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THE ROLE OF PNL2 MONOCLONAL ANTIBODIES IN THE DIAGNOSIS OF MELANOMA

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Annotation. Malignant melanoma (MM) has high aggressiveness and is difficult to diagnose, especially in amelanotic, acral, mucosal, and metastatic forms, due to morphological similarities. Immunohistochemistry (IHK) is the main auxiliary method in these cases. Such markers as C-100, HMB45, Melan-A/MART-1, tyrosinase, MITF are widely used, however, each of them has limitations in sensitivity or specificity. PNL2 is a new monoclonal antibody of the melanocytic orientation, which has practical significance due to the recognition of a stable antigen in formalin-paraffin blocks, staining melanin even after "bleaching" and decalcification. The high sensitivity of PNL2 in melanoma of the mucous membrane, its higher specificity to S-100, and its role in reducing diagnostic errors in the composition of the marker panel are highlighted.

Keywords: malignant melanoma, PNL2, immunohistochemistry, C-100, HMB45, Melan-A, mucosal melanoma, biomarkers.

Log in. Malignant melanoma, although relatively rare among skin tumors, is one of the neoplasms that contributes the most to the mortality rate. Diagnosis is easy in clinical-histological "classical" cases, but the risk of error increases sharply in the following cases:

1. amelanotic melanoma (absence of pigment),
2. mucosal melanoma (oral/nasal/genital),
3. acral melanoma (palm, heel, subungual),
4. poorly differentiated or sarcomatoid appearance,
5. Uncertainty of the primary source in metastatic foci.

For this reason, HDI has become a standard approach to confirming marker-panel melanocyte differentiation and narrowing the differential diagnosis.

Problem: diagnostic gaps in current markers

S-100

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S-100 is usually perceived as a highly sensitive marker, but its main problem is its low specificity: it can also be positively stained in various neurogenic, chondrogenic, adipocytic, and other tumors. Therefore, S-100 alone is not enough to conclude a "melanoma."

HMB45 (gp100)

HMB45 is more pronounced for the melanocyte/melanosome orientation, but the staining can be heterogeneous and negative in some melanoma. HMB45 and S-100 are widely used in mucosal melanoma, but their sensitivity profiles vary.

Melan-A/MART-1, tyrosinase, MITF

Melan-A is often beneficial, but may be lost in some metastatic/poorly differentiated melanoma; Although MITF is sensitive, it can be confusing with "non-specific" positivity due to the possibility of expression in other tumors as well. Markers are used as complementary panels.

Melanoma with negative markers

Cases have been described where C-100, HMB45, Melan-A are simultaneously negative, while another melanocyte marker (e.g., tyrosinase) is positive - this indicates the need for strictness in panel selection.

PNL2: biological and methodological features

What is PNL2?

PNL2 was described in 2003, recognizing a new antigen associated with a melanocyte resistant to fixation ("fixative-resistant") in formalin. It has been shown through proteomic approaches that the antigen complex is not identical to gp100 (HMB45). Important practical aspect: PNL2 melanin can provide reliable staining even after "bleaching" (chemical bleaching of the pigment) and decalcification.

Staining type

Cytoplasmic staining is often observed; in practice, PNL2 is added to the IHK panel to confirm melanocytic tumors.

Signal-noise in terms of specificity

Rochaix et al. showed high specificity of PNL2 to melanocytes in a wide spectrum of normal and tumor tissues, with the possibility of staining in granulocytes at high concentrations. This indicates the practical significance of the laboratory protocol and titer selection.

Clinical and diagnostic value of PNL2 in melanoma of mucosa

Separate analysis for PNL2 in melanoma of the head and neck mucosa revealed PNL2 in:

sensitivity to Melan-A and MITF may be higher,

Sensitivity comparable to HMB45,

The authors substantiated the inclusion of PNL2 as an important additional marker in the assessment of mucosal melanoma.

This indicates PNL2 as a "panel-enhancing" marker specifically for the group with the highest clinical error (mucosal melanoma).

PNL2 in metastatic melanoma and "difficult biopsies"

Morphology in metastatic foci is often confused with carcinoma/sarcoma/lymphoma. In this case, the function of the melanocyte panel is:

confirmation of melanocyte differentiation (C-100, SOX10, PNL2, HMB45, Melan-A),

Negation of alternative directions with keratin/CD45/desmin and others.

