A Publication of
MD Anderson Cancer Center
Making Cancer History®

REPORT TO PHYSICIANS
SEPTEMBER 2010 VOL. 55, NO. 9

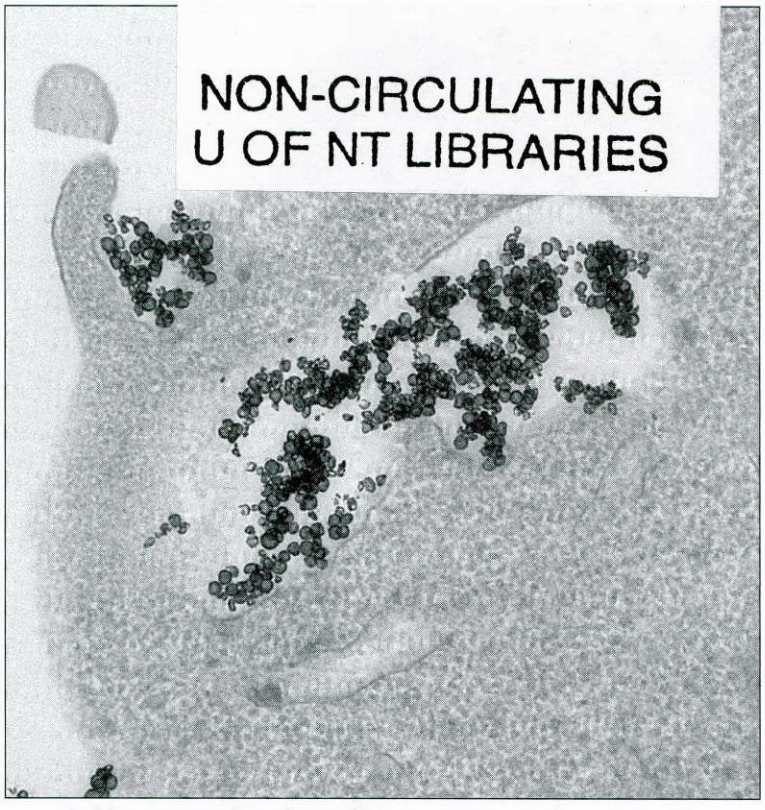
OncoLog

Tiny Particles, Vast Potential

Coming soon to the clinic: nanoparticles that deliver therapy straight to tumor cells, bypassing normal cells and many toxic effects

By Sunita Patterson

Nanotechnology has become a buzzword in the energy, computing, and fabrication fields. And now the potential use of nanotechnology in cancer therapy is also rapidly advancing. The advances build on our emerging understanding of the molecular attributes of particular tumors and our growing ability to target and even manipulate those attributes. Therapies at the nano scale—in particular, those using nanoparticles—may enable a new precision and specificity in targeting tumor cells.



Gold nanoparticles, shown here in a mouse melanoma cell by transmission electron microscopy, can kill cancer cells when heated with near-infrared light. Reprinted with permission from Lu W, et al. Clin Cancer Res *2009;15(3):876–886.*

At The University of Texas MD Anderson Cancer Center, investigators are working on nanotherapies from many different perspectives. Nanoparticles are being made of gold, biodegradable lipids, chitosan, and various other materials. Nanoparticles are being tested as vehicles for drugs, as packages for gene therapy, or as anticancer weapons themselves, activated at just the right time using radio waves or near-infrared light. And within the next year or two, several of these therapies will be available to patients in clinical trials. We highlight a few of the developing therapies here.

The blueprint

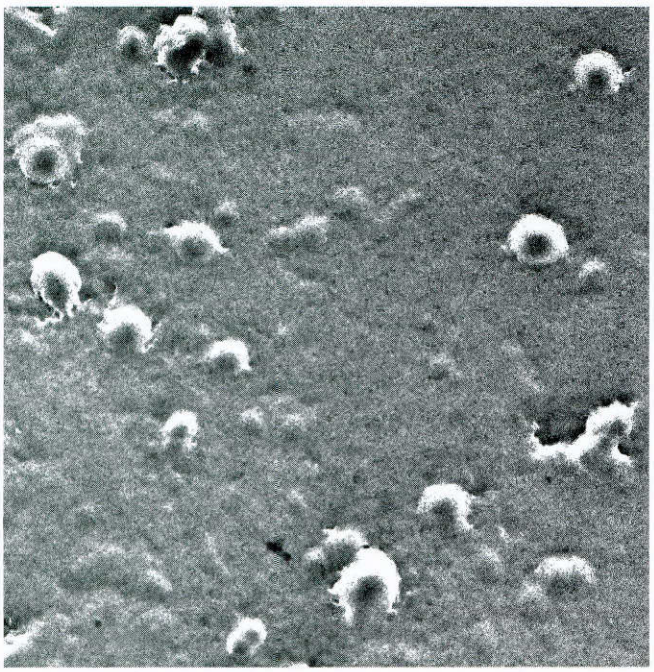
Nanoparticles are so small they are measured in nanometers (a nanometer is a millionth of a millimeter); many have diameters in the range of 5–200 nm. At that size, the particles are small enough to evade uptake by the

