

*Cytologické a bioptické laboratórium*

# XIX. Martinský bioptický seminár

Lúčky

**25.-26. október 2013**

Peter Bohuš

- 40-ročná gynekologická pacientka

## Predmet vyšetrenia

- Stena retroperitoneálnej cysty
- Myomatázny uzol.

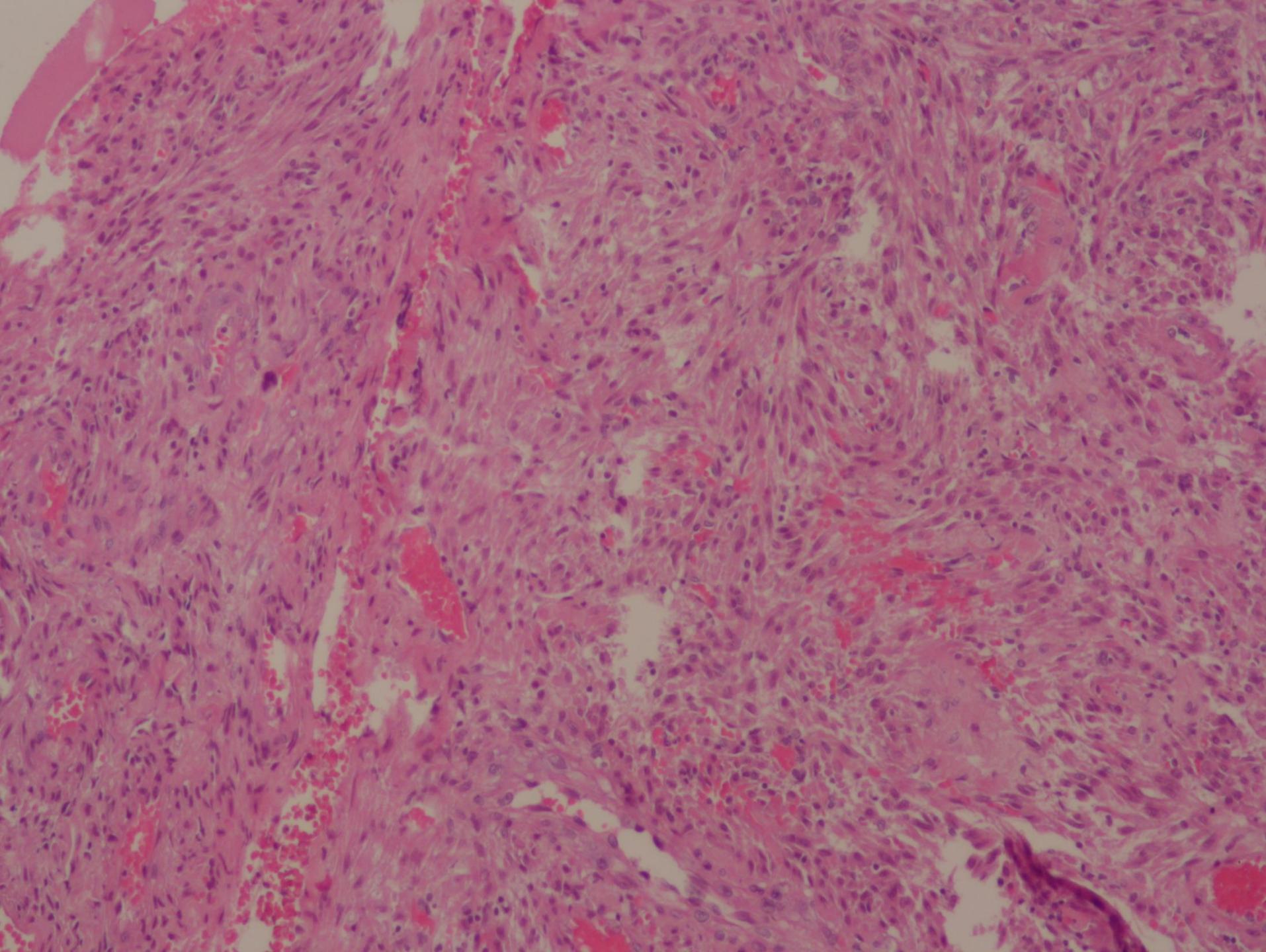
# **MAKROSKOPICKÝ OBRAZ**

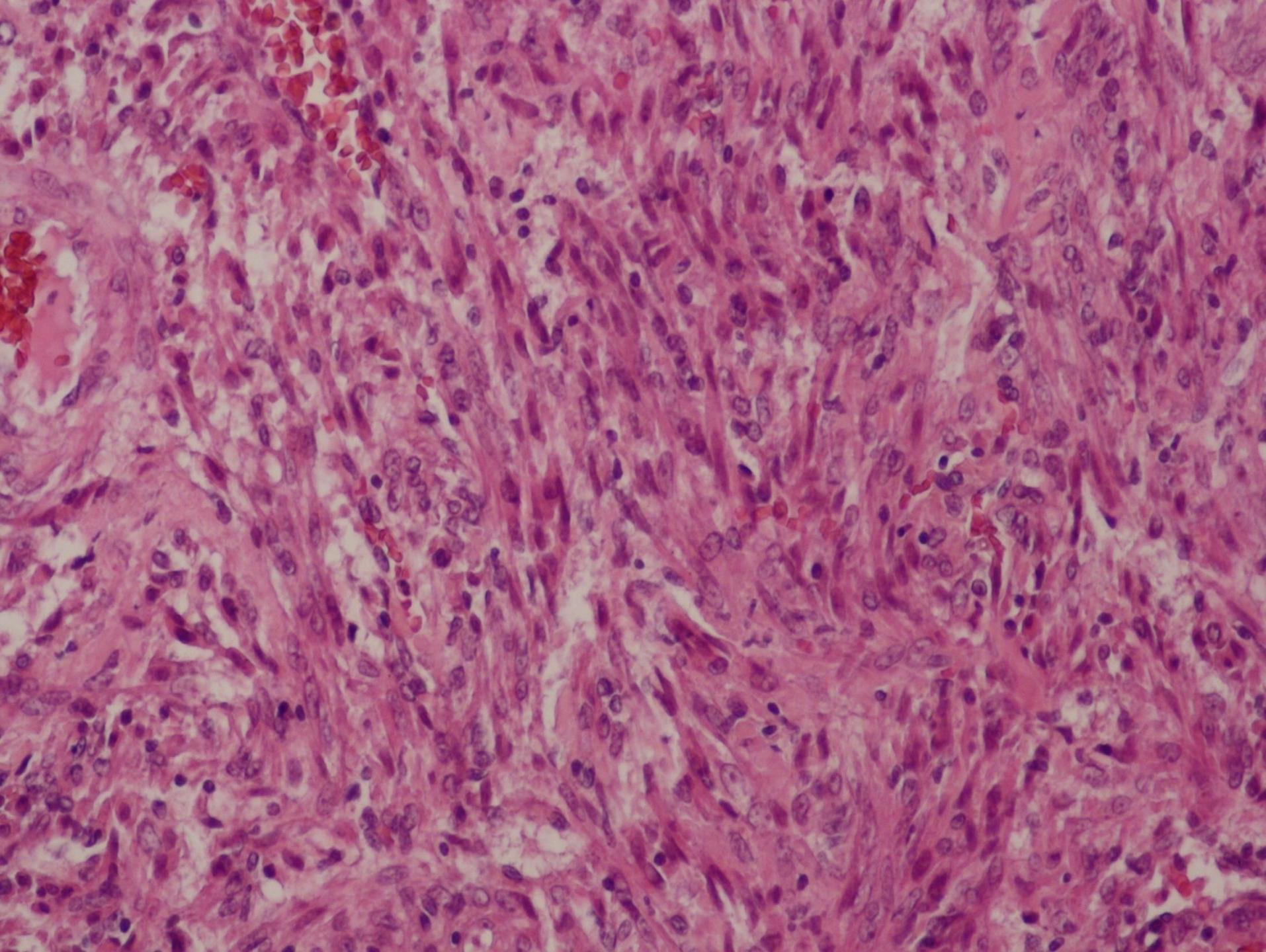
## **CYSTA**

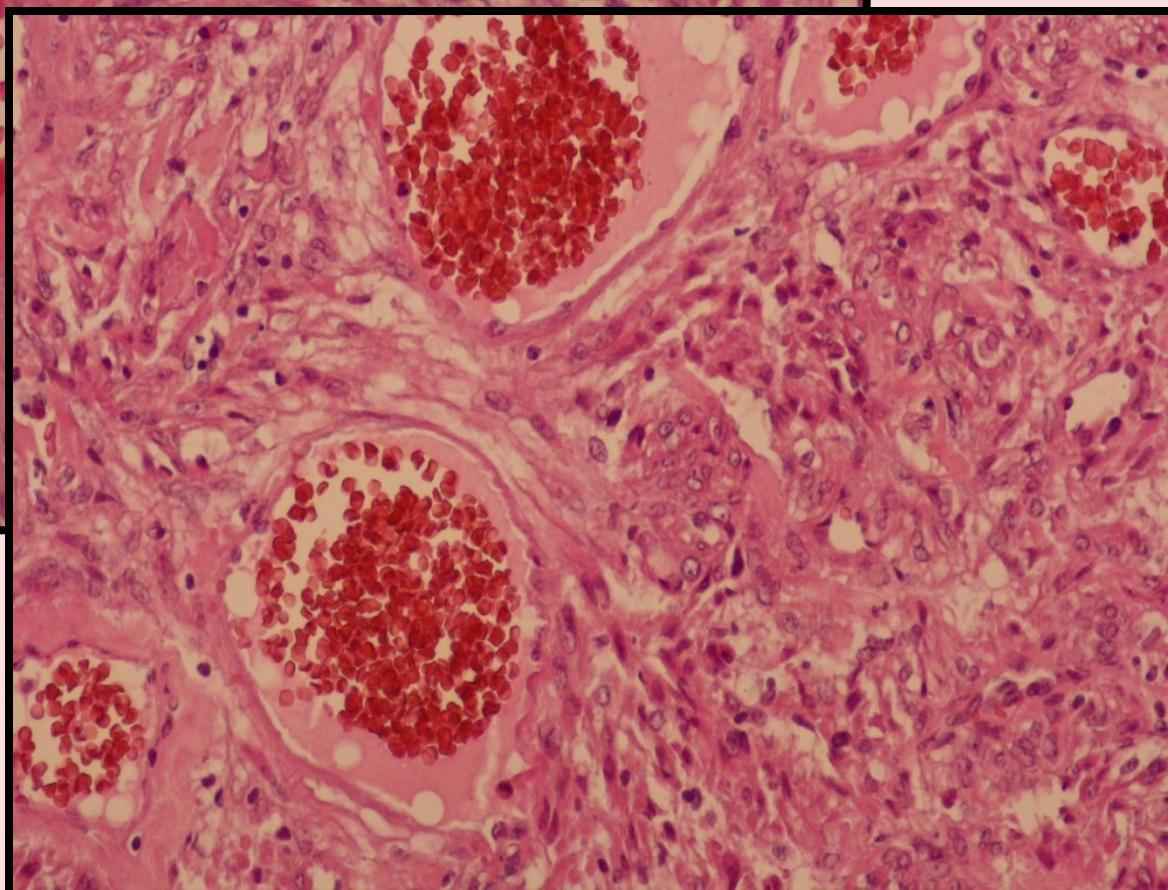
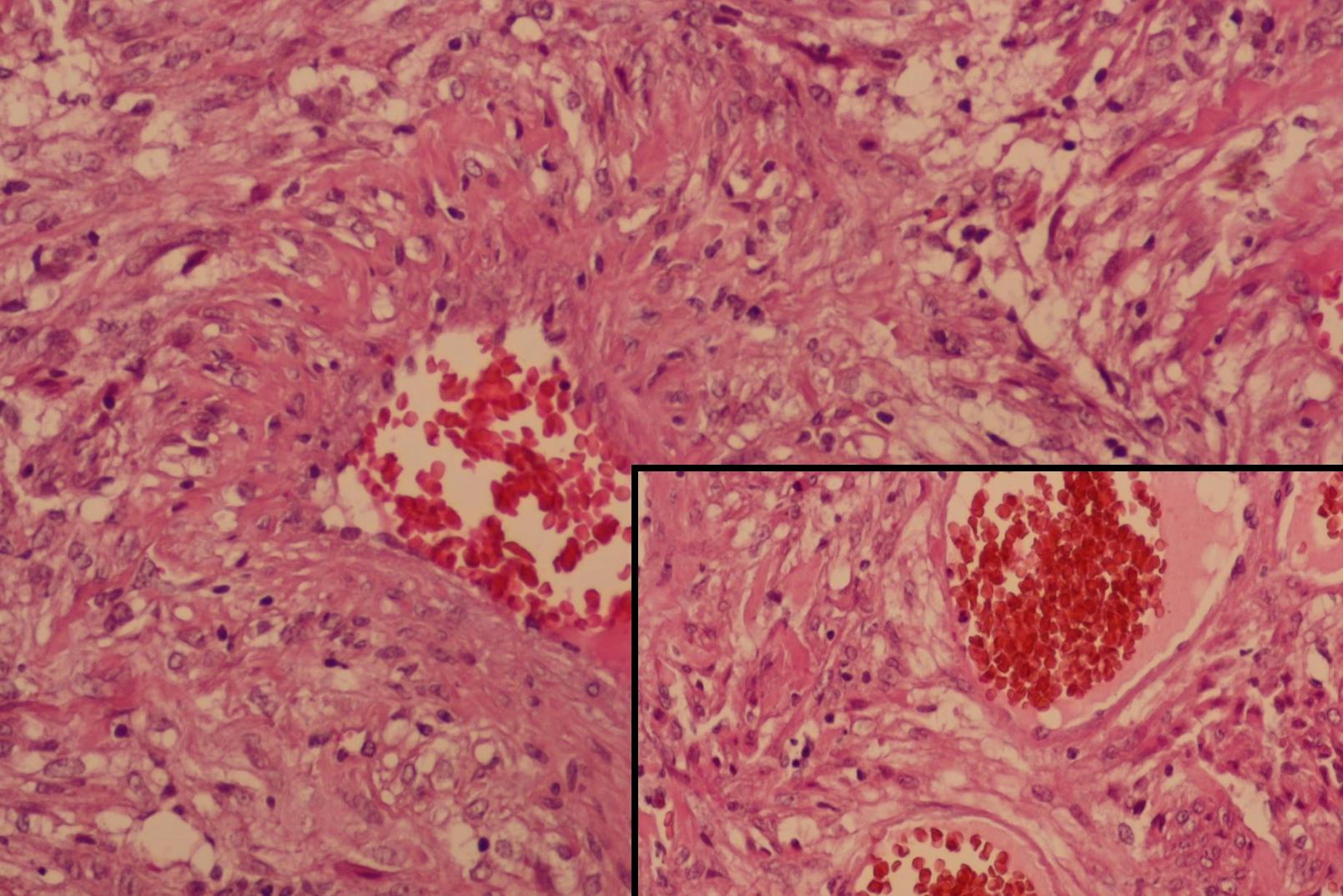
- Material blanitého charakteru veľkosti do cca 7 cm, so sivastou hladkou výstelkou a stenou miestami mierne zhrubnutou

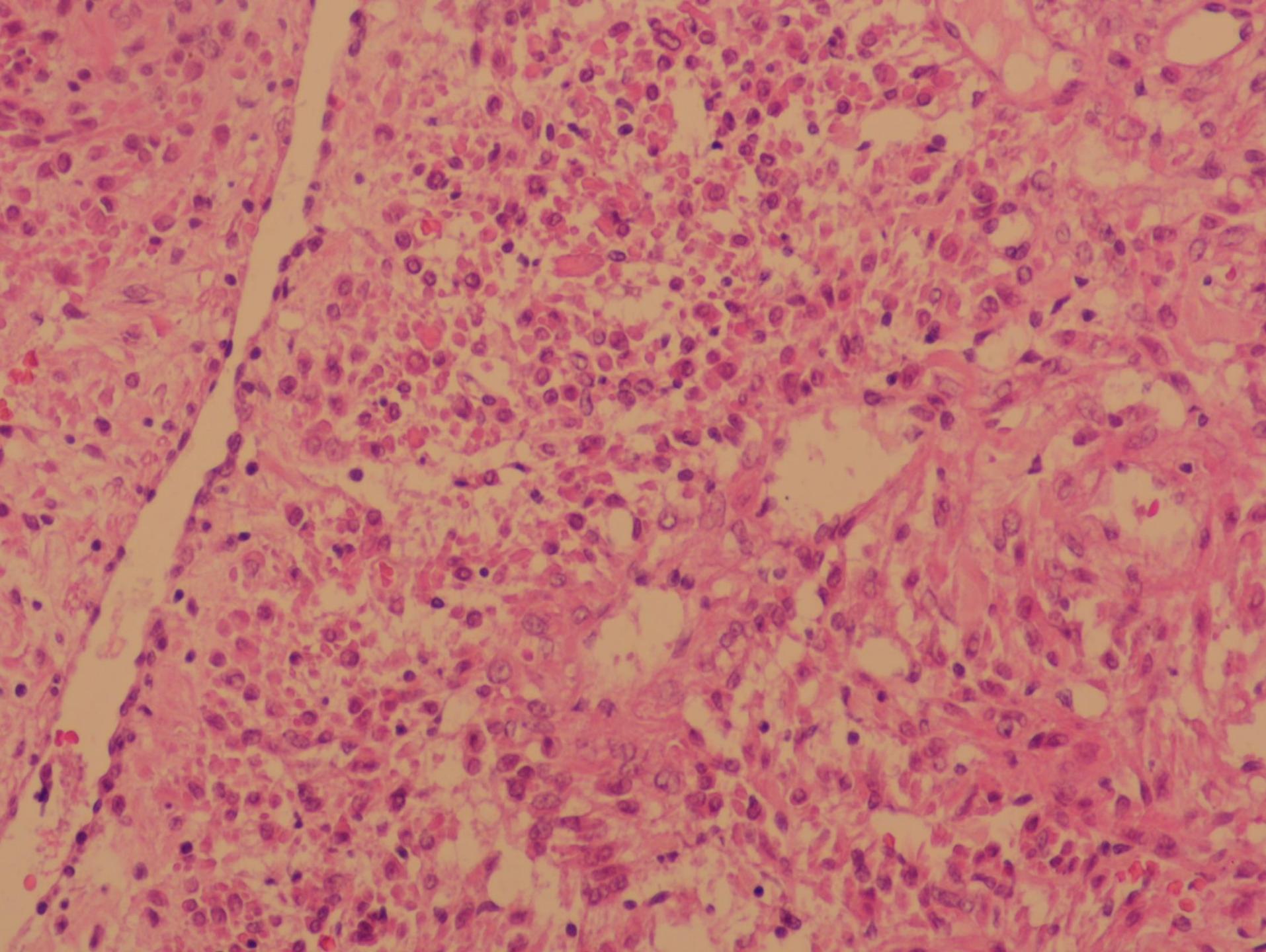
## **MYOMATÓZNY UZOL**

- Natrhnutý uzlovitý material veľkosti cca 3,8 x 2,5 x 2,1 cm, zväčša hladkého povrchu, na reze sivohnedej farby, solídnny, tuhší.
- Preparáty na seminár sú zhotovené z druhého materiálu – “myomatózneho uzla”.



