The Panel Approach to Diagnostics

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Cell Marque

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About Cell Marque:

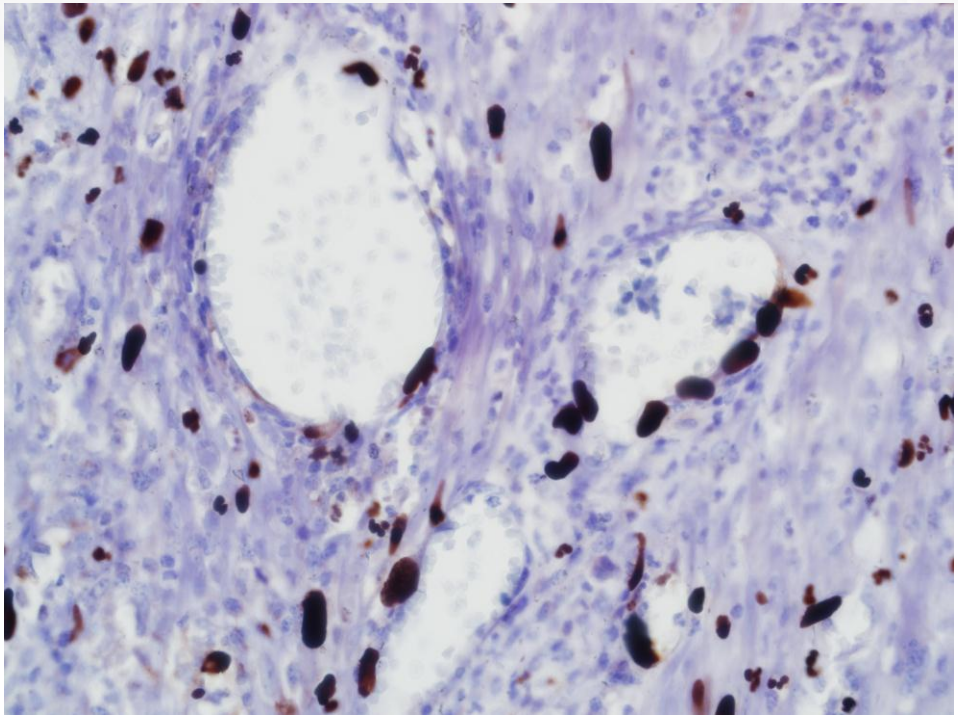
- IVD primary antibody manufacturer
- Distributors in 50+ countries
- 60+ Employees
- 2 pathologists on Staff
- Staff of primarily Biologists
- All employees trained on the science of IHC
- Focus on education, and increasing the diagnostic power of the pathologist

What is immunohistochemistry?

Immuno	• Immunology: branch of science dealing with the immune system
Histo	• Histology: branch of biology dealing with the study of organic tissues
Chemistry	• The science of the composition, structure, properties and reactions of matter

Definition of Immunohistochemistry:

Using a microscope to localize specific antigens in tissues by staining them with antibodies labeled with pigmented material.

