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Toward *Personalized* Medicine

The identification of molecular markers for different cancers holds tantalizing possibilities for the not-so-distant future of cancer medicine.

by Dawn Chalaire

For years, clinicians have noted that patients with the same type of cancer can have wildly different responses to the same treatment. Some of that variation is attributed to differences in individual physiology, such as the way patients metabolize drugs. Recently, however, molecular studies have been providing more and more evidence that genetic and proteomic differences lie at the heart of the question of who will respond to treatment and who will not.

Think of it as going beyond finding a needle in a haystack to being able to predict the kind of hay that will be found in the vicinity of a particular type of needle. Researchers are systematically sifting through approximately 25,000 genes, 300,000 single-nucleotide polymorphisms (SNPs), and 1.5 million proteins to identify the molecular signatures that are associated with certain types or stages of cancer, prognoses, and responses to treatment. Identifying these gene- or protein-based biomarkers in patients with cancer could lead to the prevention or earlier diagnosis of disease and to the selection of more effective treatments for individual patients.

"This type of research has the potential to revolutionize how we manage patients," said Gordon Mills, M.D., Ph.D., professor and chair of the Department of Systems Biology at The University of Texas M. D. Anderson Cancer Center. "The idea is to develop and implement personalized molecular medicine."

Dr. Aldape *is looking for genes that will predict response to therapy in glioblastoma.*

(Continued on **next page***)*

THE UNIVERSITY OF TEXAS
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Toward Personalized Medicine

(*Continued from* **page 1**)

Dr. Mills is the co-director of the institution's Robert J. Kleberg, Jr. and Helen C. Kleberg Center for Molecular Markers.

The center, established two years ago as part of a major research initiative at M. D. Anderson, comprises clinicians, translational scientists, and basic scientists, who—like other scientists around the country—are working to identify molecular markers that have potential applications in cancer prevention, detection, and treatment. Dr. Mills predicts that clinicians will see some tangible progress in these areas within the next five years. Ultimately, the goals are to be able to identify people at high risk for specific cancers, diagnose cancers at earlier stages of development, and better specify which patients should be treated with a particular therapeutic drug. To achieve these goals, the center supports the development of basic science research through in-house programs in leukemia and breast, ovarian, and lung cancers and facilitates the translation of basic science research performed outside the center. Programs are also being developed in glioma, prostate cancer, and renal cell carcinoma.

Finding predictors of treatment outcomes in glioblastoma

The discovery of a clinically useful marker for a certain type of cancer is the result of a long, multistep process. Ken Aldape, M.D., an associate professor in the Department of Pathology, and his colleagues have been addressing the question of why some patients with glioblastoma who receive the standard treatment (chemoradiation with temozolomide followed by adjuvant temozolomide) survive significantly longer than other patients given the same treatment.

It was recently found that the methylation status of the gene O6-methylguanine-DNA methyltransferase (MGMT) was a predictor of outcome to standard therapy in glioblastoma. Patients whose tumors were methylated at MGMT had a better outcome than patients whose tumors were not. However, the test was not specific enough to dictate what therapy an individual patient should receive, so Dr. Aldape and his colleagues began looking for other markers to complement MGMT status.

"We did some high-throughput analyses of glioblastoma tumor samples in patients with known survival data, asking the question, 'What were the genes that differed between these favorable versus nonfavorable outcomes?' One of the genes that came out of that analysis was YKL40, but there are other genes, too," Dr. Aldape said.

Genes that tend to be overexpressed in patients with poor survival represent therapeutic targets. If those genes can be neutralized, survival rates could be improved. Alternatively, patients who are genetically identified to have disease that does not respond well to the standard treatment could be selected for different treatment approaches.

