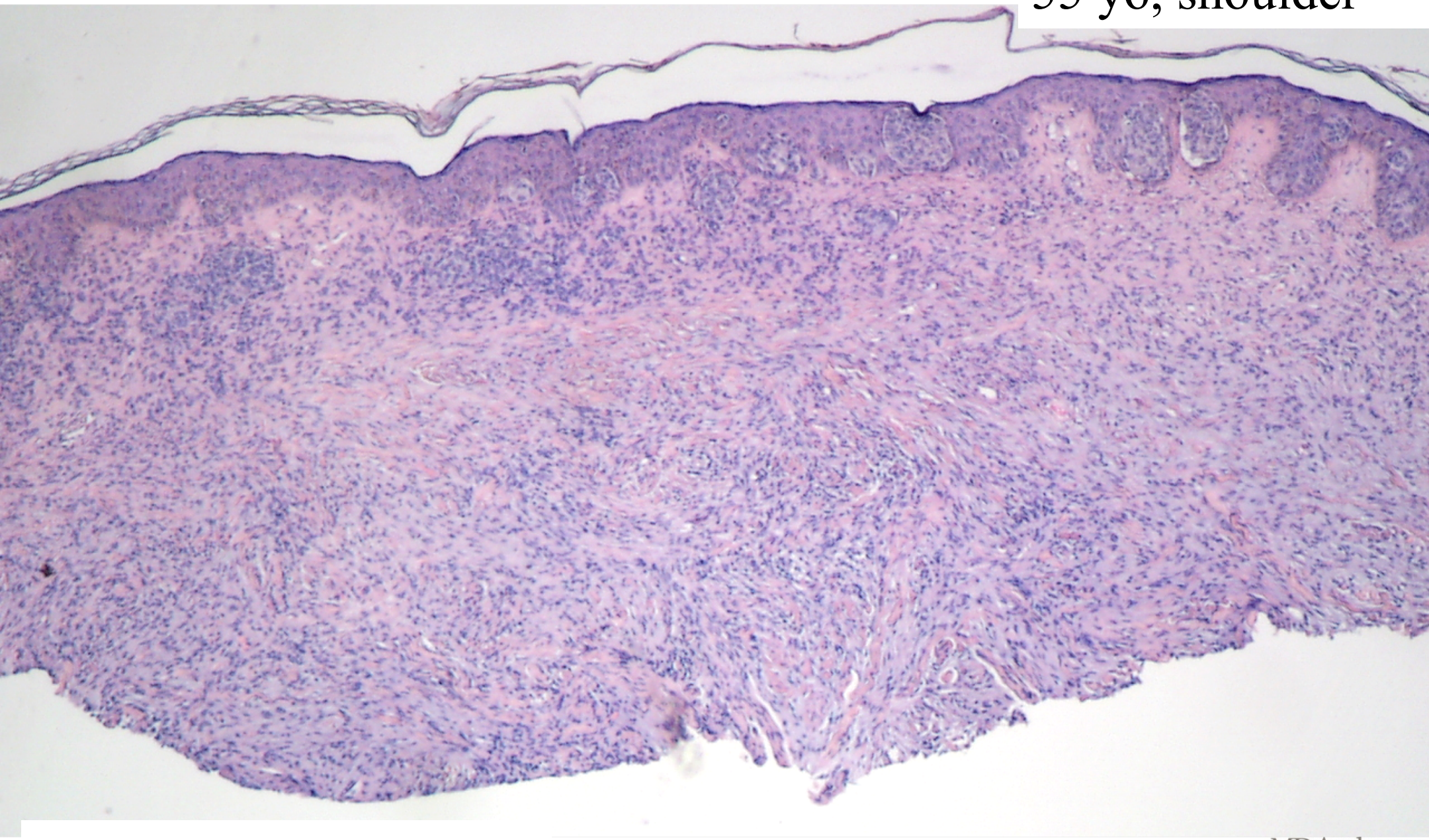
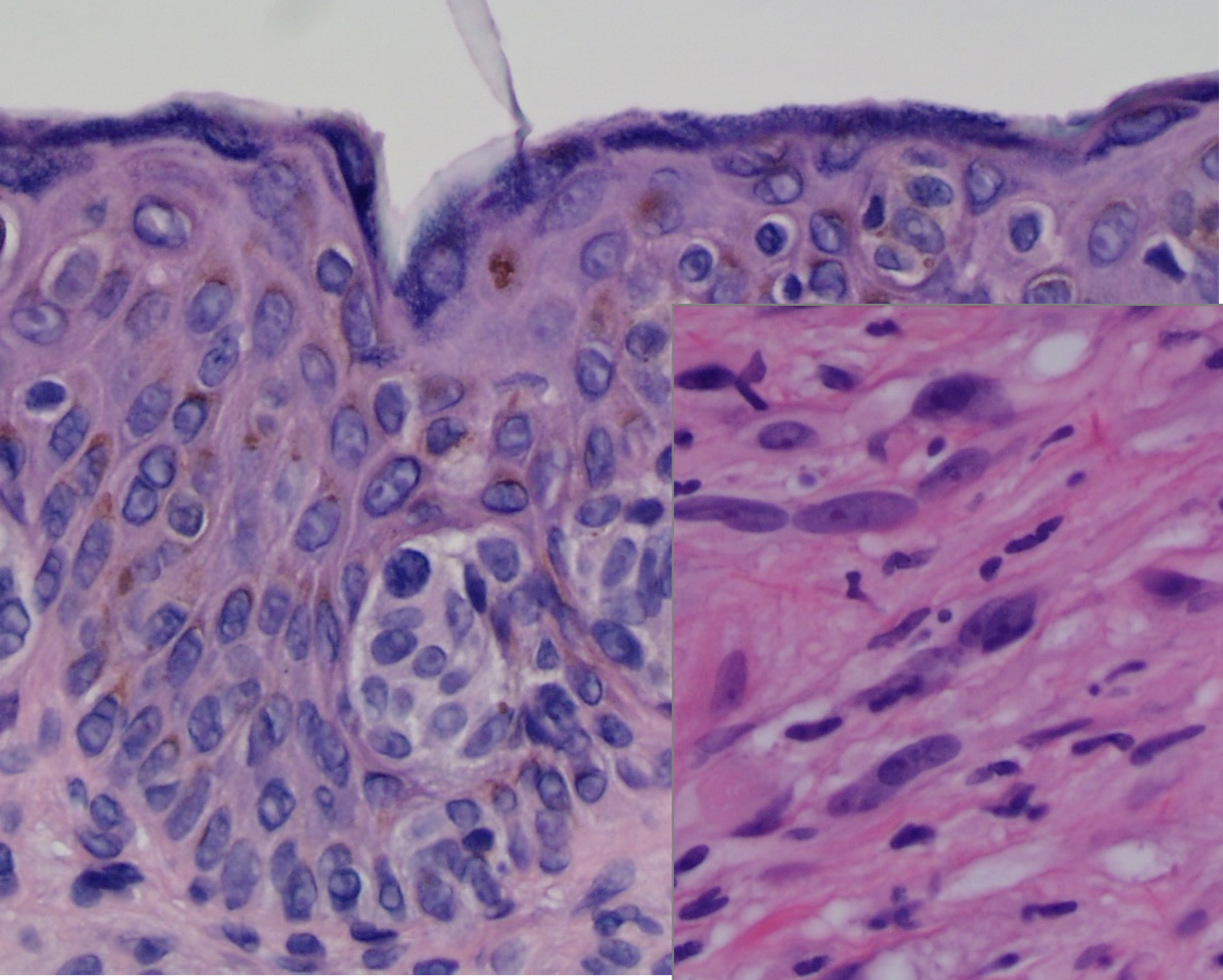
