

Subungual Melanoma

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4 y.o. boy
Japanese, Korean, Chinese



Thursday, May 23, 13



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Treatment Options?

Observation

Biopsy

Avulse nail

The Doctor's Doctor

Other

Clinical Presentations



- Rapidly spreading darkly pigmented patch with irregular border
- Invasion associated with papules, plaques and later lesions-ulceration and nail deformity
- Invasion in perieccrine adventitial dermis may remain flat
- Regression-gray white
- Hutchinson's sign-extension of pigmentation around cuticle



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ABCDE of N

- A=Age (5-7th decades), Africans, Asians, Native Americans
- B=Brown to black discoloration
Breadth of nail pigmentation >3mm
- C=Change in nail band or lack of change in nail morphology
- D=Digit most commonly involved
- E=Extension to proximal nail fold

The ABC rule for clinical detection of subungual melanoma.
Levit EK, et al. J Am Acad Dermatol. 2001 May;44(5):875.

Melanonychia Variants



- Linear
- Transverse
- Total



Epidemiology

Ethnic Group	Percentage
Africans	77%
Japanese	10-20%
Caucasians	1%

- Japanese
- African Americans
- No clear connection to UV exposure
- Usually increased moles but less incidence of AK and other sun-related lesions

Epidemiology and prognosis of subungual melanoma in 34 Japanese patients.
Kato T, et al. Br J Dermatol. 1996 Mar;134(3):383-7

Japanese Patients

Site	Numbers
Fingernails	21 (62%)
Toenails	13 (38%)
Thumb or great toe	25 (73%)

- University Hospital Study
- 34/151 melanoma cases over 25 years were subungual
- Majority Acral lentiginous histologic type followed by SS and nodular

Epidemiology and prognosis of subungual melanoma in 34 Japanese patients.
Kato T, et al. Br J Dermatol. 1996 Mar;134(3):383-7.