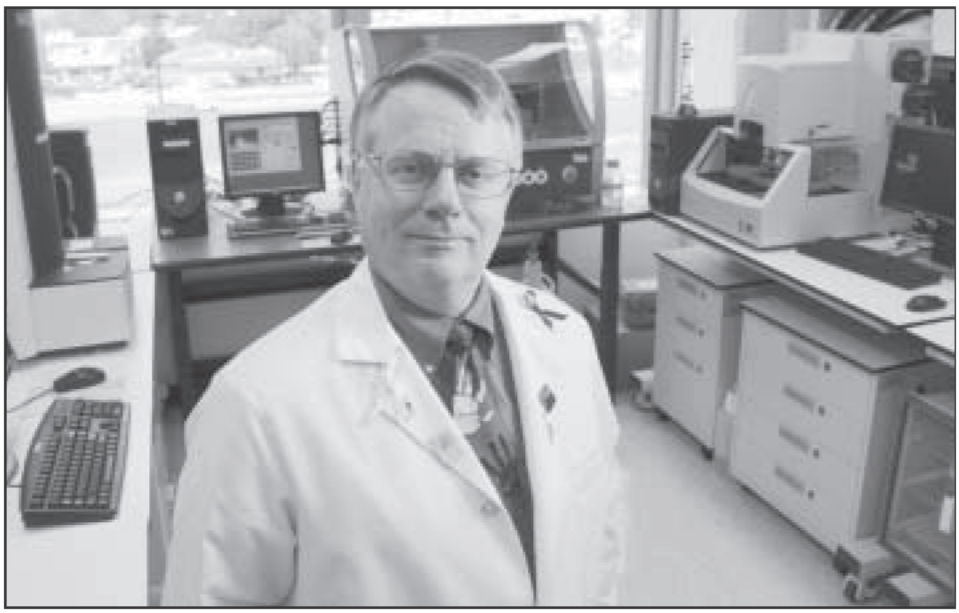
An array analysis such as the one Dr. Aldape and his colleagues performed shows only an association between a certain marker and, in this case, patient outcome. In tests, such as microarrays, that use a relatively small number of samples to search for tens of thousands of markers, some of the associations found will be due only to chance. To address this multiple comparisons problem, Dr. Aldape and his colleagues began looking at other researchers' profiling array findings to see if they identified the same genes.

"We were able to obtain four independent data sets from glioblastoma samples, and by comparing the data, we found a set of 38 genes that seem to be reproducibly predictive," Dr. Aldape said. The researchers are now trying to validate the gene markers using independent tumor samples from an ongoing Radiation Therapy Oncology Group clinical trial. Dr. Aldape said that M. D. Anderson's Center for Molecular Markers can help with these samples by looking at additional platforms, including DNA (SNP array) and microarray analyses.

Genetic signatures for tumor response

Investigators with the Breast Cancer Pharmacogenomic Program are applying genomic technology to the problem of improving breast cancer patients' responses to adjuvant chemotherapy. Several adjuvant chemotherapy regimens—including various combinations of fluorouracil, doxorubicin, cyclophosphamide (FAC); paclitaxel (T); docetaxel; and capecitabine—are virtually equal in terms of patient outcomes, and so the choice of which regimen to use is usually made on the basis of physician preference.

According to Lajos Pusztai, M.D., Ph.D., an associate professor in the Department of Breast Medical Oncology,



At the Center for Molecular Markers, **Dr. Mills** *and other scientists hope to identify markers with applications for prevention, detection, and treatment.*

about 25% of patients given any of the best preoperative chemotherapy regimens for breast cancer have no residual disease after six months of treatment and will have excellent long-term survival. By using the results of molecular analyses to match gene expression profiles of each patient's cancer to different regimens, the researchers hope to improve the pathologic complete response rate to 35% to 40%.

Fraser Symmans, M.D., an associate professor in the Department of Pathology who leads a clinical gene expression profiling laboratory, is working with Dr. Pusztai on the breast cancer study. By performing microarray analyses of fine-needle aspiration biopsy samples, the researchers have discovered genetic signatures for tumor response to different adjuvant chemotherapy regimens. The discovery of and first validation results for a 30-gene predictor of response to T-FAC have recently been reported by their group. The paper by Ken Hess, Ph.D., an associate professor in the Department of Biostatistics, showed the genomic test to be as accurate as any of the other diagnostic tests currently in use. Researchers in the Breast Cancer Pharmacogenomic Program are now performing validation studies on the predictors for FAC and FAC plus docetaxel and capecitabine and are also finalizing the design of a prospective clinical trial in which patients will be assigned to receive treatments on the basis of their tumors' genetic signatures.

In the course of their research, the investigators also identified an important mechanism of drug resistance, in which the gene that most influences response to T-FAC therapy is TAU, which blocks the binding site of paclitaxel, a key ingredient in T-FAC, and reduces the effect of the drug.

