Modern Pathology (2008) 21, S1

www.modernpathology.org

Targeted therapy of cancer: new roles for pathologists

Marc Ladanyi

Department of Pathology and Human Oncology and Pathogenesis Program, Memorial Sloan-Kettering Cancer Center, New York, NY, USA

Modern Pathology (2008) **21,** S1; doi:10.1038/modpathol.2008.12

Anatomic pathologists have always been quite familiar with the heterogeneity of human cancers, an aspect that was historically less appreciated by basic researchers interested in 'Cancer' as a single process rather than a variety of human diseases. More recently, an increasing understanding of the biological heterogeneity of human cancers by cancer biologists and molecular pathologists has set the stage for the development of therapeutic agents that target the key oncogenic abnormalities characterizing specific cancer subsets.[1] The increasing role of molecular markers of sensitivity or resistance to specific targeted agents in the management of common cancers such as breast, lung, and colon has brought these issues into everyday pathology practice.[2–4]

Many aspects of the new targeted therapies for specific cancers are therefore of increasing relevance to both molecular and anatomic pathologists, including the biology behind the specific targeted therapies, the indications for their use, their clinical impact, the eligibility criteria (as defined by histology, or by detection of the target by immunohistochemistry or molecular assays), specimen requirements and how testing is performed, histological aspects of response assessment, molecular monitoring of disease, and biologic and histopathological aspects of secondary resistance. We hope these articles will drive home the clinical importance of consolidating testing for molecular markers under the supervision of highly informed molecular anatomic pathologists or clinical pathologists. For morphology-based methods, this is self-evident, but, for tests based on DNA or RNA extraction from tumor biopsies, there is also a need to involve anatomic pathologists at the very least at the level of sample selection (and, if needed, dissection). The need for standardization and quality control to make marker studies 'transportable' between centers has also become pressing, as highlighted by some recent initiatives.[4]

It is likely that we are moving towards a time when tumors are profiled prospectively at diagnosis for panels of mutations relevant to sensitivity or resistance to specific targeted therapies,[5] much like immunohistochemistry panels are now sometimes used to enhance diagnostic certainty. These new data are becoming as pertinent to the management of cancer patients as the critical data historically provided by conventional pathological examination, namely diagnosis, grade, and pathological stage. The following articles, collected and updated from the 2007 USCAP Long Course, should provide an overview of how targeted therapies are impacting on the practice of surgical pathology in several major types of human cancer.

Correspondence: Dr M Ladanyi, MD, Department of Pathology, Memorial Sloan-Kettering Cancer Center, 1275 York Avenue, New York, NY, USA.
E-mail: ladanyim@mskcc.org
Received 11 December 2007; accepted 31 December 2007

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