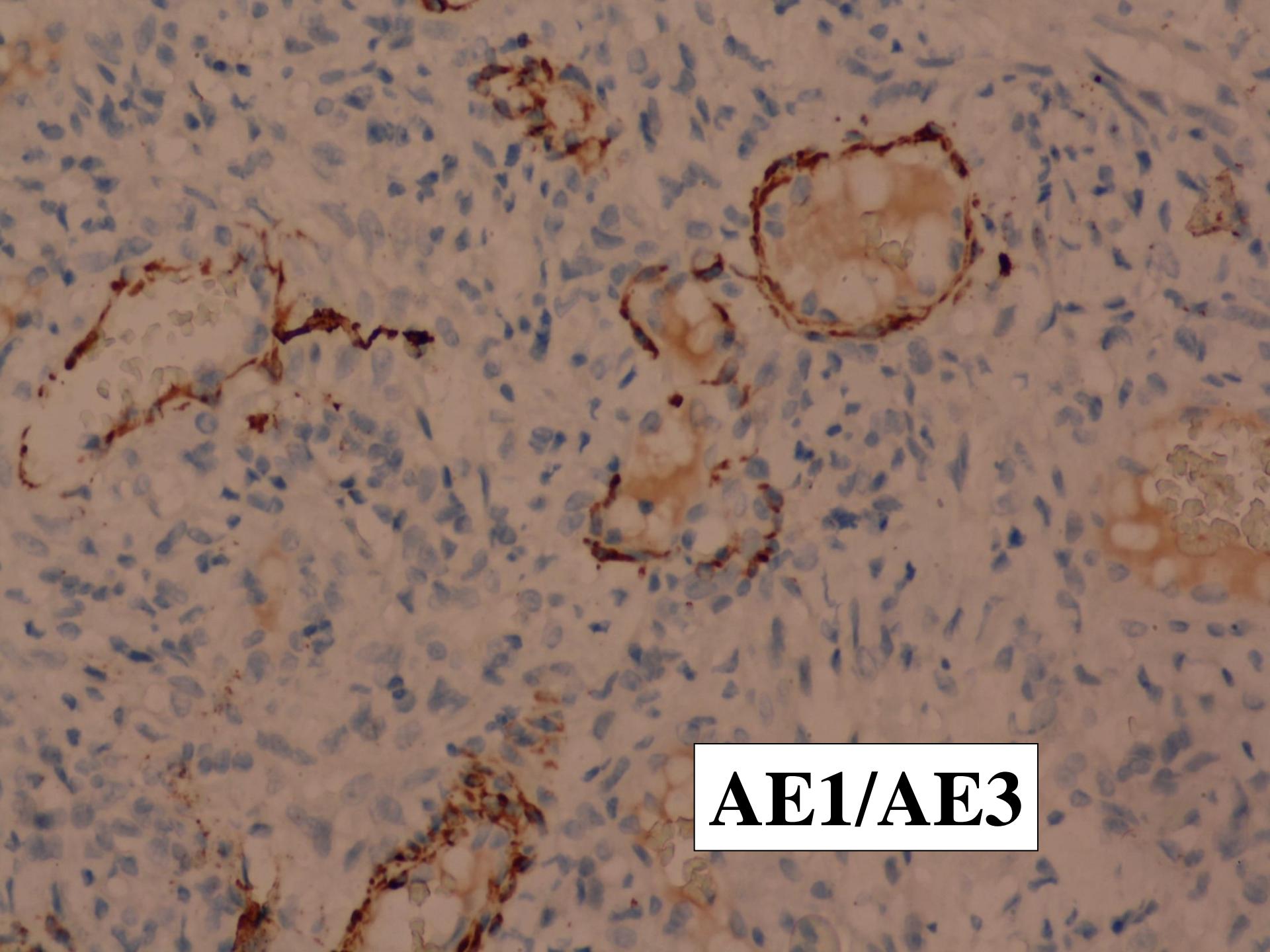




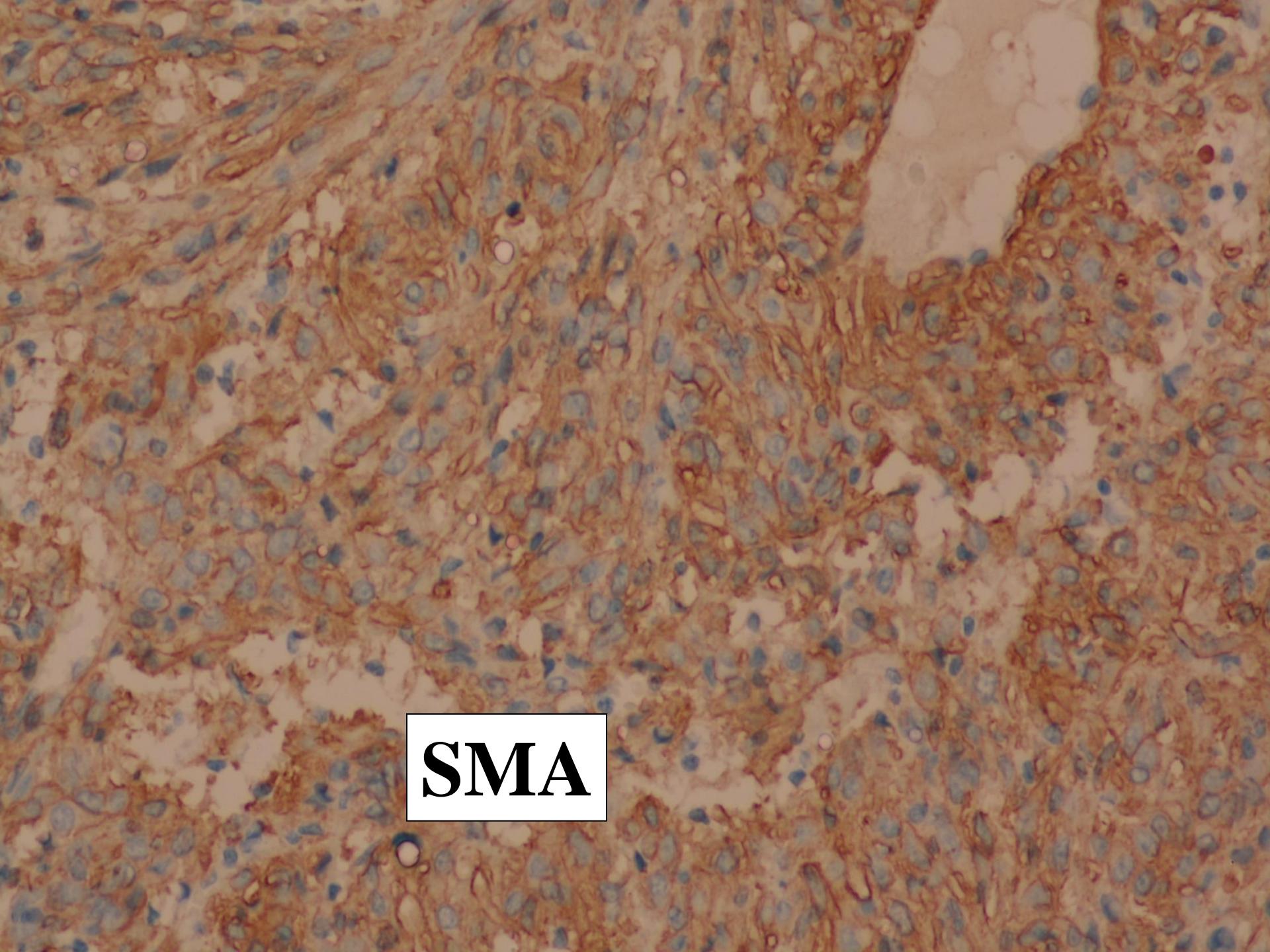


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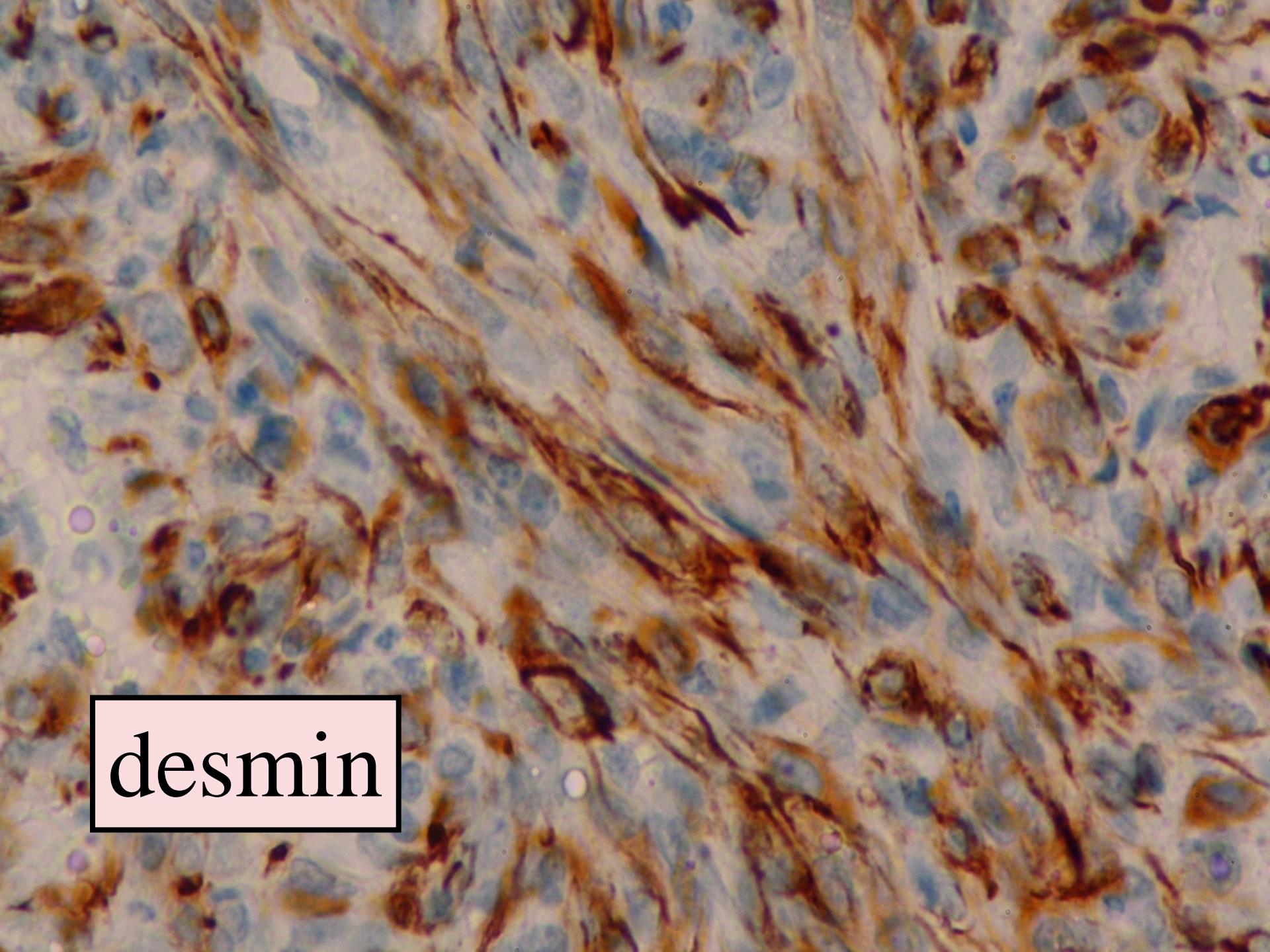




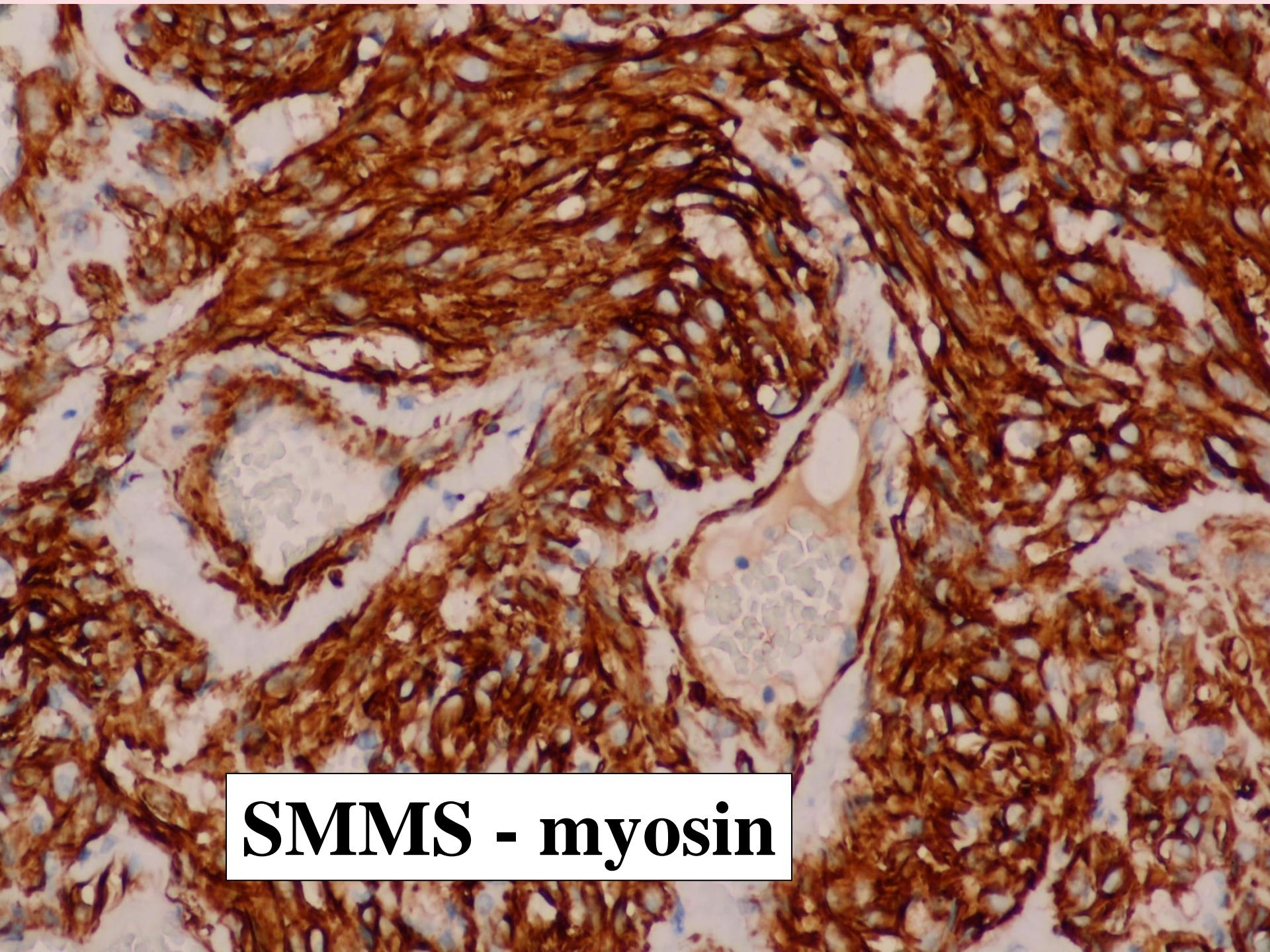
**AE1/AE3**

A histological slide showing a tissue sample with a dense network of red-stained fibers and scattered blue-stained nuclei. A white rectangular box in the lower-left corner contains the text "SMA".

