Paraffin-Section Detection of CD10 in 505 Nonhematopoietic Neoplasms

Frequent Expression in Renal Cell Carcinoma and Endometrial Stromal Sarcoma

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Abstract

We tested 505 cases of nonhematopoietic neoplasms by immunohistochemistry using a newly characterized monoclonal antibody (clone 56C6) against the CD10 antigen. CD10 was expressed widely in neoplasms of the genitourinary tract, including 41 (89%) of 46 cases of renal cell carcinoma, 13 (54%) of 24 cases of transitional cell carcinoma, and 11 (61%) of 18 cases of prostatic adenocarcinoma. In addition, 5 (100%) of 5 endometrial stromal sarcomas, 3 (60%) of 5 rhabdomyosarcomas, 7 (50%) of 14 pancreatic adenocarcinomas, 5 (45%) of 11 cases of schwannoma, and 12 (40%) of 30 cases of malignant melanoma also were positive for CD10. Similar to normal tissue, CD10 positivity was restricted to the apical surface of malignant glandular cells of well-differentiated colonic, pancreatic, and prostatic adenocarcinoma, whereas in poorly differentiated adenocarcinoma and other tumors, such as melanoma, transitional cell carcinoma, renal cell carcinoma, and endometrial stromal sarcoma, the CD10 positivity showed diffuse cytoplasmic or membranous/Golgi patterns. The monoclonal antibody clone 56C6 is a reliable marker for CD10 in paraffin immunohistochemistry after heat-induced epitope retrieval. CD10 expression in renal cell carcinoma and endometrial stromal sarcoma may be a useful marker in the differential diagnoses of these tumors because both tumors otherwise lack specific markers.

CD10, or the common acute lymphoblastic leukemia antigen, is a cell-surface neutral endopeptidase that inactivates bioactive peptides.[1,2] It is a member of the exopeptidase family that includes CD13 and CD26.[3] This antigen is expressed by lymphoid precursor cells, germinal center B lymphocytes, and some myelocytes and, thus, is used widely as a cell surface marker for the categorization of acute leukemias and subclassification of malignant lymphomas.[2] Its expression in normal nonhematolymphoid tissue also is well documented. However, for nonhematopoietic neoplasms, CD10 is used rarely as a marker in surgical pathology diagnosis, partially because CD10 has been reliably detectable only on fresh cells and frozen sections. Recently, a CD10 monoclonal antibody (clone 56C6) has become commercially available for paraffin immunohistochemistry with satisfactory results after heat-induced epitope retrieval.[4,5] We used this new CD10 monoclonal antibody to study 505 nonhematopoietic tumors. We demonstrate that CD10 antigen is expressed widely in normal tissues, as well as in carcinomas of the gastrointestinal and genitourinary tracts and some sarcomas and may be a useful marker for the differential diagnosis of these tumors.

Materials and Methods

Case Selection

We selected 505 nonhematopoietic tumors from the City of Hope National Medical Center Division of Pathology, Duarte, CA ❚**Table 1**❚. The tissues from each of the cases were fixed in 10% neutral buffered formalin and embedded in paraffin. Normal tissues adjacent to neoplasms were evaluated

❚Table 1❚
Frequency of CD10 Expression in 505 Nonhematopoietic Neoplasms

Tumor Types	No. (%) of Positive Cases
Genitourinary tract (N = 88)	65 (74)
Renal cell carcinoma (n = 46)	41 (89)
Transitional cell carcinoma (n = 24)	13 (54)
Prostate carcinoma (n = 18)	11 (61)
Gastrointestinal tract (N = 68)	12 (18)
Pancreatic carcinoma (n = 14)	7 (50)
Colonic adenocarcinoma (n = 20)	5 (25)
Gastric adenocarcinoma (n = 9)	0 (0)
Hepatocellular carcinoma (n = 13)	7 (54)
Cholangiocarcinoma (n = 12)	0 (0)
Breast (N = 26)	1 (4)
Ductal adenocarcinoma (n = 20)	0 (0)
Lobular adenocarcinoma (n = 6)	1 (17)
Malignant melanoma (N = 30)	12 (40)
Salivary gland (N = 9)	1 (11)
Mixed tumor (n = 5)	0 (0)
Warthin tumor (n = 2)	0 (0)
Acinic cell adenocarcinoma (n = 2)	0 (0)
Neuroendocrine tumors (N = 40)	1 (2)
Adrenocortical carcinoma (n = 10)	0 (0)
Neuroendocrine carcinoma (n = 9)	1 (11)
Carcinoid tumor (n = 12)	0 (0)
Merkel cell carcinoma (n = 9)	0 (0)
Spindle cell sarcoma (N = 80)	19 (24)
Endometrial stromal sarcoma (n = 5)	5 (100)
Rhabdomyosarcoma (n = 5)	3 (60)
Liposarcoma (n = 2)	1 (50)
Schwannoma (n = 11)	5 (45)
Epithelioid sarcoma (n = 14)	4 (28)
Leiomyosarcoma (n = 16)	1 (6)
Paraganglioma (n = 10)	0 (0)
Synovial sarcoma (n = 7)	0 (0)
Fibrosarcoma (n = 2)	0 (0)
Gastrointestinal stromal tumor (n = 8)	0 (0)
Lung (N = 21)	5 (24)
Adenocarcinoma (n = 11)	2 (18)
Small cell carcinoma (n = 10)	3 (30)
Female reproductive system (N = 39)	3 (8)
Ovarian carcinoma (n = 27)	3 (11)
Endometrial adenocarcinoma (n = 12)	0 (0)
Thyroid tumors (N = 55)	0 (0)
Follicular adenoma (n = 24)	0 (0)
Papillary carcinoma (n = 10)	0 (0)
Medullary carcinoma (n = 16)	0 (0)
Follicular carcinoma (n = 5)	0 (0)
Miscellaneous (N = 49)	3 (6)
Mesothelioma (n = 17)	3 (18)
Squamous cell carcinoma (n = 10)	0 (0)
Thymoma (n = 8)	0 (0)
Germ cell tumor (n = 14)	0 (0)

