

DIVISION OF NEUROPATHOLOGY

UCL QUEEN SQUARE INSTITUTE OF NEUROLOGY

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NHS FOUNDATION TRUST

Illumina 850k (v1) and 930k (v2) EPIC Array analysis

Characteristic patterns of DNA methylation of CpG Islands in the genome are key features in various tumours. The Illumina Infinium 850k/930k EPIC array assesses the DNA methylation status of over 850,000/930,000 individual CpG sites. The Heidelberg classifier distinguished brain tumour types based on their methylation profile.

We analyse tumours to establish or refine a diagnosis, and for risk stratification (meningiomas) or comprehensive methylome and copy number profiling (e.g. IDH-mutant gliomas).

For the analysis on this case, the tumour DNA was extracted and modified *in house* and the sample was processed at the UCL Genomics facility. The data file (idat file) was processed on the classifier and a report was returned.

Further information: <https://www.ucl.ac.uk/ion/research/clinical-divisions/division-neuropathology/molecular-pathology>

Meningioma classifier and risk stratification

To improve the precision of meningioma stratification in risk of recurrence groups, an integrated diagnostic approach with a three-tiered scoring has been published. It is based on the analysis of over 3000 meningiomas (Maas et al., J Clin Oncol, 2021; PMID: 34618539). The use of the 12.6 classifier have been validated for meningioma classification (Hielscher et al., Brain Pathol, 2022; PMID 36377252).

This approach integrates:

- (i) histological CNS WHO grade 1, 2, 3; corresponding to scores 0, 1, 2, respectively;
- (ii) methylation class benign, intermediate, malignant; corresponding to scores 0, 2, 4, respectively;
- (iii) loss of chromosomes 1p, 6q, 14q; if none present: score 0, 1-2 present: score 2, 3 or more present: score 3.

To predict the risk of meningioma recurrence, the summary score of all three categories is calculated.

- (i) Integrated meningioma risk stratification summary score 0,1,2 is predictive of low risk of recurrence.
- (ii) Integrated meningioma risk stratification summary score 3,4,5 is predictive of intermediate risk of recurrence.
- (iii) Integrated meningioma risk stratification summary score 6,7,8,9 is predictive of high risk of recurrence.

Weblinks to the classifiers

Weblink to the classifier versions <https://www.molecularneuropathology.org/mnp/classifiers>

Disclaimer: Classification using methylation profiling is a research tool under development, is not verified and has not been clinically validated. Implementation of the results in a clinical setting is in the sole responsibility of the treating physician.