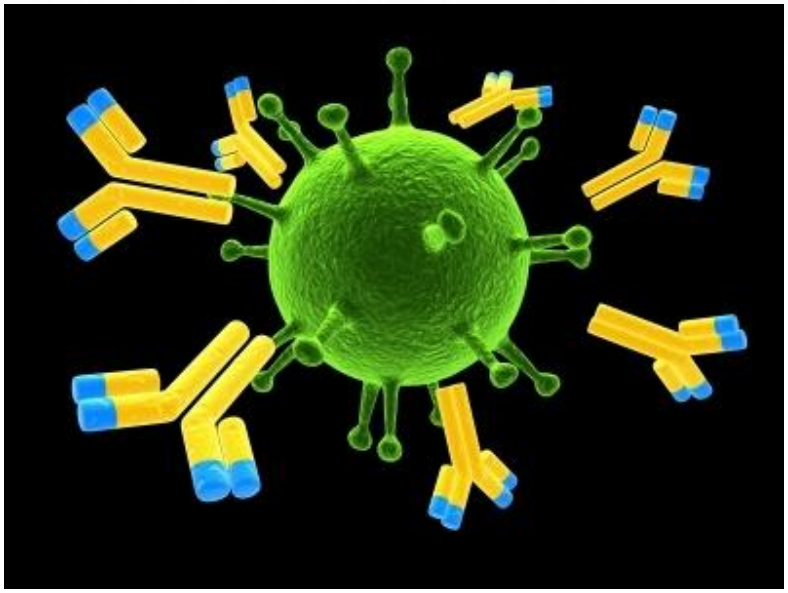


Importance of IHC

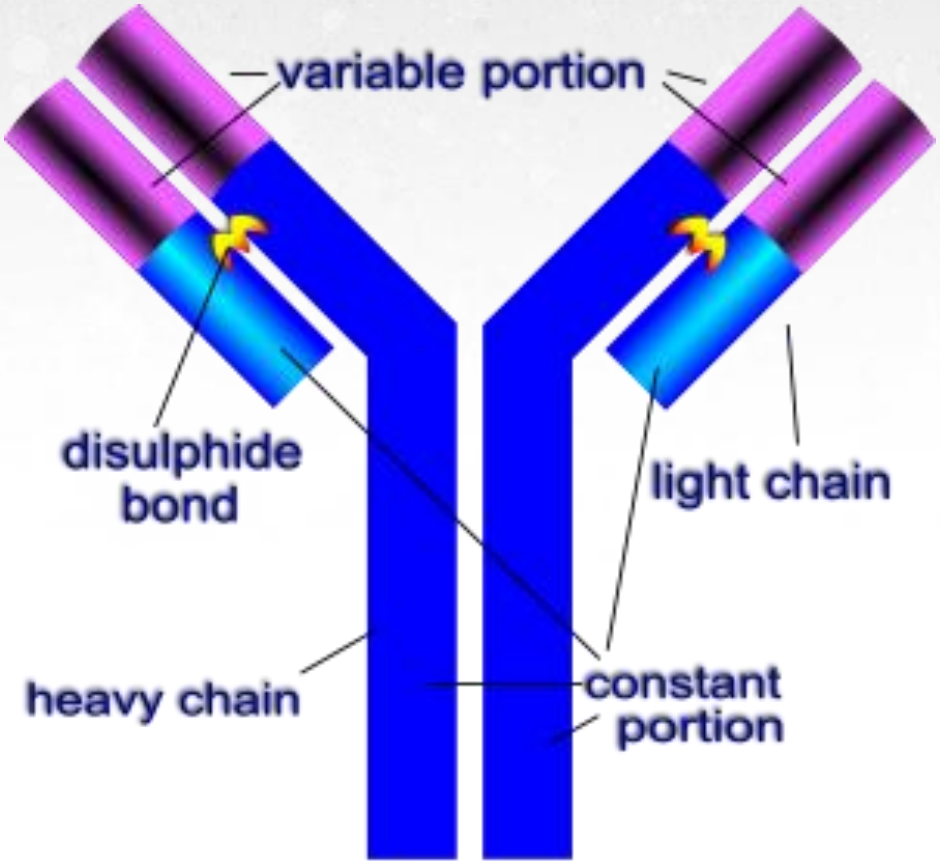
- Allows for visualization of proteins under a microscope
- Provides a diagnostic and prognostic tool for pathologists
- Detects infectious agents

What is an antibody?

Antibodies are proteins used by the immune system to identify and neutralize foreign objects.

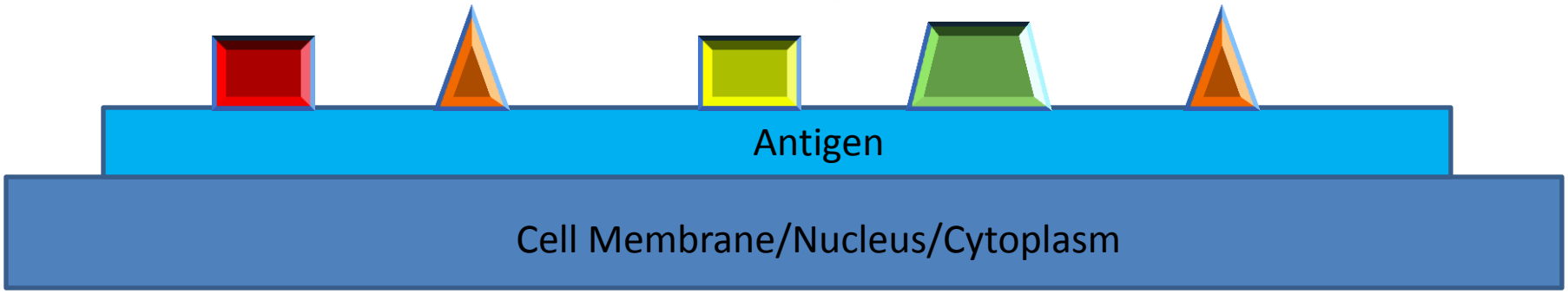


Antibody Structure



Antigens

- Antigen: a molecule that stimulates an immune response
- Epitope: three dimensional surface features found on an antigen molecule



What is a Panel?