(*Continued on* page 2)

THE UNIVERSITY OF TEXAS
MD Anderson Cancer Center

Tiny Particles, Vast Potential

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



Researchers hope to deliver siRNA to cancer cells using nanoliposomes like the ones shown in this freeze-fracture electron micrograph.

liver and spleen, enabling them to stay in the bloodstream longer. They're also able to take advantage of a unique opportunity: they can fit through the holes in the walls of the permeable, or "leaky," blood vessels that tend to form in tumors. When nanoparticles are injected intravenously, they flow right on through normal blood vessels, which have tight walls without holes, but selectively diffuse through the permeable vessels out into tumors. This selective targeting of tumor cells without affecting normal cells means that the therapy can be concentrated at the site of disease and that the systemic side effects of the therapy may be minimal.

Making a therapeutic nanoparticle involves three basic considerations. First is the design of the nanoparticle itself. The material should be biocompatible, safe to use, able to remain intact until it reaches the intended target, and, once used, able to be excreted or degraded by the body. Second, the nanoparticle should preferentially accumulate in the tissue of interest. It's common to add a targeting mechanism that, like a homing device, will find cancer cells and ignore normal cells. Finally, there must be a way to activate the particle's therapeutic potential once it has reached the target. The particle may self-destruct, or it may be activated by an external force.

Cooking tumors with gold

Two MD Anderson research groups are applying this blueprint to nanoparticles made of gold, a biocompatible material already used to treat rheumatoid arthritis. The treatments under development at MD Anderson involve injecting gold nanoparticles into the body, where they find their way to tumor cells. An energy source, such as radio waves or near-infrared light, is then applied to the body externally. As the radiation penetrates the body, the gold nanoparticles heat up, in effect "cooking" the tumor from the inside out.

Within the next few years, Steven A. Curley, M.D., a professor in the Department of Surgical Oncology, will initiate a clinical trial involving solid gold nanoparticles and radio waves. "We're finding that if we can target the gold nanoparticles to cancer cells and then treat them with a noninvasive radiofrequency field," Dr. Curley said, "it can completely control and destroy the cancer cells. And the radio waves are not harmful to patients or healthy tissue."

To increase the chances of the gold particles concentrating in cancer tissue, Dr. Curley and his team attach cancer cell–targeting antibodies and proteins to the nanoparticles. "It's very simple chemistry to add targeting molecules to the particle surface," he said. "For targets, we're looking for molecules that are abnormally expressed on the surface of the cancer cells."

The story of this therapy's genesis has been told on *60 Minutes*. Inventor John Kanzius designed the prototype radiofrequency device in 2003. An MD Anderson patient with non-Hodgkin lymphoma, he was motivated to find a treatment that lacked the side effects of chemotherapy. The first nanoparticles tested with the device were carbon particles provided by Rice University professor Richard E. Smalley, Ph.D. Dr. Smalley, who was also an MD Anderson cancer patient at the time, had been awarded the 1996 Nobel Prize in Chemistry for his role in the discovery of the complex carbon molecule buckminsterfullerene, or the "buckyball." The size, stability, and hollow structure of buckyballs and related carbon molecules make them attractive for nanotechnology research.

Neither Mr. Kanzius nor Dr. Smalley lived to see the new photothermal therapy tested in patients, but Dr. Curley has continued to pursue that aim. "This therapy has potential for treating not only localized tumors—such as pancreatic, hepatocellular, colorectal, breast, and prostate cancers—but also bloodborne cancers such as lymphomas and leukemias," he said.

Gold nanoparticles with antibodies specific to pancreatic cancer have been successfully tested by the team in cultures of human cancer cells and in mice and rabbits. Carbon nanoparticles have successfully destroyed liver tumors in rabbits, but those particles must undergo further toxicity testing before they can be considered for clinical use. Other ideas being tested by Dr. Curley's team include attaching additional elements, such as the monoclonal antibody cetuximab and siRNA (see box, "Using siRNA to Silence Genes"), to the surface of nanoparticles to make cancer cells more sensitive to the heat.