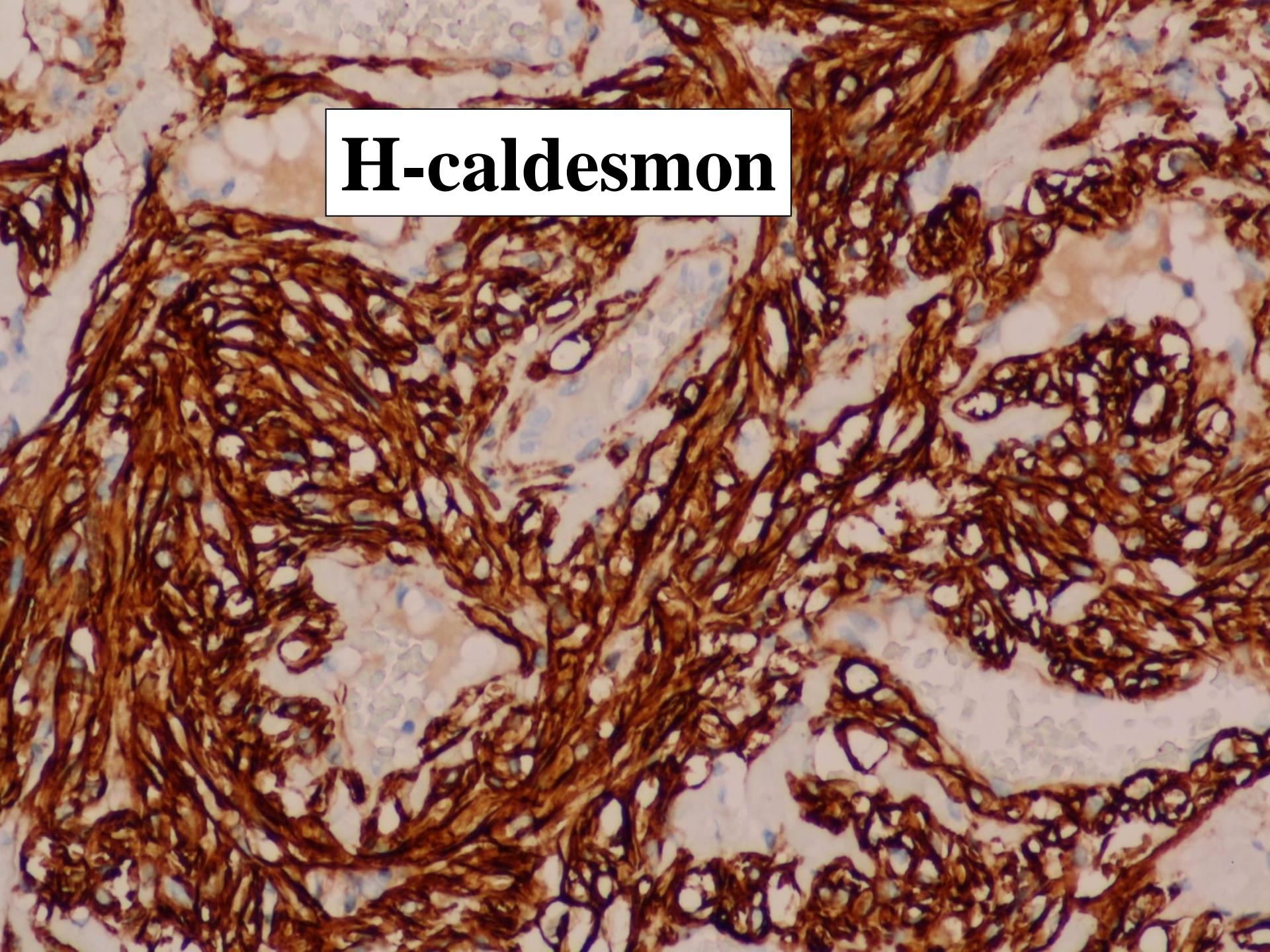
**SMA**

A light micrograph showing a tissue section stained for the protein desmin. The cytoplasm of the muscle fibers exhibits a distinct brown coloration, indicating the presence of desmin. The nuclei are stained blue, likely with hematoxylin. A white rectangular box in the bottom-left corner contains the word "desmin" in a black serif font.

desmin

A histological section stained with SMMS-myosin. The tissue shows various cellular components, with prominent brown staining indicating the presence of myosin protein. The staining is more concentrated in certain cells, particularly those with more extensive cytoplasmic processes.

**SMMS - myosin**

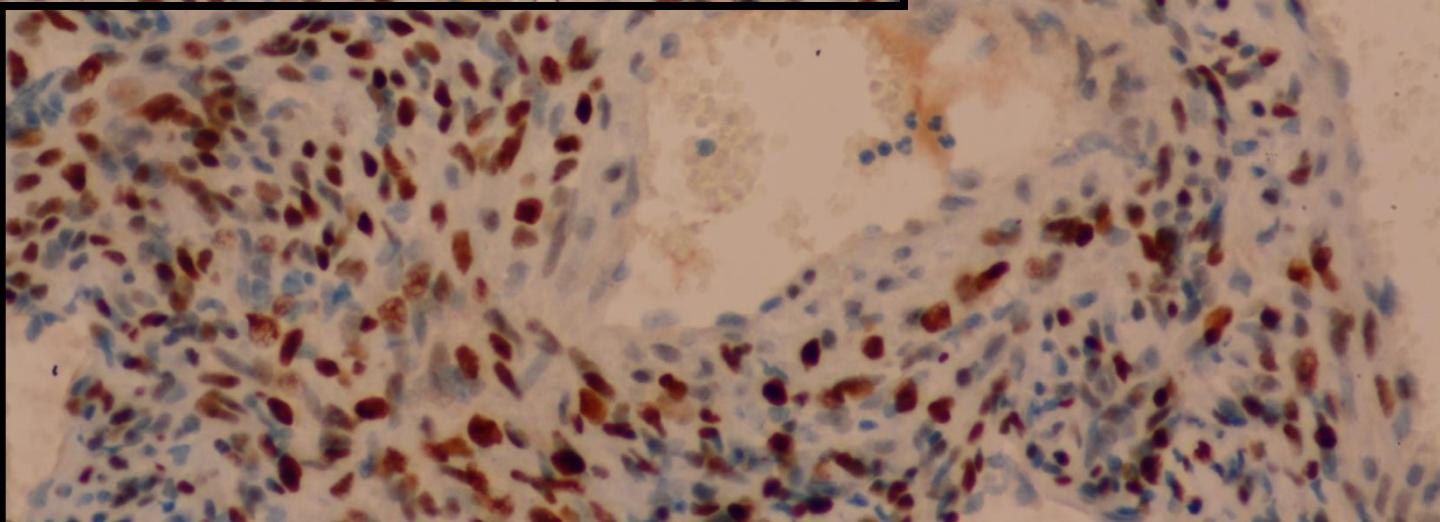
A histological section showing various tissue structures. The image is dominated by large, irregularly shaped areas of brown staining, likely representing connective tissue or cellular components. Interspersed among these brown areas are smaller, more uniform, light blue-grey regions, possibly representing different types of tissue or cellular components. The overall pattern is somewhat mottled and lacks a clear, organized structure.

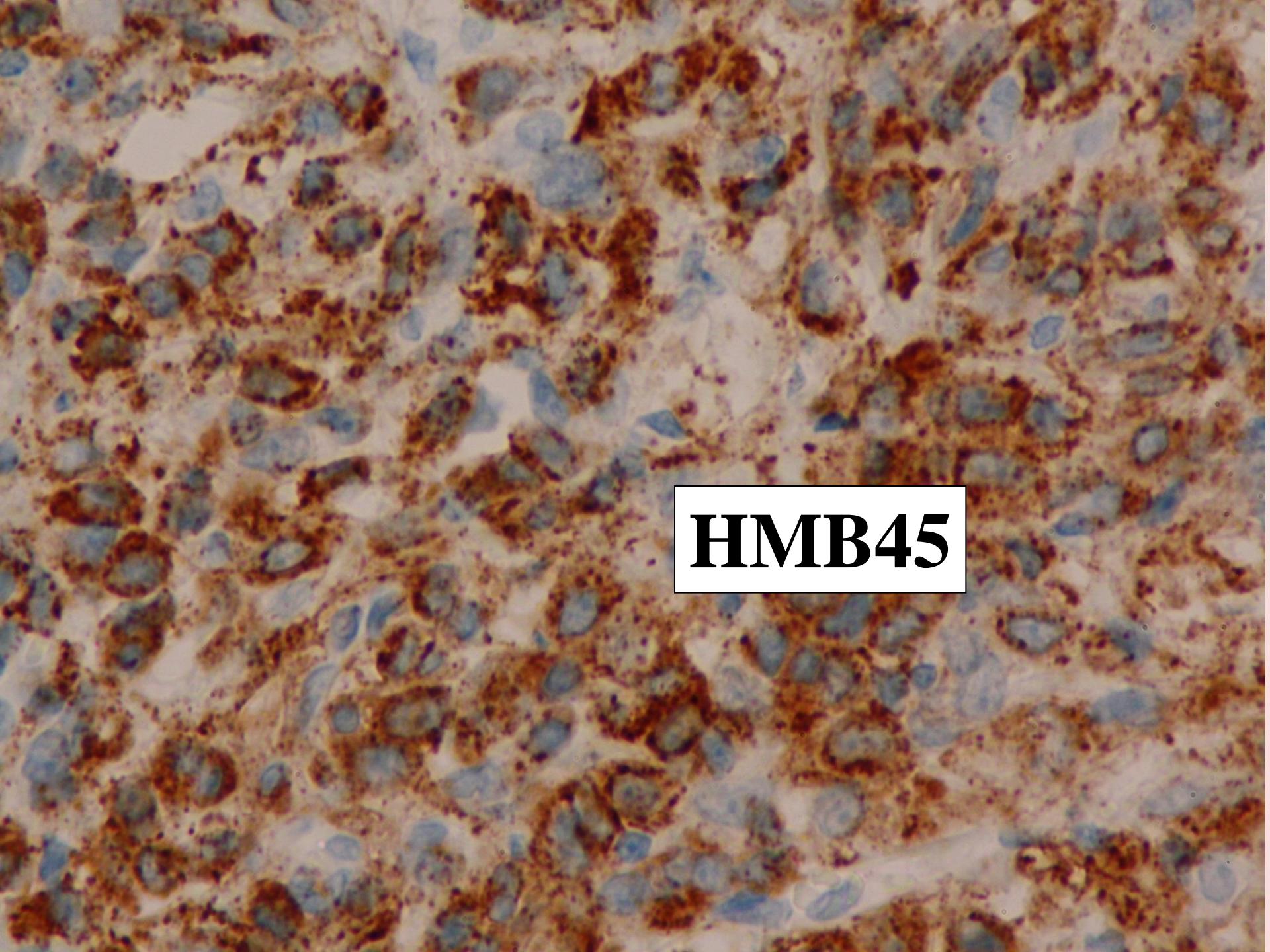
**H-caldesmon**

**PR**

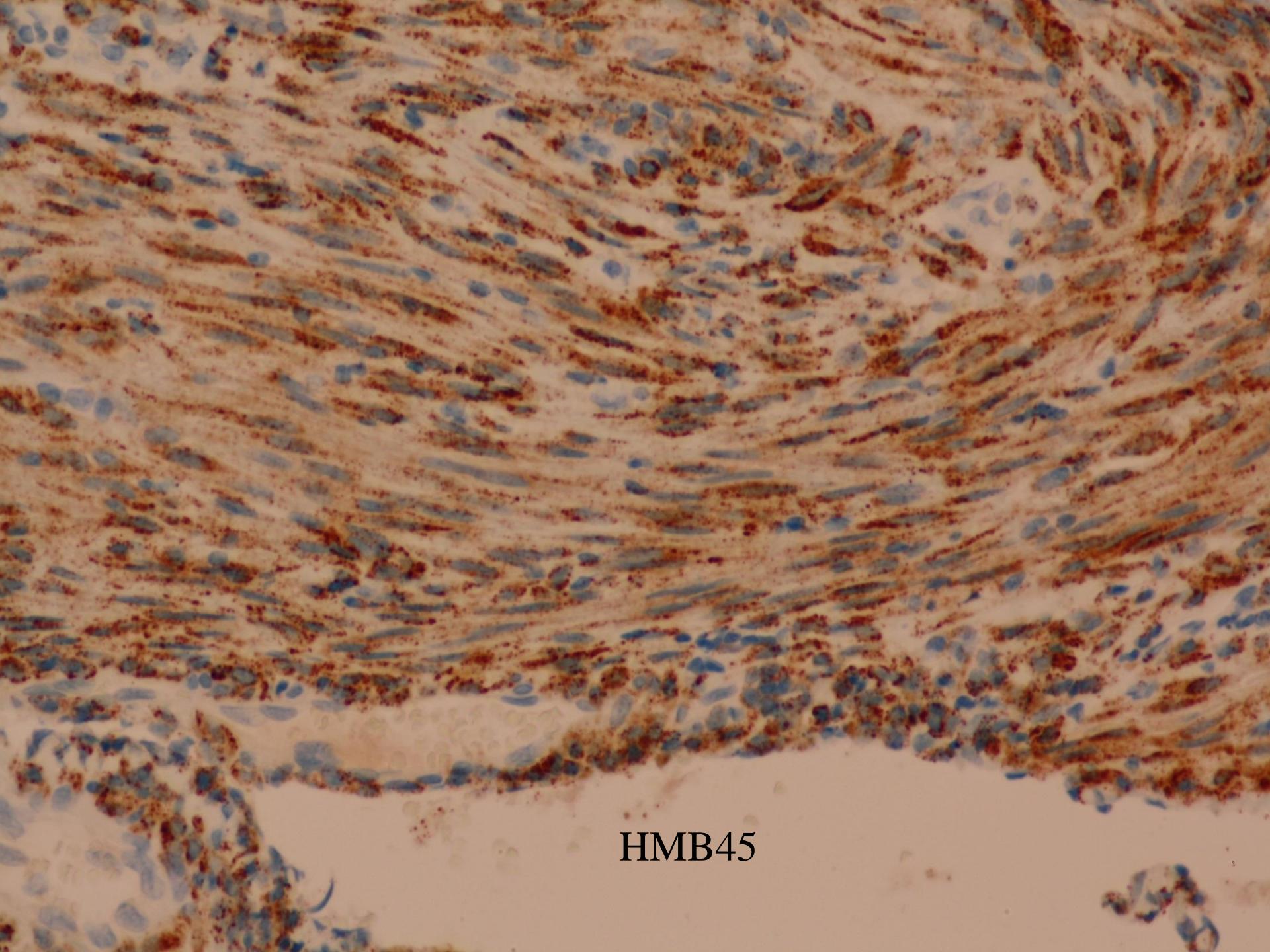
This panel shows a wide-field immunohistochemical stain of a tissue section. A large, irregularly shaped cluster of cells in the center-right is stained a bright orange-red color, indicating positive expression of the target protein. The surrounding tissue consists of smaller, more uniform cells with brown and blue staining. A white rectangular box in the upper-left corner contains the letters "PR" in bold black font.

**ER**

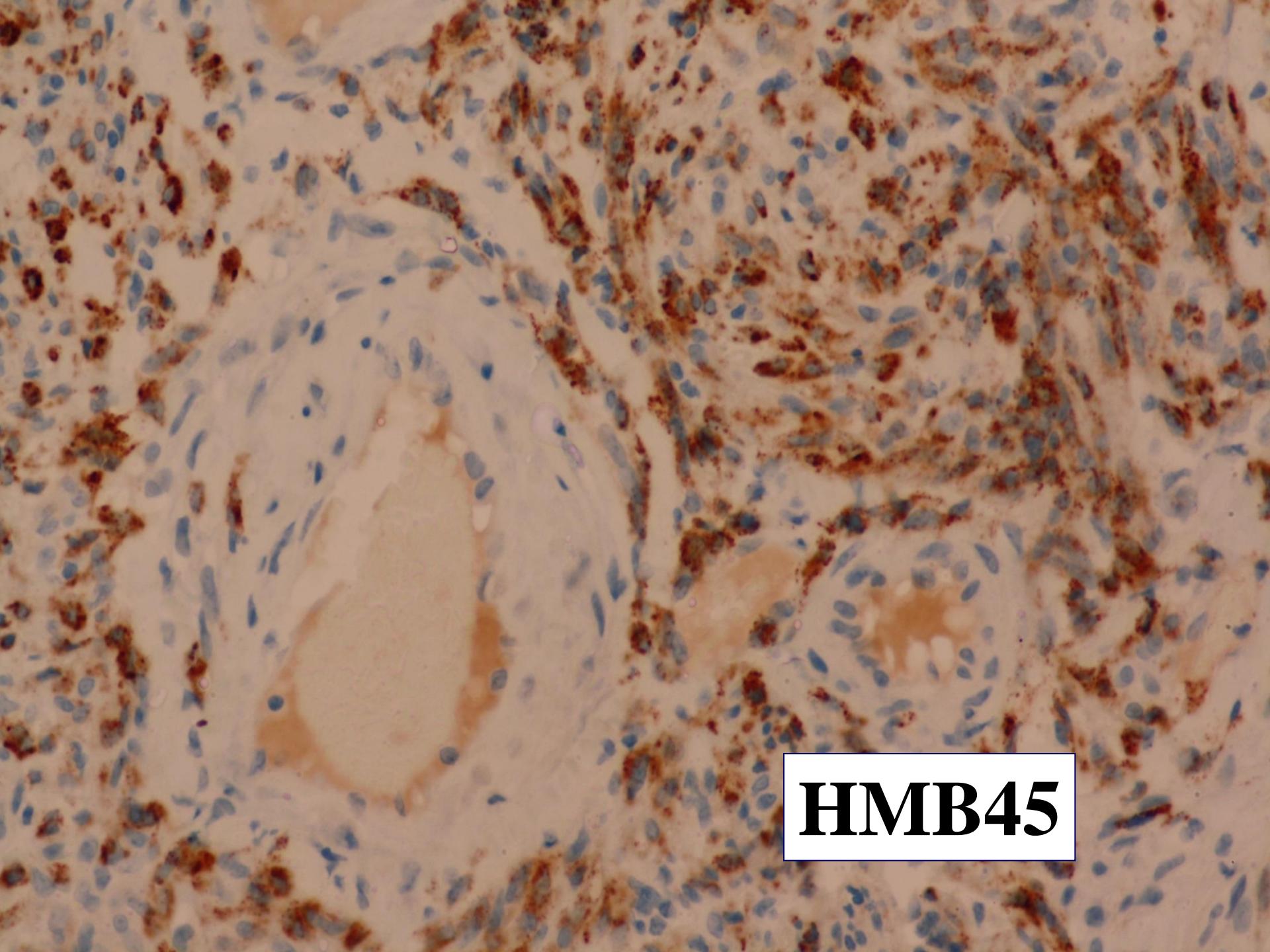
This panel shows a wide-field immunohistochemical stain of a tissue section. It features a prominent, roughly triangular cluster of cells in the lower-right quadrant, stained a bright orange-red. The rest of the tissue shows a mix of brown and blue staining. A white rectangular box in the upper-right corner contains the letters "ER" in bold black font.

This image shows a tissue sample under a microscope, likely a formalin-fixed paraffin-embedded (FFPE) section. The tissue consists of clusters of cells with dark blue nuclei and cytoplasm stained brown by hematoxylin. Interspersed among these are cells with more extensive brown staining, characteristic of melanoma. A white rectangular box is overlaid on the image, containing the text "HMB45" in a bold, black, sans-serif font.

