Methylation profiling report

Patient name: JANE DOE

MRN: nan

Date of Birth: 07/20/1969

Sex: F

Collected: 02/25/2025

Reported: 02/25/2025

Assay name: Methylation Profiling

Assay Version: 2.2.0

Brain tumor methylation classifier results

Methylation Class	Score	Interpretation
meningioma	1.00	match

The score corresponds to the probability of match to that particular class. Scores of >= 0.9 are considered a match on class and >= 0.5 for subclasses. Only classes with scores >= 0.5 are reported.

CLIA Number	Medical Director	NORTHWESTERN MEMORIAL HOSPITAL LAB
14D0666246	Gregory Retzinger, MD	251 E. Huron 7307, Chicago IL 60611

Assay name: Methylation Profiling **Assay Version:** 0.1.0

Meningioma progression risk results

Methylation Class	Score	Interpretation
LOW RISK	1.00	match

The score corresponds to the probability of match to that particular class. Scores of >= 0.75 are considered a match. Only classes with scores >= 0.5 are reported.

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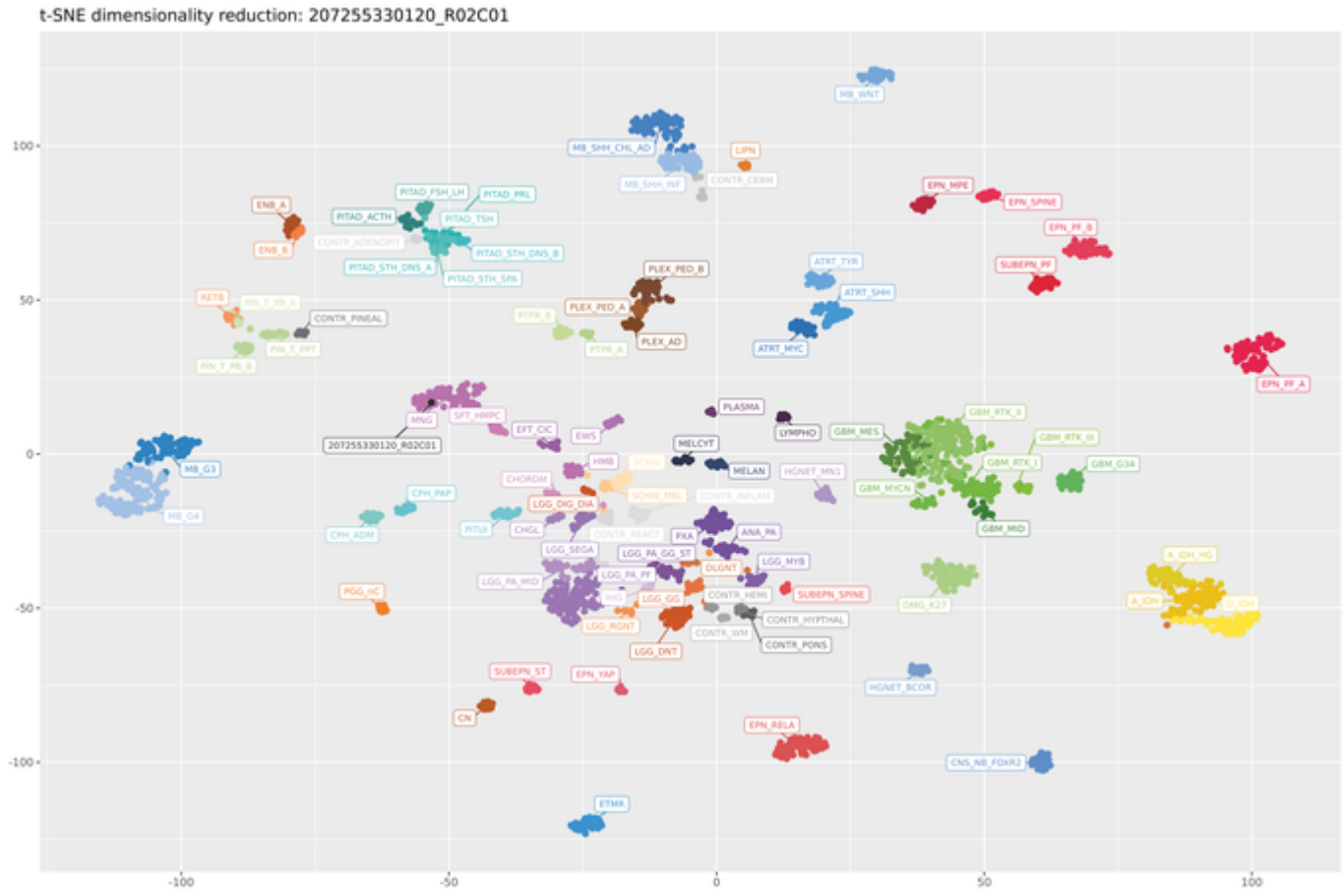
Unsupervised Clustering Analysis of CNS Classes (t-SNE)