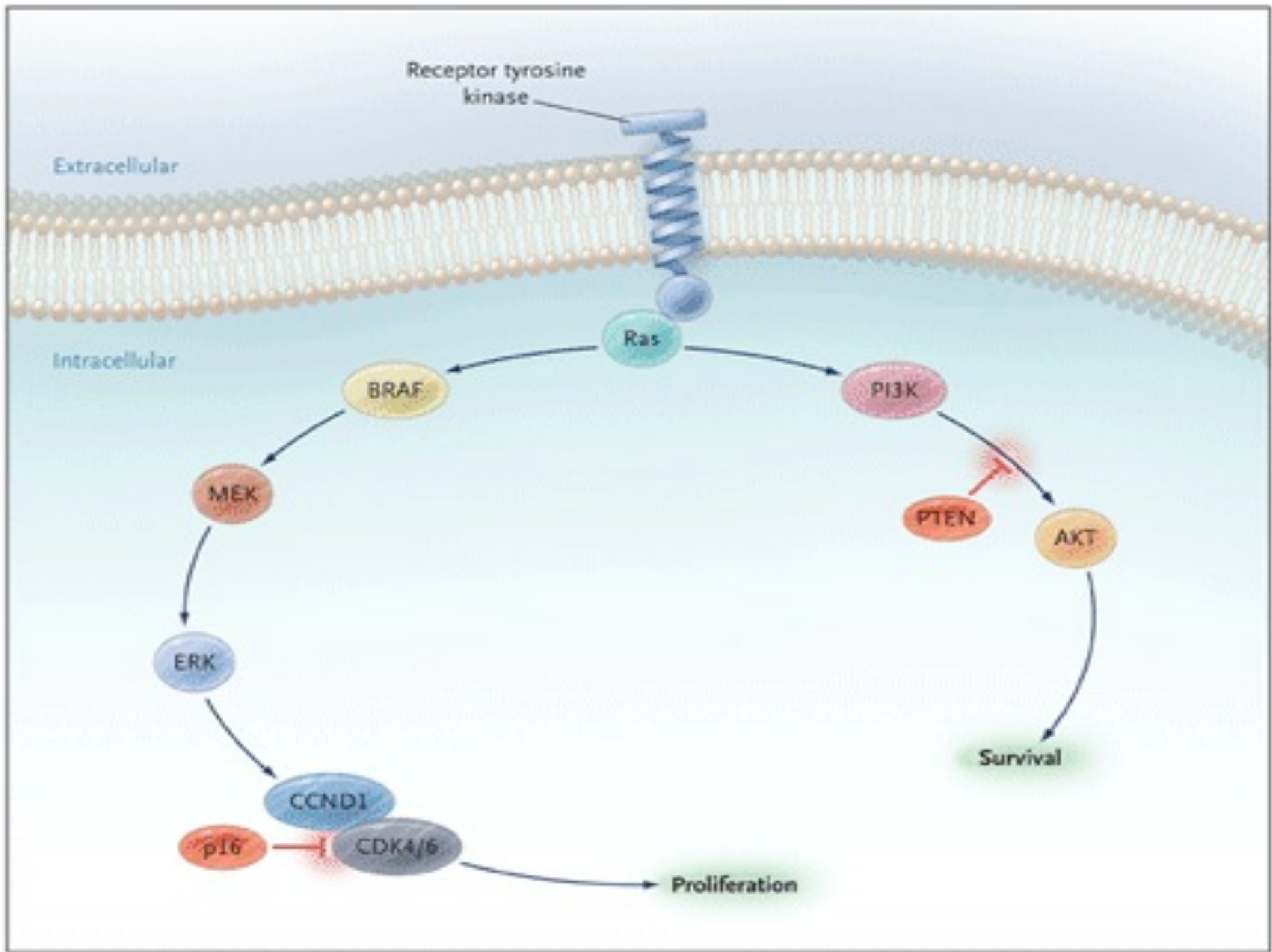
Activation vs Hyperplasia

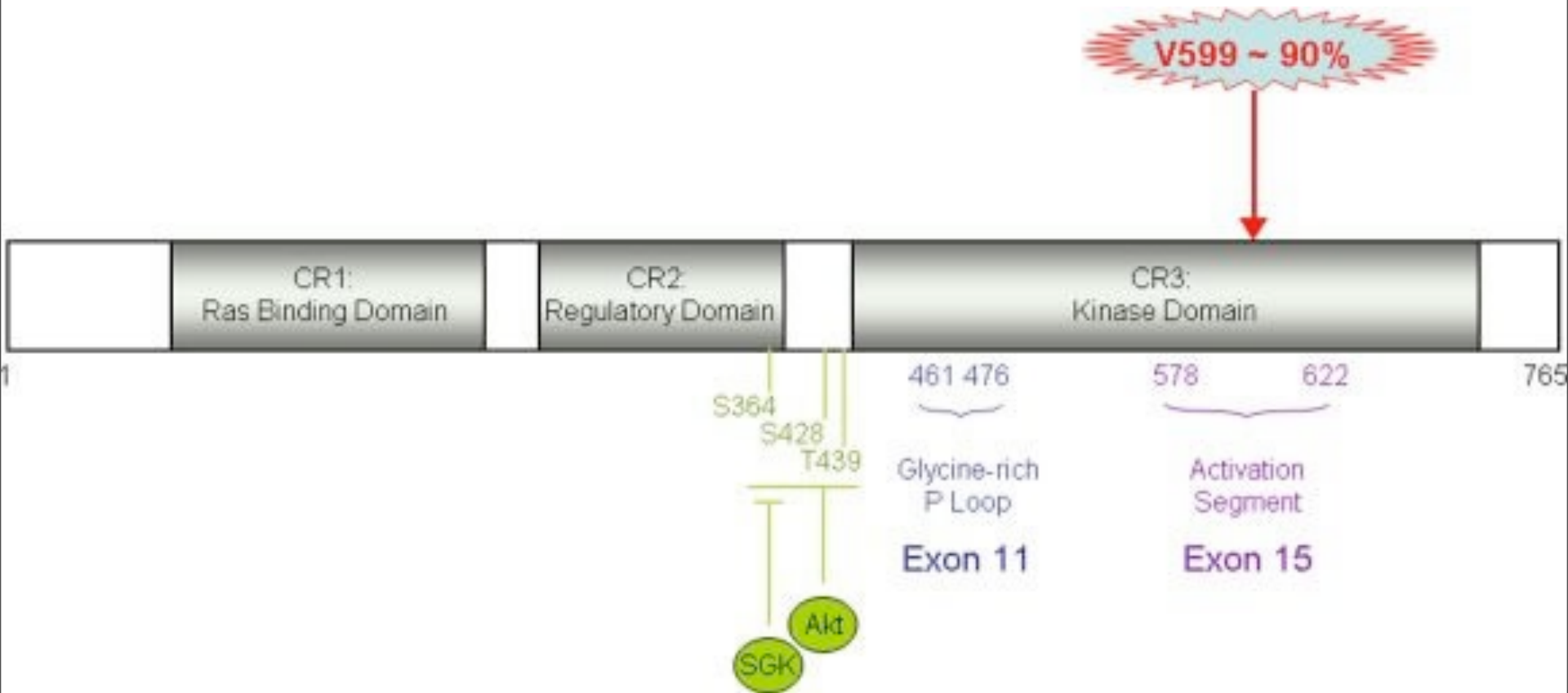
- Functional melanonychia
- 73% of LM (longitudinal melanonychia) in adults
- Physiologic-Ethnic
- Trauma
- Dermatitis
- Systemic disease
 - Addison's
 - Peutz-Jegher's
- Increased matrix melanocytes
- 77.5% of LM in children