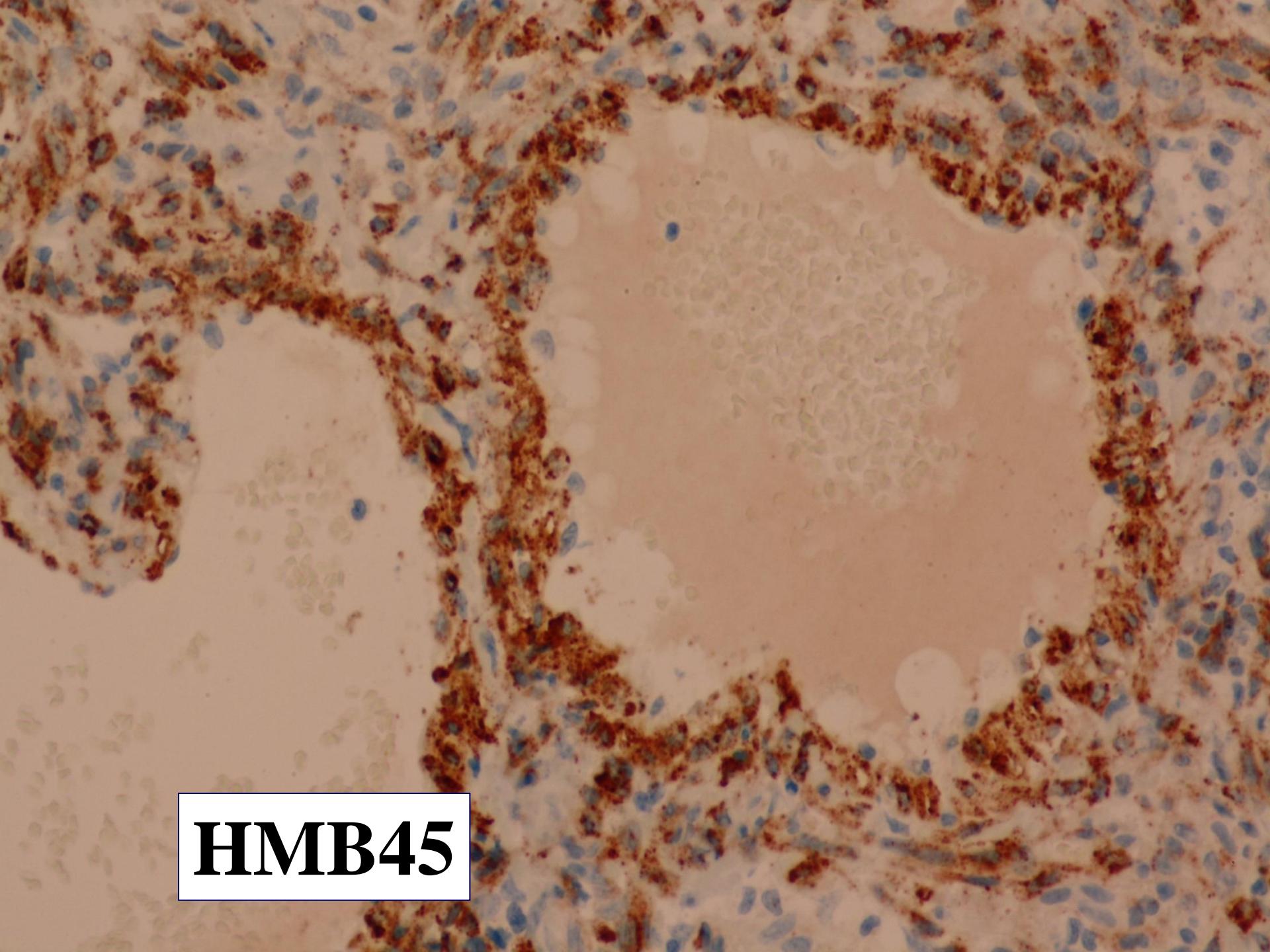
**HMB45**



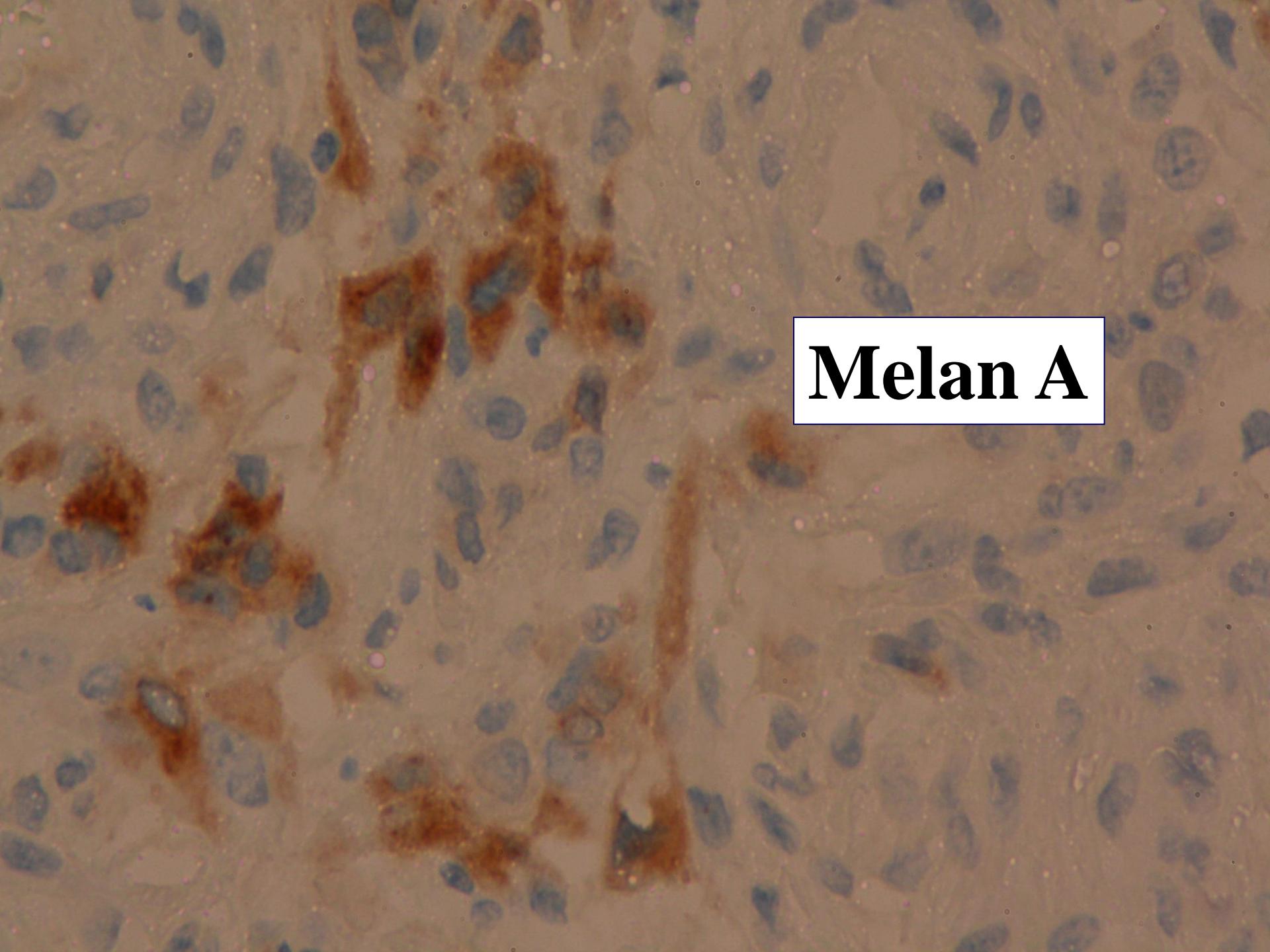
HMB45

This image shows a tissue section stained with HMB45 antibody. The staining is predominantly brown, indicating the presence of the antigen in the tumor cells. There are also some blue-stained nuclei, likely from hematoxylin counterstain. The overall pattern is somewhat mottled, with brown staining appearing in clusters and individual cells.

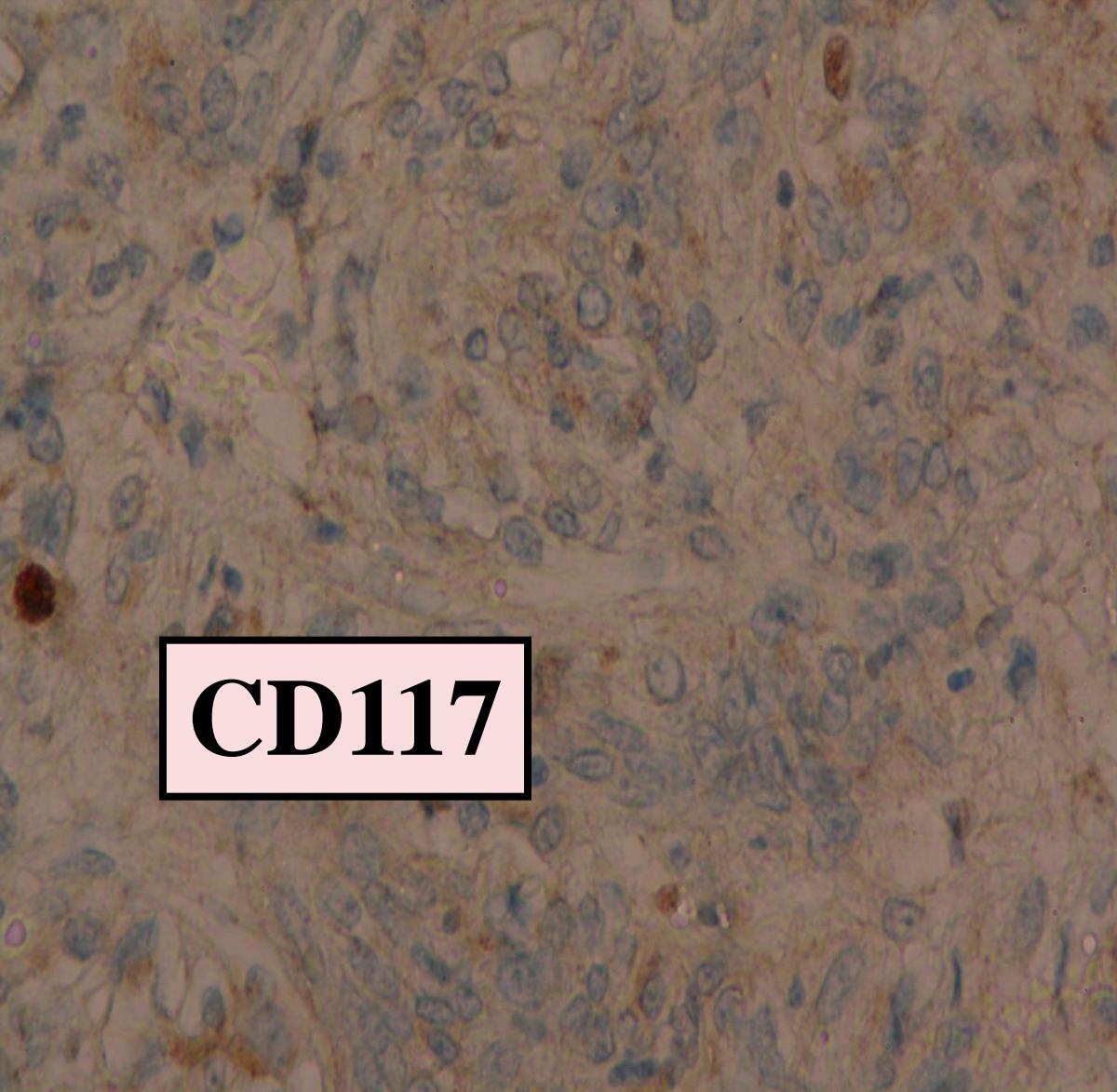
**HMB45**

A high-magnification immunohistochemical (IHC) image showing a tissue section. The majority of the cells exhibit a pale, yellowish-brown cytoplasmic staining, characteristic of a low-grade tumor. Interspersed among these are several cells with a more intense, dark reddish-brown staining, which is a hallmark of melanoma cells. A prominent feature is a large, clear, vacuolated cell located in the lower right quadrant. In the bottom left corner, there is a white rectangular box containing the text "HMB45".

**HMB45**

A light micrograph showing several clusters of brown, granular material, likely melanin, interspersed among numerous small, dark blue-stained nuclei. The overall background is a pale, mottled grey.

