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Sox10 – A marker for not only Schwannian and melanocytic neoplasms but also myoepithelial cell tumors of soft tissue. A systematic analysis of 5134 tumors

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Abstract

Sox10 transcription factor is expressed in Schwannian and melanocytic lineages and is important in their development and can be used as a marker for corresponding tumors. Additionally, it has been reported in subsets of myoepithelial/basal cell epithelial neoplasms, but its expression remains incompletely characterized. In this study, we examined Sox10 express-ion in 5134 human neoplasms spanning a wide spectrum of neuroectodermal, mesenchymal, lymphoid, and epithelial tumors. A new rabbit monoclonal antibody (clone EP268) and Leica Bond Max automation were used on multitumor block libraries containing 30–70 cases per slide. Sox10 was consistently expressed in benign Schwann cell tumors of soft tissue and the GI-tract and metastatic melanoma, and was variably present in malignant peripheral nerve sheath tumors. In contrast, Sox10 was absent in many potential mimics of nerve sheath tumors such as cellular neurothekeoma, meningioma, gastrointestinal stromal tumors, PEComa, and a variety of fibroblastic-myofibroblastic tumors. Sox10 was virtually absent in mesenchymal tumors but occasionally seen in alveolar rhabdomyosarcoma. In epithelial tumors of soft tissue, Sox10 was expressed only in myoepitheliomas, although often absent in malignant variants. Carcinomas, other than basal cell type breast cancers, were only rarely positive but included rare squamous carcinomas of head and neck and pulmonary small cell carcinomas. Furthermore, Sox10 was often focally expressed in embryonal carcinoma reflecting a primitive Sox10-positive phenotype or neuroectodermal differentiation. Expression of Sox10 in entrapped non-neoplastic Schwann cells or melanocytes in various neoplasms has to be considered in diagnosing Sox10-positive tumors. The Sox10 antibody belongs in a modern immunohistochemical panel for the diagnosis of soft tissue and epithelial tumors.

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Keywords

Sox10; Schwann cell; breast cancer; myoepithelioma; immunohistochemistry

INTRODUCTION

Sox10 transcription factor belongs to the Sox-family of transcription factors important in the development and maintenance of melanocytes and Schwann cells. The name is derived from the homology to the HMG-box of the sex-determining gene SRY on the Y-chromosome; Sox is abbreviated from SRY-related HMG-box. [1, 2]

Sox10 is important in the development and survival of Schwann cells and related cells. [3] Losses in Sox10 function lead to type IV Waardenburg syndrome with sensoneurial hearing loss, defects in the eye and hair pigment systems, and lateral displacement of the eyes (dystopia canthorum), and also cause Hirschprung disease genetic variant associated with maldevelopment of the intestinal autonomic nervous system. [4, 5]

In neuroectodermal cells, Sox10 is principally expressed in melanocytes and Schwann cells. Based on these findings, Sox10 has been explored as a marker for Schwannian and melanocytic tumors of skin and soft tissue. [6–13] Subsequently it has been recognized that Sox10 is also expressed in myoepithelial or basal cells, especially in the breast and salivary glands and in some tumors of these sites. [14–16]

However, Sox10 expression is still incompletely characterized in soft tissue tumors and carcinomas as many entities have been studied in very small numbers if at all. Increased use of minimal diagnostic specimens elevates the importance of the immunohistochemical differential diagnosis, potentially increasing the risk of misdiagnosis, if antigen patterns of tumors remain incompletely characterized. Another problem in application of Sox10 immunohistochemistry has been the lack of high quality antibodies. Some earlier antibodies were goat-derived, which makes their use more complicated, requiring species-specific detection systems.

In this study, we examined 5134 tumors for Sox10 expression and delineate its expression in neoplasia using a new rabbit monoclonal antibody. Specific areas explored here and not previously systematically studied include complete set of peripheral nerve sheath tumors and their mimics, mesenchymal tumors of the gastrointestinal tract, all types of common carcinomas, myoepitheliomas of soft tissue, skin adnexal tumors, and germ cell tumors. In addition, we describe two diagnostic pitfalls: reactive Schwann cell proliferation in various soft tissue tumors, and melanocytic colonization of basal cell carcinoma that yield focal Sox 10-positivity and should not be confused with Sox10 expressing tumors.

MATERIALS AND METHODS

Normal tissues and 5134 tumors, including nerve sheath, melanocytic, mesenchymal, epithelial, and lymphohematopoietic tumors, were obtained from anonymized surgical specimens. With few exceptions (single slide cases), the sections were derived from

multitumor blocks containing 30–70 rectangular samples each as previously described.[17] The sample size in these slides varied but was estimated to exceed the size of a single 0.6 mm^2 core by a factor of 5–12. The tumors were extensively characterized histologically and immunohistochemically. Antibodies used for this are listed in supplementary Table 1. Gliomas and related tumors were excluded from the study.

The primary rabbit monoclonal Sox10 antibody clone EP268 was obtained from Epitomics, Inc (AC-0237, Burlingame, CA) and used at a dilution of 1:250. Immunostaining was performed using the Leica Bond-Max automation and Leica Refine detection kit (Leica Biosystems, Bannockburn, IL). The approximately 3-hour protocol included in-situ deparaffinization and high-pH epitope retrieval for 25 min, primary antibody incubation for 30 min, polymer for 15 min, post-polymer for 15 min, and DAB as the chromogen for 10 min, followed by 5 min hematoxylin counterstaining. Normal tissues containing nerves, salivary gland, or breast, were used as positive controls. With the above parameters and automation platform, this antibody gave a strong, background-free, nuclear signal in the positive controls described above.

RESULTS

Normal tissues

In fetal tissue (10^{th} week) Sox10 was narrowly expressed in developing peripheral nerves, epidermal melanocytes, subsets of cells in autonomic ganglia, nerve plexuses of the intestines, and the olfactory plate (Fig. 1 A–C). It was not expressed in brain, eye, and peripheral non-neural tissues. Organs such as liver, kidney, adrenal cortex, and gonads were negative.

In normal adult tissues, Sox10 was expressed in epidermal melanocytes, peripheral nerves, and myoepithelial cells and also some luminal cells of the sweat glands (Fig. 1 D), breast, and salivary glands. In the prostate, Sox10 was only occasionally expressed in basal cells. Testicular germ cells showed focal expression in some cases. Normal squamous, glandular and parenchymal epithelia, and lymphoid tissue and histiocytes were negative. Perineurial invasion was highlighted in various carcinomas, based on Sox10-positive components in the nerves.

Neural and neuroectodermal tumors

Sox10 expression in 591 neural and neuroectodermal tumors and their selected mimics are summarized in Table 1. Sox10 was consistently expressed in peripheral and gastrointestinal schwannomas, and nerve sheath myxomas with virtually all tumor cells positive (Fig. 2A, B). In cutaneous, intraneural, and diffuse neurofibromas, it labeled subpopulations of tumor cells ranging from 20–40% of all cells.

All 47 S100 protein-positive granular cell tumors were Sox10-positive, whereas all 6 S100 protein-negative non-neural granular cell tumors, including 2 oral lesions in infants, were negative.