A one-two punch

The idea of combining modalities at the nano level is also being tested by Chun Li, Ph.D., a professor in the Department of Experimental Diagnostic Imaging. Rather than solid gold particles and radio waves, Dr. Li and his team are

working with hollow gold particles and near-infrared light. The group has fabricated and tested nanospheres (also called nanoshells or nanocages) of various thicknesses to take advantage of the near-infrared region of the electromagnetic spectrum. "At that wavelength, you have minimal absorption and scattering by tissue and water, so the light is able to penetrate deeper, and you have high absorption by the gold nanospheres," explained Dr. Li. Near-infrared radiation is already used in some clinical applications.

In an experiment reported in *Clinical Cancer Research*, Dr. Li's team tested the effectiveness of nanosphere delivery and activation in a mouse melanoma model. To heighten the selective delivery of the nanoparticles, they added a peptide that targets the melanocortin type 1 receptor, which is overexpressed in melanoma. "We found a very high level of accumulation of the particles in tumors," explained Wei Lu, Ph.D., an instructor in the Department of Experimental Diagnostic Imaging and the first author of the report. Treated tumors had much larger areas of necrosis after irradiation than did controls.

The hollowness of the particles offers a variety of possible ways to improve the efficiency of the treatment. "If you put a chemotherapy drug inside a nanosphere and then expose it to light, the drug can be released as the particle heats up," Dr. Li said. Cells that aren't killed by the heat may succumb to the chemotherapy. To test this concept of a one-two punch, Dr. Li and colleagues introduced gold nanospheres loaded with doxorubicin or paclitaxel into MDA-MB-231 breast cancer cells. Cells that were incubated with the nanospheres and irradiated with near-infrared light demonstrated increased apoptosis—cell death—caused by both photothermal ablation and drug cytotoxicity. The paclitaxel-loaded nanospheres were also tested in mice injected with MDA-MB-231 cells and were found to delay tumor growth.

Another version of the one-two punch involves loading nanospheres with siRNA rather than a drug. In April, Dr. Li's team published in *Cancer Research* the results of experiments in a HeLa cervical cancer xenograft model in mice. The team used siRNA that targets the NF-κB p65 subunit, which is thought to play a role in transcription of genes important in inflammation and cancer. Expression of NF-κB p65 receptors was reduced in tumors treated with the nanospheres and near-infrared radiation but was not affected in non-irradiated tumors.

The precision of the near-infrared light delivery allows both temporal and spatial control of nanoparticle activation. An advantage of this approach is that if nanoparticles do end up in normal tissue in a part of the body that is not irradiated, they will not be activated. "The nanoparticles are not going to have any effect if they're not exposed to near-infrared light," said Dr. Li. In the siRNA experiment, the nanospheres did not cause side effects in the liver, spleen, kidneys, or lungs.

Dr. Lu noted, "Any siRNA should be able to work with this technology. We think that because we can control the time and location of expression, it might be possible to deliver siRNAs in a sequential fashion by incorporating two different siRNAs and using different wavelengths of light to activate them."

Furthermore, the *Cancer Research* article reported the potential of a one-two-three punch: combining photothermal ablation, siRNA release, and release of a chemotherapeutic agent, irinotecan.

(Continued on **page 4***)*

Using siRNA to Silence Genes

Considering it was once classified as "junk," small interfering RNA (siRNA) has come a long way in garnering researchers' respect.

Anil Sood, M.D., explained what siRNA is. "There's a lot of genetic material that is noncoding, meaning it's not involved in making proteins. People thought that it had no purpose. It turns out that a lot of this so-called junk DNA actually plays a role in regulating or controlling the activity or the levels of many of the genes that do make proteins." siRNA is one form of this noncoding genetic material; microRNA is another. It is unknown how many of these noncoding RNAs control genes or pathways that drive tumor growth.

siRNAs, which are 20–26 bases long, bind to specific messenger RNAs (mRNAs) and break them down so the mRNAs aren't translated into proteins. siRNAs can be used to manipulate target genes in a strategy called RNA interference. "RNA interference offers an opportunity for shutting off, or silencing, genes," Dr. Sood said. Dr. Sood, along with George A. Calin, M.D., Ph.D., an associate professor in MD Anderson's Department of Experimental Therapeutics, heads the Center for RNA Interference and Non-Coding RNAs, a collaborative effort among five Houston-area research centers focused on understanding these RNAs' roles in cancer initiation, progression, and dissemination.