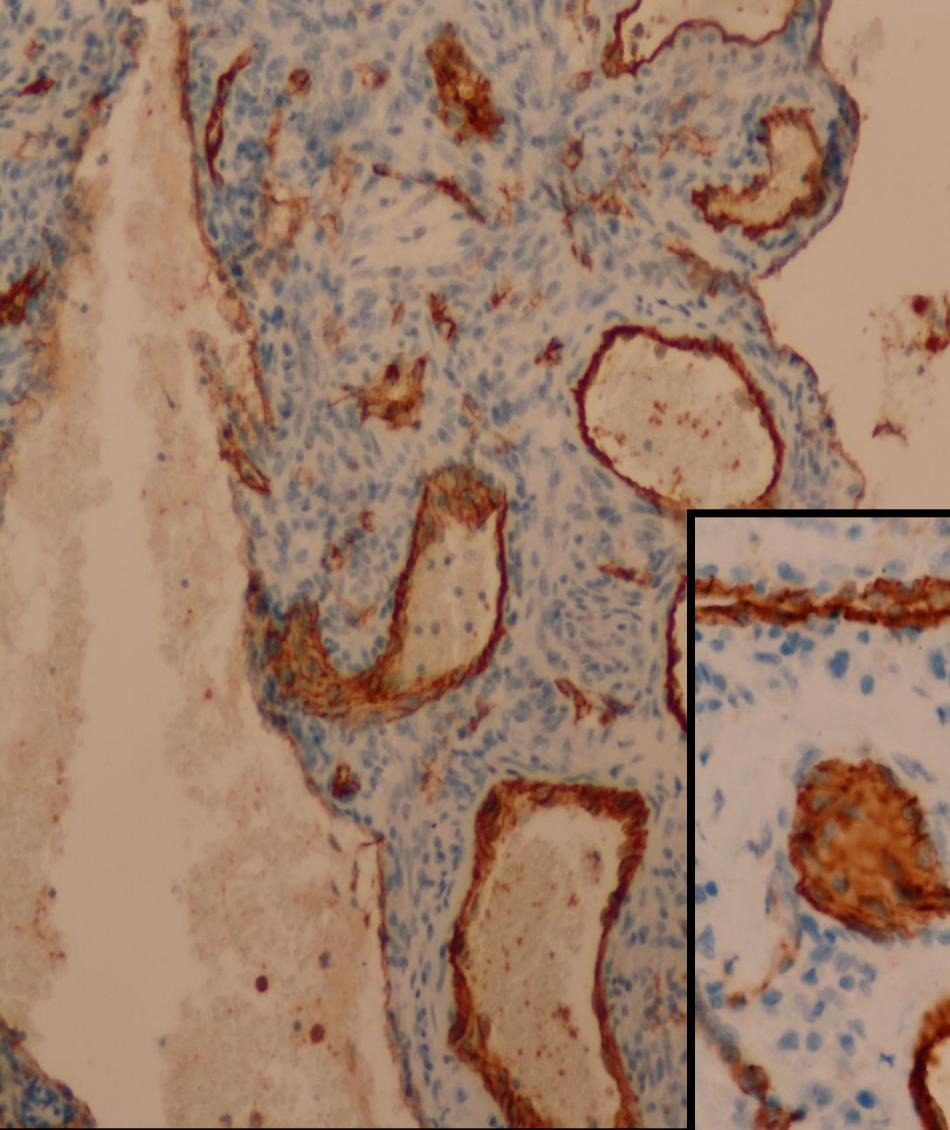
**Melan A**



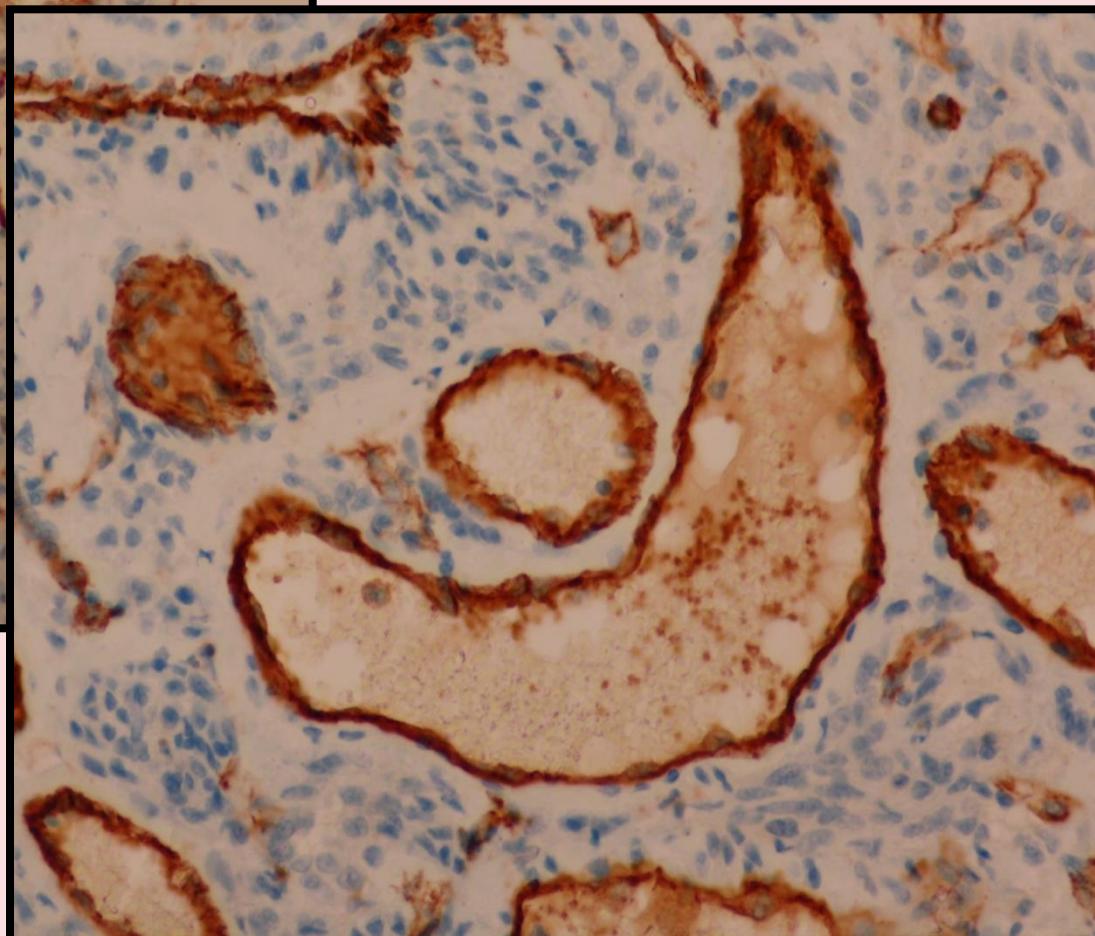
**CD117**

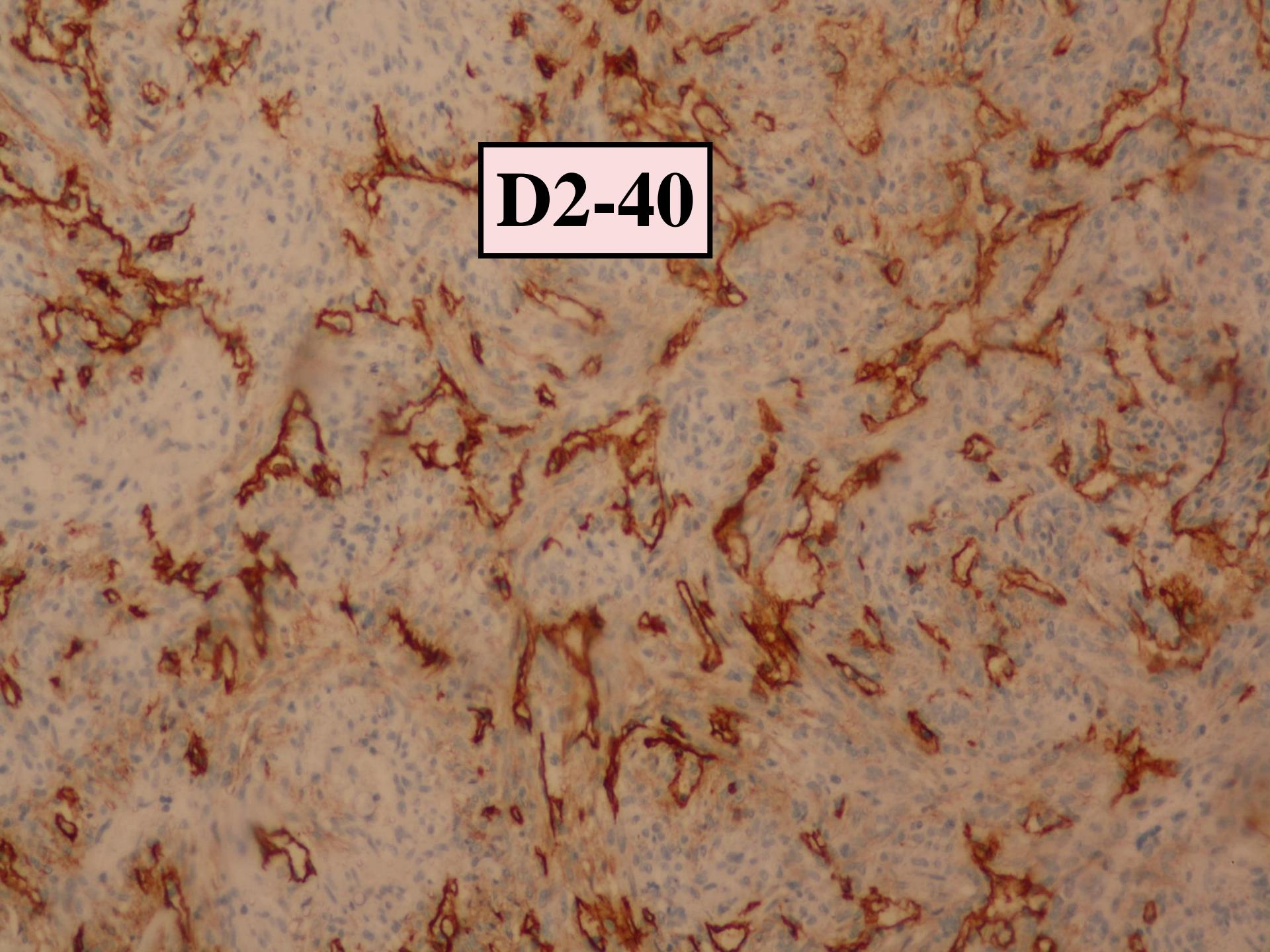


**CD34**

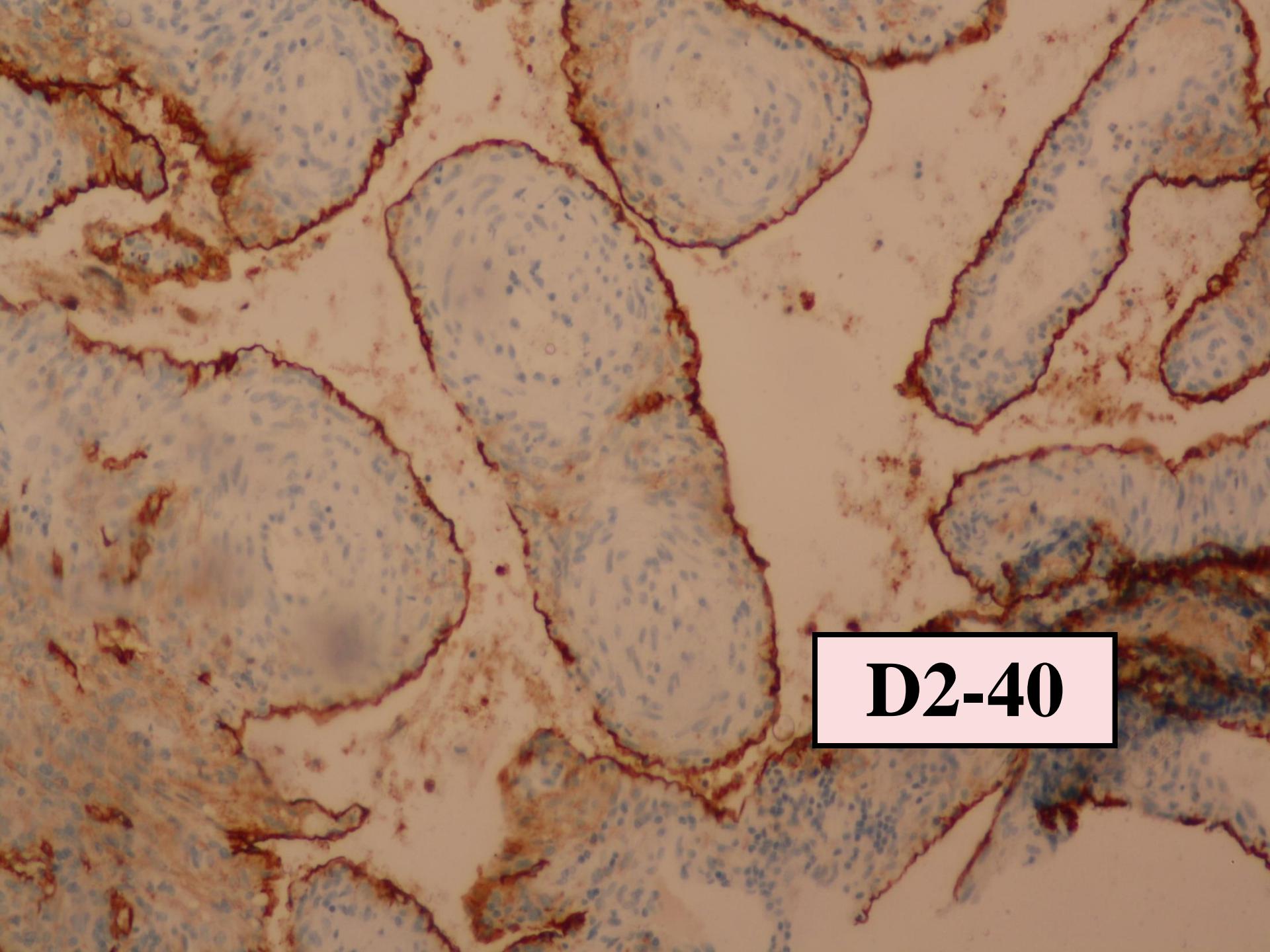


**CD31**



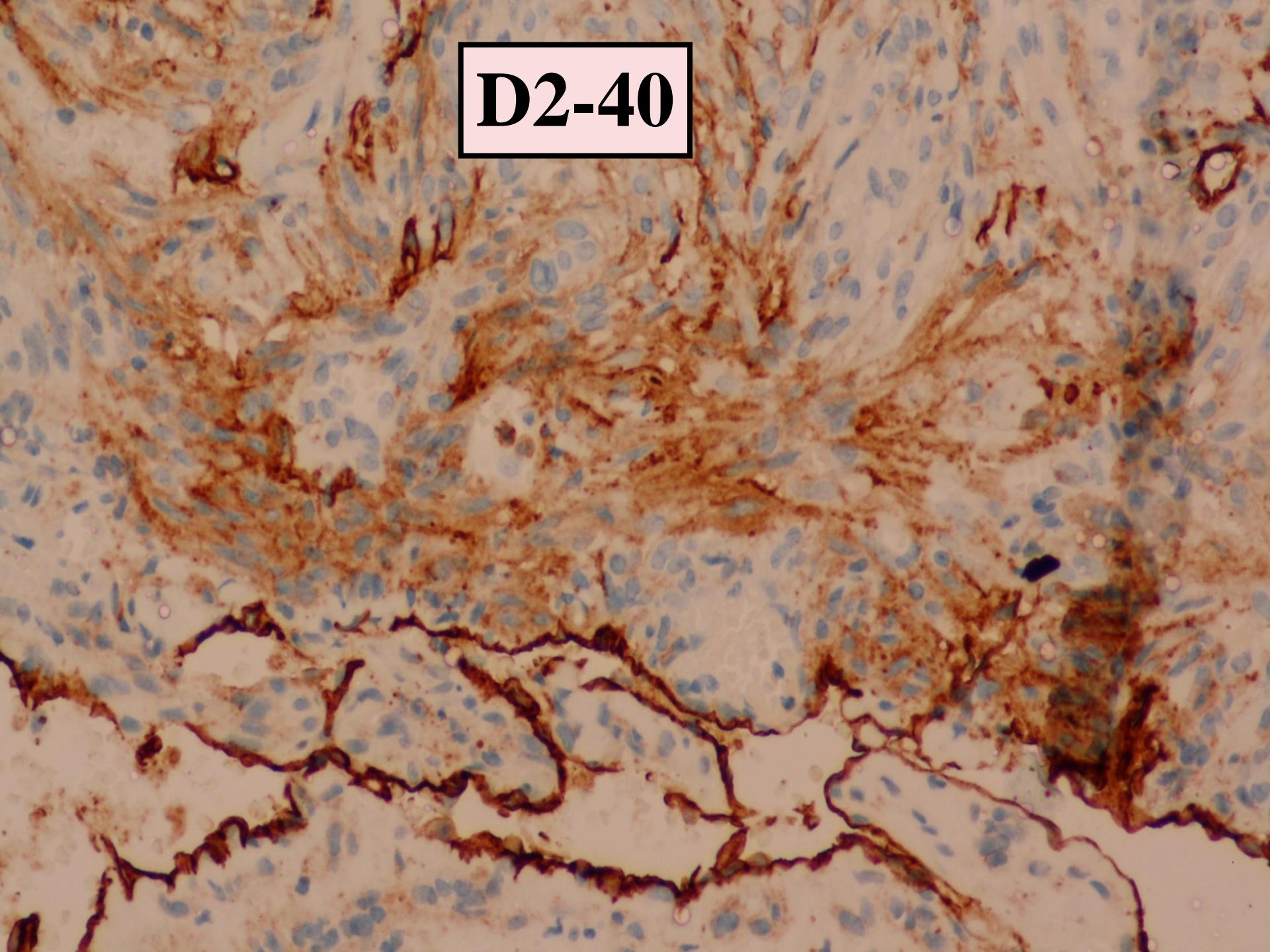


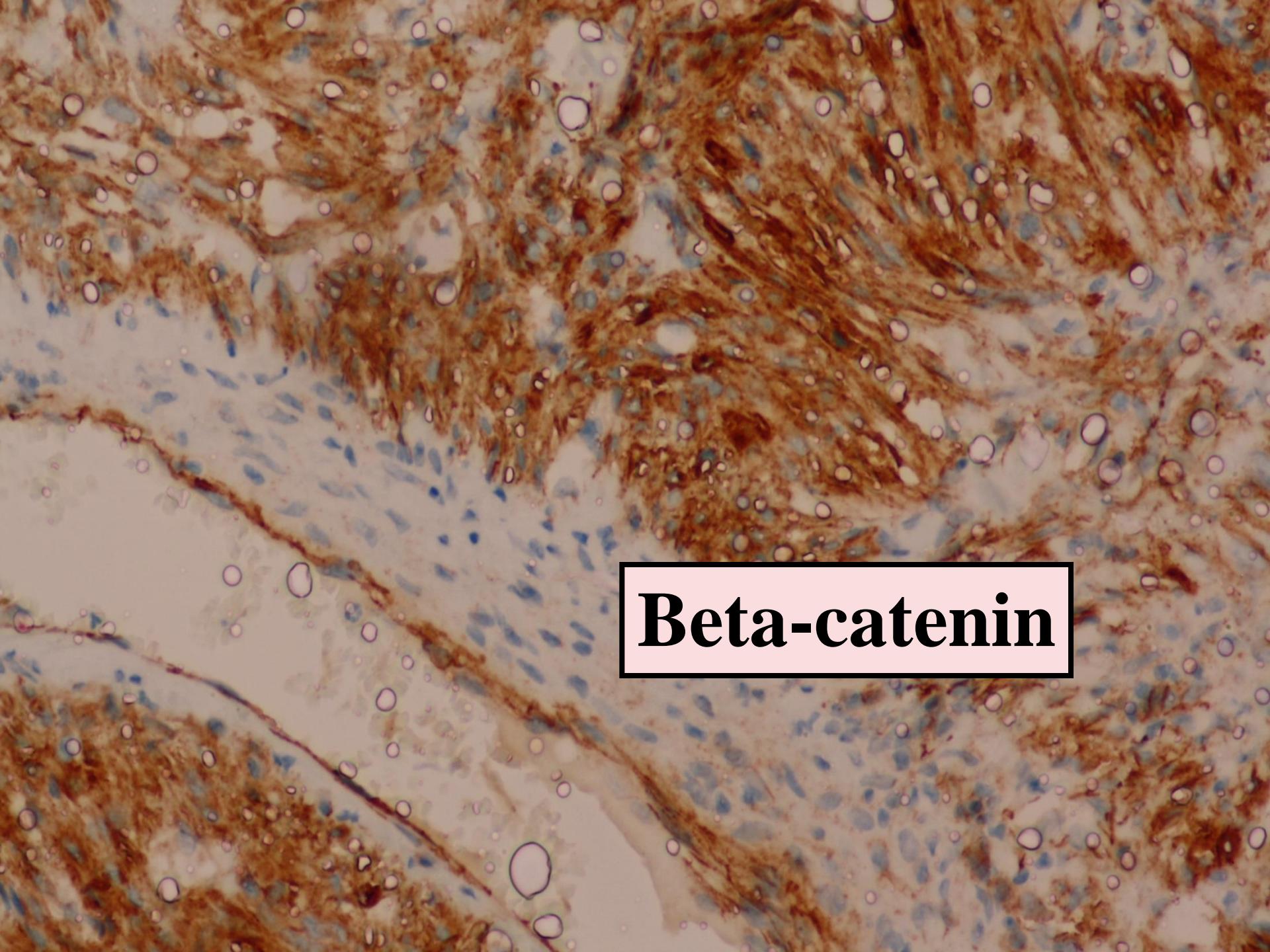
D2-40



D2-40

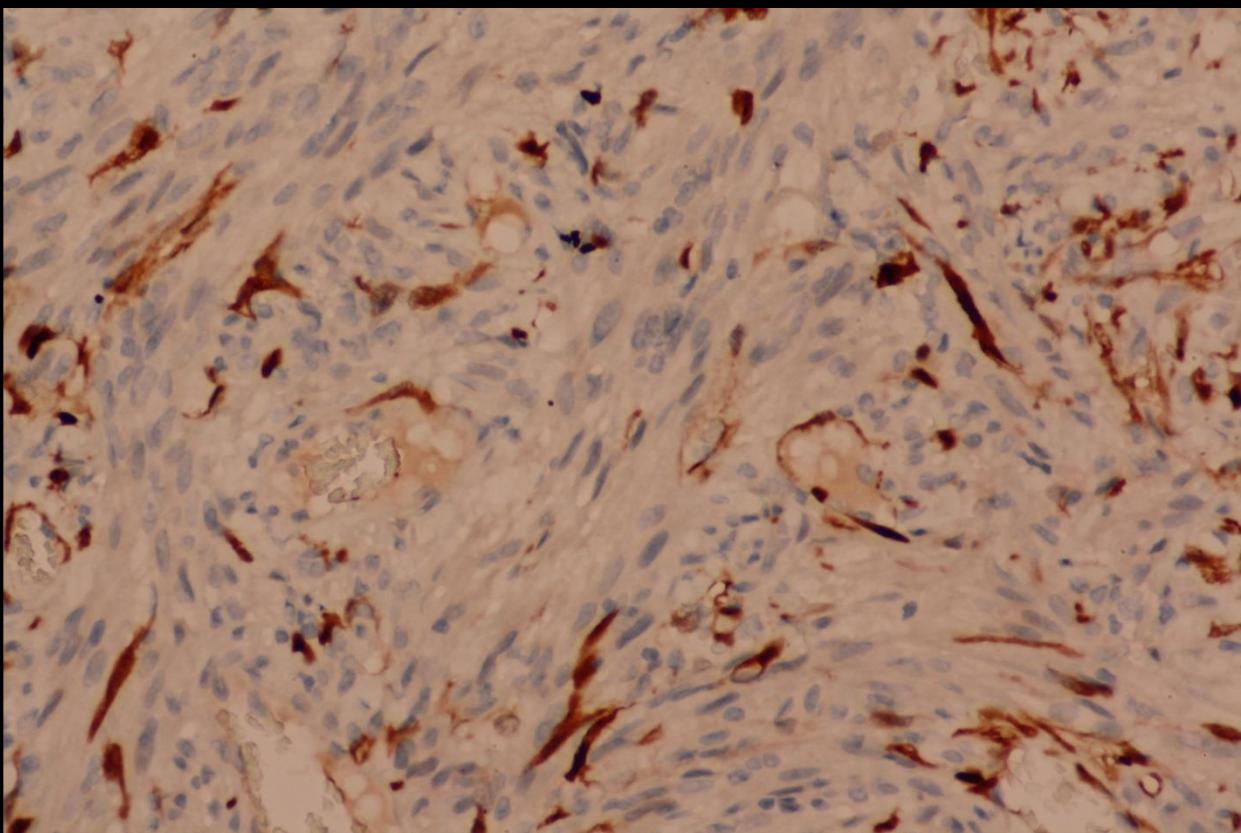
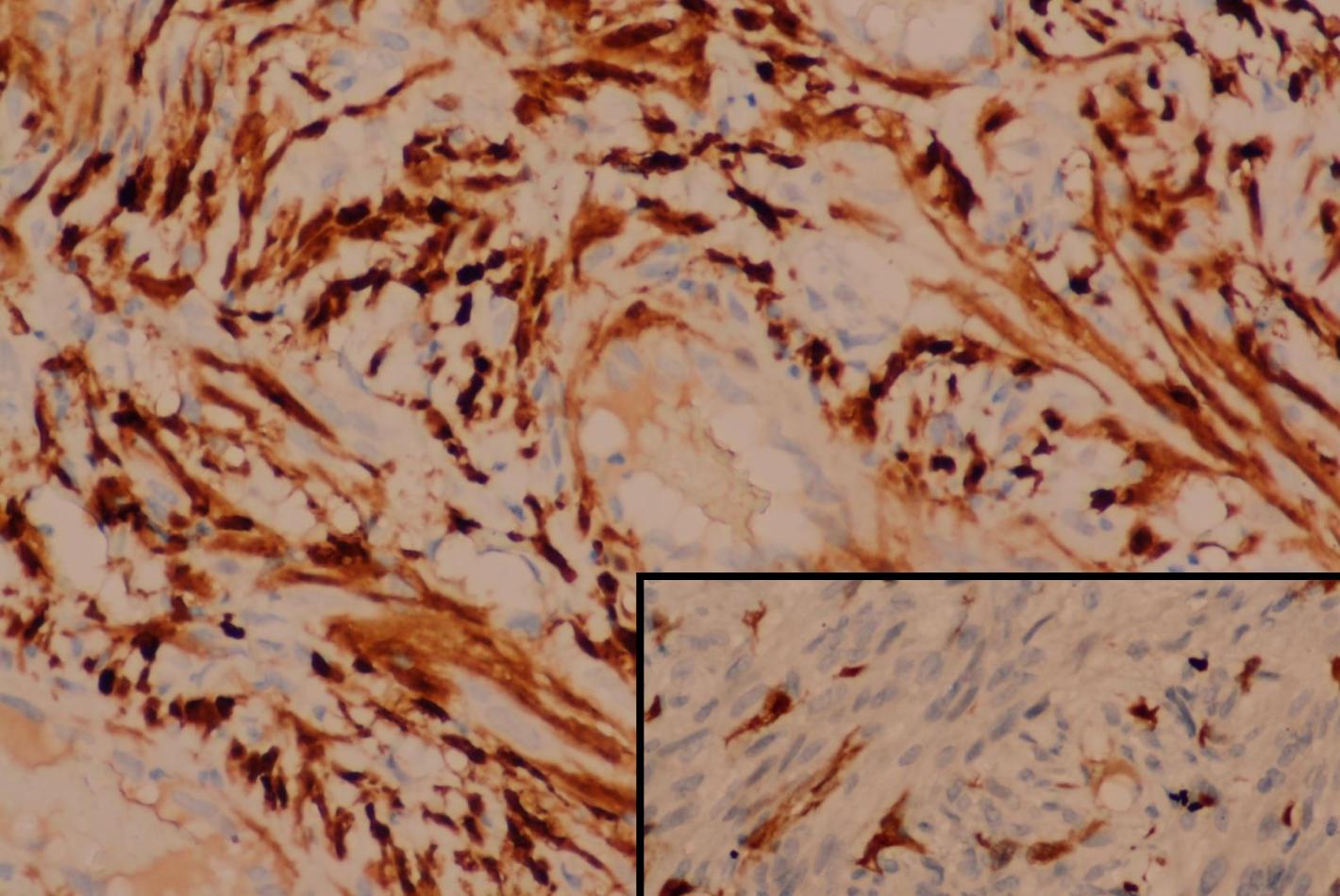
D2-40



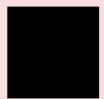
This image shows a tissue section stained with an antibody against Beta-catenin. The staining is brown and highlights various cellular structures, particularly along the boundaries of tissue compartments. A white rectangular box with a black border is overlaid on the image, containing the text "Beta-catenin".

**Beta-catenin**

**p16**



?



**LYMPHANGIOLEIOMYOMA /  
LYMPHANGIOMEIOMYOMATOSIS  
(LAM)**

# Zhrnutie / Záver patológia

- V klinicko-patologickej korelácii sa jedná o extrapulmonárne lymphangioleiomyómy / lymphangioleiomyomatózu (LAM) situované v malej panve a v retroperitoneu.
- Doporučujeme ďalšie vyšetrenia, najmä respiračného traktu.

# DEFINÍCIA (extrapulmonárne LAM)

- *WHO soft tissue*
- **LAM** patrí do **PEComa family**  
(angiomyolipoma/AML, clear cell sugar tumour of the lung/CCST, LAM and „a group of histologically and immunophenotypically similar tumours arising at variety of soft tissue and visceral sites“
  - ICD-O-codes
- PEComa                                    8714/0
- Malignant PEComa                    8714/3

# DEFINÍCIA

- Miettinen
- LAM is a *smooth muscle proliferation* of the ***lymphatic vessels and lymph nodes*** related to angiomyolipomas