Panels are diagnostic algorithms used to immunophenotype specific types of tumors and neoplasms.

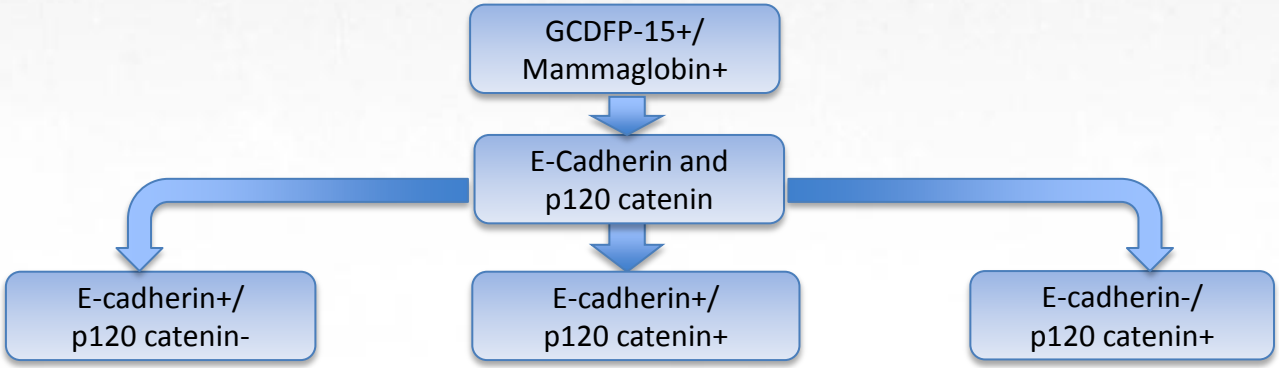
Immunophenotype

Flow Chart

Grids

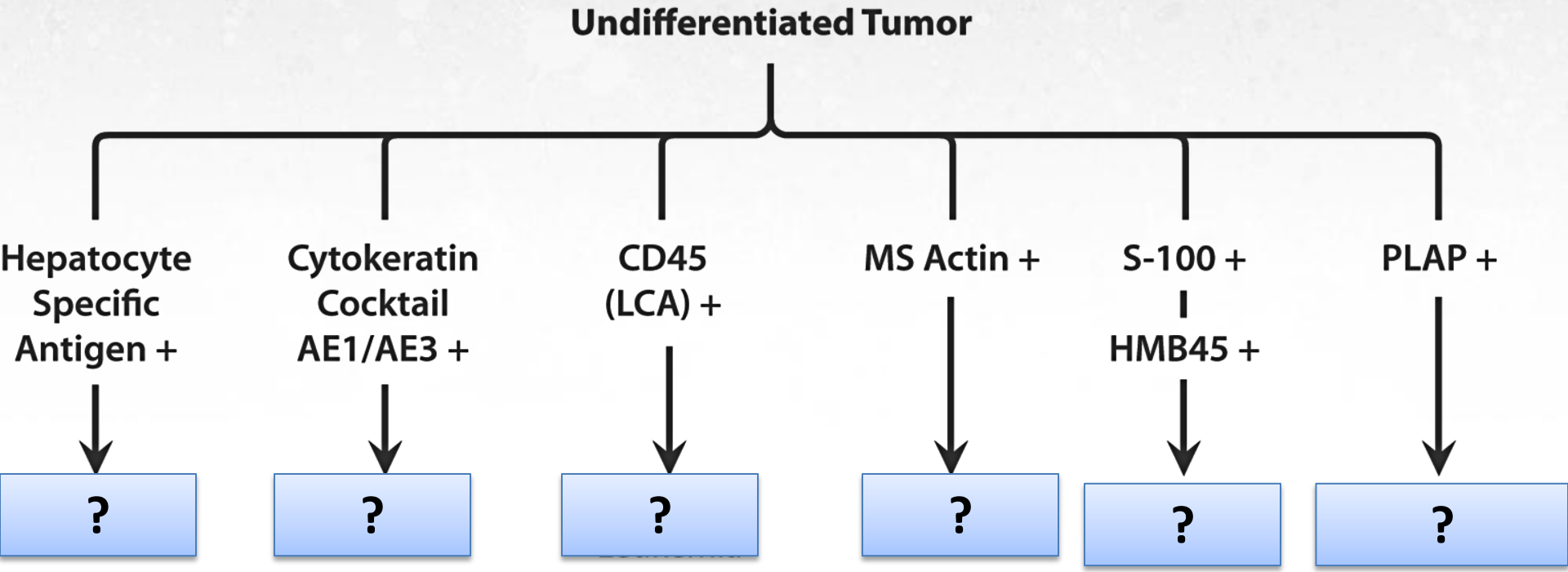
Panel Types

GCDFP15+	Mammaglobin+	E-Cadherin -	P120 Catenin -



Breast Lesion						
	GCDFP-15	Mammaglobin	B-catenin	E-Cadherin	CK, 34betaE12	p120
Lobular	+	+	-	-	+	+ (cytoplasmic)
Ductal	+	+	+ (membranous)	+	-	+ (membranous)

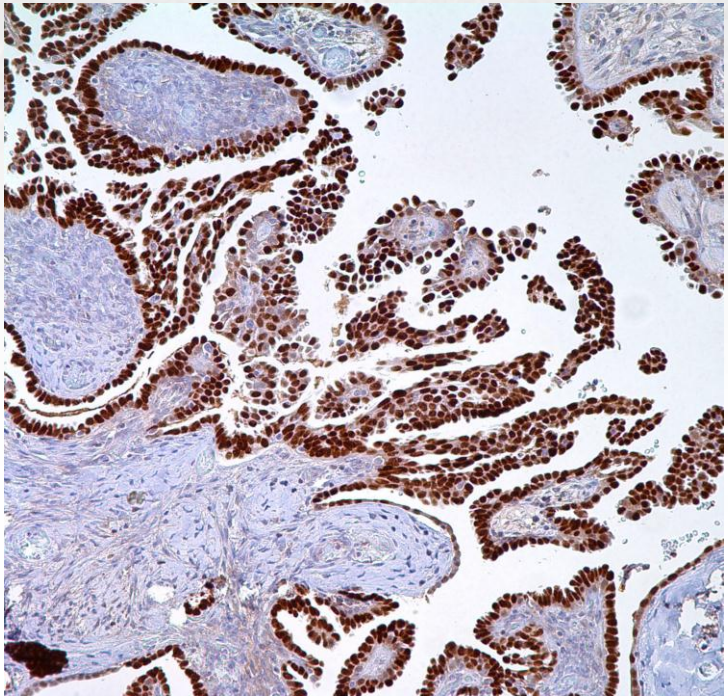
Undifferentiated Tumor Panel



Novel Markers:

Completing the Panel

PAX-8



Pax 8 on ovarian ca

- Clone: MRQ-50
- Visualization: Nuclear
- Ovarian Carcinoma (high sensitivity for serous ca)
- Thyroid transcription factor
- Kidney metastasis sensitivity over 85%
- Multiple applications
- USCAP 2010, IAP 2010

Thyroid Carcinomas

	Thyroglobulin	Calcitonin	CK 19	Galectin-3	TTF-1	HBME-1	PAX 8
Papillary Carcinoma	+	-	+	+	+	+	+
Follicular Carcinoma	+	-	-	-	+	-	+
Medullary Carcinoma	-	+	+	-	+	+	+
Benign Thyroid	+	-	-	-	+	-	+

