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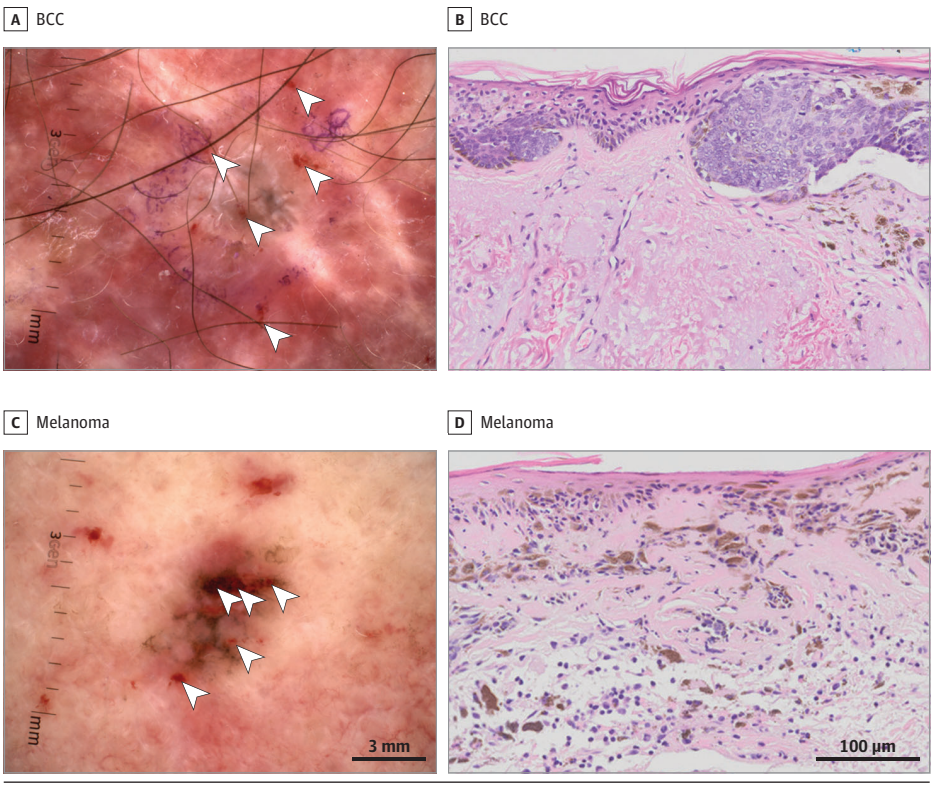
Microbiopsy Biomarker Profiling in a Superficial Melanoma Resembling a Pigmented Basal Cell Carcinoma

The skin microbiopsy device is a minimally invasive and painless technique used as an alternative to conventional biopsy techniques for collecting cells from the epidermis to the papillary dermis for molecular diagnosis and research.[1] We used microbiopsy samples and quantitative polymerase chain reaction (qPCR) analysis to differentiate between a histopathologically proven superficial pigmented basal cell carcinoma (BCC) (**Figure 1**A and B) and a superficial melanoma resembling a pigmented BCC (index lesion from the case patient) (Figure 1C and D).

Report of a Case | A man in his 80s presented with an 8 × 4-mm pigmented lesion, the index lesion, on his mid back. Dermoscopy showed gray ovoid nests in the lower half of the lesion, a spoke-wheel pattern at the 4- to 5-o'clock margin, and an atypical, irregular broad pigment network at the 2-o'clock margin (Figure 1C. Arborizing telangiectasia was absent, raising the possibility of pigmented BCC, melanoma, or, rarely, a collision lesion. We compared the index lesion with a histopathologically proven pigmented superficial and nodular BCC that was obtained and processed in the same manner (Figure 1B). Five microbiopsies were performed on representative parts across both lesions and in the perilesional skin in both lesions. The exact sites of the microbiopsies are indicated in Figure 1A and C. Using a Dermlite Cam, we obtained dermoscopic photographs of the lesions before and after microbiopsies were taken. A shave biopsy was subsequently performed for histopathological diagnosis. Three of the 5 microbiopsy specimens were pooled for qPCR analysis, looking for the expression of the melanoma signature genes *Tyr* (NM_000372), *CMIP* (NM_198390.2), and *LINC00518* (NR_027793.1)[2] and a BCC marker *Gli1* (NM_005269.2).[3]