# DEFINÍCIA

*Enzinger*

*Soft tissue tumors*

LAM – proliferation of ***PECs*** around  
**lymphatics and lymph nodes** of the  
mediastinum, retroperitoneum and  
pulmonary interstitium

# DEFINÍCIA

- Clement, Young

Uterine PEComas:

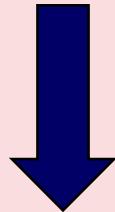
- in 15% of case evidence of tuberous sclerosis and/or lymphangioleiomyomatosis

Lymphangioleiomyomatosis:

- some such patients have other stigmata of tuberous sclerosis

# Lymphangioleiomyoma(tosis) / LAM

- Proliferácia smooth muscle-like („hladkosvalovoidných“) bb



„LAM“ cells

# LAM cells

- Fenotyp čiastočne závislý od mikro prostredia
- Potencionálne metastatické (+/- prítomné v krví, seróznych tekutinách, moči)
  - **Pôvod**
- Hypotetický pôvod v hladkej svalovine ciev
- Mikrochimérizmus (???) – pôvodne bb./ DNA fetálneho pôvodu perzistujúce v tele matky

# LAM cells

## IHC markery

- Sladkosvalové (SMA, SMMH, desmin)
- HMB45, +/- Melan A
- ER/PR
- Metaloproteinázy
- $\beta$ -catenin ([Am J Clin Pathol.](#) 2011 May;)

# **Lymphangioleiomyoma(tosis) / LAM**

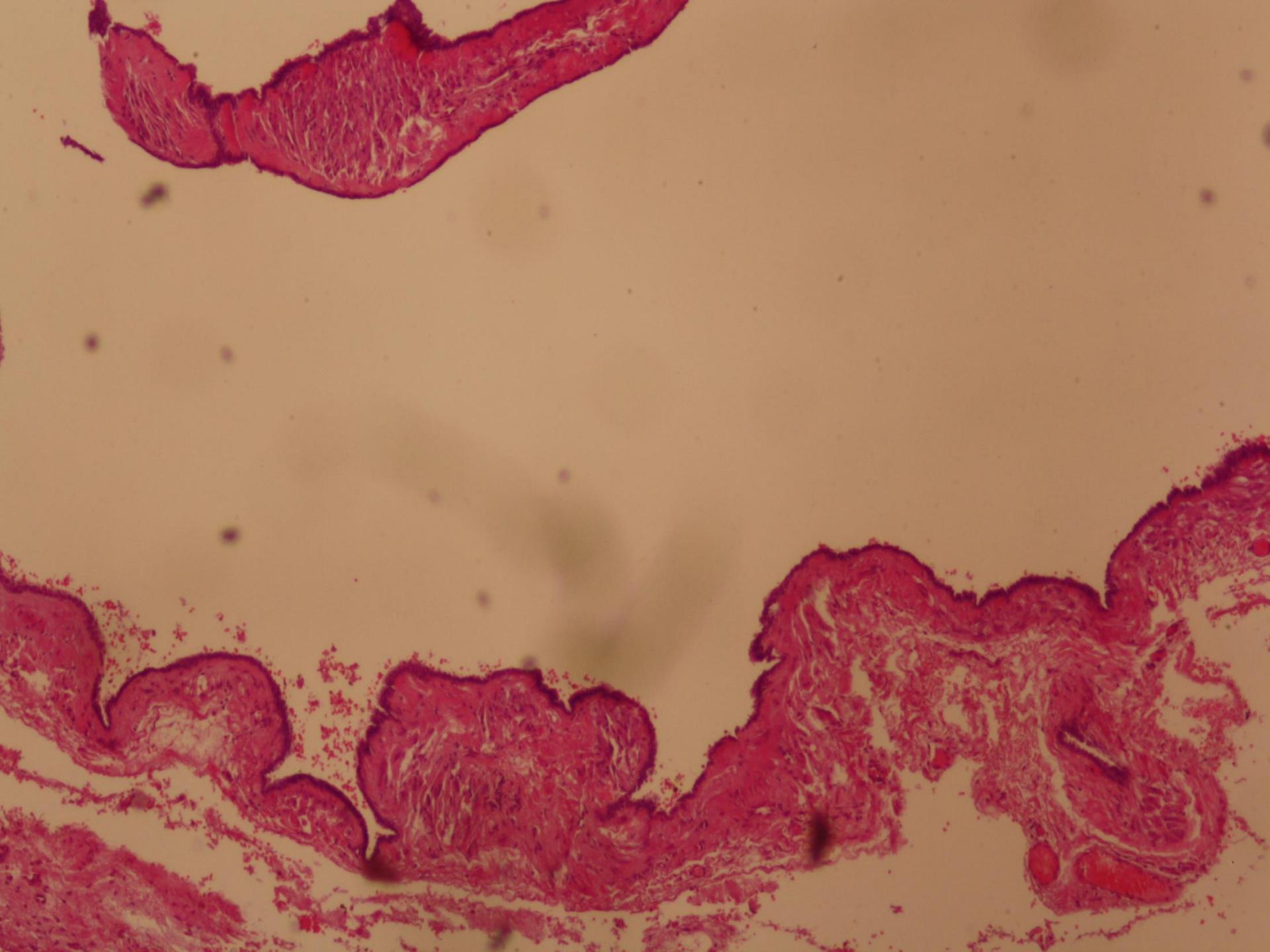
- Pulmonárna LAM
- Extrapulmonárna LAM (abdominálne tumory, postihnutie axiálnych LU)
- Kombinácia

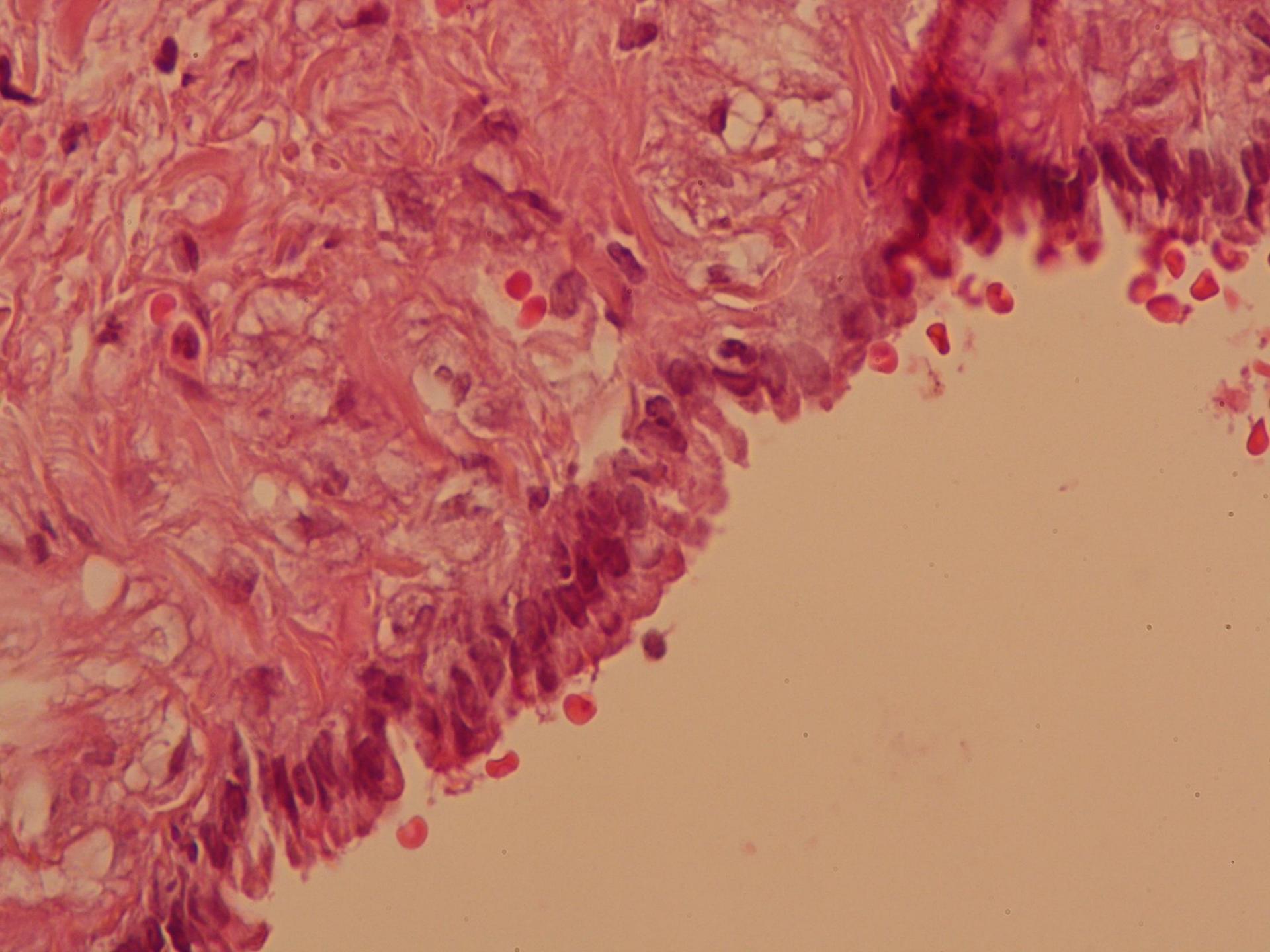
# **Lymphangioleiomyoma(tosis) / LAM**

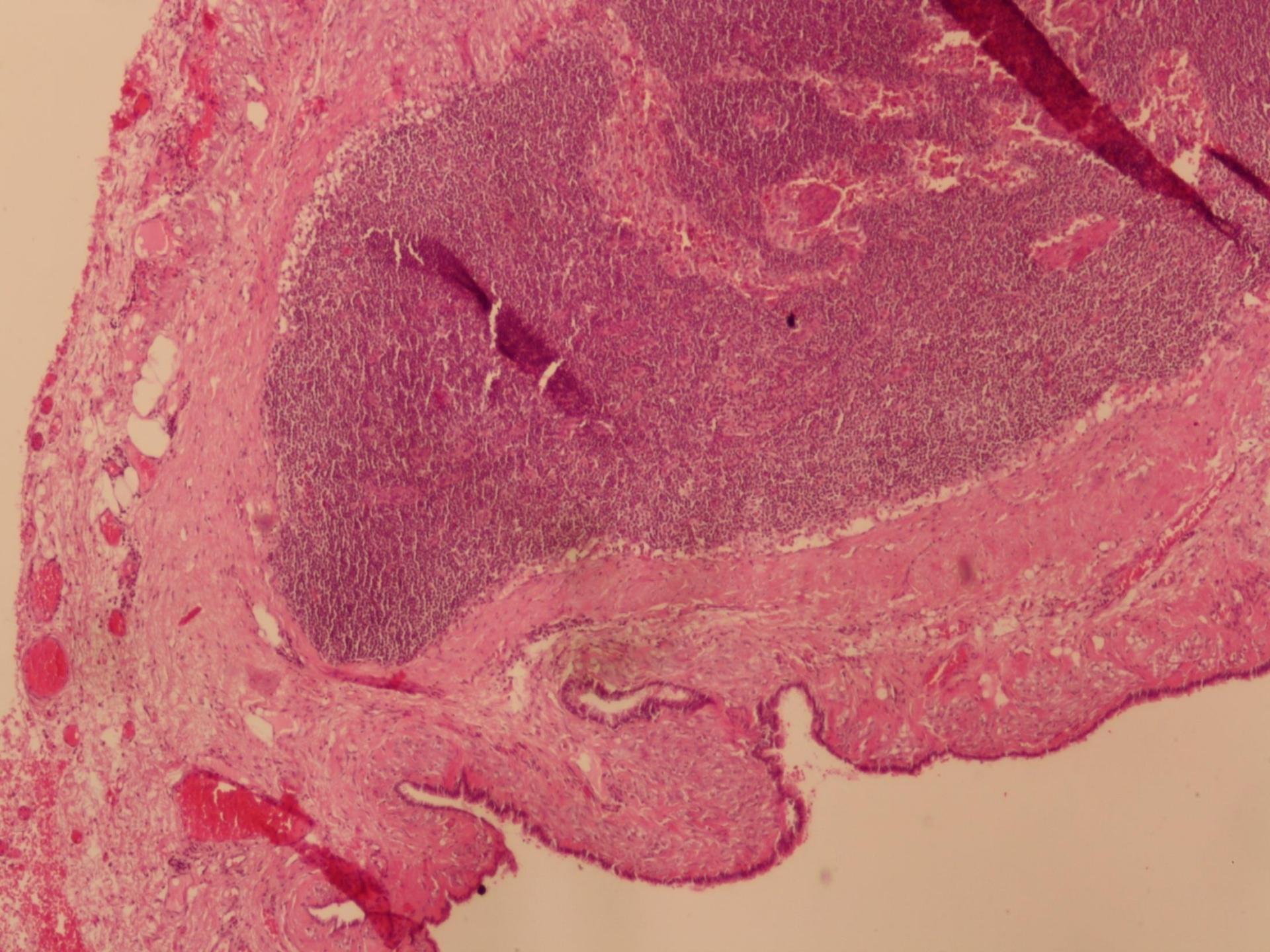
- **Formy asociované s tuberous sclerosis complex**
- vzácné multisystémové genetické, autozomálne dominantné ochorenie (mozog, obličky, koža, oči, srdce, pľúca, axiálne LU) – hamartoma-like tumory
- Mutácia génov TSC1, alebo TSC2, kódujúcich proteíny hamartín a tuberín
  
