

原発巣 ← CK7/CK20 + α

EVALUATION OF METASTATIC TUMOR BY IMMUNOHISTOCHEMICAL ANALYSIS TO DETERMINE PRIMARY SITE^a

Cytokeratin (CK)	Initial Antibody Panel	Additional Antibodies ^b	Likely Primary Tumor
CK7+/CK20-	OCT4, pankeratin (OSCAR), CD117, SALL4, PLAP ^c	CD30 (embryonal), AFP and glypican-3 (yolk sac), EMA (negative)	Germ cell tumor
	WT1, ER, PAX8 TTF1, thyroglobulin	Calcitonin (medullary), chromogranin A (medullary)	Ovarian carcinoma, nonmucinous Thyroid carcinoma
	ER, PAX8, p53 (serous)	p63 (adenosquamous), CK5/6 (adenosquamous), p16 (classic - patchy, weak; serous - diffuse, strong)	Endometrial carcinoma
	P16 (strong, diffuse), HR-HPV (in situ), m-CEA, vimentin (usually negative) ER, PR, GATA3 SMAD4/DPC4 (negative), p63, CK17 CDX2	Mammaglobin, GCDFP-1 CDX2, mesothelin and MUC5, PAX8 (pan-neuroendocrine) HepPar (hepatoid-), arginase-1 (hepatoid)	Breast carcinoma Pancreaticobiliary carcinoma (most cases) Upper GI carcinoma/ pancreaticobiliary carcinoma (minority)
	TTF1, napsin	MOC31, BerEp4	Lung adenocarcinoma
CK7-/CK20+	Synaptophysin, chromogranin A, CK20 (dot-like)	CD56, NSE, CM2B4 (anti-Merkel cell polyoma virus T antigen)	Merkel cell carcinoma
	CDX2 CDX2	Villin, SATB2 HepPar (hepatoid), arginase-1 (hepatoid)	Colorectal carcinoma Gastric carcinoma (minority)
CK7+/CK20+	CK5/6, p63, p40	Uroplakin III, GATA3, PAX8, thrombomodulin	Urothelial carcinoma
	PAX8, villin DPC4/SMAD4 (negative), p63, CK17 CDX2	CDX2, mesothelin and MUC5 HepPar (hepatoid), arginase-1 (hepatoid)	Ovarian/appendiceal mucinous carcinoma Pancreaticobiliary carcinoma (minority) Gastric carcinoma (minority)
CK7-/CK20-	HepPar, arginase 1, glypican-3 PSA, p501s	CEA-poly, CD10, TTF1 (cytoplasmic) PSAP, NKX3.1, androgen receptor, AMACR	Hepatocellular carcinoma Prostate carcinoma
	PAX8, CD10, vimentin Synaptophysin, chromogranin P63, p40	CK18, PAX2 CD56, NSE	Renal cell carcinoma Neuroendocrine carcinoma
	P63, p40 calretinin, melan-A, inhibin, SF-1	CK5/6, CK14	Squamous cell carcinoma Adrenocortical carcinoma

^aThis Table summarizes the common immunophenotypic findings in metastatic tumor sites beginning by using anticytokeratin (CK) 7 and 20 antibodies. The Table is not intended to be comprehensive, and individual tumors may vary from the patterns described.

^bThe initial antibody panel is composed of antibodies the authors believe are most helpful in the first round of immunohistochemical studies. The additional antibodies listed are also helpful, but may be better used at a later stage, based on the initial antibody results. This order of antibody use is only a suggestion and other sequences and combinations of the antibodies listed, as well as other antibodies not included in the Table, are equally valid.

^cPLAP = placental alkaline phosphatase; AFP = alpha-fetoprotein; EMA = epithelial membrane antigen; HR-HPV = high-risk human papillomavirus; CEA = carcinoembryonic antigen; ER = estrogen receptor; PR = progesterone receptor; GCDFP = gross cystic disease fluid protein; NSE = neuron-specific esterase; GI = gastrointestinal; PSA = prostate-specific antigen; PSAP = prostate-specific acid phosphatase; SF-1 = steroidogenic factor (adrenal 4-binding protein); TTF = thyroid transcription factor.

