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Rabbit Polyclonal Anti-SOX-10 is a Reliable IHC Marker for Melanoma and its Mimics

G. Yang, A. Minasyan, J. Gordon, M. Lacey, T. Knoll, O. Mego, K. Lundquist.
Cell Marque Corporation, Rocklin, CA 95677;
Western Dermatopathology, San Luis Obispo, CA 93401.

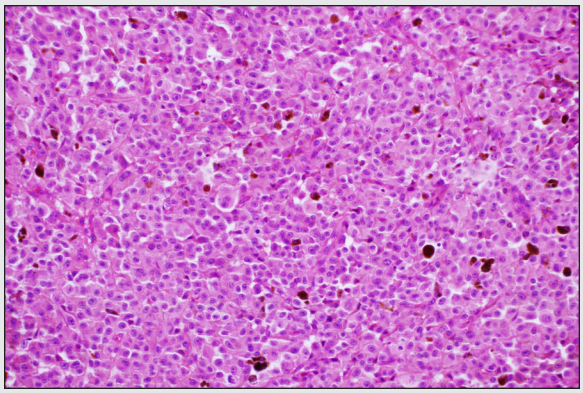

Figure 1.1 *Cutaneous melanoma.*

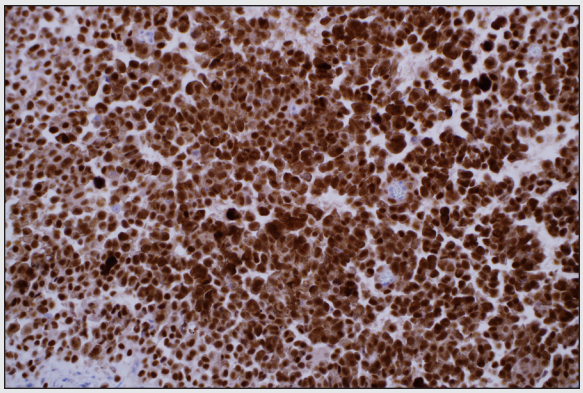

Figure 1.2 *Rabbit polyclonal SOX-10 labels melanoma cells strongly and diffusely in the nuclear location.*

Introduction

SOX-10, a member of the sex-determining region Y-related HMG-box family, is a transcription factor that is expressed in pre-migratory and migrating neural crest cells. Following migration it remains expressed in cells destined for glial, schwannian, and melanocytic differentiation. The expression of SOX-10 is ended in cells fated for neuronal differentiation, but it continues to the terminal differentiation and maintenance of the melanocytic phenotype. It has been reported that the SOX-10 antibody is a sensitive marker for melanomas, peripheral nerve sheath tumors, and breast carcinomas of basal-like and triple negative type. However, thus far the primary antibody against the SOX-10 protein discussed in research publications has been antiserum from goat, the requirement of anti-goat detection reagents for visualization hinders the antibody's acceptance, particularly in laboratories for clinical diagnosis. Here we report the assessment of SOX-10 expression of melanomas, carcinomas, mesenchymal neoplasms, nerve tumors, and mesotheliomas using a rabbit polyclonal SOX-10 antibody.

Design

In this study, we evaluated this rabbit polyclonal anti-SOX-10 for benign tissue cross-reactivity, neoplastic expression, sensitivity and specificity on whole tissue sections and tissue microarray by routine immunohistochemistry.

Results

Thirty seven of 39 conventional melanoma cases (37/39, 95%) showed strong and diffuse nuclear staining with this rabbit polyclonal antibody (Figures 1.1 and 1.2). Anti-SOX-10 highlighted

