Texas-Arizona Collaboration Between Baylor and TGen spurs “immunogenomics” revolution

Collaboration seen as essential to perfecting precision medicine model for patient care.

A remarkable precision medicine collaboration announced on May 21, 2015, matches the world-class genomics, proteomics, data analysis, and new therapeutics expertise at the Translational Genomics Research Institute (TGen) with renowned clinical investigators, immunological specialists, and the large patient population at Baylor Scott & White Health–North Texas. These combined qualities are the necessary ingredients for pursuing and perfecting precision medicine: matching the optimal treatment to the specific patient.

Alan M. Miller, MD, PhD, medical director of the Baylor Sammons Cancer Center and chief of oncology for Baylor Scott & White Health – North Texas, sees the strengths of Baylor and TGen forging a significant next step in the evolution of cancer care, enabled by tremendous strides in technology. “The reason we can do this now is because of the rapidly changing dynamics of cancer treatment and the growth of both targeted therapy and immune therapy. When we can bring together the strengths of TGen and Baylor—TGen’s strength in targets and Baylor’s strengths in immunology—we move into being at the forefront of what we call ‘immunogenomics’ and really being able to leverage these two revolutionary changes in cancer care.”

(Continued on page 3)
Cancer

From the Medical Director

As you navigate through the rest of your life, be open to collaboration. Other people and other people’s ideas are often better than your own. Find a group of people who challenge and inspire you, spend a lot of time with them, and it will change your life.

Amy Poehler

I like to begin my director’s note with a quote, usually from a notable figure, a Ben Franklin or an Abe Lincoln. This time as I searched for words to summarize the theme of the issue, I found the quote from Amy Poehler, an alum of the Saturday Night Live cast. That show in many ways has highlighted collaboration and partnership. In the early days, there were great moments with Dan Aykroyd and Jane Curtin doing “Point/Counterpoint” and the Coneheads, and of course Aykroyd and John Belushi as the Blues Brothers. More recently, Amy Poehler partnered with Tina Fey, both on SNL and afterwards, to give us brilliant comedy.

In Ms. Poehler’s quote, she notes that you should “find a group of people who challenge and inspire you, spend a lot of time with them, and it will change your life.” In TGen, we have found a group of colleagues who truly challenge and inspire us. This past weekend, over 50 scientists, physicians, and other team members from TGen and Baylor spent time together in our first scientific retreat. Hopefully the fruits of those initial collaborative discussions will change not just our lives but the lives of many with cancer and other diseases.

Decisions were made to initially fund three projects—one in breast cancer, one in ovarian cancer, and one in pancreatic cancer—each of which has co-principal investigators from Baylor and TGen. In addition, a fund was established to be able to characterize rare tumors, including the most cited in Molecular Cancer Therapeutics that year. Going forward, we are limited only by the imagination of our team, and right now that seems limitless.

Alan M. Miller, MD, PhD
Chief of Oncology, Baylor Scott & White Health – North Texas
Medical Director, Baylor Charles A. Sammons Cancer Center at Dallas

(Continued from page 1)

“You have to go back 40 years and look at when chemotherapy and radiation therapy were both emerging and when we began to look at the power of combining chemotherapy and radiation therapy,” Dr. Miller said. “We’re now, I think, seeing another revolution of that type, bringing together genomic-based targeted therapy with immune-based approaches to cancer treatment.”

The Baylor-TGen collaboration had its origins in what is widely hailed as a dramatic proof-of-concept collaboration inspired by TGen Physician-in-Chief Daniel Von Hoff, MD, FACP, whose professional roots trace back to his years as a professor at the University of Texas Health Science Center at San Antonio, where he initiated a new therapeutics unit and collaborated with doctors to help patients across the Lone Star State. That included dozens of opportunities to interact with physicians at Baylor University Medical Center at Dallas, home to the Baylor Charles A. Sammons Cancer Center.

Dr. Von Hoff drew on his knowledge of the Texas medical landscape to help match the phenomenal talents of a Texas oncologist like Baylor’s Joyce O’Shaughnessy, MD, with a proven Arizona translational scientist like TGen’s John Carpten, PhD.

Drs. O’Shaughnessy’s and Carpten’s clinical trial of 14 patients with triple-negative breast cancer produced such groundbreaking genomic and clinical research that their study paper—published in Molecular Cancer Therapeutics—became the most cited article published in that journal in 2013. “That is probably one of the more exciting clinical trials of the last 5 years,” said Dr. Miller. “That was the first major collaboration between Baylor and TGen.”

Dr. Carpten, TGen’s deputy director of basic science—who with Dr. Miller will codirect the new Baylor-TGen collaboration—agreed: “TGen had the opportunity to do our first precision medicine study using next-generation sequencing as the genomic technology for selecting patients for therapies.” Dr. Carpten recalled, “Leaning on Dan Von Hoff’s wisdom, after selecting triple-negative breast cancer as the model disease, the first name that came out of Dan’s mouth was ‘Joyce O’Shaughnessy.’”