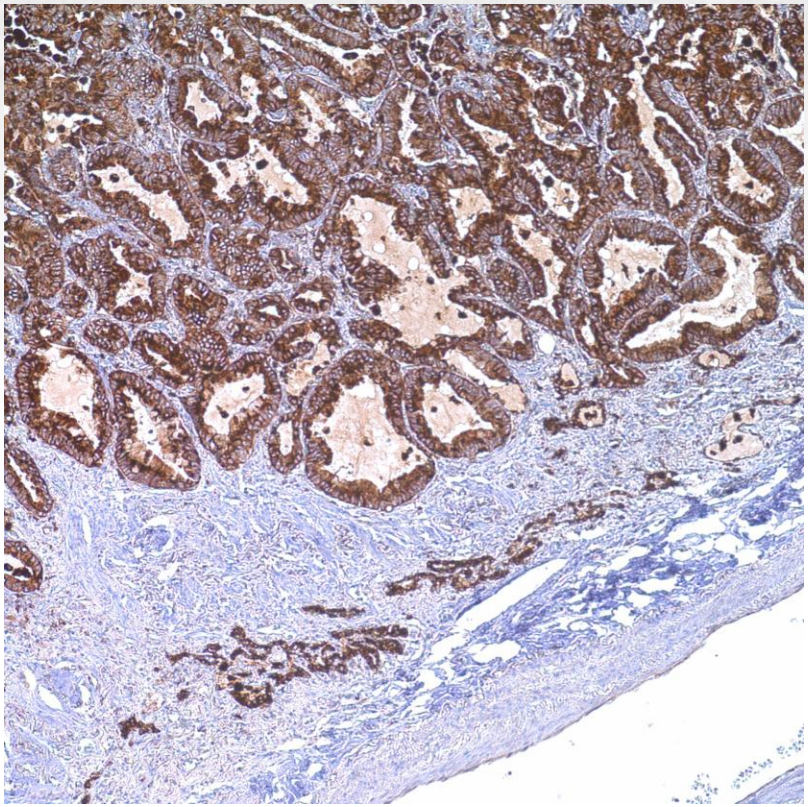
Ovarian Carcinoma

	PAX8	WT1	CA-125	CEA
Ovarian CA, Serous	**+**	+	+	+
Ovarian CA, Mucinous	**-**	-	-	-
Ovarian endometrioid CA	**+**	-	+	-
Ovarian Clear Cell Carcinoma	**+**	-	+	-

Kidney

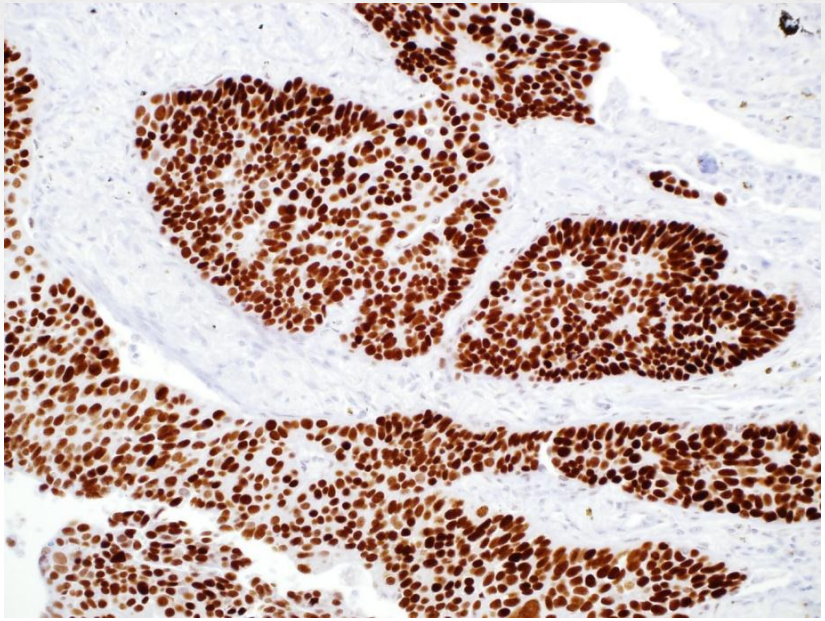
	RCC	CD10	PAX-2	**PAX-8**	Ksp-Cadherin	Ep-CAM	Caveolin-1
Clear cell	+	+	+	**+**	-	-	-
Chromophobe	-	-	-	**+**	+	+	+
Oncocytoma	-	-	-	**+**	+	-	-

Napsin A



- Clone: Polyclonal
- Visualization: Cytoplasmic
- Lung adenocarcinoma
- Multiple panel applications
- Higher sensitivity and specificity compared to TTF-1
- USCAP 2010, IAP 2010