Pathogenesis

Site	BRAF mutations	Chrom 10 loss	CCND1 gene copies
Minimal UV exposure	High	Frequent	Low
Increased UV exposure	Low	Low	Increased

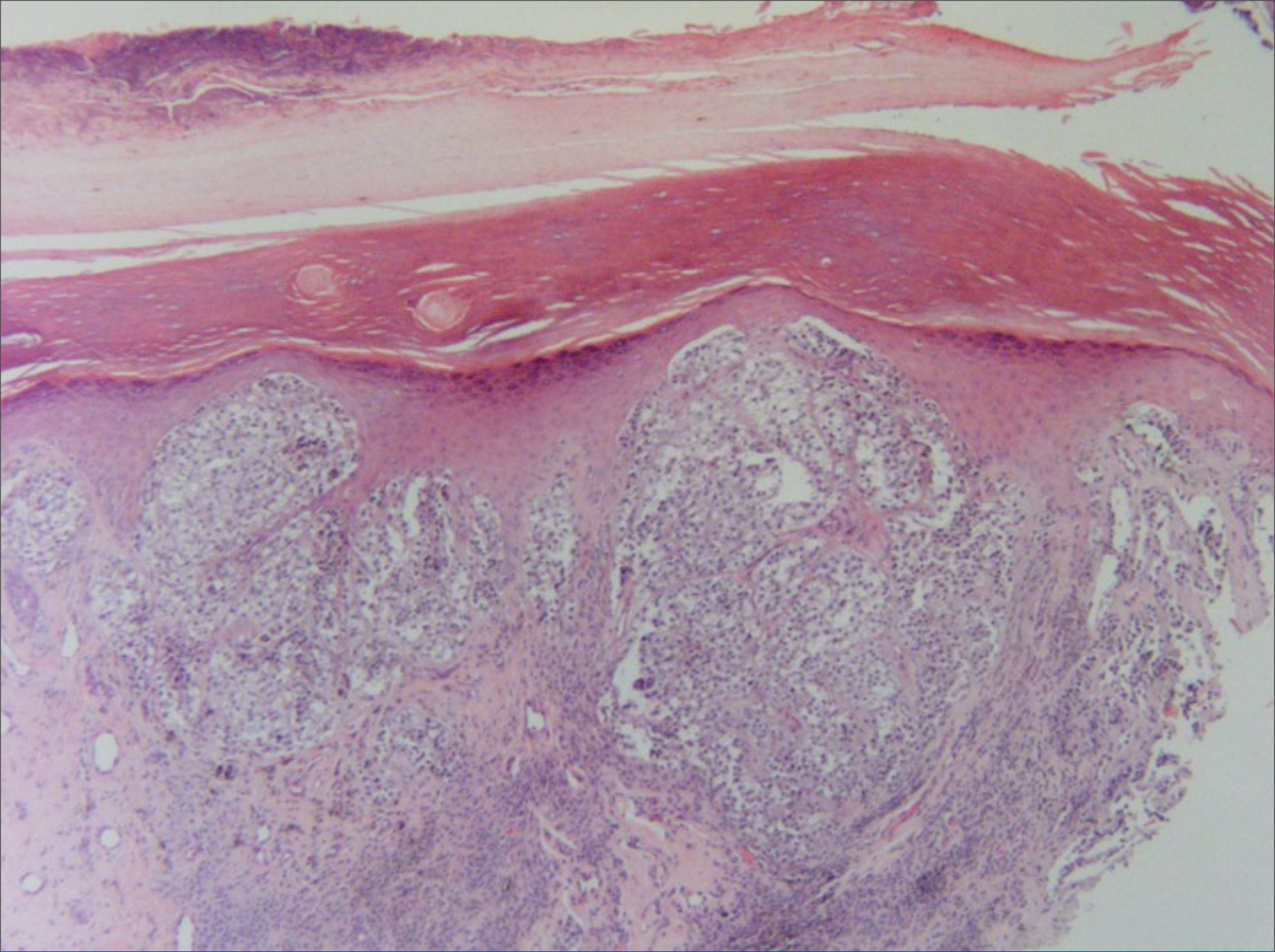
Distinct sets of genetic alterations in melanoma. Curtin JA, et al.
N Engl J Med. 2005 Nov 17;353(20):2104-7.