A challenge of developing therapy with siRNA has been figuring out how to deliver it to the tumor site. "One of the limitations of using siRNA is that if you just inject naked siRNA into the body, it gets broken down within minutes—it has no real stability," Dr. Sood said. "It gets excreted by the kidneys very quickly. So we needed a way to protect these particles so that they can be present in the body long enough to get to the needed site and actually get inside the tumor cells." Nanoparticles—whether made of gold, lipid, chitosan, or another material—may offer the protection needed to make siRNA therapy possible. ●

Tiny Particles, Vast Potential

(*Continued from* page 3)

The team believes that the photothermal and siRNA treatments sensitized the cervical cancer cells to chemotherapy.

Biocompatible and biodegradable

The concept of a therapy-loaded nanoparticle is being pursued by other MD Anderson researchers who are using different materials. Gabriel Lopez-Berestein, M.D., a professor in the Department of Experimental Therapeutics, has spent 25 years working with lipids and other biocompatible materials for delivery of therapeutic agents. He and Anil Sood, M.D., a professor in the Departments of Gynecologic Oncology and Cancer Biology, are developing two different types of therapeutic nanoparticles loaded with siRNA.

The nanoparticle closest to being available for clinical use is a nanoliposome made of 1,2-dioleoyl-sn-glycero-3-phosphatidylcholine (DOPC). This neutral lipid-based molecule has no net charge and therefore escapes filtering by immune cells. The group recently completed tests of this nanoliposome loaded with siRNA targeting the gene for EphA2, a protein involved in tumor growth, invasion, and angiogenesis. "EphA2 is present at high levels in a lot of tumors, but it's virtually absent in normal adult tissues," said Dr. Sood, "so from a toxicity perspective we thought that it was attractive." The nanoliposomes successfully accumulated in ovarian tumors in animal studies. "With this tiny fatty particle, the neutral nanoliposome, the siRNA is protected in the body," added Dr. Lopez-Berestein. "It doesn't break down, and this particular lipid is taken up avidly by ovarian cancer cells." In mice, tumor growth was reduced after treatment, and more so when the siRNA was combined with chemotherapy or with a second form of siRNA that targets a different gene. Extensive toxicology testing of the DOPC-EphA2 nanoliposomes has been conducted in mice and nonhuman primates.

Liposomal applications, such as intravenous liposomal doxorubicin injection, are already approved for clinical use, and Drs. Lopez-Berestein and Sood plan to open a nanoliposome clinical trial within a year.

> **"This therapy has potential for treating not only localized tumors ... but also blood-borne cancers such as lymphomas and leukemias."**
>
> **– Dr. Steven Curley**

Another nanoparticle the two physician-scientists are developing is made of chitosan, a polysaccharide found in crustacean exoskeletons. Chitosan nanoparticles are loaded with a different siRNA, one that targets a gene that is important in cancer cells and in tumor blood vessels. In an orthotopic ovarian cancer mouse model, the chitosan nanoparticle delivered siRNA not only into tumor cells but also into blood vessels, and the target gene was shut down. The team hopes to bring this therapy to a clinical trial within 2 years.

Drs. Sood and Lopez-Berestein continue to tweak their nanoparticle treatments to improve the treatments' efficiency. Like Dr. Li's group, they are attaching markers to the particles that can increase the particles' odds of reaching tumor cells. Drs. Sood and Lopez-Berestein will also continue to test different combinations of siRNAs customized to particular tumor types. "An advantage of this modality is you can target pretty much any gene of interest," said Dr. Sood, "so it offers a lot of flexibility."

Many possibilities

In addition to these and other therapeutic applications, nanoparticles are proving useful for imaging. "They have the potential to be multifunctional," Dr. Curley said. For example, nanoparticles are being developed to concentrate a fluorescent or contrast agent in tumor cells, providing better detail on computed tomography and magnetic resonance imaging scans. "With our colleagues in the Department of Imaging Physics," said Dr. Li, "we're looking at combining therapy and diagnostics—theranostics." The same particles would be used for imaging and for treatment; infrared light would be applied to the locations shown by either positron emission tomography or photoacoustic tomography to contain cancer cells. These approaches are being tested in small-animal models.

No one innovation discussed here is likely to become the single standard nano modality of the future. Rather, customized approaches to nanotherapy may emerge in which physicians identify the specific characteristics of an individual patient's cancer, select a modality that targets that specific set of characteristics, and select a nanoparticle that works best with that modality.