"So out of the midst of all this mathematics from microarray experiments comes a key gene that is functionally and biochemically responsible for a good part of the failure to get a complete response," Dr. Symmans said. "On its own, TAU is a decent predictor of treatment success. But combining TAU with the other genes that were identified from the microarrays into a 30-gene signature provides a much better predictor of response to T-FAC chemotherapy than we had before."

Dr. Symmans *(l) and* **Dr. Pusztai** *are designing a clinical trial in which patients will receive treatments on the basis of their tumors' genetic signatures.*

Drs. Symmans and Pusztai are also working on identifying a predictor for response to endocrine treatment in patients with estrogen receptor-positive breast cancer using molecular and biostatistical methods to identify the genes that represent estrogen receptor activity in biopsy samples. In 260 patients treated with tamoxifen only for five years, the researchers saw a clear and strong association between the expression of certain genes and how much the patients benefited from endocrine treatment.

According to Dr. Symmans, the methods and standards being established in their RNA-based microarray studies are relevant for both proteomic and DNA-based studies being conducted by other investigators through the center. "Others are investigating at the protein level what we're learning from RNA measurements of gene expression in breast cancer trials," Dr. Symmans said. "So there's good synergy occurring at scientific and clinical levels."

Bringing molecular research to the clinic

But the identification of molecules that play a role in the development and progression of cancer or in its response to treatment is only the first step in the process of developing clinically relevant applications. The road from laboratory association to clinical applicability is often long and treacherous, and many researchers simply choose not to take it.

"A lot of studies of biomarkers going back many decades show that we can measure something quite reliably and show that a particular marker is associated with a specific outcome, but that's pretty much where 95% of the literature ends," Dr. Pusztai said. "We need to translate these into clinically useful assays—to move from showing an association to developing actual tests that can be used for therapeutic decision making."

The Center for Molecular Markers works with other M. D. Anderson researchers on the design of the translational aspects of clinical trials. Dr. Mills said that the center is working with the Department of Biostatistics on a new clinical trial design that will integrate molecular marker identification and validation into clinical trials.

"In essence," Dr. Mills said, "the goal of the Center for Molecular Markers is to realize the promise of personalized molecular medicine, which is developing a treatment plan specific to the molecular makeup of each patient." It's a lofty goal, but a promising one, and progress toward it is well under way. ●

FOR MORE INFORMATION, *contact the Center for Molecular Markers at (713) 745-7041.*

Making Strides in Esophageal Cancer

by Don Norwood

In March 2006, esophageal cancer became a hot topic of conversation in Texas [redacted] announced that she had the disease and would undergo treatment at The University of Texas M. D. Anderson Cancer Center. When [redacted] died of the disease only six months later, the hard facts about the high mortality rate of esophageal cancer came into focus. The National Cancer Institute predicted that about 14,550 new cases of esophageal cancer would be diagnosed in 2006 and that 13,770 patients would die of the disease the same year, making esophageal cancer one of the most lethal types of cancer.

Although the prognosis remains bleak, advances in treatment have contributed to major improvements in both survival rates and survival duration in patients with esophageal cancer since 1970. M. D. Anderson Cancer Center has contributed to that improvement, as a multidisciplinary team of surgeons, oncologists, radiologists, and basic scientists has made great strides in the treatment of this disease.

"We emphasize a multimodality, multidisciplinary approach here at M. D. Anderson," said Wayne Hofstetter, M.D., director of the Esophageal Surgery Program and an assistant professor in the Department of Thoracic and Cardiovascular Surgery. "We've been at the forefront of that for the last 15 years. We really believe in the multidisciplinary approach because we've been able to attain a complete resection in a significantly higher number of patients through a careful combination of chemotherapy, radiation, and surgery."

Dr. Hofstetter *and colleagues have developed ways of more safely performing surgery for esophageal cancer.*

Major improvements in survival rates and duration

The numbers in an important 30-year study performed at M. D. Anderson bear out Dr. Hofstetter's assertion. In that study, Stephen Swisher, M.D., a professor in the Department of Thoracic and Cardiovascular Surgery and the previous director of the Esophageal Surgery Program, looked at patients who underwent surgery for esophageal cancer from 1970 to 2001. As surgical techniques improved over that 30-year span, the 3-year survival rate increased from 27% to 46%. Furthermore, the median survival duration rose from 17 months to 34 months. Finally, the complete resection rate increased from 76% to 95%.