Dr. Von Hoff, who since 2011 has been a senior research advisor at Baylor Sammons Cancer Center and a member of its Research Oversight Council, had known Dr. O’Shaughnessy for decades. He said the combination of Dr. O’Shaughnessy, Dr. Carpten, and David Craig, PhD, TGen deputy director for bioinformatics, was critical to the study by employing the clinical expertise at Baylor and translational research expertise at TGen. “It was an epiphany to show how much each could add. I already could see it because I work with both groups,” Dr. Von Hoff said. “And we helped some people [breast cancer patients]. That’s number 1. We had dramatic responses.”

Building on that success, and also at the urging of Dr. Von Hoff, Baylor has since joined with TGen in other projects, including a massive nationwide clinical trial of melanoma patients started this year by the Stand Up To Cancer Melanoma Dream Team and the Melanoma Research Alliance. That project is led by Jeffrey Trent, PhD, TGen president and research director.
Collaboration’s Initial Focus: Three Areas of Study

The newly formed Baylor-TGen collaboration will initially focus on three major areas of study: breast cancer and other women’s cancers; blood cancers, especially multiple myeloma; and abdominal cancers, especially pancreatic and colon cancers, with a special emphasis on new ways of detecting cancer.

Heme Malignancies Study Group

Yair Levy, MD, Baylor’s medical director of hematology malignancy clinical research, and TGen’s Jonathan Keats, PhD, will lead this group, which is a “first love” of Dr. Miller, a hematological specialist.

Baylor has a significant bone marrow transplant program, as well as an active clinical research program led by Dr. Levy with studies in leukemia, lymphoma, and myeloma. At TGen, Dr. Keats leads one of the world’s largest clinical trials in multiple myeloma, a decade-long study sponsored by the Multiple Myeloma Research Foundation.

“To get started in the collaboration, we would have liked to have covered the entire gamut of cancer, but we had to focus on areas where we already had a significant amount of research going in both institutions,” Dr. Miller said. “This was one of the naturals.”

Women’s Malignancies Study Group

Baylor’s Dr. O’Shaughnessy, medical director of Breast Cancer Research, and TGen’s Boudour Saliba, PhD, will lead this group, which Dr. Miller and Dr. Carpten described as an obvious focus following the success of the Baylor-TGen triple-negative breast cancer study. Also contributing to this study group will be Baylor’s Monique Spillman, MD, PhD, a gynecologic cancer specialist and physician on the medical staff at Baylor University Medical Center at Dallas.

“It’s another area where we had complementary strengths,” Dr. Miller said. “But rather than make it entirely about breast cancer, we included gynecological malignancies” which will include ovarian, uterine, and cervical cancers.

Abdominal Malignancies Study Group

Baylor’s Ajay Goel, PhD, Director, Center for Gastrointestinal Research; Director, Center for Epigenetics, Cancer Prevention and Cancer Genomics; and Baylor Research Institute and Charles A. Sammons Cancer Center, and Carlos Becerra, MD, medical director of Innovative Clinical Trials Center and assistant chief of Oncology, are joined by TGen’s Muhammed Murtaza, MD, PhD, in this group that will look at pancreatic cancer and colon cancer, as well as new methods of detecting cancers early when there is a greater chance of success.

“Here comes the great synergy of the Baylor-TGen collaboration, because now you’re bringing together Dr. Murtaza’s expertise in circulating tumor DNA and Dr. Goel’s expertise in microRNA,” Dr. Miller said. “And maybe it’s the combinations of those that are going to come up with the biomarker test panel that’s going to be the solution to all this.”

Liquid Biopsies, Immunology, and “Personalized Vaccines”

Coursing through all of the Baylor-TGen studies will be the use of genomic, proteomic, and epigenetic information and immune profiling to match patients to new targeted therapies, and the pursuit of clinical trials to test new treatments, Dr. Miller said. And there will be an emphasis on using new technologic breakthroughs to pursue better cancer treatments by employing new immunologic techniques and detecting cancers earlier, including the use of liquid biopsies.

“TGen has a rich history of using a particular type of immune cell—the dendritic cell—in immunotherapy. At the most basic level, these cells are extracted from a patient, programmed in the lab to identify specific antigens, and then reintroduced to the patient to help attack the cancer.”

“It’s a very specific approach,” Dr. Miller said. “I think it’s going to be evolving and we will still continue on that path. But there’s also going to be a path using a slightly different technology, and rather than take the dendritic cells out and train them in the lab, to be able to train them within the individual’s own body to attack the individual’s cancer.”

Unlike flu or polio vaccines designed to prevent disease, Dr. Miller said these “personalized vaccines” would be designed to treat an existing disease, “and hopefully prevent it from ever coming back.”

Besides the goal of detecting cancer early, another challenge is to monitor patients after treatment so if the cancer returns, intervention could start immediately.

“Liquid biopsies are emerging as a new cancer early warning system. They detect circulating tumor DNA, microRNA, and even tumor cells in the bloodstream. If you can detect them, even in very small quantities in the bloodstream, that’s your liquid biopsy,” Dr. Miller said. Such tests, when perfected, should be safer, less intrusive and less costly, and produce quicker results than scans or traditional surgical biopsies.