Classifier and t-SNE results represent two different types of analysis. The Classifier uses a random forest (RF) machine learning algorithm to classify a defined set of tumor samples into cancer classes while t-SNE is a dimensionality reduction and data visualization method. While these two approaches will often produce concordant results, discrepant results are possible. Assay validation was solely based on the RF Classifier. The t-SNE plot is provided as additional information for samples that are not a match to any of the tumor types in the RF Classifier.

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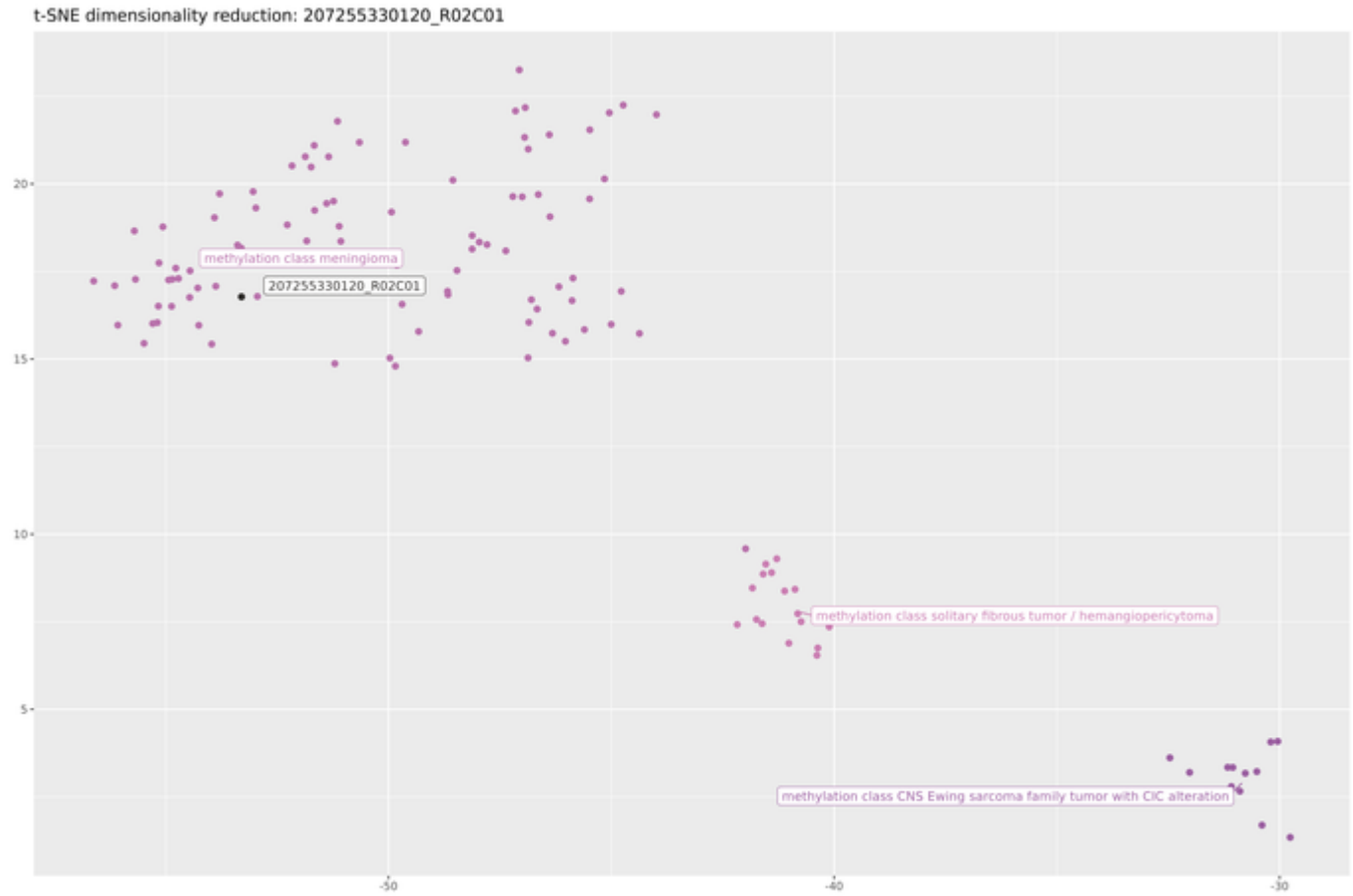
Zoomed-In t-SNE Plot of CNS Classes