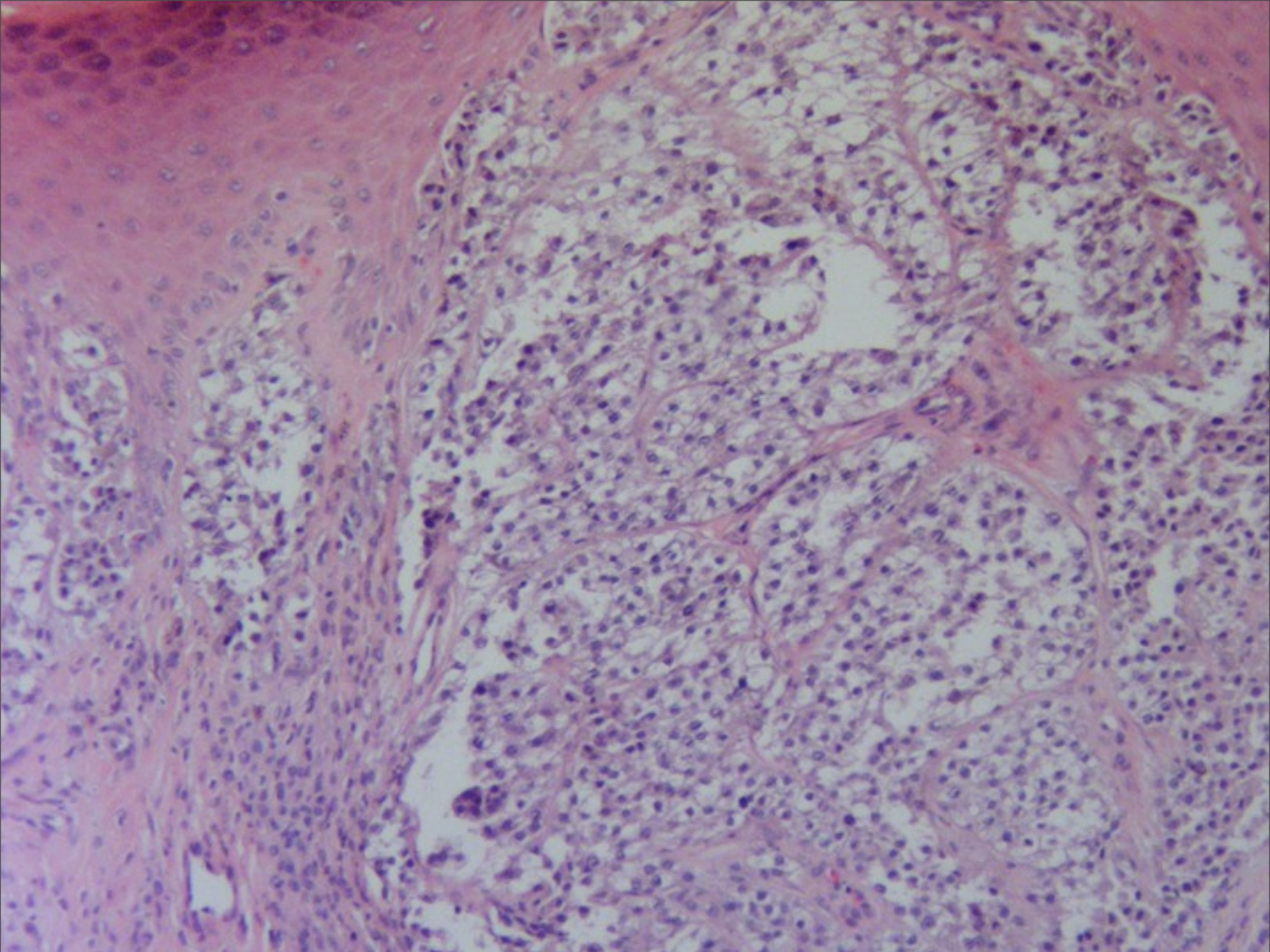


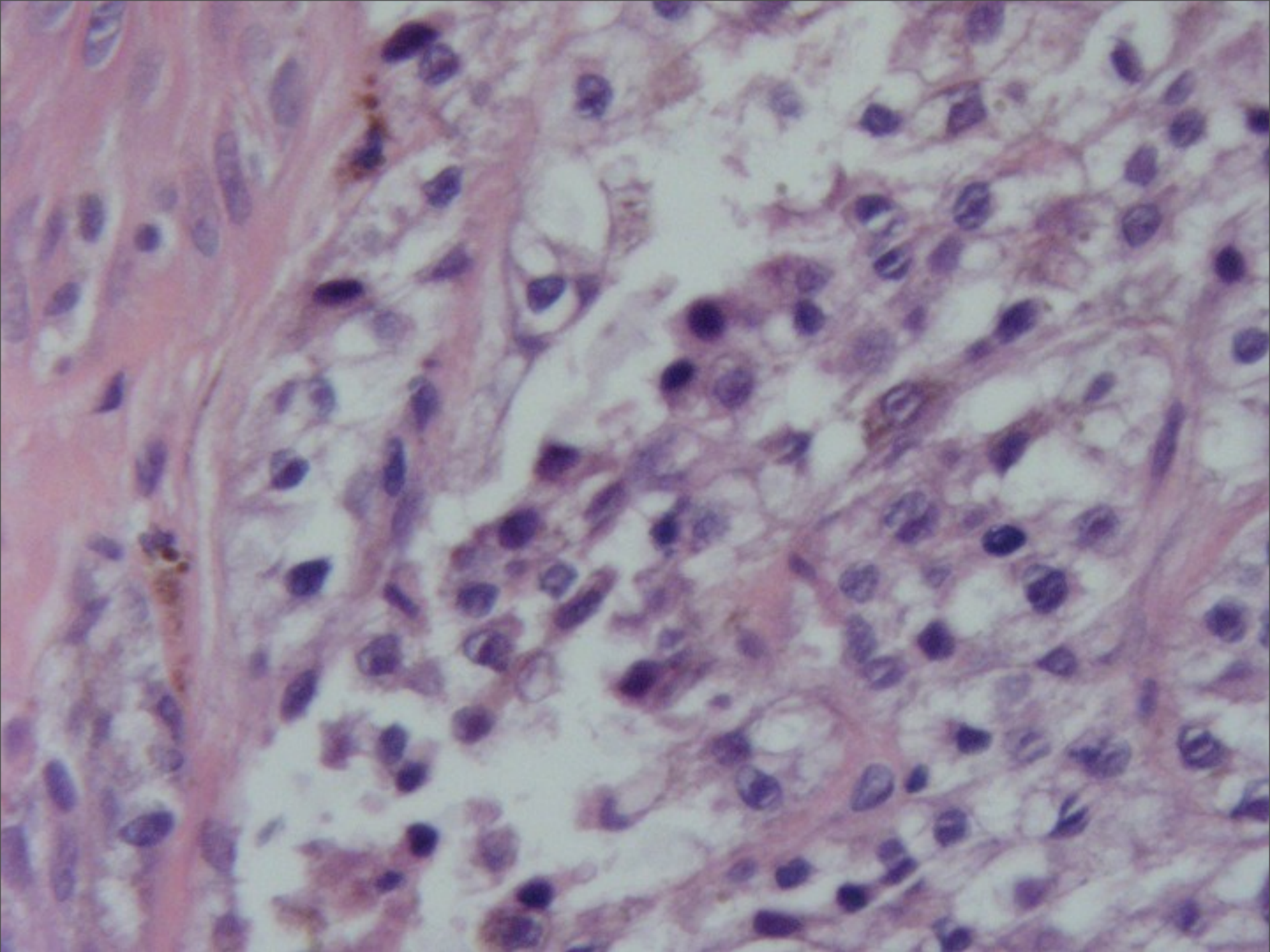


Implications

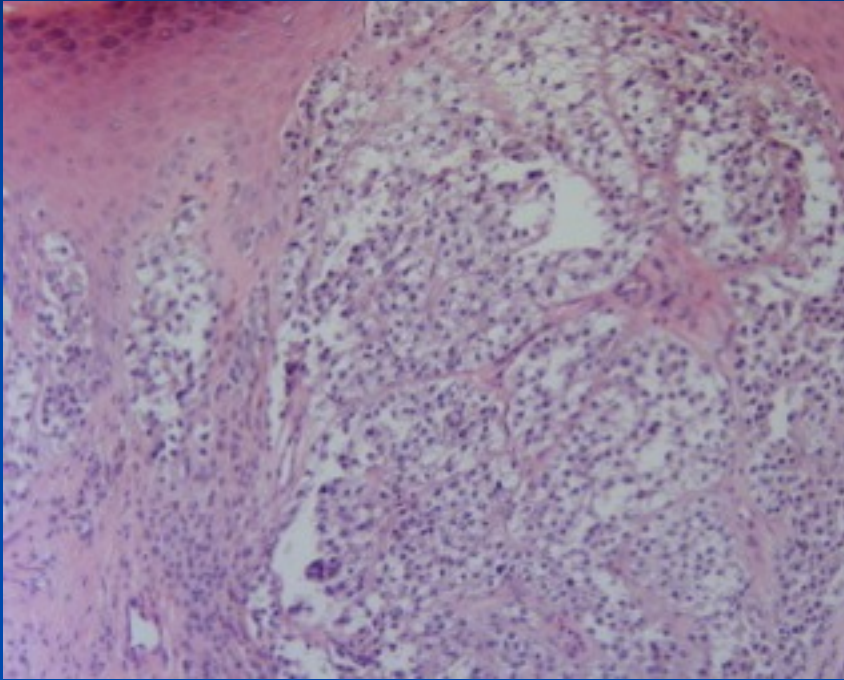
Group	Intervention
BRAF mutations frequent	Target RAS-RAF-ERK and PI3K pathways
BRAF mutations infrequent Increased copies of