SOX-2



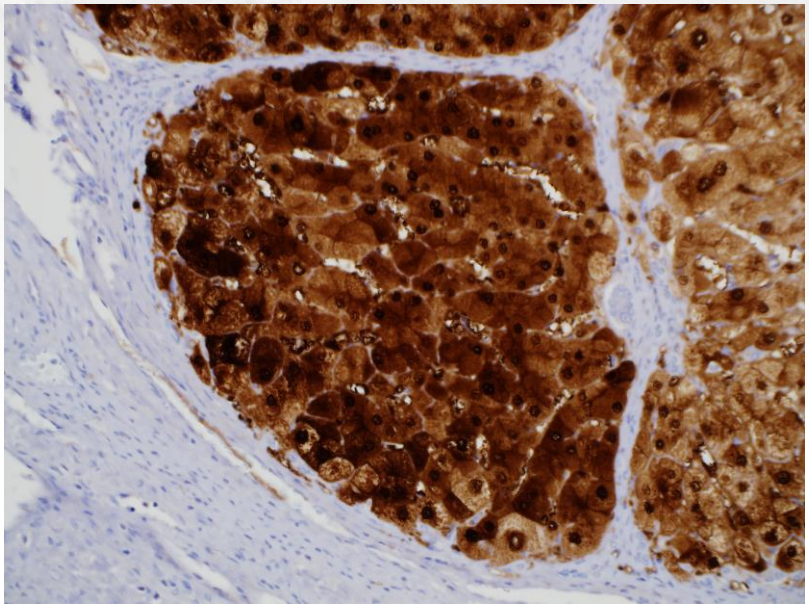
SOX-2 on Lung Squamous Cell Carcinoma

- Clone: SP76
- Visualization: Nuclear
- Rabbit Monoclonal
- Differentiates lung squamous cell carcinoma from lung adenocarcinoma
- Distinguishes embryonal carcinoma from other germ cell tumors
- Useful in the identification of astrocytomas
- Important for general pathologists and GU pathologists

Lung Adenocarcinoma vs. Squamous Cell Carcinoma

Napsin A +	TTF-1 +	CK 5/14 -	Sox-2 -	Well Differentiated Lung Adenocarcinoma
Napsin A +	TTF-1 -	CK 5/14 -	Sox-2 -	Poorly Differentiated Lung Adenocarcinoma
Napsin A -	TTF-1 +	CK 5/14 -	Sox-2 -/+	Neuroendocrine Tumor (verify w/NE marker)
Napsin A -	TTF-1 -	CK 5/14 +	Sox-2 +	Squamous Cell Carcinoma

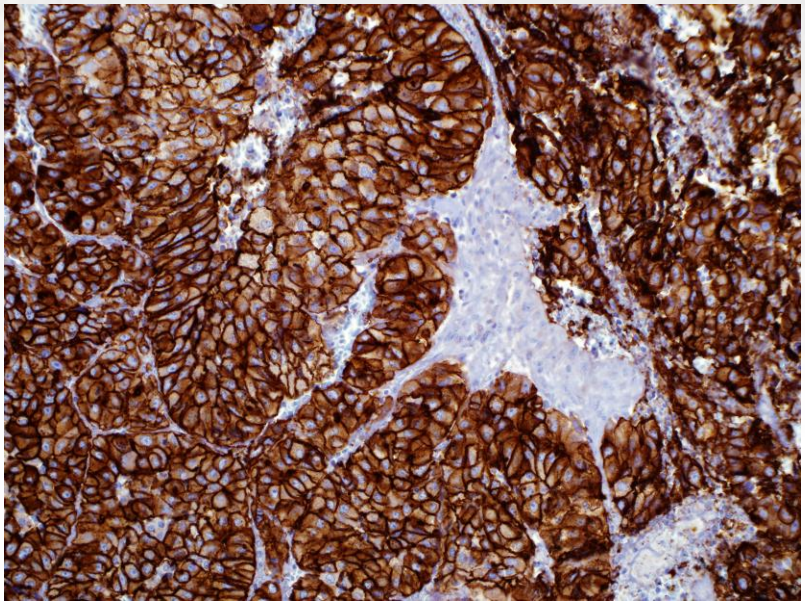
Arginase-1



Arginase 1 on cirrhotic liver

- Clone: SP156
- Visualization: cytoplasmic and nuclear
- High sensitivity for HCC
- Useful for HCC but also stains hepatic adenoma and cirrhotic liver
- Used in combination with Glypican 3 and HepPar-1 to distinguish benign from malignant

