

PREFACE

The normal precursor of malignant melanoma is the melanocyte, a cell of neural crest origin. In their embryological state, neural crest cells are unique in that they dissociate from the notochord on days 10–14 and migrate out, or “metastasize,” to numerous sites of the body as their new “homes.” These cells are known as “argentaﬀin cells” and include the melanocytes. Of interest is that melanocytes can also accumulate abnormally in clusters as nevi and thereafter reside in the lower stratum of the epithelium just above the level of the dermis (and occasionally in the dermis). The most important function of these melanocytes either singularly or in clusters is to manufacture melanin, a pigmented biopolymer that is distributed throughout the skin to protect the host from the damage of ultraviolet radiation. Indeed, the amount of pigmentation sets the background of racial groups in human beings. It is estimated that the number of melanocytes in the body is relatively constant between different racial groups, although the production of melanin varies dramatically from one race to the other. Melanocytes in lightly colored skin make the least amount of melanin, whereas melanocytes in darker skin make larger amounts of melanin, which provides significantly greater protection against the direct ultraviolet radiation at the equator and its subsequent photocarcinogenesis.

It is in the transformation and mutation of these melanocytes that melanoma cells are derived. Approximately 95% of the time, melanoma can be traced to a pre-existing nevus, but about 5% of the time, the original site may not be determined because melanoma presents as metastatic melanoma. Although melanoma is a potentially incurable disease, especially in its late stage, the overall incidence of melanoma is relatively low compared with other types of cancer. Of special interest is the incidence of cutaneous melanoma, which is dramatically lower in the more heavily pigmented populations, such as blacks and Asians. The mechanisms of melanogenesis have been studied, but are still not fully understood. It is our hope that *From Melanocytes to Melanoma: The Progression to Malignancy* presents all available evidence to date in order to establish a scholarly record of what is known about the progression of changes from melanocytes to melanoma. The intriguing differences between the lighter and darker skinned racial groups with respect to the different incidences of melanoma need to be explained. Patients with xeroderma pigmentosum (XP), a multigenic, multiallelic, autosomal recessive disease, have more than a 1000-fold increased risk of cutaneous melanoma. Thus, XP deserves special attention, since mechanisms responsible for the genesis of melanoma in these patients can be understood and applied to melanoma in general. One important goal of these studies is to understand the molecular mechanisms involved in melanogenesis and in malignant transformation of melanocytes. Potential therapeutic maneuvers may then be developed to either block these steps or use relevant specific molecules of melanogenesis as targets of attack.

From Melanocytes to Melanoma: The Progression to Malignancy is divided into three parts, with Part I addressing the basic biology of melanocytes and the molecular mechanisms involved in the development, migration, and differentiation of melanoblasts to melanocytes. Part II is devoted to elucidating processes involved in the transformation of melanocytes to malignant melanoma. Finally, Part III focuses on mechanisms

involved in the further progression of primary melanomas into invasive and metastatic melanomas. We hope that by studying the molecular signals involved in these processes, we will be able to develop model systems by which we can trace the molecular mechanisms involved in the malignant transformation of melanocytes to malignant melanoma. *From Melanocytes to Melanoma: The Progression to Malignancy* will be a valuable reference for all biologists and basic scientists who are interested in the biology of pigment cells, as well as to pathologists, dermatologists, surgeons, and medical oncologists who are interested in the diagnosis and treatment of melanoma.

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