Baylor and TGen Working Together: A Two-Way Street

“It’s finally becoming evident that precision medicine is likely going to improve outcomes for cancer patients. It’s the wave of the future for clinical management,” said Dr. Carpten. “In order to do this effectively, one would want to bring together a program that excels in basic and translational research alongside an amazing clinical facility and medical institute, and that’s what TGen and Baylor bring as a collaboration.”

Baylor, to ascend as a cancer center and become a National Cancer Institute-designated center, needs the expertise of TGen to bolster its research, Dr. Carpten said. “Instead of trying to build it from the ground up, which could take decades, why not collaborate with a group that already has established that type of basic research infrastructure?”

Dr. Carpten said, “From the TGen standpoint, Baylor brings one of the largest oncology programs in the country.” Dr. Carpten said. “For TGen to be effective as a translational institute, we must have strong clinical collaborations.”

Dr. Von Hoff said Baylor is a tremendous fit for TGen. He likes to refer to the collaboration as “a two-way street.” He considers it a privilege to work with the staff at Baylor, and admires the institute’s commitment to its community and the less fortunate. “It’s a group of people who are really dedicated to delivering the best, most compassionate care, which is where it all starts,” Dr. Von Hoff said. “It’s a medical system that is just absolutely devoted to excellence.”

Dr. Miller foresees additional opportunities for collaboration and a time when personnel will be specifically recruited to work on Baylor’s and TGen’s combined efforts. “There will be a cohort of people coming along in the next few years who will be TGen or Baylor, but they will be people who are ‘collaboration people,’” Dr. Miller said. “It will be a potential model for the rest of the nation, if we are as successful as we hope to be. Hopefully, we will continue to do our part to make cancer much more of a chronic disease, instead of a lethal disease and eventually a historic disease.”
Multiple Myeloma Is First Priority of Heme Malignancies Study Group

Baylor-TGen collaboration takes critical look at successes, and failures, to improve treatments for patients with blood cancers.

With Baylor’s extensive clinical research in leukemia, lymphoma, and other blood-related cancers, and TGen’s leadership of one of the world’s largest blood cancer clinical trials, a Heme Malignancies Study Group as part of the Baylor-TGen collaboration seemed only natural.

“I think our strength at Baylor is clinical and the availability of patients, while TGen has the expertise in correlative endpoints and the actual understanding of the molecular biology of both our successes and our failures,” said Yair Levy, MD, Baylor’s medical director of hematologic malignancy clinical research.

One of the most significant cross-pollination points for Baylor and TGen is in multiple myeloma. Both institutes are members of the Multiple Myeloma Research Consortium, and both are considered world leaders in studying this disease.

Unlike many other cancers, for which investigators continue to hunt for rapid means of telling what treatments are working, multiple myeloma already has some of the most reliable biomarkers by measuring immunoglobulin levels. "It is very easy to monitor the efficacy of new treatment interventions, as we can easily monitor the disease with a simple and cheap blood test,” explained Jonathan Keats, PhD, head of TGen’s Multiple Myeloma Research Laboratory. "As much as we talk about biomarkers, many say multiple myeloma is the only cancer with an actual biomarker.”

Further, unlike many other cancers that lack methods of early detection, the propensity to develop multiple myeloma can be predicted by identifying patients with monoclonal gamopathy of undetermined significance (MGUS). MGUS patients have an abnormal protein in their blood known as monoclonal or M protein, which indicates abnormal plasma cells in the bone marrow. The higher the level of M protein, the greater the chances that MGUS could turn into multiple myeloma. By monitoring the progression of MGUS, patients can get earlier treatment. "We don’t need a new early detection test; we just need the current test to be used as part of a routine physical,” Dr. Keats said of the serum-protein electrophoresis test that can detect MGUS.

But even when patients with MGUS are identified, he said, who is really at risk? Only about 1 in 4 eventually develop multiple myeloma. If early treatment interventions are going to be used, new ways are needed to identify the patients who will progress.

Major Challenges in Multiple Myeloma

The major challenges in multiple myeloma are identifying which patients are likely to progress from MGUS to multiple myeloma, identifying which patients will respond to various treatments, understanding why their cancer eventually progresses beyond available treatments, and discovering more effective treatments.

There has been progress in addressing the disease. Only a decade ago, the median survival was about 3 years. Dr. Keats said, “Treatments have improved so much in the last decade that median survival is now closer to 8 to 10 years. Many patients are surviving to 20 years with treatment. We have good therapies. But when patients ultimately progress beyond currently available treatments, it’s dismal.”

Dr. Levy agreed, noting that as cancers progress, they continue to mutate and become more difficult to treat: “We’re trying to identify what these characteristics are that cause this chemoresistance and try to find out what’s driving these mutational changes.” This is where Dr. Levy believes the Baylor-TGen collaboration will pay dividends.

TGen Opens Medicine’s “Next Wave”

“TGen is opening up the next wave of medicine,” Dr. Levy said. Because new treatments are expensive and not necessarily toxicity-free, TGen’s laboratory research will help advance precision medicine by recommending to clinicians the right treatment for the right patient. “Certainly, it would be better to have a good understanding of who would, and wouldn’t, benefit from treatments prior to treating them,” he said.

