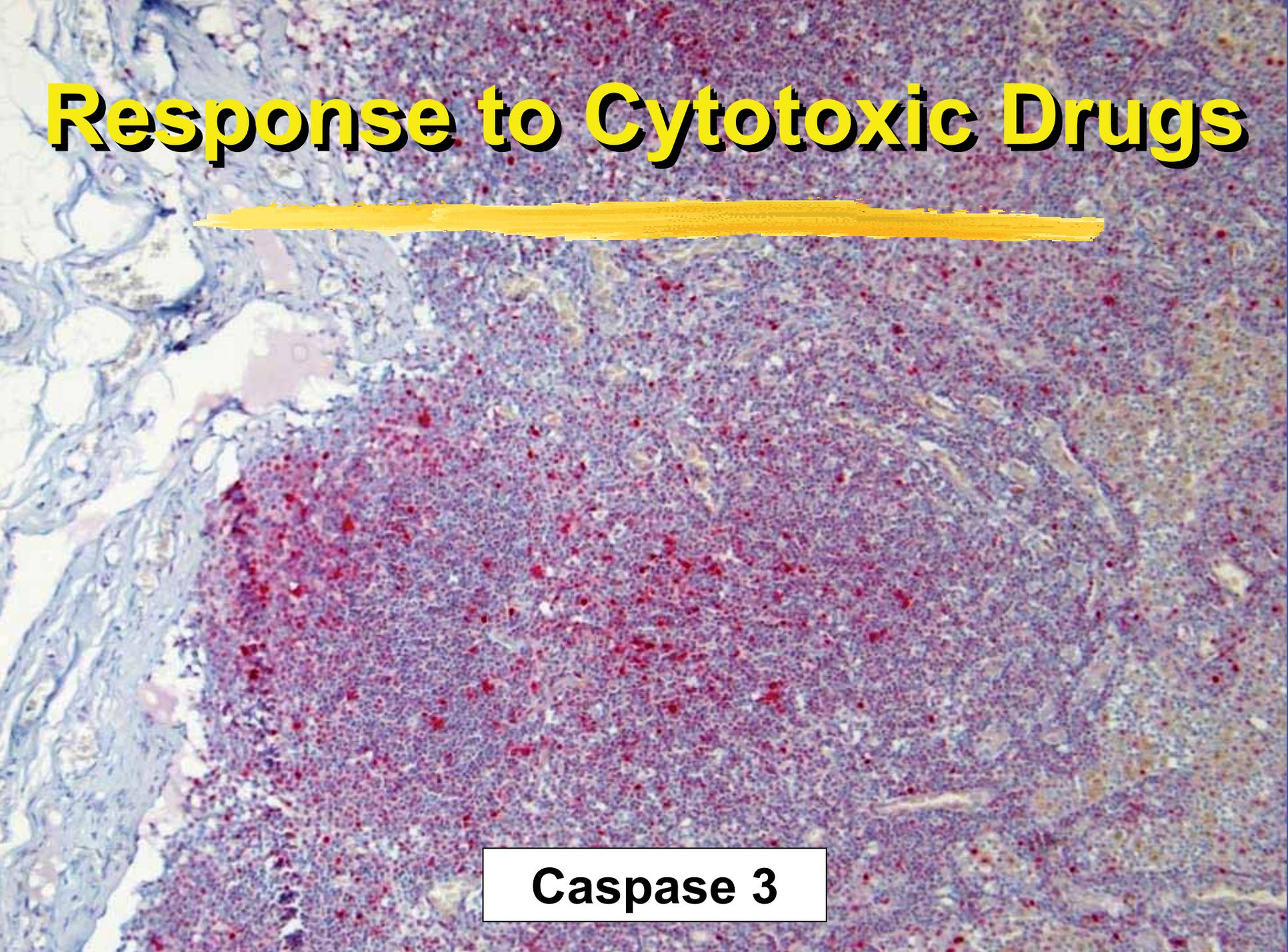
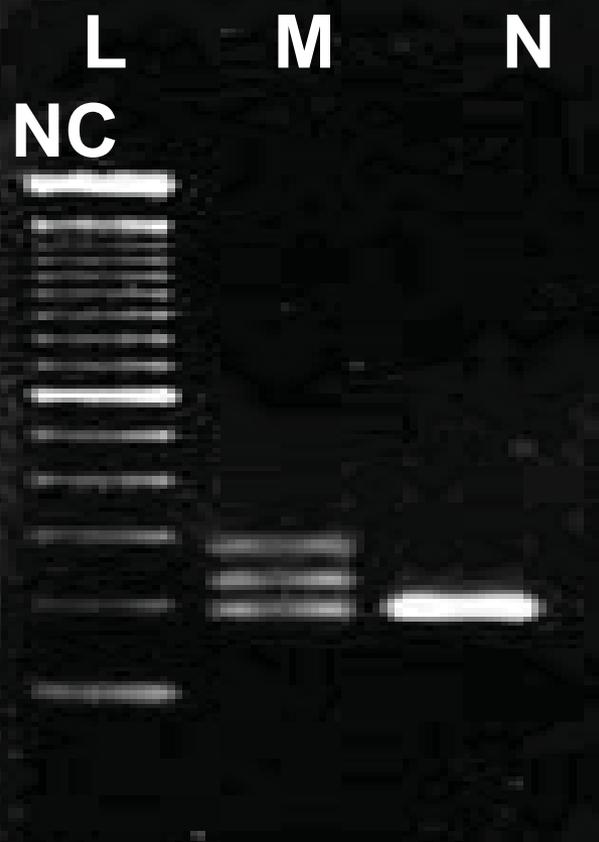


Response to Cytotoxic Drugs

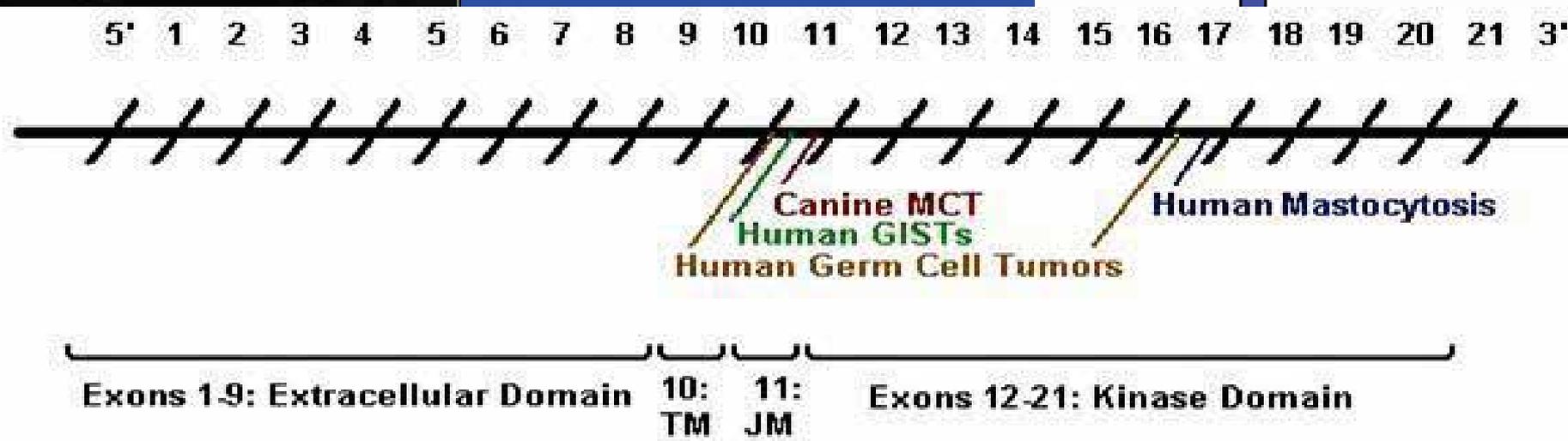
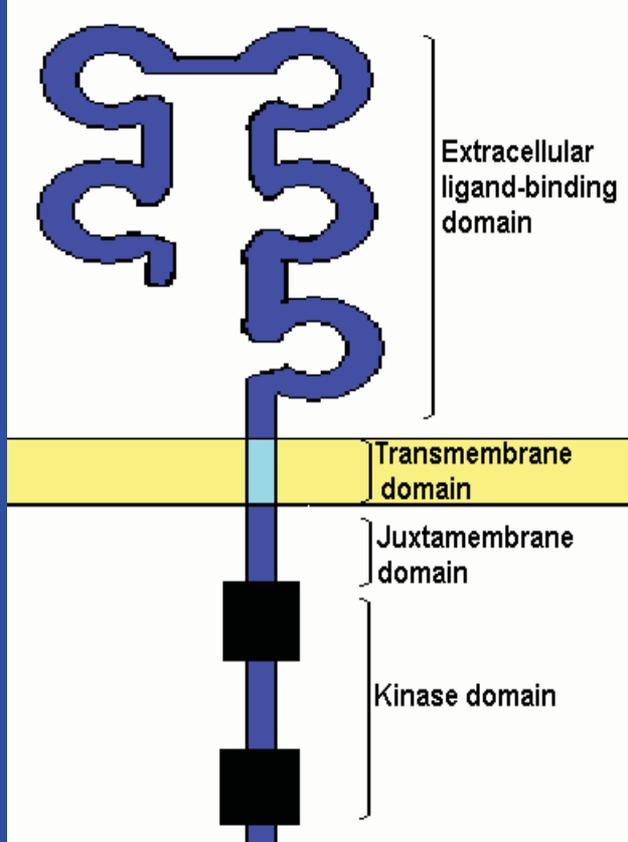
A histological slide showing tissue response to cytotoxic drugs. The image displays a dense field of cells with a prominent red coloration, likely indicating the presence of caspase 3. A yellow brushstroke underline is positioned below the title. The background is a light blue/purple hue, characteristic of hematoxylin counterstain.

Caspase 3

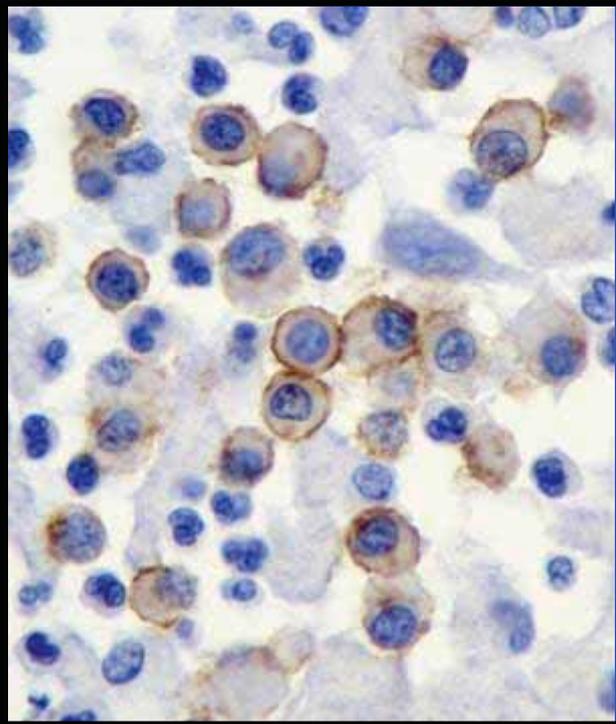


c-kit Mutations

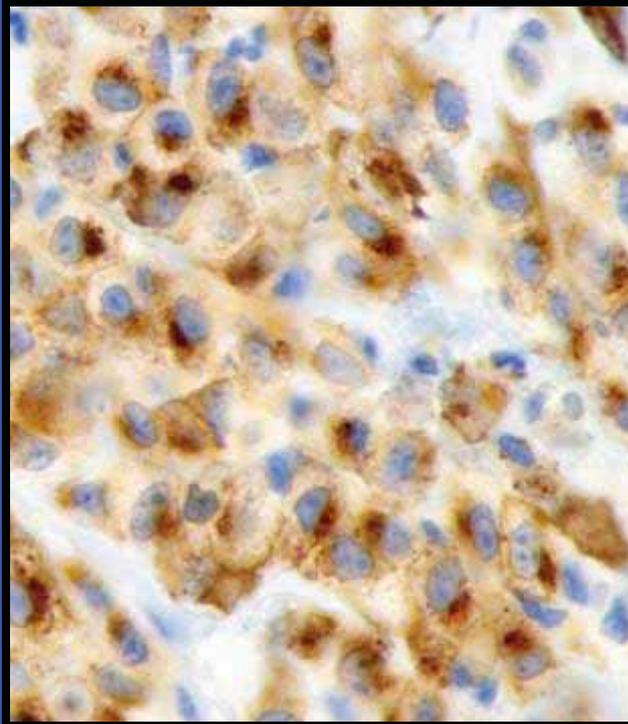
- Internal tandem duplications
 - Prevalence: 15-20% of MCTs
 - Associated with poor survival