Those amazing numbers reflect not only a better selection of candidates for surgery but also the constant advancement in therapy for esophageal cancer at M. D. Anderson. Specifically, they reflect the effect of teamwork among the different disciplines on treatment outcomes.

"Things that are offered here that aren't necessarily offered elsewhere are the innovative chemotherapy and radiation modalities in combination with surgery," Dr. Hofstetter said. "In terms of surgical therapy, we've developed ways of performing surgery more safely. We have incredibly low mortality rates of 2% to 4%, even in patients who have had chemotherapy and radiation. Many cancer centers won't perform surgery after chemotherapy and radiation because they consider it too difficult or risky. Preoperative chemotherapy and radiation therapy may make surgery more difficult, but we've been able to compensate for that with the experience that comes from being a high-volume center in surgery and perioperative care."

Another major development has been the opening of the Proton Therapy Center in September 2006, which gives patients with esophageal cancer treatment options offered in few other places. In fact, the first patient to ever receive proton beam therapy for esophageal cancer did so at M. D. Anderson. According to Dr. Hofstetter, proton beams target less normal tissue than other types of beams, allowing radiation oncologists to give higher doses to tumors and minimize the side effects to the surrounding healthy tissue. Current trials should help evaluate how well the technology meets expectations and add to oncologists' volume of experience using proton beams against esophageal cancer.

An insidious disease

The question remains, though: why is this cancer so lethal? The fact is that esophageal cancer is a very insidious disease. By the time symptoms appear, the primary tumor is local-regionally advanced; thus, the patient is often not a candidate for surgery. Dr. Hofstetter compared it to pancreatic and lung cancer, both of which are considered "silent killers."

"Esophageal cancer often doesn't become evident until it produces symptoms," said Dr. Hofstetter. "The patient may have difficulty swallowing. There may also be bleeding, anemia, or black stools, and there can be pain. By the time these symptoms come up, the tumor is usually locally advanced."

Dr. Hofstetter uses an analogy to explain the extent of esophageal cancer to his patients. He compares the wall of the esophagus to the wall in a house. Superficial lesions occur in the "paint" layer of the wall and are easily cured by scraping this layer and possibly the "drywall." However, more advanced lesions go through these layers and invade the nerves, lymphatic system, and blood vessels.

"The lesion has access then to travel along those pathways, and once it has metastasized, it becomes almost impossible to cure," said Dr. Hofstetter. "To use the house analogy, if it's just local, just in the wall, or if it's just barely gotten into the studs without invading into the plumbing and electrical circuits of the entire house, then I can remove that wall and still have a chance of cure."

Understanding risk factors

Of the two types of esophageal cancer, squamous cell carcinoma and adenocarcinoma, the squamous cell variety is associated primarily with intake of carcinogens, most notably tobacco and alcohol, whereas adenocarcinoma is associated with long-term gastroesophageal reflux disease (GERD) and Barrett's esophagus. Thus, individuals who fall into either risk category are prime candidates for esophageal cancer screening, which consists of endoscopic evaluation of the esophagus. Adenocarcinoma is the prevalent form of esophageal carcinoma in the United States. However, Dr. Hofstetter noted that not everyone with esophageal adenocarcinoma fits the typical profile: middle-aged, white, male, and slightly overweight, with a history of GERD. That presents the next challenge in esophageal cancer: determining exactly who is at risk.

"There's definitely a biological component to it, and there's got to be some way that we can more specifically filter out who's at higher risk," said Dr. Hofstetter. "Screening tests are based in part on the probability of the disease in the community, but with only 15,000 new cases of esophageal cancer in the country every year, it's just not cost-effective to screen the entire population. It's something we're continuously working on: identifying the best candidates for screening.

"What we're studying in terms of early-stage cancer is doing earlier surveillance and following people who have the markers for esophageal cancer. There are a lot of people both on the basic science side and on the clinical side here at M. D. Anderson who are trying to figure out ways to catch the disease earlier."

Providing palliative care

Another important area is preserving and even enhancing quality of life. The most common symptoms of esophageal cancer are problems swallowing and the resulting weight loss. The multidisciplinary efforts at M. D. Anderson again reap benefits in this area, resulting in improved nutrition and comfort for patients.

"We have a very good palliative care program for patients," said Dr. Hofstetter. "Chemotherapy does a very good job of opening up the esophagus, allowing patients to swallow better and maintain their weight better. We also have mechanical ways of opening the esophagus using stents, ablation, and other means.