CCND1 or CDK4	Less likely to respond to therapeutic interventions that target upstream components of the mitogen-activated protein kinase pathway including BRAF (sorafenib)





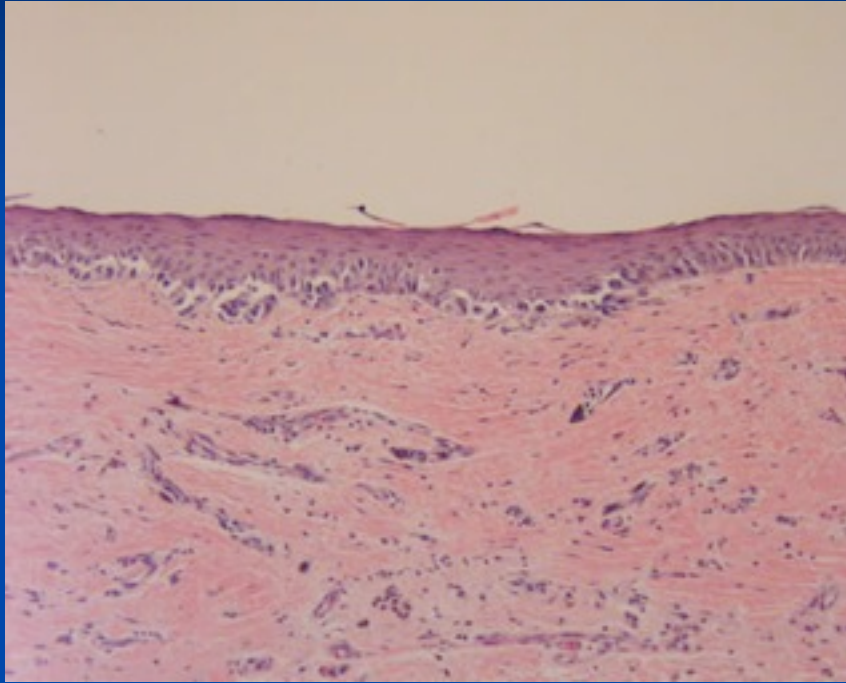


Histopathology



- Expansile nests of pleomorphic melanocytes
- Superficial spreading to lentiginous growth pattern
- Irregular pigment incontinence

Histopathologic Variants



- Two cases of regressed subungual melanoma
- Lymphoscintigraphy and sentinel lymph node (SLN) biopsies-1 positive and 1 negative