Nearest t-SNE Clusters

Methylation Class	Distance
methylation class meningioma	3.002
methylation class solitary fibrous tumor / hemangiopericytoma	15.057
methylation class CNS Ewing sarcoma family tumor with CIC alteration	26.122

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Medical Director

Gregory Retzinger, MD

NORTHWESTERN MEMORIAL HOSPITAL LAB

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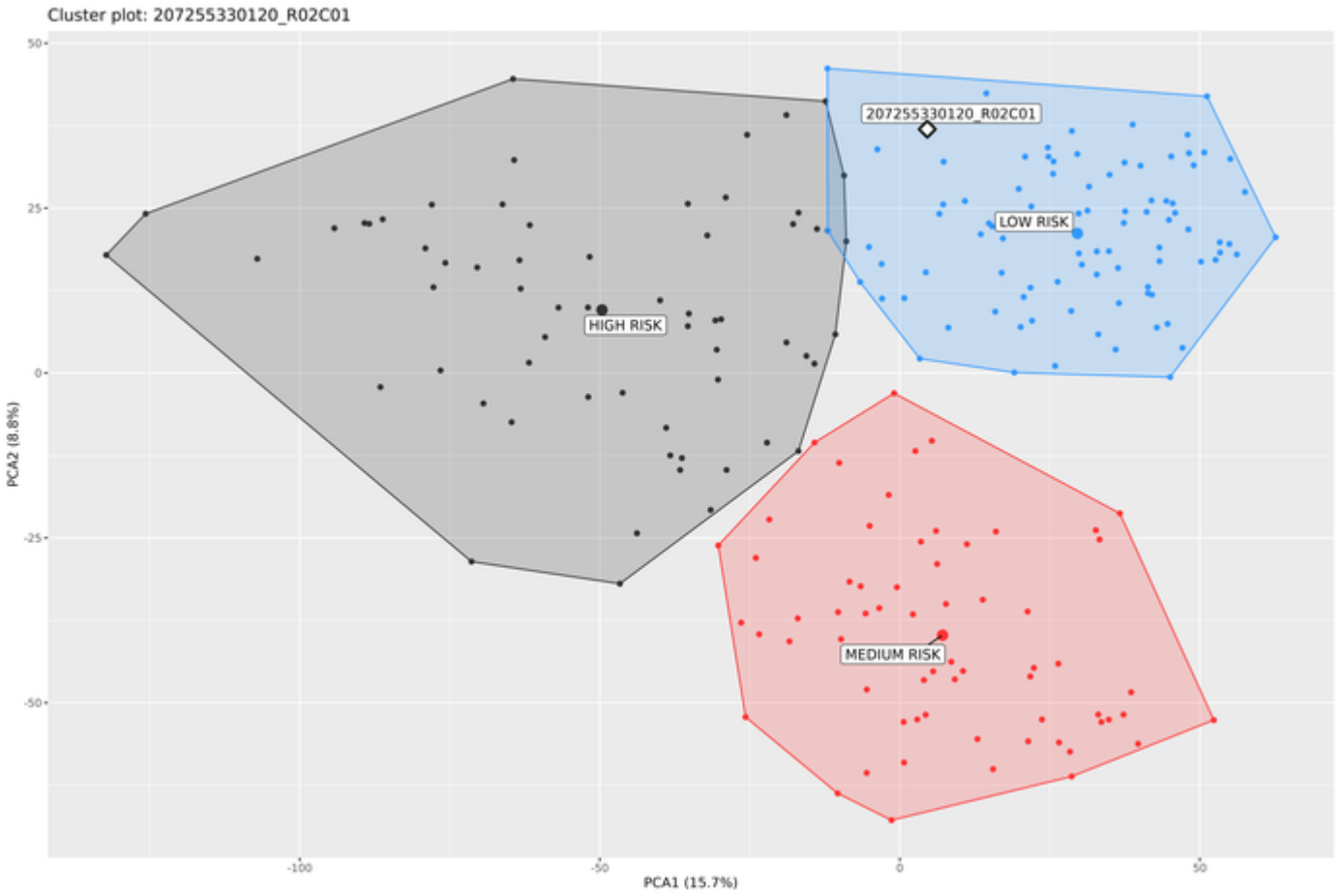
Unsupervised Clustering Analysis of Meningioma Progression Risk (PCA)



