

Evaluation of a Pigmented Nail Lesion

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and

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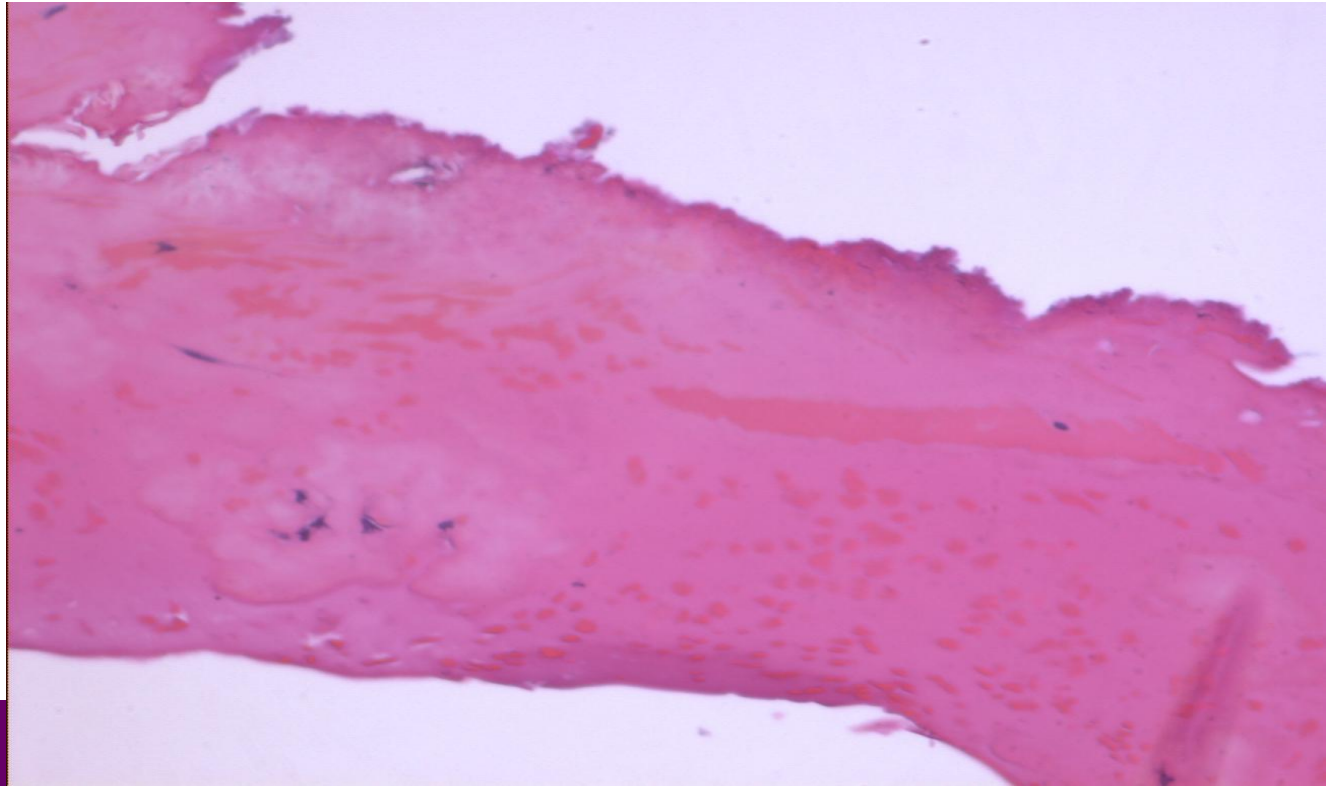
What is the source of the pigment?



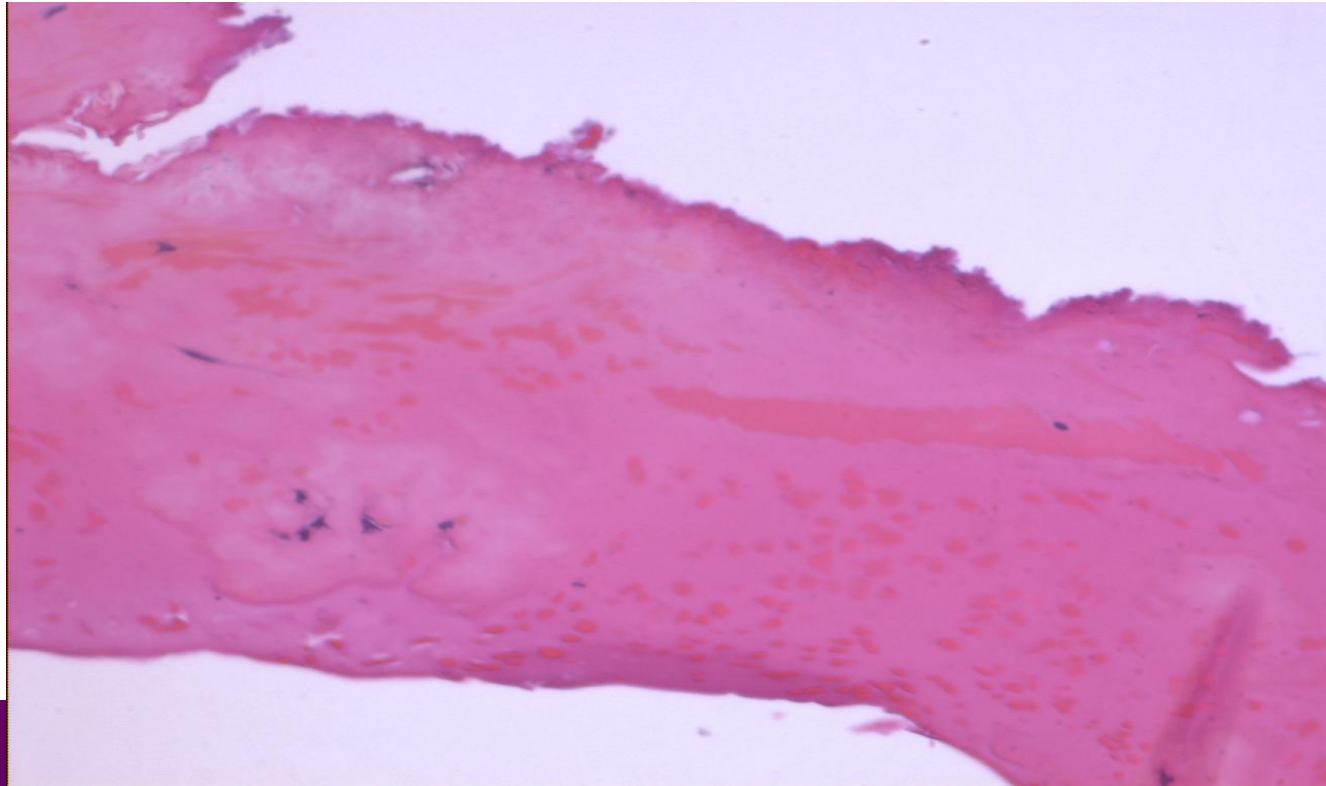
What is the source of the pigment?

- Melanocytic neoplasm
 - Benign
 - Malignant
- Melanocyte 'activation'

Blood in nail plate



Perl's iron stain does not work.

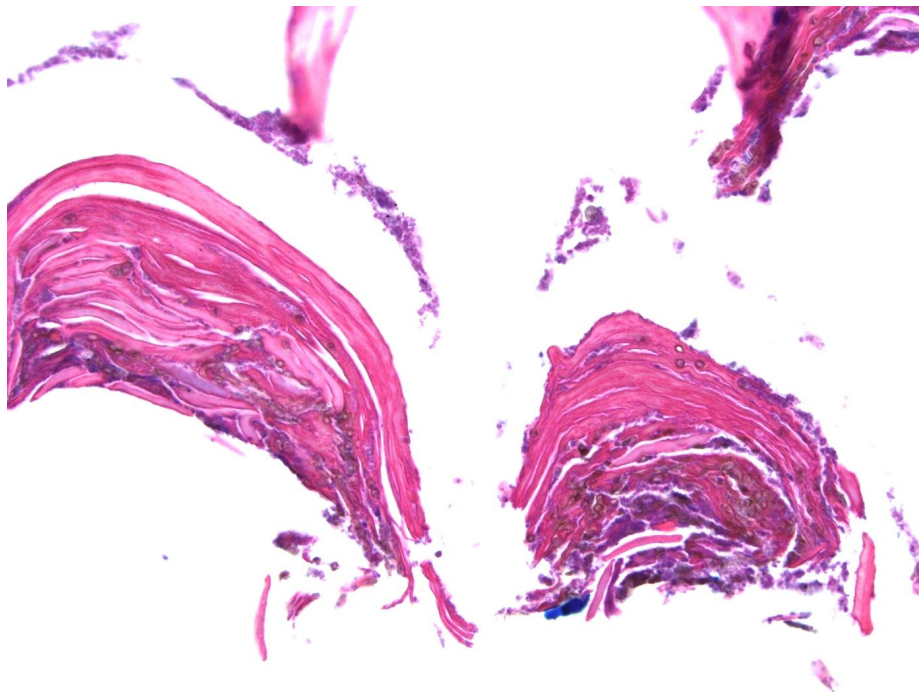


What is the source of the pigment?

- Non-melanocytic
 - Trauma—blood



Pigmented fungus



What is the source of the pigment?

- Non-melanocytic
 - Trauma—blood
 - Infection
 - Pigmented fungus

What is the source of the pigment?



Pseudomonas *aeruginosa*



What is the source of the pigment?

- Non-melanocytic
 - Trauma—blood
 - Infection
 - Pigmented fungus
 - Bacteria (*Pseudomonas*)



Drug deposition



Drug deposition

- Multiple nails
- Iron and melanin may be present



Drug Deposition

- Deposition
- Change in growth rate of nail
- Hemorrhage

Drug Deposition

- Deposition
- Change in growth rate of nail
- Hemorrhage (splinter or subungual)
 - Anticoagulants and antiplatelet agents
 - Taxanes
 - Tetracyclines
 - EGFR inhibitors (imatinib, etc)

What is the source of the pigment?

- Non-melanocytic
 - Trauma—blood
 - Infection
 - Pigmented fungus
 - Bacteria (*Pseudomonas*)
 - Drug

What is the source of the pigment?

- Melanocytic neoplasm
 - Benign
 - Malignant
- Melanocyte 'activation'

Longitudinal melanonychia



Challenge

- Identifying source of clinical pigmentation



Finding the pigment

- H&E with initial levels
- MelanA IHC
- Fontana-Masson
- PAS fungus
- Unstained slides





Print template from www.ctapathology.com.

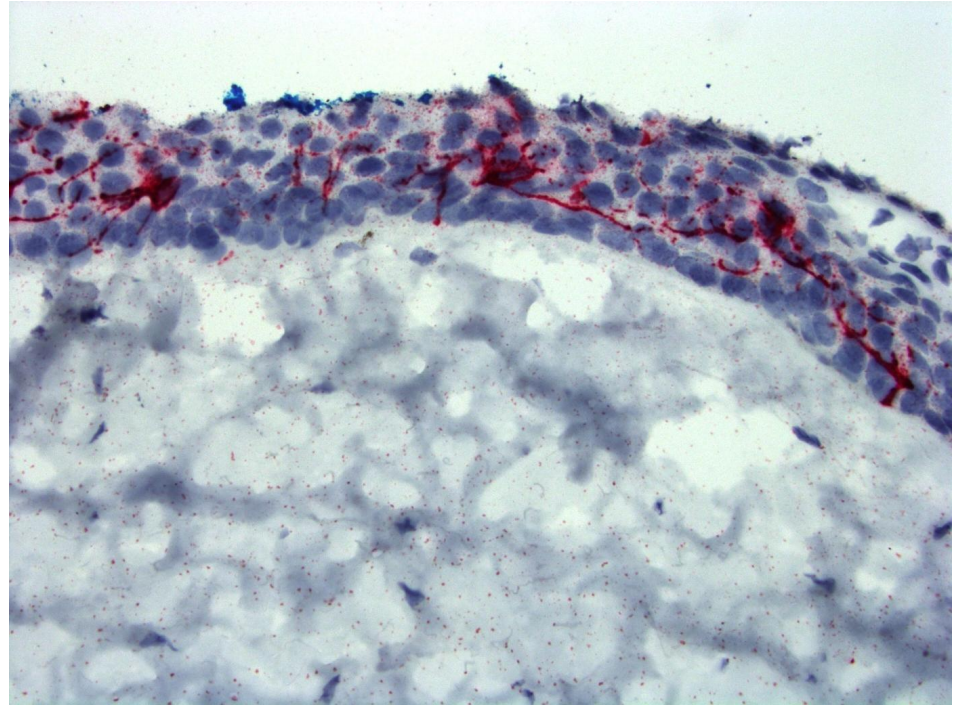
How to find the pigment



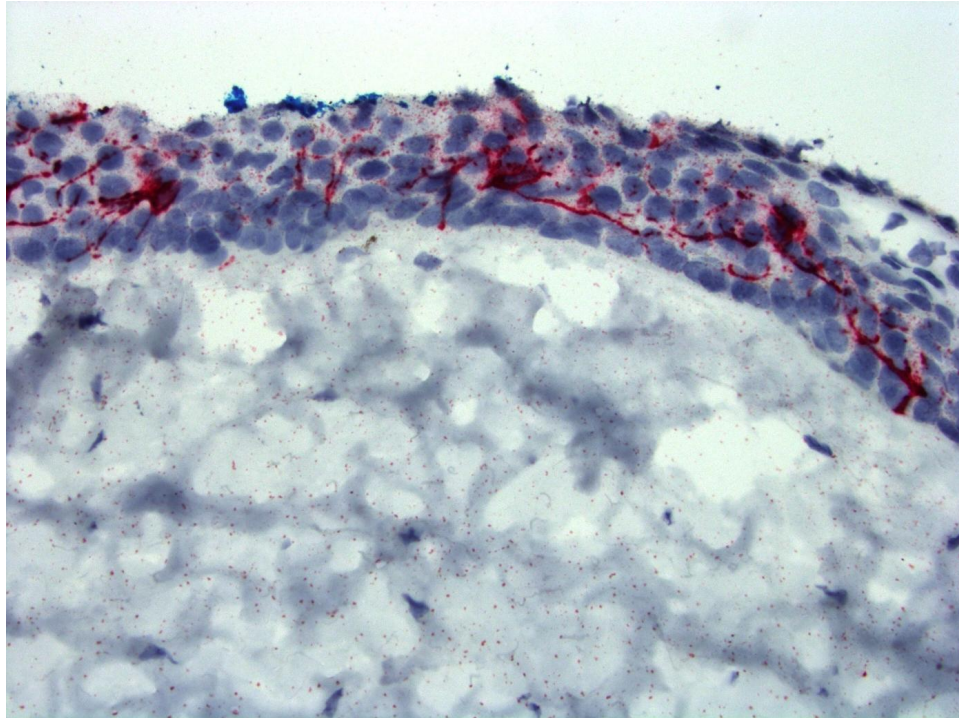
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MelanA/Mart1

