

Chapter 1

Introduction

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Although special techniques have been applied for more than a century to aid the diagnosis of pathology specimens, it is only within the past 10–20 years when the field of ancillary techniques has exploded to the current levels. From the beginning of histology and pathology, morphologists have used a wide range of special techniques such as silver stains to detect the presence of axons, colloidal iron stain to detect mucin deposits in the dermis, or Steiner stain to detect spirochetes. During the 1960 and 1970s, electron microscopy allowed examination of the subcellular structures to detect, among others, the capsids of viruses, organelles associated with a particular neoplasm (Birbeck granules in Langerhans cell histiocytosis), or alteration of the basement membrane area in the different subtypes of epidermolysis bullosa. Since the 1980s immunohistochemistry has become widely used to detect antigens, with applications to neoplastic (e.g., differentiation between Paget disease and melanoma), inflammatory (differentiation among the different subtypes of cutaneous immunobullous diseases), and infectious conditions (detection of spirochetes in cutaneous lesions of syphilis). In a sense, we can consider immunohistochemistry as an early “molecular” technique since it allows the detection of specific antigens (i.e., “molecules”).

In the past 10–15 years, molecular techniques such as genomic sequencing have become much more available. From an original very expensive price and long-processing times, significant advances have much reduced their turnaround time and cost and thus have made them very attractive to diagnostic applications. The range of genetic or molecular tests that can be performed on skin specimens include polymerase chain reaction (PCR), fluorescence in situ hybridization (FISH), comparative genomic hybridization (CGH), gene arrays, routine cytogenetics, and mass spectrometry.

A very significant advance in the field of molecular techniques has been their progressive adaptation to formalin-fixed, paraffin embedded tissue specimens. As

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it is well known, due to standard tissue processing (formalin fixation, successive heating periods, and embedding in paraffin), the genetic material is partially degraded so most tests were originally developed on fresh tissue or cell suspensions, thus limiting their practical use in dermatopathology. However, by developing successive modifications, many of these tests can now be utilized on standard, formalin-fixed, paraffin embedded tissue (the material most easily available in pathology departments).

As an example of the importance of these molecular techniques, genomic analysis has allowed to confirm that the old morphologic classification of lentigo maligna, superficial spreading, and acral-lentiginous melanoma correlates with a different genetic signature. Thus, melanomas arising in skin chronically exposed to the sun (i.e., lentigo maligna melanoma) have c-kit and NRAS mutations; melanomas arising in skin intermittently exposed to the sun (i.e., superficial spreading type) typically have BRAF mutations; and melanomas arising in the acral locations or mucosae (i.e., acral-lentiginous mucosal type) most commonly show c-kit mutations. Furthermore, this analysis has not only resulted in better knowledge of the pathogenesis of cutaneous melanoma but has also provided with identification of therapeutic targets in an area surely needed of new treatments.

In summary, this book reviews the most popular and useful techniques, in our opinion, for diagnosis, prognosis, and therapeutic purposes in the field of dermatopathology. Although almost any area of dermatopathology can benefit of the use of molecular techniques, they are currently preferentially used in some conditions, and thus this book devotes one chapter each to cutaneous hematolymphoid, mesenchymal, epithelial, infectious, melanocytic, and miscellaneous lesions. We are aware that it is certainly impossible to discuss all the possible applications of these techniques to the field of dermatopathology; however, we expect that this book will serve as a tool to familiarize the readers with these techniques and help them to add these tools to the diagnostic armamentarium in pathology.

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