"A surgical form of palliation is putting in a feeding jejunostomy. Most of the time, when we first see patients, they can't swallow, and they lose a lot of weight. The average person in the United States is a little bit overweight and can afford to lose 15, 20, 25 pounds, but that's not true for everyone. And as patients continue to lose weight, their nutrition declines, and they can't fight the cancer anymore. Poor nutrition equals a shortened life span. Therefore, surgically, we'll put in a feeding tube so they can go on to get treatment or palliative care, which can help maintain their nutrition for the rest of their lives."

The treatment of and screening for esophageal cancer remain high priorities at M. D. Anderson. This is evident in the growing multidisciplinary efforts that are aimed at further reducing the mortality of this now high-profile disease. ●

FOR MORE INFORMATION, *contact Dr. Hofstetter at (713) 563-9130.*

ESOPHAGEAL CANCER PROTOCOLS

- Phase II randomized trial of preoperative chemotherapy and chemoradiotherapy versus preoperative chemoradiotherapy for potentially resectable adenocarcinoma of the stomach and gastroesophageal junction (2003-0769). Physician: Jaffer Ajani, M.D.
- Phase Ib randomized, double-blinded, placebo-controlled, dose escalation study of Polyphenon E in patients with Barrett's esophagus (2004-0907). Physician: Robert S. Bresalier, M.D.
- Computer-assisted analysis of brush biopsy specimens (EndoCDx) in the detection of esophageal dysplasia: a multicenter prospective clinical trial (2005-0737). Physician: Sharmila Anandasabapathy, M.D.
- Nonoperative therapy of local-regional carcinoma of the esophagus: a randomized phase II study of two paclitaxel-based chemoradiotherapy regimens. (RTOG 0113). Physician: Ritsuko R. Komaki, M.D.

FOR MORE INFORMATION *and a broader listing of clinical trials, visit www.clinicaltrials.org or call askMDAnderson at (877) MDA-6789.*

Lapatinib Shows Promise for Inflammatory Breast Cancer

In a multicenter and international clinical trial of the experimental biological agent lapatinib, researchers have discovered that it is active against inflammatory breast cancer (IBC), an aggressive and often lethal form of the disease.

Massimo Cristofanilli, M.D., associate professor in the Department of Breast Medical Oncology at M. D. Anderson Cancer Center, reported the findings of the international phase II trial at the San Antonio Breast Cancer Symposium in December.

IBC is a fast growing cancer. According to Dr. Cristofanilli, only 40% of women with IBC will survive five years. Until now, no therapies specific to IBC have been studied in multicenter clinical trials. Therefore, no proven therapies—standard or experimental—currently exist for women with IBC.

"We did this phase II study because lapatinib is one of the few drugs that has shown any activity in phase I studies in patients with recurrent IBC. It appeared that this agent could become the first to offer hope for women newly diagnosed with the disease," said Dr. Cristofanilli, the study's principal investigator.

Lapatinib is an epidermal growth factor receptor (EGFR) and HER2neu tyrosine kinase inhibitor. An experimental drug that has shown promise in patients with metastatic HER2-positive breast cancer in whom trastuzumab (Herceptin) has failed, the oral agent blocks the activity of the HER2 protein as well as EGFR by binding to the part of the protein found inside breast cancer cells, explained Dr. Cristofanilli.

The study reports that 30 of the 35 patients, or 86%, had a clinical response (defined as a 50% or greater reduction in tumor size) to the lapatinib-chemotherapy drug regimen. Just as interesting and important is the finding that 25% to 30% of the patients receiving lapatinib alone responded in the first two weeks, said Dr. Cristofanilli.

"With lapatinib, we finally have a drug on which to build effective therapy—we just have to refine the most effective way to use it," said Dr. Cristofanilli.

Further studies are planned with lapatinib that will likely include the agent in combination with different chemotherapy regimens.

New Molecule Targets Leukemia

Researchers at M. D. Anderson Cancer Center report that a novel multi-kinase inhibitor, MK-0457 (VX-680), is clinically active against multiple target mutations in two types of leukemia and myeloproliferative disorders and produces few side effects.

Francis J. Giles, M.D., professor in the Department of Leukemia at M. D. Anderson, presented the phase I/II trial data at the annual meeting of the American Society of Hematology in December.