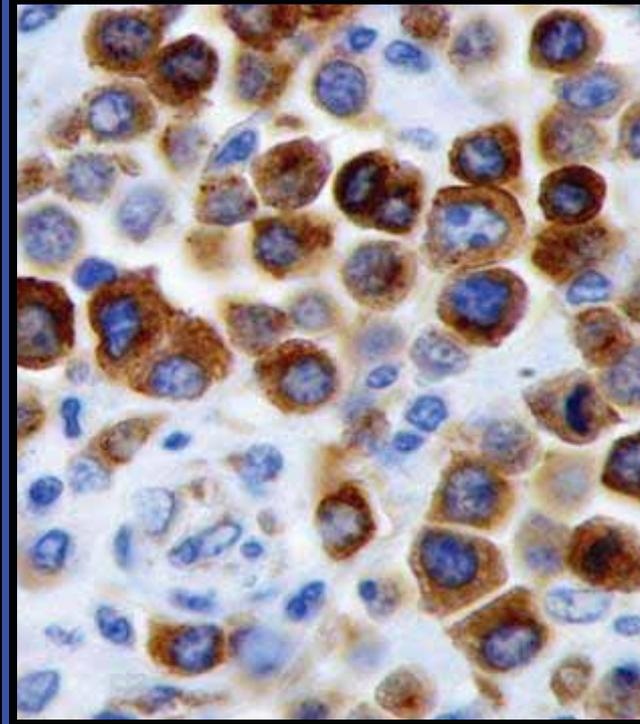
KIT Staining Patterns



**KIT Staining
Pattern 1**



**KIT Staining
Pattern 2**

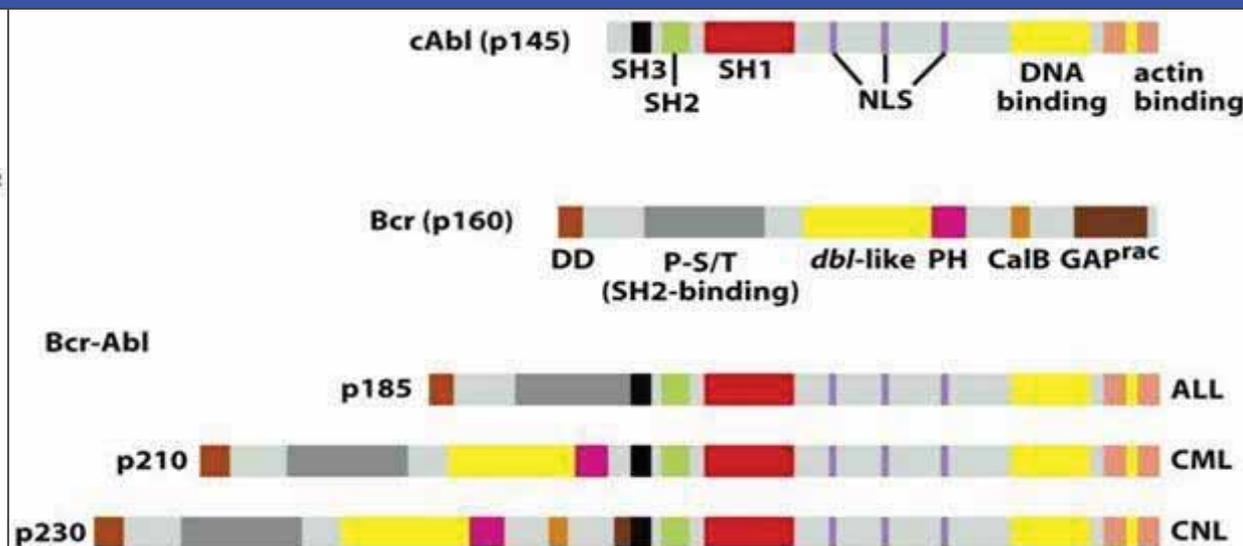
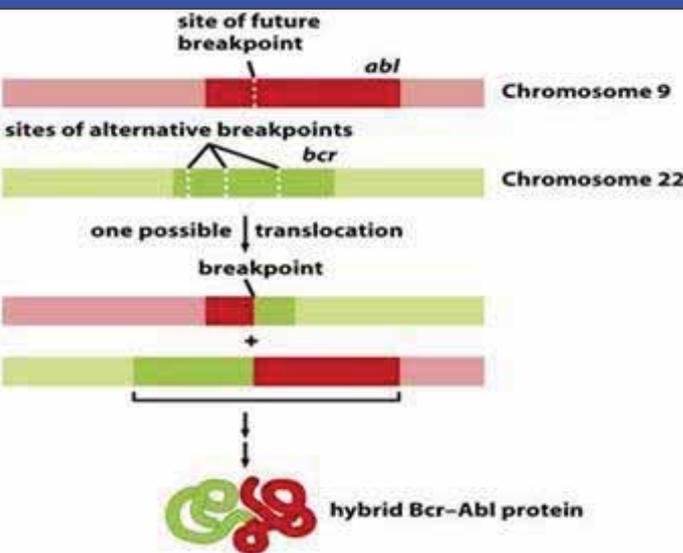


**KIT Staining
Pattern 3**

(Kiupel et. al., The Use of KIT and Tryptase Expression Patterns as Prognostic Tools for Canine Cutaneous Mast Cell Tumors. Vet Pathol 2004)

***bcr-abl* Translocations Producing a Fusion Protein**

- *abl* gene (Abelson murine leukemia virus), rapidly tumorigenic retrovirus, maps to chromosome 9q34
- Fused with sequences clustered at 22q11, called breakpoint cluster region = *bcr* (both are multidomain, multifunctional proteins)
- Identified in 95% of Chronic myelogenous leukemia (CML)
- Expression of *bcr/abl* gene driven by *bcr* gene promoter, produced transcript represents a chimera consisting of 5' portion of *bcr* gene, and 3' portion of *c-abl*
- *bcr/abl* protein expresses enhanced tyrosine kinase signaling activity compared to the normal ABL protein (gain of function)



Molecular Clonality - Indications

- **Morphological, cytological, immuno-phenotypic properties inconclusive**
 - **Lack of architectural effacement in organized lymphoid tissue - MZL or TZL**
 - **Lympho-histiocytic proliferations in skin**
 - **Lamina proprial or intra-epithelial lymphocytosis in the small intestine**

Feline TCRG V-N-J alignment CDR3 region

Moore et al., Vet Immunol Immunopathol 106: 167-178, 2005

PCR $\xrightarrow{\text{5' primer}}$

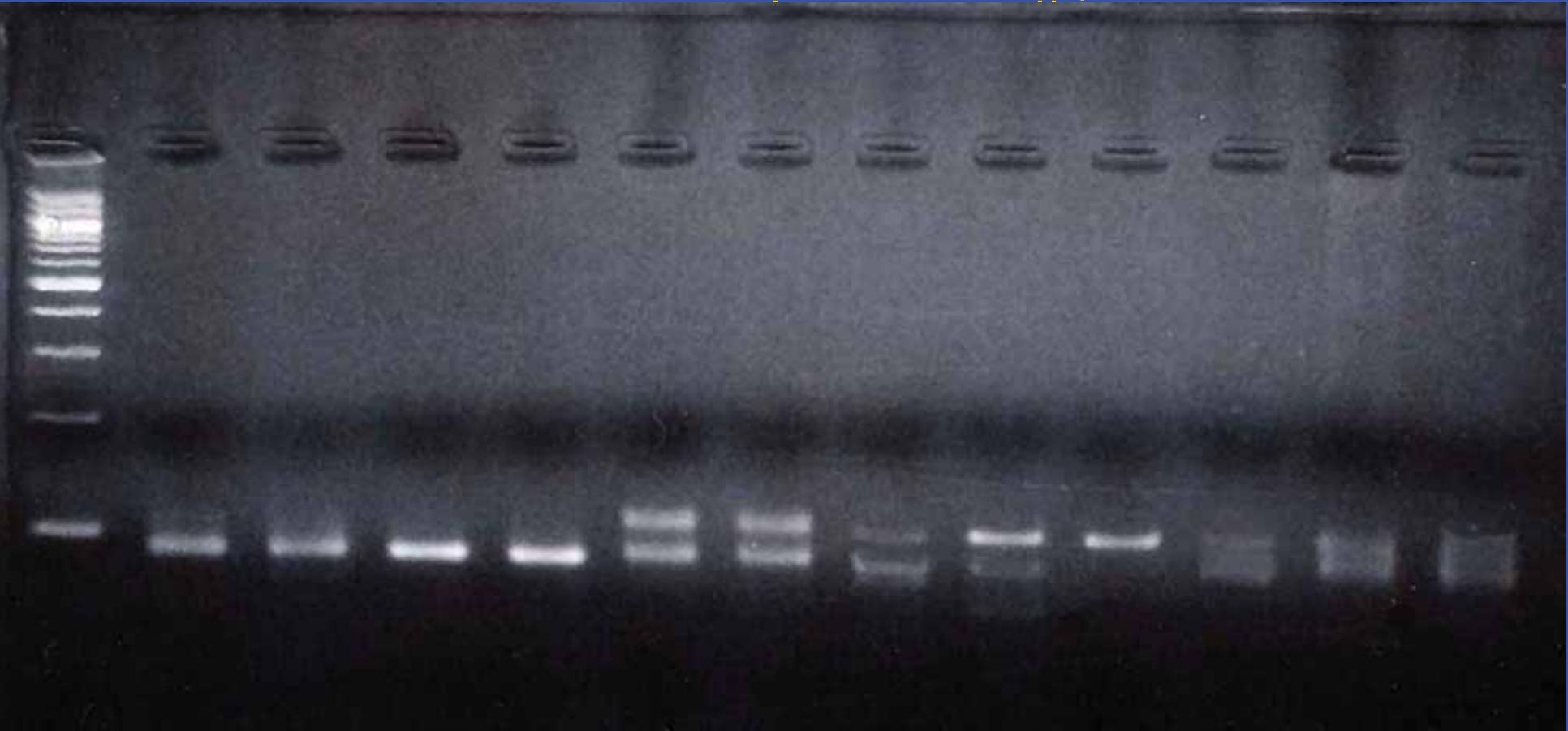
$\xleftarrow{\text{3' primer}}$

	118	128	138	148	158
(H-81)	K L Q K S D E G V Y Y C A A W E A	S - - - - -	L I T Y	G W A H K V F G P G T L L R V T	
(H-82)	K L Q K S D E G V Y Y C A A W E A	S - - - - -	L I T H	G W A H K V F G P G T L L R V T	
(H-83)	K L Q K S D E D V Y Y C A A W E F	- - - - -	- - - - -	R G W A H K V F G P G T L F R V T	
(H-84)	K L Q K S D E G V Y Y C A A W E A	R G T - - - - -	F G Y	G W A H K V F G P G T L L R V T	
(H-85)	K L Q K S D E G V Y Y C A A Y D - - - - -	- - - - -	- - - - -	- W A H K V F G P G T L L R V T	
(H-86)	K L Q K S D E G V Y Y C A A W E A	R G T - - - - -	F G Y	G W A H K V F G P G T L L R V T	
SFL-89	K L Q K S D E G V Y Y C A A W E A	C G T - - - - -	V Y C	C W C H K V F G A G T L L R V T	
SFL-810	K L Q K S D E G V Y Y C A A W E V	V T V C - - - - -	- - - - -	Y G W A H K V F G P G T L L R V T	
SFL-811	K L Q K S D E G V Y Y C A A F A N - - - - -	- - - - -	- - - - -	Y S G W A H K V F G P G T L L R V T	
SFL-812	K L Q K S D E G V Y Y C A A T C C - - - - -	- - - - -	- - - - -	- W A Y K V F G A G T L L S V T	
SFL-813	K L Q K S D E G V Y Y C A A W E A	R - - - - -	C Y	G W A Y K V F G A G T L L R V T	
SFL-814	K L Q K S D E G V Y Y C A A W E A	S A S I R L G W T V H	G W A H K V F G P G T L L R V T		
SFL-815	K L Q K S D E G V Y Y C A A W E A	S T - - - - -	R R	G W A H K V F G P G T L L R V T	
SFL-829	K L Q K S D E G V Y Y C A A W C - - - - -	- - - - -	- - - - -	G W A H K V F G P G T L L R V T	
SFL-833	K L Q K S D E G V Y Y C A A W E A	R G T - - - - -	F G Y	G W A H K V F G P G T L L R V T	
SFL-840	K L Q K S D E G V Y Y C A A W D S L G - - - - -	- - - - -	- - - - -	F G W A R K V F G P G T L L R V T	
SFL-81	K L E K S D E G V Y Y C A A W E A	R - - - - -	R Y	G W A R K V F G P G T L L R V T	
SFL-832	K L A K S D E G V Y Y C A V W E D - - - - -	- - - - -	W D C	W W C H K V F G P G T L L R V T	
SFL-834	K L A K S D E G V Y Y C A V W E D F A D - - - - -	- - - - -	Y W D C	W W C H K V F G P G T L L R V T	
SFL-837	K L A K S D E G V Y Y C A V W E V C - - - - -	- - - - -	F W D C	W W C H K V F G P G T L L R V T	
	K L Q K S D E G V Y Y C A A W E A	C T I R L G		C W A H K V F G P G T L L R V T	