A critical mass of interest and funding has contributed to the profusion of nanomedicine projects. MD Anderson is involved in the Alliance for NanoHealth, an effort involving hundreds of researchers within eight institutions centered on Houston's Texas Medical Center. Headed by Mauro Ferrari, Ph.D., a professor in the Department of Experimental Therapeutics, the alliance's goal is to foster collaboration on nanotechnology applications in medicine. "We're trying to join forces to gain a deeper understanding of how nanomaterials interact with the body, how they are transported to the cells, and how they are cleared from the body," Dr. Li said.

These small particles have the potential to make a large impact in the clinic soon. ●

For more information, call Dr. Curley at 713-794-4957, Dr. Li at 713-792-5182, Dr. Lopez-Berestein at 713-792-8140, or Dr. Sood at 713-745-5266. A more comprehensive list of ongoing nanotherapy research at MD Anderson is available at www.mdanderson.org/oncolog.

Non-Hodgkin Lymphomas: Targeted Therapies Leading Treatment Advances

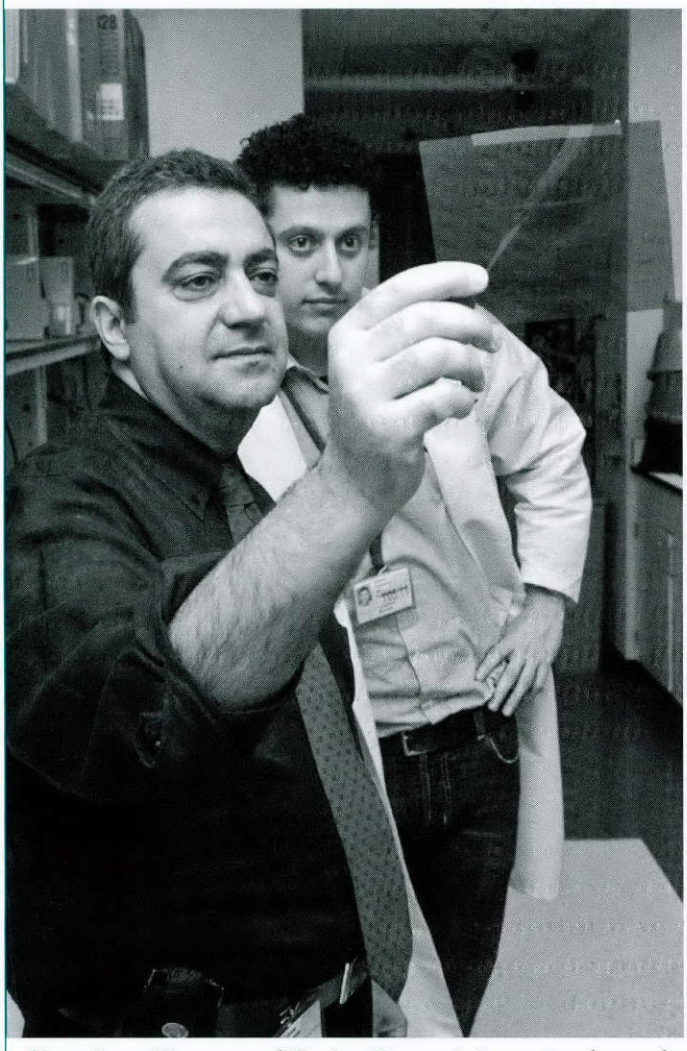
By John LeBas

For years, oncologists have attacked non-Hodgkin lymphomas with varying combinations of chemotherapy, radiation, stem cell transplants, and surgery, trying to find optimal regimens for a group of diseases that are often difficult to cure. While survival rates have improved as a result of these efforts, most non-Hodgkin lymphoma specialists agree that there is much more to be done for patients affected by this diverse group of lymphomas.

In recent years, new hope has emerged from positive clinical trials of targeted therapies, which have been shown to work on their own or to boost the effectiveness of established treatments. These newer drugs attack cancer via its biology, targeting specific molecular characteristics to impede malignant proliferation.

Targeted therapies are being tested in most types of non-Hodgkin lymphoma and at all disease stages. Most of these agents are monoclonal antibodies, which are laboratory-developed proteins that seek out proteins or receptors expressed by cancer cells; or small molecules that interfere with key cell survival machinery.

"We and others are actively involved in finding new treatments for lymphoma that preferentially kill the tumor cells while sparing normal cells. These new drugs have the potential of improving treatment efficacy while reducing treatment toxicity," said Anas Younes, M.D., a professor and director of clinical and translational research in the Department of Lymphoma and Myeloma at MD Anderson Cancer Center.



