From the Editor's Desk

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Who Will Tailor Therapy?

Here is a business opportunity: Someone will devise a business (perhaps not in the profit-making sense, but in the organizational sense) to streamline the value chain that results in therapy specifically tailored to your patients and their tumor. Though oncologists have tailored targeted therapy for over 30 years, we are at the tail end of a disorganized, haphazard value chain to deliver this service.

This value chain starts with the decision regarding source and timing of obtaining a tissue sample, continues with patient preparation and with procuring and processing the specimen, and finally, with interpreting the result and tailoring a therapy. Because of the rapidly emerging changes in our field, there exists a business opportunity to add value and to control more of the value chain. A few examples may be illustrative:

For more than 30 years, we have been asking that breast cancer samples be evaluated to determine whether a predictive target (the estrogen and progesterone receptors) are present in quantities sufficient for successful manipulation by tamoxifen. Currently, our contribution at the tail end of this value chain is using this binary information (ie, is estrogen receptor present? Yes or no?) to prescribe a medication, and to manage the side effects.

Recently, there has been a struggle to obtain reliable predictors of response to another targeted therapy, trastuzumab. Does the immunohistochemistry (IHC) assay predict response to trastuzumab, or should we insist on fluorescence in-situ hybridization (FISH) testing? Do we test the primary tumor or a metastasis? Is HER-2/*neu* expression influenced by processing of the specimen or by previous therapies? Who assumes the cost of requesting the specimen for testing and the liability if it is not tested or is tested incorrectly?

Today, we know of specific single-nucleotide polymorphisms (SNPs) that predict, with high certainty, the chance that a patient who sits before you with chronic myelogenous leukemia will benefit from one of the three active tyrosine kinase inhibitors, or that your patient with lung cancer may benefit from one of at least two tyrosine kinase inhibitors. By the time you read this, there will undoubtedly be additional examples.

Before long, not only will we have to sort out targets, but also tailor therapies based on drug activation and metabolism as well as unusual potential toxicities. Irinotecan may be the prototype for the use of SNPs to predict toxicity, and tamoxifen and fluorouracil may not be far behind.

We can legitimately add value, not just by prescribing therapy, but in the choice and timing of sample acquisition, in assuring that results are reported in a timely fashion, and in a meaningful format with sufficient context. Our field is continually evolving. Each issue of our scientific journals contains one or more articles describing a new biomarker, genetic polymorphism, or isoenzyme that may provide prognostic information or predict response to one of our therapies.

Why shouldn't control of these assays rest with clinical laboratories? Clinical laboratories excel at specimen processing and quality control, and should continue to perform these functions. Oncology provides context. Consider the following:

Many of these assays measure RNA levels. Handling of the specimen before, during, and after its acquisition is being recognized as important. Many of the genes that give cancer cells a growth advantage are expressed in normal cells in response to stress. Does the in vivo stress of biopsy and general anesthesia change gene expression? Does the stress of ex vivo existence (even in the short time between biopsy and fixation) change gene expression?

Other medications, herbs, and "supplements" that our patients take can influence enzyme activity (particularly "CYPs" or enzymes of the cytochrome P450 system). It is likely that there will be other pharmacologic and pharmacogenetic interactions. The treating oncologist is in a position to both control the conditions of acquisition and storage of tissue and serum specimens, and have relevant contextual information available.

Someone will design a way to enhance this value chain. It may be a for-profit entity, which bundles services in a sophisticated way; perhaps an automated leukemia algorithm that would operate on a peripheral blood specimen, start with a histologic interpretation, directly informing FISH or other appropriate DNA sequence testing, determine any relevant drug metabolism polymorphisms, then make a treatment recommendation and suggest a monitoring schedule. A commercial product with these features would save time and money, cut down on duplicate and unnecessary testing and add value. Wouldn't you want this if you were a patient?

Alternatively, our professional societies may develop general diagnostic and treatment algorithms and monitoring recommendations and leave it to oncologists—individually or in groups—to thoughtfully implement them.

Alternately, we could default to the ad hoc and haphazard current development path. Wouldn't it be wonderful if the information we have so painstakingly entered into our medical records be used seamlessly to inform choice of assays. It would be even better if we were compensated for the work of creating this information, which we now add to the value chain.

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