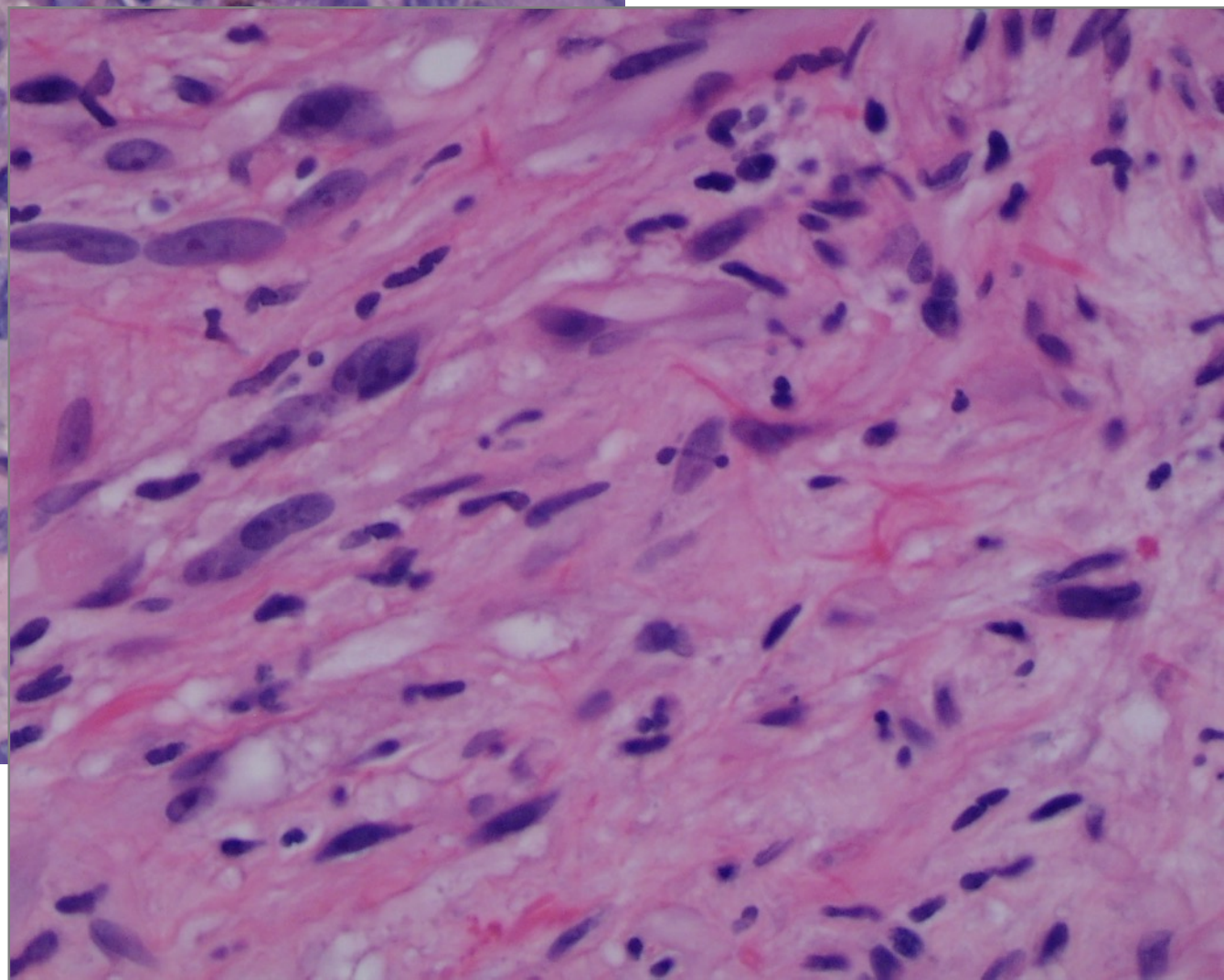
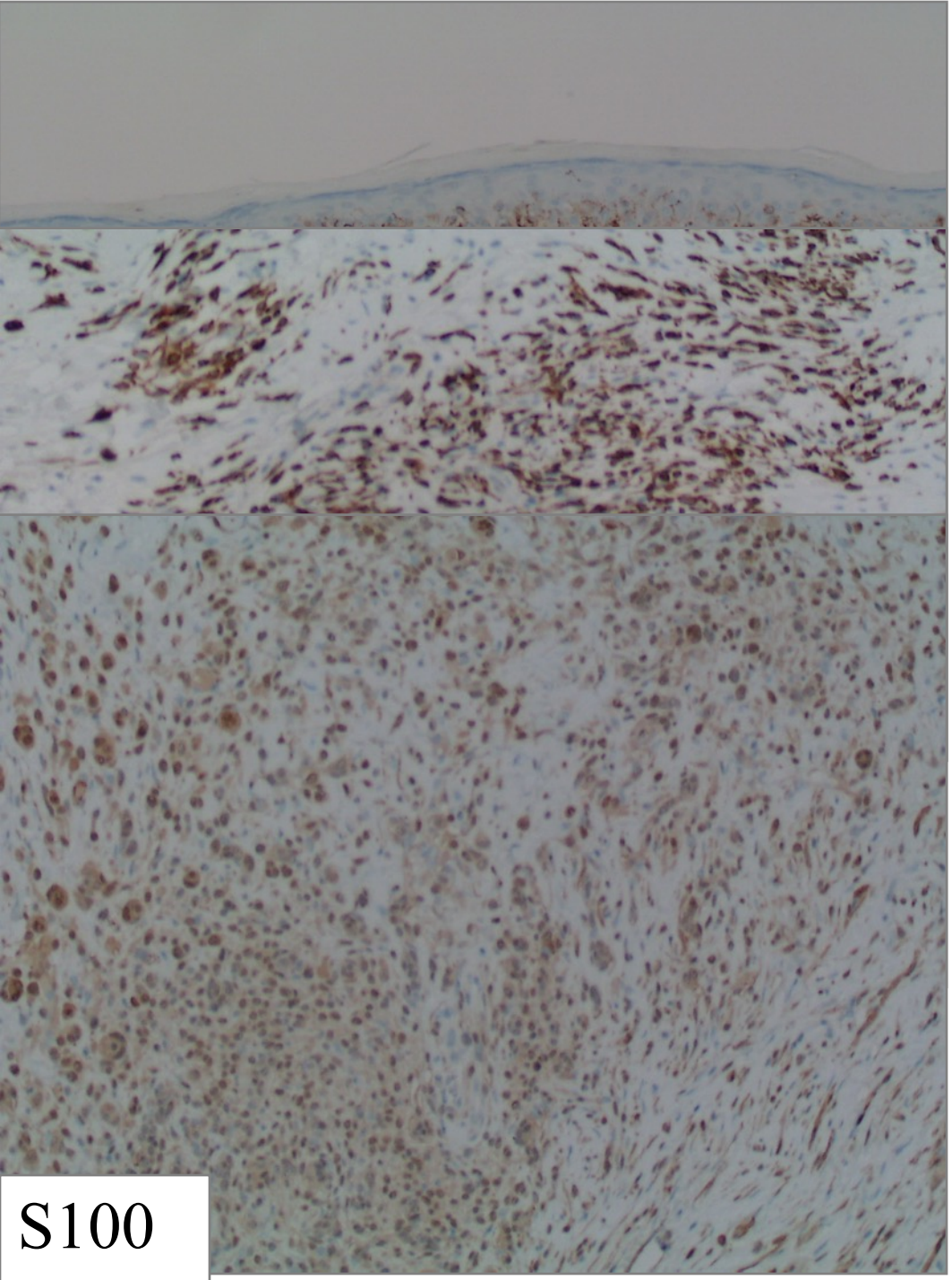