Dermatol Surg. 2006 Apr;32(4):577-80

Clinical Differential Diagnosis



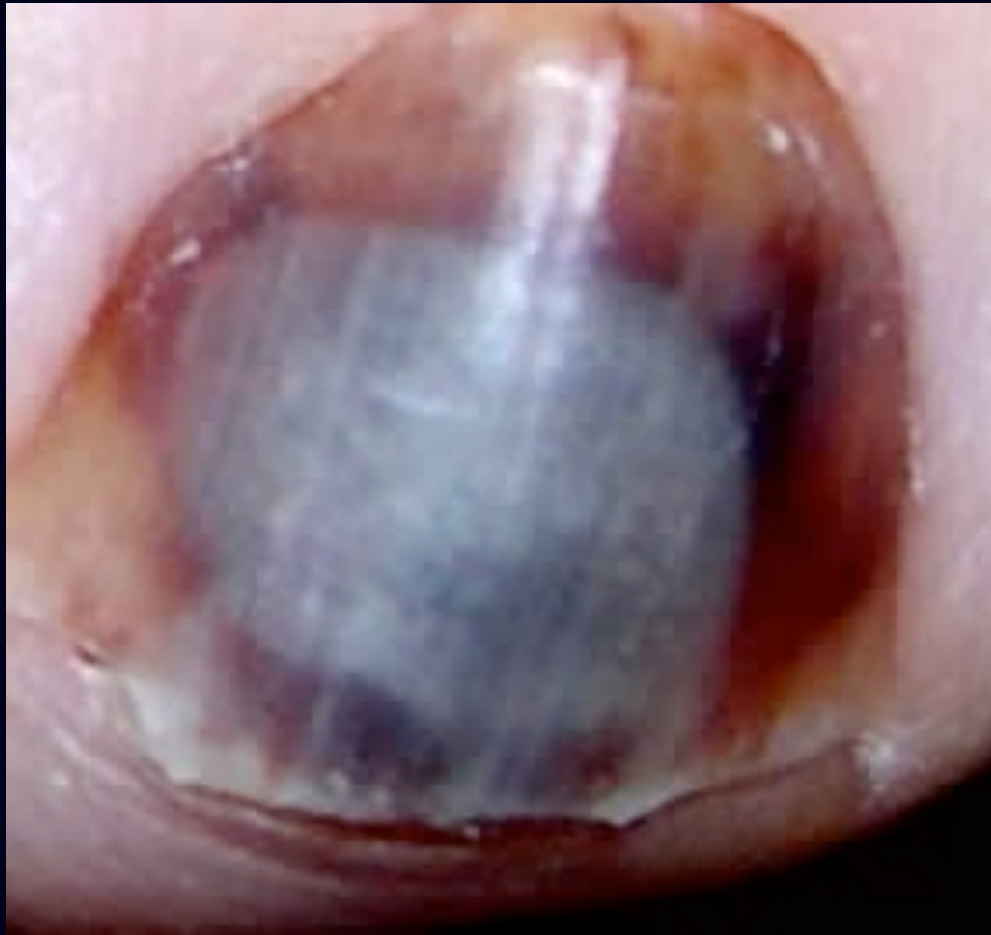
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Melanonychia Striata



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Frictional Melanonychia



Coumadin-Associated Melanonychia



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Longitudinal Chromonychia (Melanonychia)



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Tinea Nigra

(*T. rubrum* var *nigricans*)

Pseudo-Hutchinson Signs



- Racial
- Lauzier-Hunziker and Peutz-Jeghers syndromes
- Radiation therapy
- Malnutrition
- Minocycline
- AIDS
- Congenital nevus
- Trauma
- Pseudomonas and Proteus infections
- Bowen's disease

Prognosis



- Worse than conventional melanomas?
- Subungual worse than other acral melanomas?
- Variables
 - Delayed diagnosis
- Poorer prognosis:
 - Breslow thickness
 - Male
 - Amelanosis
- Mets to CNS, liver lungs, bone, and LN

**Acral lentiginous melanoma: a clinicoprostic study of 126 cases.
Phan A, etal. Br J Dermatol. 2006 Sep;155(3):561-9**

Delay in Diagnosis

- 5YS

- 88% <2.5mm
- 40% >2.5mm

Site	Mean Thickness
Non-acral	<1.0 mm
Acral	3.05 mm

Nail apparatus melanoma. Thai KE, etal Australas J Dermatol 2001;42:71-81
The incidence and prognosis of nail apparatus melanoma. A retrospective study of 105 patients in four English regions. Banfield CC, etal. Br J Dermatol 1998;139:276-279.

Subungual vs. Acral

67 Japanese cases of acral malignant melanomas

>40% palmoplantar and subungual

80% acral lentiginous type

15% nodular malignant melanoma

3% superficial spreading

No difference in prognosis of acral malignant melanomas vs other body sites

Palmoplantar and subungual malignant melanoma

Women younger, better survival rates

No significant difference with thickness

Biological behavior and natural course of acral malignant melanoma.