Malignant peripheral nerve sheath tumors, defined here as a tumors arising in pre-existing neurofibroma, varied in Sox10 expression. Nearly half of the cases (31/65) contained some Sox10-positive cells. However, most commonly, Sox10 expression was seen in pre-existing anatomically detectable neurofibroma components (Fig. 2) or sprinkled throughout the tumor as smaller Sox10-positive nuclei than those belonging to the high-grade MPNST component. In only 14/65 cases was Sox10 expression recognized in unequivocally malignant high-grade components, sometimes in a mosaic manner with only a portion of tumor cells being positive (Fig. 2D).

Great majority of metastatic melanomas (119/125, 95.2%) were Sox10 positive with nearly uniform nuclear labeling. Exceptions were 6 poorly differentiated examples that were mainly composed of sarcomatoid spindle cells. Three of these tumors were also S100 protein negative and 4 were negative for both HMB45 and MelanA. Because 3 other Sox10-positive melanomas were S100 protein-negative, Sox10 and S100 protein were equally sensitive for metastatic melanoma in this study. One of the Sox10-negative metastatic melanoma was positive for BRAF V600E mutation similar to the corresponding primary tumor supporting the diagnosis of melanoma. All but one desmoplastic melanoma were also Sox10-positive, and the immunostain often highlighted a trabecular growth pattern (Fig. 3 A).

The principal cells of paragangliomas and neuroblastomas were Sox10-negative. However, sustentacular cells, present in a majority of paragangliomas, were positive (Fig. 3B). A somewhat similar Sox10-positive population was also present in many olfactory neuroblastomas, but the principal tumor cells were negative (Fig. 3 C). The schwannian stromal elements variably present in differentiating neuroblastomas were also Sox10-positive (Fig. 3 D).

Mesenchymal tumors

Sox10 expression in 1645 mesenchymal non-neurogenic tumors is summarized in Table 2. Among non-nerve sheath tumors alveolar rhabdomyosarcoma was one of only exceptions showing positive tumor cells (2/27, Fig. 4). Two S100-positive tumors classified as ossifying fibromyxoid tumors were also positive. Fibroblastic-myofibroblastic tumors such as nodular fasciitis, benign fibrous histiocytoma and its variants, solitary fibrous tumor / hemangioperi-cytoma of the peripheral soft tissues and intracranial space and undifferentiated pleomorphic sarcomas were always negative for Sox10. Mimics of nerve sheath tumors, such as cellular neurothekeomas, fibrous hamartomas of infancy, and meningiomas were negative.

Lipomatous, smooth muscle, glomus /perivascular cell tumors, and other sarcomas studied were consistently negative. However, synovial sarcomas and glomus tumors often showed a small number (<5%) of Sox10-positive nuclei that were small and likely represented entrapped neural (schwannian) elements.

All 177 lymphomas studied were negative, including large B-cell (n = 50), small B-lymphocytic (n = 32), follicular (n = 30), and miscellaneous T-cell lymphomas including

large cell anaplastic lymphomas (n = 65). Also negative were 5 cases of Langerhans cell histocytosis.

Epithelial neoplasms

Sox10 expression in 2716 epithelial neoplasms is summarized in Table 3. Sox10 was prominently expressed in pleomorphic adenomas/mixed tumors of the salivary gland with a majority of tumor cells positive. This included positivity in ductal and solid epithelioid elements as well as chondroid components. In cutaneous and soft tissue myoepitheliomas/mixed tumors the expression was variable. Nevertheless, 28/34 non-malignant cases were positive. However, malignant myoepitheliomas were less frequently (6/20) positive. Examples with epithelioid cells in a myxoid stroma and those composed of spindled cells were strongly positive (Fig. 5). For comparison, these malignant tumors expressed other myoepithelial markers as follows: keratins AE1/AE3 (17/20), S100 protein (10/20), GFAP (7/20), p63 (5/20).

Skin adnexal neoplasms related to sweat glands had variable expression. While cylindromas (including cases from patients with cylindromatosis of the scalp) and eccrine spiradenomas were uniformly Sox10-positive, hidradenomas (eccrine acrospiromas) were usually negative. Ectopic hamartomatous thymoma (branchial anlage mixed tumor) showed focal Sox10 expression in epithelial cords, but the spindle cell components were negative.

Of ductal carcinomas of the breast, 57/486 (12%) expressed Sox10, typically in all tumor cells (Fig. 6 A), but in 3 cases <50% of the tumor cells were positive. These tumors were high-grade, and the majority (60%) were ER-negative or had low ER expression (<5% of tumor cells). A majority of Sox10-positive ductal carcinomas expressed CK5/6 (69%) or Trim29 (71%) at least focally, consistent with a basal cell type. None of the lobular carcinomas were positive. In addition, ducts with in situ-carcinoma were typically bordered by Sox10-positive myoepithelial cells.

Sox10 expression was rare in other carcinomas. However, it was detected in occasional squamous cell carcinomas of the head and neck and lungs, and pulmonary small cell carcinomas (Fig. 6 B). The only pulmonary adenocarcinoma showing a small number of positive tumor cells was a well-differentiated fetal adenocarcinoma in a 35-year-old man that had glands with subnuclear vacuolization somewhat reminiscent of secretory endometrium (Fig. 6 C).

In embryonal carcinomas of testis, a subpopulation of tumor cells (<10%) were Sox10-positive in 8/23 cases. This included positivity inside and in the lining element of the embryoid bodies (Fig. 6 D). Among teratomatous elements, squamous and glandular epithelia showed rare, focal positivity. All seminoma and choriocarcinoma components were negative.

Scattered non-neoplastic Sox10-positive cells in non-expressing tumors

Scattered Sox10 labeled scattered Sox10-positive perivascular cells, presumably Schwann cells were detected in some but not all desmoid tumors (Fig. 7 A) and synovial sarcomas. Also, Sox10-positive melanocytes (also positive for MelanA) were variably present around

and inside the cellular nests of basal cell carcinoma (Fig. 7 B). Many but not all glomus tumors also contained Sox10-positive elements representing Schwann cells. Sox10 did not label the S100-positive dendritic histiocytes variably present in most malignant neoplasms.

DISCUSSION

In this study, we examined Sox10 expression with a new rabbit monoclonal antibody offering an excellent signal quality with minimal if any background. Two major groups of tumors emerged that were nearly consistently Sox10-positive and strong diagnostic targets: nerve sheath and melanocytic neoplasms among mesenchymal/neuroectodermal tumors, and myoepithelial or basal cell –related neoplasms among epithelial neoplasms.