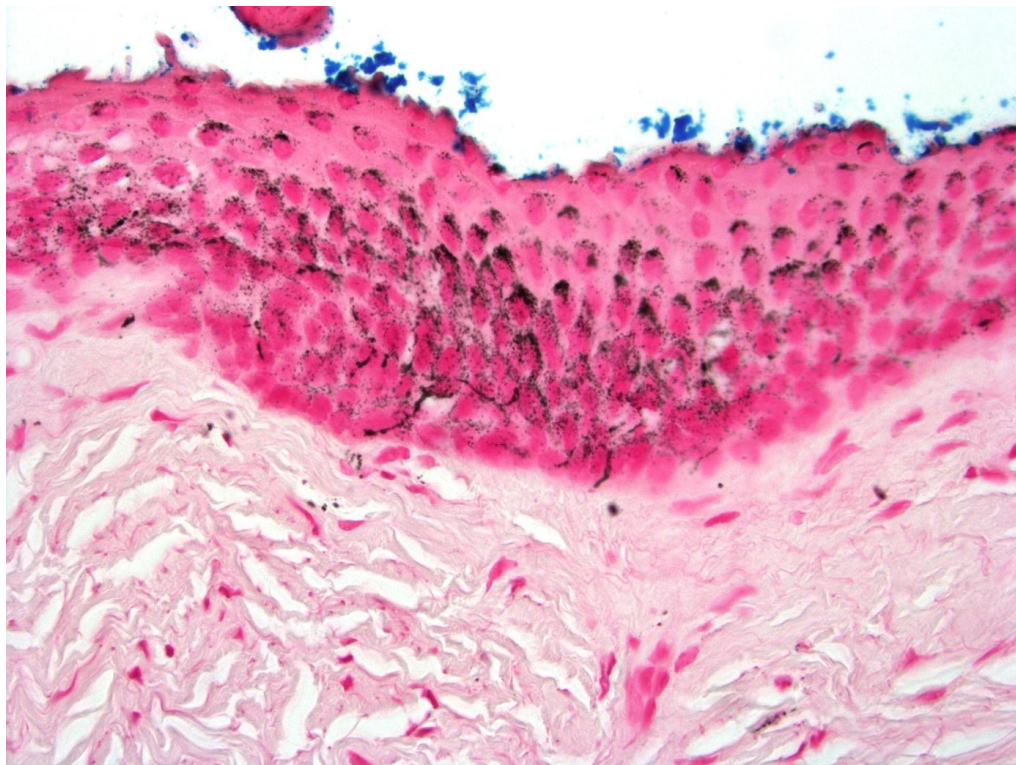
- Melanocyte density
- Red chromogen



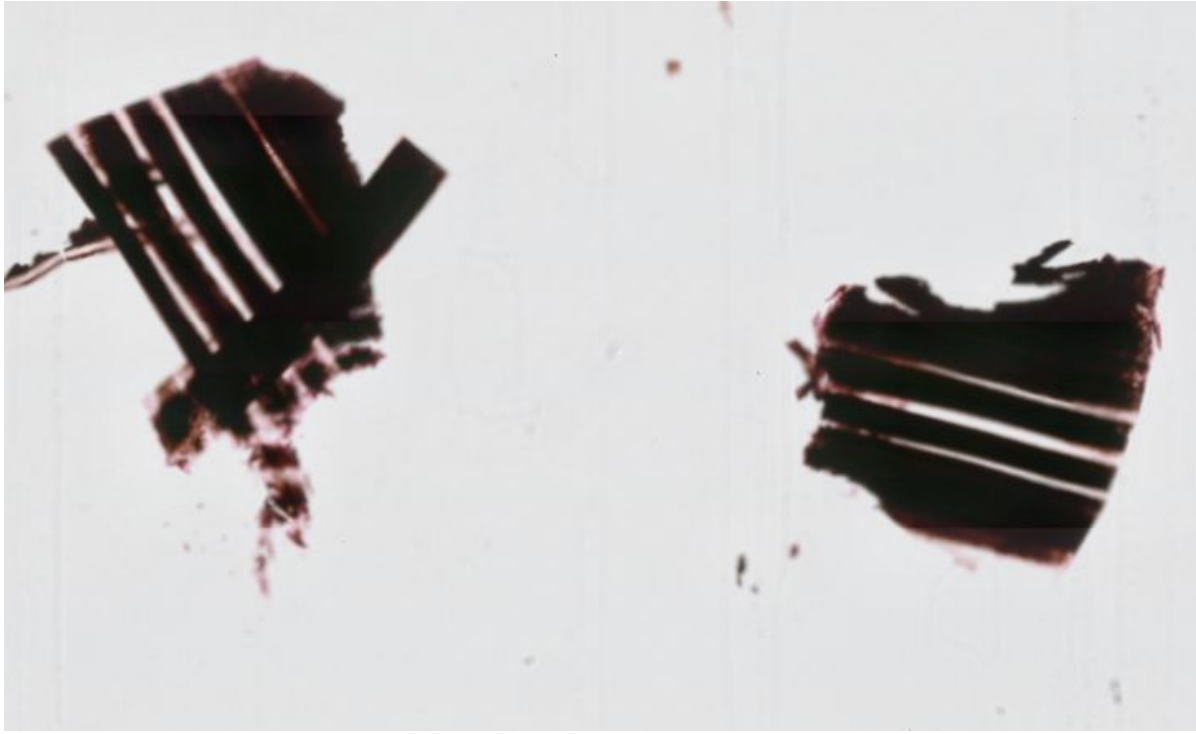
melanA/Mart-1 is better than SOX-10



Fontana-Masson Stain



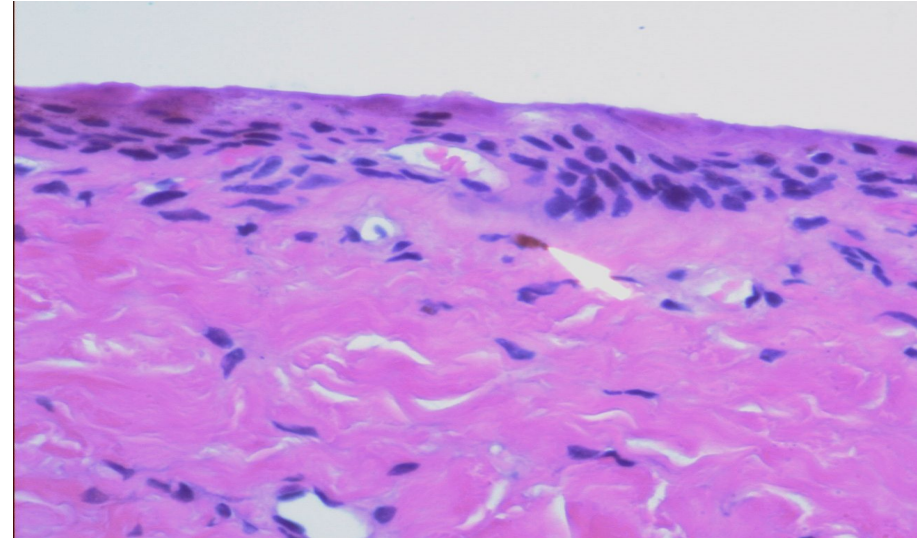
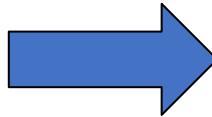
Special stains for pigment do not work in nail plate



Fontana-Masson—must dilute



Finding subtle pigment



Benign Activation of Junctional Melanocytes

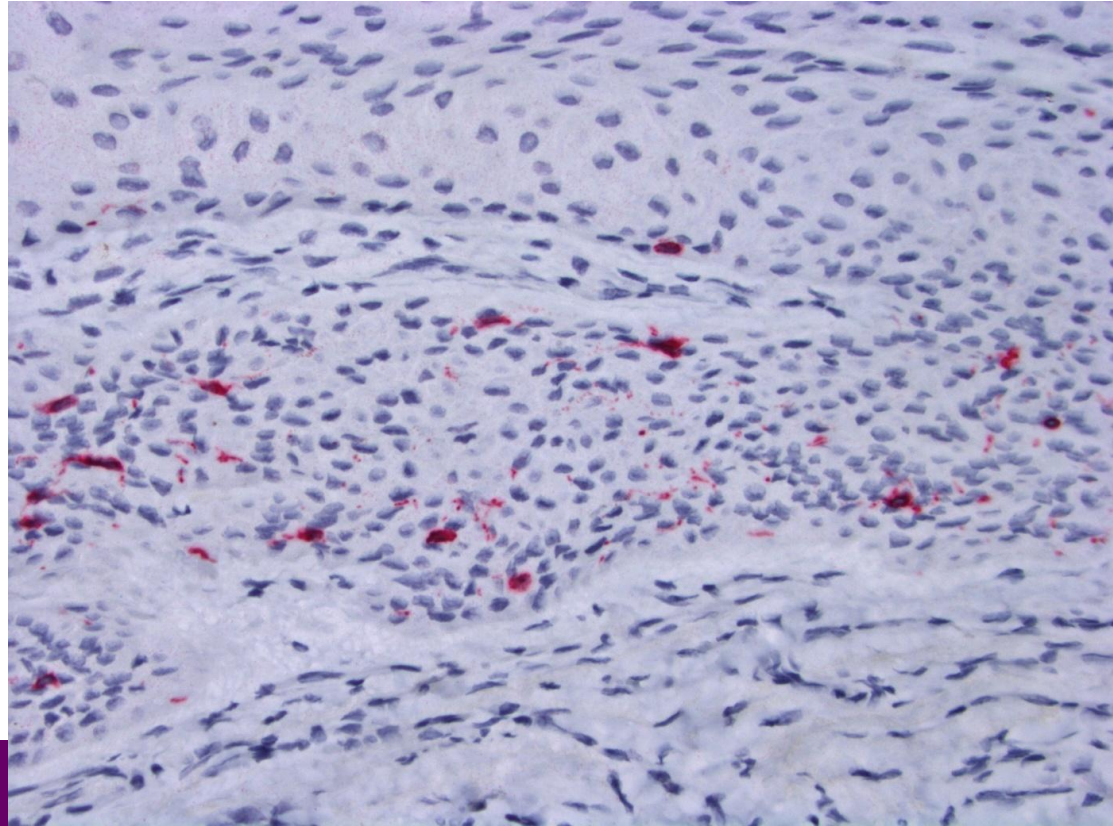
- Synonyms
 - Melanotic macule of the nail
 - Nail unit lentigo