← 3' V segment → N region → J segment →

← CDR3 →

PCR amplicons to demonstrate TCRG rearrangements



1 2 3 4 5 6

Molecular clonality - Limitations

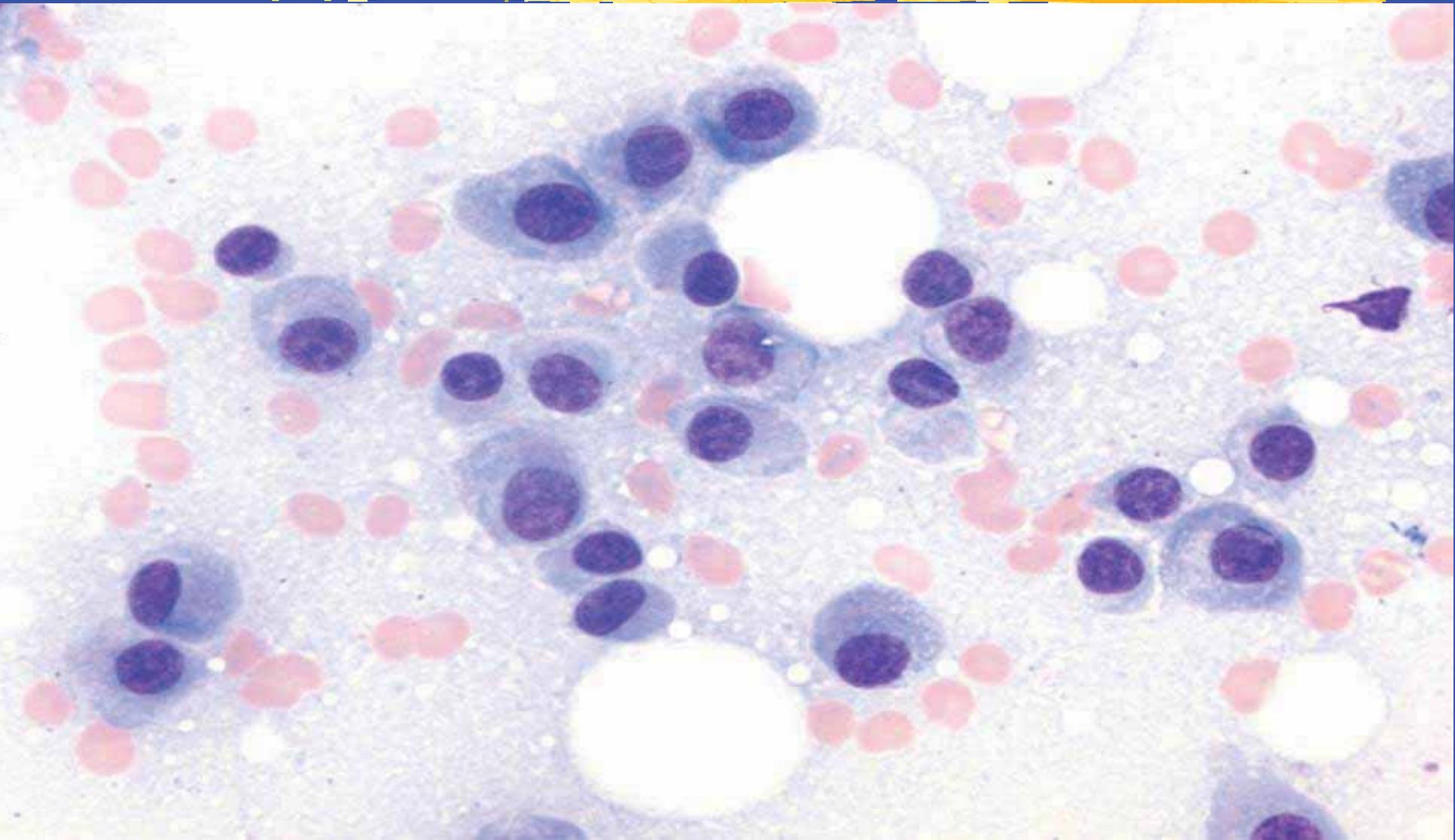


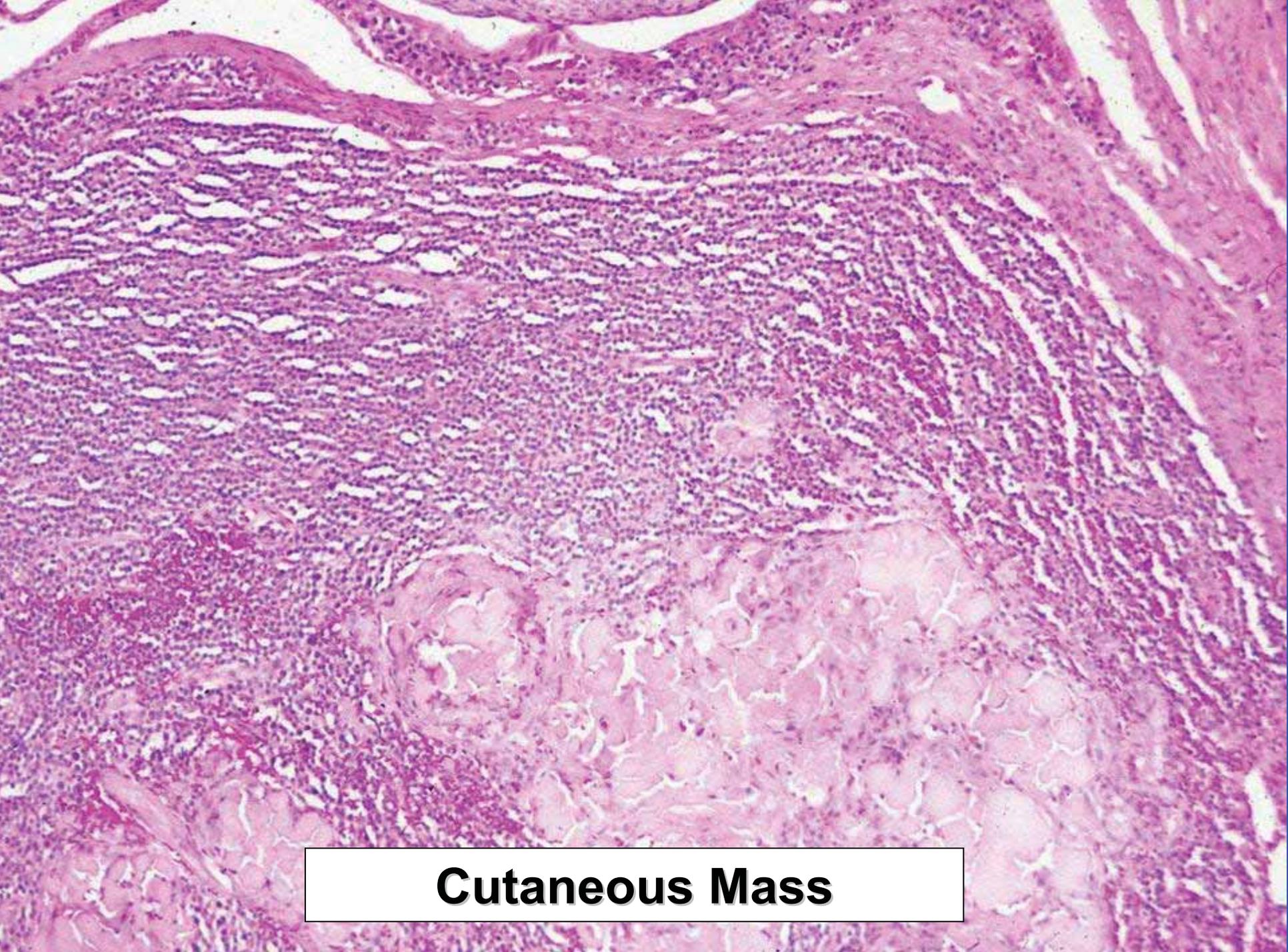
- Sensitivity limited with high polyclonal background
 - Miss small clonal populations
- Sensitivity limited- B cells - *IGH* V mutation
- Clonality is not equivalent to malignancy
 - Interpret results in context
- *IGH* and *TCRG* rearrangements are not markers of lineage
 - Cross lineage rearrangements in lymphoid and myeloid malignancies