simultaneously ❚Table 2❚. We cut 5-μm sections from each case, and 1 was stained with H&E.

Immunohistochemistry

CD10 immunophenotypic studies were performed with a newly available CD10 monoclonal antibody clone 56C6 (Novocastra, Burlingame, CA), which is reactive in routine paraffin-embedded sections, using the avidin-biotin complex technique augmented by heat-induced epitope retrieval.[6,7] Immunohistochemical staining was performed with a 1:20 dilution of CD10 on an automated immunostainer (TechMate 1000, Ventana, Tucson, AZ). Briefly, deparaffinized 5-μm sections first were rehydrated through

xylene and graded alcohol series. The slides then were rinsed with tap water for 5 minutes and steamed in a 1-mmol/L concentration of EDTA buffer (pH 8.0) in a food steamer (HH90, Black and Decker, Shelton, CT) for 20 minutes at 100 C. The following staining procedures then were performed in the automated immunostainer: (1) slides were washed 3 times for 10 minutes, blocked with normal mouse serum, and washed 3 times for 10 minutes; (2) incubated with CD10 antibody for 25 minutes at room temperature and washed 3 times for 10 minutes; (3) incubated with secondary antibody provided by the manufacturer (Ventana) and washed 3 times for 10 minutes; (4) quenched with quenching buffer for 10 minutes and washed 3 times for 10 minutes; (5) incubated with the avidin-biotin complex reagent provided by the manufacturer (Ventana) and washed 3 times for 10 minutes; and (6) incubated with diaminobenzidine for 15 minutes, rinsed 3 times for 10 minutes, counterstained with Mayer hematoxylin for 1 minute, dehydrated, cleared, and mounted with mounting media. All washing buffers and the quenching buffer were provided by the manufacturer (Ventana).

A section of lymph node with lymphoid hyperplasia was used as control tissue. Additional immunohistochemical studies were performed on some cases with antibodies directed against prostate-specific antigen (Biogenex, San Ramon, CA) at a 1:5 dilution, CEA Gold-5 (obtained from John E. Shively, PhD, City of Hope Beckman Institute, Duarte, CA) at a 1:1,500 dilution, and Melan A (Dako, Carpinteria, CA) at a 1:25 dilution with the procedure as described and appropriate controls.

Brown staining of the cell membrane, cytoplasm, or apical surface was considered positive.

Results

Staining Pattern

The CD10 immunohistochemical staining results for various neoplasms and normal tissue are summarized in

❚Table 2❚
Normal Tissue in Which CD10 Antigen Was Detected

Myoepithelial cells of breast and parotid glands
Apocrine metaplasia of breast tissue
Normal glandular apical surface of small and large intestines
Glomerular cells and proximal convoluted tubules of kidney
Apical surface of large prostate ducts
Apical surface of epididymal ducts
Endometrial stromal cells
Bone marrow stroma cells
Liver canaliculi
Lung alveolar epithelial cells

Tables 1 and 2. The cases with more than 5% tumor cells staining were considered positive.