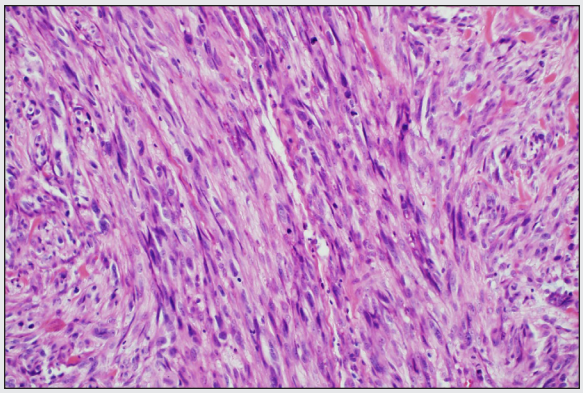

Figure 2.1 *Desmoplastic melanoma.*

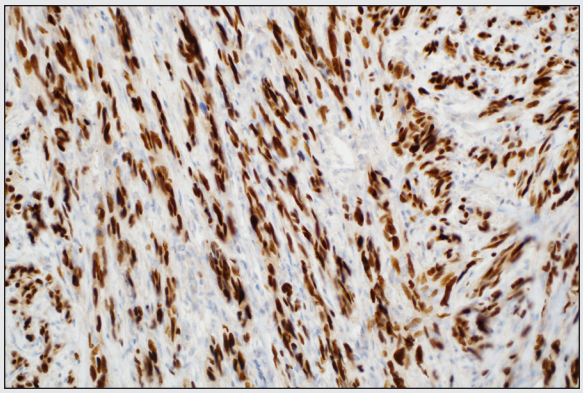

Figure 2.2 *Desmoplastic melanoma cells express SOX-10. Note fibroblasts, fibrocytes and macrophages are negative.*

spindle-shaped tumor nuclei strongly and diffusely in all 11 cases of desmoplastic melanoma (100%) (Figures 2.1 and 2.2). Melanoma markers S-100, CD63, and KBA.62 have demonstrated a moderate-to-strong and focal-to-diffuse staining of tumor cells. However, in comparison to SOX-10, these antibodies also stained other cellular components, such as fibrocytes, fibroblasts, macrophages, and interdigitating dendritic cells by S-100 (Figures 3.1, 3.2, and 3.3) and CD63, and endothelial cells, fibrocytes, and smooth muscle cells by KBA.62. The staining patterns interfered with the accurate interpretation of desmoplastic melanoma. Other melanoma markers such as HMB-45, MART-1, MiTF, tyrosinase, and PNL2 showed no immunoreactivity in 10 cases of desmoplastic melanoma. Only one case was weakly and focally positive in less than 10% of tumor cells for HMB-45, MART-1, MiTF, and tyrosinase. PNL2 was completely negative in all cases of desmoplastic melanoma. Three cases of spindle cell melanoma (3/3, 100%) were positive for anti-SOX-10. Malignant peripheral nerve sheath tumors display strong immune-reactivity to the antibody (3/4, 75%) (Figures 4.1 and 4.2). All schwannoma (15/15, 100%), neurofibroma (20/20, 100%), and granular cell tumor (5/5, 100%) were stained with rabbit polyclonal anti-SOX-10. Additional immunostaining was performed on 47 breast invasive ductal carcinoma cases and 43 colorectal adenocarcinoma cases with no reactivity (0/47, 0%), (0/43, 0%), respectively. No other carcinomas of GI, respiratory, genitourinary tract, reproductive tract primaries were found positive for anti-SOX-10. However, seven cases of colorectal carcinoma showed cytoplasmic dot-like, para-Golgi region staining. All lymphomas, mesenchymal tumors, and mesotheliomas were negative. The results are summarized in Table 1.

For normal benign tissue, 36 different tissues were used. The rabbit polyclonal SOX-10 antibody stained benign melanocytes, nerve sheath cells, and myoepithelial cells in sweat gland, mammary duct and salivary gland. Prostate basal cells are not stained. Three cases of dermal scar were studied and stained with the antibody. Spindle cells, such as fibrocytes, fibroblasts, and macrophages did not stain with rabbit polyclonal anti-SOX-10.