Better analysis could reduce the time a patient is treated with a drug that is not working—time that could allow the cancer to become more resistant to treatment, and time that the patient could be using to receive a better treatment.

One tactic Dr. Levy said he would employ with Dr. Keats is to work backwards, "a type of reverse engineering. He explained: "We’re going to look at our successes, especially our unexplained successes, when the patients have had a more robust response than we typically see. What in particular is allowing this treatment to work better? We’re also going to look at people who are not responding to anything. What are the mechanisms? What do they have in common in the gene expression level, or the proteomic level, or anything—what are the commonalities?”

Baylor Among CoMMpass Study’s 120 Clinical Trial Sites

At TGen, Dr. Keats is supervising a 10-year study, sponsored by the Multiple Myeloma Research Foundation, which includes a clinical trial that in September 2015 had enrolled all of its planned 1,000 multiple myeloma patients at 120 sites worldwide. One of the first and largest clinical trial sites in this study is at Baylor.

"Relating Clinical Outcomes in Multiple Myeloma to Personal Assessment of Genetic Profile,” or CoMMpass StudySM, started in 2011. It is one of the first studies of this disease with a proportional number of African American patients, who are nearly twice as likely to develop it.

One phenomenon noted in the CoMMpass StudySM, said Dr. Keats, is that many distinct DNA abnormalities are being detected that are not directly associated with the cancer. “What we’ve been seeing through one of the assays in CoMMpass is that there are many more cells with DNA abnormalities in the bone marrow of a patient than there are cells with the phenotype of the tumor cells.”

Following a Clue That Could Prevent Relapse

Dr. Keats said that these cells might be the cause of eventual relapse, and that studies in conjunction with Baylor—which runs one of the nation’s most active bone marrow transplant programs—could help determine if that is true.

Dr. Keats also plans to leverage Baylor’s immunotherapy expertise with TGen’s expertise in genomics. He is especially interested in Dr. Levy’s work in radiolabeled antibodies, which work like “smart bombs” against individual blood tumor cells, avoiding healthy cells.

Beyond multiple myeloma, there are plans for the Baylor-TGen collaboration to address other blood-related cancers as well. “As people work together more, more projects snowball from one project to another, and even if it’s a project that’s a failure, it may lead you to something else,” said Dr. Levy.

He added that Dr. Keats already has helped him provide the scientific justification for a new clinical trial on the horizon, by finding a common target for a drug that worked in one acute myeloid leukemia case and may have a use in treating multiple myeloma.

Dr. Keats said he believes the Baylor-TGen collaboration could also lead to a new way of addressing cancer. "It’s ultimately my hope, in the next 10 to 15 years, that we’re not necessarily going to have hematological tumors vs. solid tumors. We would describe tumors, instead of their tissue of origin, by their aberrant cellular pathway,” he said. "Here’s what’s going wrong with these cells, which may be the same in a colon cancer, a breast cancer, and a lymphoma, so that we identify things based on the abnormalities that occur, instead of the tissue of origin.”

“I think our strength at Baylor is clinical and the availability of patients, while TGen has the expertise in correlative endpoints and the actual understanding of the molecular biology of both our successes and our failures.”

Yair Levy, MD
Within the new Baylor-TGen collaboration, the Women’s Cancer Study Group is building on initial successes, and already is poised to pursue new discoveries in precision medicine.

A unique in-depth Baylor-TGen clinical trial of 14 metastatic triple-negative breast cancer patients—the most cited paper in 2013 in the American Association for Cancer Research’s Molecular Cancer Therapeutics—showcased the creative power of the two institutes.

“I think it was a pioneering trial because we had the privilege of being able to completely characterize, molecularly, the metastatic triple-negative breast cancers,” said Joyce O’Shaughnessy, MD, cochair of breast cancer research at Baylor. “TGen thoroughly analyzed them at the DNA and RNA levels. It was fairly unique to do whole-genome and transcriptome sequencing back then.”

“It was used to evaluate this ‘genome-forward’ concept, where you start with the genome first and then you choose the therapy based on the patient’s genome,” said Dr. O’Shaughnessy, who also is codirector of the Baylor-TGen Women’s Cancer Study Group. “That study of just 14 metastatic triple-negative patients has led me in very important directions regarding the next steps I need to pursue in designing clinical trials. It showed that we clinicians should be working with people like the scientists at TGen who can give us novel insights into these cancers.”

Bodour Salhia, PhD, an assistant professor in TGen’s Integrated Cancer Genomics Division and the other coconvener of the Women’s Cancer Study Group, was a coauthor of the Baylor-TGen triple-negative breast cancer study. “Our interests are aligned, especially in the area of breast cancer metastasis, and specifically when it spreads to the brain. What we want to do as a collaboration is to expand that to cover other forms of metastasis from breast cancer: to liver, lung, and possibly bone,” Dr. Salhia said. “While Dr. O’Shaughnessy runs clinical trials, I can run correlative studies. We can really help each other.”