Sox10 transcription factor is known to be important in the development and maintenance of the peripheral nervous system, and it is strongly expressed in Schwann cells.[6, 7] In this study, benign nerve sheath tumors such as schwannomas, neurofibromas, granular cell tumors, and nerve sheath myxomas were strongly positive with rare exceptions. It is possible that technically insufficient or antigenically poorly preserved samples played a role in the isolated negative examples. These observations confirm previous studies based on smaller series of cases. [6, 12]

Because nearly all other mesenchymal tumors were negative, Sox10 helps to differentiated Schwannian neoplasms from a variety of other entities. In the intracranial space, distinction of schwannoma or neurofibroma from meningioma is greatly assisted, as up to 20–30% of meningiomas may express S100 protein. [18] In the gastrointestinal tract, Sox10 detects GI-Schwannomas and distinguishes them from GISTs that are occasionally S100 protein-positive. Distinction of nerve sheath myxoma from the non-schwannian neurothekeomas is aided by Sox10 immunohistochemistry as previously suggested. [9] Sox10-negativity of S100 protein-positive tumors such as ossifying fibromyxoid tumor argues against their Schwannian or myoepithelial derivation.

Neurofibromas are composed of a heterogeneous admixture of cells with Schwann cells and CD34-positive fibroblasts being the primary components. Neurofibromas, in general, differ from Schwannomas in that they contain a much smaller proportion of Schwann cells, as clearly shown by the percent of Sox10-positive cells. This is in strong contrast with many mesenchymal tumors, such as fibrous histiocytoma variants and dermatofibrosarcoma protuberans (DFSP), among which not a single Sox10-positive case was found in this study. However, certain variants with melanocyte-like components, such as pigmented DFSP, could be focally positive but such cases were not included in this study.

Malignant peripheral nerve sheath tumors are a more difficult diagnostic problem even with immunohistochemistry, because the majority of high-grade examples are negative for S100 protein. [19] Similarly, they are also often negative for Sox10, necessitating additional clinicopathologic correlation such as tumor location in a nerve trunk or origin from neurofibrma or association with neurofibromatosis 1. Based on our observations, it seems likely that Sox10-positive cells in MPNST often are entrapped Schwann cells or residual

Schwann cells from a pre-existing neurofibroma. This is supported by the observation that the Sox10-positive cells often have small non-atypical nuclei.

Metastatic malignant melanoma and desmoplastic melanoma involving skin or soft tissue and sinonasal melanomas nearly always retain Sox10-expression, so Sox10 is an excellent positive marker for most melanomas. However, there are rare undifferentiated or "dedifferentiated" melanoma metastases that do not express Sox10, S100 protein or melanoma-specific markers, so that their specific identification may be difficult. In some cases, additional sampling for more differentiated components, or BRAF V600E mutation analysis, could be helpful.[20] Nevertheless, the specificity of this molecular genetic test is not certain, as examples of malignant peripheral nerve sheath tumor have been reported that carry this mutation. [21] Because Sox10 is equally expressed in benign nevi, it cannot be used to distinguish benign and malignant melanocytic lesions. [6, 7, 9]

Entities that can enter into differential diagnosis of nerve sheath tumor, melanoma or clear cell sarcoma based on their positivity for S100 protein include low-grade sinonasal sarcoma with neural and myoid features. [22] HMB45 or MelanA-positivity is typical of PEComa, which often raises the differential diagnosis of a melanocytic neoplasm. As all these tumors were Sox10-negative in our study, Sox10 is helpful in their distinction from nerve sheath and melanocytic neoplasms.

While early studies suggested that all carcinomas are Sox10-negative[6], subsequent studies pointed out that a subset of breast cancer with basal cell type features can express Sox10. [13, 15] In our study, we found that 12% of ductal carcinomas are strongly Sox10-positive, and these tumors often had focal positivity for basal cell markers such as keratins 5/6 and Trim29. We also found that lobular carcinomas are invariably Sox10-negative. Also, other basal cell-type carcinomas, such as adenoid cystic carcinoma of salivary gland are also usually Sox10-positive. [14]

Other carcinomas were only rare Sox10 positive. Such examples include a small percentage (<10%) of squamous cell carcinomas of the head and neck, occasional small cell carcinomas, and rare pulmonary adenocarcinomas. However, other common carcinomas, such as colorectal, pulmonary, pancreatic, prostatic, and urothelial carcinomas, were not found to be Sox10-positive in this study, indicating high basal cell/myoepithelial cell specificity for Sox10. Because Sox10 is generally so narrowly expressed in carcinomas but consistently present in nerves, it could be useful in pinpointing perineurial invasion in the prostate and other anatomic sites.

Embryonal carcinomas were among rare carcinomas that often contained Sox10-positive elements. Such components could be analogous to Sox10 expression in early embryogenesis or possibly reflect early neurogenic differentiation.

Among non-nerve sheath soft tissue tumors mixed tumors and myoepitheliomas were typically Sox10 positive. Sox10 expression was also consistently prominent in pleomorphic adenomas of the salivary gland and was also expressed in a great majority of cutaneous mixed tumors and myoepitheliomas. Furthermore, Sox10 aided in the identification of myoepitheliomas among potential tumor mimics such as extraskeletal myxoid

chondrosarcoma, ossifying fibromyxoid tumor, and chordoma. Occasional Sox10-positive ossifying fibromyxoid tumors will need further characterization as they might in fact represent myoepitheliomas. This could also be suspected based on the fact that many investigators have included keratin-positive cases under this diagnosis. [23] Because malignant myoepithelioma is often Sox10-negative, the use of other myoepithelial markers, such as keratins, GFAP, p63, SMA, and calponin, is necessary in proper identification. These markers can also be useful in separating spindled myoepitheliomas and nerve sheath tumors, although some entities have overlapping expression patterns for some of these markers.

Skin adnexal tumors have divergent patterns of Sox10 expression. While cylindromas and eccrine spiradenomas are uniformly positive, expression seems rare in hidradenomas (eccrine acrospiromas). The potential application of Sox10 in the accurate subclassification of skin adnexal neoplasm should be validated in a larger study.

Even if Sox10 is highly specific for Schwann cells, melanocytes, and myoepithelial cells and therefore an excellent marker for tumors with these types of differentiation, its expression in non-neoplastic elements can sometimes be potentially confounding. Examples of this include Sox10-positive melanocytes colonizing basal cell carcinomas and some other skin adnexal tumors; these cells have been shown positive for other melanoma markers. [24] Also, Sox10 immunostain detects Schwann cell proliferation in tumors such as synovial sarcoma, glomus tumor, and desmoid fibromatosis. However, such Sox10 expression is always seen in a minority of cells in those settings, and should not lead into confusion with nerve sheath or melanocytic neoplasms. The problem of non-neoplastic positive cells is much smaller with Sox10 than with S100 protein, as the S100 protein-positive antigen presenting cells are nearly ubiquitous and sometimes prominently expressed in tumors prompting one to potentially assess such tumors as focally S100 protein-positive.