Benign Activation of Junctional Melanocytes

- Similar to benign solar lentigo

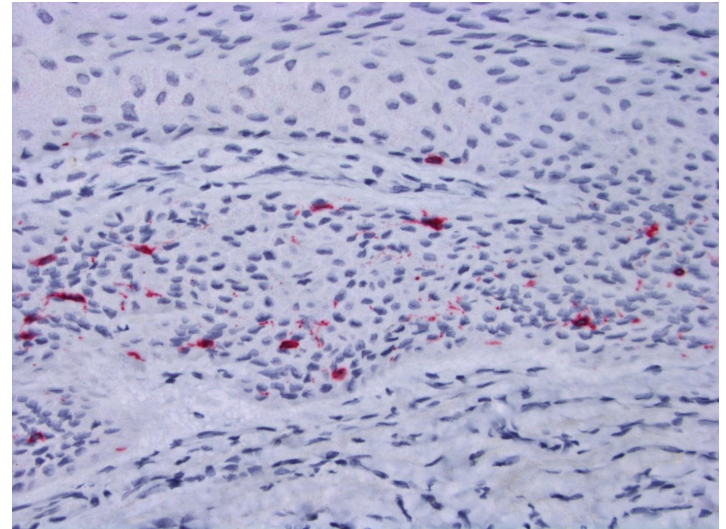


Density of melanocytes

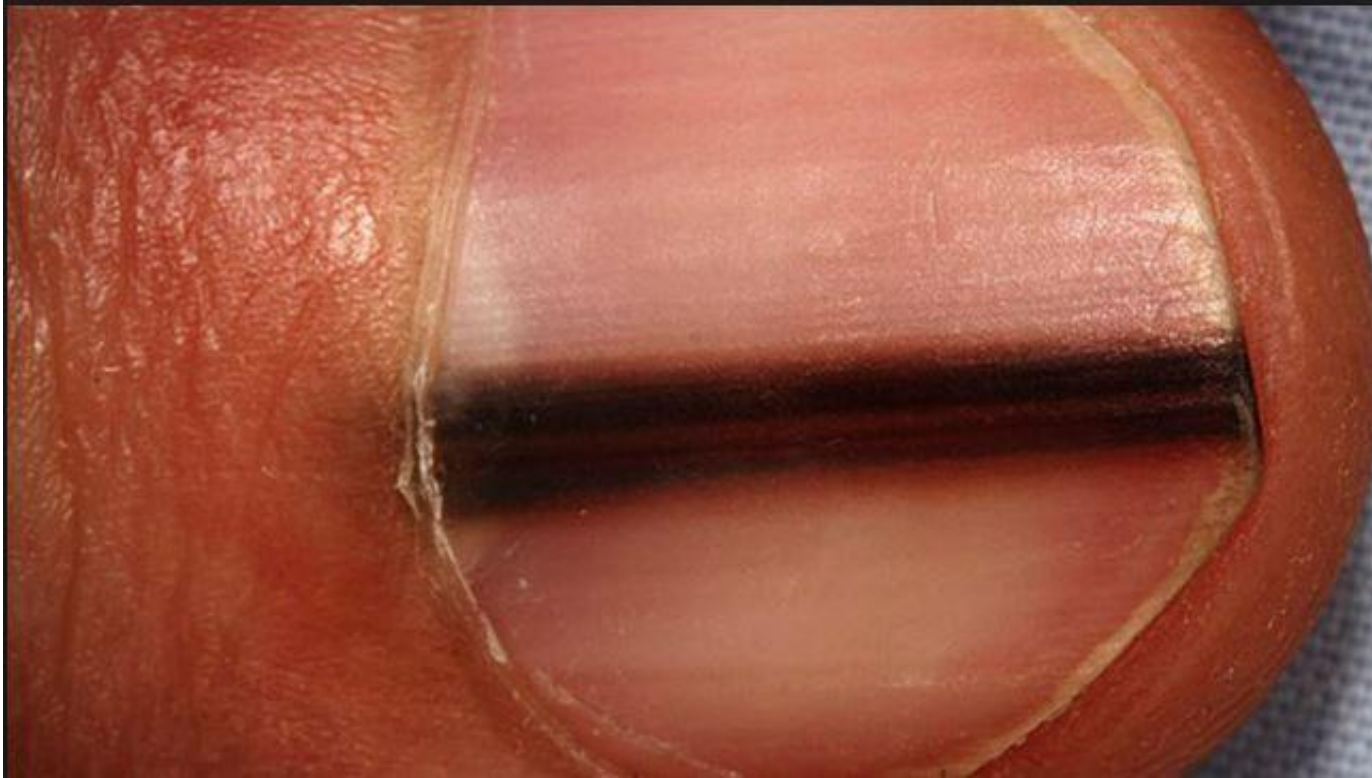


Density of melanocytes

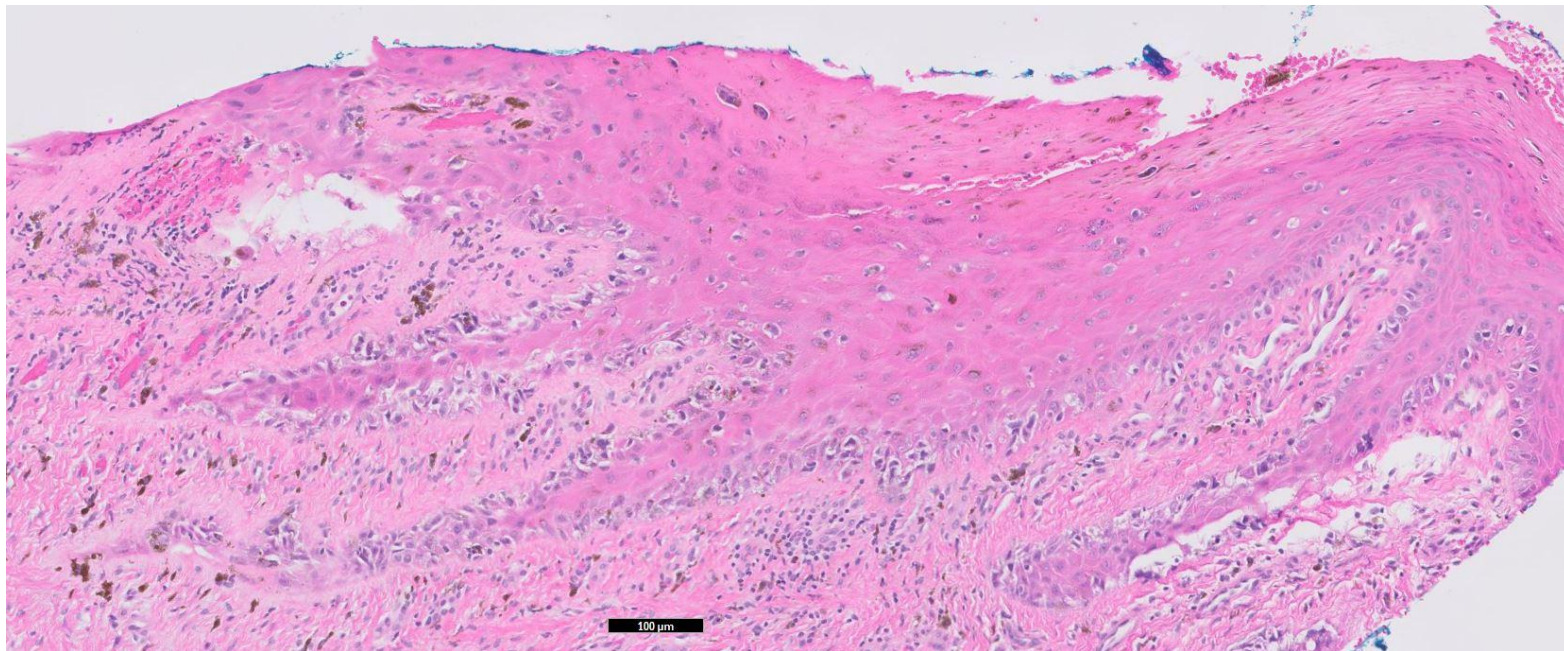
- Depends upon skin type



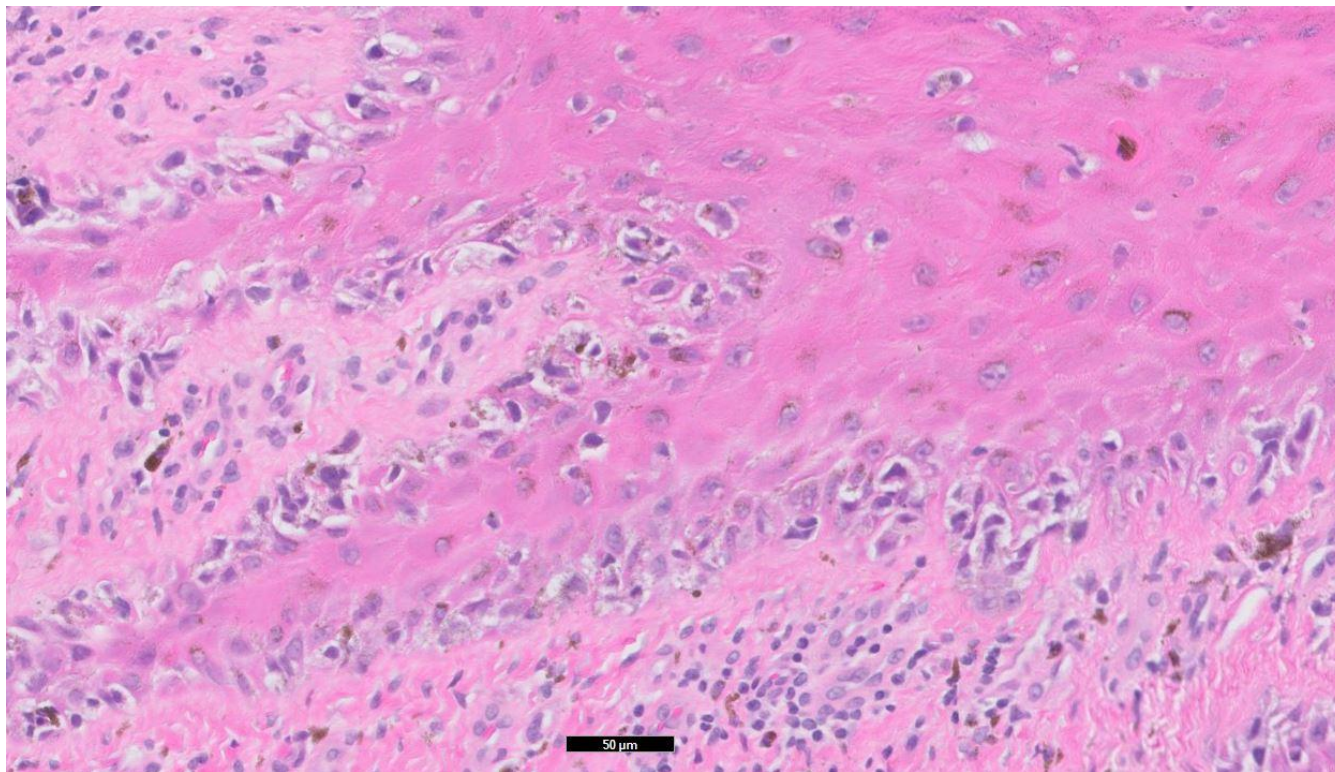
60 y/o left thumbnail



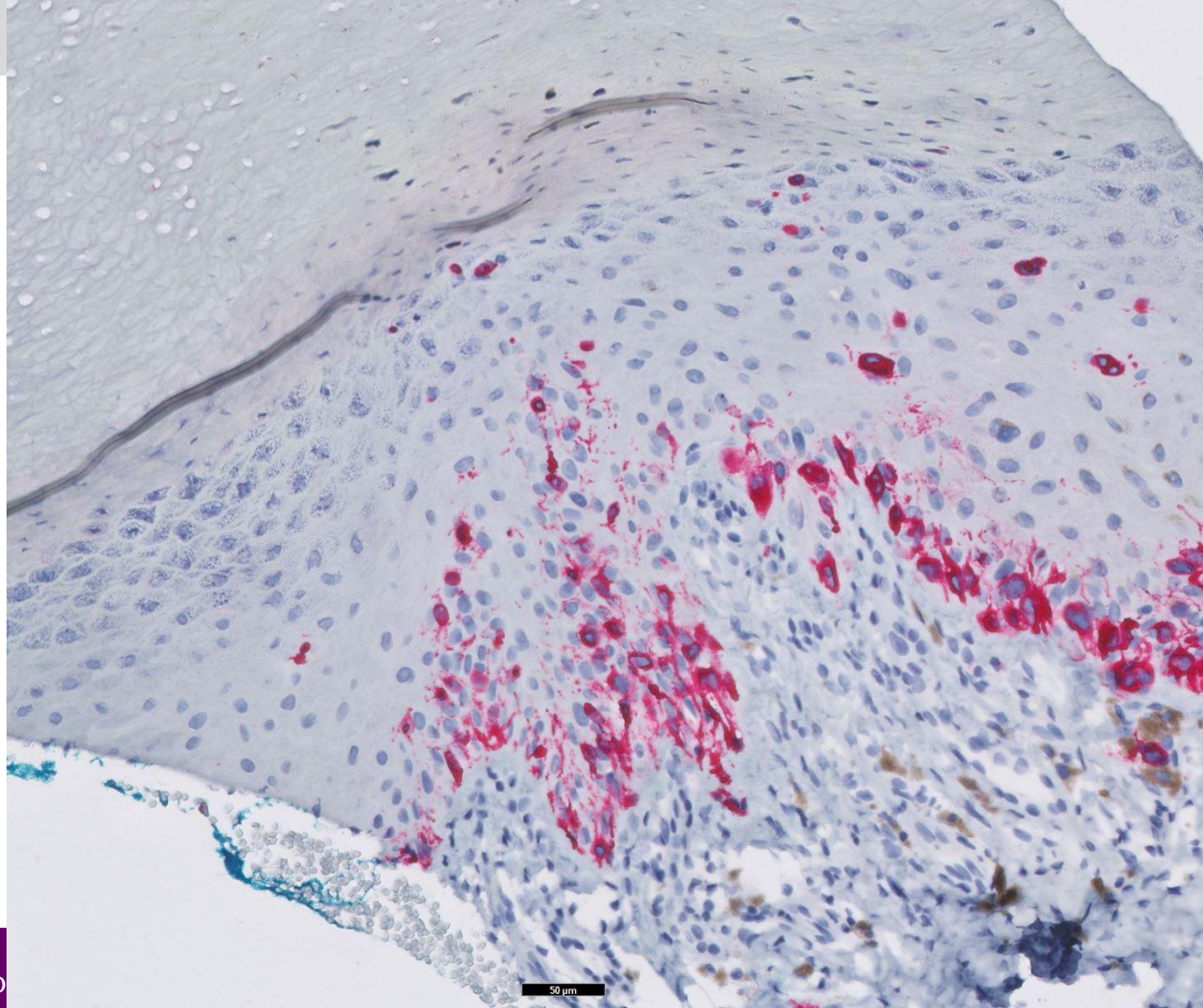
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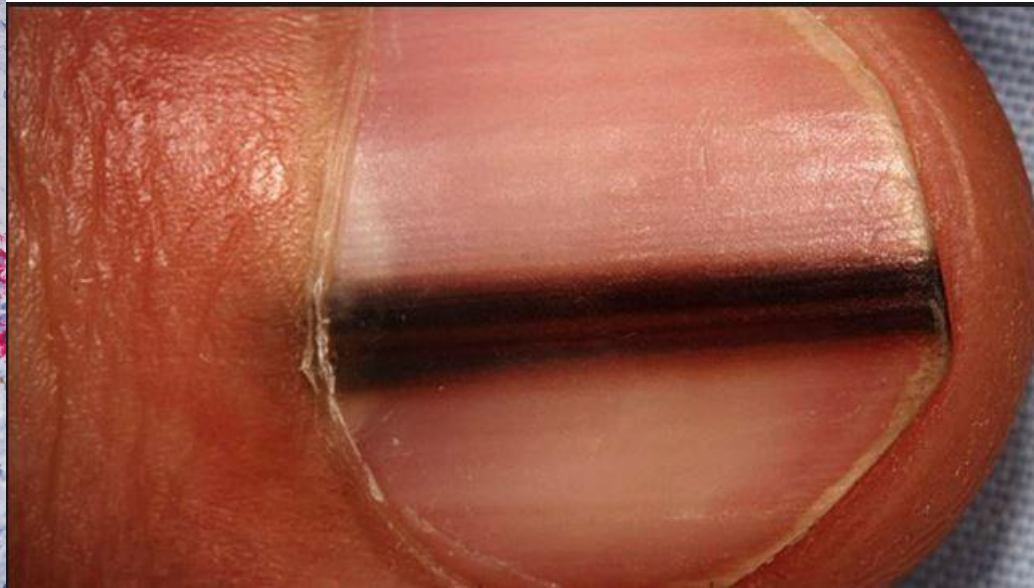
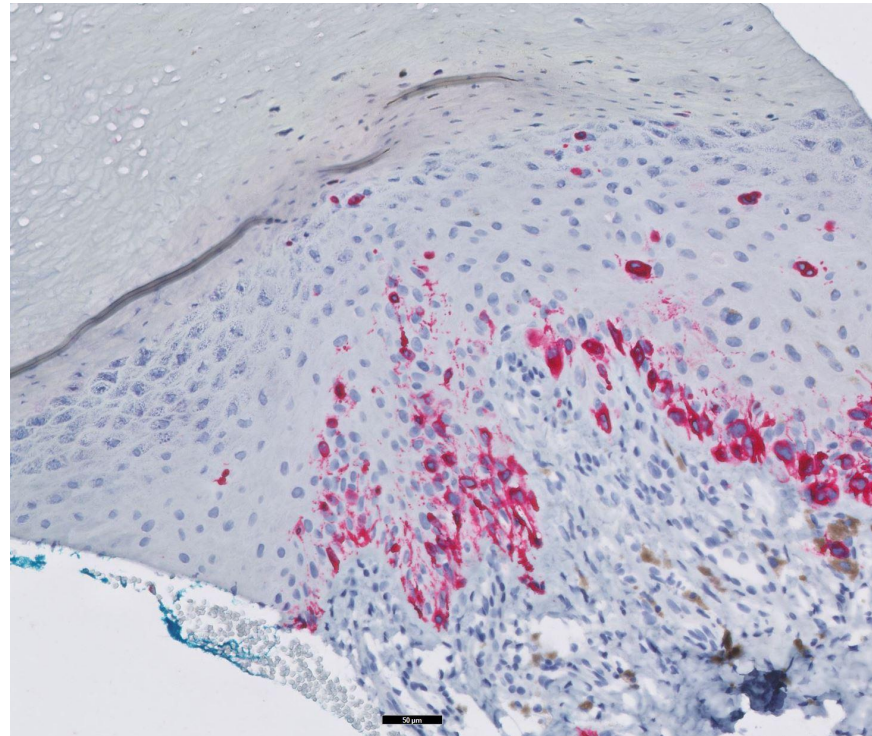
60 y/o left thumbnail



60 y/o



Melanoma in-situ



Histologic distinction between subungual lentigo and melanoma

Bijal Amin ¹, Kishwer S Nehal, Achim A Jungbluth, Bushra Zaidi, Mary S Brady, Daniel C Coit, Quin Zhou, Klaus J Busam

Affiliations + expand

PMID: 18391745 DOI: 10.1097/PAS.0b013e31815c8578

Abstract

The distinction between a benign subungual pigmented macule (lentigo) and an early lesion of melanoma in situ can be difficult. To identify histologic parameters of potential diagnostic value, we retrospectively reviewed biopsies and excisions of 35 pigmented nail lesions. We studied 20 melanomas (10 invasive and 10 noninvasive) and 15 benign subungual melanotic lentigines. Ten specimens of normal nail apparatus obtained for reasons other than melanonychia were also examined as controls. The parameters, which were analyzed, included the density of melanocytes, the presence of multinucleated cells, pagetoid spread, cytologic atypia, inflammation, and the distribution of melanin pigment. The density of melanocytes was measured as the number of cells per 1 mm stretch of subungual dermo-epithelial junction [=melanocyte count (MC)]. The MC for invasive melanomas was as follows: mean=102, median=92.5, and range 52 to 212. For noninvasive (only in situ) melanoma, the mean MC was 58.9, median 51, and range 39 to 136. For benign subungual melanotic macules, the mean MC was 15.3, median 14, and range 5 to 31. In normal controls, the mean MC was 7.7, median 7.5, and range 4 to 9. Qualitative features associated with in situ melanoma and useful for its distinction from benign subungual melanotic macules included the presence of confluent stretches of solitary units of melanocytes, multinucleated melanocytes, lichenoid inflammatory reaction, and florid pagetoid spread of melanocytes.

Histologic distinction between subungual lentigo and melanoma

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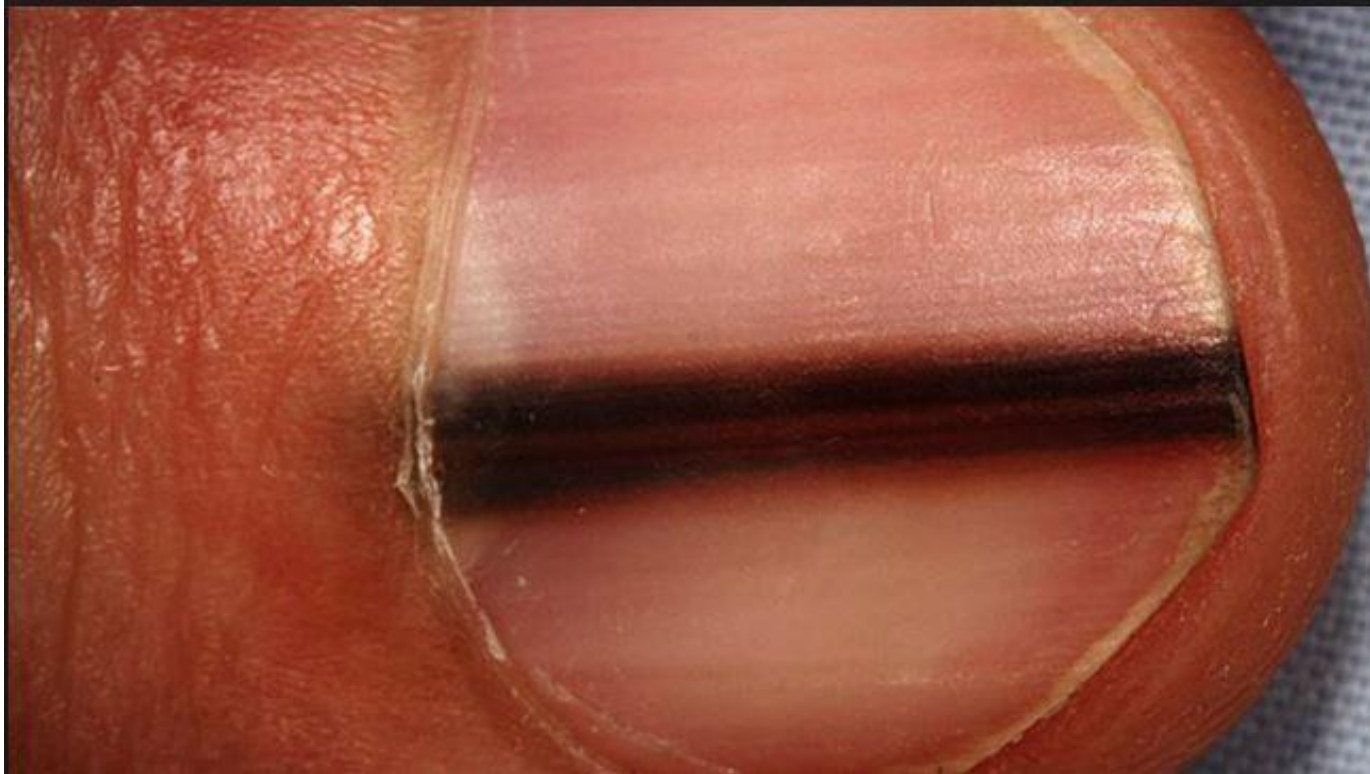
Abstract

The distinction between a benign subungual pigmented macule (lentigo) and an early lesion of melanoma in situ can be difficult. To identify histologic parameters of potential diagnostic value, we retrospectively reviewed biopsies and excisions of 35 pigmented nail lesions. We studied 20 melanomas (10 invasive and 10 noninvasive) and 15 benign subungual melanotic lentigines. Ten specimens of normal nail apparatus obtained for reasons other than melanonychia were also examined as controls. The parameters, which were analyzed, included the density of melanocytes, the presence of multinucleated cells, pagetoid spread, cytologic atypia, inflammation, and the distribution of melanin pigment. The density of melanocytes was measured as the number of cells per 1 mm stretch of subungual dermo-epithelial junction [=melanocyte count (MC)]. The MC for invasive melanomas was as follows: mean=102, median=92.5, and range 52 to 212. For noninvasive (only in situ) melanoma, the mean MC was 58.9, median 51, and range 39 to 136. For benign subungual melanotic macules, the mean MC was 15.3, median 14, and range 5 to 31. In normal controls, the mean MC was 7.7, median 7.5, and range 4 to 9. Qualitative features associated with in situ melanoma and useful for its distinction from benign subungual melanotic macules included the presence of confluent stretches of solitary units of melanocytes, multinucleated melanocytes, lichenoid inflammatory reaction, and florid pagetoid spread of melanocytes.