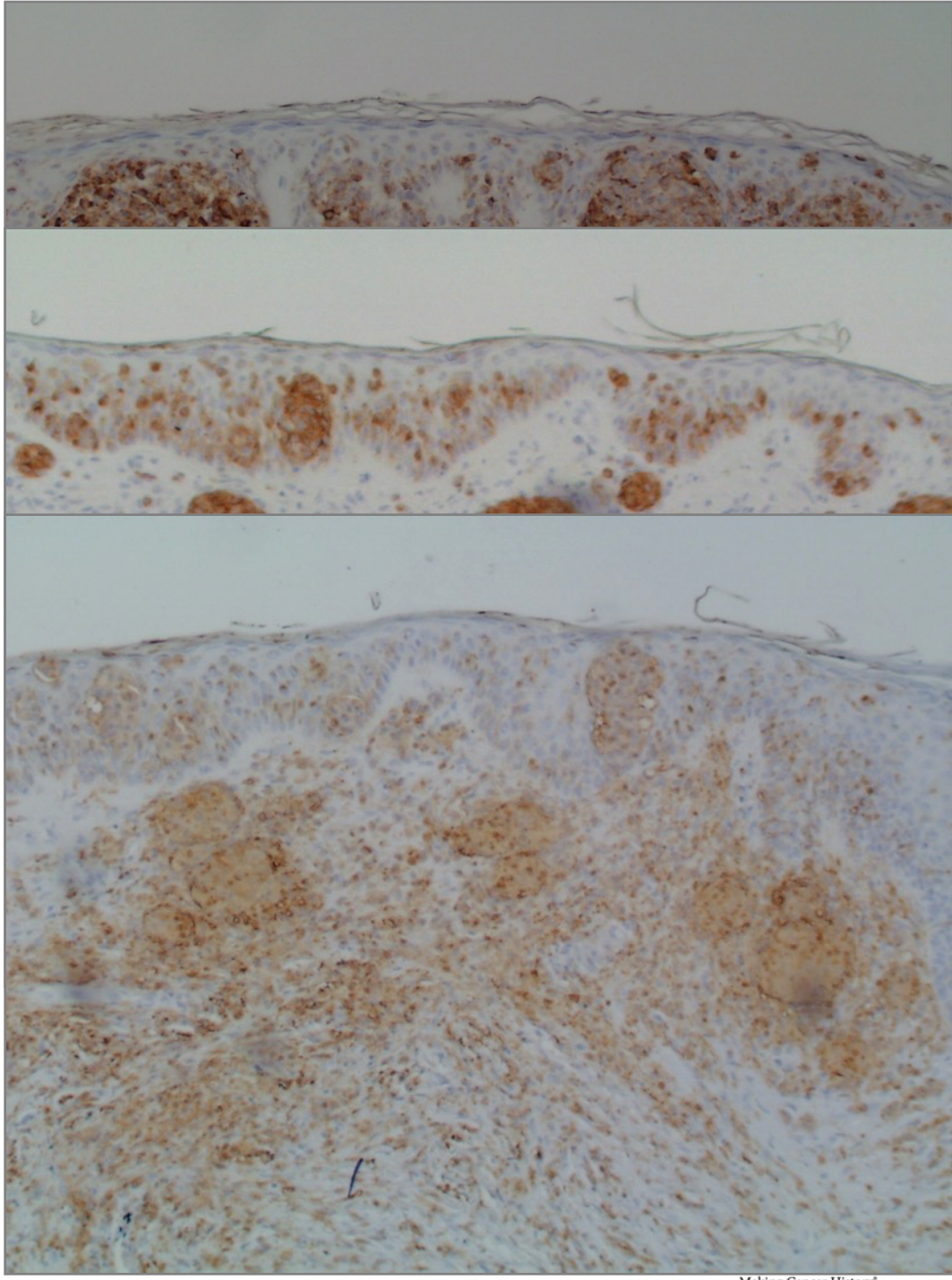
Dense cellular infiltrate





Junctional component
Cellular atypia

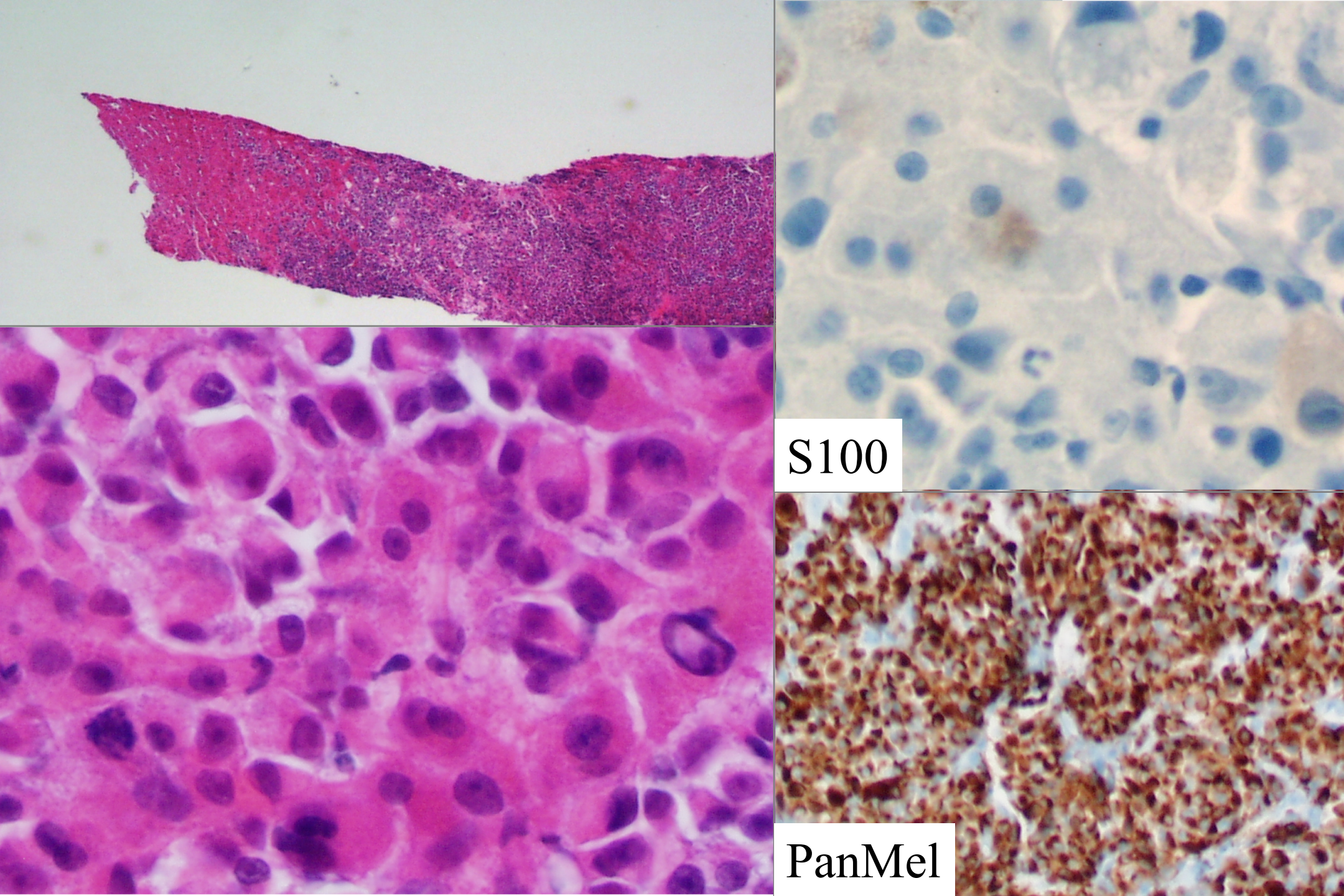

S100

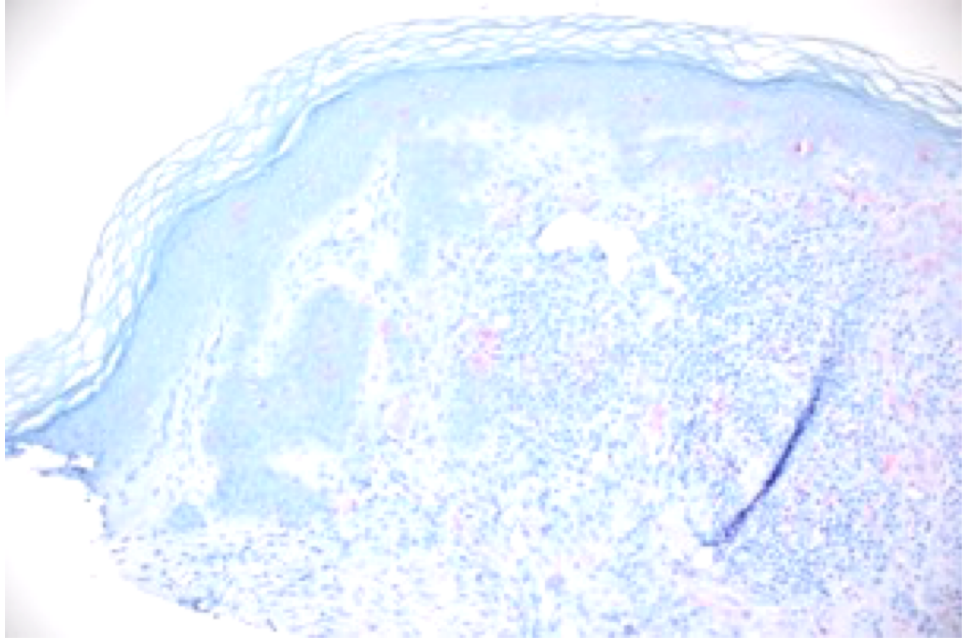

Making Cancer History®

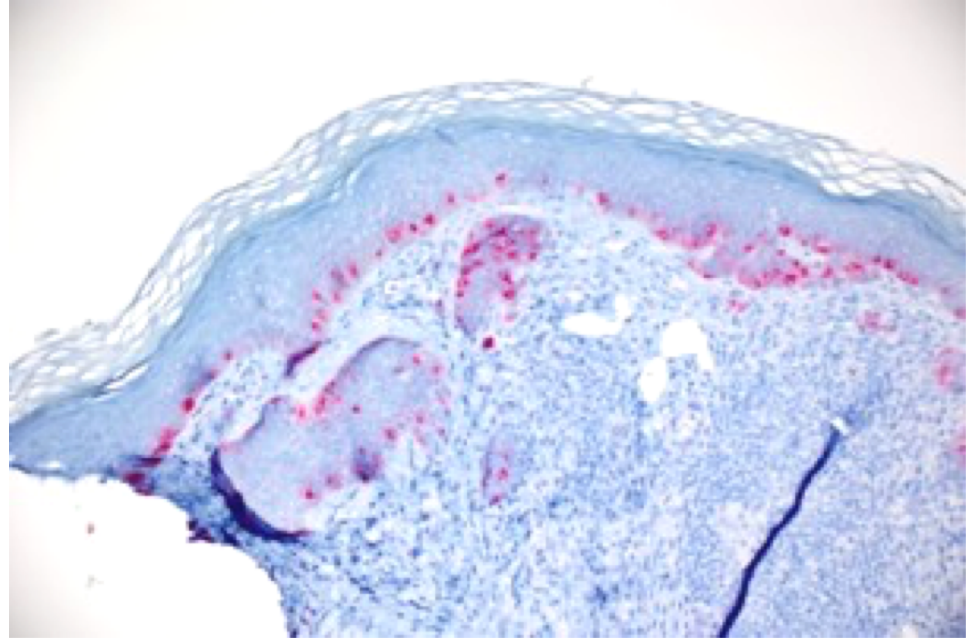
Immunohistochemical Features (VI)

S100 protein may be lost with under- or overfixation or after freezing

- Such false negative may result in misdiagnosis
- The epitope expressed in melanocytes is sometimes more labile than the one expressed in other cells (Schwann cells, neurons):
  - Check internal controls (preferably melanocytes

