Pathologic and Molecular Techniques Used in the Diagnosis and Treatment Planning of Sarcomas

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2.1 Introduction

The purpose of this chapter is to describe briefly the histopathologic and genetic tools currently available to establish a specific cancer diagnosis, to predict prognosis and response to therapy and, ultimately, to identify potential novel therapeutic targets. The diagnosis of cancer has traditionally been rendered based upon the morphologic characteristics of an individual tumor interpreted within a given clinical setting. Over the years, the evaluable morphologic features have expanded from light microscopic appearance by routine hematoxylin and eosin (H&E) staining to include special and immunohistochemical stains and ultrastructural features. While these phenotypic attributes have allowed the pathologist to classify the majority of tumors, the classification is relatively subjective in some cases, maybe a “diagnosis of exclusion” in others, and does not allow reliable prediction of biologic behavior in most.

As the repertoire of techniques and tools traditionally used by the pathologist has expanded, so have those utilized by the research community. These latter advancements, such as karyotyping, PCR, FISH, DNA sequencing, and microarrays (of tissue or DNA probes), frequently result in observations about specific tumors at the genetic level that provide potentially invaluable, ancillary, diagnostic information. Concomitant development of methods that allow reliable and reproducible assessment of these additional tumor characteristics has resulted in the current global approach to cancer diagnosis – one based upon the integration of molecular genetic, histologic and clinical features. The approach is fluid in two respects – first of all, the types of information used depend upon the differential diagnosis of the tumor.
itself and, secondly, as new information is generated and proven to be clinically useful, it is incorporated into the diagnostic process. Moreover, as the ability to refine our diagnostic capabilities increases, it carries with it the wonderful benefit of providing prognostic and therapeutic information as well, facilitating the ultimate goal of individualized tumor therapy (Brandt 2002; Cordon-Cardo 2001; Hicks et al. 2004; Millar et al. 2004).

2.2 Standard Histopathology

2.2.1 Light Microscopy

The foundation and initial step in cancer diagnosis remains the formalin fixation, routine processing to paraffin and examination of an H&E stained section of tumor tissue on a glass slide (Triche et al. 2005). In most cases, the process is an overnight procedure with generation of slides usually occurring the day following a surgical procedure or biopsy. However, if tumors are large, an additional day of formalin fixation may be needed prior to processing, and in the case of some bone-forming tumors the specimen may need to be decalcified prior to processing – a procedure that may take days or even weeks, depending upon the extent of ossification.

Interpretation of H&E stained section(s) of tumor is the “art” of surgical pathology and is based upon pattern recognition. Figure 2.1 shows the dramatic difference in appearance of a typical embryonal rhabdomyosarcoma (panel a) versus a typical alveolar rhabdomyosarcoma (panel b). Depending upon the light microscopic appearance and clinical setting...