ Glio assay successfully found CGCs in 23 out of 25 (92%) cases diagnosed with Glial malignancies.
- EGFR amplification was found in approximately one-third of glioblastoma cases (4/11; 40%) and one-half of astrocytoma Grade 3 cases (1/2; 50%).
- In a matched cohort, EGFR copy gain was detected in tumor tissue in 8 (36%) among 22 cases of malignant glial tumors, and EGFR gain was also detectable in corresponding blood analysis, indicating 100% concordance
- Among the remaining 14 samples with normal EGFR tissue status according to FISH, the CGCs also exhibited normal EGFR status.
- Further, among the 22 cases of benign tumors, there were no instances of EGFR copy gain detected by FISH on tumor tissue. All 22 samples were also negative for CGCs indicating high specificity.

CONCORDANCE FOR DIAGNOSIS OF GLIAL MALIGNANCY BY TRINETRA™ GLIO ASSAY vs HISTOPATHOLOGY (HPE)



CONCORDANCE FOR EGFR COPY NUMBER STATUS BY TISSUE vs CGC FISH ANALYSIS

CNS tumor type (n=44)	EGFR copy number gain	
	Tissue	CGCs
Malignant (n=22)	8/22 (36%)	8/22 (36%)
Benign (n=22)	0/22 (0%)	0/22 (0%)

CONCLUSIONS

- **We demonstrate a reliable method for detecting Circulating Glial Cells. This can offer valuable insights into diagnosis of suspected glial malignancies in cases where performing a biopsy is not possible.**
- **Furthermore, FISH analysis of CGCs shows the potential in providing diagnostic insights that align with the current WHO classification system for central nervous system.**