This study was performed using slides from multitumor blocks so that the sample size was smaller than typically seen in resections specimens but larger than that in some needle biopsies and 5–12 times larger than present in a single 0.6 mm^2 core in tissue microarrays. Nevertheless, this could result into failed detection of very focal immunostaining. However, the results of nerve sheath and melanocytic tumors compare will with the data in previous series. [6, 9, 11]

In conclusion, we analyzed 5134 tumors for Sox10 expression and conclude that it is fairly specific for Schwannian, melanocytic, and myoepithelial/basal cell epithelial neoplasms. A new rabbit monoclonal Sox10 antibody with strong immunohistochemical labeling is an excellent marker for these tumors, as most other carcinomas, sarcomas, and all hematopoietic tumors are Sox10 negative. Table 4 lists potential morphologic mimics that show contrasting patterns of Sox10 expression highlighting its potential diagnostic applications.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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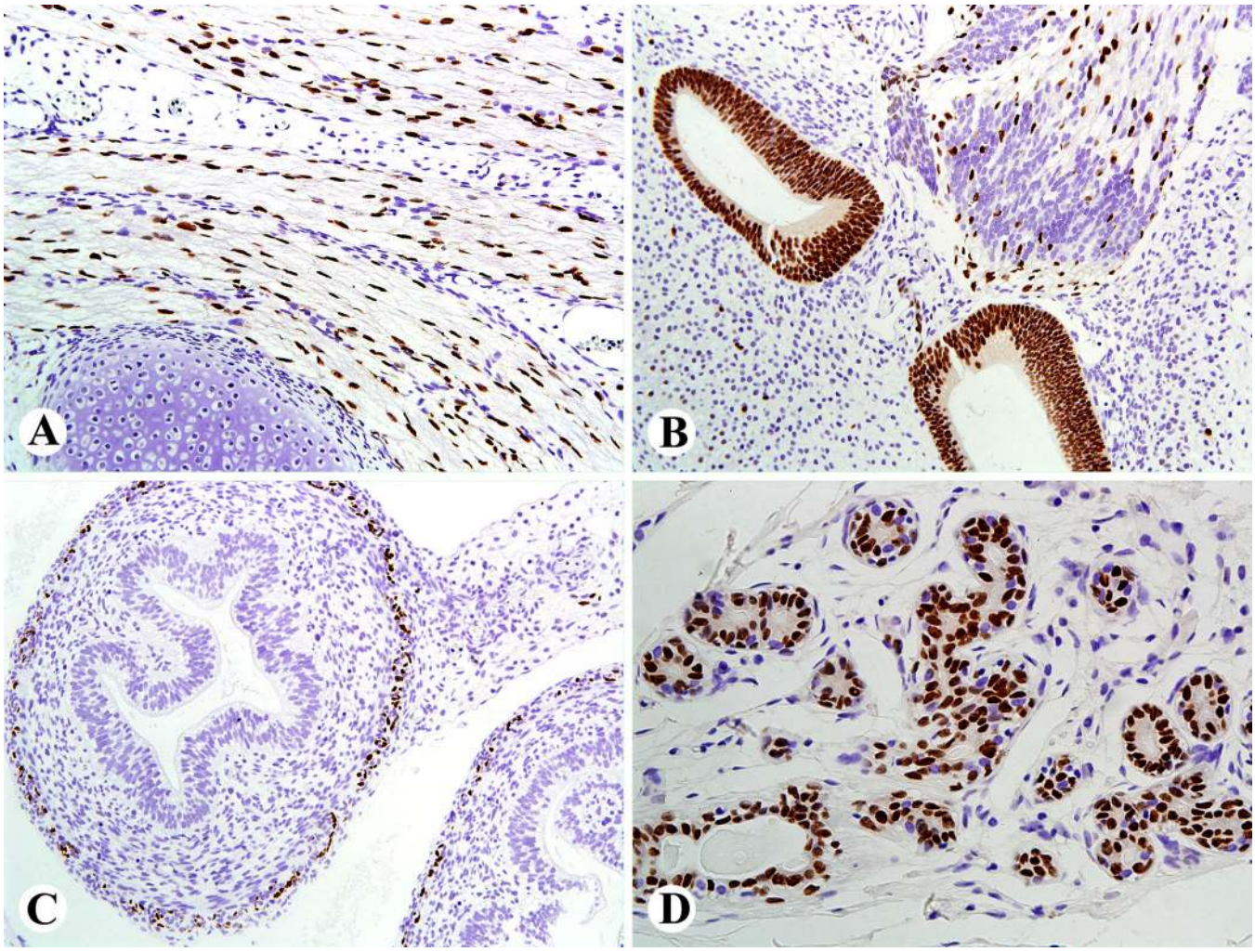

Fig. 1.

Sox10 expression in normal fetal and adult tissue. A. Developing nerve trunks contain Sox10-positive Schwann cells, whereas cartilage, connective tissue and blood vessels are negative. B. Olfactory plate and Schwannian elements in a nerve ganglion are positive. C. In developing intestines, Sox10 is restricted to myenteric plexus elements. D. Adult sweat glands express Sox10 in myoepithelial cells and many luminal cells.