Enough of Lymphomas

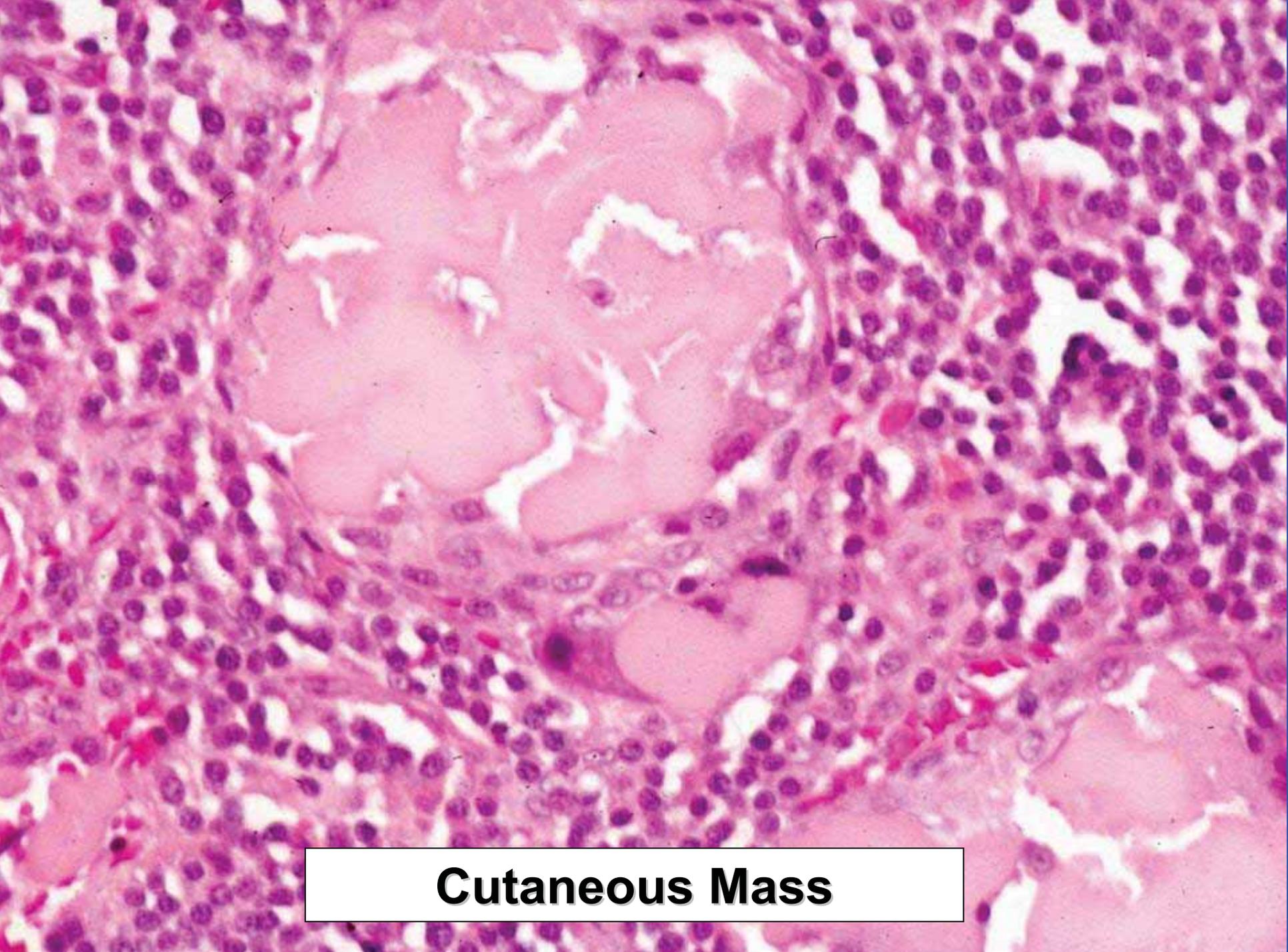


Cutaneous Mass

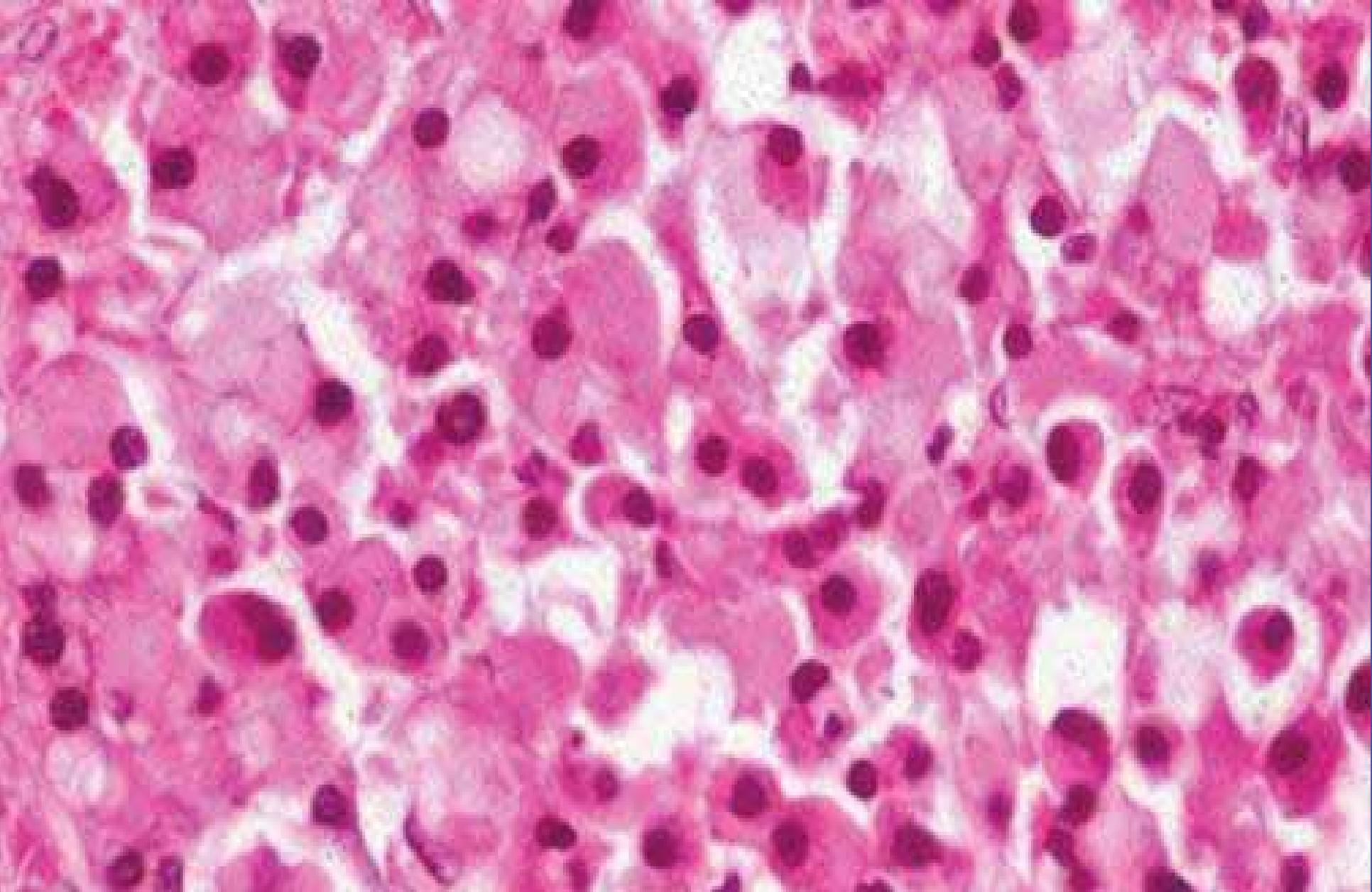




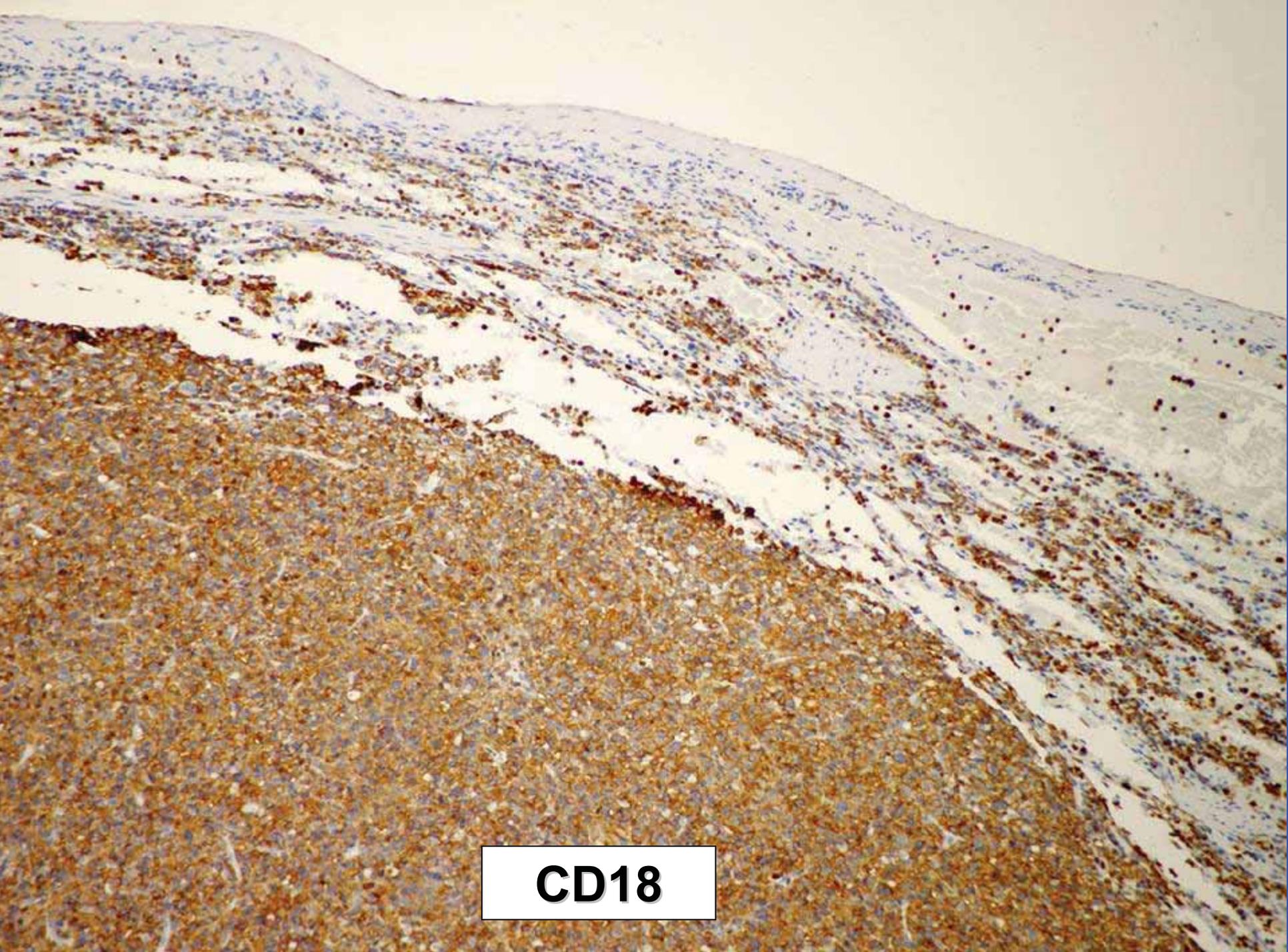
Cutaneous Mass



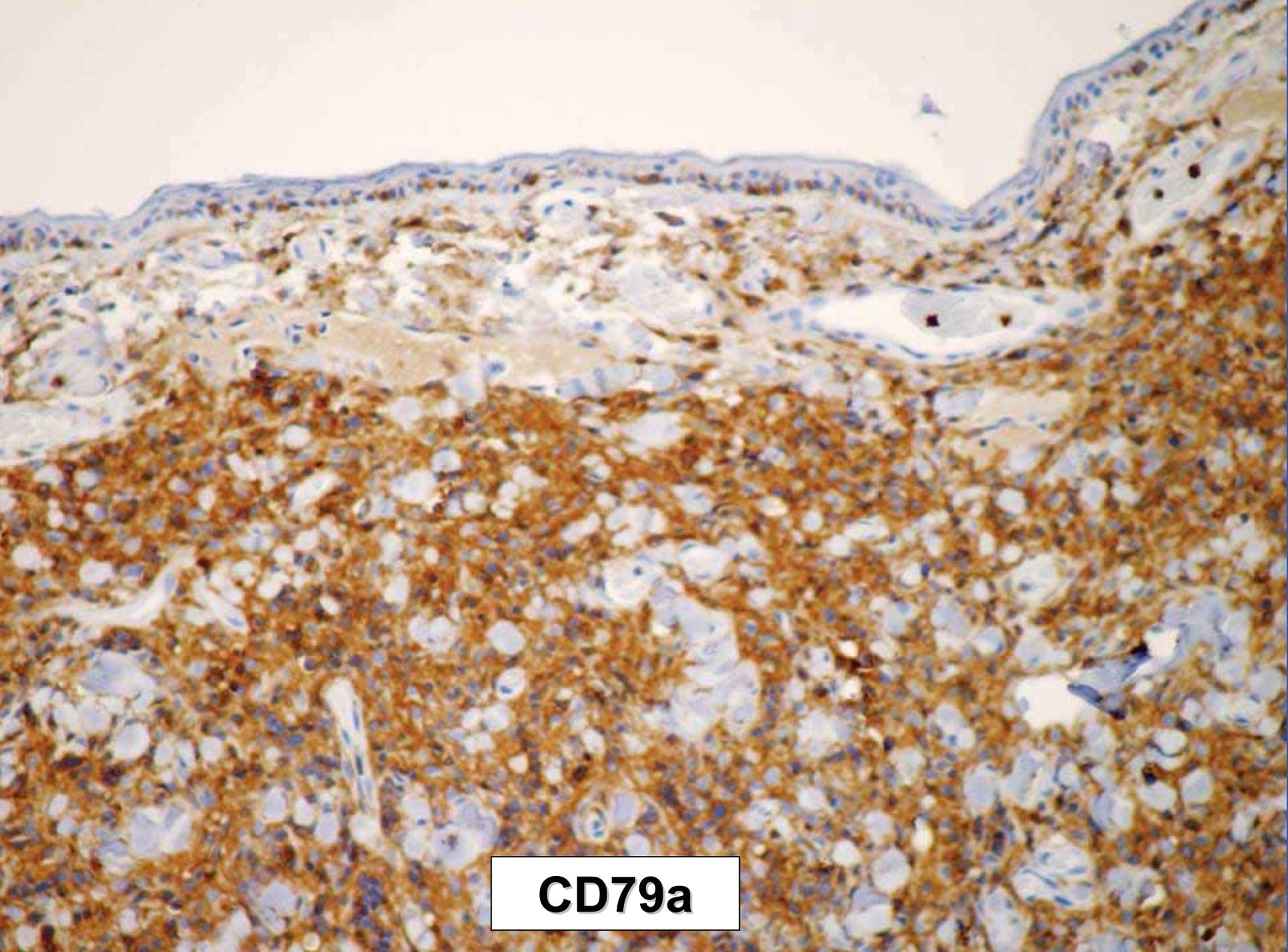
Cutaneous Mass



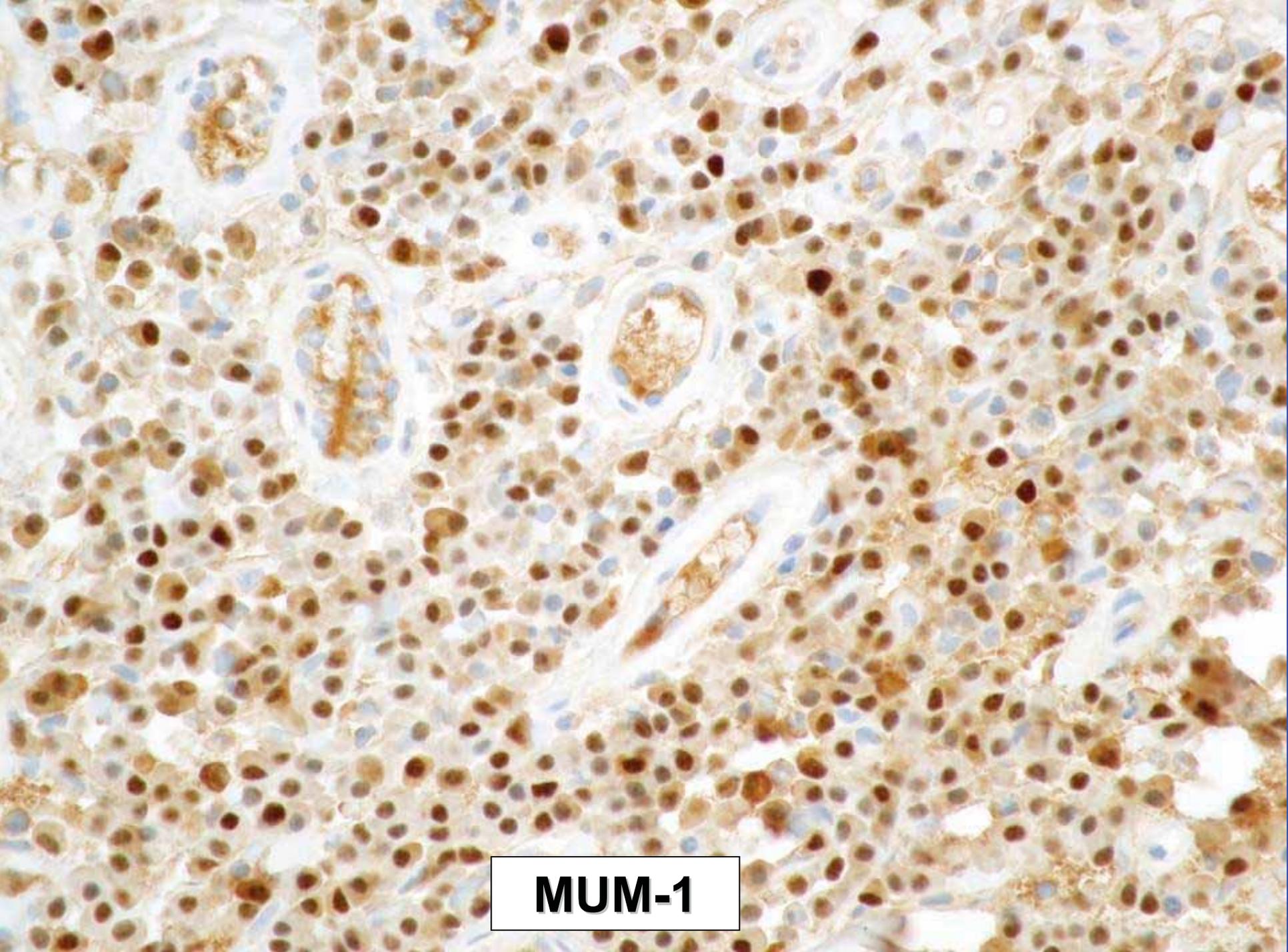
Cutaneous Mass



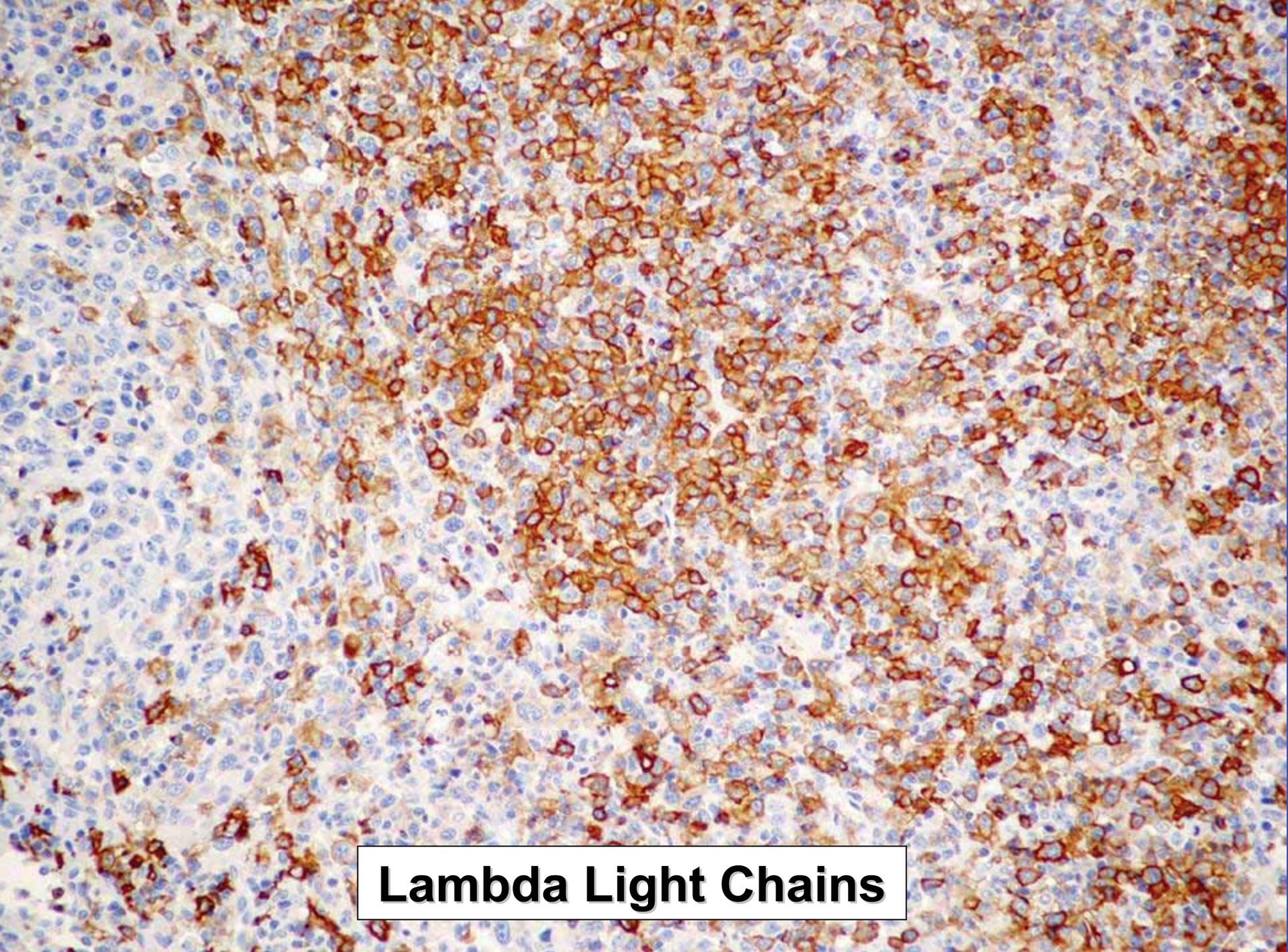
CD18



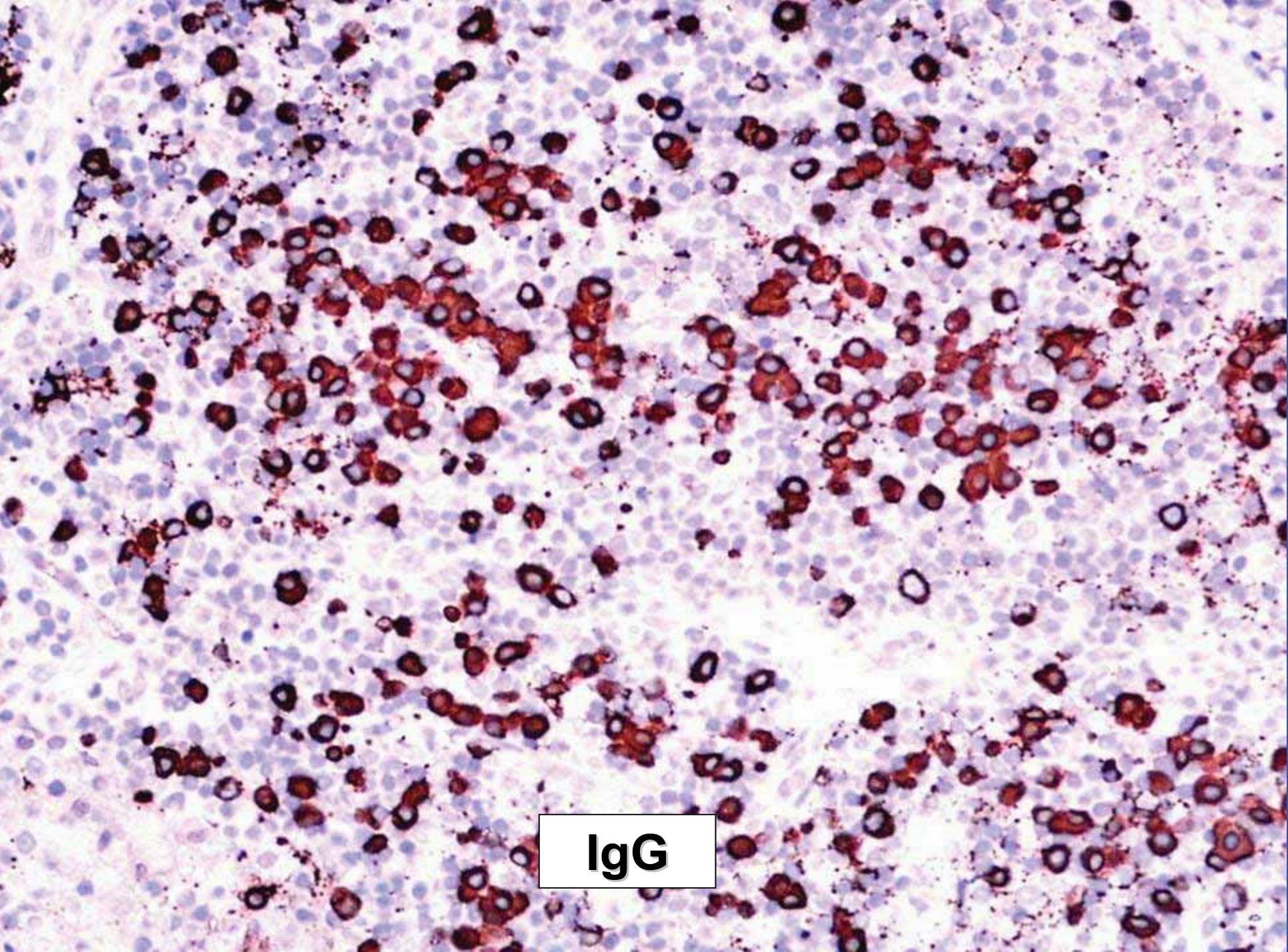
CD79a



MUM-1



Lambda Light Chains

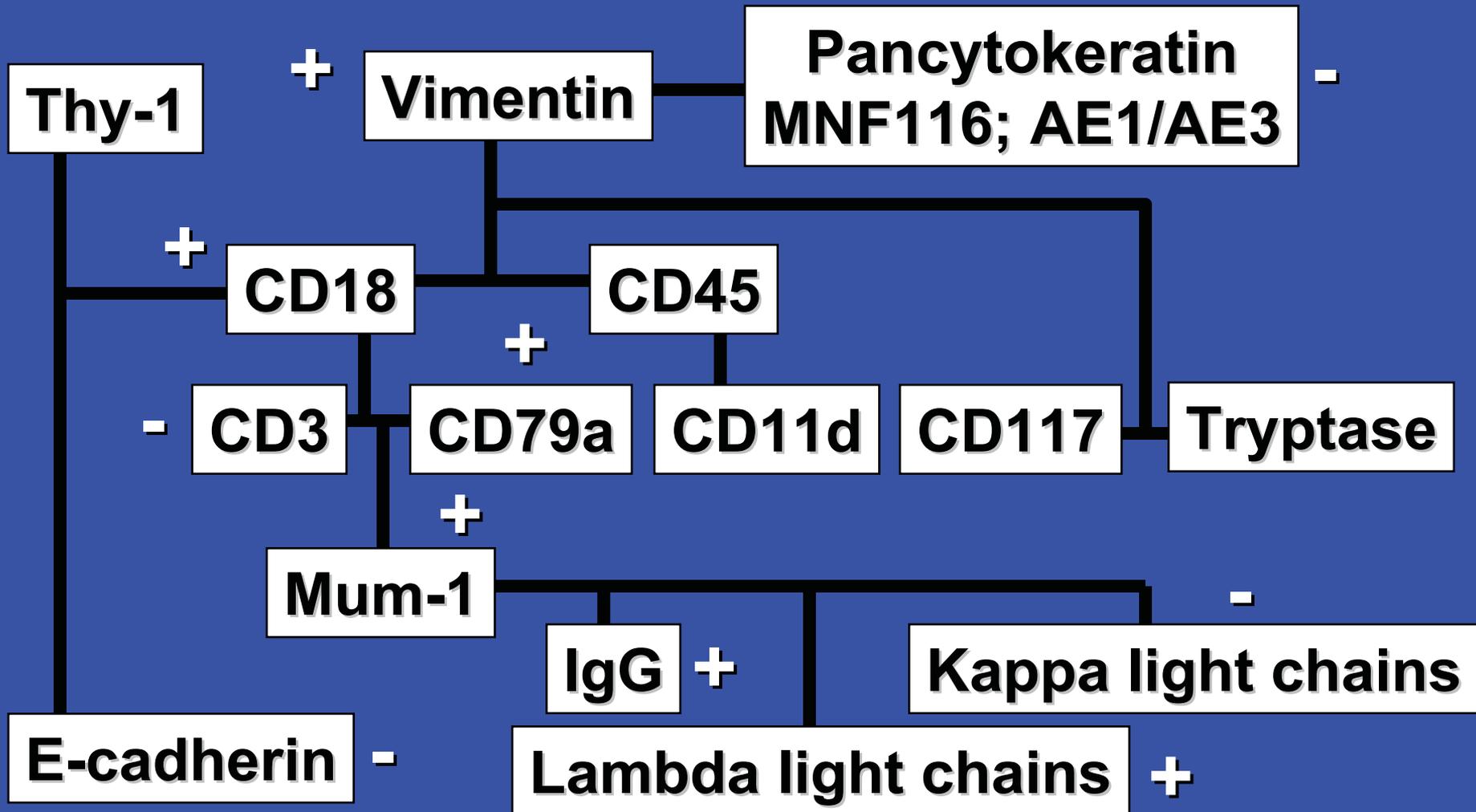


IgG

**What's
your
Diagnosis**



Cutaneous Plasmacytoma



Cutaneous Plasmacytoma

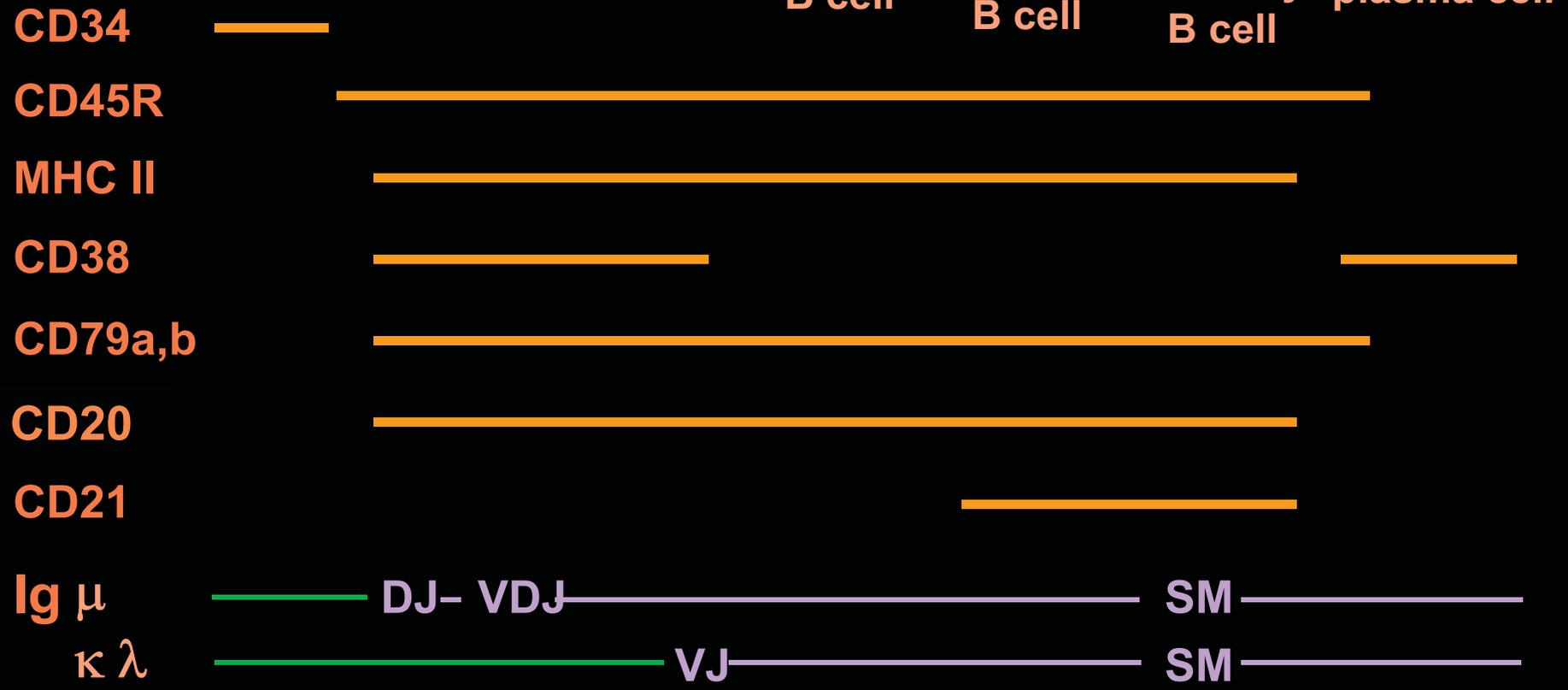
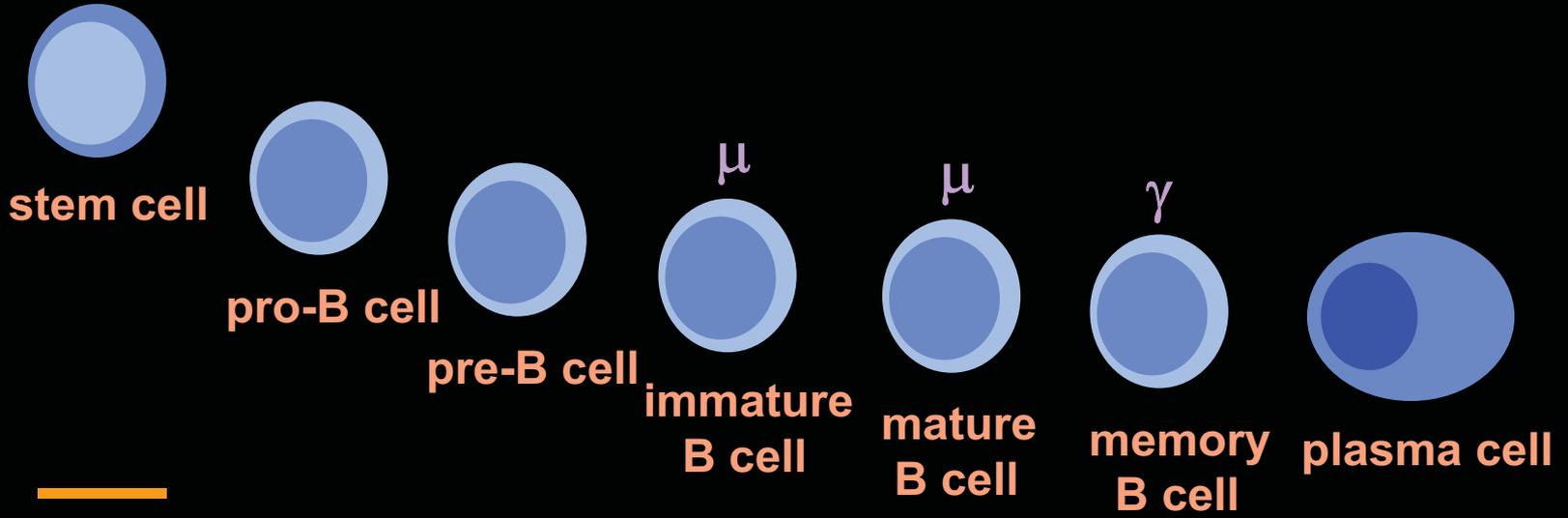


- Most common tumor of B cell lineage in skin
- Mostly benign
- Often multiple or sequential tumors
- Predilection for digits, ear canal, lip, mouth
- Histology
 - well circumscribed, dermal tumors
 - arranged in small lobules by delicate stroma
 - marked cellular pleomorphism with perinuclear halo
 - common presence of giant cells

Cutaneous Plasmacytoma



- CD79a expressed in 70% of cases
- CD20 expressed in less than 50% of cases
- CD45RA expressed in 90% of cases
- Multiple myeloma oncogene 1/interferon regulatory factor 4 (MUM-1/IRF4) is expressed in 95% cases
- IgG is demonstrable in many cases (amyloid AL present in some)
- Many are positive for kappa or lambda light chains