According to Dr. Giles, the study of 44 patients, conducted at M. D. Anderson and Duke University Medical Center, showed the first clinical activity of a kinase inhibitor against the T315I BCR-ABL mutation found in chronic myeloid leukemia and acute lymphocytic leukemia. In addition, the trial showed the first activity against the JAK-2 mutation found in myeloproliferative disorders.

"The drug was very well tolerated and showed a clinical response not only in patients but in terms of pharmacodynamics."

– Dr. Giles

The findings could potentially lead to effective treatments for diseases resistant to imatinib (Gleevec), nilotinib (Tasigna), and dasatinib (Sprycel). The T315I mutation is known to be responsible for the aggressive biological growth cycle and resistance to these drugs.

Dr. Giles reported that patients on the study experienced minimal side effects, such that no maximum tolerated dose was defined. Mild side effects included lowering of white blood cell counts, hair loss, nausea, and inflammation of the mouth.

"This drug produces clinical and biologic activity where we have not seen it before—in T315I-positive chronic myeloid and acute lymphocytic leukemias and JAK-2-positive myeloproliferative disorders," Dr. Giles said.

"While we went into this trial to determine the safety and dosage of the drug, it became apparent quite quickly that the drug was very well tolerated and showed a clinical response not only in patients but in terms of pharmacodynamics," said Dr. Giles. "As a result, we ended the phase I aspect of the trial earlier than anticipated and moved into phase II with a range of different doses. We are quite hopeful that this drug will ultimately prove to be clinically beneficial for this segment of patients, but additional research will be needed."

Though chronic myeloid leukemia, acute lymphocytic leukemia, and myeloproliferative disorders are relatively rare cancers, they are very aggressive and often fatal after standard therapy fails, said Dr. Giles. For the subset of leukemia patients who have the T315I mutation or for patients with myeloproliferative disorders with the JAK-2 mutation—about 10% of patients with the respective diagnoses—there are no therapies available to specifically attack these key mutations.

"This is a relatively small population that can potentially benefit from the drug, but for those who have these mutations, this research opens the door to a tremendous option for them," said Dr. Giles.

Dr. Giles and his team are planning an international phase II study of MK-0457 in patients with the T315I mutation.

HOUSE•CALL

Eat Well, Live Longer

The food you eat can help reduce your risk of developing cancer. Experts estimate that between 30% and 40% of all cancers could be prevented if people ate the right foods, exercised enough, and maintained a healthy body weight.

Research studies have found that people who routinely eat large amounts of fruits and vegetables are half as likely to develop cancer as people who don't. In fact, the latest American Cancer Society (ACS) Nutrition and Physical Activity Guidelines for Cancer Protection recommend that individuals eat a plant-based diet to reduce cancer risk and maintain a healthy weight.

Two major benefits of plant-based diets

The ACS guidelines are updated every five years to take into account the latest research. Each new version ranks health recommendations in order of importance, said Sally Scroggs, a registered dietician and senior health education specialist in M. D. Anderson Cancer Center's Prevention Center. The first recommendation in the latest guidelines is "maintain a healthy weight throughout life." Being overweight or obese is linked with an increased risk of breast cancer (in postmenopausal women) and cancers of the colon, uterus, esophagus, and kidney.

The foods within a plant-based diet, mostly fruits and vegetables, contain a variety of nutrients and phytochemicals—fiber and plant chemicals—that protect against cancer and other diseases. The ACS guidelines recommend getting these nutrients through foods rather than vitamins or artificial supplements.

Eating healthier one meal at a time

If what you're eating right now is less than ideal, you may be thinking it would be too difficult to change to a healthier diet—which includes eating five or more servings of fruits and vegetables each day, according to the new guidelines. Good news: it's simpler than it seems. Including fruits and vegetables at every meal and having them as snacks can help make it easier to reach your goal. "If you eat a salad consisting of one cup of raw leafy vegetables and one-half cup of chopped vegetables, that's two servings of vegetables right there," Ms. Scroggs said. "That's two of the three servings of vegetables you should eat, at a minimum, each day, along with at least two servings of fruit."

Eat a plant-based diet to reduce cancer risk and maintain a healthy weight.

The latest evidence also supports eating an assortment of fruits and vegetables to maximize health benefits. For example, cruciferous vegetables, such as broccoli, cauliflower, brussels sprouts, and kale, contain chemicals thought to reduce colorectal cancer risk.