Classifier and PCA results represent two different types of analysis. The Classifier uses a K-nearest neighbor (KNN) machine learning algorithm to classify a defined set of meningioma tumor samples into risk classes while PCA is a dimensionality reduction and data visualization method. While these two approaches will often produce concordant results, discrepant results are possible. Assay validation was solely based on the KNN Classifier. The PCA plot is provided as additional information for samples that are not a match to any of the risk categories in the KNN Classifier.

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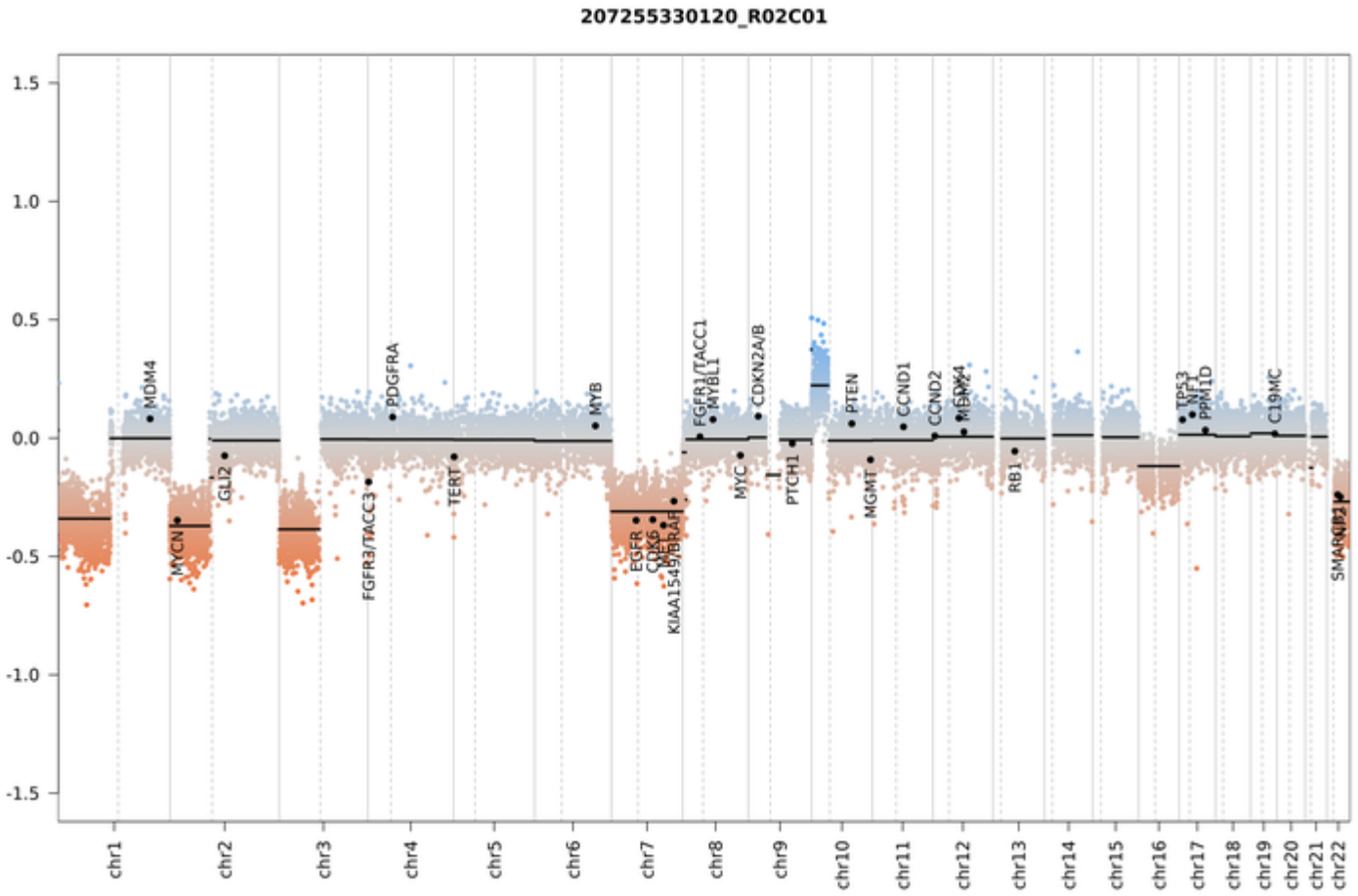
Copy Number Analysis