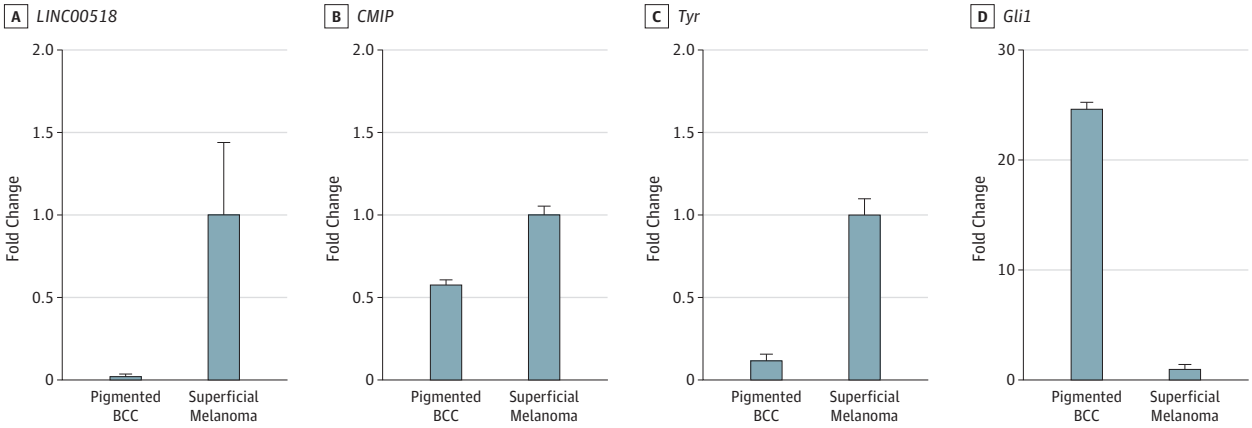
Results of qPCR showed that *LINC00518* was upregulated in the index sample by 47-fold (**Figure 2**A). There was no significant difference in the expression of *CMIP* between these

Figure 1. Dermoscopic and Hematoxylin-Eosin–Stained Histopathologic Images of the Lesions



Clinical (A) and histopathologic (B) images of pigmented superficial basal cell carcinoma (BCC): A, locations of the microbiopsies (arrowheads); B, histopathologic analysis demonstrates aggregations of basaloid cells, palisading of nuclei, and clefting. Clinical (C) and histopathologic (D) images of superficial melanoma: C, locations of the microbiopsies (arrowheads); D, histopathologic analysis reveals individual melanocytes and irregularly distributed nests predominantly along the basal layer of the epidermis. Scale bars present in panels C and D apply also to panels A and B, respectively.

Figure 2. The Expression of *LINC00518* and *CMIP*, *Tyr*, and *Gli1* in Superficial Melanoma and Pigmented BCC



A, *LINC00518* expression level in the melanoma was 47-fold higher than in the pigmented basal cell carcinoma (BCC) control lesion. B, *CMIP* expression profiling revealed no significant differences in fold change between the pigmented BCC and the melanoma. C, *Tyr* expression was 10-fold higher in the index melanoma lesion than in pigmented BCC. D, The pigmented BCC control lesion had 24-fold higher *Gli1* expression than the melanoma. Error bars indicate standard error.

samples (Figure 2B). The expression of *Tyr* in the index sample was 10-fold higher than in the pigmented BCC sample (Figure 2C). *Gli1* was significantly overexpressed in the pigmented BCC sample by 24-fold (Figure 2D).

Histopathologic analysis showed a lentiginous melanoma arising from moderately to severely sun-damaged skin; Breslow thickness, 0.2 mm; Clark level, 2 (Figure 1D).

Discussion | Pigmented BCC and melanoma can be difficult to differentiate, both clinically and dermoscopically. Gene expression profiling has been performed to improve the diagnostic accuracy of melanoma[4] and BCC.[5]

For this report, we used microbiopsy technology combined with biomarker profiling to differentiate 2 lesions. Our results showed that the expression of *Tyr* in the index samples was 10-fold higher than in the pigmented BCC control specimens, suggesting that the index lesion contained a signature for melanoma.[6] *Gli1*, a critical transcriptional factor of the Hedgehog/Patched signaling pathway,[3(p132)] is considered to be a molecular marker for BCC.[3(p135)] *Gli1* expression was detected in our index sample but was 24-fold lower than in the BCC control specimens. The high-level *Tyr* expression and low expression of *Gli1* suggested that the index sample was indeed a melanoma and not a BCC.

To confirm this hypothesis, we used a set of 2 markers, *LINC00518* and *CMIP*. This 2-gene molecular signature approach was designed to differentiate melanoma from nevi using an adhesive patch test method that samples the epidermis with a sensitivity of 97.6% and a specificity of 72.7%.[2(p240)] *LINC00518* has been reported to be upregulated in melanoma, whereas *CMIP* is relatively downregulated. Between the index lesion from the present patient and the BCC lesion, we observed a significant difference in the expression of *LINC00518*, but we did not observe a difference in expression of *CMIP* levels, which may reflect differences in biomarker sampling sites from previously published reports.

Conclusions | Observations from our study suggest that microbiopsy is a promising sampling technique for skin cancer research. It provides enough RNA for performing rapid, sensitive, and specific qPCR and has potential clinical applications in research that may lead to future development for diagnostic sampling in small, multiple lesions or in cosmetically sensitive areas.