While most breast cancers are manageable, researchers cannot predict with certainty—even among the most treatable types of breast cancer—when the cancer might recur. And metastatic breast cancer remains the leading cause of breast cancer-related death, said Dr. Salhia. “Everybody has a risk of relapse. We don’t know who.”

Developing a Liquid Biopsy for Metastatic Breast Cancer

The ability to predict relapse could change, following the September 16, 2015, publication by Dr. Salhia in the journal Clinical Epigenetics, in which she described a new 21-gene test panel. Her study showed that metastatic breast cancer patients experienced significantly higher levels of methylation in certain genes than either healthy individuals or cancer-free survivors. Further, patients could be evaluated based on a simple blood test, a liquid biopsy.

“I have a circulating DNA methylation signature that might actually tell us whether a woman is at risk of relapse,” said Dr. Salhia. “What we’ve identified is a potential signature of metastasis in blood. We now want to validate that 21-gene signature to see if it would be predictive. The signature looks really strong.” Such a test would have profound implications for improving the future treatment of women with all types of breast cancer, a disease that impacts 1 in 8 American women.

The goal is to predict metastases at the time of diagnosis and in a noninvasive way, Dr. Salhia said. It also could be a test that is taken following surgery or chemotherapy. Clinicians would be able to tell if any residual micrometastases are detectable in the blood. Such a test will either spare women unnecessary therapies or indicate additional therapies for prevention. Since metastasis prevention therapies are not available, we would be able to develop these new strategies as part of this program.

“We want to predict. We want to prevent. And we want to develop curative therapies,” she said. “We really need to change the course of metastatic breast cancer. I believe we can make a difference—even for one patient at a time.”

Developing New Treatments for Patients

Drs. O’Shaughnessy, Salhia, and Spillman all foresee exciting possibilities for new treatments springing from the Baylor-TGen collaboration. “Breast cancer metastasizes to the brain or liver, regardless of subtype. We are pretty desperate for treatments,” Dr. O’Shaughnessy said. “We need to know what it is that makes breast cancer spread to those two sites. What are the key driving cellular pathways? What’s driving those cancers, and how can we better treat the patients?”

She is hopeful about Dr. Salhia’s new test panel. “We don’t have any good way of understanding, right now, who needs ongoing therapy because they are at risk for breast cancer recurrence for the rest of their life, and who may be having a very early recurrence.” Imaging studies simply don’t pick up the cancers early enough, she said. There is a need for better methods of early detection. By the time a tumor is big enough to confirm with a scan, at least a half centimeter in size, there are already 500 million cancer cells.

With the Baylor-TGen collaboration, Dr. O’Shaughnessy said, “You’ve got the scientists educating the clinicians about what’s specifically going on in these cancers, so that the clinicians can design clinical trials. But you’ve also got the clinicians saying to the scientists: These are the problem cancers. This is why the treatments are not working. This is what’s happening when our treatments fail the patients.”

Dr. Salhia agreed: “My hope with this very symbiotic relationship is that the process from bench to bedside becomes so streamlined that we’re going to have many more clinical tools available and enough cumulative data where we will be able to go from patient to clinical trials quickly.”

Dr. Spillman said she believes the spirit of openness, the shared goals, and a common language fostered at both Baylor and TGen could help them become one of the top research collaborations in the nation. “I think this collaboration has the ability to do that. It’s the best of the clinical world and the best of the basic science and clinically related translational science world,” she said. “I think both are nimble enough to do it.”

References


Abdominal Malignancies Study Group Includes New Ways to Test Cancer Patients

Developing liquid biopsies to analyze cancer is a major focus of the Baylor-TGen collaboration.

One of the three main study groups in the Baylor-TGen collaboration covers abdominal malignancies, and a major focus of this group will be how to use emerging technologies to provide all cancer patients with better care.

Cancer patients are often now evaluated using biopsies, which essentially are minor surgeries. They can be invasive, costly, time-consuming, painful, and dangerous. Operating rooms must be booked, and surgeons must be scheduled. In the case of lung cancer, for example, patients run the risk of a collapsed lung. And the patient is usually given general anesthesia, which carries its own risks. In the end, the results are limited and may not provide the answers oncologists are looking for, since a biopsy extracts a sample of one small part of a tumor, at one place and at one point in time.

“The biopsy is limited to where the needle goes,” said Muhammed Murtaza, MD, PhD, codirector of TGen’s Center for Noninvasive Diagnostics and one of two coleaders of the Baylor-TGen Abdominal Malignancies Study Group. “We know that tumors within a person are heterogeneous. If a tumor has already spread outside the lung, then we already know that there is a very good chance, if the cancer has spread to the liver, that what you biopsy from the lung may no longer be representative of what is in the liver,” Dr. Murtaza said. “The cancer evolves. Even within the same tumor, different regions can have different genetic signatures.”

How much better patient care would be if there were a virtually instant test, derived from a simple blood sample, that could screen for all tumor types in a patient’s circulation—and be easy enough to administer that attending physicians could order an updated test every month, every week, and every day if needed.

“Rather than putting patients through these invasive biopsies, eventually the goal would be to develop these liquid biopsies,” said Ajay Goel, PhD, director of Baylor’s Center for Gastrointestinal Research, director of Baylor’s Center for Epigenetics, Cancer Prevention and Cancer Genomics, and the other coleader of the study group.

