PERSPECTIVES IN PATHOLOGY

Embracing the Digital Realm

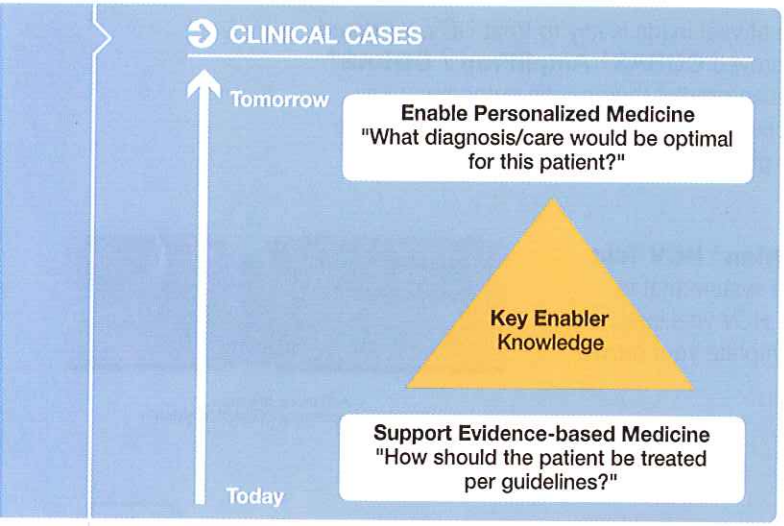
By Ajit Singh, PhD, and Rob Monroe, MD

Editor's note: This is the conclusion of a two-part column that began in the February issue.

Traditionally, pathologists have provided rough eyeball estimates for various patterns or features in tissues assessed through standard manual microscopic examination. Image analysis can more accurately and reproducibly quantify such features in different types of studies, including immunohistochemistry, immunofluorescence and FISH. These studies are being used by the pathologist not only to arrive at a specific diagnosis, but to guide clinicians in therapeutic decisions for a subset of their patients. Depending on the results of these studies, therapies are personalized for patients, leading to more precise, targeted treatment and monitoring of that treatment.

Digital pathology is poised to be a crucial enabler of personalized medicine through its central role in selecting patients for specific therapies.

The burden of testing for specific biomarkers to predict patient response to given therapeutic agents will fall to the pathologist, due mostly to the pathologist's central role in tissue processing and analysis. Given the critical role of these tests, the need for accurate, reproducible, quantitative results is paramount.



Digital pathology can provide these results. Only a handful of therapeutic decisions are based on results of specific biomarker assays. However, the number of these tests is expected to expand rapidly in the coming years as a result of the increased number of drugs being developed with companion diagnostics. This will ensure that the correct subsets of patients are being studied in clinical trials and that the correct patients are treated with the appropriate drugs once they are approved.

Implementing clinical use cases in personalized medicine (Figure) is based on the premise that the relevant data is available in a digital, mineable form so the knowledge pertinent to the clincal decision can be extracted and made available at the point of care to allow physicians and caregivers to make the most appropriate decisions.

Prime Example

Herceptin is one of the best examples of personalized medicine to date and highlights the important role that digital pathology can play in selecting patients for a given therapy. Based on the pattern and quantity of the HER2/*neu* protein in the membrane compartment of breast cancer cells as assessed by immunohistochemistry, patients are selected for treatment with the monoclonal antibody Herceptin or, in equivocal cases, for a second FISH-based assay that assesses amplification of the HER2/*neu* gene.

Interpretation of both the immunohistochemistry and FISH tests relies on quantitative assessments greatly facilitated by the use of digital pathology and image analysis. Misinterpretation of results, for example, by under- or over-estimating HER2/*neu* signals can lead to suitable patients not being treated with a potentially life-saving therapy and unsuitable patients being treated with an unnecessary and high-cost drug with potentially devastating cardiac side effects.

Additional Evidence

Several other therapeutics have been developed for specific conditions that also rely on the results of pathology-performed diagnostic assays for proper patient selection. These include Gleevec for the treatment of gastrointestinal stromal tumors and certain leukemias, anti-EGFR based drugs for the treatment of colorectal and lung cancers and anti-hormone therapies for the treatment of breast cancer.

Decisions on treatment with all of these agents—similar to the Herceptin example—rely on quantitative assessments by the pathologist that can be more accurate through the use of digital pathology and image analysis. Thus, digital pathology is poised to be a crucial enabler of personalized medicine through its central role in selecting patients for specific therapies. Moreover, assays are being developed that require quantitation not possible with the human eye, including immunofluorescence and multi-biomarker assays for which image analysis will be a necessary component of interpretation. ■

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