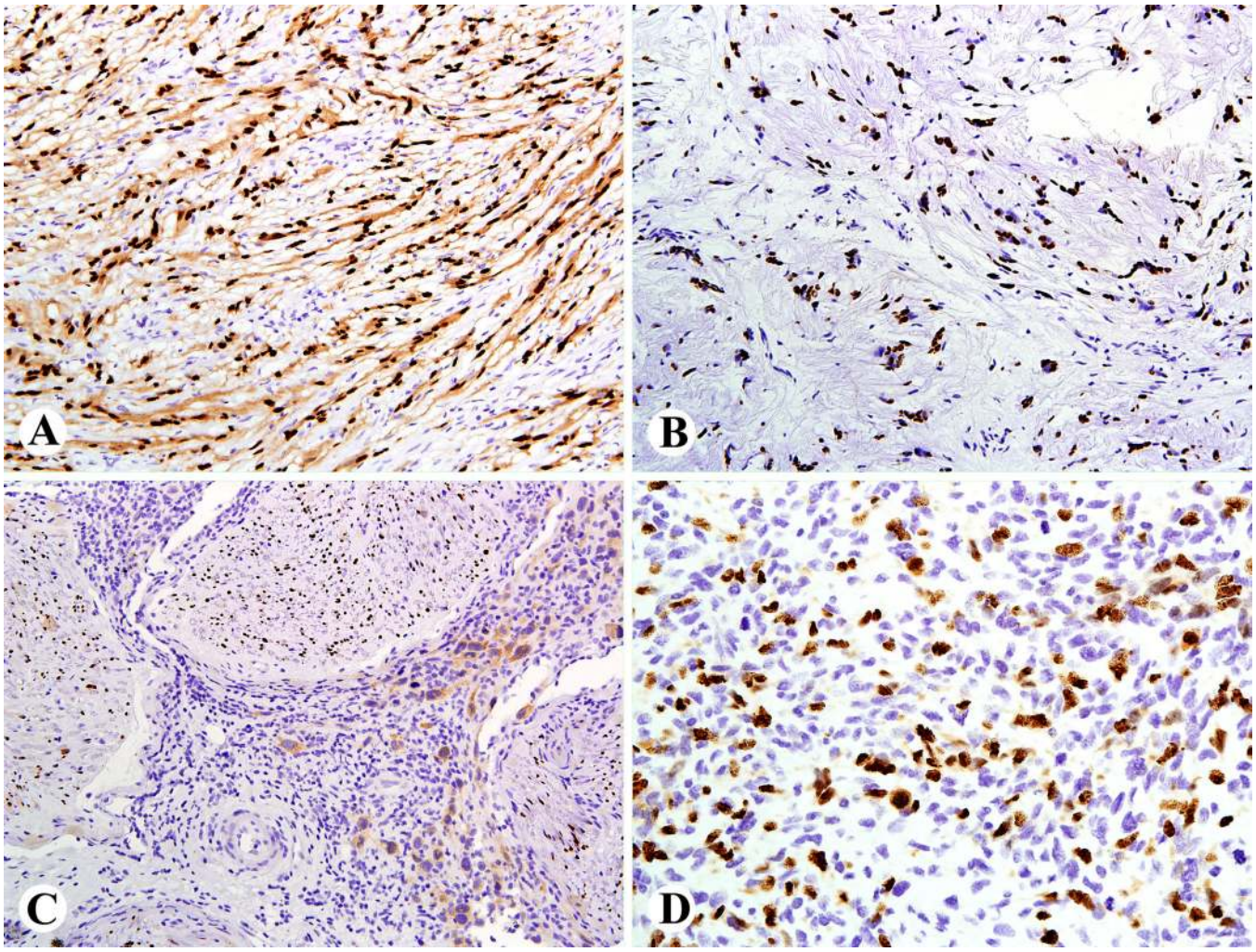

Fig. 2.

Sox10-positive nerve sheath tumors. A. Gastric schwannoma composed of spindled cells forming trabecular arrangements. B. Nerve sheath myxoma with spindled cells in corded patterns containing syncytial formations. C. Malignant peripheral nerve sheath tumor with positive plexiform neurofibroma elements but negative high-grade component. D. This MPNST shows Sox10 expression in nearly half of the tumor cells.

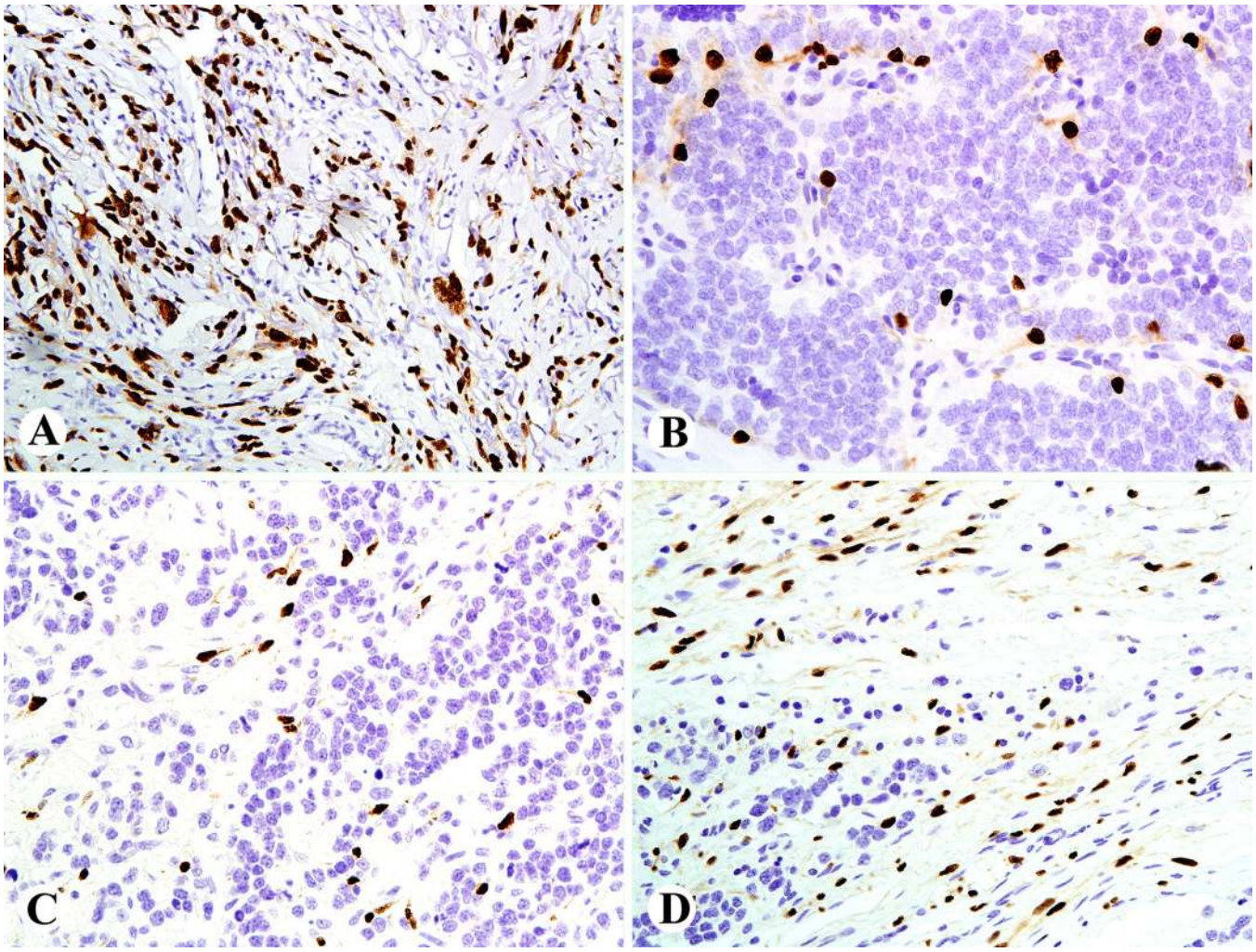

Fig. 3.

Sox10 in melanocytic and neuroectodermal tumors. A. The tumor cells of desmoplastic melanoma are positive. B. In olfactory neuroblastoma, Sox10 highlights a sustentacular cell-like element in the periphery of cellular nests. C. Poorly differentiated stroma-poor neuroblastoma contains small numbers of Sox10-positive cells. D. In differentiating neuroblastoma, the more abundant Schwann cell stromal elements are Sox10-positive.