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SMALL CELL TUMORS: DIFFERENTIAL DIAGNOSIS AND IMMUNOHISTOCHEMISTRY

Tumor	Initial Antibodies	Additional Antibodies/Studies
Poorly differentiated carcinoma	Pancytokeratin (CK)	(See Table 67-1)
Neuroendocrine carcinoma	CK, synaptophysin, chromogranin	CD56, CK20 (dot-like positivity)
Neuroblastoma	Neurofilament protein (NF), NB84, ALK1	
Ewing sarcoma/PNET ^a	CD99, FLI1	Genetic analysis
Rhabdomyosarcoma, small cell	Desmin, myogenin, MyoD	Genetic analysis
Wilms tumor	CK, CD56, WT1	Desmin (blastema), genetic analysis
Desmoplastic small round cell tumor	WT1, CK	Genetic analysis
Liposarcoma, small round cell	S-100 protein	
Small cell lymphoma	CD3, CD20, cyclin D1, BCL6	BCL2, CD5, CD23; Genetic analysis, flow cytometry
Lymphoblastic lymphoma	TdT, CD3 (T cell), PAX5 (B cell)	CD34, CD19; flow cytometry, genetic analysis
Myeloid sarcoma	Myeloperoxidase, CD68, CD117, lysozyme	CD11c, CD34, CD43, flow cytometry, genetic analysis

^aPNET = peripheral neuroectodermal tumor.

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EPITHELIOID TUMORS: DIFFERENTIAL DIAGNOSIS AND IMMUNOHISTOCHEMISTRY

Tumor	Initial Antibodies	Additional Antibodies
Carcinoma	Pancytokeratin	(See Table 67-1)
Melanoma	S-100, SOX10, HMB-45, melan A	Tyrosinase, MITF
Seminoma	OCT4, SALL4	CK, CD117, PLAP
Myeloid sarcoma	Myeloperoxidase, CD68, CD117, lysozyme	CD11c, CD34, CD43, flow cytometry, genetic analysis
Large cell lymphoma	CD3 (T cell), CD20 (B cell)	CD2 and CD5 (T cell), CD22 and CD79a (B cell), CD30, CD45/LCA
Plasmacytoma	CD138, kappa/lambda, MUM1/IRF4	CD38, VS38, BLIMP1
Epithelioid sarcoma	CK, INI1 (loss)	CD34, genetic analysis
Epithelioid angiosarcoma	CD31, CD34, ERG, FLI1	Thrombomodulin, CK, factor VIII antigen
Epithelioid fibrosarcoma	MUC4, CK (focal, weak)	
Epithelioid leiomyosarcoma	SMA ^a , desmin	
Perivascular epithelioid cell tumor (PEComa)	Desmin, HMB-45	

^aSMA = smooth muscle actin; MITF = microphthalmia-associated transcription factor; PLAP = placental alkaline phosphatase.

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ANAPLASTIC TUMORS: DIFFERENTIAL DIAGNOSIS AND IMMUNOHISTOCHEMISTRY

Tumor	Initial Antibodies	Additional Antibodies
Anaplastic carcinoma	Pancytokeratin (CK)	(See Table 67-1)
Nasopharyngeal carcinoma	CK, EBV ^a (in situ)	
Melanoma	S-100, SOX10, HMB-45, melan A	
Angiosarcoma	CD34, ERG, WT1, FLI1	CD31, factor VIII antigen
Leiomyosarcoma	Desmin, SMA	
Malignant fibrous histiocytoma		
Embryonal rhabdomyosarcoma	Desmin, MyoD1, myogenin	
Osteosarcoma	SATB2	
Malignant epithelioid hemangioendothelioma	CD34, factor VIII antigen, ERG	
Seminoma	OCT4, SALL4	CK, CD117, PLAP
Anaplastic large cell lymphoma	CD30	ALK, CD2, CD4, CD43, cytotoxic antigens
Classic Hodgkin lymphoma	CD15, CD30, CD45 (negative), PAX5 (weak)	EBV (in situ; subset of cases)
Follicular dendritic cell sarcoma	CD21, CD23, CD35, clusterin	Fascin, D2-40/podoplanin, EGFR
Interdigitating dendritic cell sarcoma	S100, CD68, CD163	
Histiocytic sarcoma	CD68, CD163, CD11c	CD4, lysozyme

^aEBV = Epstein-Barr virus; SMA = smooth muscle actin; SATB2 = special AT-rich sequence binding protein 2; ALK = anaplastic lymphoma kinase; EGFR = epidermal growth factor receptor.