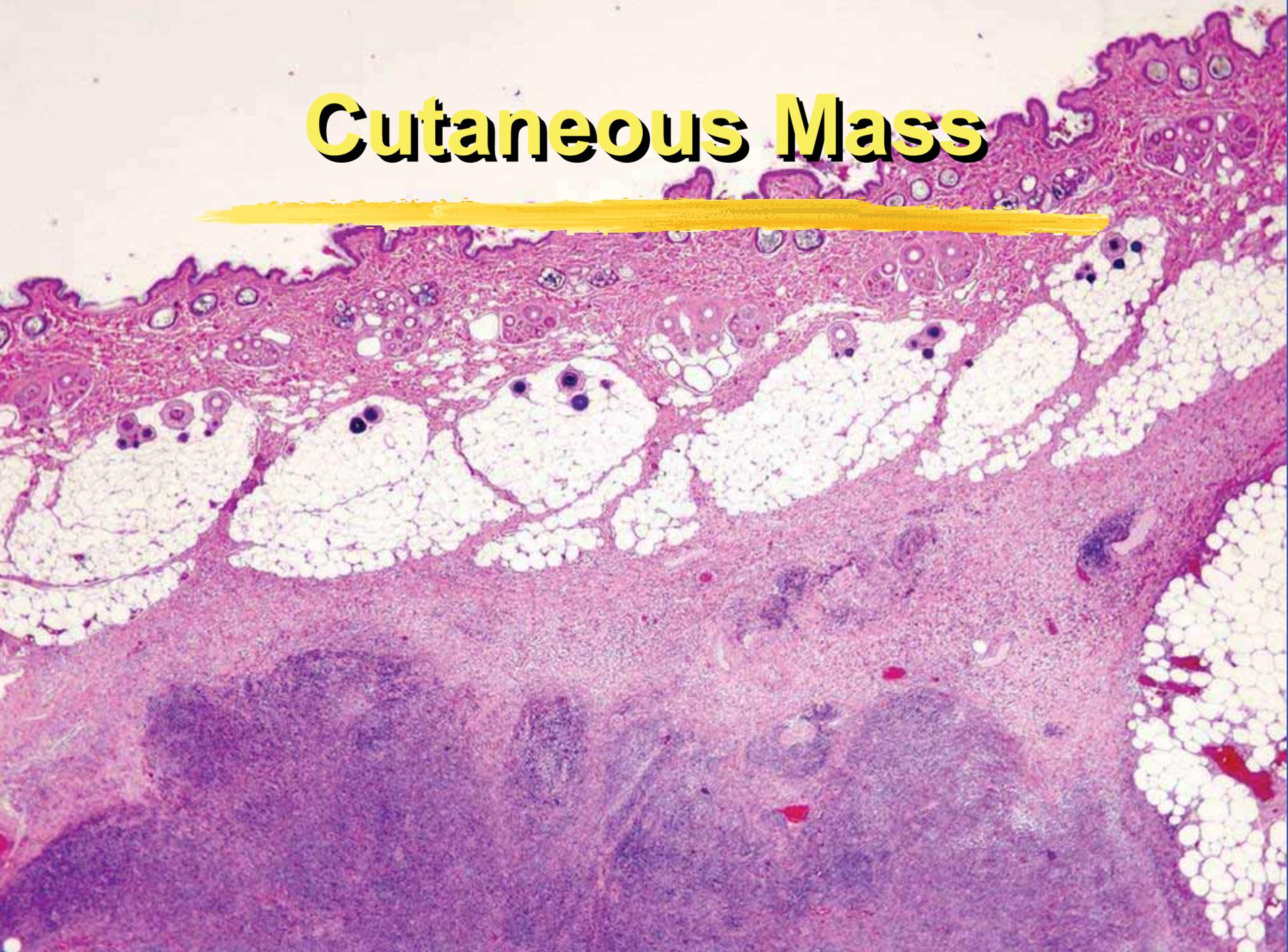


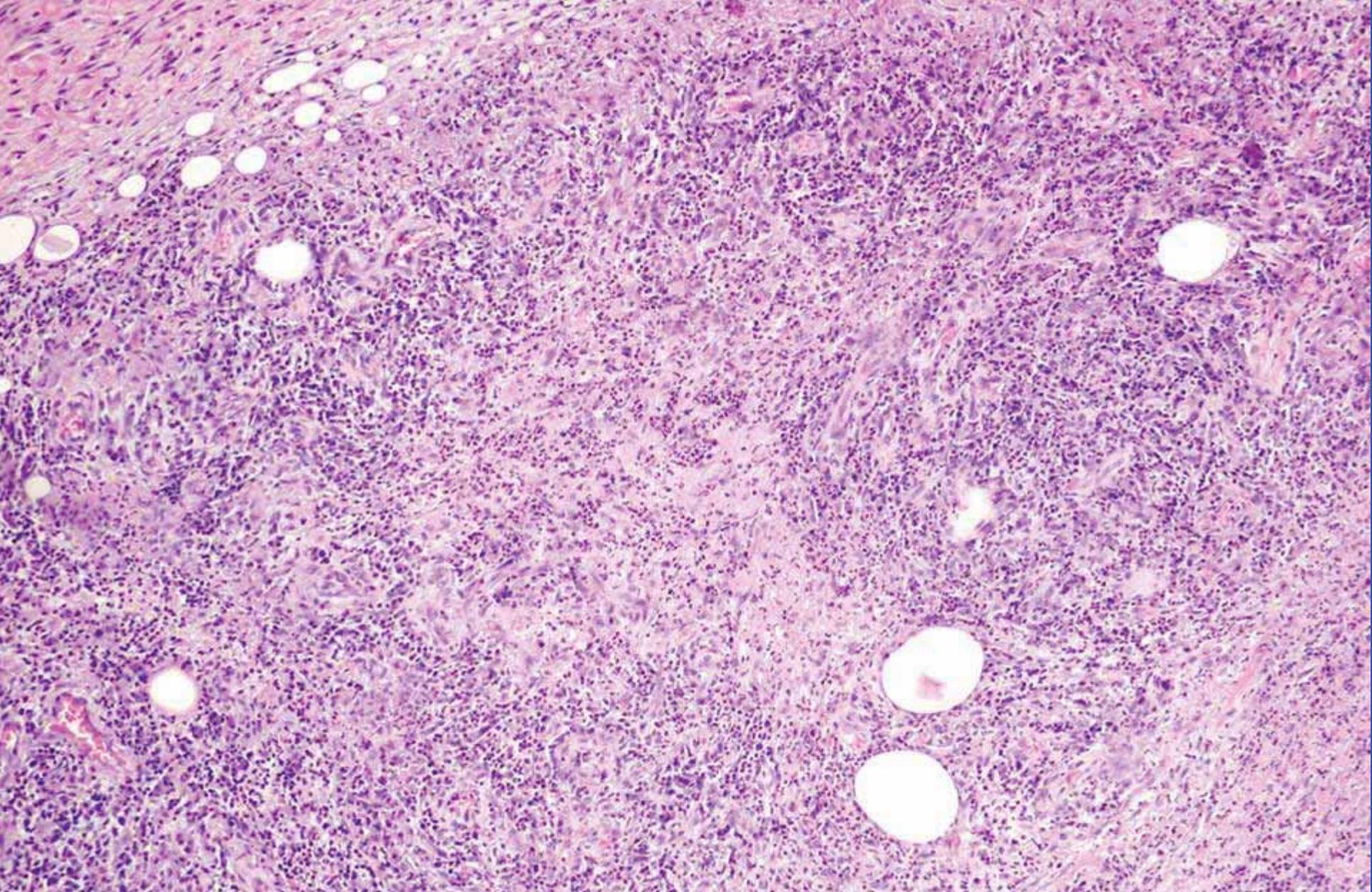
Multiple Myeloma



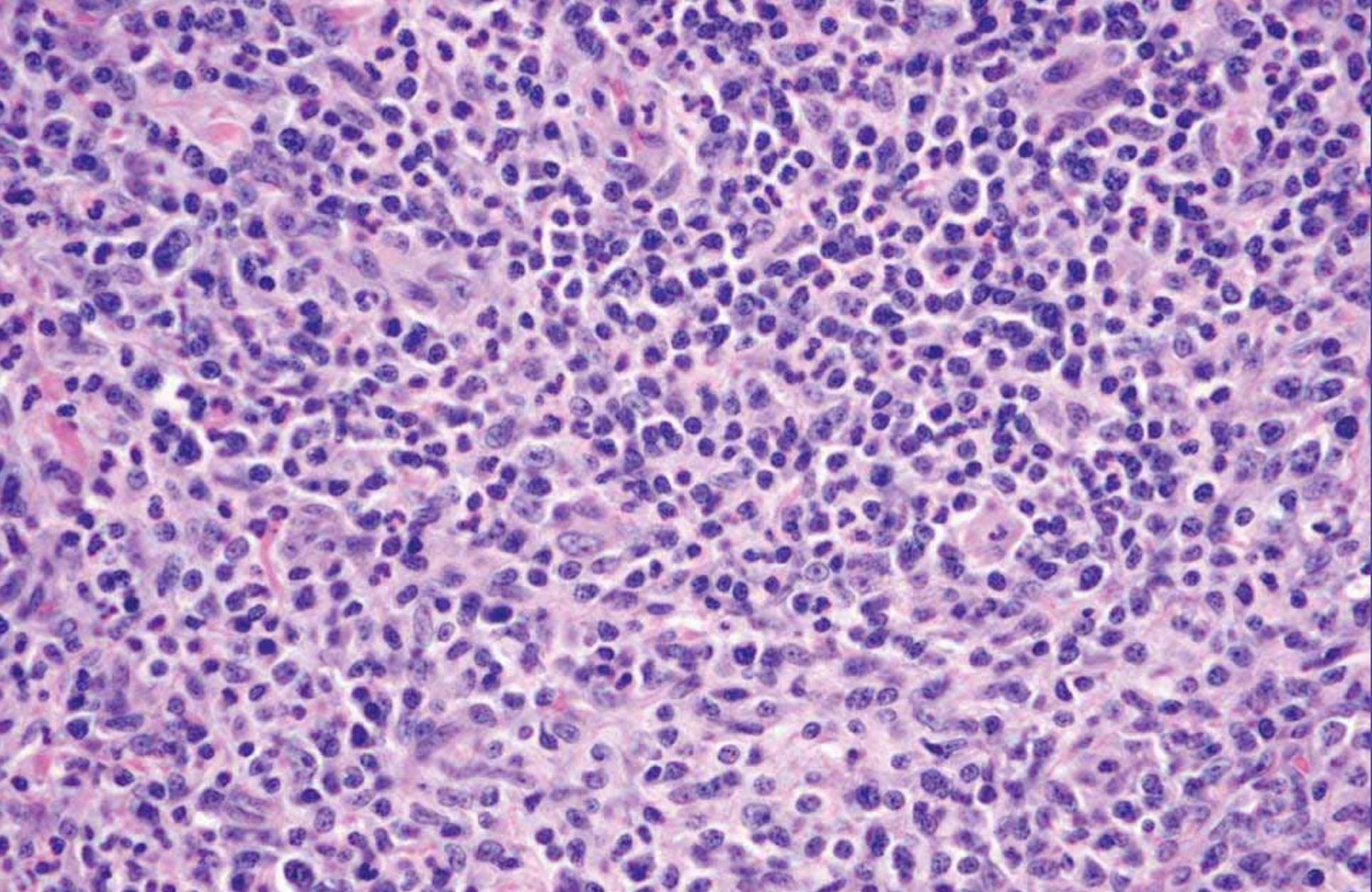
- Discrete, multicentric lytic lesions in bones with active hematopoiesis
- Dogs >>> cats, horses
- Adult males >> females
- Monoclonal gammopathy (not required)
- Hypercalcemia (uncommon)
- X-ray: Punch-out foci of osteolysis → Vertebrae, femur, pelvis, humerus, ribs
- Histo: Plasma cells (well or poorly differentiated), MUM-1 positive

