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Identification of *HRAS* mutations and absence of *GNAQ* or *GNA11* mutations in deep penetrating nevi

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***HRAS* is mutated in ~15% of Spitz nevi, and *GNAQ* or *GNA11* is mutated in blue nevi (46–83% and ~7% respectively). Epithelioid blue nevi and deep penetrating nevi show features of both blue nevi (intradermal location, pigmentation) and Spitz nevi (epithelioid morphology). Epithelioid blue nevi and deep penetrating nevi can also show overlapping features with melanoma, posing a diagnostic challenge. Although epithelioid blue nevi are considered blue nevic variants, no *GNAQ* or *GNA11* mutations have been reported. Classification of deep penetrating nevi as blue nevic variants has also been proposed, however, no *GNAQ* or *GNA11* mutations have been reported and none have been tested for *HRAS* mutations. To better characterize these tumors, we performed mutational analysis for *GNAQ*, *GNA11*, and *HRAS*, with blue nevi and Spitz nevi as controls. Within deep penetrating nevi, none demonstrated *GNAQ* or *GNA11* mutations (0/38). However, 6% revealed *HRAS* mutation (2/32). Twenty percent of epithelioid blue nevi contained a *GNAQ* mutation (2/10), while none displayed *GNA11* or *HRAS* mutation. Eighty-seven percent of blue nevi contained a *GNAQ* mutation (26/30), 4% a *GNA11* mutation (1/28), and none an *HRAS* mutation. Within Spitz nevi, none demonstrated *GNAQ* or *GNA11* mutations (0/30). Seventeen percent contained an *HRAS* mutation (5/30). All *GNAQ* and *GNA11* mutations were p.Q209L (c.626A>T) point mutations, except 2 *GNAQ* mutations, which contained novel c.625_626CA>TT double mutations. Four *HRAS* mutations were in exon 2, and three in exon 3. This is the first study to identify *HRAS* mutations in deep penetrating nevi. The presence of *HRAS* mutations and absence of *GNAQ* or *GNA11* mutations in deep penetrating nevi suggests classification of these unusual nevi within the Spitz nevus category of melanocytic tumors, rather than the blue nevus category.**
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Melanocytic nevi with epithelioid cytomorphology include epithelioid and spindle cell (Spitz) nevi, epithelioid blue nevi, and deep penetrating nevi. Deep penetrating nevus, a term first coined by Seab *et al*,[1] are unusual melanocytic neoplasms difficult to classify. Deep penetrating nevi are uncommon but are of importance due to their histological and clinical overlap with melanoma. They most commonly present on the extremities, followed by the head and neck and upper trunk.[2] The age range at presentation is wide; however, as with Spitz nevi, deep penetrating nevi most commonly present in younger patients (adolescence and young adults). They typically present as predominantly dermal to focally compound melanocytic proliferations with extension into the reticular dermis particularly along adnexal structures and neurovascular bundles, often extending into the subcutis. They tend to have a relatively symmetric wedge-shaped nodular growth pattern, although superficial variants can occur.[2] A plexiform disposition is also often present. Deep penetrating nevi are composed of epithelioid melanocytes with abundant finely pigmented cytoplasm with associated pigment-laden macrophages. There is often a minor component of banal nevocellular nevus admixed with the deep penetrating nevus component (so-called 'combined nevus'). Random cytological atypia can be present in deep penetrating nevi,

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