Epignostix Skin Tumor Methylation Classifier

Training iteration 10

Preliminary Version June 2026

- **51 distinct methylation classes**
- Training set: **1,588 methylation profiles**
- 89.61% class-level accuracy
- One tier hierarchical output structure
- Proposed evidence level annotation
- **150,000+ patient cases** analyzed
- 500+ institutions worldwide use the classifier

Sample Collection
(Fresh Frozen / FFPE)
Tumor assesment (>= 50%)

↓

Pre-analytical procedure
(DNA extraction)

↓

Raw data generation
(idat file)

↓

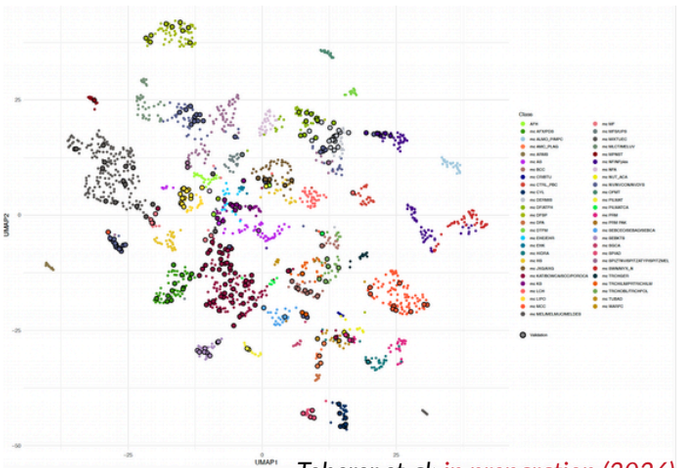
Epignostix Skin Tumor Methylation Classifier
(QC, Tumor classification, CNV analysis)

↓

PDF and html Report

List of Classes training iteration 10

1. Angiomatoid fibrous histiocytoma
2. Atypical fibroxanthoma/pleomorphic dermal sarcoma
3. Angioleiomyoma peripheral/myopericytoma
4. Apocrine mixed tumor PLAG-fused
5. Alveolar rhabdomyosarcoma
6. Angiosarcoma
7. Basal cell carcinoma
8. Cribriform tumor
9. Control whole blood leukocytes
10. Cylindroma
11. Control dermis
12. Dermatofibroma/atypical fibrous histiocytoma
13. Dermatofibrosarcoma protuberans
14. Digital papillary adenocarcinoma
15. Desmoid type fibromatosis
16. Epithelioid hemangioendothelioma/retiform hemangioendothelioma
17. Kaposiform hemangioendothelioma
18. Hidradenoma
19. Histiocytic sarcoma
20. Juvenile xanthogranuloma/adult xanthogranuloma
21. Keratoacanthoma/Bowen carcinoma/cutaneous squamous cell carcinoma/porocarcinoma
22. Kaposi sarcoma
23. Langerhans cell histiocytosis
24. Lipoma
25. Merkel cell carcinoma
26. Melanoma/mucosal melanoma/desmoplastic melanoma
27. Mycosis fungoides
28. Myxofibrosarcoma/undifferentiated pleomorphic sarcoma
29. Eccrine mixed tumor
30. Melanocytoma/melanoma uveal
31. Malignant peripheral nerve sheat tumor
32. Cutaneous neurofibroma/plexiform neurofibroma
33. Nodular fasciitis
34. Adnexal NUT carcinoma
35. Naevus/naevus dysplastic/naevus congenital
36. Ossifying fibromyxoid tumor
37. Pilomatricoma
38. Pilomatrix carcinoma
39. Poroma
40. Poroma PAK-fused
41. Sebaceoma/sebaceous adenoma/sebaceous carcinoma
42. Seborrhoic keratosis
43. Sweat gland carcinoma
44. Spiradenoma
45. Spitz naevus/atypical Spitz naevus/spitzoid melanoma
46. Schwannoma/nerve sheath myxoma
47. Trichogerminoma
48. Trichilemmoma/proliferating trichilemmoma
49. Trichoblastoma/trichofolliculoma
50. Tubular adenoma
51. Wnt/betacatenin activated rosette forming carcinoma



Toberer et al; in preparation (2026)

- On-premise version for routine use
- Compatible with standard laptops
  An installation guide is included.
- RUO Platform freely accessible for academic research and scientific use
- Register here:
  https://app.epignostix.com/
- Contact for more information
  info@epignostix.com

Publications connected to the Epignostix Skin Tumor Methylation Classifier

Advancing skin tumor diagnostics with DNA methylation-based classification
T*oberer F. et al., in preparation (2026)*

Background: DNA promoter methylation-based classification has recently proven to substantially impact precision diagnosis of brain tumors and sarcomas. Here we explore this approach for the evaluation of cutaneous tumors.
Objective: To generate a methylation-pattern based landscape defining DNA methylation classes for skin tumors and developing a classifier algorithm.
Methods: Multicentre, retrospective study investigating genome-wide DNA methylation patterns in 1,546 benign and malignant skin tumors belonging to different 72 cutaneous and subcutaneously occurring tumor entities.
Results: DNA promoter methylation patterns of skin tumors reveal a detailed landscape with 50 distinct tumor methylation classes that clearly separate morphologically defined entities. Of special interest is separation of melanocytic lesions with melanoma, spitzoid tumors and naevi forming distinct methylation clusters. Performance of the skin tumor classifier v10.1 was validated employing a series of 274 tumors. Employing a stringent value exceeding 0.9 for the calibrated classifier score, a prediction was reached in 66% of the cases of which 95% matched the histological diagnoses. Reducing the calibrated score to higher than 0.7 resulted in a prediction rate of 77% with 91% of predictions matching.
Limitations: While major tumor groups are included, the series does not comprise all skin tumor entities.
Relevance: DNA promoter methylation patterns are entity specific. This can be used for classifying cutaneous and subcutaneous tumors lacking typical morphological features or for entities sharing morphological features thereby impeding precise classification.

Integrated Genomic Classification of Melanocytic Tumors of the Central Nervous System Using Mutation Analysis, Copy Number Alterations, and DNA Methylation Profiling
Griewank. *et al., Clinical Cancer Research (2018)*

Purpose: In the central nervous system, distinguishing primary leptomeningeal melanocytic tumors from melanoma metastases and predicting their biological behavior solely using histopathologic criteria may be challenging. We aimed to assess the diagnostic and prognostic value of integrated molecular analysis.
Experimental Design: Targeted next-generation sequencing, array-based genome-wide methylation analysis, and BAP1 IHC were performed on the largest cohort of central nervous system melanocytic tumors analyzed to date, including 47 primary tumors of the central nervous system, 16 uveal melanomas, 13 cutaneous melanoma metastases, and 2 blue nevus-like melanomas. Gene mutation, DNA-methylation, and copy-number profiles were correlated with clinicopathologic features.
Results: Combining mutation, copy-number, and DNA-methylation profiles clearly distinguished cutaneous melanoma metastases from other melanocytic tumors. Primary leptomeningeal melanocytic tumors, uveal melanomas, and blue nevus-like melanoma showed common DNA-methylation, copy-number alteration, and gene mutation signatures. Notably, tumors demonstrating chromosome 3 monosomy and BAP1 alterations formed a homogeneous subset within this group.
Conclusions: Integrated molecular profiling aids in distinguishing primary from metastatic melanocytic tumors of the central nervous system. Primary leptomeningeal melanocytic tumors, uveal melanoma, and blue nevus-like melanoma share molecular similarity with chromosome 3 and BAP1 alterations, markers of poor prognosis.

Contact us!
info@epignostix.com

www.epignostix.com