Simple substitutions for renovating your diet

Other dietary guidelines include choosing whole grains instead of processed grains and sugars, limiting the consumption of processed and red meats, and limiting alcohol intake to one drink a day for women and two drinks a day for men:

✓ **Eat whole grains.** Fortunately for those interested in getting healthier, the whole-grain foods recommended by experts—which include whole-grain rice, bread, pasta, and cereals—are now common in supermarkets. Still, try to limit your consumption of refined carbohydrates, such as those in pastries, sweetened cereals, and other high-sugar foods.

✓ **Limit consumption of processed and red meat.** As much as possible, eat fish, poultry, or beans, instead of beef, pork, and lamb. When you do eat meat, choose lean cuts and smaller portions. Bake, broil, or poach meat instead of frying or charbroiling.

✓ **Limit alcohol intake.** Cut down on the alcohol you drink, or don't drink at all. Research has documented that alcohol can cause cancers of the mouth, throat, larynx, esophagus, liver, and breast and may increase the risk of colon and rectal cancer.

Remember: what you eat and drink can either increase or decrease your risk of getting cancer. Making a few simple changes to your diet can do a great deal of good for your health.

For further information about what you can do to prevent cancer, visit www.mdanderson.org/prevention. The American Cancer Society's Web site (www.cancer.org) outlines the latest nutrition and physical activity guidelines. The American Institute of Cancer Research's Web site (www.aicr.org) provides tips on how to make these dietary changes. ●

For more information, talk to your physician, or:

- *call askMDAnderson at (877) MDA-6789*
- *visit www.mdanderson.org.*

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K. Stuyck

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The Secret of Good "Person-Doctoring"

Robert Buckman, M.D., Ph.D.
Adjunct Professor of Neuro-Oncology, M. D. Anderson
Professor, University of Toronto

The oldest equation that describes the entire breadth of the clinical interaction is actually quite simple. It is this: Patient = Person + Disease.

In our clinical practice, we are not simply taking care of a disease process—we are taking care of a disease as experienced by a particular person.

We have all—appropriately—spent multiple years learning our "disease-doctoring" skills, and we are justifiably proud of our knowledge in managing, for example, node-positive, receptor-negative, HER2-positive breast cancer or recurrent ovarian cancer. The trouble, however, is that we almost certainly didn't get any specific training in "person-doctoring"—and that poses a problem.

The solution to that problem is actually straightforward: we have to show that we see the patient as a person first and not simply as another case of "node-positive breast cancer." Even though that sounds like a rather vague objective, there are some simple and straightforward guidelines that you can use right now which will help.

The secret of "making contact" with or "engaging" the patient is to acknowledge the emotion the patient is experiencing. Whatever it is they express—be it shock, disbelief, fear, anger, frustration, dismay, denial, sadness—it's important that we as clinicians demonstrate that we have observed that emotion and that we note it as something that needs to be on the agenda between us.

The best and most practical way of doing this is called "the empathic response," and it consists of three steps. Step 1 is to *identify the emotion*. Since emotions are almost always mixed, you can identify the strongest component. In Step 2, *identify the cause* or the source of that emotion—usually it is related to news you have just given the patient. Then, in Step 3, you respond in a way that shows you have *made the connection* between Steps 1 and 2.

For example, you might say, "This news is obviously scary," or "Clearly this is difficult to believe," or "What I've just said is obviously very upsetting."

Any response that acknowledges and identifies the emotion will help the situation and label you as an effective communicator and part of the patient's support system. Any response that ignores or invalidates the patient's emotion ("You're so brave—I know you'll do fine!") will probably label you as somewhat insensitive—and will make engaging the patient more difficult.

The empathic response is actually relatively straightforward. It simply requires an active decision to respond to the emotion in the room. If you aren't using the technique very much at present, try it. I think you will be very pleasantly surprised at how easy it is and what a big difference it makes. ●

OncoLog, M. D. Anderson Cancer Center's report to physicians, is a monthly newsletter sent to more than 30,000 physicians throughout the nation and the world. Published by the Department of Scientific Publications, *OncoLog* reports on innovative developments in research and treatment at M. D. Anderson. Current and previous issues are available online in English and Spanish at www2.mdanderson.org/depts/oncolog. For editorial information, call (713) 792-3305 or email scientificpublications@mdanderson.org. To refer a patient or request information, call (800) 392-1611 or (713) 792-6161, or visit www.mdanderson.org.

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