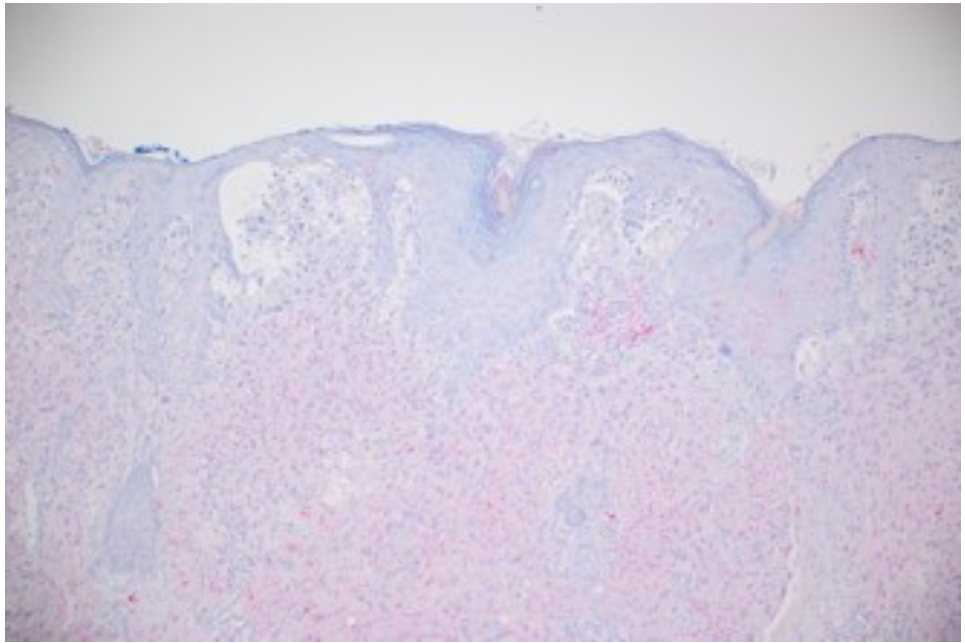

S100
PanMel

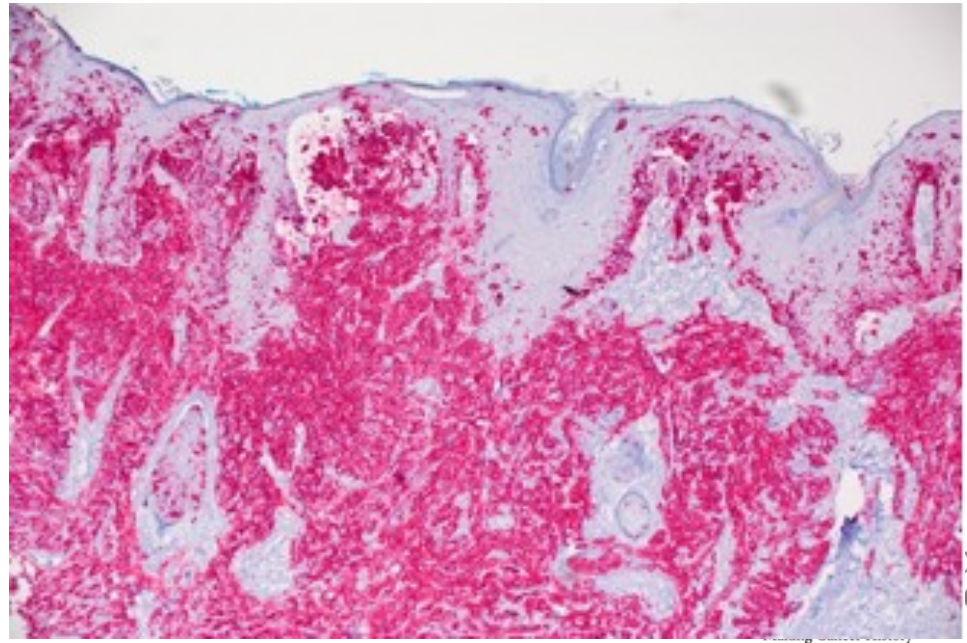




S100

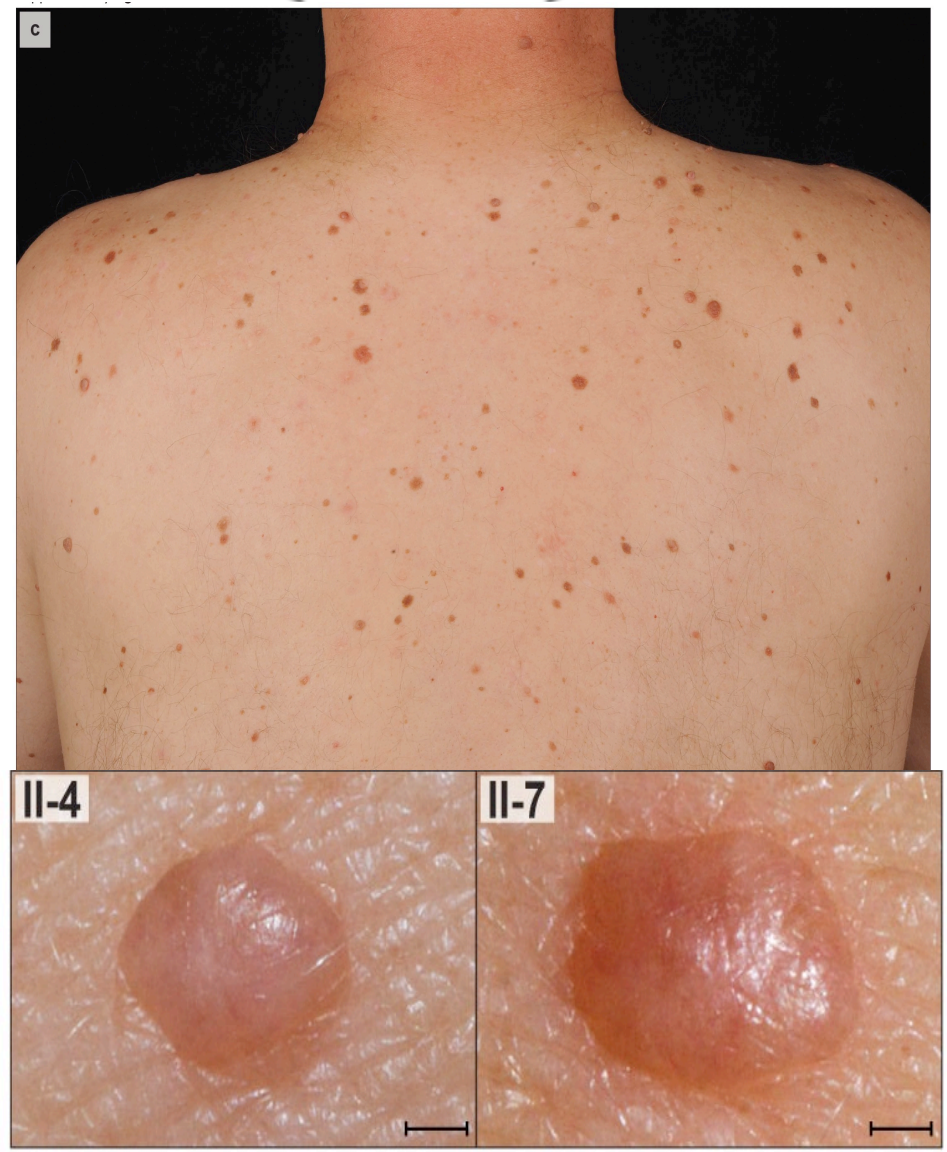
MART1





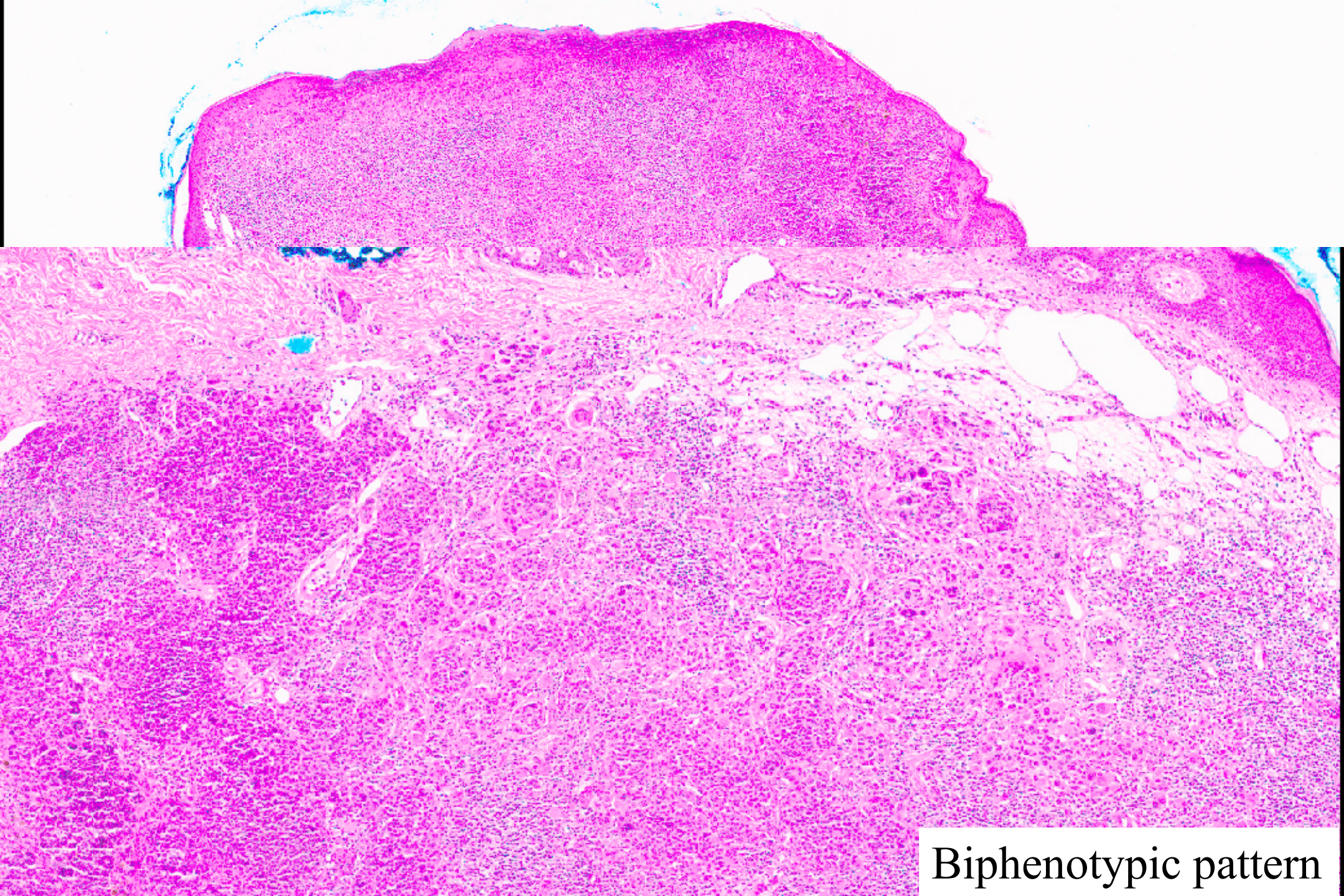
Immunohistochemical Features (VII)