Three CD10 staining patterns were observed: apical surface/luminal, cytoplasmic, and membranous/Golgi ❙**Image 1**❙. The *apical/luminal* staining pattern was observed on brush borders of small intestine, large intestine, proximal convoluted tubules of kidney, and in well to moderately differentiated adenocarcinomas of the colon, pancreas, and prostate. A layer of dark brown deposit was present at the apical surface or within the apical lumina of neoplastic glands (Image 1A). The diffuse *cytoplasmic* staining pattern was seen mainly in transitional cell carcinoma, poorly differentiated adenocarcinoma of various origins, melanoma, and sarcoma (Image 1B). A *membranous/Golgi*–staining pattern was seen in the majority cases of renal cell carcinoma (Images 1C and 1D).
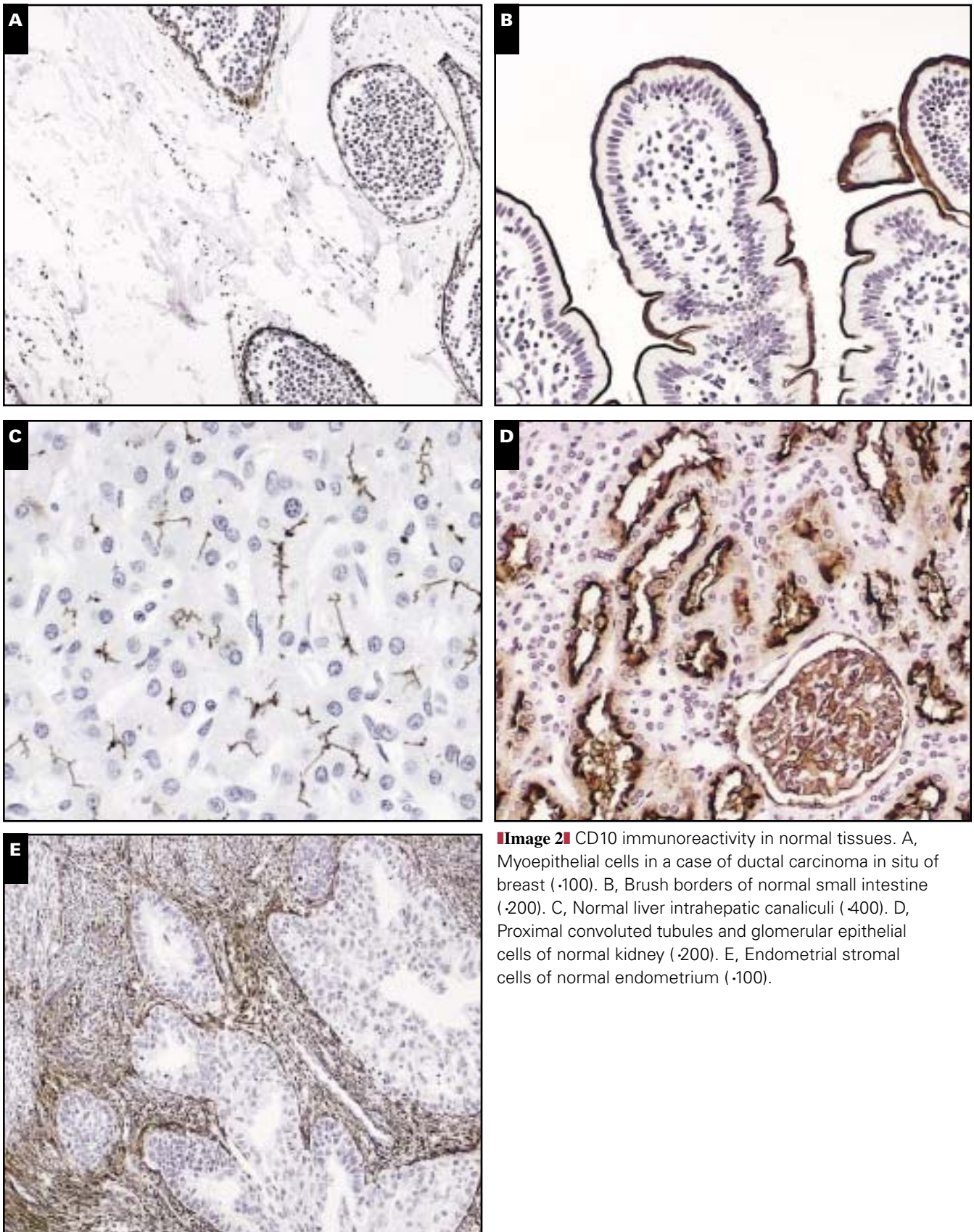
CD10 in Normal Tissue

