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A Newly Developed Mouse Monoclonal SOX10 is a Highly Sensitive Marker for Malignant Melanoma, including Spindle Cell and Desmoplastic Melanoma

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Introduction

SOX10 is a nuclear transcription factor that participates in neural crest development and in the differentiation of cells of melanocytic and schwannian lineage. Recently, SOX10 has been shown to be expressed in malignant tumors such as melanoma, malignant peripheral nerve sheath tumors, and a subset of breast carcinomas.[1-7] Importantly, SOX10 has been shown to be a sensitive and specific marker for spindle cell and desmoplastic melanomas.[4-6] However, to date, the majority of publications for SOX10 are limited to a goat polyclonal antibody which may hinder its acceptance in the clinical arena. In this study a mouse monoclonal SOX10 hybridoma has been developed for immunohistochemistry (IHC) and was evaluated for sensitivity and specificity in melanomas, and in various normal and neoplastic tissues.

Materials and Methods

Tissue microarrays (TMAs) and whole tissue biopsies of malignant melanoma, spindle cell and desmoplastic melanoma, schwannoma and nevis were evaluated by IHC using a mouse monoclonal mouse SOX10 [BC34] (Biocare Medical Concord, CA). Additionally, both normal and neoplastic tissues were also evaluated for specificity with SOX10. Formalin-fixed, paraffin-embedded (FFPE) whole tissues and tissue TMAs were deparaffinized and hydrated to water. TMAs were placed in an antigen retrieval solution (modified citrate buffer, pH 6.0) and placed in a pressure cooker (Decloaking Chamber) at 125 °C for 30 seconds. SOX10 [BC34] was diluted and optimized at 1:100, and tissues were incubated for 30 minutes and then rinsed in TBS. A goat anti-mouse horseradish peroxidase (HRP) or alkaline phosphatase polymer detection was applied to tissue sections for 30 minutes. Sections were then rinsed in TBS and sections were incubated for 5 minutes in 3, 3'-Diaminobenzidine (DAB) or 10 minutes in fast red chromogen.

Scoring Method: Each case was deemed "positive" if more than >1% of cells stained. Conversely, a case was deemed "negative" if <1% of tumor cells stained. Only nuclear staining was considered positive.

Results

In normal tissues (n=34), SOX10 stained skin melanocytes, a portion of eccrine glandular epithelial and myoepithelial cells, breast myoepithelial cells as well as a subset of lobular epithelial cells, salivary gland myoepithelial cells, peripheral nerve, Schwann cells, and brain glial cells.

SOX10 stained 93.1% (258/277) of all melanomas (Table 1, Figure 1A-D). Notably, 98.0% (50/51) spindle cell and desmoplastic melanomas were positive for SOX10 (Table 1, Figure 2A, B). SOX10 was positive in 20/20 (100%) nevi (Table 1, Figure 2C).

In other neoplasms (Table 2), SOX10 was expressed in 16.5% (18/109) infiltrating ductal breast cancers (Figure 3A) and in myoepithelial cells in breast ductal cell *in situ* carcinoma (DCIS) (Figure 3B). SOX10 was also expressed in 50.0% of CNS neoplasms (Table 2, Figure 3C); and was negative in all other carcinomas, including lung (n=158), colon (n=24), prostate (n=13), bladder (n=48), kidney (n=15), liver (n=57), esophagus (n=10), ovary (n=17), cervix (n=11) thyroid (n=10), adrenal (n=4), pancreas (n=12), skin (n=40), neuroendocrine (n=20) and testicular seminoma (n=12). Carcinoid tumors in the digestive tract and in the lung were negative, except for staining of sustentacular cells (Figure 3D). In addition, SOX10 was expressed in 100% (28/28) of schwannomas, in 4.5% (1/22) of rhabdomyosarocomas and in 6.5% (2/31) of leiomyosarcomas (Table 3).

Discussion

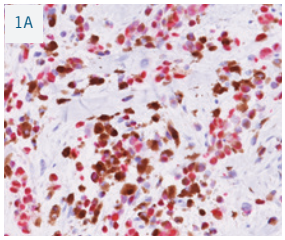
In our study, SOX10 stained 96.6% (115/119) of primary cutaneous melanomas. This compares well with the study by Nonaka *et al.*, as SOX10 nuclear expression was found in 76 of 78 melanomas (97%).[4]

Desmoplastic melanoma (DM) and spindle cell melanoma (SCM) can present diagnostic challenges for the pathologist due to histologic mimics and limitations with immunohistochemical staining. Although S100 usually stains DM, other melanoma markers such as HMB45 and Melan-A has been shown to be negative in most cases.[6] Other histologic mimics of DM include spindled fibroblasts or histiocytes within prior excision scars.

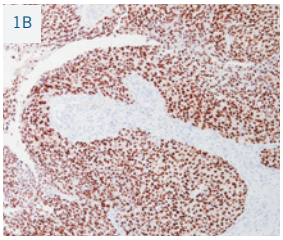
In our study, SOX10 was negative in the vast majority of non-melanocytic tumors (Table 2). These findings show concordance with other studies.[1, 4] SOX10 has been demonstrated in a subset of breast carcinomas, including basal-like or triple-negative carcinomas, and in metaplastic carcinomas.[7] This finding supports the concept that these neoplasms may show myoepithelial differentiation. In our study, SOX10 nuclear staining was expressed in normal breast myoepithelial cells, as well as a subset of breast lobular epithelial cells; and SOX10 was expressed in 16.5% of infiltrating breast cancers. SOX10 has also been shown to stain various types of brain tumors.[2, 3] Bannykh SI *et al.*, demonstrated the majority of oligodendrogliomas, and a large fraction of astrocytomas and glioblastomas that expressed SOX10,[3] thus correlating with our results.