- **Formy sporadické**
- výskyt výhradne u žien zväčša v reprodukčnom veku
- Taktiež mutácia TSC1, alebo TSC2

- strata heterozygosity *TSC2* génu na 16. chromozóme
- pri sporadických LAM
- pri LAM asociovaných s tuberous sclerosis

# **Stena retroperitoneálnej cysty**

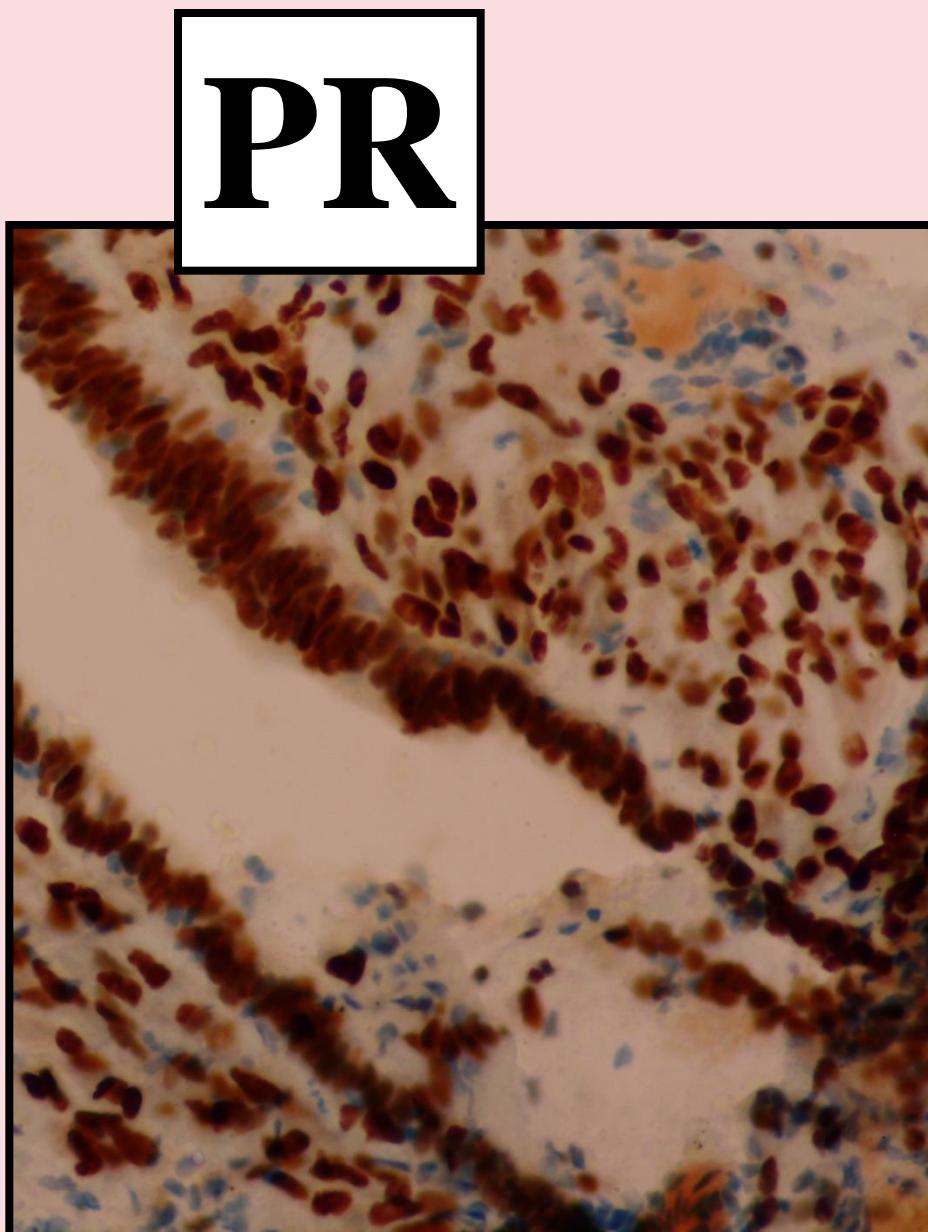
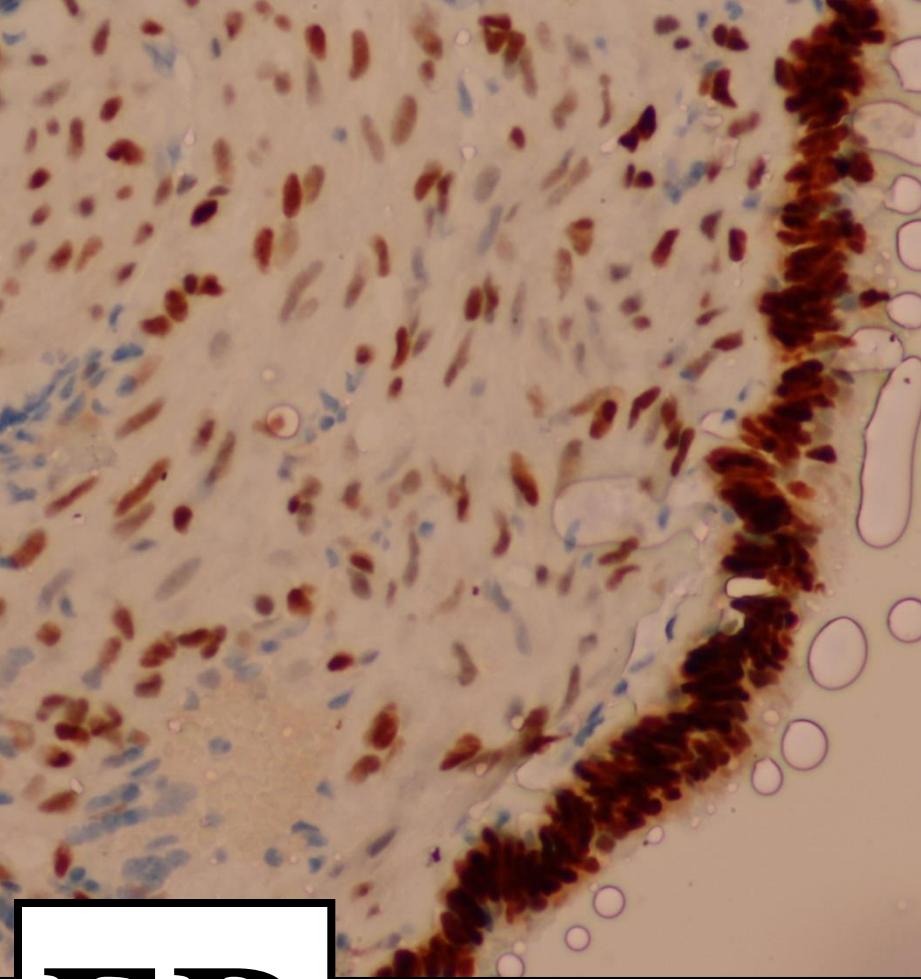


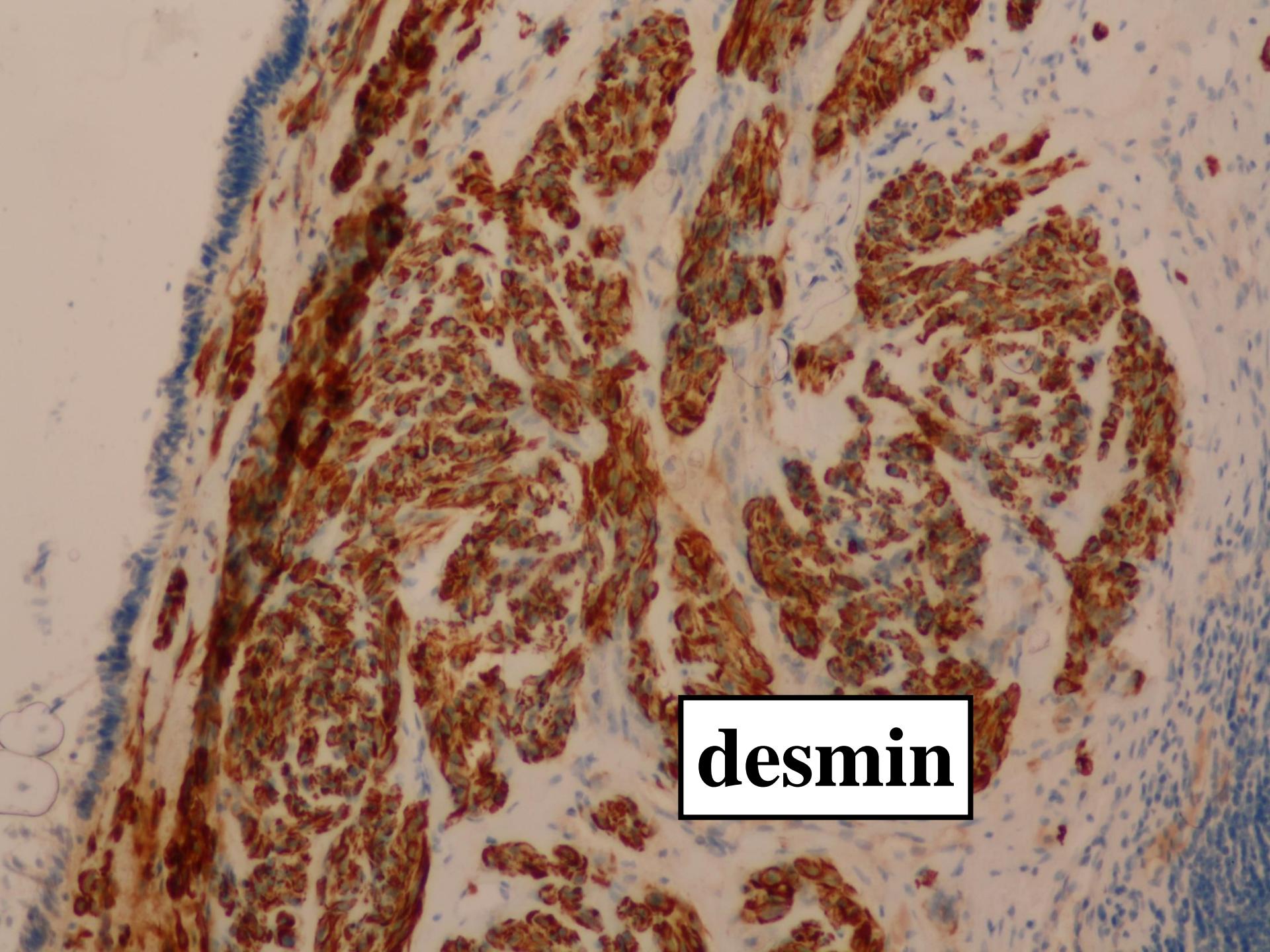




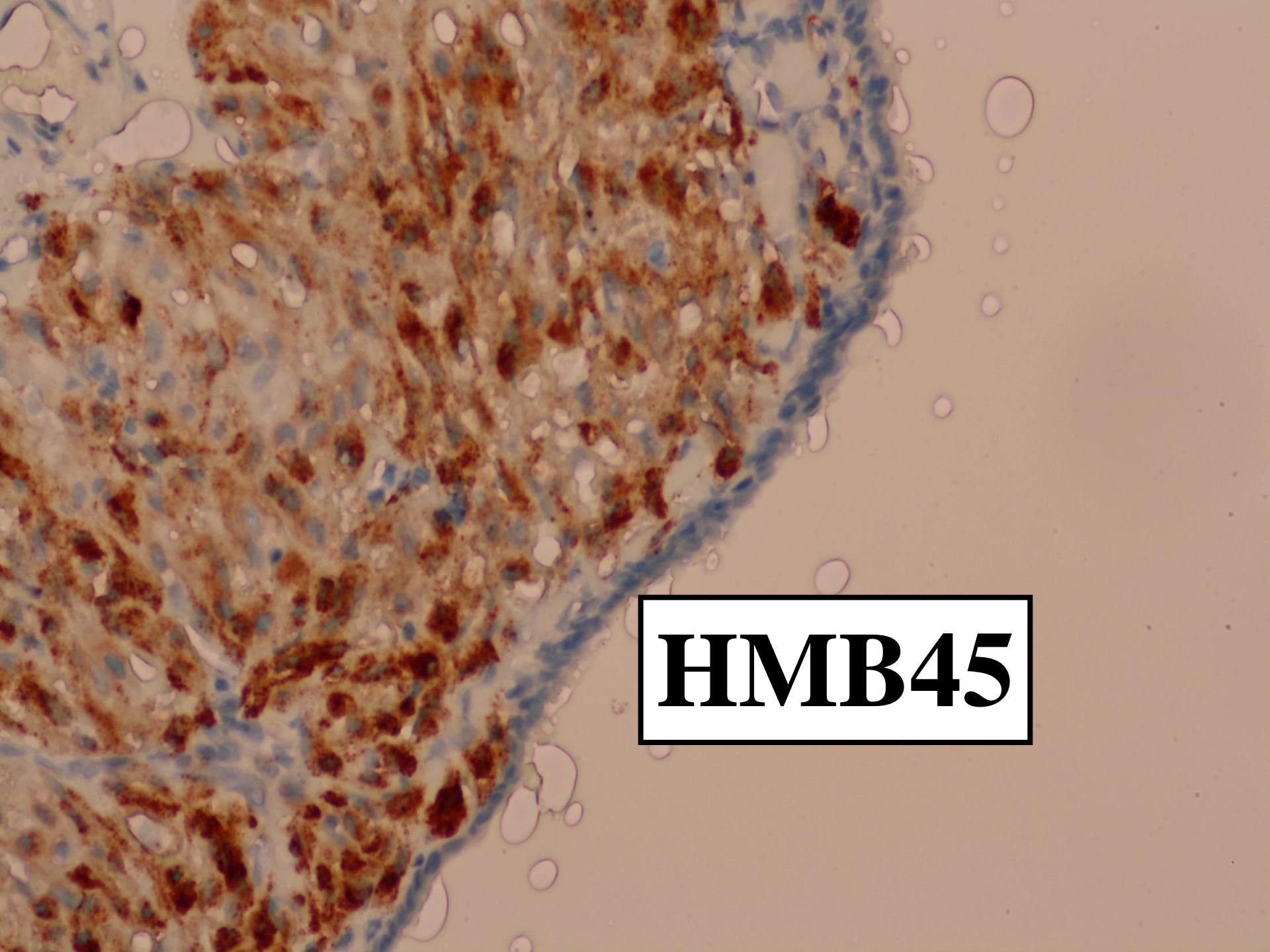
CK7

This image shows a tissue section stained for the cytokeratin marker CK7. The staining is localized to the apical portions of the epithelial cells lining the glandular structures, appearing as dark brown, granular deposits. The nuclei of these cells are stained blue with hematoxylin. The background shows a dense population of small, blue-stained nuclei. A white rectangular box with a black border contains the text "CK7" in a large, bold, black serif font.



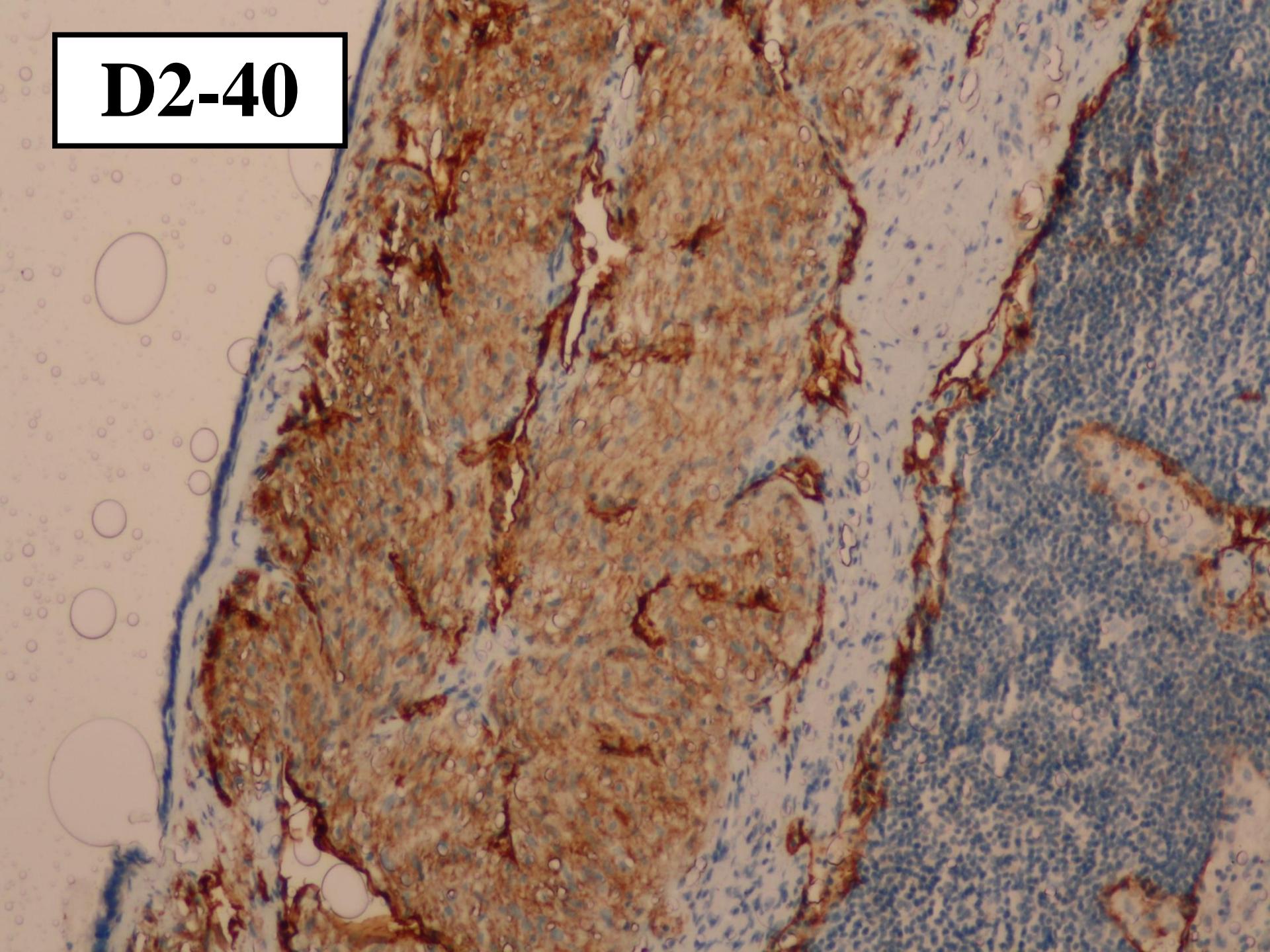
A light micrograph of a tissue section stained for the protein desmin. The stain is applied to the cytoplasm of muscle fibers, appearing as brownish-red patches against a blue-stained background. The muscle fibers are arranged in a somewhat disorganized, infiltrative pattern. A white rectangular box is overlaid on the image, containing the word "desmin" in a bold, black, sans-serif font.