In the breast, CD10 expression was seen in ductal and lobular myoepithelial cells of normal breast tissue, in situ adenocarcinoma ❙**Image 2A**❙, and apocrine metaplasia. In the gastrointestinal tract, CD10 positivity was seen on the brush borders of the small intestine epithelium ❙**Image 2B**❙ and the apical surface of large intestine epithelium. In the liver, CD10 positivity had a characteristic canalicular pattern similar to that of CEA Gold-5 staining ❙**Image 2C**❙. The hepatocytes and bile ductal epithelial cells, however, were negative. Positive CD10 staining was found in many organs of the genitourinary tract. It stained glomerular epithelial cells and proximal convoluted tubular epithelial cells of the kidney ❙**Image 2D**❙ and prostatic large ductal epithelial cells (apical surface). The endometrial stromal cells ❙**Image 2E**❙ and alveolar lining cells of the lung
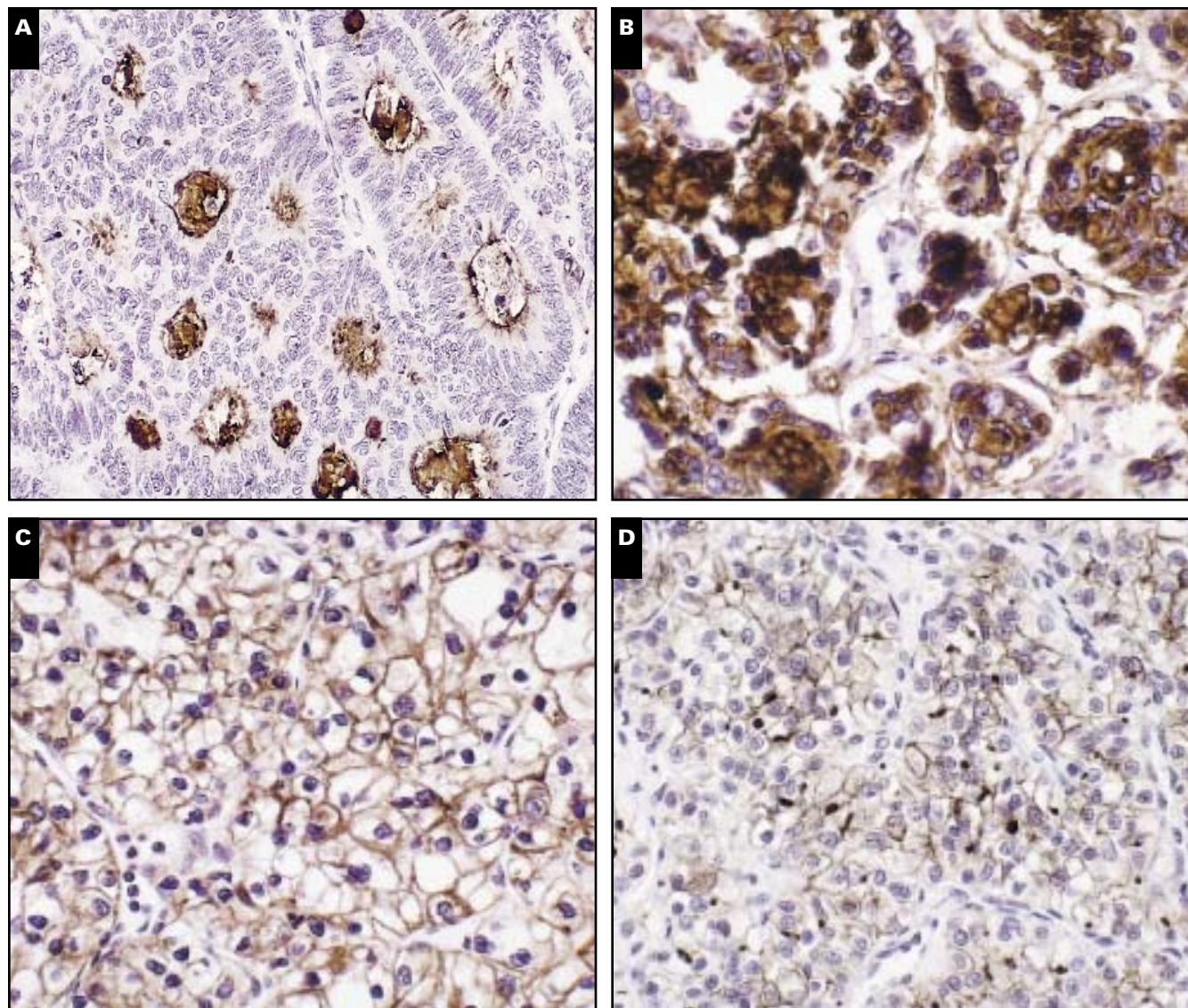
❙**Image 1**❙ Three main CD10 staining patterns. A, Strongly *apical* surface and *luminal* positivity in a case of well-differentiated colon adenocarcinoma (×200). B, *Cytoplasmic* positivity in a case of pancreatic adenocarcinoma (×400). C, *Membranous* positivity in a case of renal cell carcinoma (×400). D, *Membranous/Golgi* positivity in a case of renal cell carcinoma (×400).