Assay Description

The Methylation Profiling assay is a micro-array-based test developed and validated at Northwestern Medicine. For CNS classification, methylation data is analyzed by a Machine Learning algorithm that classifies the sample into one of 91 possible central nervous system (CNS) tumors. Direct comparison to the DKFZ classifier (Capper et al Nature 555, 469–474 (2018)) using an independent validation cohort of 1104 samples showed high concordance (92%) and comparable accuracy (specificity 94.0% v. 84.9% for DKFZ, sensitivity 88.6% v. 94.7% for DKFZ).

CNS Methylation Classes: astrocytoma (A_IDH), high grade astrocytoma (A_IDH_HG), anaplastic pilocytic astrocytoma (ANA_PA), MYC (ATRT_MYC), SHH (ATRT_SHH), TYR (ATRT_TYR), methylation class chordoid glioma of the third ventricle (CHGL), methylation class chordoma (CHORDM), methylation class central neurocytoma (CN), methylation class CNS neuroblastoma with FOXR2 activation (CNS_NB_FOXR2), methylation class control tissue, pituitary gland anterior lobe (CONTR_ADENOPIT), methylation class control tissue, cerebellar hemisphere (CONTR_CEBM), methylation class control tissue, hemispheric cortex (CONTR_HEMI), methylation class control tissue, hypothalamus (CONTR_HYPTHAL), methylation class control tissue, inflammatory tumor microenvironment (CONTR_INFLAM), methylation class control tissue, pineal gland (CONTR_PINEAL), methylation class control tissue, pons (CONTR_PONS), methylation