Glypican-3



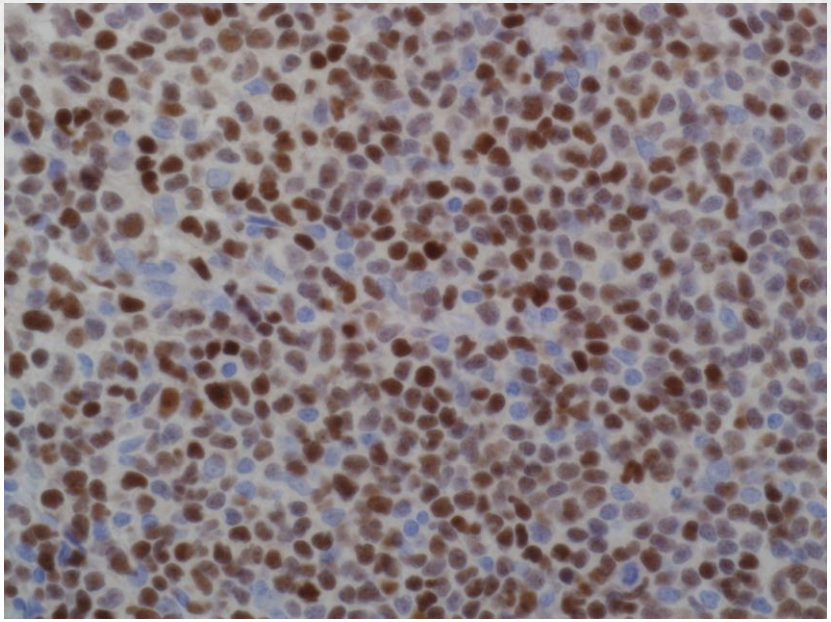
Glypican-3 on HCC

- Clone: 1G12
- Visualization: Cytoplasmic
- Differentiates benign liver from hepatocellular ca
- Also useful in identifying choriocarcinoma and yolk sac tumor
- Benign vs. malignant marker
- Unique to Cell Marque

Liver Neoplasms

	Arginase-1	Hep Par-1	Glypican-3	CD10	pCEA
Hepatic Adenoma	+	+	-	+	+
Hepatocellular Carcinoma	+	+	+	+	+
Metastatic Adenocarcinoma	-	-	-	-/+	-/+

Sox-11



Sox-11 on Mantle Cell Lymphoma

- Clone: MRQ-58
- Visualization: Nuclear
- Positive in 93-100% of all cyclin D1+ Mantle Cell Lymphomas and 100% of cyclin D1- MCL
- Also useful in defining pathological features of CD5+DLBCL(-)
- Stains Burkitt's and Lymphoblastic lymphoma that cyclin D1 does not