❚Image 2❚ CD10 immunoreactivity in normal tissues. A, Myoepithelial cells in a case of ductal carcinoma in situ of breast (×100). B, Brush borders of normal small intestine (×200). C, Normal liver intrahepatic canaliculi (×400). D, Proximal convoluted tubules and glomerular epithelial cells of normal kidney (×200). E, Endometrial stromal cells of normal endometrium (×100).

were strongly CD10+. In the bone marrow, stromal cells were positive for CD10. The number of positive stromal cells and staining intensity varied from case to case.

CD10 in Carcinomas

CD10 immunoreactivity was detected mainly in neoplasms of the gastrointestinal and genitourinary tracts (Table 1).

In the gastrointestinal tract, 7 of 14 cases of pancreatic adenocarcinomas showed focal to diffuse CD10 positivity with apical and cytoplasmic staining patterns (Image 1B). Five of 20 cases of colonic adenocarcinoma were CD10+ with an apical and luminal staining pattern. The well-differentiated adenocarcinomas tended to have apical staining, whereas poorly differentiated adenocarcinomas had cytoplasmic staining. In some cases, the positive CD10 precipitate was accumulated in the lumen (Image 1A). In the liver, CD10 antibody characteristically stained the canaliculi between hepatocytes (6 of 7 positive cases; Image 2C). This staining pattern was seen in normal liver tissue and in hepatocellular carcinoma. Only 1 case of hepatocellular carcinoma showed strong cytoplasmic CD10 staining. All 13 cases of hepatocellular carcinoma showed a canalicular staining pattern for CEA-Gold 5 ▮**Table 3**▮. All 9 cases of gastric adenocarcinomas and 12 cases of cholangiocarcinoma were negative for CD10.

Forty-one of 46 cases of renal cell carcinoma were positive for CD10. The CD10 immunoreactivity was in a membranous or perinuclear Golgi zone pattern, regardless of tumor subtypes (Images 1C and 1D). The majority of cases had a predominantly membranous pattern (Image 1C), whereas a few cases showed a primarily Golgi or membranous/Golgi (Image 1D) pattern. Virtually all classic renal cell carcinomas (clear cytoplasm, alveolar architecture, and rich in microvessels) and papillary variants were CD10+ (41/44 [93%]). Sarcomatoid renal cell carcinomas (2 cases) were negative. None of 46 cases of renal cell carcinomas were positive for Melan A. In comparison, 6 of 10 cases of adrenocortical tumor were positive for Melan A, and none were CD10+ (Table 3). In the prostate, CD10 positivity delineated 2 groups of adenocarcinomas.

Prostatic adenocarcinomas composed of predominantly small glands tended to be CD10–, whereas the adenocarcinomas made up of large ducts with cribriform intraluminal configurations were (apical and cytoplasmic) CD10+. However, all cases of both types of prostatic carcinoma were positive for prostate-specific antigen. Thirteen of 24 cases of transitional cell carcinomas were CD10+ with a cytoplasmic pattern.

Outside the gastrointestinal and genitourinary tracts, rare cases of lung small cell carcinoma and adenocarcinoma, mesothelioma, ovarian adenocarcinoma, and lobular breast carcinoma were CD10+.

CD10 in Melanoma and Sarcomas

Approximately one third of malignant melanomas (12/30) showed cytoplasmic positivity for CD10 ▮**Image 3A**▮. The positive cases had a primarily epithelioid component, while spindle cell melanomas usually were CD10–.

All 5 cases of endometrial stromal sarcomas were CD10+ ▮**Image 3B**▮. The positive stain usually was strong cytoplasmic in spindled cells between the spiral arteriole-like vessels. Only 1 of 16 cases of leiomyosarcoma of various origins (including uterine cases) was CD10+. Four of 14 cases of epithelioid sarcoma showed cytoplasmic CD10 positivity. Among other types of sarcomas, most CD10+ cases were high-grade with pleomorphic features ▮**Image 3C**▮.

An immunostaining comparison of CD10 and CEA Gold-5 in 13 cases of hepatocellular carcinoma is given in Table 3, along with the comparison for CD10 and Melan A in 10 cases of adrenocortical carcinoma and 46 cases of renal cell carcinoma. Like most cases with CD10, CEA Gold-5 showed a canalicular staining pattern in hepatocellular carcinomas and normal hepatocytes. Melan A showed a diffuse cytoplasmic staining pattern.