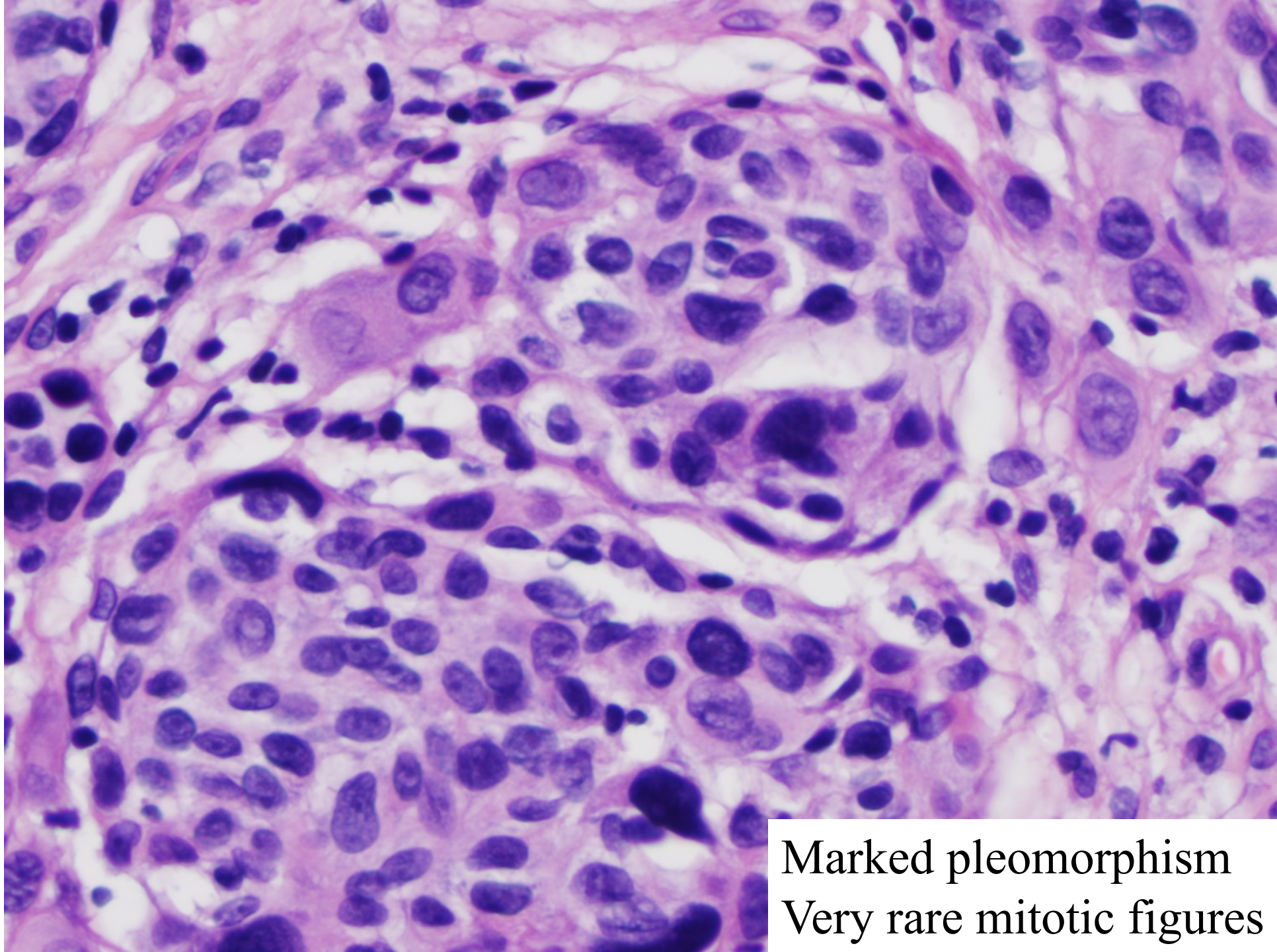
- BAP1
- Multiple nevi (5-50), tan-colored, reddish to brown, papular
- Second decade
- Similar to Spitz nevus but some differences