class control tissue, reactive tumor microenvironment (CONTR_REACT), methylation class control tissue, white matter (CONTR_WM), methylation class craniopharyngioma, adamantinomatous (CPH_ADM), methylation class craniopharyngioma, papillary (CPH_PAP), methylation class diffuse leptomeningeal glioneuronal tumor (DLGNT), methylation class diffuse midline glioma H3 K27M mutant (DMG_K27), methylation class CNS Ewing sarcoma family tumor with CIC alteration (EFT_CIC), methylation class esthesioneuroblastoma, subclass A (ENB_A), methylation class esthesioneuroblastoma, subclass B (ENB_B), methylation class ependymoma, myxopapillary (EPN_MPE), methylation class ependymoma, posterior fossa group A (EPN_PF_A), methylation class ependymoma, posterior fossa group B (EPN_PF_B), methylation class ependymoma, RELA fusion (EPN_RELA), methylation class ependymoma, spinal (EPN_SPINE), methylation class ependymoma, YAP fusion (EPN_YAP), methylation class embryonal tumor with multilayered rosettes (ETMR), methylation class Ewing sarcoma (EWS), methylation class glioblastoma, IDH wildtype, H3.3 G34 mutant (GBM_G34), mesenchymal (GBM_MES), midline (GBM_MID), MYCN (GBM_MYCN), RTK I (GBM_RTK_I), RTK II (GBM_RTK_II), RTK III (GBM_RTK_III), methylation class CNS high grade neuroepithelial tumor with BCOR alteration (HGNET_BCOR), methylation class CNS high grade neuroepithelial tumor with MN1 alteration (HGNET_MN1), methylation class hemangioblastoma (HMB), methylation class infantile hemispheric glioma (IHG), methylation class low grade glioma, desmoplastic infantile astrocytoma / ganglioglioma (LGG_DIG_DIA), methylation class low grade glioma, dysembryoplastic neuroepithelial tumor (LGG_DNT), methylation class low grade glioma, ganglioglioma (LGG_GG), methylation class low grade glioma, MYB/MYBL1 (LGG_MYB), methylation class low grade glioma, subclass hemispheric pilocytic astrocytoma and ganglioglioma (LGG_PA_GG_ST), midline pilocytic astrocytoma (LGG_PA_MID), posterior fossa pilocytic astrocytoma (LGG_PA_PF), methylation class low grade glioma, rosette forming glioneuronal tumor (LGG_RGNT), methylation class low grade glioma, subependymal giant cell astrocytoma (LGG_SEGA), methylation class cerebellar liponeurocytoma (LIPN), methylation class lymphoma (LYMPHO), group 3 (MB_G3), group 4 (MB_G4), SHH A (children and adult) (MB_SHH_CHL_AD), SHH B (infant) (MB_SHH_INF), WNT (MB_WNT), methylation class melanoma (MELAN), methylation class melanocytoma (MELCYT), methylation class meningioma (MNG), 1p/19q codeleted oligodendroglioma (O_IDH), methylation class paraganglioma, spinal non-CIMP (PGG_nC), methylation class pineoblastoma group A / intracranial retinoblastoma (PIN_T_PB_A), methylation class pineoblastoma group B (PIN_T_PB_B), methylation class pineal parenchymal tumor (PIN_T_PPT), methylation class pituitary adenoma, ACTH (PITAD_ACTH), methylation class pituitary adenoma, FSH/LH (PITAD_FSH_LH), methylation class pituitary adenoma, prolactin (PITAD_PRL), methylation class pituitary adenoma, STH densely granulated, group A (PITAD_STH_DNS_A), methylation class pituitary adenoma, STH densely granulated, group B (PITAD_STH_DNS_B), methylation class pituitary adenoma, STH sparsely granulated (PITAD_STH_SPA), methylation class pituitary adenoma, TSH (PITAD_TSH), methylation class pituicytoma / granular cell tumor / spindle cell oncocytoma (PITUI), methylation class plasmacytoma (PLASMA), adult (PLEX_AD), paediatric A (PLEX_PED_A), paediatric B (PLEX_PED_B), methylation class papillary tumor of the pineal region group A (PTPR_A), methylation class papillary tumor of the pineal region group B (PTPR_B), methylation class (anaplastic) pleomorphic xanthoastrocytoma (PXA), methylation class retinoblastoma (RETB), methylation class

schwannoma (SCHW), methylation class melanotic schwannoma (SCHW_MEL), methylation class solitary fibrous tumor / hemangiopericytoma (SFT_HMPC), methylation class subependymoma, posterior fossa (SUBEPN_PF), methylation class subependymoma, spinal (SUBEPN_SPINE), methylation class subependymoma, supratentorial (SUBEPN_ST).

For meningioma progression risk classification, methylation data is analyzed by a Machine Learning algorithm that classifies the sample into one of 3 possible meningioma risk categories. Classifier validation resulted in high accuracy (96.1% concordant, 90.8% match) in a cohort of 76 meningioma samples.

Meningioma progression risk classes include LOW RISK, MEDIUM RISK, and HIGH RISK based on k-means clustering of methylation data from 217 meningioma samples and represent significant differences in progression free survival (PFS).

This test was developed and its performance characteristics determined by Northwestern Memorial Hospital Pathology Laboratory. It has not been cleared or approved by the U.S. Food and Drug administration. Since reagents and/or equipment that are not FDA approved are utilized for this testing, these results should only be used adjunctively for patient management.