A Question of Ownership

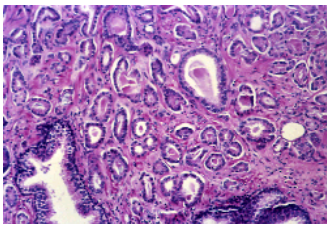
By Daniel D. Von Hoff, MD, and J. Lyle Bootman, PhD

There is no question that the recent sequencing of the human genome will have a major impact on the practice of oncology—and that impact will likely be faster than anyone can now predict. Certainly this is true for colorectal cancer (discussed in this issue), where a large variety of genetic alterations have been described.[1] Currently, we have at least four techniques to evaluate patients' tumors, including routine histology, immunohistochemistry (protein), mRNA expression (by microarray), and protein expression (by proteomics) (see Figure 1).[2,3,4]

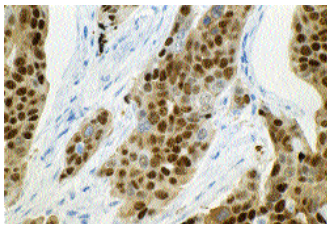
Clearly, additional technologies will become available to characterize patients' tumors. Characterization of patients' tumors can be very helpful in the clinic for:

A) Determining prognosis for the patient. This is best exampled by patients with *HER-2/neu* positive tumors or estrogen receptor-negative breast cancer, who have a worse prognosis than other breast cancer patients.[5,6] More recently, Hedenfalk and colleagues have shown that cluster analysis of microarray data can clearly delineate those patients with melanoma who will do well vs those who will not.[7] Of course, if the patient is in a poor prognostic group, more aggressive therapy to prevent recurrence may be indicated. In contrast, those patients who are in a good prognostic group would not have to be treated with anything to prevent recurrence, and would be saved the side effects of therapy that is not needed.

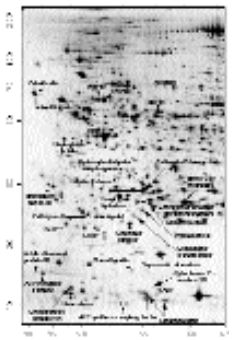
FIGURE 1. VARIOUS, CURRENT METHODS FOR CHARACTERIZING PATIENTS' TUMORS



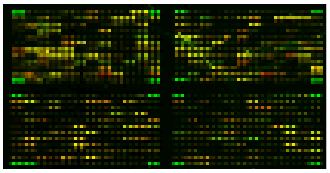
Routine pathology



Immunohistochemistry



Proteomics



Microarray

Oncology Spectrums. Vol 2. No 4. 2001.

Daniel D. Von Hoff, MD is director of the Arizona Cancer Center at the University of Arizona in Tucson, and the co-editor of Oncology Spectrums.

J. Lyle Bootman, PhD, is dean of the University of Arizona College of Pharmacy in Tucson, and the co-editor of Oncology Spectrums.

The editors wish to thank Dr. David Bearss for the illustrations and scientific review, and Elva Apodaca for the preparation of this editorial.

B) Determining therapy for the patient. This use for characterization of patients' tumors is still in its infancy. The best examples are once again in the breast cancer arena. For example, the presence of the estrogen receptor (now usually detected by immunohistochemistry) predicts for response to a hormonal manipulation, such an anti-estrogen or an aromatase inhibitor.[8] Another example for the patient with breast cancer is the presence of *HER-2/neu* (most reliably detected by in situ hybridization), which predicts for response to the agent trastuzumab.

Curiously, and relevant to this issue of *Oncology Spectrums*, there really has been very little molecular characterization of patients' colon or colorectal cancers. None of the few characterizations that have been done have been adapted for routine clinical use to predict prognosis or to define a therapeutic target. This fact brings us to the point of this editorial.

All of a sudden there is a tremendous increase in the demand for patients' tumors. Multiple companies are approaching surgeons, pathologists, cancer center directors, or anyone who has access to patients' tissues and serum, to ask them to make these specimens available to their commercial entities. While it is commendable and totally above board that people are trying to identify new genetic abnormalities in patients' tumors vs patients' normal cells—so those genetic abnormalities can be used to develop new diagnostics, new tumor markers, new prognostic factors, or indeed to discover new therapies—there are numerous problems that are developing around this approach. Some of these tumor specimens were collected from patients and kept in repositories. Informed consent for their use was most likely given for research purposes, but was unlikely given for commercial purposes. Since it is vitally important for research on tumor characterization to continue, and since this research is likely to be in the best interest of patients everywhere, many people are struggling to determine a fair way to have access to patients tumors. Without such a method, this important research will certainly be stymied.

What we propose in this editorial is that we go back to a basic premise—that this is the individual patient's tumor. It grew in their body, was taken out of their body, and belongs to them. They need to be in control and given options as to where where their tumor or serum is sent, as well as what tests are carried out on the specimen.

We propose that at the time of tumor or serum removal that the patient be given the option to have their tumor: (1) stored in pathology, as is routinely done, so that others can utilize the tumor (at the discretion of the pathologist); (2) given to them in the form of paraffin blocks so they may keep the tumor and, subsequently, submit it for any testing they deem necessary; or (3) a combination of both, with half of the specimen stored in pathology and half given to the patient.

If the patient selects either the second or third option, the patient is in control. They can decide where they want to submit their tumor to allow the latest technologies to be applied to characterize their tumor. The specimen could be submitted to either a national, government-sponsored laboratory that is fully equipped and would give the prognostic/therapeutic target information back to the patient and their physician(s), or a not-for-profit consortium (very much like the Single Nucleotide Polymorphism Consortium, which has worked so well for polymorphisms) that would be put together to characterize patients' tumors.

Empowering patients to be in control of their own tumors or serum, so they have the option to submit them where they wish, is what needs to be done. This will drive all of us to do what is best for our patients—give them access to the most information. Power to the patients! Whose tumor is it any way?

Daniel D. Von Hoff, MD

Lyle Bootman, PhD

REFERENCES

1. Arends JW. Molecular interactions in the Vogelstein model of colorectal carcinoma. *J Pathol.* 2000;190(4):412-416.
2. Ridolfi RI, Jamehdor MR, Arber JM. HER-2/neu testing in breast carcinoma: a combined immunohistochemical and fluorescence *in situ* hybridization approach. *Mod. Pathol.* 2000;13(8):866-873.
3. Iyer VR, Eisen MB, Ross DT, et al. The transcriptional program in the response of human fibroblasts to serum. *Science.* 1999;283(5398):83-87.
4. Pandey A, Mann M. Proteomics to study genes and genomes. *Nature.* 2000;405(6788):837-846.
5. Slamon DJ, Clark GM, Wong SG, Levin WJ, Ullrich A, McGuire WL. Human breast cancer: correlation of relapse and survival with amplification of the HER-2/neu oncogene. *Science.* 1987;235(4785):177-182.
6. Knight WA, Clark GM, Osborne CK, McGuire WL. Adjuvant therapy for stage II, estrogen receptor negative breast cancer. *Breast Cancer Res Treat.* 1981;1(2):131-134.
7. Hedenfalk I, Duggan D, Chen Y, et al. Gene-expression profiles in hereditary breast cancer. *N Engl J Med.* 2001;344(8):539-548.
8. Elledge RM, Green S, et al. Estrogen receptor (ER) and progesterone receptor (PgR), by ligand-binding assay compared with ER, PgR and pS2, by immunohistochemistry in predicting response to tamoxifen in metastatic breast cancer. *Int J Cancer.* 2000;89(2):111-117.