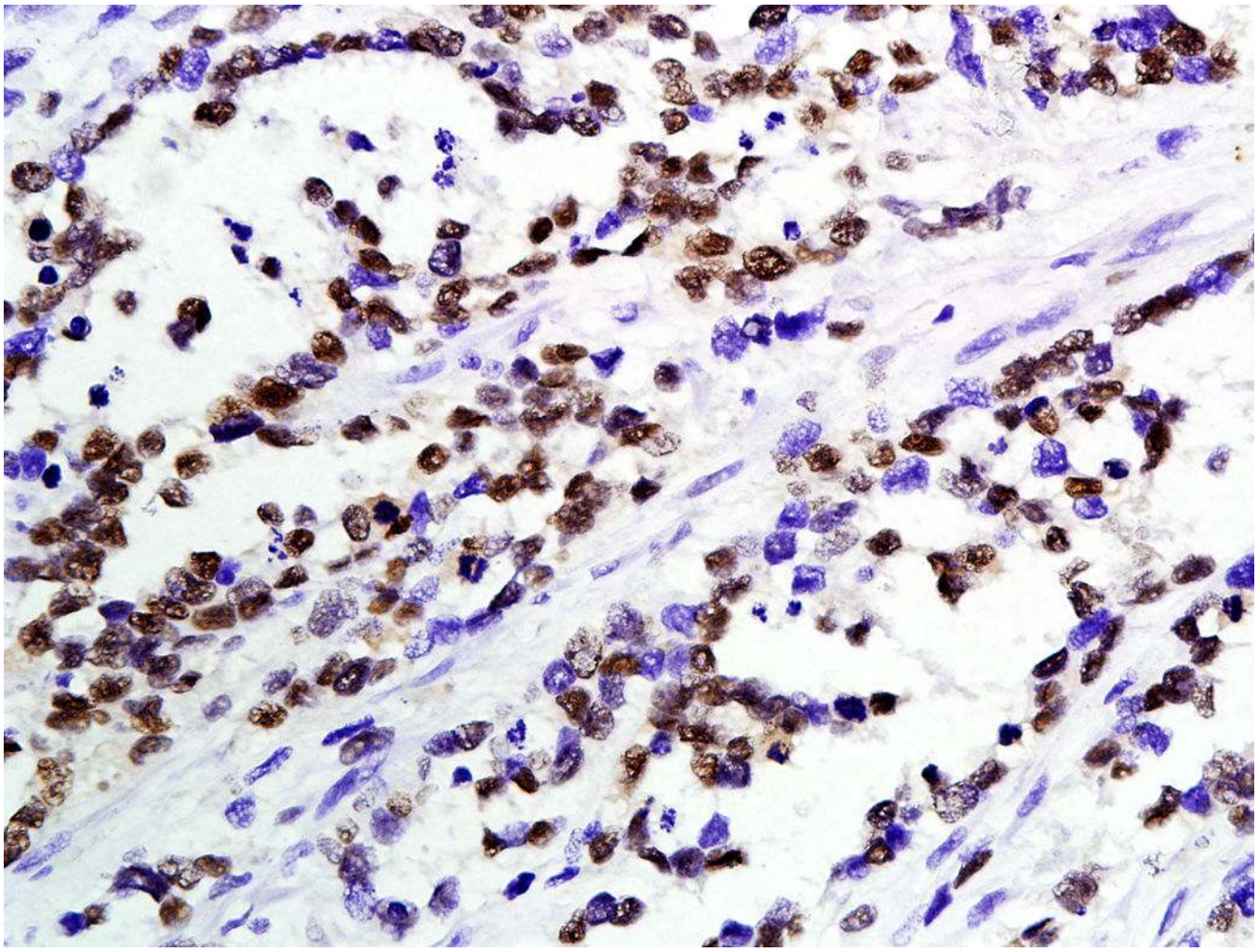

Fig. 4.
Rare alveolar rhabdomyosarcomas were Sox10-positive.

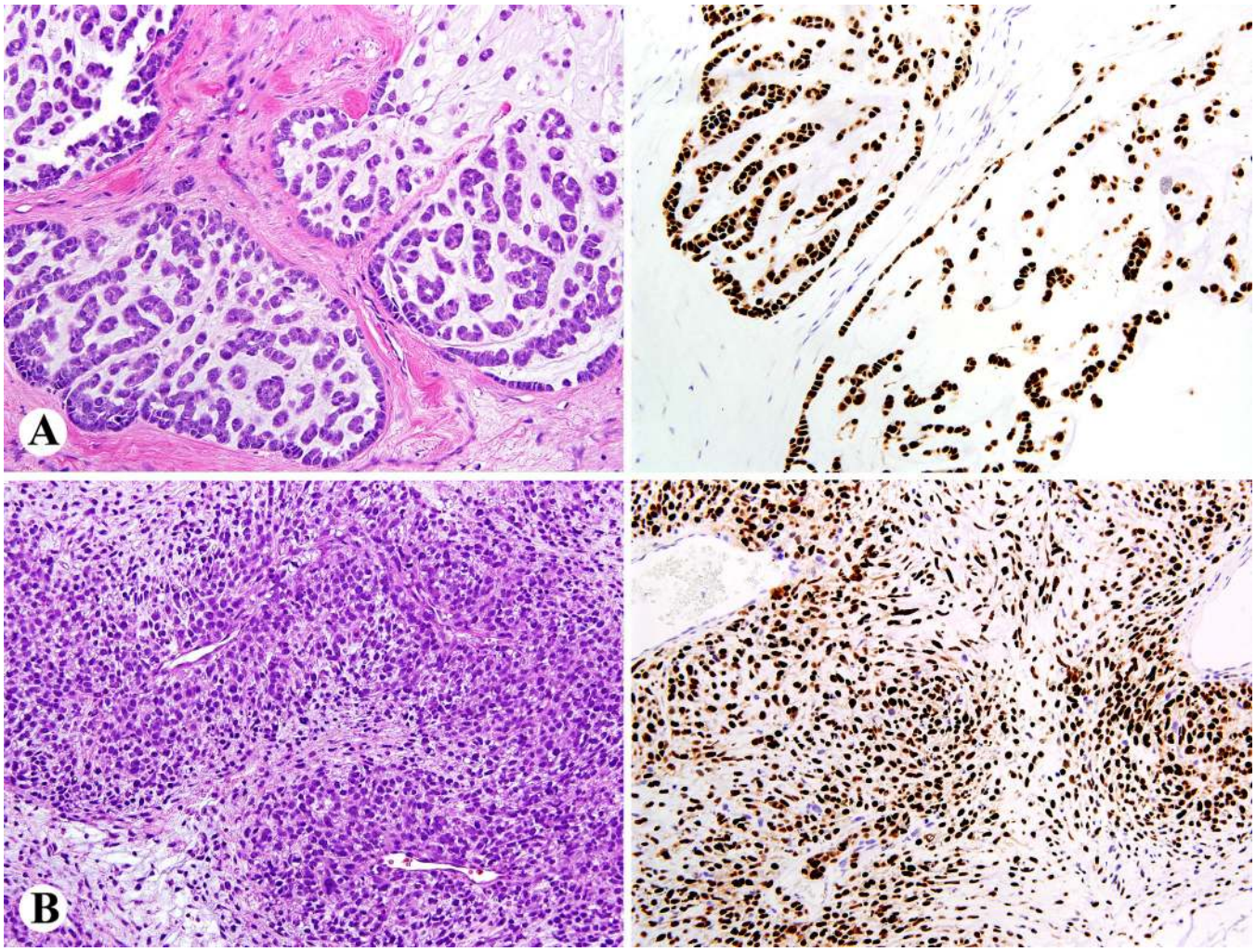

Fig. 5.

Two examples of Sox10-positive malignant myoepitheliomas with the corresponding H&E stain. A. A sarcomatoid example with a spindle cell pattern (tumor was also positive for keratins, S100 protein, GFAP, and p63). B. An example composed of epithelioid cells in myxoid matrix arranged in a trabecular pattern (this tumor was positive for keratins and S100 protein only).