Time is critical. Now, when a cancer patient is treated with a new drug, oncologists might wait 6 to 8 weeks before they know whether the drug is working, said Carlos Becerra, MD, medical director of Baylor’s Innovative Clinical Trials Center and a co-principal investigator of the study group’s first clinical trial. “But if we develop new lab techniques where I can determine—within 24 hours—that Drug X is not working, we would not expose the patient to the potentially toxic effect of the drug, and there would be less time for the cancer to grow,” Dr. Becerra said.

First Project Seeks Liquid Biopsies for Pancreatic Cancer

Dr. Murtaza’s expertise in detecting circulating tumor DNA in blood is something new at Baylor. Dr. Goel’s work has mostly been in using RNA to create tests that screen patients for specific cancer biomarkers. “What we hope to come up with, it’s not going to be one or two markers, but a panel of markers—a combination of genomic endpoints, a mixture of DNA, proteins, RNA, microRNA, and DNA methylation markers,” Dr. Goel said. “All of this encompassed together to make a much more reliable, much more sensitive, much more specific test.”

The first project of this study group will be to develop sophisticated markers that could determine the response to different treatments in pancreatic cancer patients, he said. It will initially involve about 20 patients with pancreatic cancer who undergo surgery and/or chemotherapy. Their progress will be followed for as long as 2 years. Their blood will be periodically drawn in the process of developing biomarkers, including circulating tumor DNA markers, as well as RNA and DNA methylation markers, Dr. Goel said.

The study may eventually grow to more than 100 patients, include other gastrointestinal cancers, especially colon cancer, and build on early cancer detection efforts being developed at TGen. Eventually, the study group would build a biobank of blood and tissue samples, he said.

With patients’ consent, we will have access to any patient who walks into the clinic and is diagnosed with pancreatic cancer,” Dr. Goel said. “We will have access to their tissue, their blood, which will allow us to generate additional data, to further build upon this whole concept of early detection of cancers.”

A Powerful Contrast to the Way Things Are

Dr. Murtaza said the goal is to eventually come up with better ways to classify patients, so their treatments can be tailored to maximize efficacy and minimize side effects.

“It would be a powerful contrast to the way things are,” he said. “By the time a cancer becomes obvious, when it becomes symptomatic and a patient comes to the clinic, by that point the cancer is already a moving target. It makes little sense to guide treatment of a moving target using a test that is static in time and space, which is a biopsy.”

Dr. Becerra said the Baylor-TGen collaboration could lead to a model for the nation of cancer care collaboration. “It’s basically bringing people together so they can synergize and do the problem solving. It happens in industry, it happens in academia, and now it will happen at a private hospital in the community, where it can benefit patients immediately,” he said. “We’re working hard to develop screening programs and techniques to try to detect the cancer very early, way before it metastasizes, when it’s just beginning—to try to cure it.”

“We’re working hard to develop screening programs and techniques to try to detect the cancer very early, way before it metastasizes, when it’s just beginning—to try to cure it.”