68 y/o female—new black line

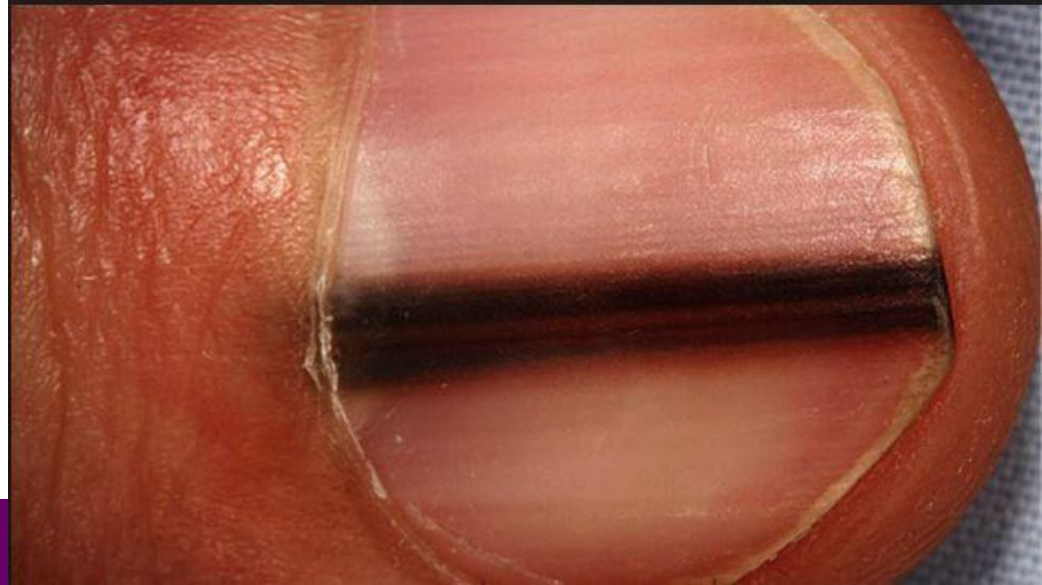


Clinical presentation important



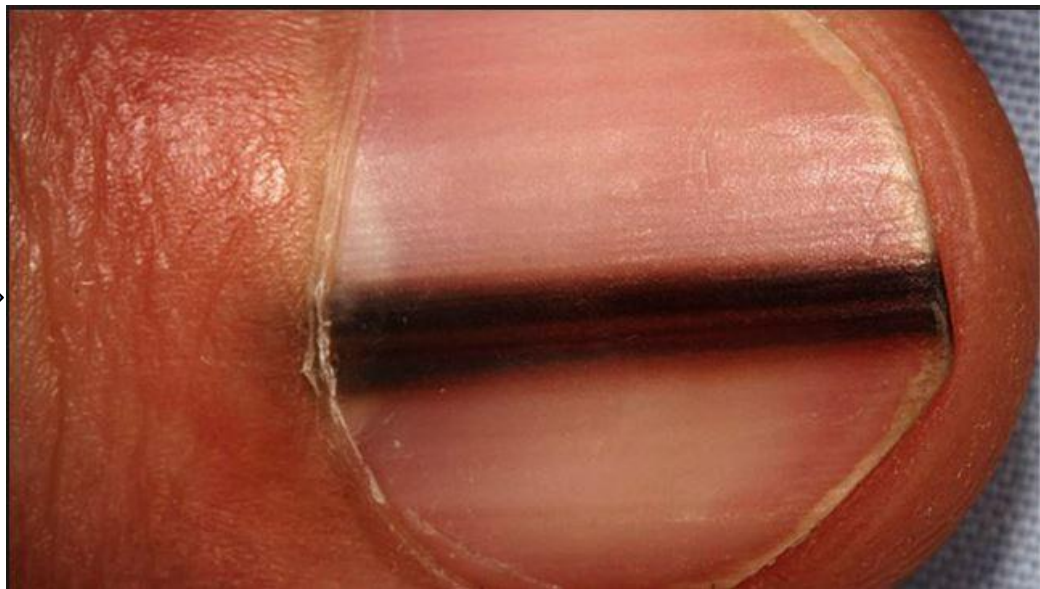
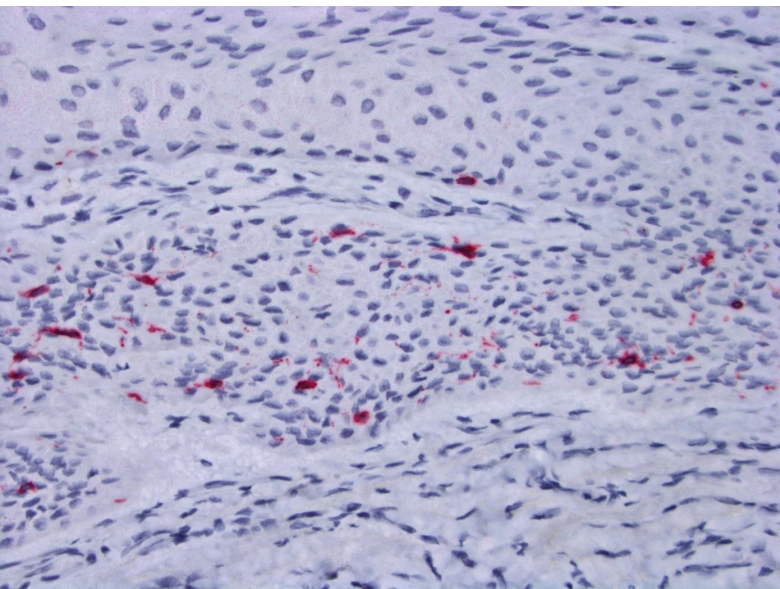
Clinical presentation important

- New pigment
- Older age
- Skin type

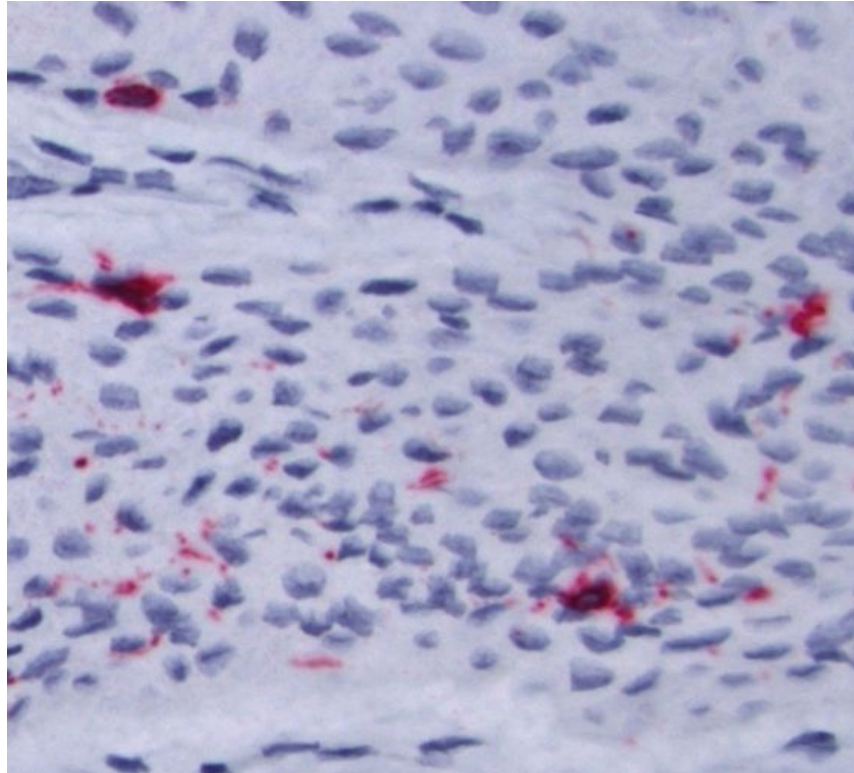


Clinical presentation important

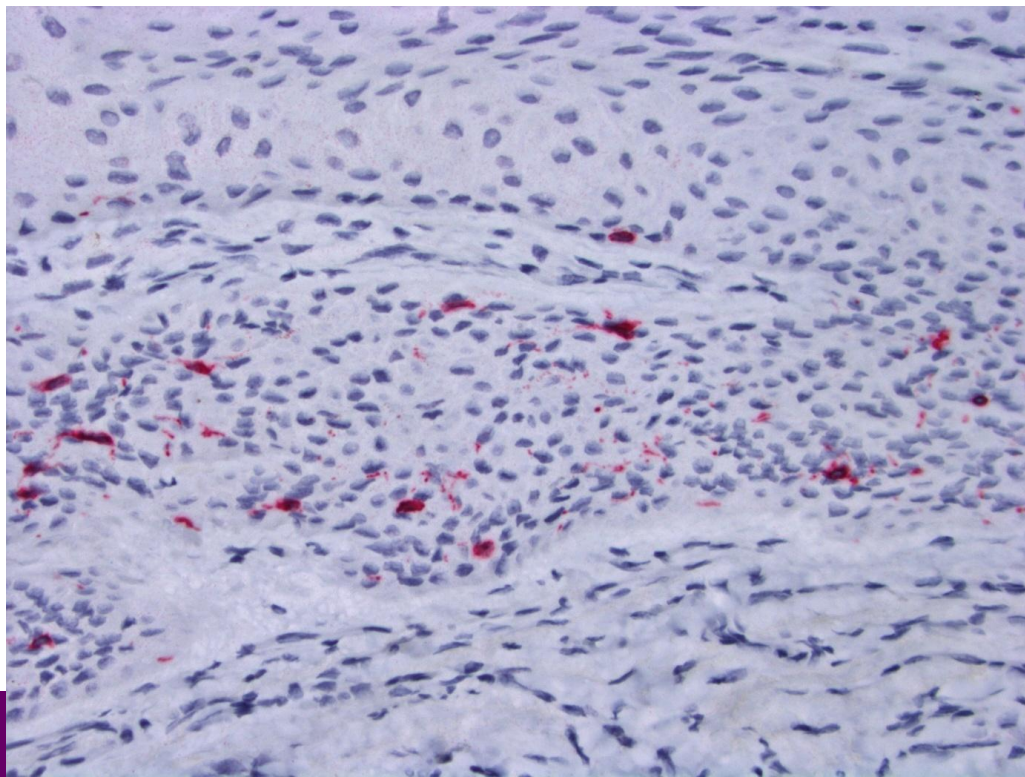
- New lesion in older patient



Dendritic melanocytes in B9 and malignant



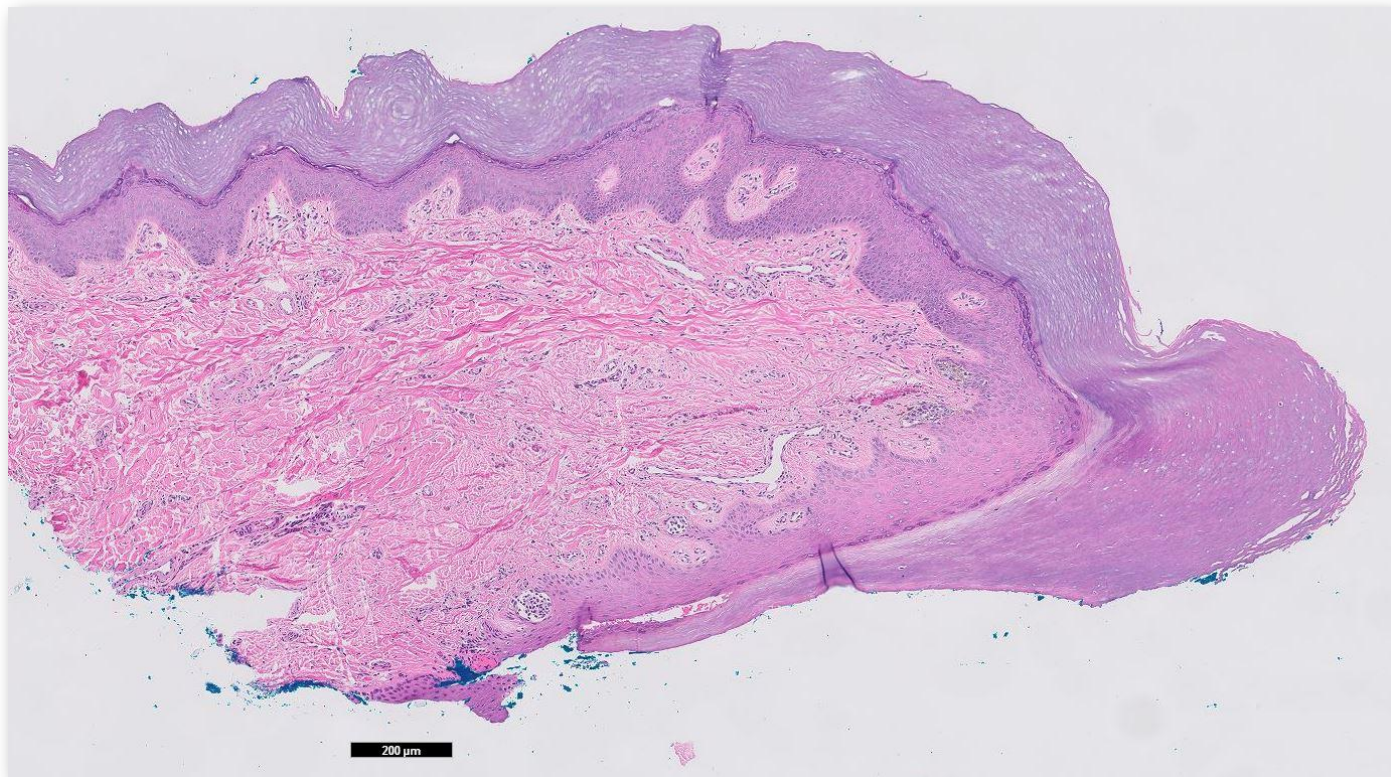
Margin assessment may be challenging

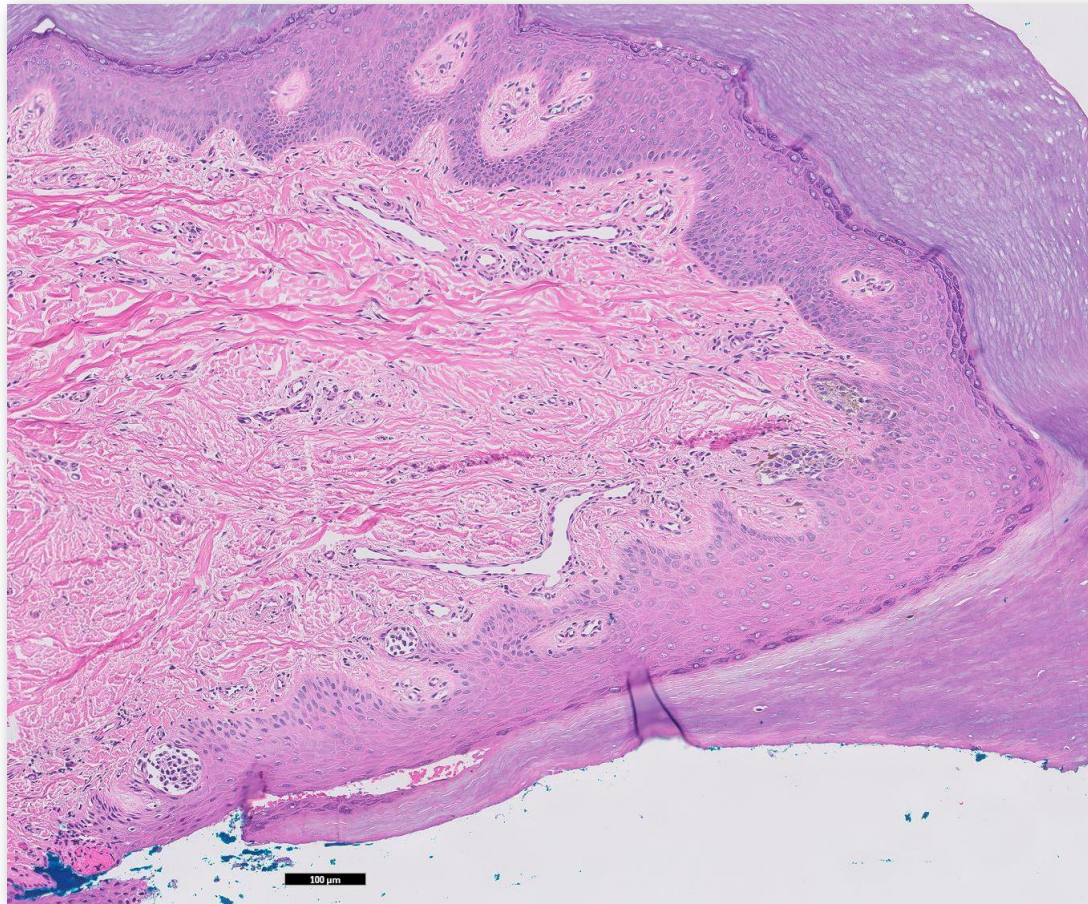


- 10 y/o male with pigmented nail of great toe. It appeared at age 3.

