

An Update in Molecular Diagnostics of Solid Tumors

Sanja Dacic, MD, PhD

Histologic diagnosis of tumors is usually straightforward, but current clinical practice in the era of personalized medicine goes beyond basic histologic diagnosis. New discoveries about genes and signaling pathways in tumors affect our profession daily. Currently available targeted therapies, diagnostic assays used in clinical laboratories for molecular profiling of tumors, and morphologic-molecular correlations are part of 21st century pathology. Pathology reports provide more than just a histologic diagnosis. Based on morphologic-molecular characteristics of the tumor, reports also provide information about predictors of therapy response and the patient's prognosis. The development of targeted therapies and their link to specific genetic alterations have resulted in an unexpected revolution in our understanding of tumor responses to novel therapies. This places additional demands on pathologists who must now be aware of advances in the molecular diagnostics of solid tumors. We must be certain that we, as pathologists, understand the role of new molecular diagnostic and prognostic tools and, most important, understand the significance of data generated by these new tools, which should be conveyed to our clinicians as clearly as possible. Molecular diagnostics of solid tumors is a rapidly evolving field, and many questions still need answers.

The purpose of this special section is to update pathologists on the molecular diagnostics of common solid tumors. The first article, by Kelly B. Engel, PhD, and Helen M. Moore, PhD, addresses the issue of preanalytical variables, such as tissue processing and time of fixation, which may influence the results of ancillary studies. A standardized approach to specimen collection, fixation,

processing, and storage to preserve the DNA, RNA, and protein necessary for ancillary testing is crucial. These variables are clearly defined in studies of *HER2* in breast cancer, and Aaron M. Gruver, MD, PhD, Bryce P. Portier, MD, PhD, and Raymond R. Tubbs, DO, take us beyond *HER2* to the world of gene expression and proteomics. Marina N. Nikiforova, MD, and Ronald L. Hamilton, MD, review the significance of molecular testing in brain tumors, as an instructive example of diagnostic and therapeutic applications of genetic events to specific tumor types. Similarly, management of patients with thyroid or colon cancers depends greatly on tumor molecular profiling, as summarized by Yuri E. Nikiforov, MD, PhD, and by Ahmed Bedeir, MD, and Alyssa M. Krasinskas, MD, respectively. Classic cytogenetics has been part of a diagnostic workup of soft tissue tumors for decades. However, classic cytogenetics has been replaced by molecular cytogenetics, as reviewed in depth by Julia A. Bridge, MD, and Allison M. Cushman-Vokoun, MD, PhD. Jennifer L. Hunt, MD, reviews the molecular perspective in head and neck cancers. Prostate cancer is one of the most common cancers and certain genetic events can be of potential diagnostic use as discussed by George J. Netto, MD, who also extensively reviews the status of molecular markers in other malignancies of the genitourinary tract. In the last article, I address the status of molecular testing in lung cancer and the great need to standardize this testing nationally and internationally. Our European colleagues have already made the first step toward standardized testing of *EGFR* in patients with lung carcinoma. The College of American Pathologists, the International Association for the Study of Lung Cancer, and the Association for Molecular Pathology are collaborating to provide an international guideline for biomarker testing in lung cancer.

Indubitably, pathology practice has passed a point of no return. Pathologists of the 21st century must not only render histologic diagnoses but also be knowledgeable about molecular pathology and its clinical implications for patient care.

Alea iacta est!

Accepted for publication January 14, 2011.

From the Department of Pathology, University of Pittsburgh Medical Center—Presbyterian Hospital, Pittsburgh, Pennsylvania.

The author has no relevant financial interest in the products or companies described in this article.

Reprints: Sanja Dacic, MD, PhD, Department of Pathology, University of Pittsburgh Medical Center—Presbyterian Hospital, 200 Lothrop St, Room A610, Pittsburgh, PA 15213 (e-mail: dacics@upmc.edu).



Sanja Dacic, MD, PhD, is associate professor of pathology and director of the FISH (fluorescent in situ hybridization) laboratory in the Department of Pathology at the University of Pittsburgh Medical Center (Pittsburgh, Pennsylvania). Dr Dacic received her medical degree and a doctor of philosophy degree with a thesis on the *EGFR* signaling pathway in lung carcinomas at the University of Zagreb (Zagreb, Croatia). She completed her residency training at the University of Pittsburgh and joined the faculty immediately after her fellowship in surgical pathology. She started her career in diagnostic pulmonary pathology and has been involved in many basic and translational research projects on molecular profiling of lung carcinomas that resulted in more than 100 peer-reviewed scientific articles, book chapters, and reviews. She was recently appointed deputy editor-in-chief of *Archives of Pathology & Laboratory Medicine* and is a member of editorial boards for *Advances in Anatomic Pathology* and *American Journal of Clinical Pathology*. She has been an officer of the Pulmonary Pathology Society for the past 6 years and is currently serving as program chair.