The presence of clinical case images indicating that S-100/HMB45/Melan-A may remain negative increases the need for broader paneling.

PNL2 Performance Results (Based on Information You Provided)

In the clinical material we presented (47 melanoma, 10 normal skin), PNL2:

positive staining in the melanoma group: **87.23% (41/47)**

positive staining on normal skin: **10% (1/10)**

sensitivity: **87.23%**

Uniqueness: **90%**

It was also noted that the positivity is associated with age and the Clark stage, and not with sex/ethnicity/lymph metastasis. These results justify PNL2 not as a "universal marker," but as a highly beneficial marker within the panel (especially in the mucosal group). (These numbers are from the text you provided; no external source link is provided for them.)

Discussion

1) When is PNL2 most profitable?

Mucosal melanoma: PNL2 is often beneficial in the group where other markers are poorly functioning.

Melanin-rich biopsy (conditions requiring bleaching): The chemical stability of the PNL2 antigen provides a practical advantage.

Sample requiring decalcification (e.g., bone infiltration): PNL2 staining may persist.

2) what does PNL2 not "substitute"?

PNL2 does not completely replace "broadly sensitive" markers such as S-100 or SOX10; it is a diagnostically reliable component in the line of melanocyte-specific markers such as HMB45/Melan-A. In practice, the conclusion with a single marker is not scientifically justified; **a panel with at least 2-4 markers** necessary.

3) Restrictions

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Incomplete detection of the antigen makes standardization difficult in some laboratories (titre, antigen retrieval, protocol differences).

The possibility of accidental staining (granulocyte) at high concentrations requires protocol control.

Practical recommendation: diagnostic algorithm (HHK panel)

Step 1 (screening, high sensitivity):

S-100 or SOX10 (if any) + PNL2

Stage 2 (melanocyte-specific confirmation):

HMB45 + Melane-A ± tyrosinase

Stage 3 (differential negation):

Pan-keratin (carcinoma), CD45 (lymphoid), desmin/SMA (myogen), CD68 (histiocytic)

Note: in case of suspected mucosal melanoma, early inclusion of PNL2 in the panel is advisable.

Conclusion. PNL2 is an IHD marker with high practical value in the diagnosis of monoclonal antibody melanoma, partially compensating for the limitations of other markers, especially in mucosal melanoma. Stable staining of PNL2 in formalin-paraffin blocks, functioning even after melanin bleaching and decalcification, expands diagnostic capabilities. PNL2 provides the highest clinical effectiveness not as a single marker, **but in combination with C-100/COX10 and HMB45/Melan-A** .

References

1. Rochaix P, Lacroix-Triki M, et al. PNL2, a new monoclonal antibody directed against a fixative-resistant melanocyte antigen. *Modern Pathology.* 2003.

2. Morris, L.G., et al. PNL2 melanocytic marker in immunohistochemical diagnosis of head and neck mucosal melanoma. *[PubMed indexed]* 2008.

3. Giudice, C. et al. Immunohistochemical investigation of PNL2 reactivity of canine melanocytic neoplasms and comparison with Melan A. 2010.

4. Yu CH, et al. HMB-45 may be a more sensitive marker than S-100 or Melan-A for immunohistochemical diagnosis of primary oral and nasal mucosal melanoma. 2005.

5. Ricci C, et al. Skin melanoma: review on immunohistochemistry in diagnosis and characterization. *International Journal of Molecular Sciences*. 2022.

6. Shinohara M, et al. S100, HMB-45, and Melan-A negative primary melanoma (case report). 2009.

7. Ramos-Vara JA, et al. Immunohistochemical expression of melanocytic antigen markers and notes on PNL2 sensitivity/specificity. 2014.

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8. Quilaqueo N, et al. Immunohistochemical markers S-100, HMB-45, MART-1 in differential diagnosis of melanoma and nevi. 2021.

9. Bolovan L.M., et al. Correlation studies between soluble S100B/MIA and tissue melanocytic markers (S100, gp100/HMB45, MelanA). 2023.

10. Sigma-Aldrich. Anti-PNL2 monoclonal antibody product background and cited performance notes (metastatic melanoma sensitivity data cited in product literature).