Drs. Anas Younes *and* **Enrico Derenzini** *examine the results of a Western blot of HDAC3 protein expression in cancer cells.*

About non-Hodgkin lymphoma

Non-Hodgkin lymphoma refers collectively to malignancies of the lymphocytes, a subset of white blood cells. It is the fifth most common group of cancers, with new diagnoses in the United States exceeding 65,000 annually, according to the U.S. National Cancer Institute. About 20,200 Americans die of these diseases each year. Most patients with new non-Hodgkin lymphoma are age 60 years or older, and there are no known environmental or behavioral causes.

About 40 drugs, most of them cytotoxic chemotherapeutic agents, are approved to treat non-Hodgkin lymphomas, and the growing number of available treatments has contributed to improved survival over the past 30 years. Still, most lymphoma subtypes are currently not cured with standard chemotherapy regimens; one of the most curable types of non-Hodgkin lymphoma, diffuse large B cell lymphoma, can be cured in only about half of patients, Dr. Younes said.

Monoclonal antibodies in lymphoma therapy

The treatment landscape began to change more rapidly a few years ago, with the approval by the U.S. Food and Drug Administration of rituximab (Rituxan) for certain patients with non-Hodgkin lymphoma. Rituximab, a monoclonal antibody that targets cells expressing the protein CD20, has since become one of the most successful targeted therapies for these diseases. It is used alone or is added to established chemotherapy regimens for optimal effect, and clinical trials using rituximab in various combinations and for various disease types are ongoing.

In addition to having activity against some new and recurrent non-Hodgkin lymphomas, rituximab was recently found in an international phase III trial to be effective as a maintenance therapy for newly diagnosed advanced

(Continued on **page 6***)*

(*Continued from* page 5)

follicular lymphomas (a group of non-Hodgkin lymphomas). The study showed that rituximab maintenance yielded a significant improvement in progression-free survival duration among patients whose disease responded to initial immuno-chemotherapy. A separate study showed that rituximab maintenance therapy yielded better progression-free survival after autologous stem cell transplant therapy for some patients with recurrent follicular lymphoma.

Further study of the safety of rituximab given over long periods and in different types of non-Hodgkin lymphoma is needed, Dr. Younes said. The agent does not work in some non-Hodgkin treatment scenarios, having been shown, for example, to have no benefit as a maintenance therapy following initial remission in newly diagnosed diffuse large B cell lymphoma.

Future developments with small molecules

Still, the successes of rituximab against non-Hodgkin lymphoma have encouraged clinical testing of other targeted agents, Dr. Younes said. And positive results have begun adding up: several new small molecules being tested in clinical trials at MD Anderson and elsewhere are demonstrating promising clinical activity in patients with lymphoma. These agents include drugs that target mTOR, histone deacetylases, Jak/STAT signaling, and B cell receptor signaling.

> **"These new drugs have the potential of improving treatment efficacy while reducing treatment toxicity."**
>
> **– Dr. Anas Younes**

For example, in a phase I study whose preliminary results were presented this year at the American Society of Clinical Oncology annual meeting, the experimental agent PCI-32765 (an oral inhibitor of Bruton tyrosine kinase) showed activity in patients with relapsed B cell lymphomas. Complete or partial responses were seen in 23% of the patients with follicular lymphoma, 69% of those with chronic lymphocytic leukemia/small lymphocytic lymphoma, 75% of patients with mantle cell lymphoma, and 1 of 7 patients with diffuse large B cell lymphoma. Newer clinical trials are combining multiple small molecules to increase the anti-lymphoma efficacy.

Historically, phase I trials have been designed to gauge tolerance and side effects of an experimental agent, with the possible benefit of disease response. However, in phase I trials of non-Hodgkin lymphoma therapies, researchers have come to expect treatment response in a high percentage of patients, Dr. Younes said. "This gives us hope that we will be able to one day make significant improvements in patient survival with targeted agents and other therapies now undergoing early testing," he said. ●

For more information, contact Dr. Younes at ayounes@mdanderson.org. You can also follow Dr. Younes on Facebook (www.facebook.com/pages/Anas-Younes-MD) and on Twitter (DrAnasYounes).

Clinical Trials in Lymphoma

The following selected clinical trials of targeted therapy for lymphoma are available at MD Anderson:

A Phase I/II Study of Immunotherapy with Milatuzumab (hLL1) in Patients with Non-Hodgkin's Lymphoma (NHL) and Chronic Lymphocytic Leukemia (CLL) (2008-0075). Principal investigator (PI): Felipe Samaniego, M.D. This clinical trial is testing dosing, safety, and efficacy of an anti-CD74 monoclonal antibody.