Carlos Becerra, MD
<table>
<thead>
<tr>
<th>Site</th>
<th>Study ID</th>
<th>Location</th>
<th>Principal investigator</th>
<th>Title</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>13033</td>
<td>Texas Oncology – Dallas</td>
<td>Joyce A. O'Shaughnessy, MD</td>
<td>(USO 13033/ Millenium X14021) A Phase II, Multi-center, Randomized, Parallel Group Study to Compare Aisertib in Combination with Paclitaxel vs. Paclitaxel Alone in Patients with Metastatic or Locally Recurrent Breast Cancer</td>
</tr>
<tr>
<td></td>
<td>14052</td>
<td>Texas Oncology – Dallas</td>
<td>Joyce A. O'Shaughnessy, MD</td>
<td>A Phase 2, Open-Label, Single-Arm, Multi-center Study to Evaluate the Efficacy and Safety of Eribulin Mesylate Administered Biweekly (Q2W) for Subjects with Human Epidermal Growth Factor Receptor 2 (HER2)-Negative Metastatic Breast Cancer (E7389-M001-216)</td>
</tr>
<tr>
<td></td>
<td>15072</td>
<td>Texas Oncology – Dallas</td>
<td>Joyce A. O'Shaughnessy, MD</td>
<td>A Phase II Clinical Trial of Pembrolizumab (MK-3475) as Monotherapy for Metastatic Triple-Negative Breast Cancer (mTNBC) - (KEYNOTE-086)</td>
</tr>
<tr>
<td>Carcinoid</td>
<td>014-277</td>
<td>Baylor Dallas</td>
<td>Andrew David, McCollum, MD</td>
<td>Prospective Randomized Phase II Trial of Pazopanib (NSC # 737754, IND 75648) vs Placebo in Patients with Progressive Carcinoid Tumors</td>
</tr>
<tr>
<td></td>
<td>14124</td>
<td>Texas Oncology – Dallas</td>
<td>C. Lance Cowey, MD</td>
<td>Expanded Access Program With Nivolumab for Subjects With Histologically Confirmed Stage III (Unresectable) or Stage IV Melanoma Progressing Post Prior Systemic Treatment Containing an Anti-CTLA-4 Monoclonal Antibody (CA209168)</td>
</tr>
<tr>
<td>GU</td>
<td>14182</td>
<td>Texas Oncology – Dallas</td>
<td>Thomas E. Hutson, DO</td>
<td>(42756493BLC2001) A Phase 2, Two-arm Multi-center, Open-Label Study to Determine the Efficacy and the Safety of Two Different Dose Regimens of a pan-FGFR Tyrosine Kinase Inhibitor JNJ-42756493 in Subjects with Metastatic or Surgically Unresectable Urothelial Cancer with FGFR Genomic Alterations (IND #117490)</td>
</tr>
<tr>
<td></td>
<td>15006</td>
<td>Texas Oncology – Dallas</td>
<td>Thomas E. Hutson, DO</td>
<td>WC029637: A Phase III, Open-Label, Randomized Study of MPDL3280A (Anti–PD-L1 Antibody) in Combination with Bevacizumab vs Sorafenib in Patients with Untreated Advanced Renal Cell Carcinoma</td>
</tr>
<tr>
<td></td>
<td>14210</td>
<td>Texas Oncology – Dallas</td>
<td>Eric S. Nadler, MD</td>
<td>D4193C00002: A Phase III Randomized, Open-Label, Multi-Center, Global Study of MEDI4736 Monotherapy and MEDI4736 in Combination with Tremelimumab Versus Standard of Care Therapy in Patients with Recurrent or Metastatic Squamous Cell Carcinoma of the Head and Neck (SCCHN)</td>
</tr>
<tr>
<td></td>
<td>15024</td>
<td>Texas Oncology – Dallas</td>
<td>Eric S. Nadler, MD</td>
<td>A Phase 2 Proof-of-Concept Study of the Combination of ACP-196 and Pembrolizumab in Subjects with Advanced Head and Neck Squamous Cell Carcinoma - Acerta ACE-ST-006</td>
</tr>
<tr>
<td>Heme</td>
<td>14184</td>
<td>Texas Oncology – Dallas</td>
<td>Joseph W. Fay, MD</td>
<td>ACE-LY-005: A Phase 1b/2 Proof-of-Concept Study of the Combination of ACP-196 and Pembrolizumab in Subjects with B-cell Malignancies</td>
</tr>
<tr>
<td></td>
<td>14111</td>
<td>Texas Oncology – Dallas</td>
<td>Moshe Y. Levy, MD</td>
<td>A Randomized Controlled Phase 3 Study of Oral Pacritinib versus Best Available Therapy in Patients with Thromboocytopenia and Primary Myelofibrosis, Post-Polychtemia Vera Myelofibrosis, or Post-Essential Thrombocythemia Myelofibrosis (PAC326)</td>
</tr>
<tr>
<td></td>
<td>014-258</td>
<td>Baylor Dallas</td>
<td>Moshe Y. Levy, MD</td>
<td>A Phase 1b dose-escalation study of SGN-CD33A in combination with standard-of-care for patients diagnosed with acute myeloid leukemia (AML)</td>
</tr>
<tr>
<td></td>
<td>014-188</td>
<td>Baylor Dallas</td>
<td>Moshe Y. Levy, MD</td>
<td>A Phase 1 Study of Iplimumab in relapsed and refractory high risk myelodysplastic syndrome and acute myeloid leukemia with minimal residual disease</td>
</tr>
<tr>
<td></td>
<td>014-182</td>
<td>Baylor Dallas</td>
<td>Brian Berryman, MD</td>
<td>A Phase 3, Randomized, Placebo-Controlled, Double-Blind Study of Oral Ixazomib Citrate (MLN9708) Maintenance Therapy in Patients With Multiple Myeloma Following Autologous Stem Cell Transplant</td>
</tr>
<tr>
<td></td>
<td>014-267</td>
<td>Baylor Dallas</td>
<td>Estill A. Vance, MD</td>
<td>A Prospective Observational Study for the Long-term Follow-up of Subjects Previously Enrolled in Selected Clinical Studies of CMX001 (“The Chimera CMX001 Registry”)</td>
</tr>
<tr>