Discussion

The common acute lymphoblastic leukemia antigen (CD10) initially was described as a tumor-specific antigen

▮**Table 3**▮
Immunohistochemical Comparison of CD10, Carcinoembryonic Antigen (CEA) Gold-5, and Melan A in Various Carcinomas[*]

Type of Carcinoma	CD10	CEA Gold-5	Melan A[†]
Hepatocellular (n = 13)	7 (54)‡	13 (100)	ND
Adrenocortical (n = 10)	0 (0)	ND	6 (60)
Renal cell (n = 46)	41 (89)	ND	0 (0)

ND, not done.
[*] Data are given as number (percentage) positive.
[†] Dako, Carpinteria, CA.
‡ Six of 7 cases demonstrated a canalicular pattern only, the pattern seen in all cases with CEA Gold-5.

found in acute lymphoblastic leukemia. Since its initial description by Greaves et al[8] in 1975, CD10 antigen has been found to be associated widely with precursor B-cell acute lymphoblastic leukemias,[9] T-cell acute lymphoblastic leukemias,[10,11] and various types of lymphoma, especially follicular lymphoma and Burkitt lymphoma.[12-14] In contrast with the hematopoietic neoplasms, CD10 expression in nonhematopoietic neoplasms was less well explored until recently. There are 2 main reasons: (1) Nonhematologic neoplasms usually are diagnosed via routine paraffin histologic examination, because frozen section immunophenotyping and flow cytometry, methods widely used in leukemia and lymphoma diagnoses, are used less commonly for nonhematopoietic neoplasms. (2) Commercially available CD10 antibodies did not work consistently on paraffin sections until very recently.

Early experiments have shown that some normal human tissues or cell lines express the CD10 antigen. Metzgar et al[15] detected CD10 expression in renal tubular and glomerular cells and epithelial cells of the small intestine. The CD10 antigen also was detected in myoepithelial cells of breast[15-17] and salivary gland,[15] cultured marrow stromal cells,[18] glandular epithelium of the prostate and epididymides,[19] alveolar lining cells of the lung,[20] amniotic membrane cells,[21] and first-trimester endometrial cells.[22] The present study confirms many of these previous findings.

An increased number of human nonhematopoietic neoplasms and cell lines were shown to express CD10 antigen in recent years. The low-level expression of CD10 by small cell carcinoma of the lung may regulate tumor cell proliferation.[23,24]

By using radioimmunoassay, Carrel et al[25] showed that 6 of 15 cultured melanoma cell lines expressed CD10 antigen. After studying a series of skin melanocytic lesions and 15 cases of ocular melanomas, Carrel et al[26] also found that 63% of ocular melanomas and 38% of cutaneous melanomas expressed CD10 antigen.
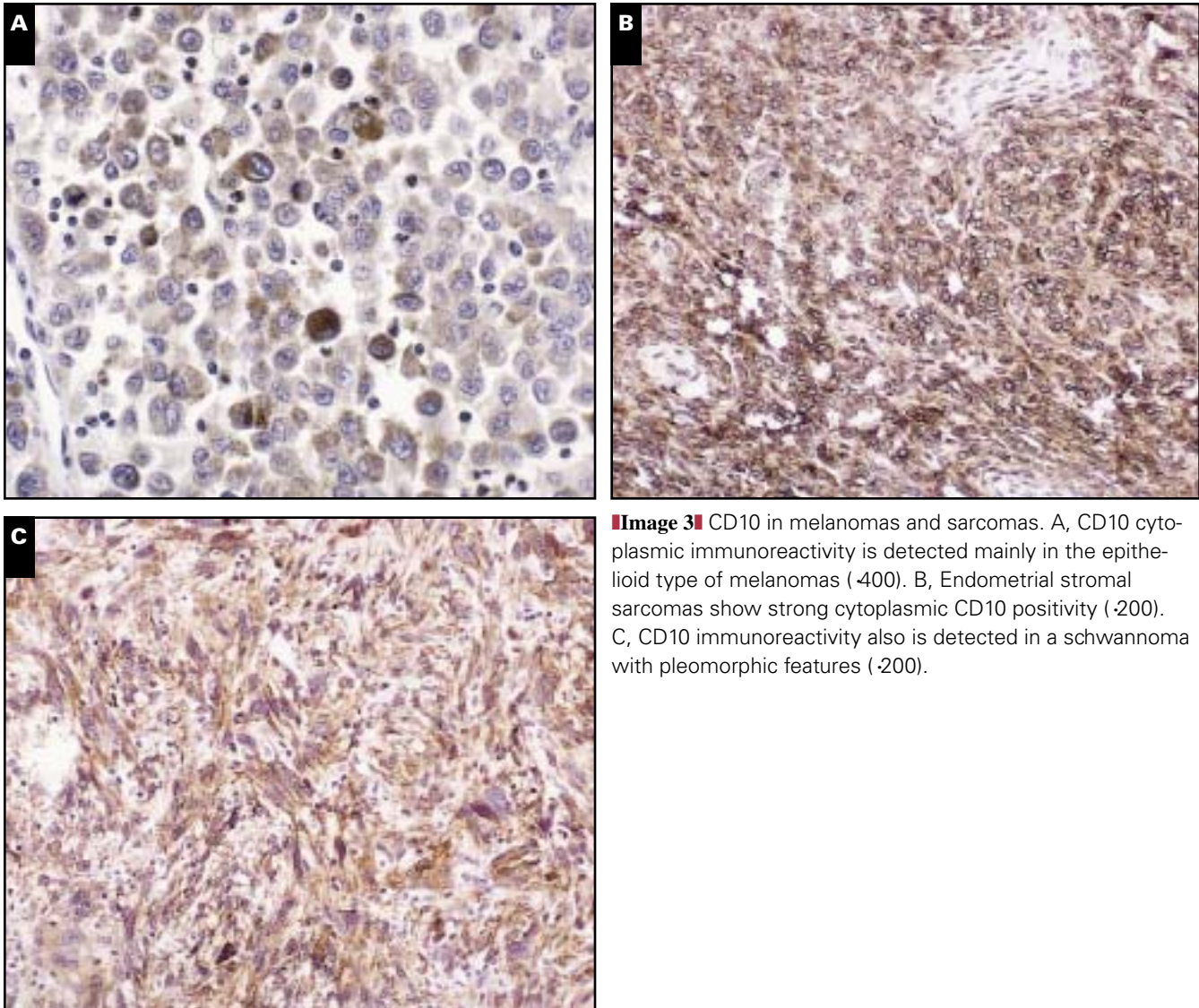
∎**Image 3**∎ CD10 in melanomas and sarcomas. A, CD10 cytoplasmic immunoreactivity is detected mainly in the epithelioid type of melanomas (×400). B, Endometrial stromal sarcomas show strong cytoplasmic CD10 positivity (×200). C, CD10 immunoreactivity also is detected in a schwannoma with pleomorphic features (×200).