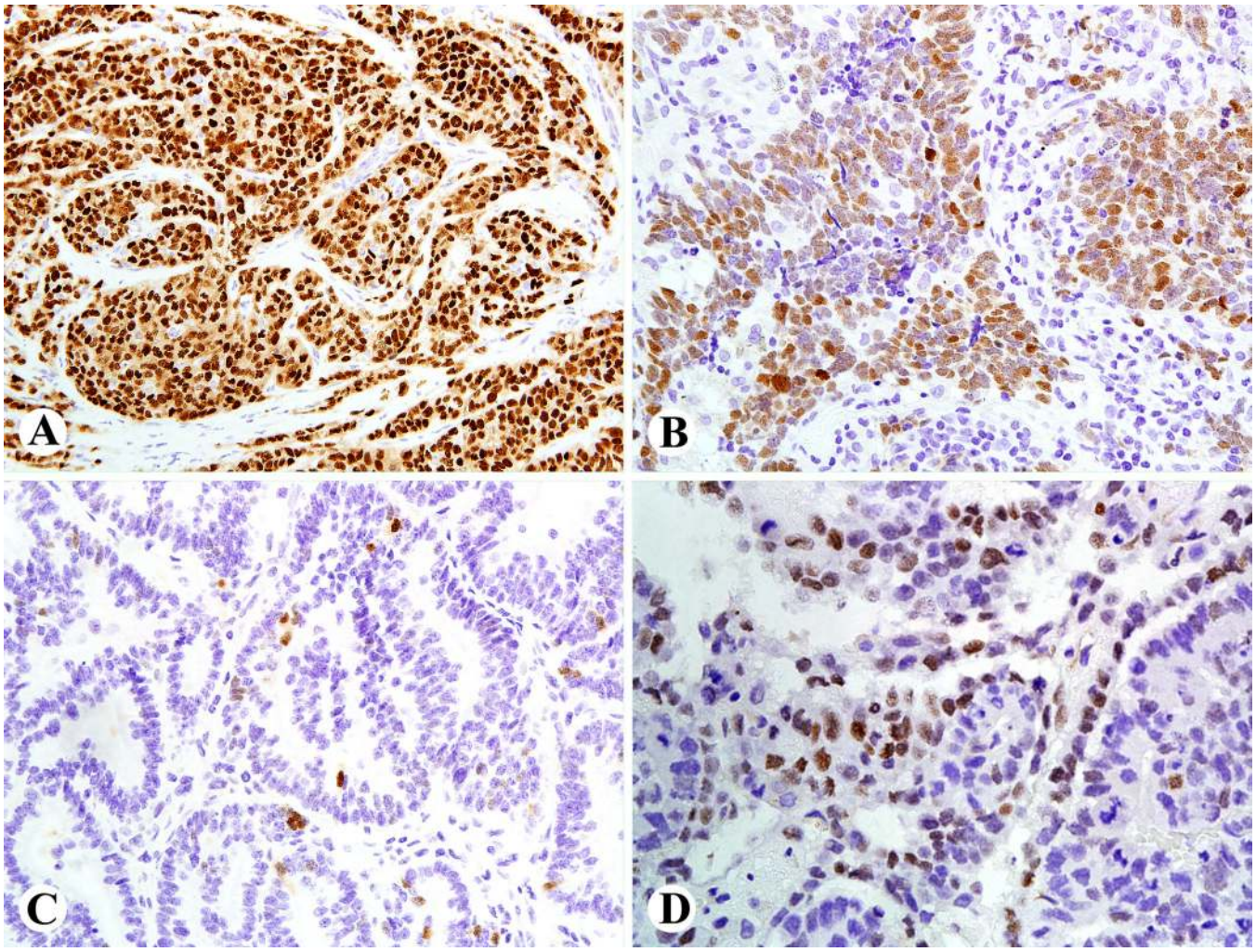

Fig. 6.

Sox10-positive epithelial neoplasms. A. A subset of ductal carcinomas of the breast closely corresponding to basal cell type carcinomas, were strongly Sox10-positive. B. Rare examples of pulmonary small cell carcinomas were also positive. C. Sox10-positive cells in a fetal type of pulmonary adenocarcinoma. D. Embryonal carcinomas of the testis showed varying numbers of Sox10-positive cells, here seen in embryoid bodies and the surrounding cuboidal cell layer.