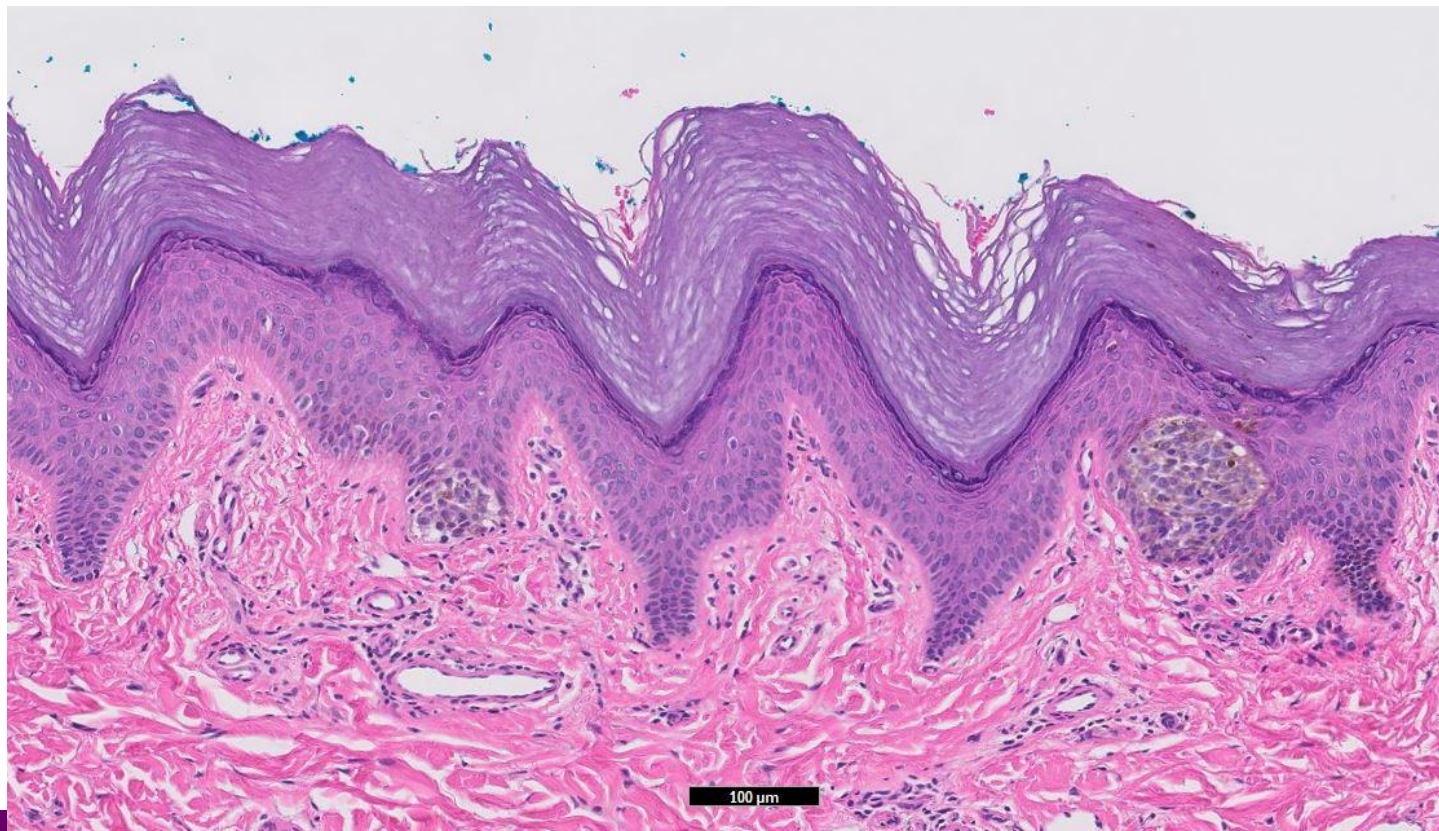


10 y/o boy

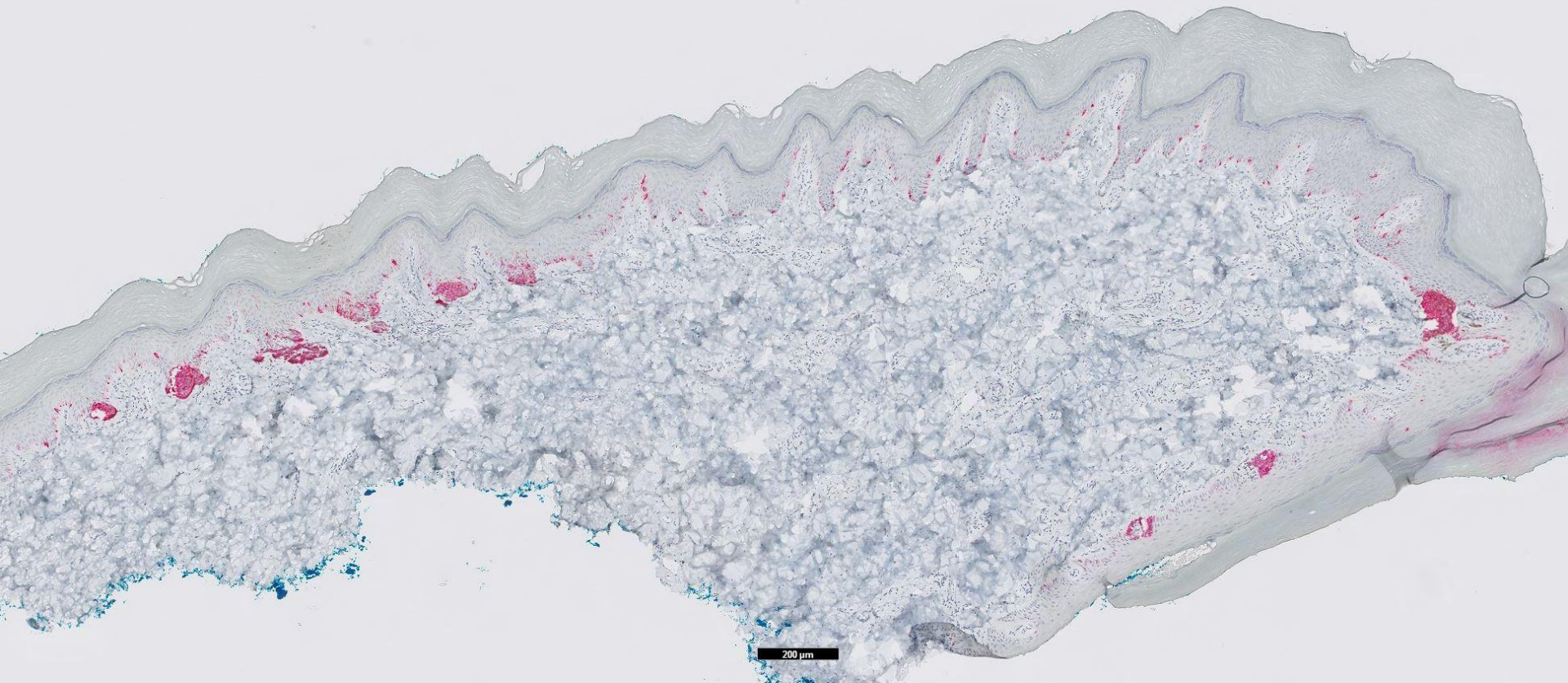




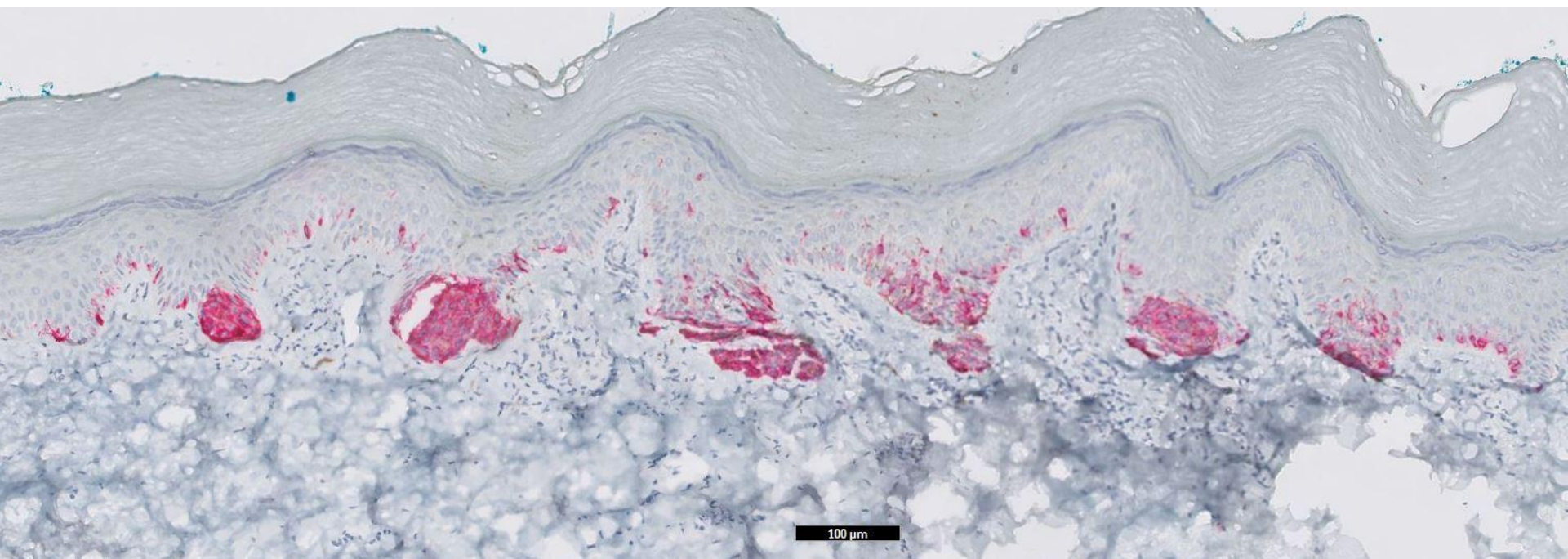
Proximal nail fold



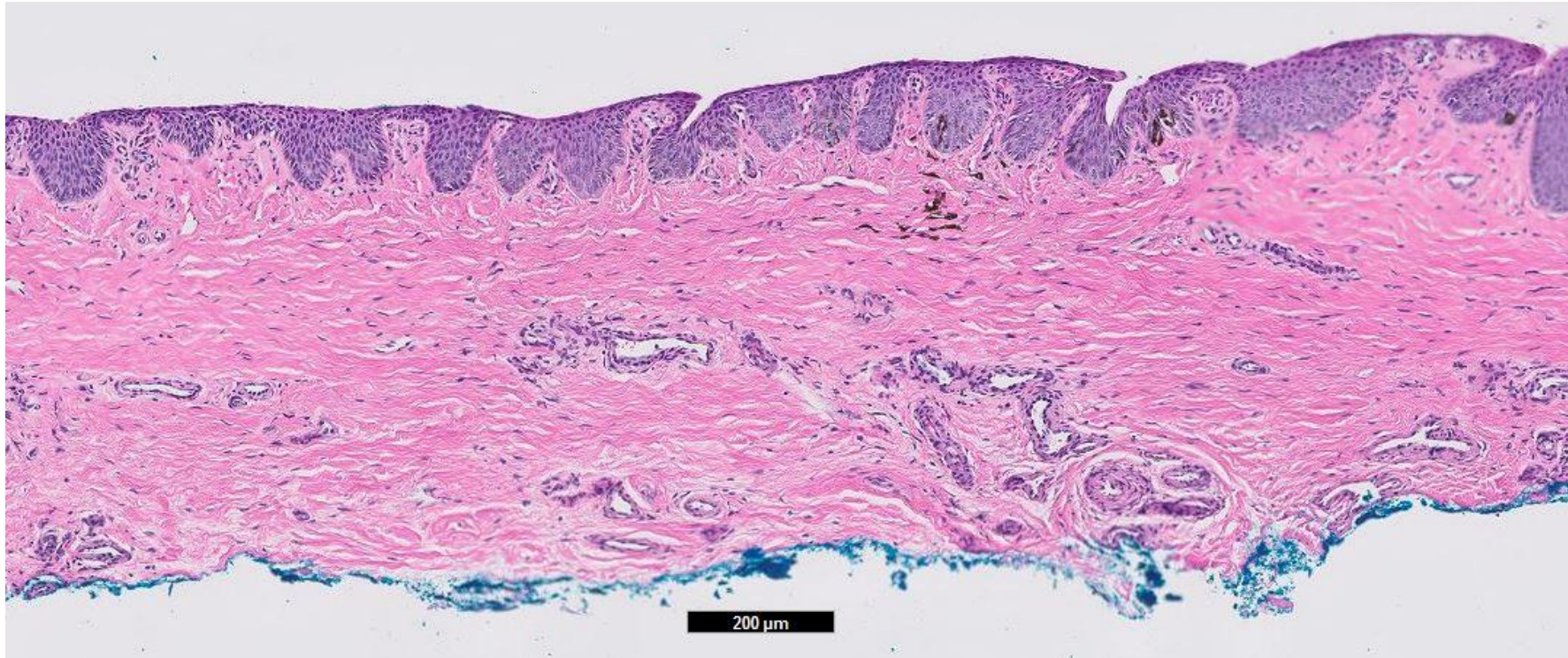
10 y/o



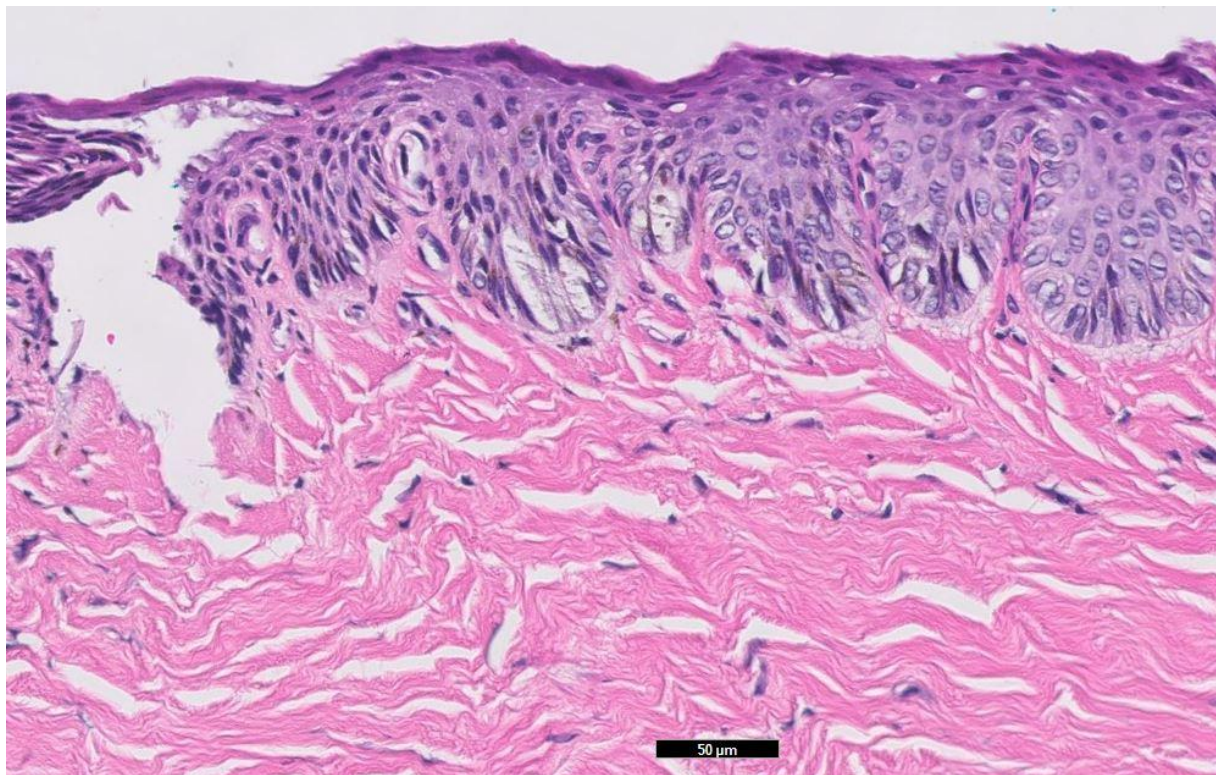
Proximal nail fold



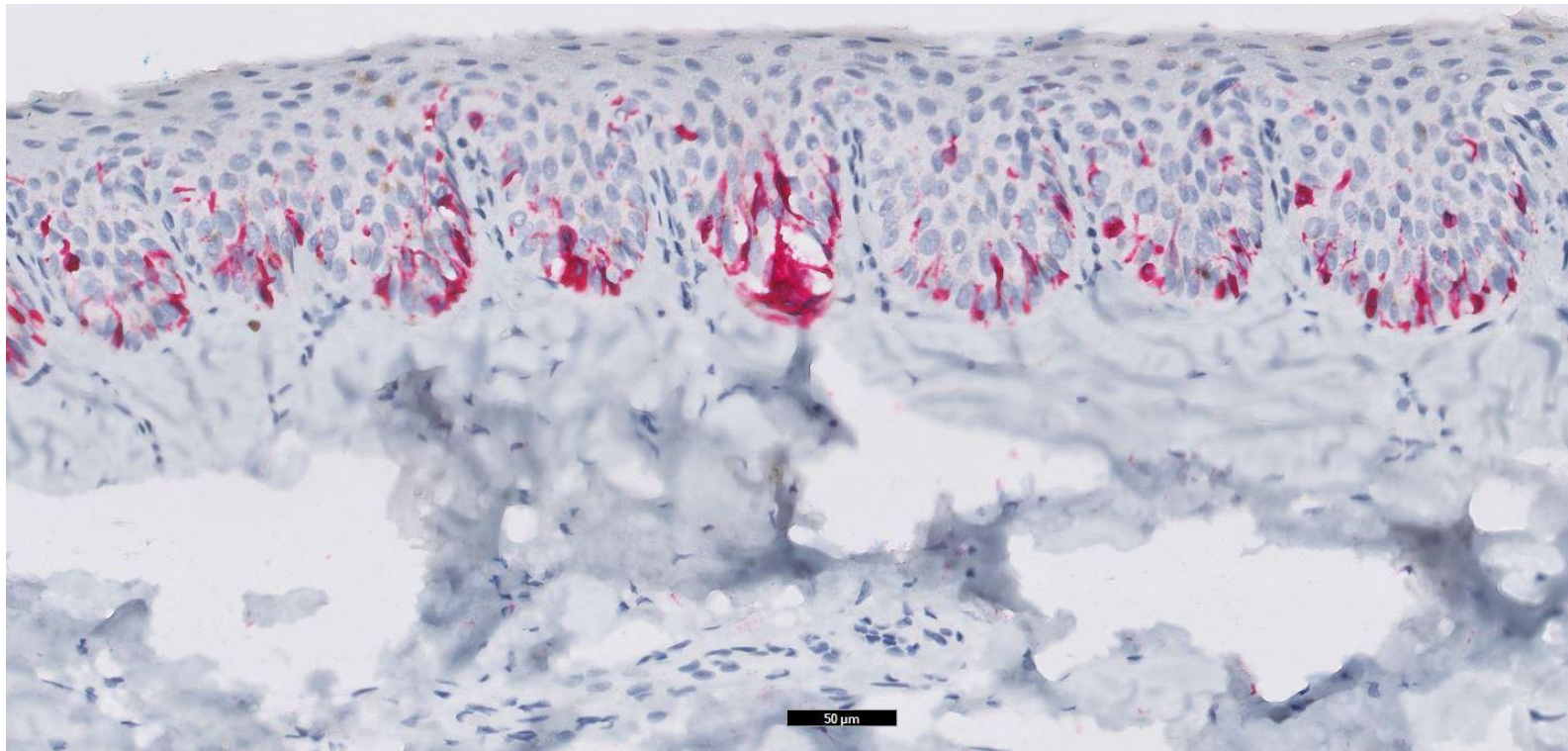
Nail bed/matrix



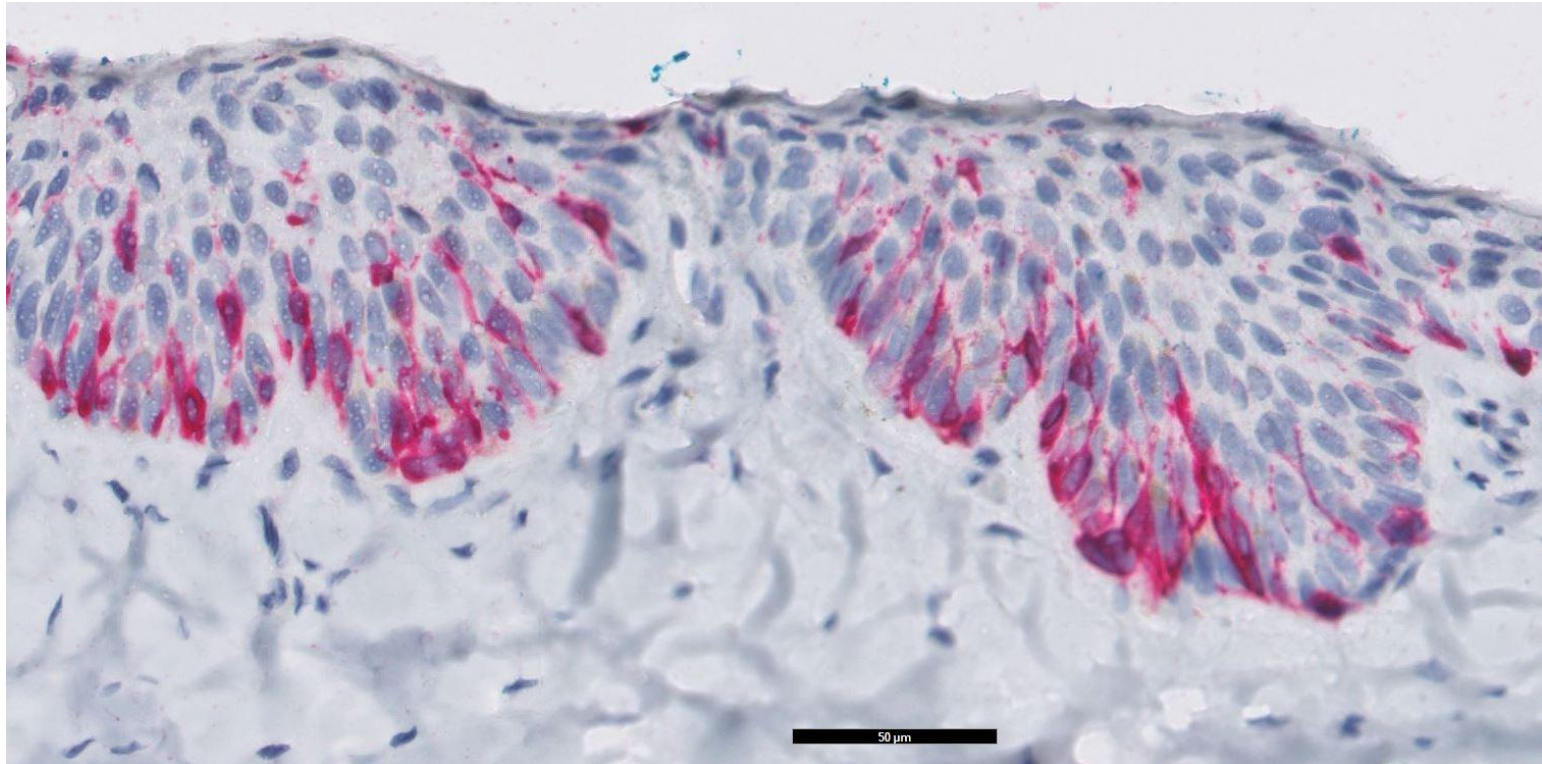
10 y/o nail bed/matrix



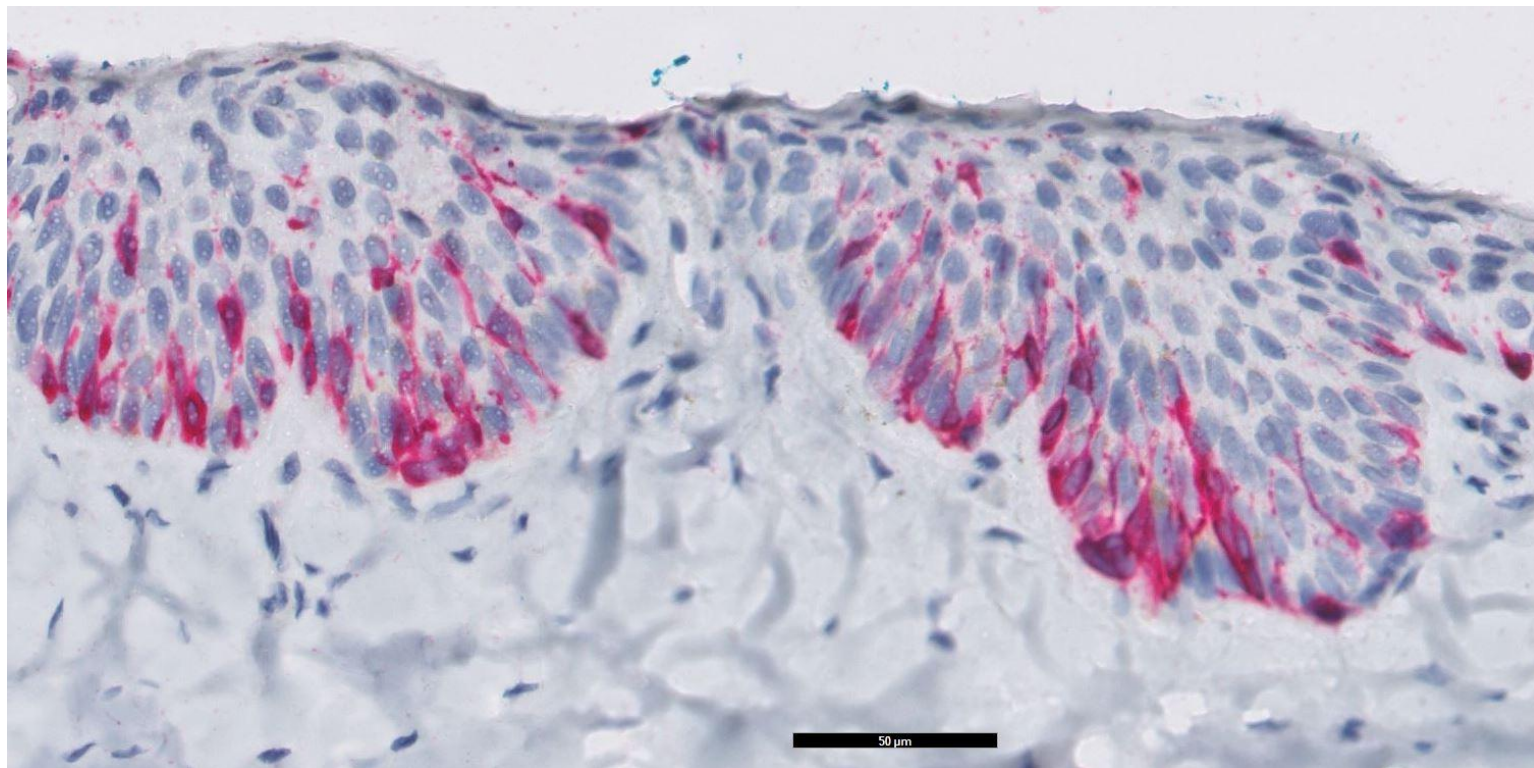
Nail bed/matrix



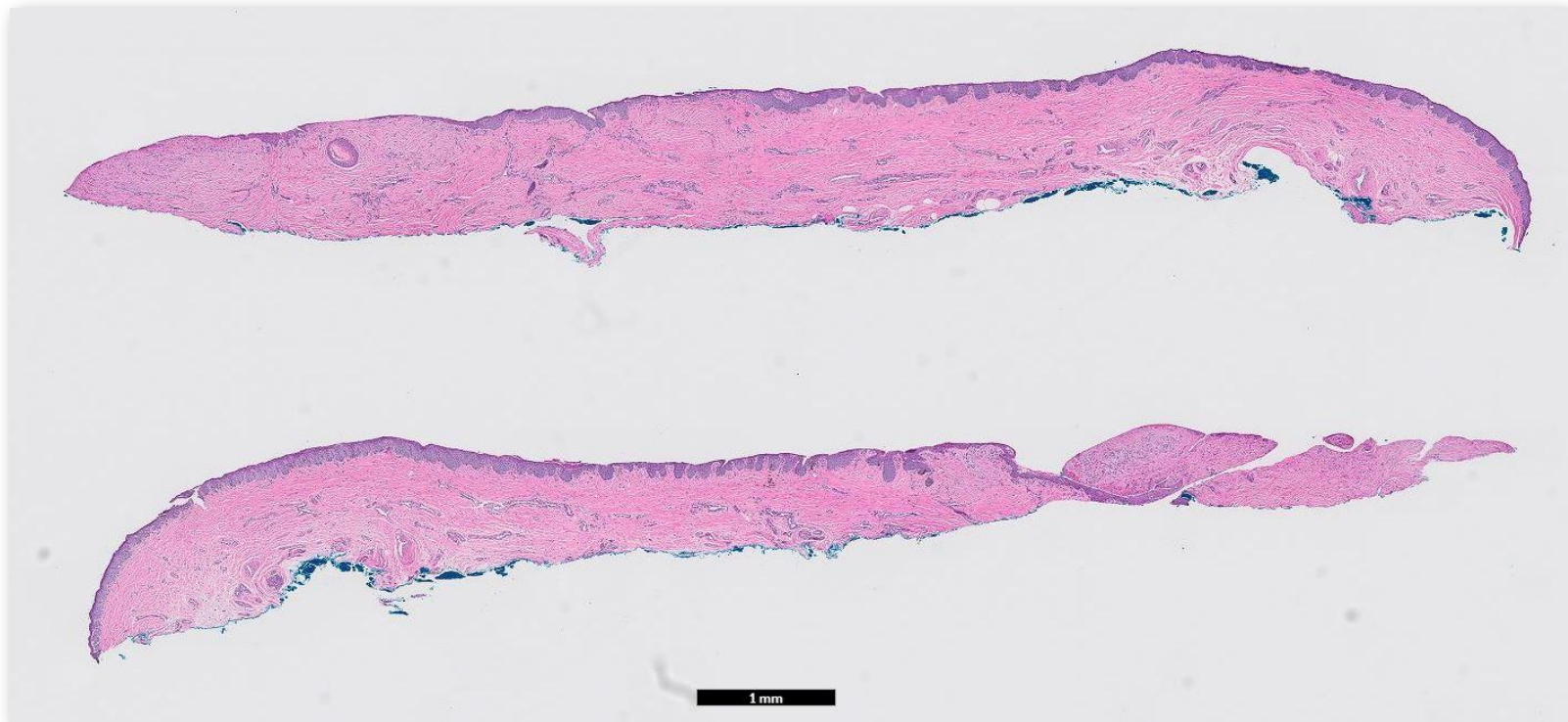
Nail bed/matrix



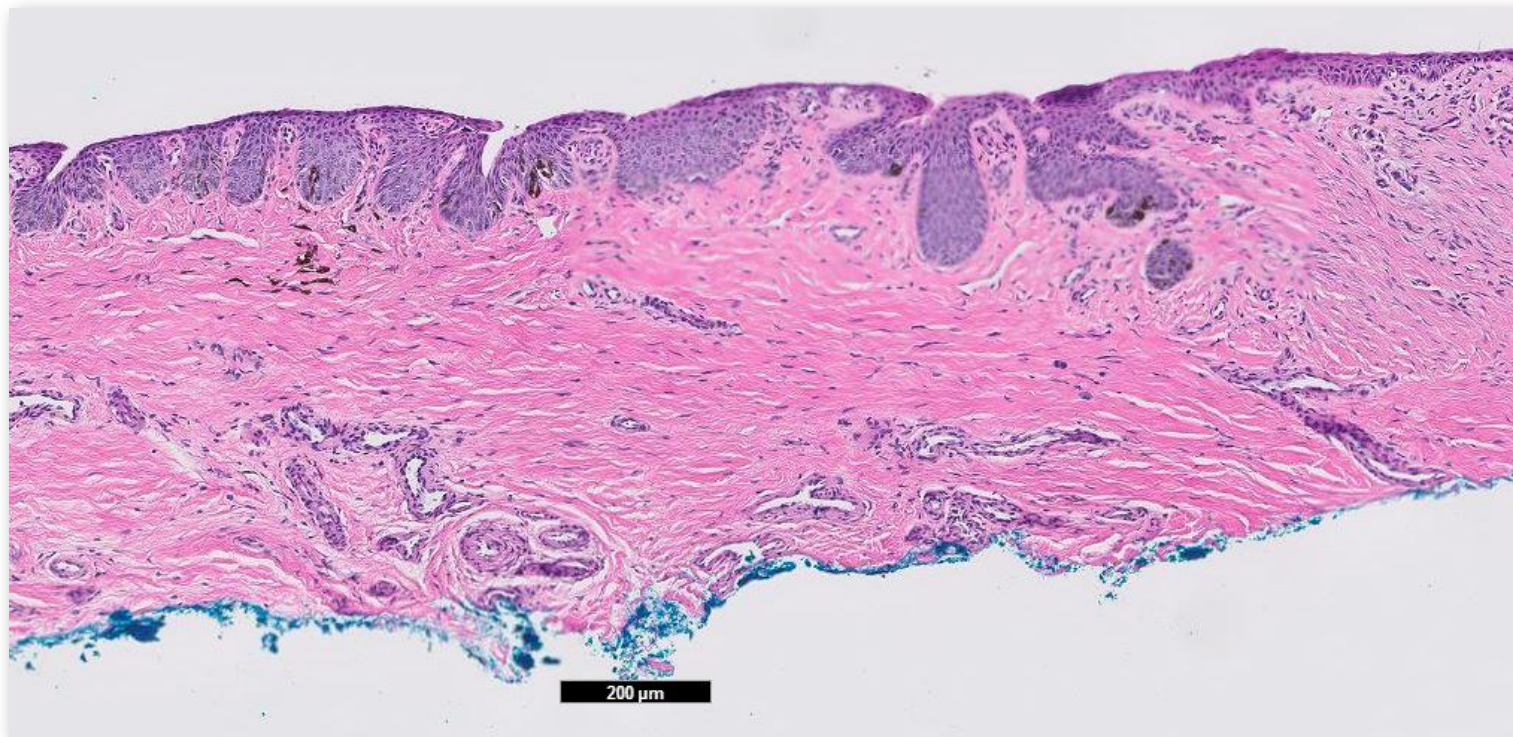
Benign nevus in 10 y/o



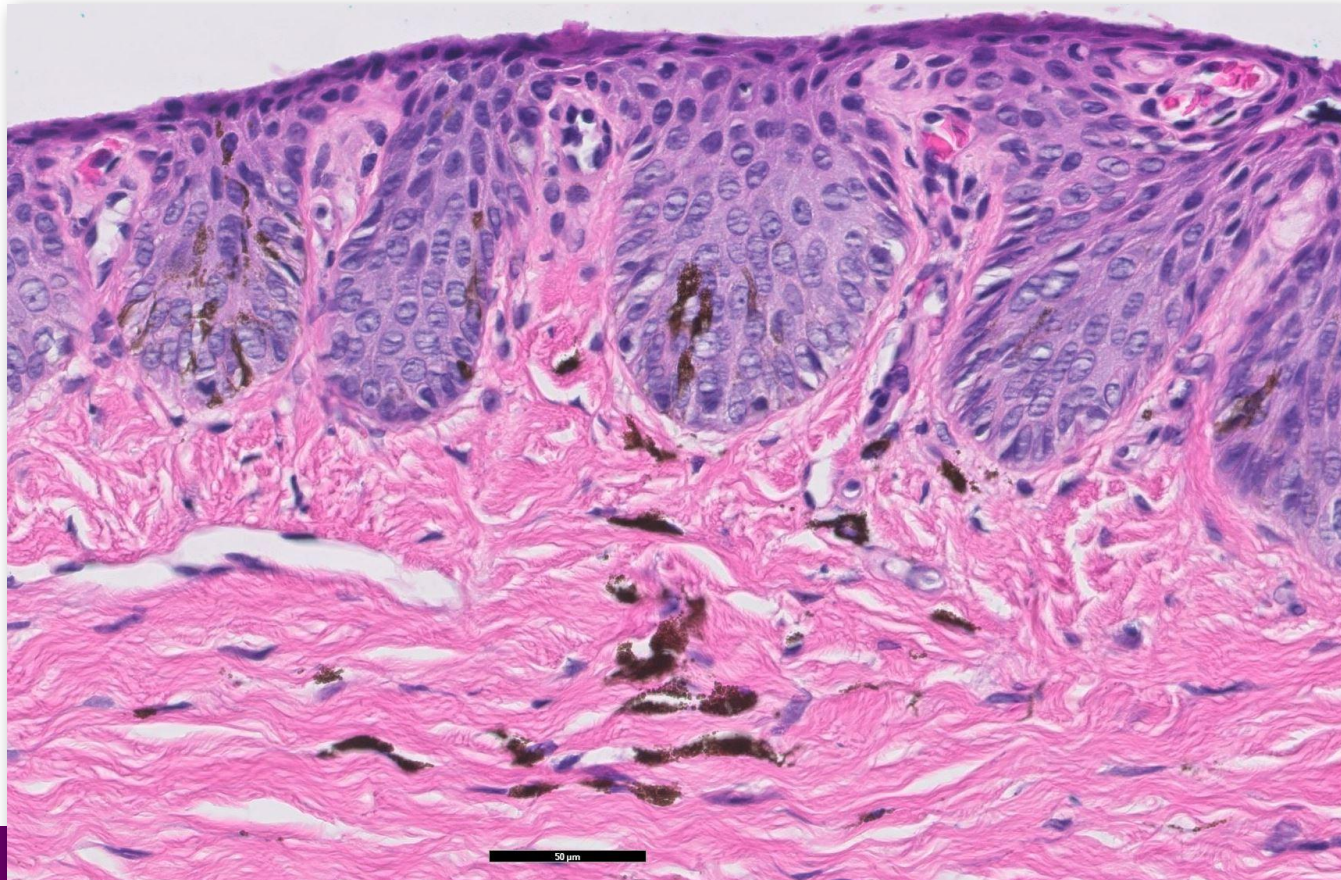
13 y/o male



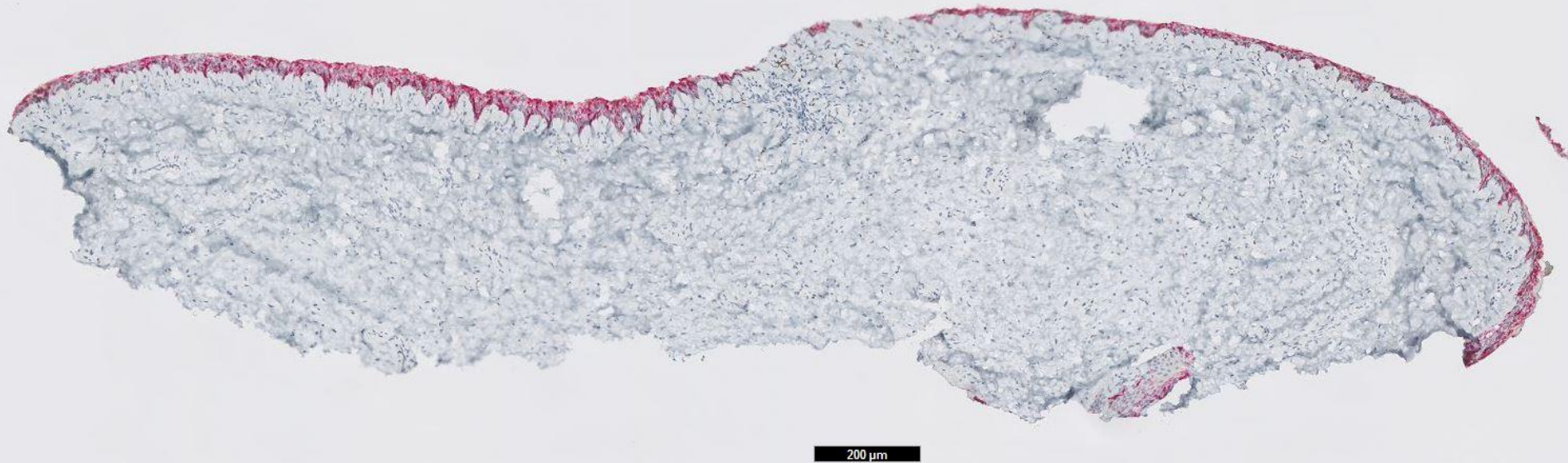
13 y/o male



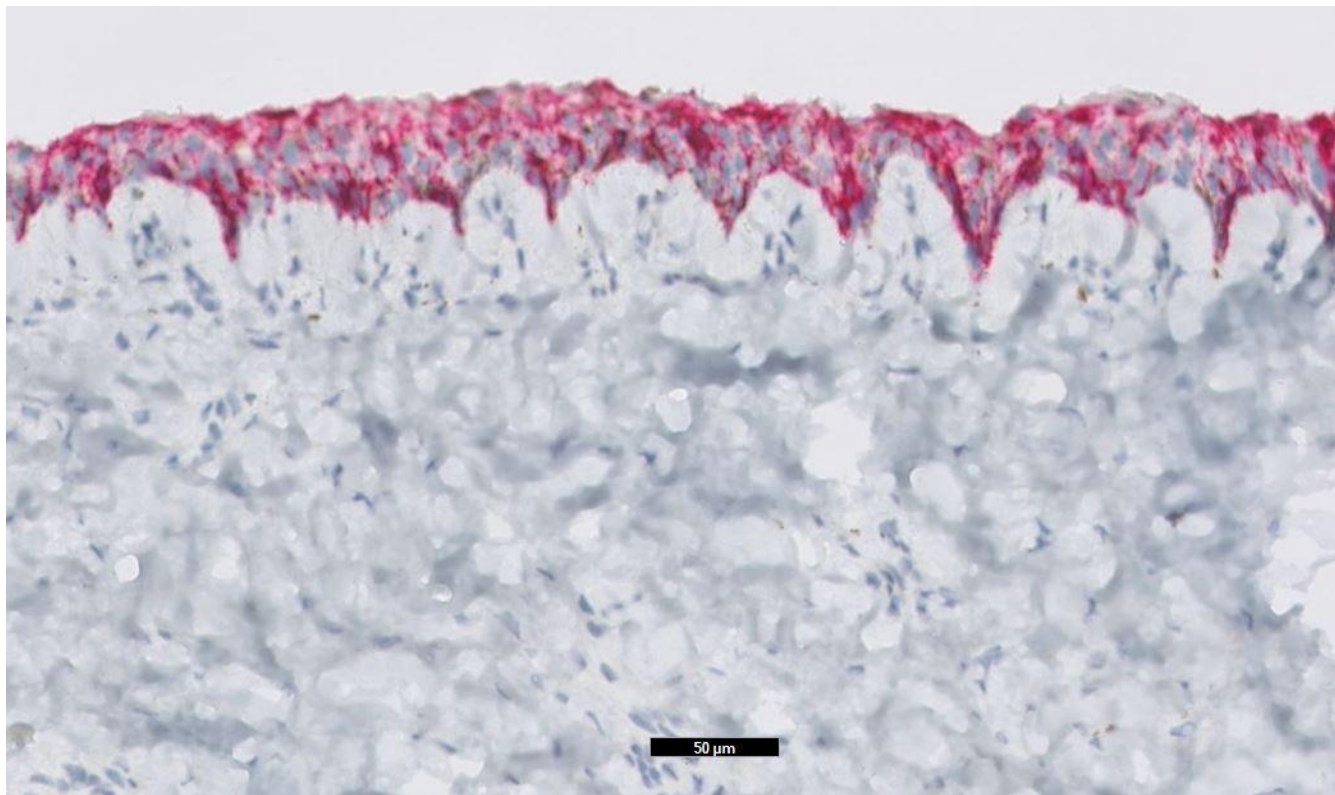
13 y/o male



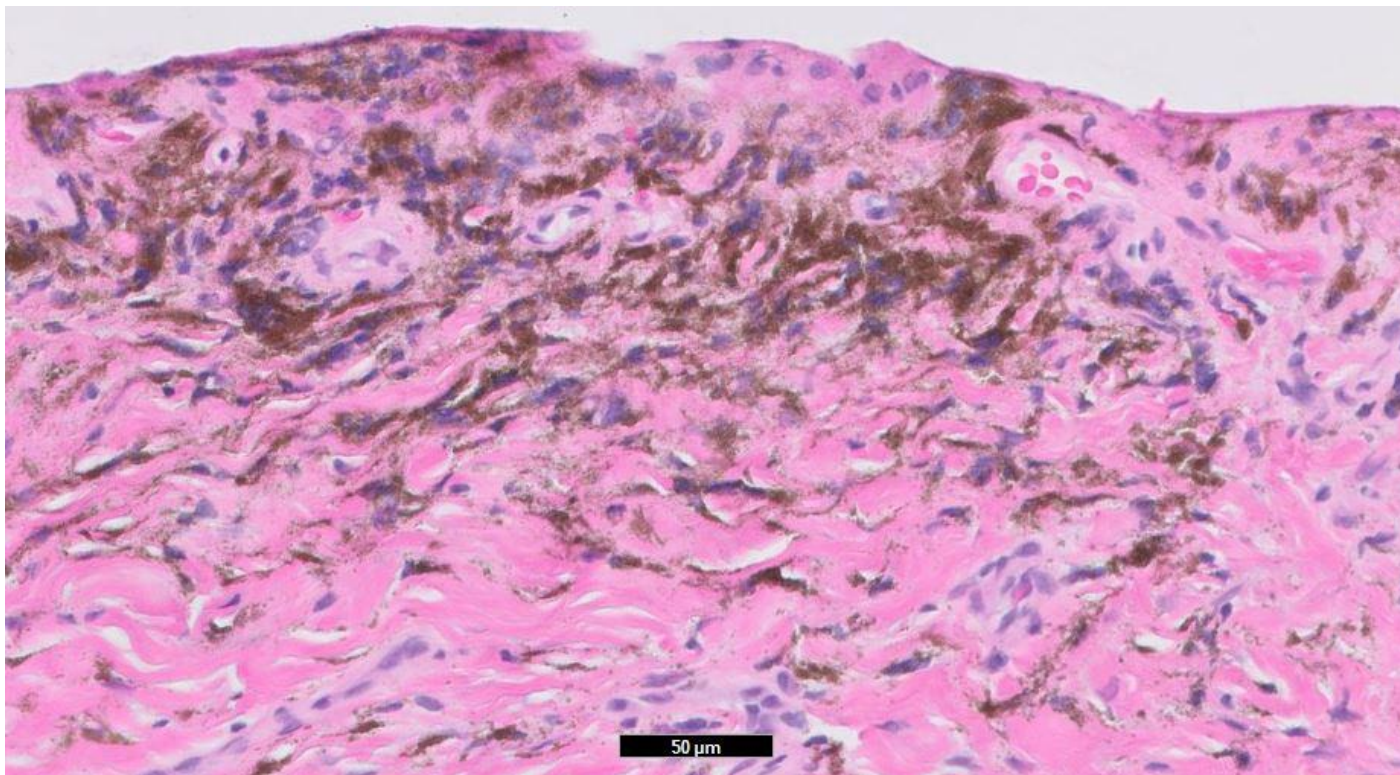
13 y/o nailbed



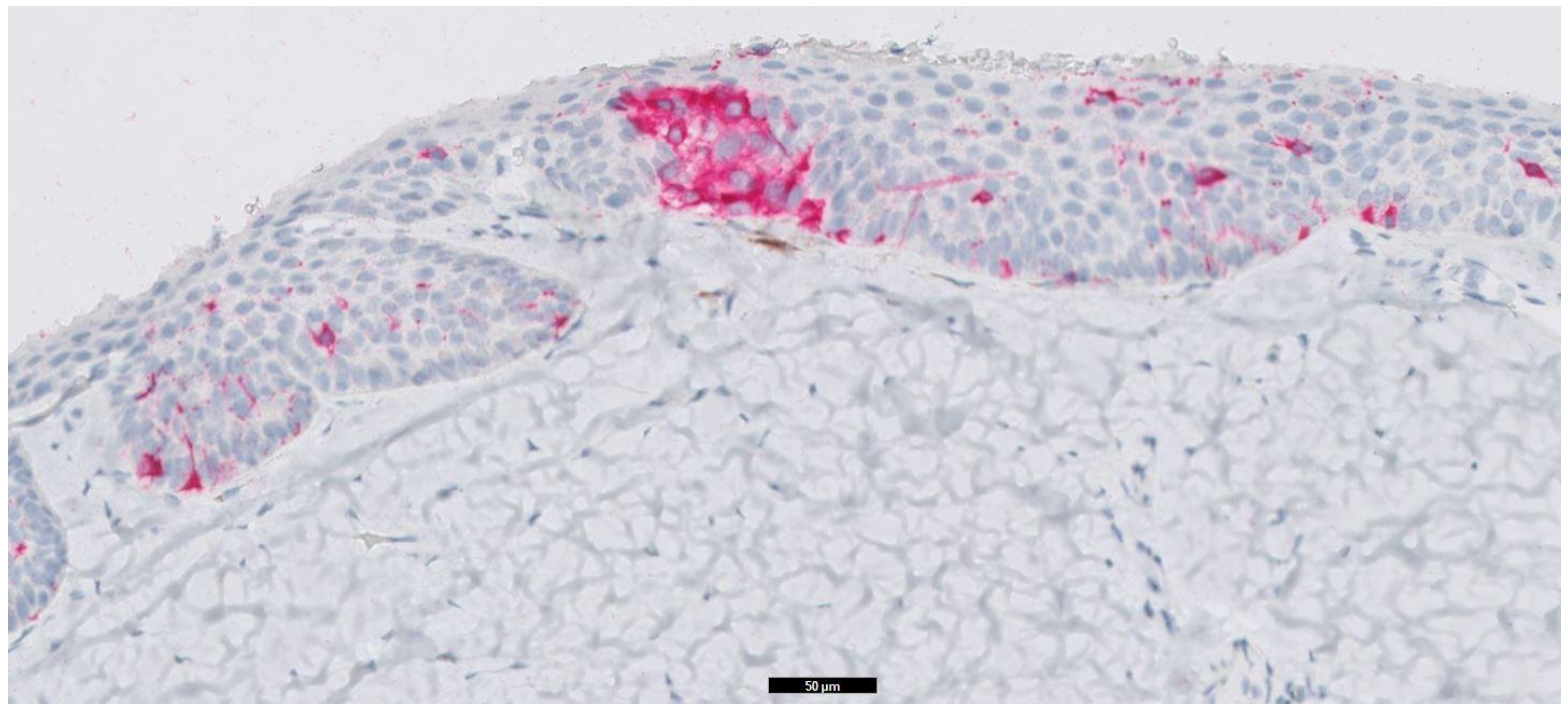
13 y/o nailbed



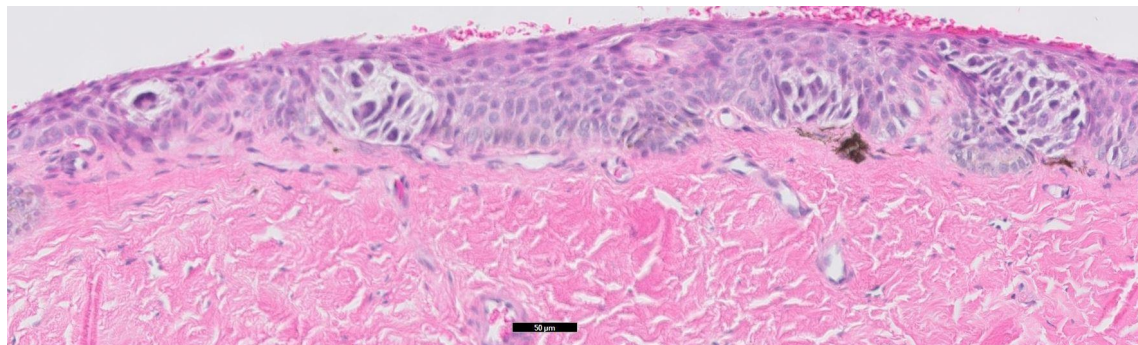
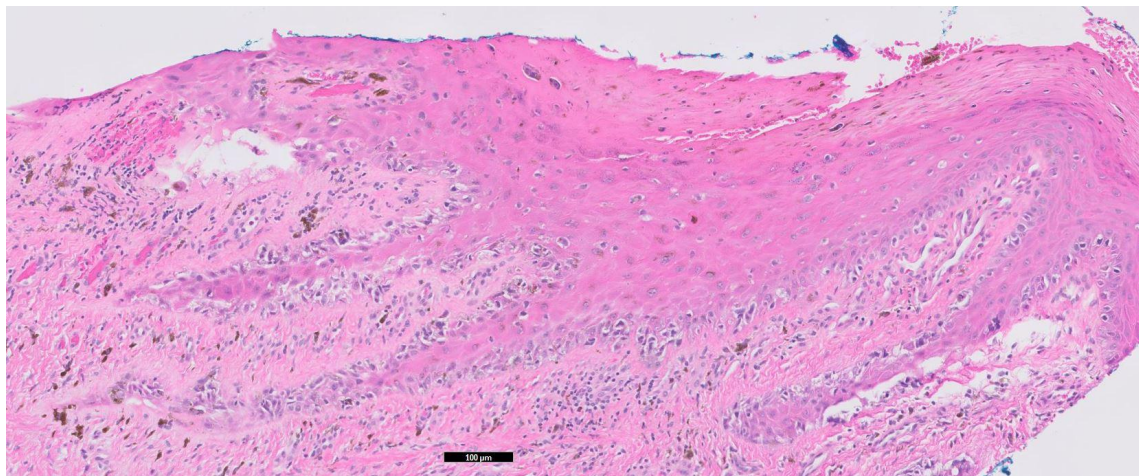
18 y/o



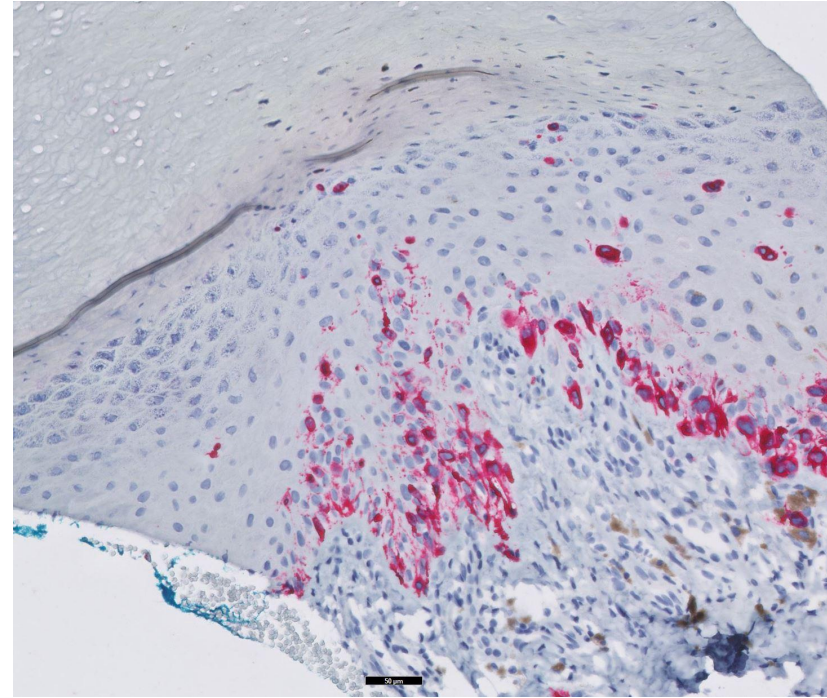
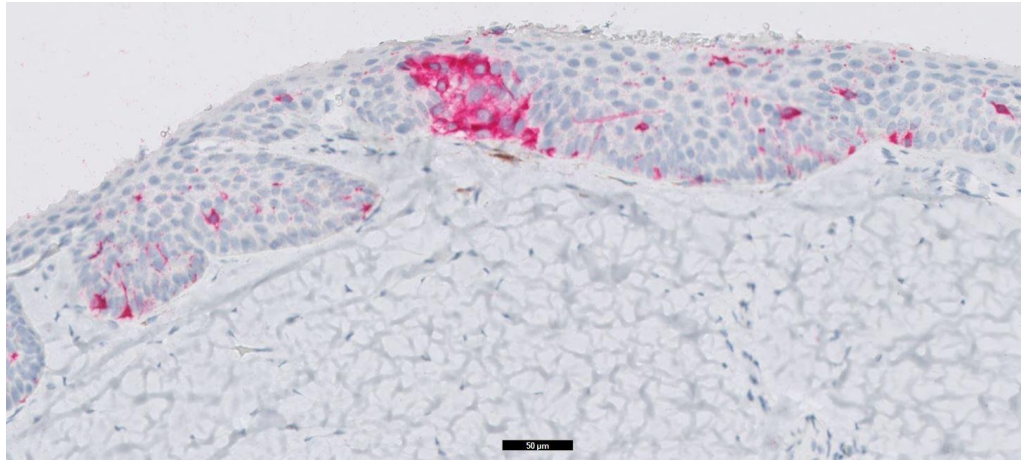
18 y/o nail



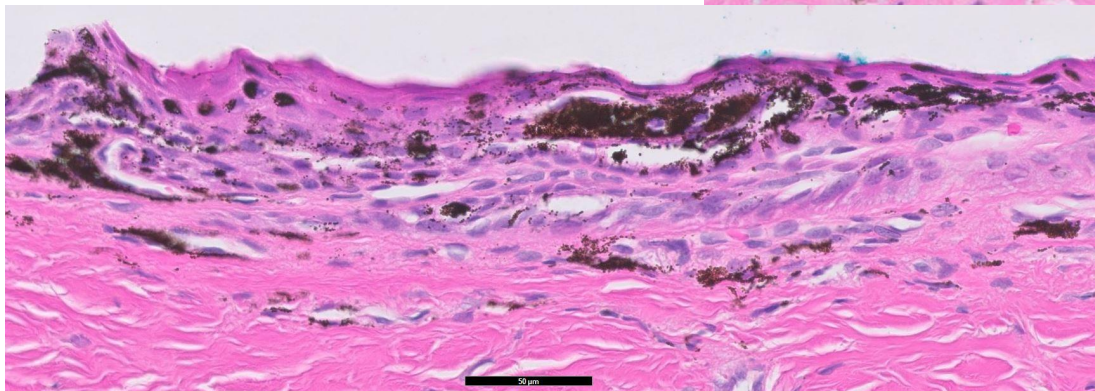
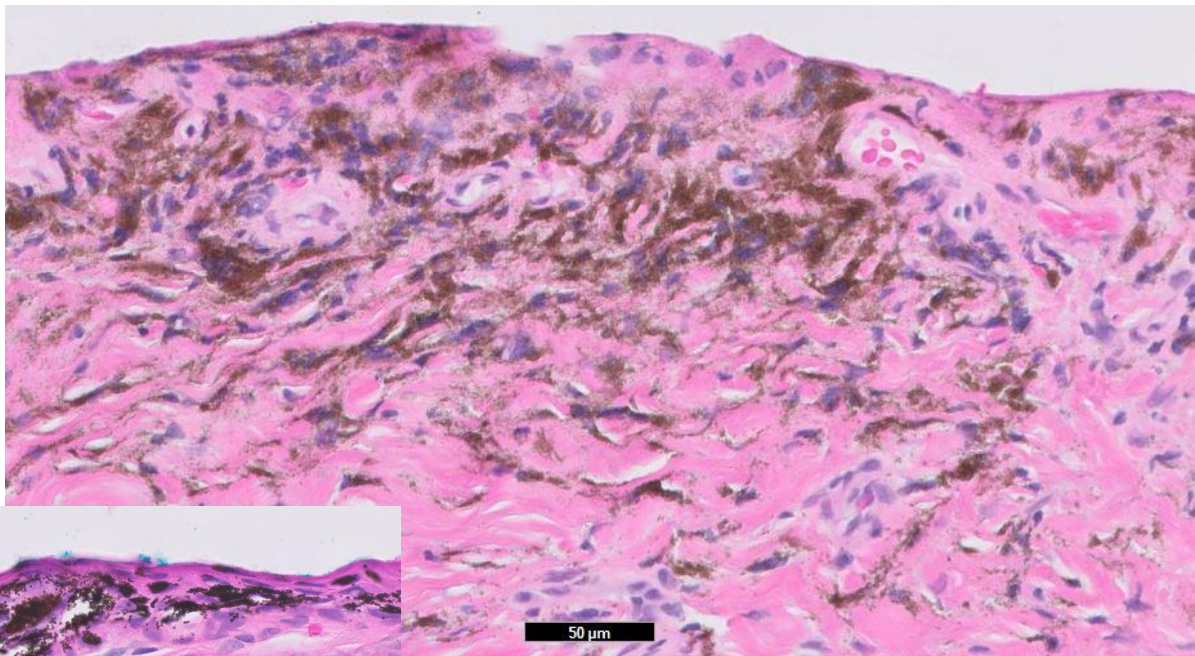
**Benign?
Atypical?
Malignant?**



Benign?
Atypical?
Malignant?



**Benign?
Atypical?
Malignant?**