In the colon, almost all well and moderately differentiated adenocarcinomas reported by Sato et al[27] tended to be positive for CD10 by Western blot analysis, whereas the expression level clearly was decreased in poorly differentiated adenocarcinomas. Dragovic et al[28] found that 14 of 18 hepatocellular carcinomas, but not normal hepatocytes, were CD10+. Furthermore, mediastinal germ cell tumors and cultured glioma cell lines also are reported to express the CD10 antigen.[29,30]

In the present study, we found a similar CD10+ rate in lung small cell carcinoma and extraocular melanomas. However, unlike Dragovic et al,[28] who found 78% of hepatocellular carcinomas were CD10+ by frozen section immunohistochemistry, we found that 7 of 13 cases of hepatocellular carcinomas were CD10+, only 1 of 7 positive cases showed cytoplasmic CD10 positivity, and the other 6 positive cases showed a canalicular staining pattern. We stained all 13 cases of hepatocellular carcinoma with CEA-Gold 5 in parallel with CD10 (Table 3). We found that the CD10 staining pattern in hepatocellular carcinomas was the same as that for CEA-Gold 5 in well to moderately differentiated hepatocellular carcinomas. However, in poorly differentiated hepatocellular carcinomas, CEA-Gold 5 usually was positive, whereas CD10 usually was negative. CEA Gold-5 has been described[31] and has a staining pattern similar to the commercially available polyclonal CEA antibodies.

We also observed a much lower CD10+ rate in gastric and colon adenocarcinomas in comparison with the reported CD10+ rate of 100% in 18 cases of well to moderately differentiated adenocarcinomas by Western blot analysis.[27] In fact, we found none of 9 cases of gastric carcinoma and only a quarter of the cases of colon adenocarcinoma to be CD10+. All 14 cases of germ cell tumors in the present series were CD10– as well.

The present study shows that many CD10+ neoplasms arise from tissues that normally express the CD10 antigen, with the exception of transitional cell carcinoma. During tumorigenesis, malignant cells still maintain certain functions and molecules of their predecessors, which is helpful for surgical pathology diagnosis.

Functionally, CD10 is a cell surface enzyme that reduces cellular response to peptide hormones by regulating local peptide concentrations.[32,33] In hematopoietic cells, CD10 functions as a regulator of B-cell development.[34] In nonhematologic tissue and neoplasms, the expression of CD10 has a close relationship to the secretory process and genitourinary tract.[19] Previous studies suggested that CD10 reduces the cellular responses to peptide hormones and regulates peptide-mediated cellular proliferation.[23,35] It has been postulated that the function of CD10 in the kidney may be to cleave peptides, such as bradykinin and angiotensin, that function in renal autoregulation in the maintenance of water and sodium metabolism.[19] However, the functional role of CD10 in the

gastrointestinal tract is unknown. The secretory activities of the pancreas and small and large intestines are regulated largely by endocrine and paracrine hormones. As in the kidney, CD10 also may regulate the hormonal effects on enterocytes. Other organs with secretory functions, such as the breast, stomach, and salivary gland, are CD10–. The CD10 pattern of reactivity suggests that CD10 is involved in the secretory process with strong Golgi, apical, and luminal positivity in many carcinomas arising from these organs, especially the well and moderately differentiated cases.