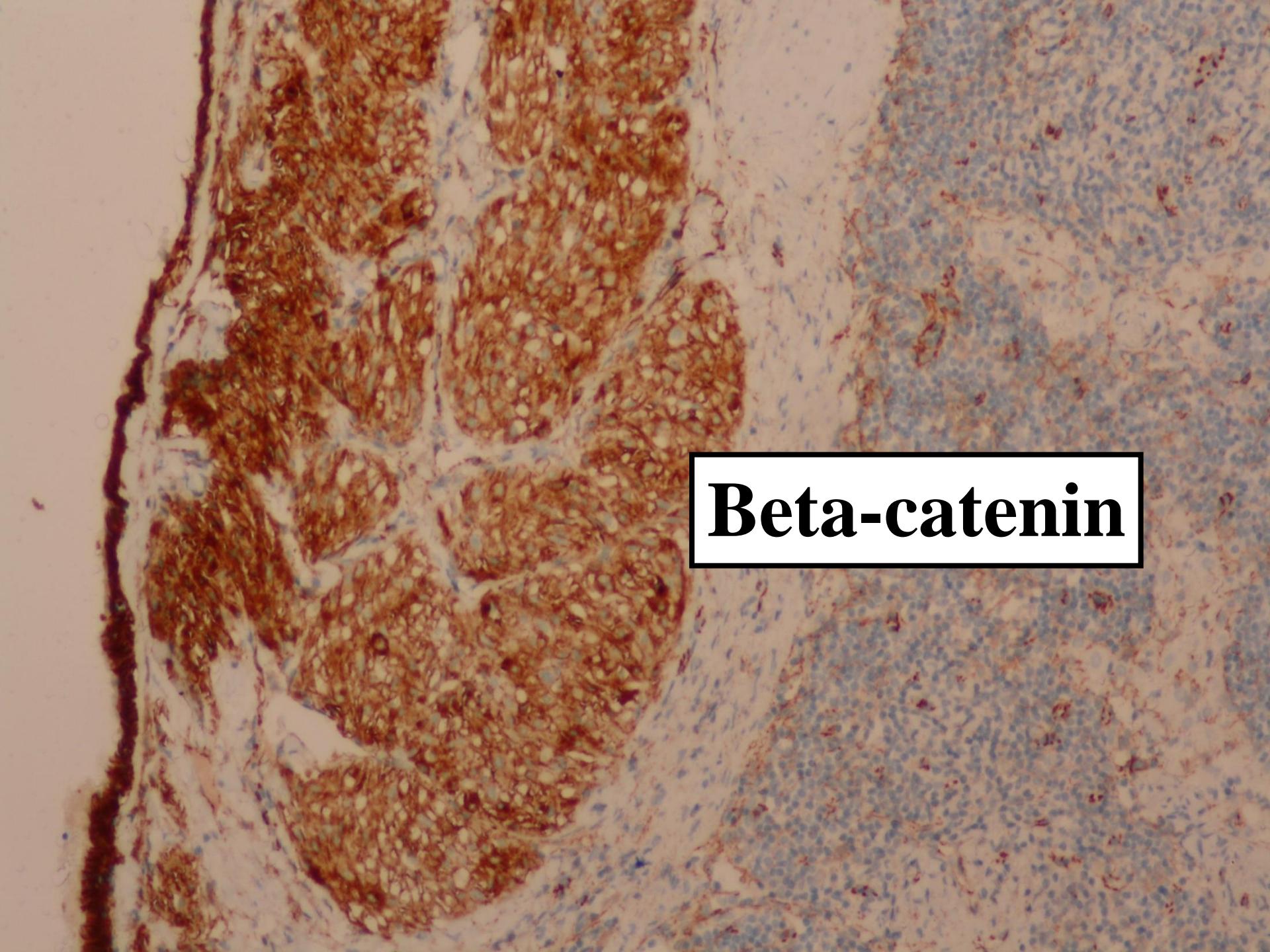
**desmin**

A light blue background with numerous small, irregularly shaped, reddish-brown spots scattered across it. These spots vary in size and density, creating a mottled pattern. Some larger clusters of these reddish-brown areas are visible on the left side.

**HMB45**

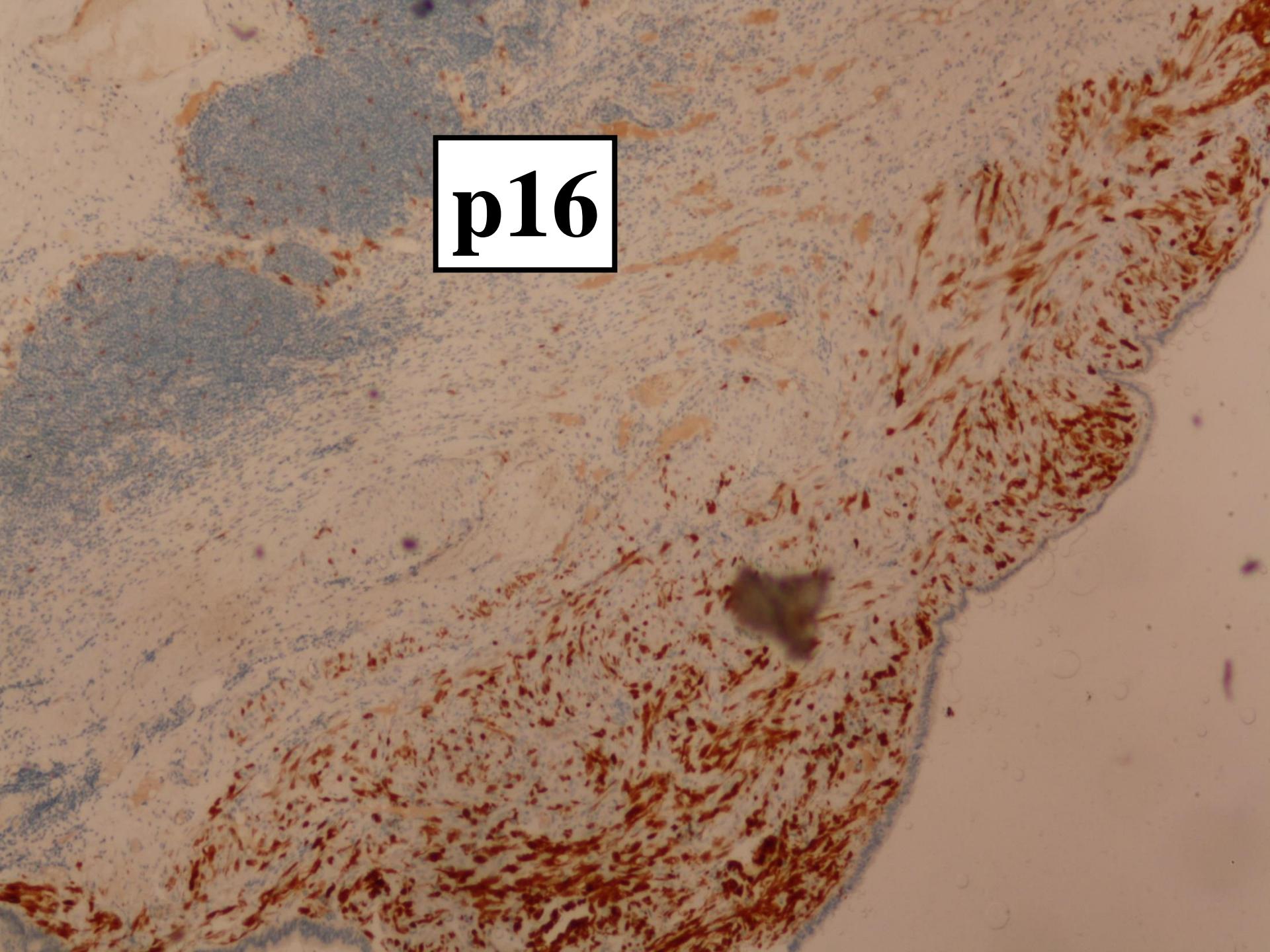
**D2-40**

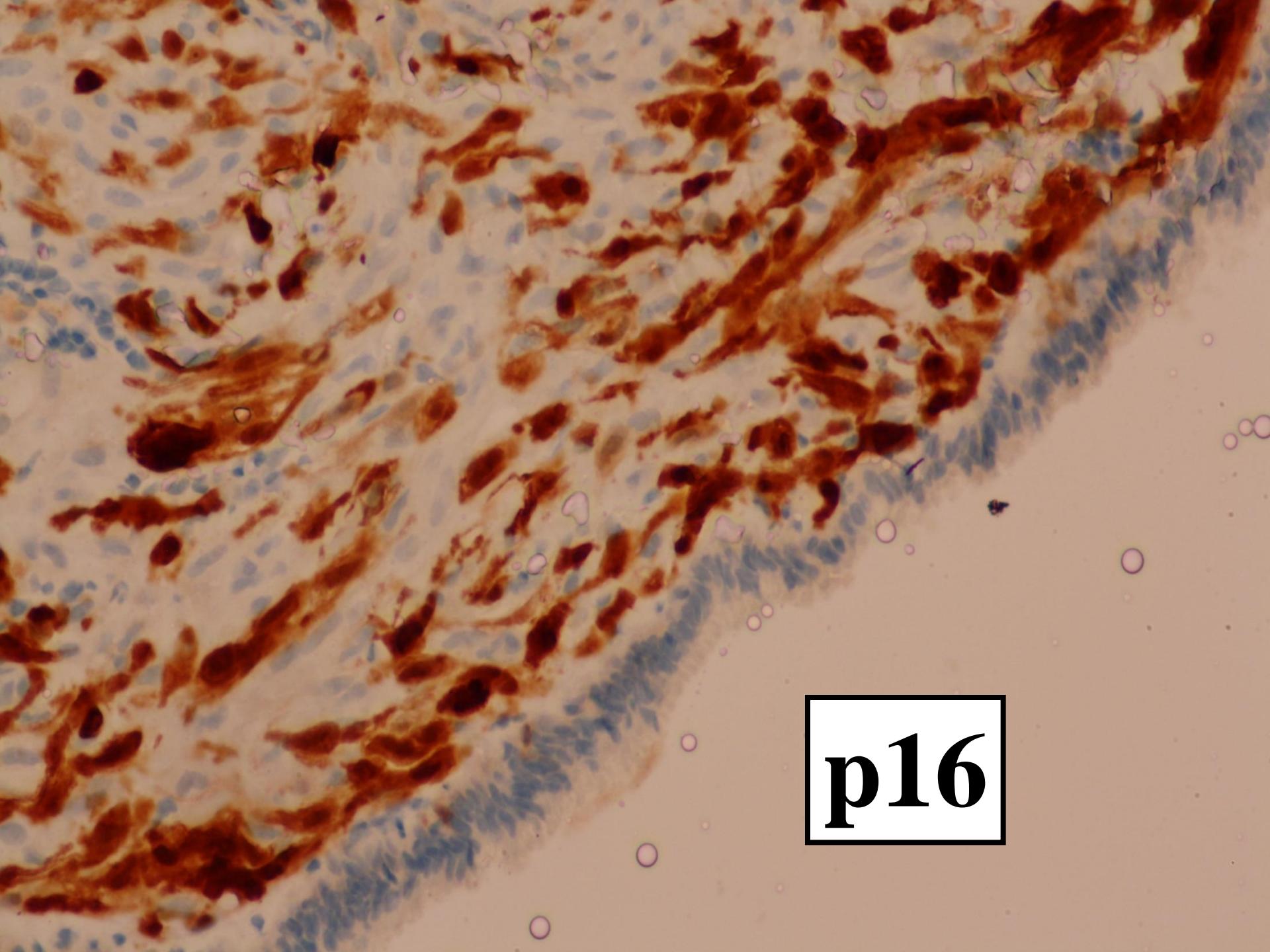


This image shows two adjacent tissue sections stained with Beta-catenin. The left section displays a high density of brown-stained nuclei, indicating strong Beta-catenin expression. The right section shows a much lower density of brown-stained nuclei, indicating lower expression. Red staining is visible in the blood vessels of both sections.

**Beta-catenin**

p16





**p16**

# Stena retroperitoneálnej cysty

?

- LAM retroperitoneálnej LU s mulleriánskou inklúziou; resp. endosalpingiózou
- .....asi najsôr tak.....

- Int J Surg Pathol. 2001 Apr;9(2):155-62.
- **Association of lymphangioleiomyomatosis (LAM) with endosalpingiosis in the retroperitoneal lymph nodes: report of two cases**
- Matsui K, Travis WD, Gonzalez R, Terzian JA, Rosai J, Moss J, Ferrans VJ.
- Pathology Section, National Heart, Lung and Blood Institute, Bldg. 10/2N240, National Institutes of Health, 10 Center Dr. MSC-1518, Bethesda, MD 20892-1518, USA.

- [APMIS.](#) 2007 Dec;115(12):1460-5. doi: 10.1111/j.1600-0463.2007.00668.x.
- **Retroperitoneal lymphangioleiomyomatosis associated with endosalpingiosis.**
- [Fukunaga M](#), [Mistuda A](#), [Shibuya K](#), [Honda Y](#), [Shimada N](#), [Koike J](#), [Sugimoto M](#).
- Department of Pathology, Jikei University School, Tokyo, Japan. maasafu@jikei.ac.jp

# TERAPIA

- Chirurgia
- Inhibitory m-Tor
- Inhibitory VEGF
- Antiestrogénna th

# Pôvod LAM cells / PEC cells

- Možný pôvod z neurálnej lišty (neural crest)
- vysoká migračná schopnosť progenitorových bb neurálnej trubice počas embryonálneho vývoja
- [Mol Med.](#) 2007 Mar-Apr;13(3-4):160-5.
- **Expression of the neural stem cell markers NG2 and L1 in human angiomyolipoma: are angiomyolipomas neoplasms of stem cells?**
- [Lim SD](#), [Stallcup W](#), [Lefkove B](#), [Govindarajan B](#), [Au KS](#), [Northrup H](#), [Lang D](#), [Fisher DE](#), [Patel A](#), [Amin MB](#), [Arbiser JL](#).
- Department of Urology, Emory University School of Medicine, and Atlanta VA Medical Center, Georgia 30322, USA.

# Pôvod LAM cells / PEC cells

- Možný zdroj „primárneho tumoru“ ....

## 1.) UTERUS (?)

vysoká prevalencia uterínnych PECómov pri S-LAM aj pri TSC-LAM

## 2.) AML obličky (?)

## 3.) Lymfatický systém (?)

pri pitve časté postihnutie ductus thoracicus;

LAM bb v chylóznej tekutine – zhluky obalené lymfatickými endotelovými bb

- [World J Surg Oncol.](#) 2004 Oct 19;2:35.
- **Perivascular epithelioid cell tumor (PEComa) of the uterine cervix associated with intraabdominal "PEComatosis": A clinicopathological study with comparative genomic hybridization analysis.**
- [Fadare O](#), [Parkash V](#), [Yilmaz Y](#), [Mariappan MR](#), [Ma L](#), [Hileeto D](#), [Qumsiyeh MB](#), [Hui P](#).
- Department of Pathology, Yale University School of Medicine, New Haven, CT, USA.  
oluwole.fadare@yale.edu

- [Int J Surg Pathol.](#) 2008 Oct;16(4):443-6. doi: 10.1177/1066896908316067. Epub 2008 May 21.
- **Multifocal PEComa (PEComatosis) of the female genital tract associated with endometriosis, diffuse adenomyosis, and endometrial atypical hyperplasia.**
- [Froio E](#), [Piana S](#), [Cavazza A](#), [Valli R](#), [Abrate M](#), [Gardini G](#).
- Department of Pathology, Arcispedale Santa Maria Nuova, Reggio Emilia, Italy.
- \_\_\_\_\_
- PS: pacientka s TSC

- [Int J Gynecol Pathol.](#) 2011 Mar;30(2):121-8. doi: 10.1097/PGP.0b013e3181fa5a99.
- **The morphologic spectrum of uterine PEC-cell associated tumors in a patient with tuberous sclerosis.**
- [Lim GS, Oliva E.](#)
- Department of Pathology, National University Hospital, Singapore.
- \_\_\_\_\_

- PS: pacientka mala:
- 1. AML
- 2. Sclerosing PEComa
- 3. diffuse LAM

- [Int J Gynecol Pathol.](#) 2011 Jan;30(1):71-5. doi: 10.1097/PGP.0b013e3181efe08d.
- **Microscopic uterine lymphangioleiomyomatosis perivascular epithelioid cell neoplasm: a case report with the earliest manifestation of this enigmatic neoplasm.**
- [Clay MR](#), [Gibson P](#), [Lowell J](#), [Cooper K](#).
- Department of Pathology at Fletcher Allen Health Care, University of Vermont, College of Medicine, Burlington, VT 05401, USA. Michael.clay@uvm.edu

## 3.diferenciačná línia

- [J Histochem Cytochem.](#) 2013 Aug;61(8):580-90. doi: 10.1369/0022155413489311. Epub 2013 Apr 22.
- **Lymphatic endothelial differentiation in pulmonary lymphangioleiomyomatosis cells.**
  - [Davis JM](#), [Hyjek E](#), [Husain AN](#), [Shen L](#), [Jones J](#), [Schuger LA](#).
  - Department of Pathology, Biological Sciences Division, University of Chicago, Chicago, Illinois 60637, USA.
  - \_\_\_\_\_
  - PS: LAM cells:
  - D2-40+ (12/12);
  - PROX1, LYVE1, VEGFR3 ... immunoreactivity varied from scarce to abundant
- lymphatic endothelial differentiation is a feature of LAM and provide evidence of a *previously unidentified third lineage of differentiation (!)*

## 3.diferenciačná línia (?)

- PEComa - všeobecne
- Myo-melanocytic tumor
  - LAM
- Myo-melano-**lympho**.... tumor

# Follow up

- Viac ako po roku
- Telefonát obvodnému gynekológovi
- Bez respiračných problémov
- Bez iného nálezu

Ďakujeme za pozornosť