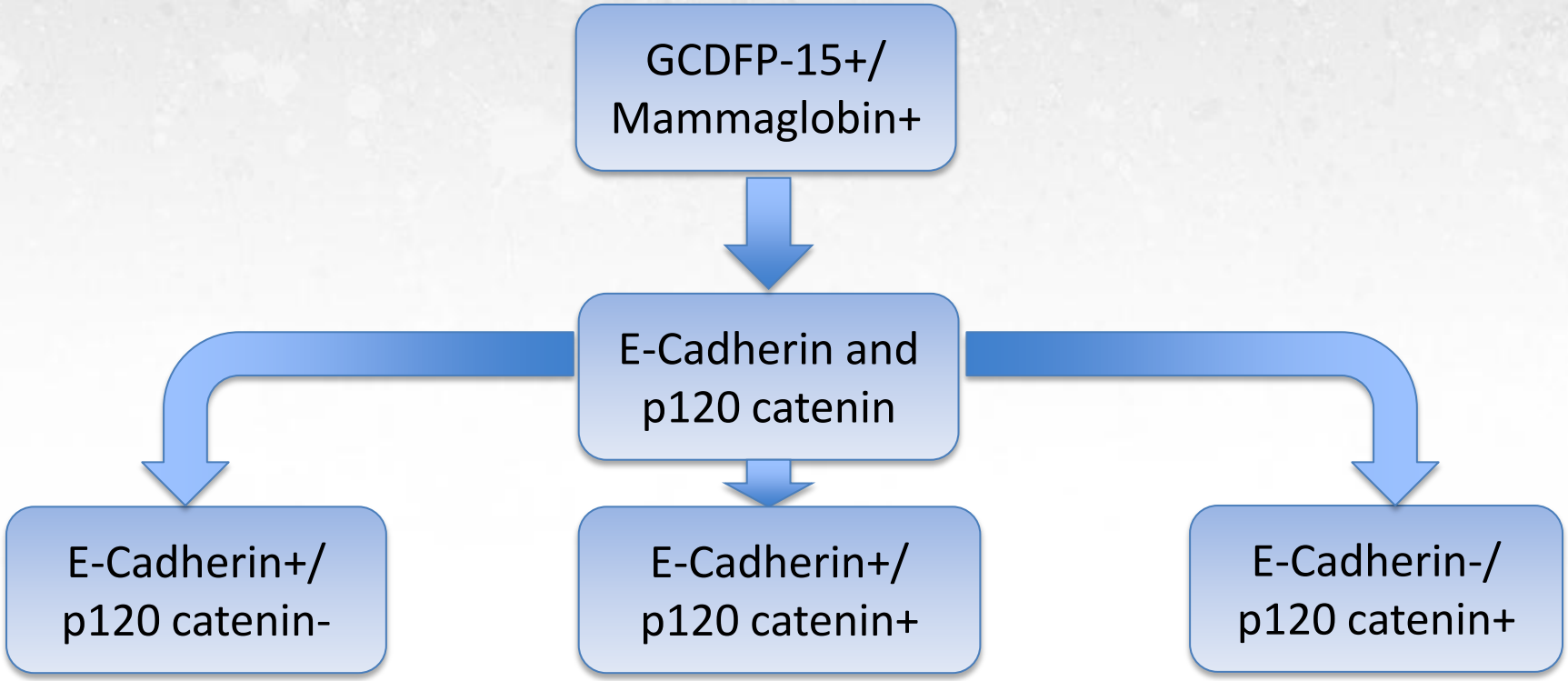
Hematolymphoid Neoplasm

	Sox-11	CD20	CD5	CD10	CD23	Cyclin D1
MCL	+	+	+	-	-	+
FL	-	+	-	+	-	-
SLL/CLL	-	+	+	-	+	-
MZL	-	+	-	-	-	-
LBL	+	+	-	+/-	-	-
BL	-/+	+	-	-	-	-
CD5+ DLBCL	-	+	+	+	-	-
Blastoid Variant MCL	+	+	+	-	-	+

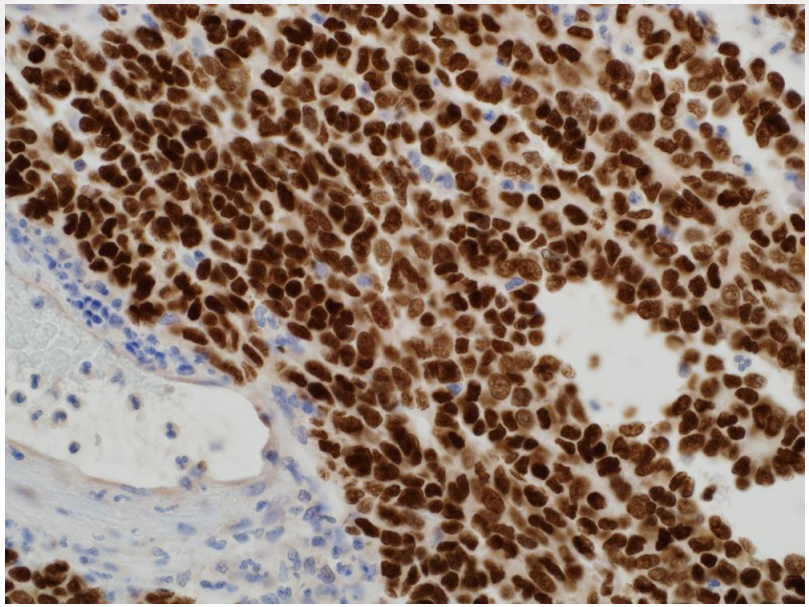
E-Cadherin/p120 Catenin Dual Stain

E-cadherin-DAB, p120 catenin-Red

Breast Carcinoma



SOX-10



SOX-10 on Melanoma

- Clone: Polyclonal
- Visualization: Nuclear
- Sensitive marker for melanoma (including conventional, spindle cell and desmoplastic subtypes)
- Superior to other immunostains in detecting residual invasive and in situ melanoma
- Useful in detecting in situ and invasive components of desmoplastic melanoma
- Antibody unique to CM

Cutaneous Lesion

	SOX-10	CK Cocktail	HMB-45	S-100	MART-1 (Melan A)
Conventional Melanoma	+	-/+	+	+	+
Desmoplastic Melanoma	+	-	-	+/-	-
Squamous Cell Carcinoma	-	+	-	-/+	-
Basal Cell Carcinoma	-	+	-	-	-
Merkel Cell Carcinoma	-	-/+	-	-/+	-

Why are panels important?

- Increase the number of diagnostic tools for the pathologists
- See a macroview of the disease state
- Faster turn around time
- No single antibody is 100% sensitive and specific
- More specific diagnosis leads to more specific treatment

Questions?