Of particular interest is that many neoplasms from the genitourinary tract are CD10+. CD10 positivity has been shown in various normal male genital tract cell types and fluids,[19] including the epithelial lining and in the lumen of the prostate and epididymis ducts, and in seminal fluid. Based on CD10 positivity, prostatic adenocarcinomas may be divided into those with small glands (CD10–), and those with medium-sized and cribriform glands (CD10+). In both cases, tumor cells are positive for prostate-specific antigen.

The characteristic membranous/Golgi–staining pattern of renal cell carcinoma has not, to our knowledge, been reported previously. The unique staining pattern was observed in classic clear renal cell carcinomas and in other variants. Both low and high nuclear grade renal cell carcinomas expressed the CD10 antigen. The typical apical surface positivity seen in other adenocarcinomas, such as those of the colon, pancreas, and prostate, was not seen in renal cell carcinoma. In normal kidney tissue, the brush border of proximal convoluted tubules is strongly CD10+.[15] This further supports the long-held impression that most renal cell carcinomas arise from proximal convoluted tubules[36,37] but not distal convoluted tubules.

The differential diagnosis of renal cell carcinomas from other neoplasms usually is not a problem. The difficulties arise primarily when tumors are not the classic type (papillary, oncocytic, or collecting duct types) or are metastatic. Although all cases of renal cell carcinomas in the present study were primary tumors, metastatic renal cell carcinomas would be expected to have a similar CD10 staining pattern. However, more studies should be done to confirm this assumption.

In the differential diagnosis of renal cell carcinoma vs adrenocortical carcinoma, CD10 immunohistochemistry may be extremely helpful. All 10 cases of adrenocortical carcinoma were CD10–, whereas 41 (89%) of 46 cases of renal cell carcinoma were CD10+. A study by Busam et al[38] showed that all 34 cases of adrenocortical tumors were positive for Melan A, including 5 cases of adenoma, 16 cases of primary adrenocortical carcinoma, and 13 cases of metastatic adrenocortical carcinoma, whereas all 14 cases of renal cell carcinoma of the clear cell type were negative for Melan A. We found only 6 (60%) of 10 cases of adrenocortical carcinomas were positive for Melan A (Table 3). All 46 cases of renal cell carcinoma were negative with this antibody. Since Melan A and CD10

stain adrenocortical tumors and renal cell carcinomas, respectively, without cross-reactivity, the combined use of these 2 markers may be useful for the differential diagnosis of these tumor types.

All 5 cases of endometrial stromal sarcoma, as well as normal endometrial stroma, were CD10+. The CD10 positivity was cytoplasmic and varied from focally positive to diffuse strongly positive. In contrast, 15 of 16 cases of leiomyosarcoma (including uterine cases) were CD10–. Endometrial stromal sarcoma typically consists of oval to spindled cells with numerous small vessels resembling spiral arterioles. A metastatic endometrial stromal sarcoma may lack this characteristic vasculature, making diagnosis more difficult. These endometrial stromal sarcomas may be confused with smooth muscle tumors, synovial sarcomas, gastrointestinal stromal sarcomas, and fibrosarcomas. These other tumors usually were CD10– (Table 1). This observation indicates that CD10 may be a useful marker for the differential diagnosis of these sarcomas.

Some pediatric small cell sarcomas, such as Wilms tumor, Ewing sarcoma, rhabdomyosarcoma, and neuroblastoma, are reportedly CD10+ by frozen section immunohistochemistry using a different CD10 antibody.[39] We found frequent CD10 expression (3 of 5 cases) in rhabdomyosarcoma, but the number of small round cell tumors in the present study is too small for further comment. More studies should be done with this new CD10 antibody to show its histologic distribution in different pediatric small cell sarcomas.

Although usually negative in breast carcinoma, CD10 expression by myoepithelial cells was demonstrated consistently in the present study, indicating that this antibody may be used as an alternative marker (other than smooth muscle actin and collagen, type IV) for the diagnosis of invasive vs in situ breast carcinoma.

The CD10 antigen is expressed in a variety of nonhematopoietic tumors. The relatively broad range of CD10 reactivity limits its usefulness. However, in paraffin sections, it may be most useful for the differential diagnosis of renal cell carcinoma vs adrenocortical carcinoma and for differentiating endometrial stromal sarcoma from other sarcomas, because renal cell carcinoma and endometrial stromal sarcoma lack specific markers. In addition, other markers always should be applied in combination with CD10. For example, for the differential diagnosis of adrenocortical carcinoma vs renal cell carcinoma, an antibody panel that includes CD10 and Melan A may be useful. The use of CD10 for differentiating invasive vs in situ carcinoma of the breast and for the differential diagnosis of hepatocellular carcinoma vs nonhepatocellular carcinoma warrants further study.

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