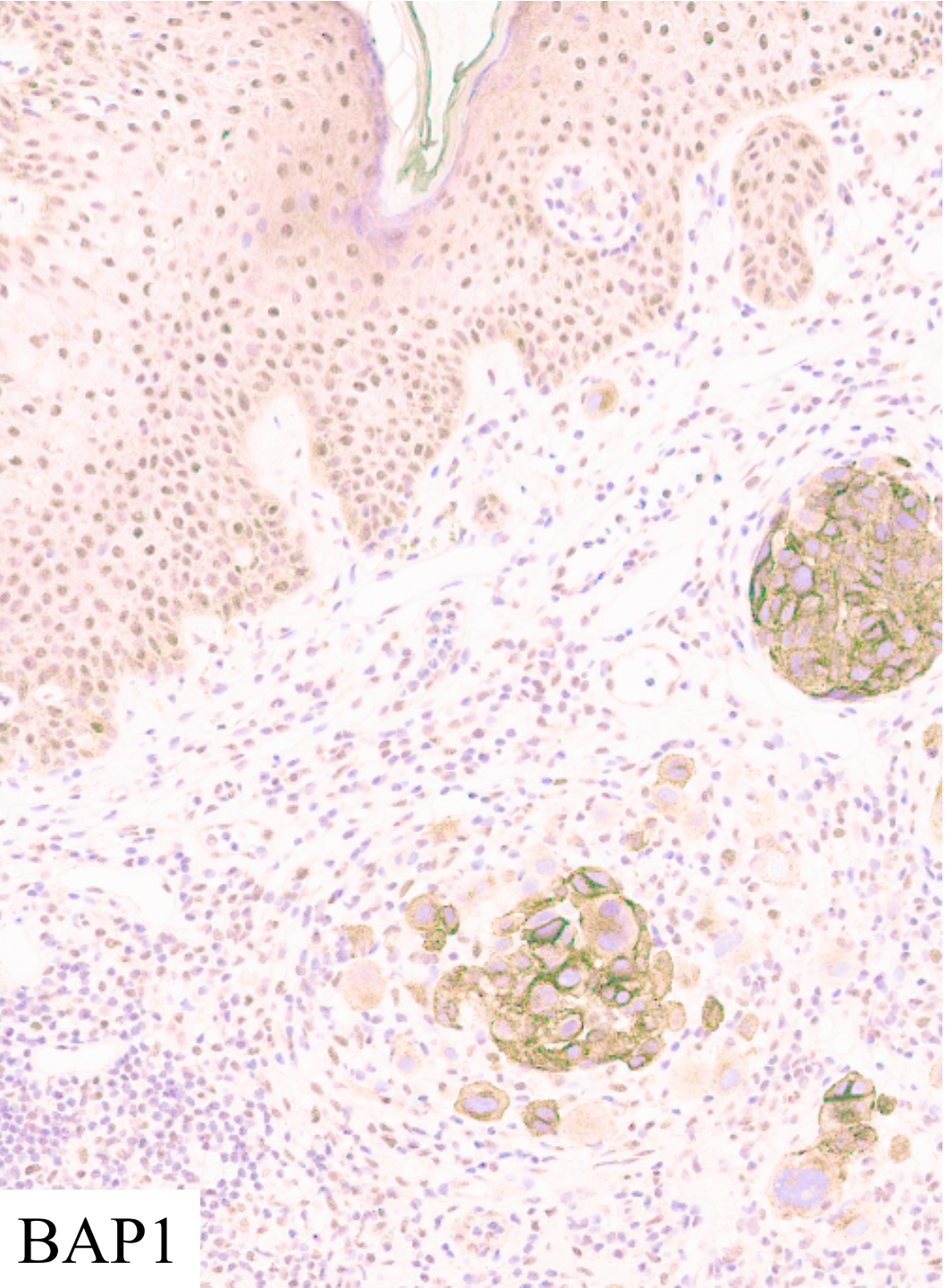


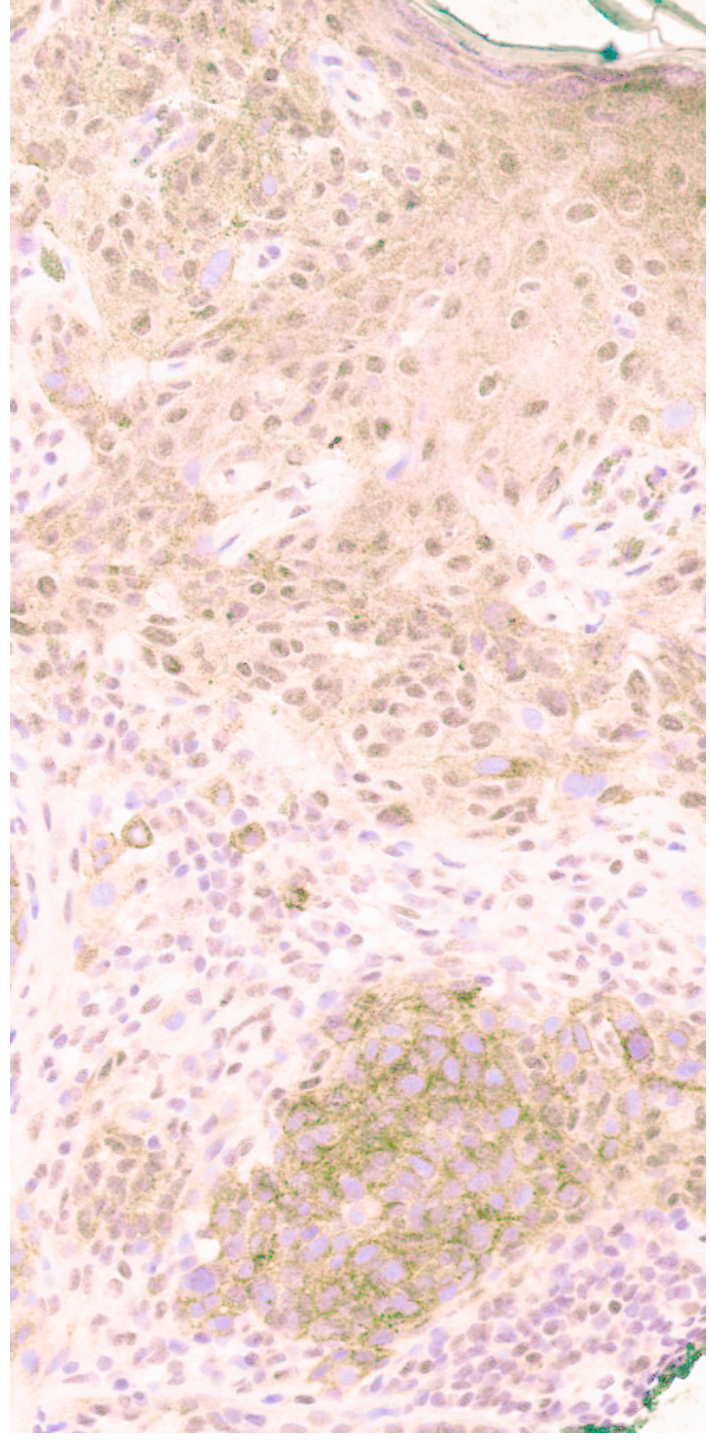
BAP1

- Dermal lesions, inflamed
- Biphenotypical:
  - Standard melanocytes
  - Epithelioid melanocytes with pleomorphic, large nuclei, prominent nucleoli
- 89% loss of BAP1 *and* BRAF V600E mutation
- Overwhelmingly benign


Biphenotypic pattern


Marked pleomorphism
Very rare mitotic figures





BAP1

THE UNIVERSITY OF TEXAS
MD Anderson Cancer Center
Making Cancer History®

Other Techniques
CGH Requirements

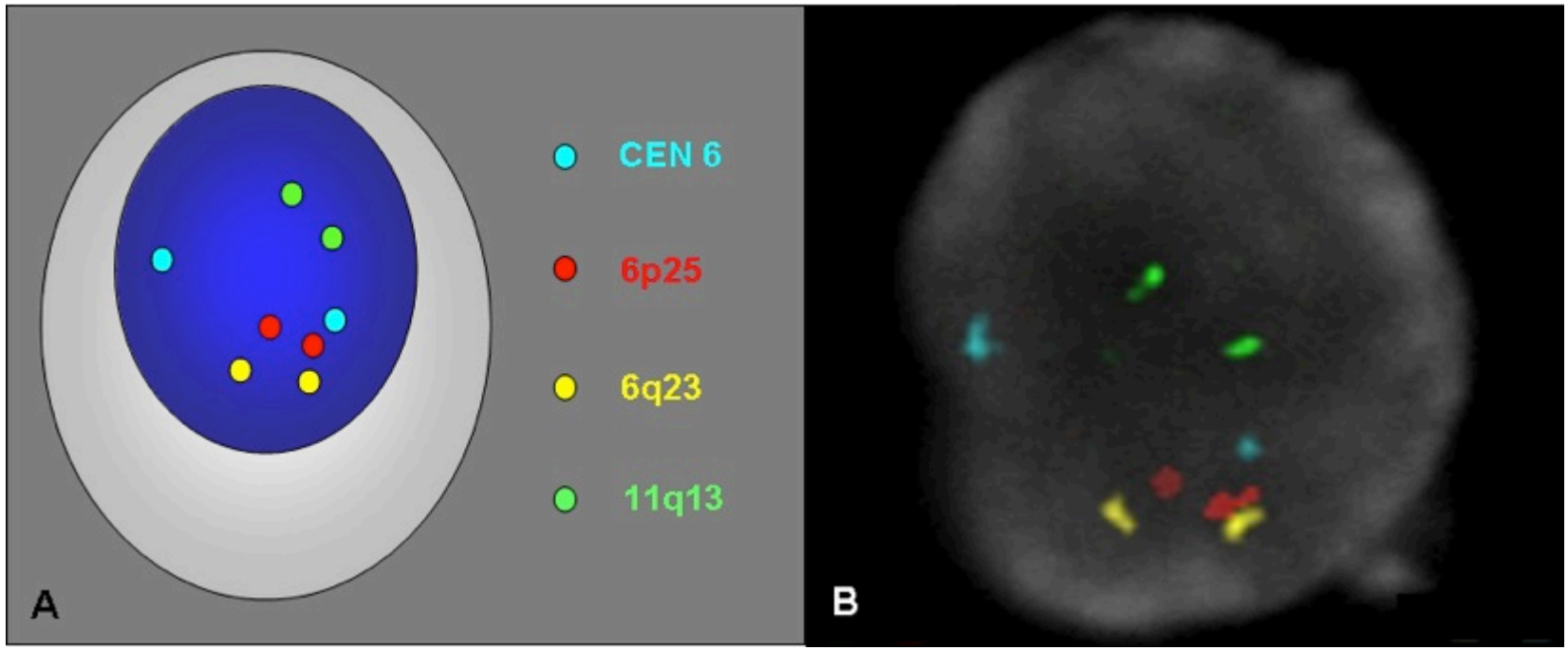
- Relatively large amount of pure tumor cells (conflict with histologic analysis)
- Difficult if numerous admixed inflammatory or stromal cells
- The abnormality must be present in a sufficient number of tumor cells
- DNA must be suitable for subsequent enzymatic manipulations for fluorescent labeling reactions