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Secukinumab for Acrodermatitis Continua of Hallopeau

Acrodermatitis continua of Hallopeau (ACH) was first described in 1890 by Henri Hallopeau.[1] He had observed a single patient with an undulating but recalcitrant pustular destruction of the fingertips and toes.[1] Nowadays, this condition is considered a subtype of localized pustular psoriasis.

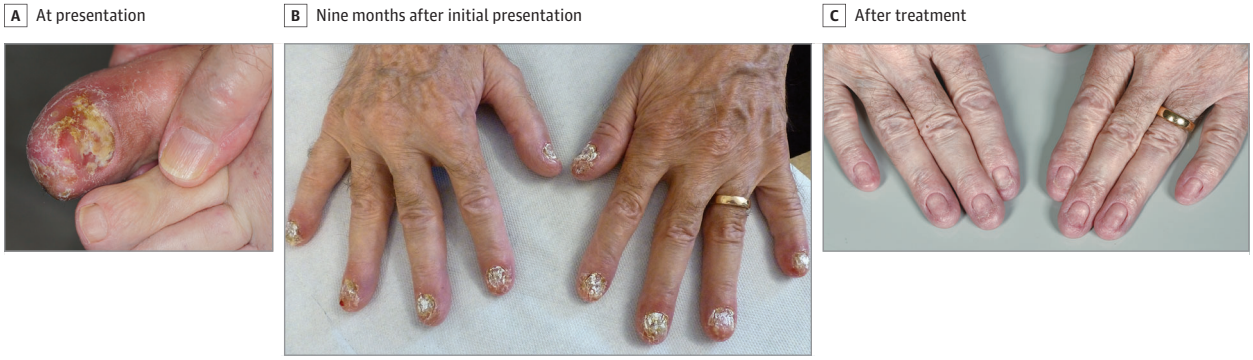
There are no treatment guidelines available for ACH, and the condition is refractory to many conventional topical and systemic treatments.[2] Several patients have been treated with biologic agents with variable success. Targeted treatment strategies based on pathogenic cytokine expression patterns have not been evaluated for ACH.

Report of a Case | An 87-year-old retired electrical engineer had recurrent episodes of redness, swelling, and purulent discharge in the area of the left hallux with progressive degeneration of the toenail for 2 years. Other digits were not involved. Antibiotic treatment had been ineffective. The affected toe showed onychodystrophy, and the erythematous perionychium was beset with pustules (**Figure 1**A). All other toes and fingers were normal. Findings of mycologic and bacterial swabs were negative. No signs of systemic inflammation were present.

A medial longitudinal biopsy of the nail bed of the left hallux revealed numerous neutrophils within the stratum corneum, psoriasiform dermatitis with epidermal hyperplasia, a lacking granular layer, and compact hyperkeratosis and parakeratosis. These findings are compatible with the diagnosis of acrodermatitis continua of Hallopeau (ACH). The patient, a nonsmoker, did not have plaque-type psoriasis but had a family history of this condition. After ineffective treatment with topical steroids, UV-B phototherapy, and acitretin for 9 months, the ACH flared to involve all fingers (Figure 1B). The Nail Psoriasis Severity Index score reached the maximum score of 80 points. On the pain visual analog scale, the patient reported the maximum score, 10 of 10.

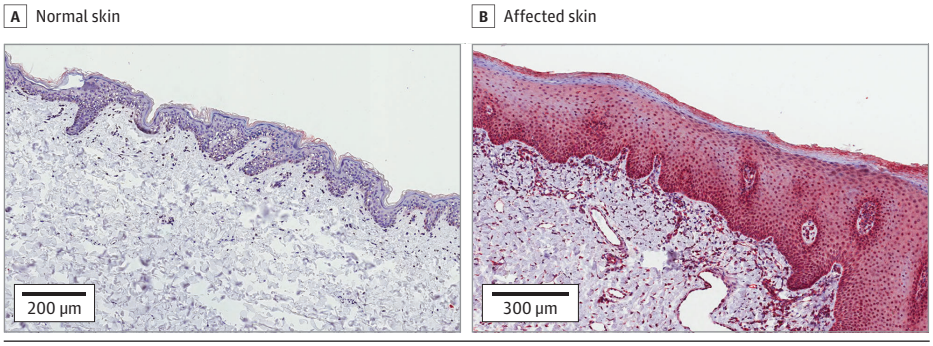
In generalized pustular psoriasis (GPP), interleukin (IL)-17 mRNA levels are elevated.[3] Even though they are distinct clinical entities, ACH and GPP are closely related on the

Figure 1. Clinical Findings



A, Patient's left big toe on initial presentation. B, Involvement of the fingers 9 months later and shortly before initiation of treatment with secukinumab. C, Nine weeks after treatment with secukinumab.

Figure 2. Histopathologic Findings



A, Normal (uninvolved) non-acral skin sample (interleukin [IL]-17 stain, original magnification x400). B, Acrodermatitis continua of Hallopeau (involved) skin sample from the left big toe (IL-17 stain, original magnification x400).