Our findings of SOX10 expression in malignant melanomas (96.6%) and in benign nevi and schwannomas (100%) demonstrated a high concordance with other studies using the well published SOX10 goat polyclonal antibody.[1, 4-6] The use of a research use only (RUO) goat primary antibody may be satisfactory for research purposes; however, it may not be generally accepted in a clinical setting. Polyclonal antibodies are also notorious for lot-to-lot variation and may produce unwanted non-specific background staining.

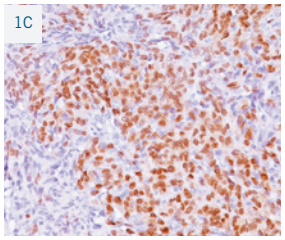
Figure 1: SOX10 in Classic Melanoma



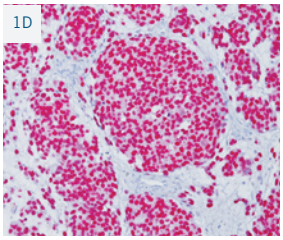
Melanoma with melanin pigment (FR)



Melanoma with melanin pigment (DAB)

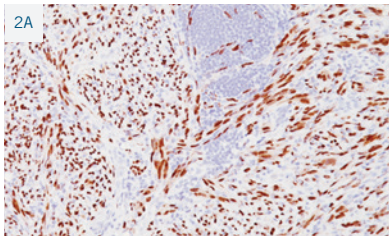


Metastatic melanoma in lymph node (DAB)

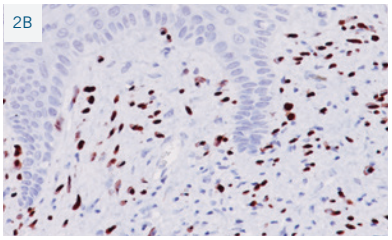


Epithelioid melanoma in lymph node (FR)

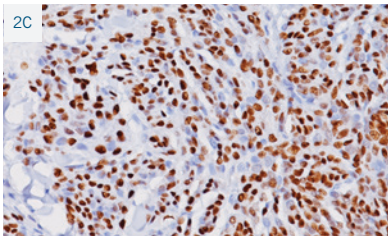
Figure 2: SOX10 Expression in Spindle Cell/Desmoplastic Melanoma



Spindle cell melanoma, 10X

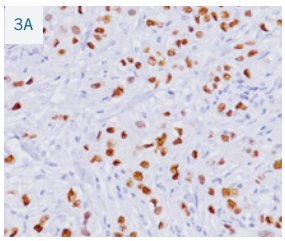


Desmoplastic melanoma, 20X

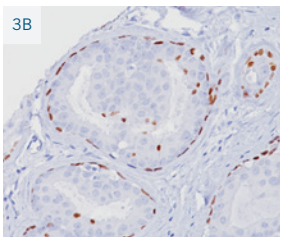


Benign nevus

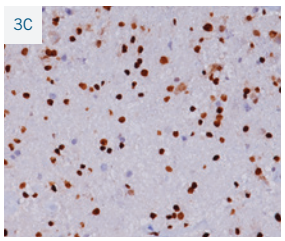
Figure 3: SOX10 Expression in Various Neoplasms



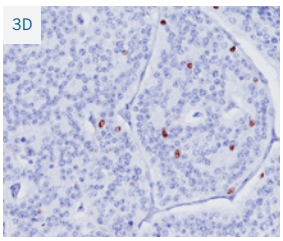
Invasive ductal carcinoma (breast)



Myoepithelal cells surrounding DCIS (breast)



Astrocytoma



Intestinal carcinoid, sustentacular cells

Table 1: Melanocytic Lesions (n=277)

Melanoma	Cases	SOX10 (+)	% (+)
Melanoma (cutaneous)	119	115	96.6
Metastatic melanoma	87	73	83.9
Spindle cell melanoma	19	19	100
Desmoplastic melanoma	29	28	96.6
Desmoplastic/Spindle cell mixed features	3	3	100
Benign Nevus (various)	20	20	100

Table 2: SOX10 Expression in Carcinomas (n=610)

Carcinoma	Cases	SOX10 +	% (+)
Breast carcinoma	109	18	16.5
CNS Neoplasms			
Astrocytoma	41	22	53.7
Glioblastoma	7	2	28.6
Ependymoma	2	1	50
All other carcinomas*	451	0	0

*See Results

Table 3: SOX10 Expression in Soft Tissue Tumors (n=127)

Soft Tissue Tumors	Cases	SOX10 +	% (+)
Schwannoma (Neurilemmoma)	28	28	100
Leiomyosarcoma	31	2	6.5
Rhabdomyosarcoma	22	1	4.5
Fibrosarcoma	7	0	0
Dermatofibrosarcoma protuberans	9	0	0
Malignant fibrous histiocytoma	13	1	7.7
Liposarcoma	14	0	0
Angiosarcoma	1	0	0
Neurofibrosarcoma	2	0	0

Conclusion

This is the first report of a newly developed mouse monoclonal SOX10 immunohistochemical antibody. In this study, SOX10 appears to be a highly sensitive and specific marker for melanoma and its variants, including desmoplastic and spindle cell melanomas.

References

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