<td></td>
<td>15024</td>
<td>Texas Oncology – Dallas</td>
<td>Eric S. Nadler, MD</td>
<td>A Phase 2 Proof-of-Concept Study of the Combination of ACP-196 and Pembrolizumab in Subjects with Advanced Head and Neck Squamous Cell Carcinoma - Acerta ACE-ST-006</td>
</tr>
<tr>
<td></td>
<td>015-037</td>
<td>Baylor Dallas</td>
<td>Joseph W. Fay, MD</td>
<td>Phase I Study of MPDL3280A (ANTI-PD-L1) in Multiple Myeloma Patient Populations: Relapsed, Post-Autologous Stem Cell Transplantatation</td>
</tr>
<tr>
<td>Site</td>
<td>Study ID</td>
<td>Location</td>
<td>Principal investigator</td>
<td>Title</td>
</tr>
<tr>
<td>-------------</td>
<td>----------</td>
<td>-------------------</td>
<td>------------------------</td>
<td>----------------------------------------------------------------------</td>
</tr>
<tr>
<td>015-016</td>
<td>Baylor   Dallas</td>
<td>Moshe Y. Levy, MD</td>
<td>A phase 1 trial of SGN-CD33A in patients with CD33-positive acute myeloid leukemia</td>
<td></td>
</tr>
<tr>
<td>015-116</td>
<td>Baylor   Dallas</td>
<td>Houston Holmes, MD</td>
<td>A Two-arm, Phase Ib/II Study of Investigational Product Administered in Combination with Rituximab or Obinutuzumab in Subjects with Previously Untreated CD20+ Follicular Lymphoma</td>
<td></td>
</tr>
<tr>
<td>T0-1414</td>
<td>Texas Oncology – Dallas</td>
<td>Carlos H. Roberto Becerra, MD</td>
<td>MRX34-101: A Multicenter Phase I Study of MRX34, MicroRNA miR-RX34 Liposomal Inclusion</td>
<td></td>
</tr>
<tr>
<td>12028</td>
<td>Texas Oncology – Dallas</td>
<td>Carlos H. Roberto Becerra, MD</td>
<td>A 3-Arm Phase 2 Double-Blind Randomized Study of Carboplatin, Pemetrexed Plus Placebo versus Carboplatin, Pemetrexed plus 1 or 2 Truncated Courses of Dexamethasone in Subjects with Non-Squamous Non-Small Cell Lung Cancer (M18-007/DENALI)</td>
<td></td>
</tr>
<tr>
<td>13185</td>
<td>Texas Oncology – Dallas</td>
<td>Kartik Konduri, MD</td>
<td>59RS-003: A Phase 1b/II Study of OMP-59RS in Combination with Etoposide and Platinum Therapy in Subjects with Untreated Extensive Stage Small Cell Lung Cancer</td>
<td></td>
</tr>
<tr>
<td>14106</td>
<td>Texas Oncology – Dallas</td>
<td>Kartik Konduri, MD</td>
<td>A Phase III, Randomised, Double-blind, Placebo-controlled, Multi-centre, International Study of MED4736 as Sequential Therapy in Patients with Locally Advanced, Unresectable Non-Small Cell Lung Cancer (Stage III) Who Have Not Progressed Following Definitive, Platinum-based, Concurrent Chemoradiation Therapy (PACIFIC) AstraZeneca - D4191C00001</td>
<td></td>
</tr>
<tr>
<td>T0-1434</td>
<td>Texas Oncology – Dallas</td>
<td>Kartik Konduri, MD</td>
<td>A Randomized Open-Label Phase III Trial of Pembrolizumab versus Platinum based Chemotherapy in LS Subjects with PD-L1 Strong Metastatic Non-Small Cell Lung Cancer</td>
<td></td>
</tr>
<tr>
<td>014-111</td>
<td>Baylor   Dallas</td>
<td>Karen Fink, MD, PhD</td>
<td>A Phase Ib, Randomized, Multi-Center, Open-Label Study of a Conditionally Replicating Adenovirus (DNX-2401) and Interferon Gamma (IFN-y) for Recurrent Glioblastoma or Gliosarcoma</td>
<td></td>
</tr>
<tr>
<td>014-155</td>
<td>Baylor   Dallas</td>
<td>Karen Fink, MD, PhD</td>
<td>Immunological targeting of CD-133 in recurrent glioblastoma: A multi-center Phase I translational and clinical study of a autologous CD-133 DC vaccine</td>
<td></td>
</tr>
<tr>
<td>015-119</td>
<td>Baylor   Dallas</td>
<td>Carlos H. Roberto Becerra, MD</td>
<td>A Phase I, Safety Trial of Dendritic Cell Vaccine and Chemotherapy for Patients with Pancreatic Cancer</td>
<td></td>
</tr>
</tbody>
</table>

### Online Access to Clinical Trials

Physicians and patients can now access information about open clinical trials in oncology at Baylor Sammons Cancer Center with these steps:

- Go to BaylorHealth.edu/Sammons.
- Click on "Research" on the left-hand menu, then click on "Clinical Trials" in the drop-down menu.
- Select a condition (e.g., "Cancer") and then select a specific disease (e.g., "Breast Cancer").

For additional details or questions about the studies, please contact the Office of Clinical Oncology Research Coordination at 214.818.8472 or 817.698.8472, or via e-mail at cancer.trials@baylorhealth.edu.
Recent Publications from Baylor Sammons Cancer Center at Dallas

February 16, 2016 to September 28, 2015


30. Guileyardo J, Bertucci F, Carney P. Expression of FANG Immunotherapy in Ewing’s Sarcoma of the Inferior Vena Cava. Proc (Bayl Un...


Welcome to new Members of the Medical Staff at Baylor Charles A. Sammons Cancer Center at Dallas

Jana M. Reynolds, MD  Internal Medicine/Medical Oncology  Baylor University Medical Center

Gary Schwartz, MD  Surgery/Surgical Oncology  Baylor University Medical Center