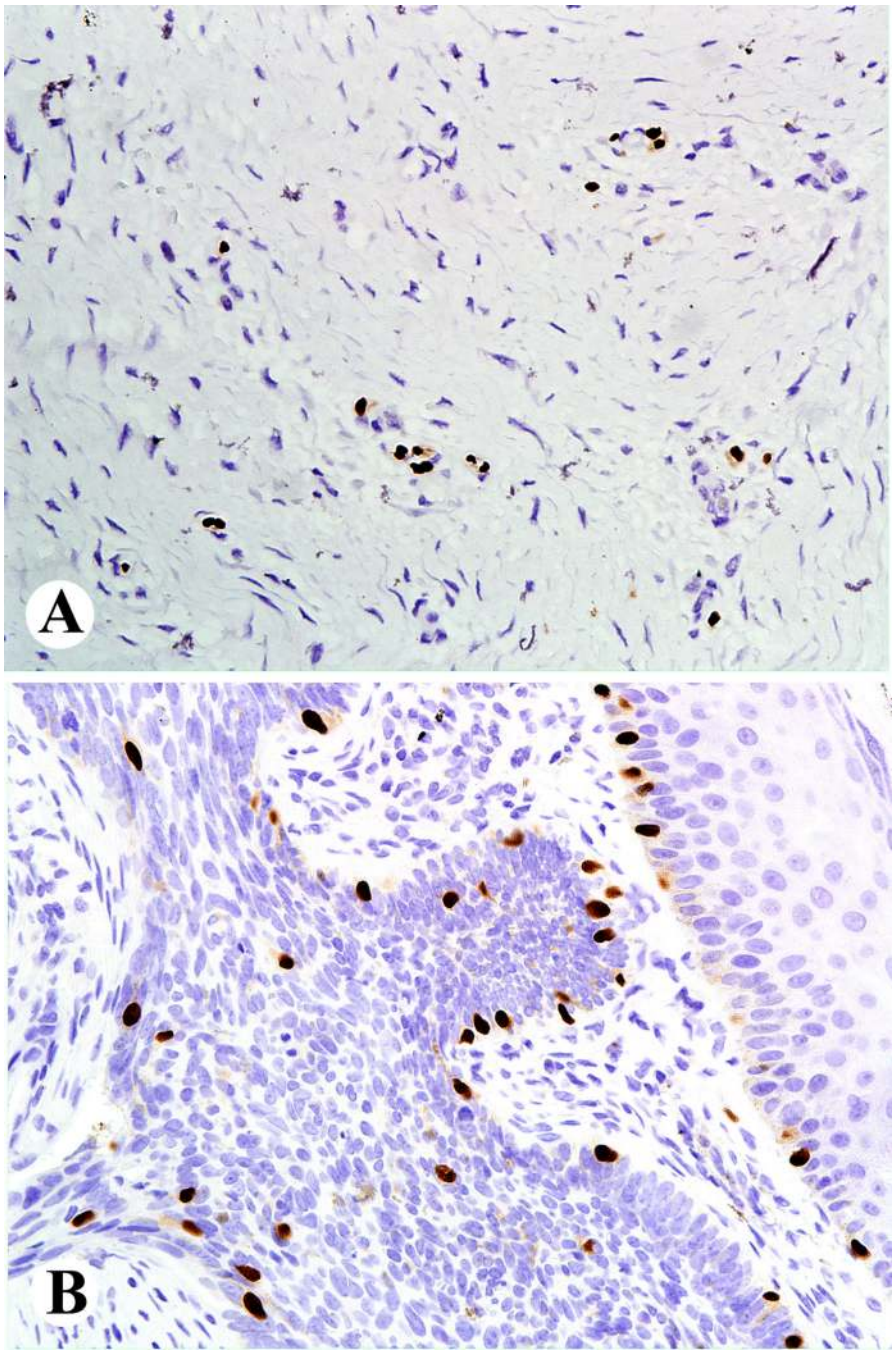

Fig. 7.

Examples of Sox10-positive scattered cells in Sox10-negative tumors. A. Sox10 positive perivascular cells in desmoid fibromatosis are probably Schwann cells of nerves. B. Scattered Sox10-positive cells present in most basal cell carcinomas are entrapped melanocytes (MelanA-positive, not shown).

Table 1

Expression of Sox10 in 591 neurogenic and selected related tumors or mimics.

Benign epithelioid PNST	15/15
Cellular blue nevus	3/3
Clear cell sarcoma (includes 5 in GI-tract)	19/20
Granular cell tumor, S100 protein positive	47/47
Granular cell tumor, S100-negative, non-neural	0/6
Malignant peripheral nerve sheath tumor	14/65 (31/65)**
Melanoma, metastatic	119/125
Melanoma, desmoplastic	24/25
Melanoma, sinonasal	36/41
Nerve sheath myxoma	6/6
Neuroblastoma	16/26*
Neurofibroma	31/31
Neurothekeoma, cellular and myxoid	0/19
Olfactory neuroblastoma	5/7*
Paraganglioma	36/48*
Perineurioma	0/6
Schwannoma, soft tissue	80/81
Schwannoma, GI-tract	20/20

* Positive cells represent sustentacular cells or Schwann cells.

** The numbers in parentheses include expression in entrapped Schwann cells.

PNST = peripheral nerve sheath tumor.

Table 2

Expression of Sox10 in 1645 mesenchymal tumors.

Alveolar soft part sarcoma	0/12
Angiosarcoma	0/21
Benign fibrous histiocytoma	0/198
Chondrosarcoma, bone	0/56
Chondrosarcoma, extraskeletal myxoid	0/41
Dermatofibrosarcoma protuberans	0/40
Desmoid fibromatosis*	0/31
Desmoplastic small round cell tumor	0/14
Epithelioid hemangioendothelioma	0/19
Epithelioid sarcoma	0/20
Ewing sarcoma	0/32
Fibrous hamartoma of infancy	0/9
Gastrointestinal stromal tumor	0/94
Glomus tumor*	0/62
Glomangiopericytoma	0/9
Hemangioma (different variants)	0/22
Inflammatory myofibroblastic tumor	0/14
Kaposi sarcoma	0/34
Leiomyoma (57 uterine, 15 esophageal)	0/72
Leiomyosarcoma, soft tissue	0/63
Liposarcoma, dedifferentiated	0/49
Liposarcoma, myxoid	0/24
Low-grade fibromyxoid sarcoma	0/31
Meningioma (including 32 atypical ones)	0/219
Myofibroma	0/19
Nodular fasciitis	0/43
Ossifying fibromyxoid tumor	2/47
Perivascular epitheluioid tumor (PEComa)	0/21
Pleomorphic undifferentiated sarcoma	0/75
Proliferative fasciitis	0/29
Rhabdomyosarcoma, alveolar	2/27
Rhabdomyosarcoma, embryonal	0/43
Sinonasal low-grade polyphenotypic sarcoma	0/12
Solitary fibrous tumor/HPC	0/85
Synovial sarcoma*	0/58

*Small numbers of positive cells seen in these tumors were entrapped or proliferating Schwann cells.

Table 3

Sox 10 expression in 2716 epithelial neoplasms

Adenoma, parathyroid	0/27
Adenoma, pleomorphic, salivary gland	111/112
Adenoid cystic carcinoma, head and neck	35/36
Adrenocortical carcinoma	0/38
Basal cell carcinoma, skin	0/53*
Breast, ductal carcinoma	57/486
Breast, lobular carcinoma	0/50
Chordoma	0/39
Colorectal adenocarcinoma	0/164
Ectopic hamartomatous thymoma	2/7
Endometrium, adenocarcinoma	0/103
Germ cell tumor, seminoma	0/30
Germ cell tumor, choriocarcinoma	0/5
Germ cell tumor, embryonal carcinoma	8/23
Liver, cholangiocarcinoma	0/40
Liver, hepatocellular carcinoma	0/46
Lung, adenocarcinoma	1/86
Malignant mesothelioma	0/45
Merkel cell carcinoma	0/16
Mixed tumor/myoepithelioma, soft tissue	28/34
Mixed tumor/myoepithelioma, malignant	6/20
Ovary, endometrioid carcinoma	0/38
Ovary, serous carcinoma	0/94
Pancreas, adenocarcinoma	0/150
Pancreas, neuroendocrine tumor	0/42
Prostate, adenocarcinoma	0/124
Renal cell carcinoma/oncocytoma*	0/270
Salivary gland, ductal carcinoma	2/33
Small cell cell carcinoma, lung	2/30
Squamous cell carcinoma, skin	0/40
Squamous cell carcinoma, head and neck	7/118
Squamous cell carcinoma, lung	2/71
Skin adnexal tumor, cylindroma/spiradenoma**	10/10
Skin adnexal tumor, hidradenoma	1/11
Stomach, adenocarcinoma	0/33
Thymoma	0/38
Thyroid, papillary carcinoma	0/36
Urothelial carcinoma	0/118

* Includes the following carcinomas: 60 Clear cell low-grade, 50 high-grade, 57 Papillary type 1, 8 papillary type 2, 52 Chromophobe, 15 miscellaneous, and 28 oncocytomas.

** Included 5 cases of each.

Table 4

Examples of diagnostic applications of Sox10 with tumors showing contrasting patterns of expression.

Sox10-positive	**Sox10-negative**
Nerve sheath myxoma	Cellular/myxoid neurothekeoma
Gastrointestinal schwannoma	GIST
Schwannoma	Meningioma
Neurofibroma	Fibrous histiocytoma
Granular cell tumor (neural, S100 protein+)	Granular cell tumor, non-neural
Myoepithelioma/mixed tumor	Extraskeletal myxoid chondrosarcoma
Myoepithelioma/mixed tumor	Hidradenoma
Metastatic melanoma/Clear cell sarcoma	PEComa, alveolar soft part sarcoma