Table 1:
Immunostaining of rabbit polyclonal anti-SOX-10 in neoplasms

Neoplasm	Positive Cases/ Total Cases Tested	Sensitivity
Melanoma	37/39	95%
Desmoplastic melanoma	11/11	100%
Spindle cell melanoma, metastasis to lymph node	3/3	100%
Peripheral nerve sheath tumor	43/44	98%
Neurofibroma	20/20	100%
Schwannoma	15/15	100%
Malignant peripheral nerve sheath tumor	3/4	75%
Granular cell tumor	5/5	100%
Carcinoma	0/153	0%
Skin squamous carcinoma	0/8	0%
Basal cell carcinoma	0/5	0%
Colorectal adenocarcinoma	0/43	0%
Breast invasive ductal carcinoma	0/47	0%
Lung adenocarcinoma	0/5	0%
Lung squamous carcinoma	0/4	0%
Renal cell carcinoma	0/6	0%
Transitional cell carcinoma	0/5	0%

Table 1:
Immunostaining of rabbit polyclonal anti-SOX-10 in neoplasms

Neoplasm	Positive Cases/ Total Cases Tested	Sensitivity
Pancreatic ductal adenocarcinoma	0/5	0%
Prostatic adenocarcinoma	0/1	0%
Hepatocellular carcinoma	0/3	0%
Gastric adenocarcinoma	0/3	0%
Papillary thyroid carcinoma	0/3	0%
Medullary thyroid carcinoma	0/3	0%
Esophageal adenocarcinoma	0/1	0%
Esophageal squamous carcinoma	0/3	0%
Small cell lung carcinoma	0/2	0%
Merkel cell carcinoma	0/7	0%
Ovarian serous carcinoma	0/5	0%
Endometroid endometrial carcinoma	0/5	0%
Pancreatic neuroendocrine tumor	0/1	0%
Lymphoma	0/14	0%
Anaplastic large cell lymphoma	0/1	0%
Burkitt lymphoma	0/1	0%
Primary mediastinal large B cell lymphoma	0/1	0%
Small lymphocytic lymphoma	0/1	0%
Hairy cell leukemia	0/1	0%
Classic Hodgkin lymphoma	0/2	0%
Lymphoblastic lymphoma/ leukemia	0/2	0%
Peripheral T cell lymphoma, NOS	0/5	0%
Sarcoma	0/15	0%
Alveolar soft part sarcoma	0/1	0%
Leiomyosarcoma	0/2	0%
Rhabdomyosarcoma	0/2	0%
Gastrointestinal stromal tumor	0/6	0%
Solitary fibrous tumor	0/2	0%
Fibrosarcoma	0/1	0%
Ewing's sarcoma	0/1	0%
Other		
Mesothelioma	0/5	0%
Seminoma	0/4	0%
Spindle cell lipoma	0/1	0%
Sebaceous adenoma	0/1	0%

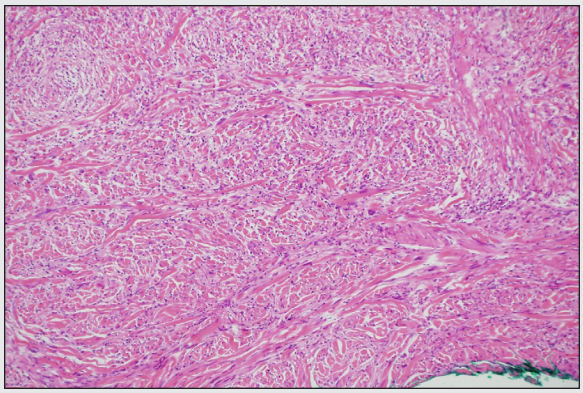

Figure 3.1 *Desmoplastic melanoma is suspicious present at the resection margin.*

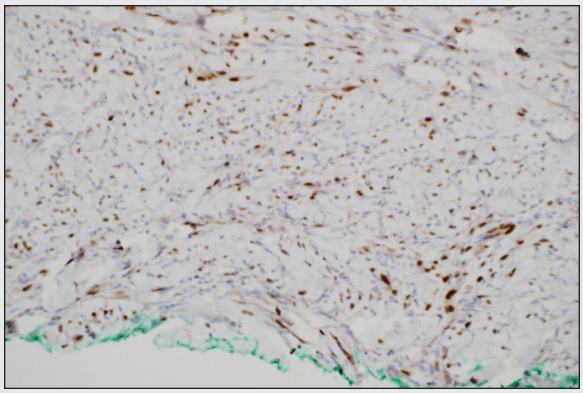

Figure 3.2 *Immunostaining of rabbit polyclonal anti-SOX-10 demonstrates tumor cells at the margin.*