A Phase I Study of SB1518 for the Treatment of Advanced Lymphoid Malignancies (2008-0105). PI: Anas Younes, M.D. This clinical trial is testing dosing and safety of an oral JAK2 inhibitor.

Phase I Dose-Escalation Study of Bruton's Tyrosine Kinase (Btk) Inhibitor PCI-32765 in Recurrent B Cell Lymphoma (2008-0494). PI: Nathan Fowler, M.D. The primary objective of this clinical study is to find the maximum tolerated dose of a Btk inhibitor.

An Open-Label, Dose Escalation, Phase I Study of MLN4924, A Novel Inhibitor of NEDD8-Activating Enzyme, in Adult Patients with Lymphoma or Multiple Myeloma (2008-0135). PI: Jatin J. Shah, M.D. This clinical study is the first of the NEDD8-activating enzyme inhibitor MLN4924 in humans.

A Phase IA/II, Multi-Center, Open-Label Study of HCD122 Administered Intravenously Once Weekly for Four Weeks in Adult Patients with Advanced Non-Hodgkin's or Hodgkin's Lymphoma Who Have Progressed After at Least Two Prior Therapies (2008-0062). PI: Michelle A. Fanale, M.D. This clinical trial is testing an anti-CD40 fully humanized IgG1 antibody.

An Open-Label, Phase I Study of MLN8237, a Novel Aurora A Kinase Inhibitor, in Patients with Advanced Hematological Malignancies (2008-0278). PI: Dr. Fowler. This clinical trial is testing dosing, safety, and response.

Phase I/II Study of Panobinostat (LBH589) Plus Everolimus (RAD001) in Patients with Relapsed and Refractory Lymphoma (2008-0805). PI: Dr. Younes. The primary objectives of this clinical study are to determine the highest tolerable dose and safety of an HDAC inhibitor/mTOR inhibitor combination. ●

For more information about clinical trials available at MD Anderson, visit www.clinicaltrials.org.

HOUSE•CALL

Writing for Wellness: Keeping a Journal

When facing a serious illness like cancer, anyone can find it difficult to express personal feelings to others and sort through complicated emotions. If you find yourself in that position, one safe and private way to do both is to write in a journal. Keeping a journal allows you to come to terms with your situation at your own pace and in your own way, potentially helping you regain a sense of control in your life.

"Our culture seldom allows us to voice our real feelings," said Sandi Stromberg, who has facilitated several journaling sessions at MD Anderson's Place … *of wellness*. "So I encourage patients and caregivers to process what they are experiencing—to write down their anger and sadness, their frustrations and fears. I also suggest they write down three gratitudes at the end of the day, even if it's something as small as a good cup of coffee or less traffic on the road."

Research has shown that writing about stressful experiences, such as illness, may boost patients' health and psychological well-being. When people confront and work through an experience, they understand it more clearly. This can improve coping and sleep quality, reduce stress, and enhance social interactions, all of which result in a better quality of life.

How do I start journaling?

Follow the steps below to help you get started.

1. **Make a plan.** Choose a time of day that is most convenient for you. Then make a goal to write twice a week, for 15 minutes each time. Once that becomes a routine, try adding a day.

2. **Find a spot.** Choose a place to write that is comfortable and relaxing, where you can be alone and focus on your thoughts.

3. **Start writing.** Write down whatever comes to mind. Let your mind wander and your words flow. Don't edit yourself.

Once you are comfortable journaling, do not limit yourself to certain days or times. Journal whenever you have time or when you feel it can help you the most. Some people find it helpful to journal while waiting for appointments, as it helps to calm nerves and pass the time.

Keeping a journal can help some patients cope with their illness.

©iStockphoto.com/busypix

Journaling Tips

- Don't be hard on yourself if you miss a day.
- Always date your entries.
- If you prefer journaling on a computer, print the pages and keep them in a notebook. (This makes it easier to look back at later.)
- Write what you want to write. Remember, the journal is for you.
- Allow yourself to buy a nice journal. Your words are worth it!

What should I write?

If you find yourself staring at the blank page without knowing how to start, write "I don't know what to write" over and over. Eventually, other words will come. Another way to begin the writing process is to try writing stories about your past. For example, you can journal about your first car or your experiences on your first day of school. You might record the unexpected humor of daily life or simply insights and observations. Don't feel pressured to tell the whole story—you can always expand on the bits and pieces you choose at a later time.

"I give patients and caregivers suggestions for topics during our sessions to remind them they were fully functional people with productive lives before cancer," Ms. Stromberg said. "It's so easy for them to tell about who they are in terms of their illness when the truth is that they are and have been so much more. Journaling helps them remember that."