FISH in Melanocytic Lesions

Five probes:

- CEN9 (centromere 9)
- MYB (6q23)
- p16 (9p21)
- RREB1 (6p25)
- CCND1 (11q13)

Gerami et al. Am J Surg Pathol 2013; 37: 676-84



FISH in Melanocytic Lesions

- FISH + should not modify treatment
- FISH - does not exclude melanoma (if there are histologic features of melanoma) Tetzlaff et al Am J Surg Pathol 2013;37:1783–1796
- Homozygous deletions of 9p21 in spitzoid lesions is associated with malignant behavior Gerami et al Am J Surg Pathol 2013;37:1387–1394
- Amelanotic melanomas with amplification of MYC 8q24 Pouryazdanparast et al Modern Pathology 2012;25, 1221–1226

Mass Spectrometry

- Use of mass spectrometry to determine the protein profile (MALDI: Matrix-assisted laser desorption ionization)
- MelaPro®

Lazova R, et al. Am J Dermatopathol 2012; 34: 82-90

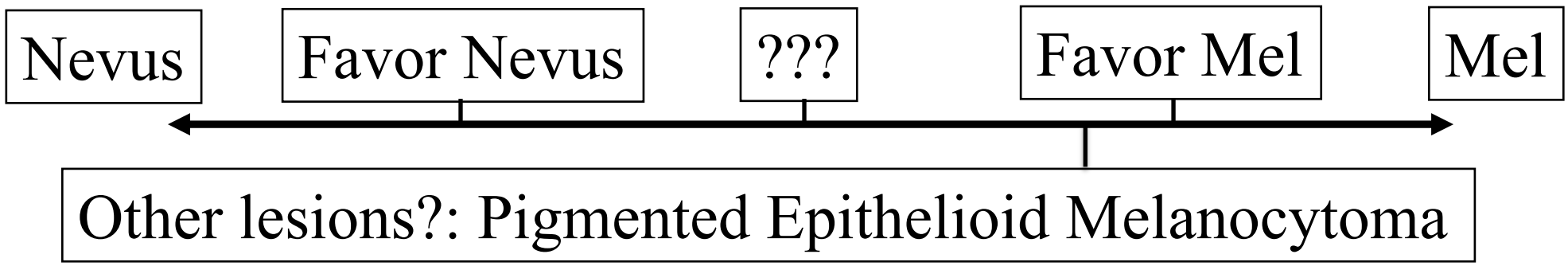
MyPath® (Myriad)

- Expression of 14 genes:
  - Inflammatory
  - Melanocytic
  - Prame (preferentially expressed antigen in melanoma; inhibitor of retinoid acid receptors)
- Very useful in sun-damaged and in spitzoid lesions

Decision Dx®

- Analysis of 31 genes (gene expression profile):
  - Class 1: low risk of metastasis at 5y
  - Class 2: 69% recurrence/metastasis at 5y
- Similar to breast carcinoma
- More significant than SLN?
- More studies and follow-up

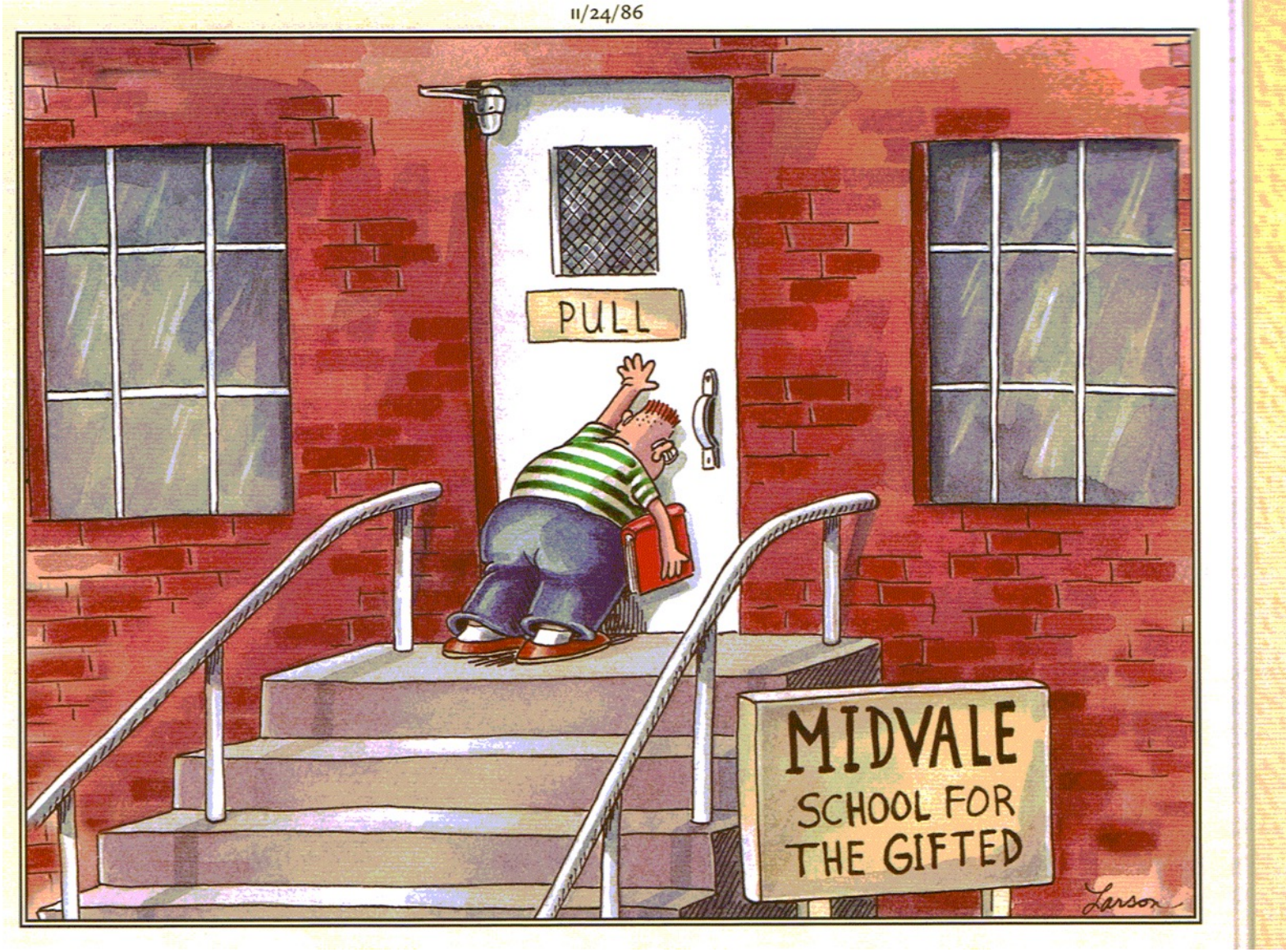
Spectrum of Melanocytic Lesions



- Histologic features
- Clinical features
- IHC
- Newer techniques FISH, CGH, etc.

Summary

- Invisible gorilla: Use a systematic approach and look at the entire slide
- *Histologic* diagnosis
- Correlation with special studies and clinical features
- Maturation with HMB45 / low Ki67
- Preserved MART1
- CGH, FISH, Myriad, MelaPro, Decision Dx



Need to pay attention to details…

Dank je

Summary

- Invisible gorilla: Use a systematic approach and look at the entire slide
- *Histologic* diagnosis
- Correlation with special studies and clinical features
- Maturation with HMB45 / low Ki67
- Preserved MART1
- CGH, FISH, Myriad, MelaPro, Decision Dx