Pigmented lesion in a child

- Often type III skin type or above (worry about acral lentiginous MM)
- Concern to parents—pressure to biopsy
- Biopsy shows large, single, Spitzoid melanocytes (?Atypia?)

Pigmented lesion in a child

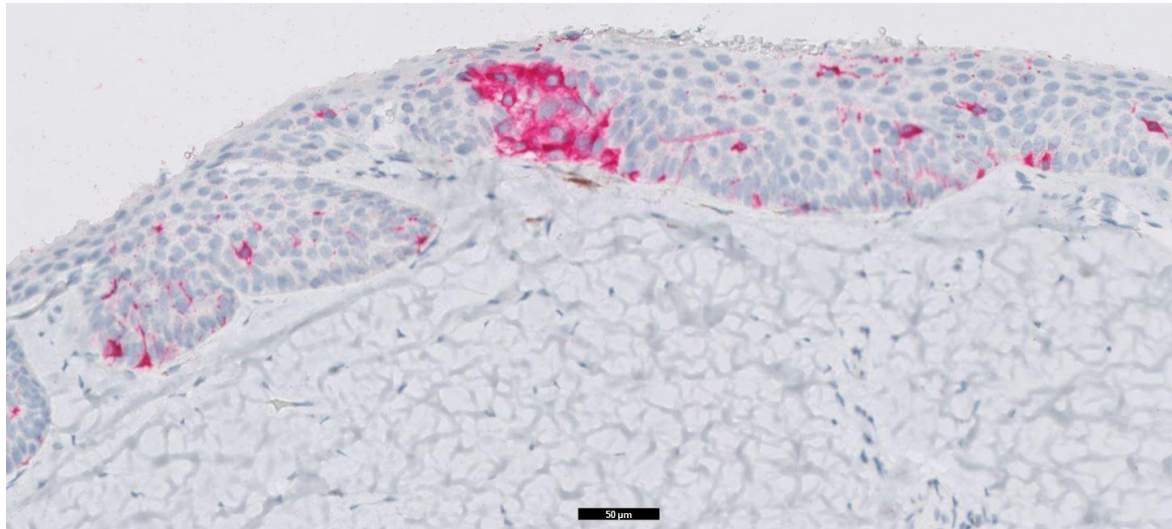
- Few pediatric melanocytic tumors sampled—nail experts do not sample
- Traditional criteria for benign vs atypical vs malignant do not apply

Current histopathology assessment is of limited utility.

- H&E
- Immunohistochemistry
- Genetic analysis—not yet possible

Immunohistochemistry

- Most only highlights melanocytes
- MelanA (Mart1), SOX-10, HMB45




Molecular markers—B9 vs malignant

- p16
- Not useful

ORIGINAL ARTICLE

Immunohistochemical characterization of benign activation of junctional melanocytes and melanoma in situ of the nail unit

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³Department of Dermatopathology, University Hospital Brugmann, Brussels, Belgium

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Background: Immunohistochemical (IHC) stains that distinguish benign, pigmented nail lesions from malignancy are needed. Candidate markers of malignant transformation include p16, HMB45, and Ki-67, with p16 being of particular