If writing does not come naturally to you, try making lists of things that come easily to mind, such as:

- your best qualities,
- what you need and want from your doctor,
- things that make you happy,
- ten people who've had the greatest impact on your life, or
- your favorite books. ●

For information about cancer, talk to your physician, or:

- *visit www.mdanderson.org*
- *call* askMDAnderson *at 1-877-632-6789*

OncoLog, September 2010
S. Stromberg and L. Classen

The University of Texas
MD Anderson Cancer Center
OncoLog—1421/18417601
PO Box 301439
Houston, TX 77230-1439

ADDRESS SERVICE REQUESTED

IN BRIEF

Study Shows Abnormal Cells in Blood Increase with Lung Cancer Stage

Using a novel approach to detect genetically abnormal cells in the blood of patients with non–small cell lung cancer, a team of scientists at MD Anderson Cancer Center found that the number of circulating cells with genetic abnormalities matching those of tumor cells increases with the severity of the cancer. Cancer patients in the study also had many times the number of these circulating abnormal cells per microliter of blood than did healthy volunteers in a closely matched control group.

"Blood tests for these circulating cytogenetically abnormal cells could be used to diagnose lung cancer earlier, monitor response to therapy, and detect residual disease in patients after treatment," said Ruth Katz, M.D., a professor in MD Anderson's Department of Pathology and corresponding author of the study's report in a recent issue of *Clinical Cancer Research*.

The report describes what Dr. Katz and colleagues believe to be the first study to use a technique called fluorescence in situ hybridization (FISH) to detect circulating cells that have the same genetic aberrations as non–small cell lung cancer cells. FISH detects and quantifies abnormal cells using dye-labeled DNA probes that cause cells with the targeted genetic abnormalities to light up when viewed under a fluorescence microscope. Color photomicrographs of these abnormal cells are available online at www.mdanderson.org/oncolog.

> "Blood tests for these circulating cytogenetically abnormal cells could be used to diagnose lung cancer earlier."
>
> **– Dr. Ruth Katz**

"We were surprised to find many more abnormal circulating cells in lung cancer patients compared with what had been seen previously using other techniques," Dr. Katz said.

Using 12 biomarker probes that target aberrations previously connected to lung cancer, the researchers analyzed blood samples from 59 patients with non–small cell lung cancer and 24 people without lung cancer. Both groups included smokers and non-smokers.

In addition to finding that patients with stage IIIB or IV lung cancer had higher mean levels of circulating abnormal cells than did patients with early-stage disease, the researchers found that some biomarkers were associated with lung cancer recurrence and overall survival duration. Dr. Katz said work is under way to develop a clinical test to detect lung cancer based on abnormalities in the peripheral blood mononuclear cells revealed by FISH. ●

OncoLog

The University of Texas MD Anderson Cancer Center

President
John Mendelsohn, M.D.

Provost and Executive Vice President
Raymond DuBois, M.D., Ph.D.

Senior Vice President for Academic Affairs
Stephen P. Tomasovic, Ph.D.

Director, Department of Scientific Publications
Walter J. Pagel

Managing Editor
Bryan Tutt

Assistant Managing Editor
Joe Munch

Contributing Editors
Melissa G. Burkett, Sunita Patterson, John LeBas, Lionel Santibañez, Ann M. Sutton

Design
Janice Campbell, The Very Idea®

Photography
Barry Smith

Editorial Board
Michael Fisch, M.D., Chair
Lyle Green, Vice Chair
Therese Bevers, M.D.
Robert Gagel, M.D.
Beverly Handy, M.D.
Patrick Hwu, M.D.
Charles Koller, M.D.
Maurie Markman, M.D.
Shreyaskumar Patel, M.D.
David Schwartz, M.D.
Rena Sellin, M.D.
Randal Weber, M.D.
Christopher Wood, M.D.

Physicians: To refer a patient or learn more about MD Anderson, please contact the Office of Physician Relations at 713-792-2202, 1-800-252-0502, or www.physicianrelations.org.

Patients: To refer yourself to MD Anderson or learn more about our services, please call 1-877-632-6789 or visit www.mdanderson.org.

For questions or comments about *OncoLog*, please e-mail scientificpublications@mdanderson.org or call 713-792-3305. Current and previous issues are available online in English and Spanish at www.mdanderson.org/oncolog.

Made possible in part by a gift from the late Mrs. Harry C. Wiess.

NCI® CCC A Comprehensive Cancer Center Designated by the National Cancer Institute