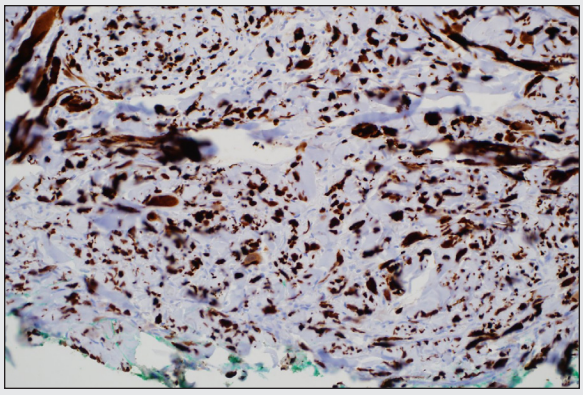

Figure 3.3 *S-100 not only stains tumor cells but also other tissues and shows little specificity.*

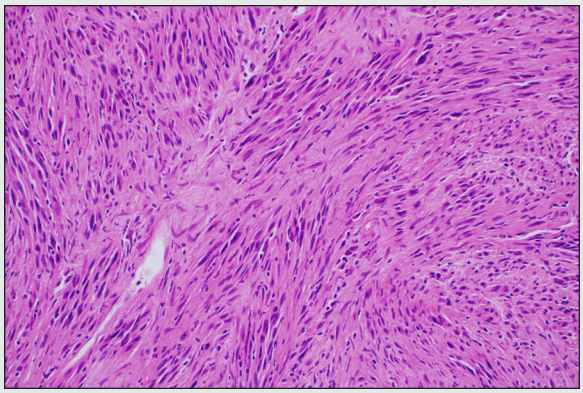

Figure 4.1 *Malignant peripheral nerve sheath tumor.*

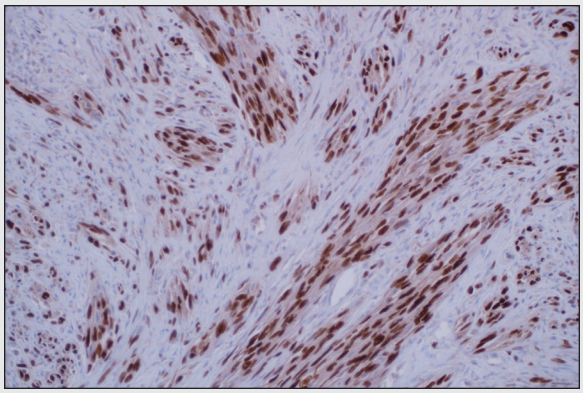

Figure 4.2 *Malignant peripheral nerve sheath tumor is strongly positive for rabbit polyclonal SOX-10.*

Conclusion

Our results show that rabbit polyclonal anti-SOX-10 antibody is a reliable, sensitive, and specific IHC biomarker for melanocytic and schwannian lesions. Rabbit antibody as a primary antibody is more suitable for routine diagnostic use in clinical laboratories due to readily available detection reagents and automation compatibilities.

In summary, the rabbit SOX-10 antibody showed the following important clinical utilities:

1. Melanocytic tumors, including melanocytic nevus, malignant melanoma, *in situ* and invasive
2. Desmoplastic melanoma, especially when the tumor mimics other spindle cell lesions with S-100 positivity and does not express melanoma-specific markers, such as HMB-45 and Melan A, tyrosinase, and MiTF
3. Metastatic melanoma in sentinel lymph node for distinguishing from S-100-positive interdigitating dendritic cells, follicular dendritic cells and Langerhans cells in the lymph node
4. Benign peripheral nerve sheath tumor with schwannian differentiation, such as neurofibroma and schwannoma
5. Malignant peripheral nerve sheath tumor for which SOX-10 shows higher sensitivity and specificity than S-100