interest. There is limited knowledge about the spectrum of p16 expression in pigmented lesions, especially junctional melanocytic proliferations of the nail. The objective of this study was to determine if any of these markers demonstrate diagnostic utility in distinguishing between benign activation of junctional melanocytes (BAM) and melanoma in situ (MIS) of the nail unit.

Methods: In this retrospective study, ten cases of BAM and eight cases of MIS were identified. Archival slides available for review included H&E (hematoxylin and eosin), Fontana-Masson, and MelanA (Mart1) IHC slides. IHC studies for p16, HMB45, and dual-color Ki-67/MelanA (Mart1) were then performed.

Results: None of the tested IHC stains distinguished BAM from MIS. p16 IHC expression was uniformly negative with the exception of two cases of MIS. HMB45 was positive in all BAM and

Molecular markers—B9 vs malignant

- PRAME?

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PRAME Expression in Melanocytic Tumors

[Cecilia Lezcano](#), MD,* [Achim A. Jungbluth](#), MD,* [Kishwer S. Nehal](#), MD,† [Travis J. Hollmann](#), MD, PhD,* and [Klaus J. Busam](#), MD*

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Abstract

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PRAME (PReferentially expressed Antigen in MELanoma) is a melanoma-associated antigen that was isolated by autologous T cells in a melanoma patient. While frequent *PRAME* mRNA expression is well documented in cutaneous and ocular melanomas, little is known about PRAME protein expression in melanocytic tumors. In this study we examined the immunohistochemical expression of PRAME in 400 melanocytic tumors, including 155 primary and 100 metastatic melanomas, and 145 melanocytic nevi. Diffuse nuclear immunoreactivity for PRAME was found in 87% of metastatic and 83.2% of primary melanomas. Among melanoma subtypes, PRAME was diffusely expressed in 94.4% of acral melanomas, 92.5% of superficial spreading melanomas, 90% of nodular melanomas, 88.6% of lentigo maligna melanomas, and 35% of desmoplastic melanomas. When in situ and nondesmoplastic invasive melanoma components were present, PRAME expression was seen in both. Of the 140 cutaneous melanocytic nevi, 86.4% showed PRAME expression. © 2018 Wolters Kluwer Health | Lippincott Williams & Wilkins

Summary

- Melanocytic vs Non-melanocytic
- Find the pigment and the melanocytes
- Avoid biopsies in children

Thanks!

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