Lay Summary

BRAIN UK Ref: 19/001

Molecular analyses of glial and glioneuronal tumours by DNA methylation profiling and next generation sequencing (NGS).

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We want to improve the way brain tumours are diagnosed. Currently clinicians make a diagnosis by looking at a tumour tissue under a microscope but cannot always identify the correct diagnostic category patients should be placed into. In about a quarter of the brain tumour cases using an algorithm has made a different diagnosis, which has significantly changed the treatment of some of our patients. It is predicted that a deeper look into these tumours will significantly improve the clinical management of patients with CNS tumours and open the doors towards possible options for novel targeted therapies.

This study will provide tissue which will be used to improve a recently established computer based algorithm that can better diagnose tumours arising within the central nervous system (CNS). Here, patterns of chemical tags (DNA methylation) are detected within the tumour. This new technique will enable doctors to place patients more precisely into specific risk groups and make more accurate therapy decisions.

Our centre has previously contributed to the development of the brain tumour classifier– one of only two centres in the UK to use it. Patients treated at UCLH/NHNN have already benefitted from this novel technology and the clinical team (pathologists) have contributed to identifying DNA methylation patterns in rare brain tumour classes.

In the present study we want to contribute again to this novel and exciting development, which will significantly improve the way we diagnose tumours within the CNS and identify new diagnostic biomarkers as well as potentially targetable alterations.

Publications:

Date	**Publication title**
2019	Isomorphic diffuse glioma is a morphologically and molecularly distinct tumour entity with recurrent gene fusions of MYBL1 or MYB and a benign disease course
2019	Posterior fossa pilocytic astrocytomas with oligodendroglial features show frequent FGFR1 activation via fusion or mutation
2019	Rosette-forming glioneuronal tumors share a distinct DNA methylation profile and mutations in FGFR1, with recurrent co-mutation of PIK3CA and NF1
2019	MYCN amplification drives an aggressive form of spinal ependymoma

2021	Recurrent fusions in PLAGL1 define a distinct subset of pediatric-type supratentorial neuroepithelial tumors
2021	Cross-Species Genomics Reveals Oncogenic Dependencies in ZFTA/C11orf95 Fusion–Positive Supratentorial Ependymomas
2021	Glioblastomas with primitive neuronal component harbor a distinct methylation and copy-number profile with inactivation of TP53, PTEN, and RB1