Cutaneous Mass

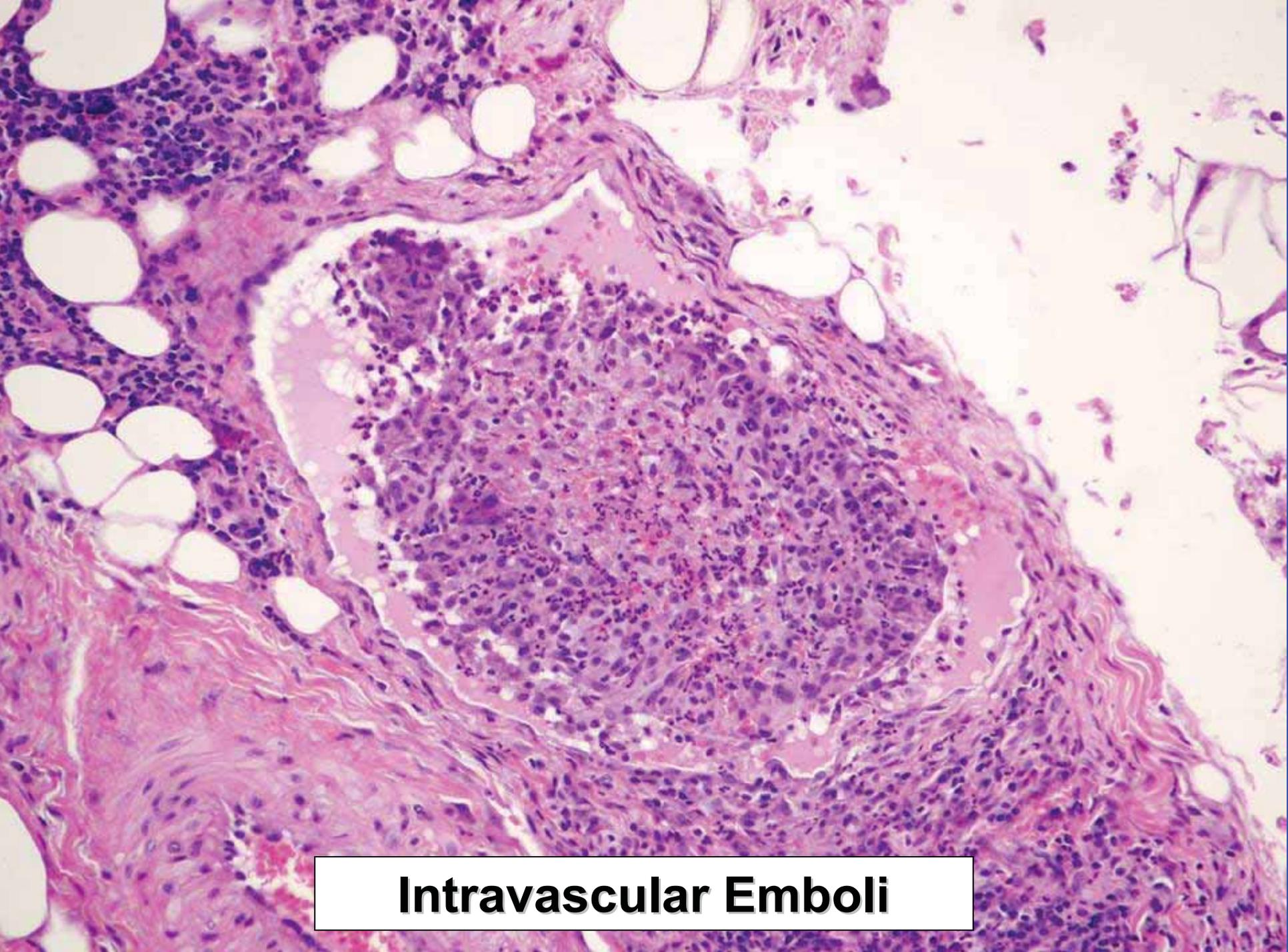




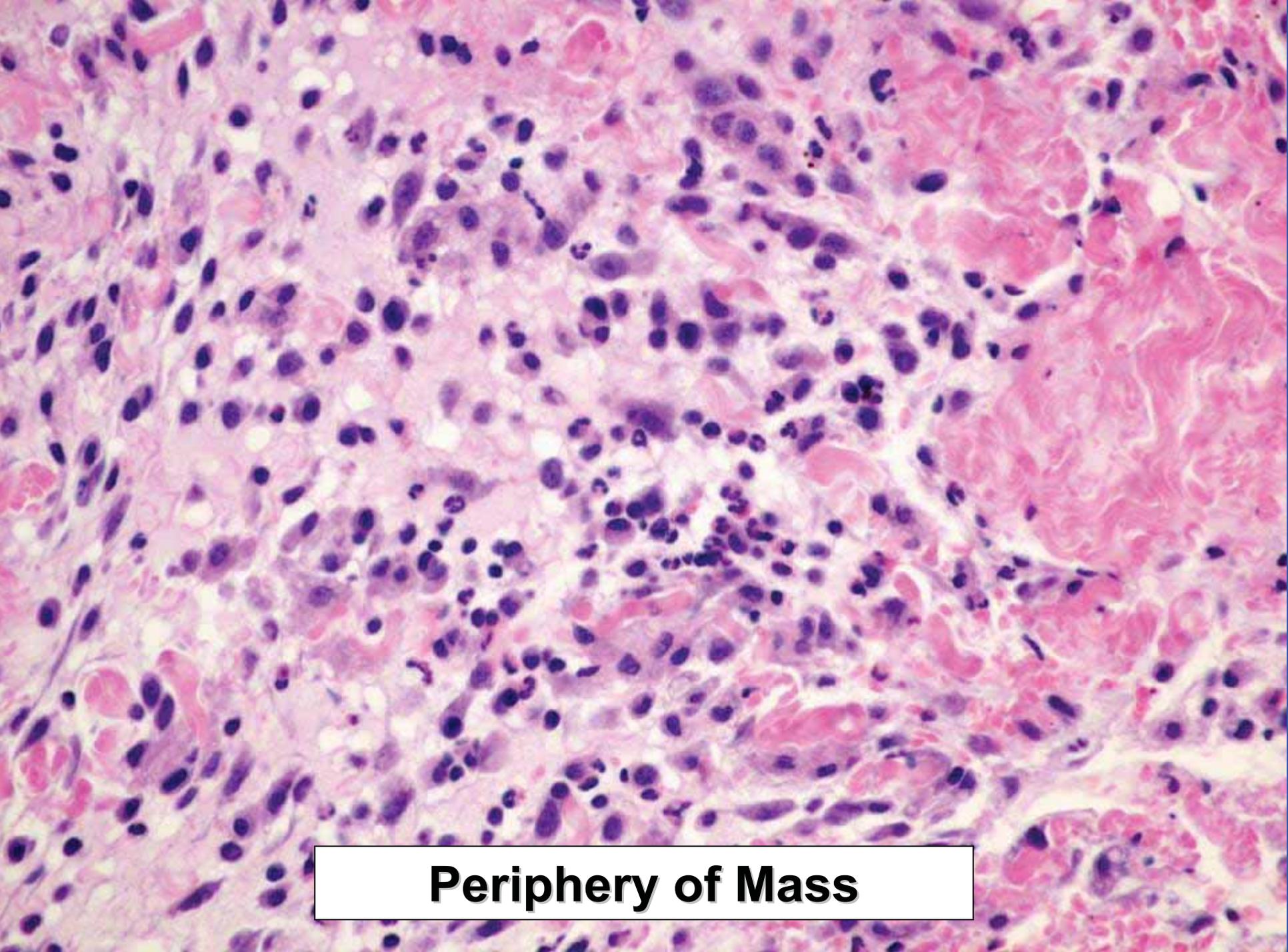
Cutaneous Mass



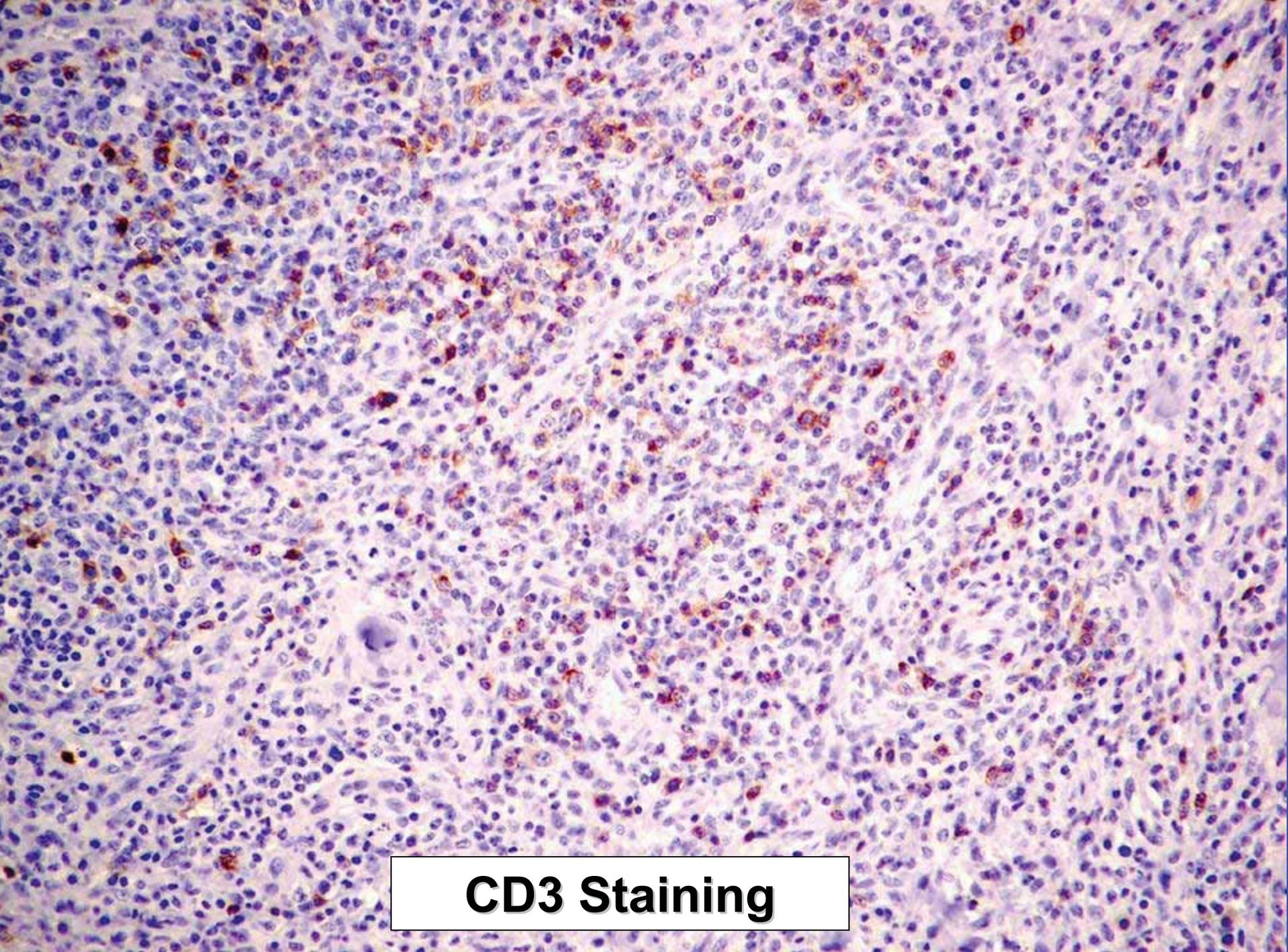
Mixed Inflammation/Eosinophils



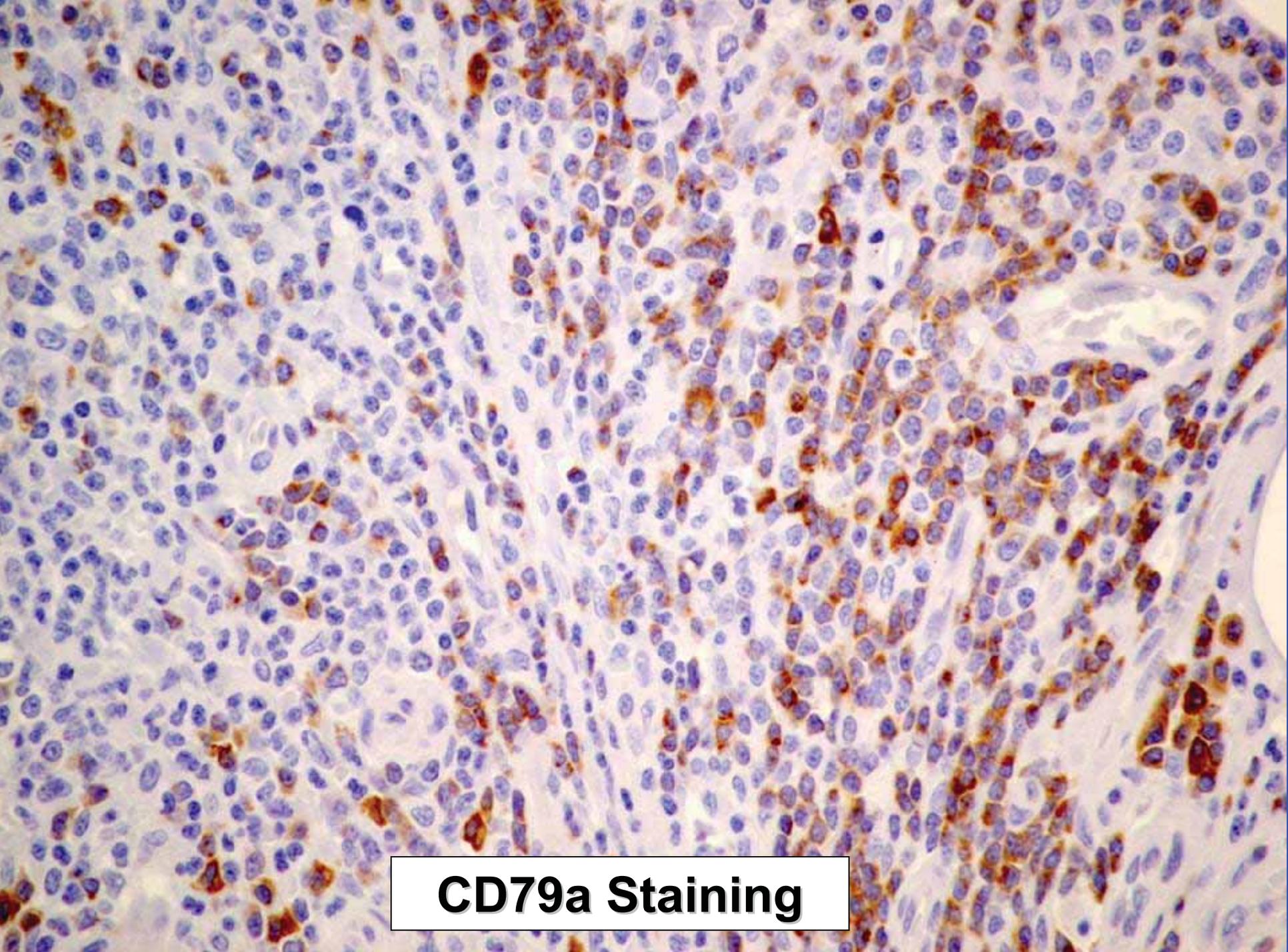
Intravascular Emboli



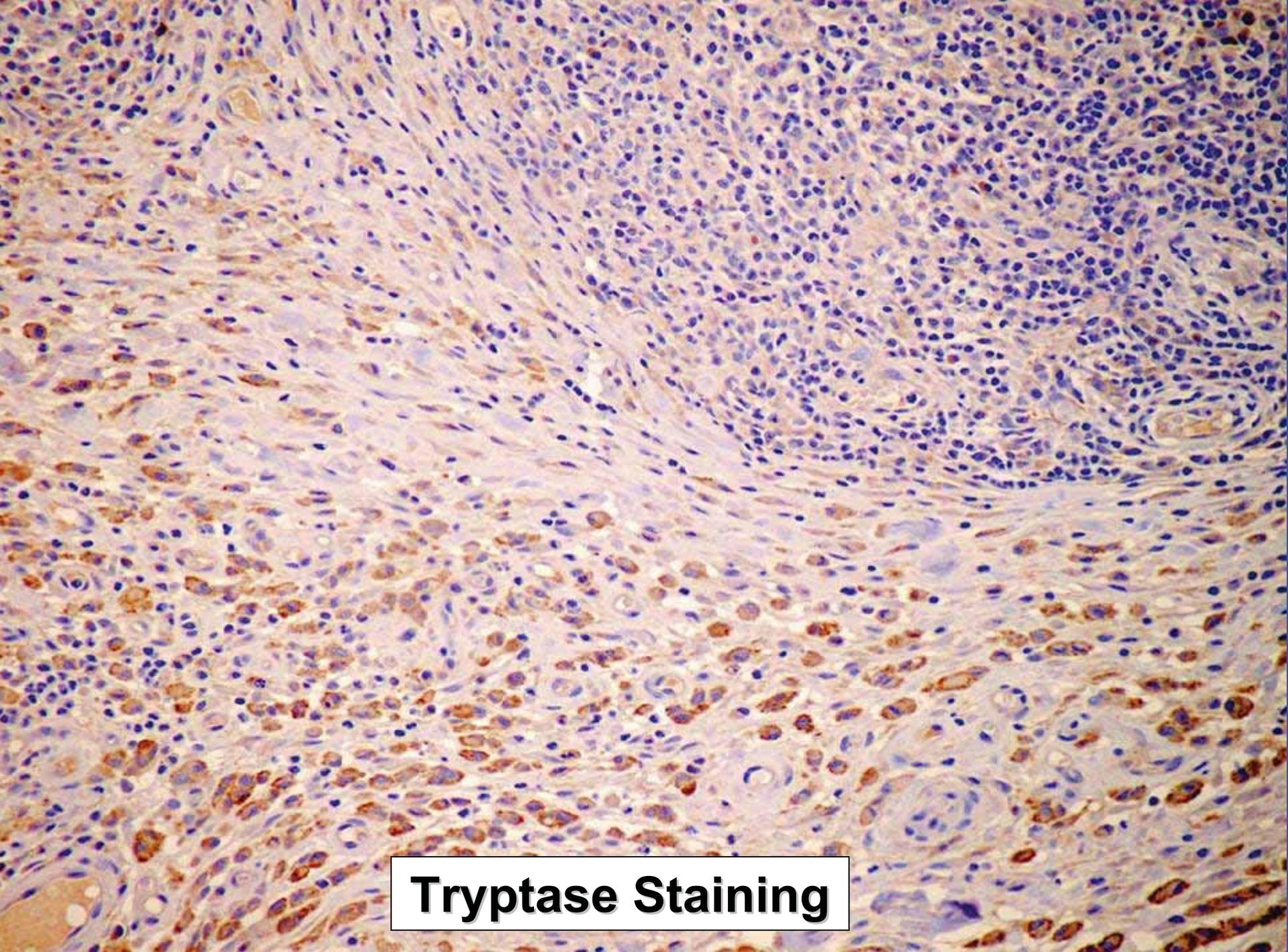
Periphery of Mass



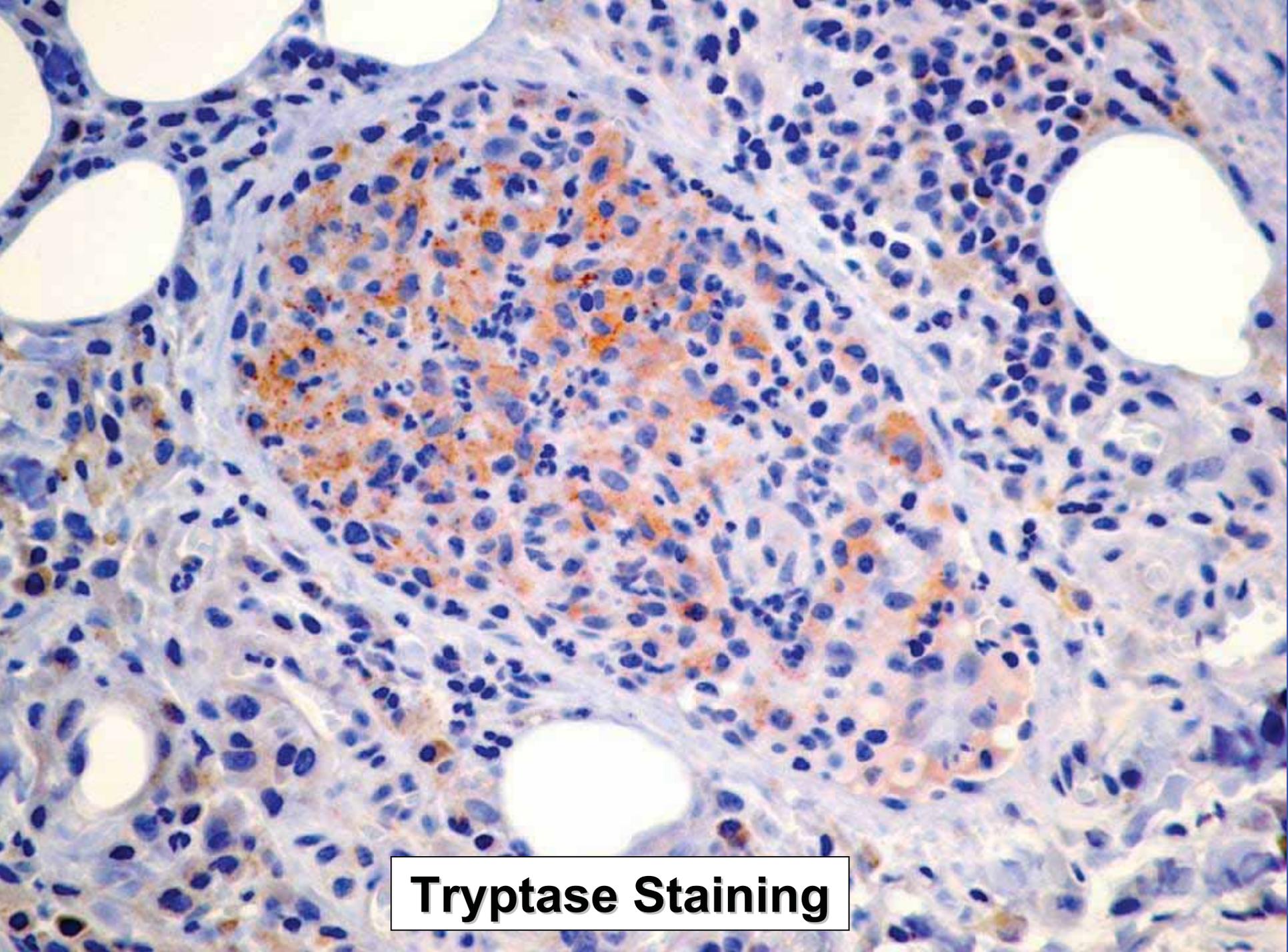
CD3 Staining



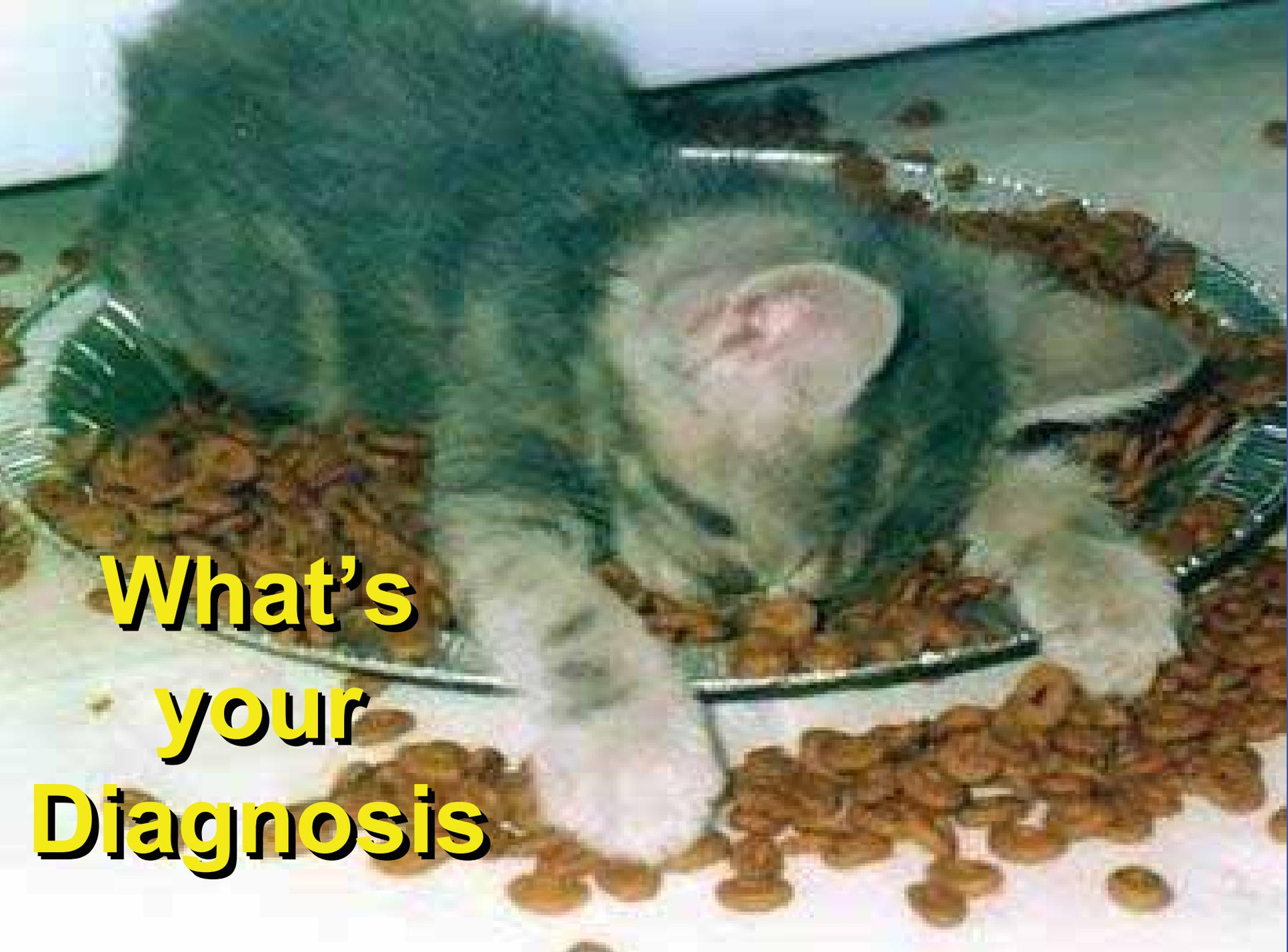
CD79a Staining



Tryptase Staining

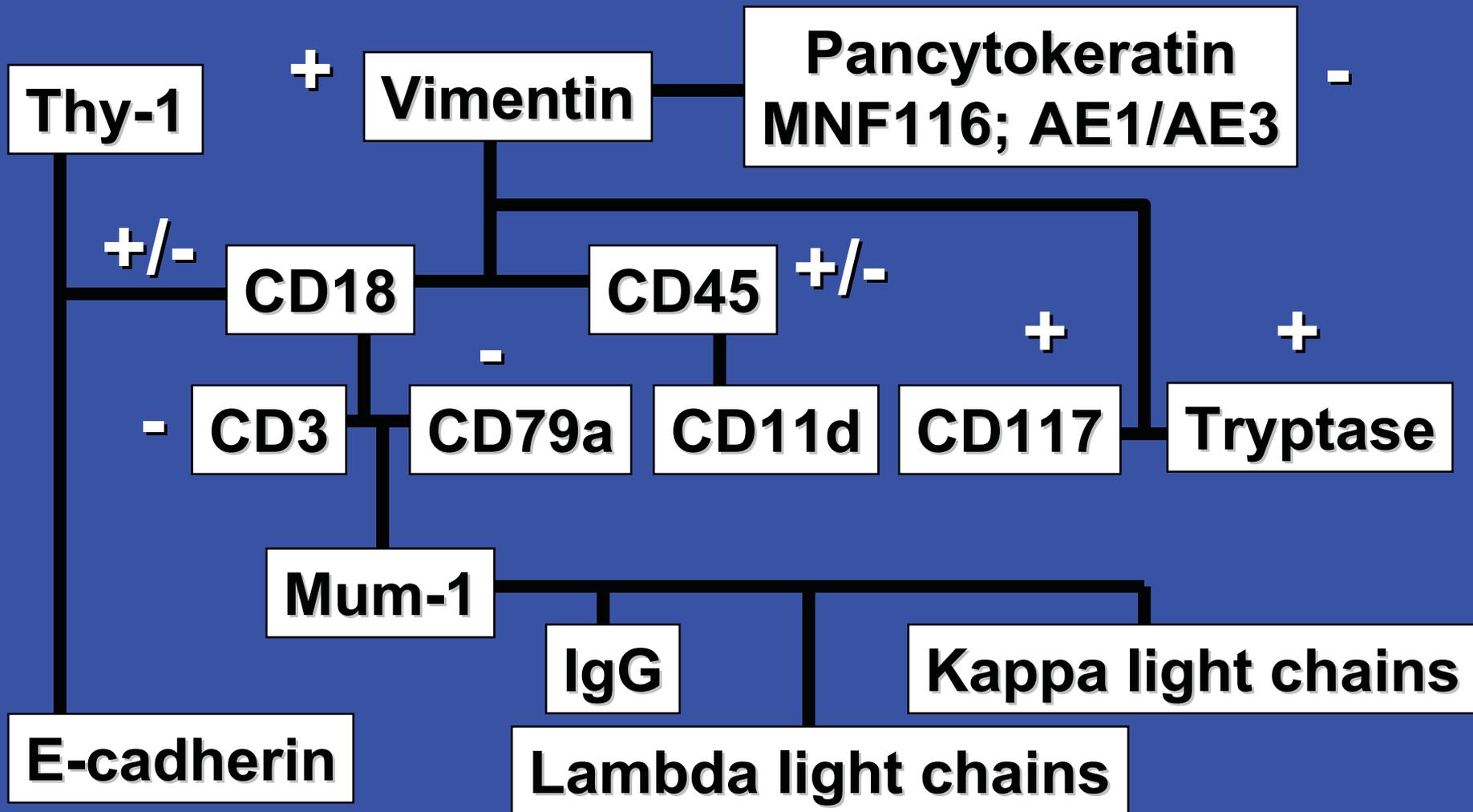


Tryptase Staining



**What's
your
Diagnosis**

Cutaneous Mast Cell Tumor



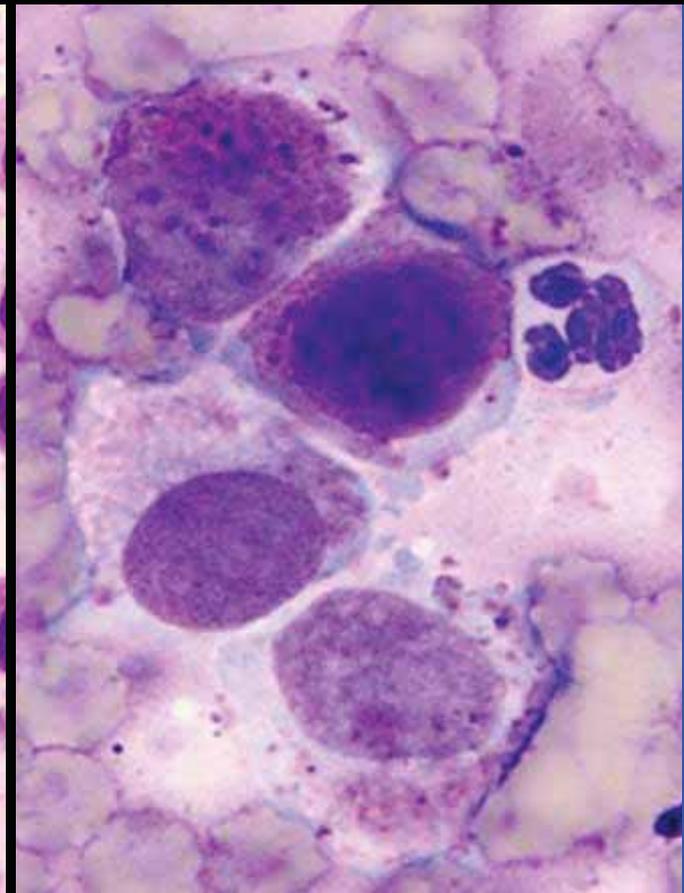
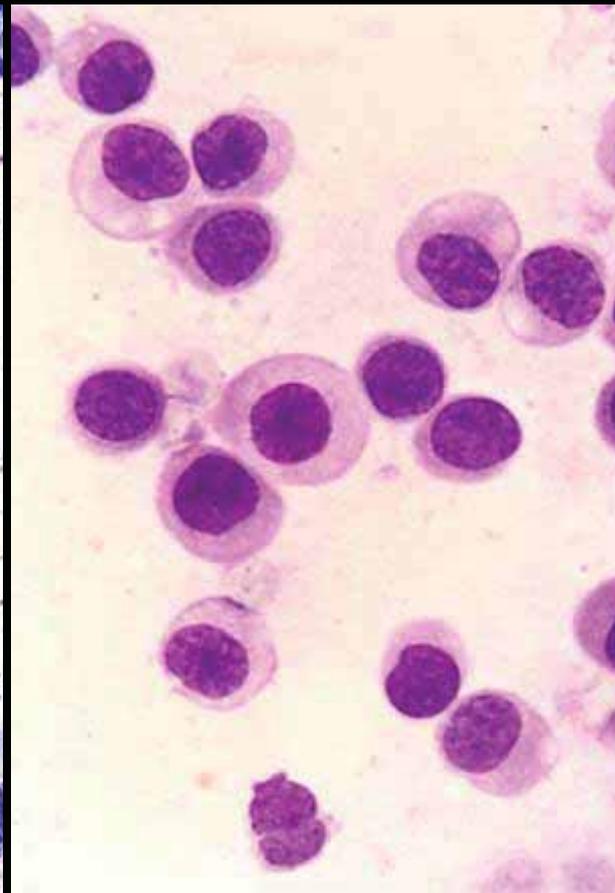
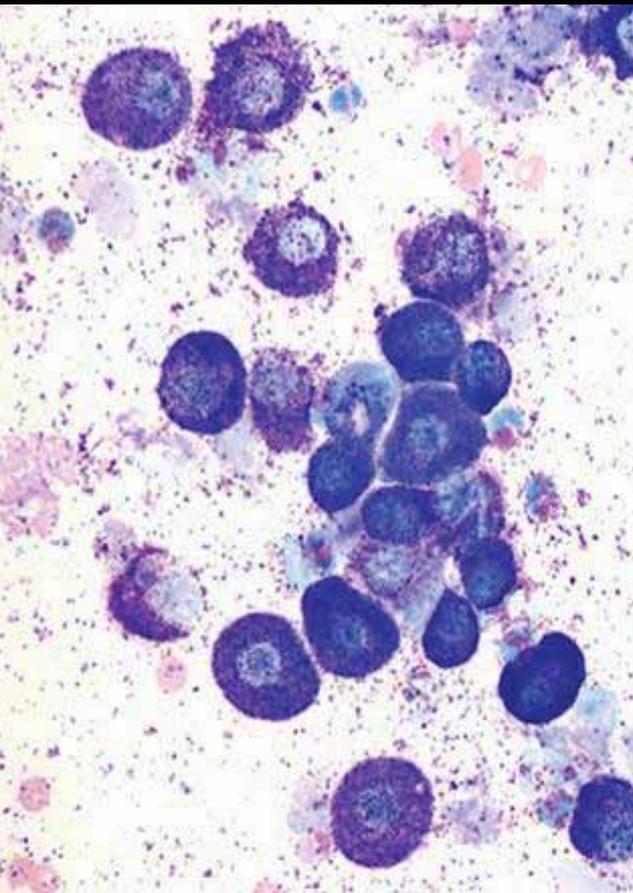
Canine Cutaneous MCTs

- 7-21% of canine cutaneous neoplasms
- Variable biologic behavior
 - Solitary
 - Multi-centric
 - Locally invasive
 - Systemic metastases
 - Para-neoplastic syndrome
- No sex predisposition
- Mean age 9 years
- Breed predisposition:
 - Boxer
 - Weimaraner
 - Labrador retriever
 - Boston terrier
 - Brachycephalic breeds



Diagnosis

- Usually easily diagnosed cytologically
- Grading requires histologic evaluation



Diagnosis

- **Stains for cytologic evaluation:**
 - **DiffQuik**
 - **Most commonly used**
 - **Granules may not stain**
 - **Wright-Giemsa**
 - **Granules easily recognized**
 - **More expensive and takes longer**
 - **Toluidine Blue**
 - **Excellent stain for poorly granulated MCTs**