Clinical and histologic features and prognosis of palmoplantar, subungual, and other acral malignant melanomas. Jimbow K, etal. Am J Dermatopathol

Acral Melanomas vs. Other Sites

84, 836 cases

National Cancer Data Base (1985-1994)

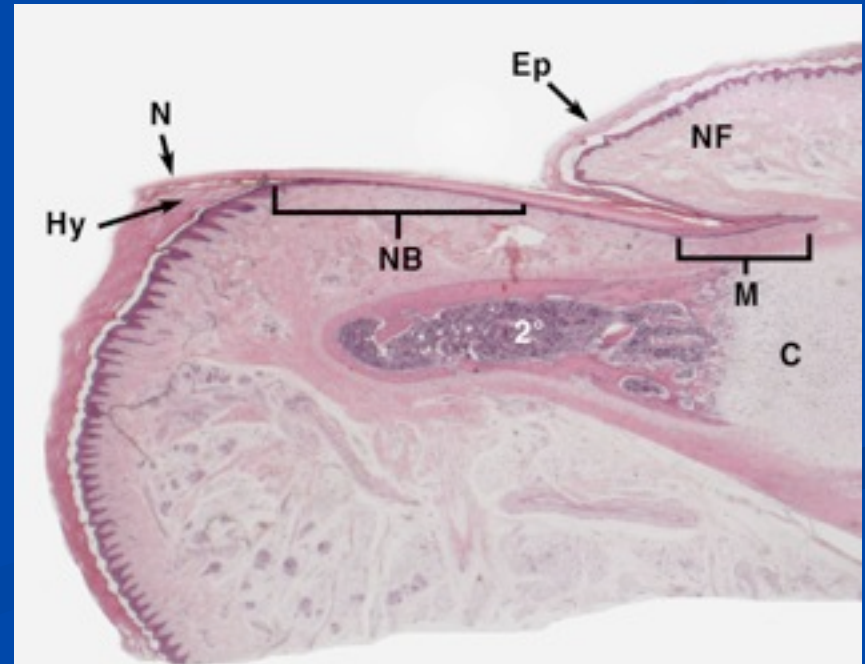
Nodular MM and Acral MM decreased survival

Independent prognostic variable

The National Cancer Data Base report on cutaneous and noncutaneous melanoma: a summary of 84,836 cases from the past decade. Chang AE, etal. Cancer 1998;83:1664-1678.



Nail Biopsy



Technique



- Must biopsy proximal nail fold, location where tumor usually arise
- Incisional bx of nail plate or proximal fold
- Punch bx of proximal fold

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Patient's Mother's Solutions

- 1) **Do Nothing & Monitor? = DISAGREE - Delay in treatment increases severity if Melanoma is found/treatment more invasive**
- 2) **Do Another Biopsy? = DOESN'T MAKE SENSE - b/c anesthesia will still have to be used**
- 3) **REMOVE NAIL NOW? = LOGICAL - Eliminates Melanoma risk BUT Increases Anesthesia risk (If nail is benign - future risk**
- 4) **Transplantation with Toenail? = Derm knew about recent success & wanted to investigate - DON'T LIKE - creates 2 trauma sites**

Remove Now!

A = Age (Low - child); Race (High - Japanese/Asian)

B = Band (High - visible bands); Pigment (High - brown/black), Breadth (High - 9 mm size); Border

C = Change (High - rapid/esp 1st yr); Dystrophy (High - Mostly biopsy caused but is brittle, weak,

D = Digit (High - single digit); Dominant Hand (Low - is not dominant hand)

E = Extension/Hutchinson's sign (High - visible pigment in fold)

Family history is unknown.

Parallels most cases in literature - starting with 1 line, widening rapidly, completely covering nail

Literature Support



A rapidly growing pigmented nail streak resulting in diffuse melanosis of the nail. A possible sign of subungual melanoma in situ. Kato T, et al. *Cancer*. 1989 Nov 15;64(10):2191-7.

Childhood subungual melanoma in situ in diffuse nail melanosis beginning as expanding longitudinal melanonychia. Antonovich DD, et al. *Pediatr Dermatol* 2005;22;210-212.

Solutions

- Dr. Beth Rubin, Dermatopathologist UCSF
 - Dr. Scher and Dr. Tosti
- Dr. Stefani Takahashi-UCLA



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