

# Immunostaining for tyrosinase and nestin in melanocytic nevi as a model for melanocyte differentiation and neovogenesis

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Histological analysis allows an accurate classification of most melanocytic lesions as benign or malignant. However, a challenging diagnosis can be faced when differentiating a nevus from a melanoma, mostly due to the heterogeneous histological appearance of melanomas. It is thus necessary to use immunohistochemistry as a complementary tool. The immunohistochemical expression of tyrosinase, the key melanogenic enzyme in melanocytes, has often been useful in formulating a differential diagnosis thanks to the peculiar staining pattern in nevocytes compared with melanoma cells. The expression pattern of tyrosinase in nevi appears to parallel the cytoarchitectural changes typically observable within the lesion: nevus cells in the epidermis or in the superficial dermis are more likely to be larger and strongly express melanocytic differentiation antigens, such as tyrosinase, compared with deeper nevocytes [1]. Our study aimed to evaluate the immunohistochemical expression pattern of the tyrosinase antigen (clone T311) in different histological types of acquired dysplastic melanocytic nevi, including junctional, compound, and intradermal nevi, as well as in a panel of normal skin tissues. Moreover, to evaluate whether the expression of tyrosinase by nevus cells, pointing out the acquisition of melanin-producing capabilities, was associated with the differentiation state of nevocytes, we likewise investigated the immunohistochemical expression of the two markers of pluripotency, CD34 and nestin. Our results revealed a prominent immunoreactivity for tyrosinase in junctional and superficial dermal nevocytes and a decreasing gradient of staining in dermal nevocytes, up to become negative in the deeper dermis. All junctional and dermal nevocytes were negative for CD34. Nestin immunostaining showed an opposing pattern compared with tyrosinase, leading us to look into the melanocytic nevus as a “histopathological model” to trace the final stages of the differentiation pathway that neural crest-derived melanocyte precursors undertake toward their ultimate anatomical and functional site into the epidermis, consistently with Cramer’s dermal precursor model of melanocytic origin and the stem cell-based concept of neovogenesis [2]. Both CD34 and nestin intensely stained the small aggregates of cells, resembling “niches”, adjacent to the bulge area of hair follicles, that may represent the reservoir of neural crest-derived melanocyte stem cells residing in the dermis.

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## References

- [1] Grichnik (2008) Melanoma, Neovogenesis, and Stem Cell Biology. *J Invest Dermatol* 128: 2365-2380
- [2] Kinsler et al. (2013) Immunohistochemical and ultrastructural features of congenital melanocytic naevus cells support a stem-cell phenotype. *Br J Dermatol* 169: 374-383

## Key words

Tyrosinase, nestin, dysplastic melanocytic nevi, immunohistochemistry, neovogenesis, neural crest.