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SPINDLE CELL TUMORS: DIFFERENTIAL DIAGNOSIS AND IMMUNOHISTOCHEMISTRY

Tumor	Initial Antibodies	Additional Antibodies
Sarcomatoid carcinoma	Pancytokeratin (CK)	(See Table 67-1)
Melanoma	SOX10, HMB-45, melan A, S-100 (often negative)	MITF ^a
Kaposi sarcoma	CD34, ERG, HHV-8	CD31, factor VIII-related antigen
Follicular dendritic cell sarcoma	CD21, CD23, CD35, clusterin	Fascin, D2-40/podoplanin, EGFR
Sarcoma	S-100, CD34, CD117, desmin, SMA	
Non-Hodgkin lymphomas with fibrosis	CD3 (T cell), CD20 (B cell), CD45/LCA	CD2 and CD5 (T-cell), CD22 and CD79a (B cell), CD30
Nodular sclerosis Hodgkin lymphoma	CD15, CD30, CD45 (negative), PAX5 (weak)	EBV (in situ; subset of cases)

^aMITF = microphthalmia-associated transcription factor; HHV = human herpesvirus; SMA = smooth muscle actin; EGFR = epidermal growth factor receptor; EBV = Epstein-Barr virus.

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HEMATOPOIETIC-ASSOCIATED MARKERS THAT MAY BE EXPRESSED
IN NONHEMATOPOIETIC TUMORS AND NORMAL TISSUES^a

Hematopoietic Marker	Other Tissues and Tumors	Notes
CD5	Thymoma, thymic epithelium	Expressed in about 10% of non-hematopoietic tumors.
CD7	Subset of carcinomas and melanoma	Expressed in about 20% of non-hematopoietic tumors
CD10	Large variety of tumors and tissue types	
CD15	Broad range of carcinomas	
CD20	Thymoma	B cells intermixed with epithelial cells that often have asteroid/dendritic features; also can focally highlight epithelial cells
CD30	Embryonal carcinoma, other carcinomas, some yolk sac tumors, rare mesotheliomas, rare sarcomas	
CD43	Mesothelioma, adrenocortical carcinoma, lung carcinoma	
CD56 (NCAM)	Neuroendocrine tumors, CNS ^b tumors, neural crest-derived cells, adrenocortical tumors, thyroid tumors, variety of sarcomas	
CD138	Large variety of tumor and tissue types	~60% of carcinomas are positive
ALK	Inflammatory myofibroblastic tumors, rhabdomyosarcoma, lipogenic tumors, Ewing/PNET, leiomyosarcoma, lung adenocarcinoma (small subset)	
BCL2	Large variety of tumors and tissue types	
BCL6	Bronchial epithelium, some lung tumors, squamous cell carcinoma, urothelial carcinoma	
Cyclin D1	Wide variety of proliferating epithelial and mesenchymal tissues	Endothelial cells in lymph nodes are positive and serve as internal control
MUM1/IRF4	Melanoma	
PAX5	Merkel cell carcinoma, alveolar rhabdomyosarcoma	Small cell carcinoma of lung usually negative
TdT	Merkel cell carcinoma, small cell carcinoma	Reactivity can be bright and uniform (similar to lymphoblastic lymphoma)

^aThis Table is a general summary of antigens commonly used in the diagnosis of hematopoietic tumors that also may be positive in nonhematopoietic tumors and normal tissues. The Table is not intended to be comprehensive.

^bCNS = central nervous system; PNET = peripheral neuroectodermal tumor.



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**TUMORS OF THE
LYMPH NODES AND SPLEEN**

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