



Local Immunotherapy

By James Strauss, M.D.,
 Clinical Research Director

A persistent challenge in the treatment of cancer is how to fully activate the immune system to engage and destroy a tumor. Although research has been ongoing for decades, recently there have been findings and accomplishments that are the basis for studies now open in the Clinic.

The development of antibodies that can reverse certain immune suppression signals has provided new impetus for vaccine studies. These antibodies, called checkpoint inhibitors, block certain signals that can be displayed by cancer cells to inhibit lymphocytes in the immune system. Several drugs in this class have now been approved and are part of standard care for certain types of cancer.

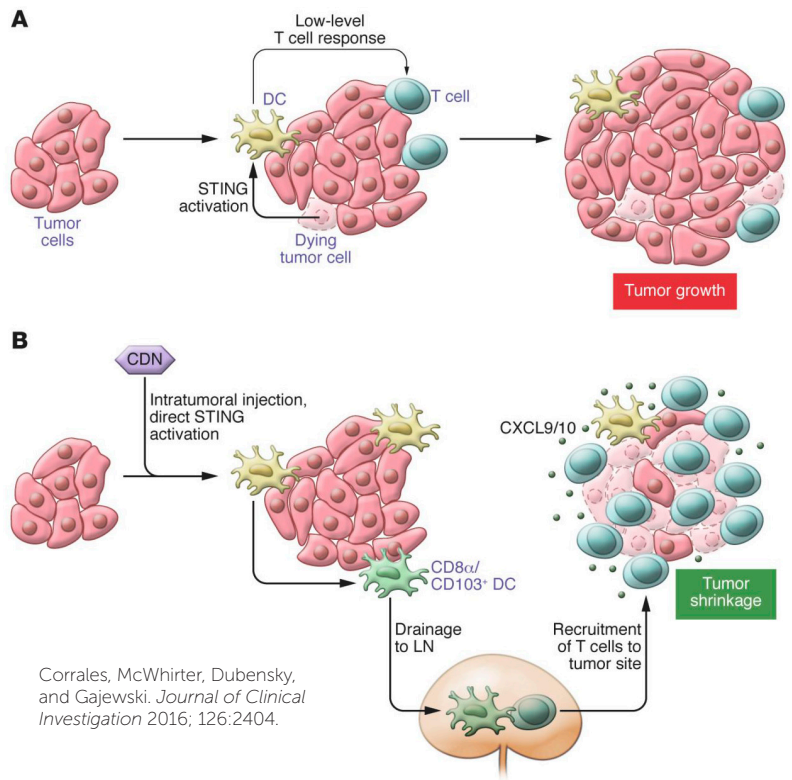
There are several ideas that are directed at the problem of extending the benefit of checkpoint inhibitor antibodies to more kinds of cancer. One approach is to start with what has been called "local immunotherapy" to initiate an immune response. **Local immunotherapy uses an injection into a tumor with a drug to stimulate the immune cells.** Cells in the immune system have receptors to detect certain substances. One of these receptors, called TLR9, can be stimulated by a fragment of DNA. SD101, a drug constructed from DNA components, is used in study #15-31 to stimulate TLR9. Injection of SD101 into the melanoma is followed by treatment with intravenous checkpoint inhibitor antibody.

Another receptor system in lymphocytes is called STING (for STimulator of Interferon Genes). In study #16-39, MK1454 is injected into a tumor to activate the STING pathway. The treatment is combined with intravenous checkpoint inhibitor antibody.

The third study of local immunotherapy has a different approach. Study #17-04 uses direct injection into a tumor of a genetically engineered virus. The virus has been modified to take advantage of the difficulty tumor cells may

have compared with normal cells stopping the multiplication of viruses. The viral infection should be controlled readily by normal cells. The proliferation of viruses in the tumor should start a strong immune reaction that could potentially attack tumor cells throughout the body.

All three studies are using injection into a tumor as a way to initiate the immune response. **In a sense this is an attempt to vaccinate by using the tumor itself as the vaccination site.** Lab studies in recent years have revealed more details regarding the steps in activation of the immune response. These insights are now being tested in real world treatment studies at Mary Crowley Cancer Research.



FIVE QUESTIONS

with **Donna German,**
Mary Crowley COO



Where did you grow up?

I grew up in Kansas in a very rural environment. I learned how to drive when I was 12 because I got to drive the tractor on the farm.

How did you first hear about Mary Crowley? After years in the corporate world, what inspired you to pivot to cancer research?

A friend invited me to attend an event for the Mary Crowley Women's Auxiliary a decade ago. My career was 35 years in corporate America, as a banker for 20 years and then 15 years as Treasurer and

Chief Risk Officer. You get to a point in your life when you want to spend your time on something that is personally significant to you. Cancer is a big part of my family's story. I had an early-stage breast cancer experience about 7 years ago; my dad passed from multiple myeloma in 2009; and my mother at age 93 is a 40+ year breast cancer survivor. So the message of Mary Crowley has always resonated with me.

How is Mary Crowley is different from other cancer research organizations?

Mary Crowley is a gem in Dallas that isn't as well-known as it should be. Several large institutions do some form of cancer research, but it's really hard for the average patient to understand the difference. Mary Crowley offers specialized expertise in late stage cancer and implementing first-in-human therapies through clinical research trials.

The differentiator is the specialized expertise it takes to focus on the Phase I & II arena. For example, we have an onsite pharmacy. A patient's vaccine is customized based on that particular patient's genetics versus "one size fits all" standard therapy given to every patient.

What is personalized medicine, and how does Mary Crowley give HOPE to cancer patients?

Personalized medicine is widely recognized as the wave of the future in cancer research. It examines a patient's own genetic makeup, identifies the abnormal genetic sequence, and devises a strategy to target and interrupt the cells allowing cancer growth.

Most of our patients have few standard care options; a clinical trial option gives them HOPE for a new therapy that wouldn't otherwise be available. There's great HOPE in extending time with your loved ones and your quality of life. Also it's very powerful to be part of the process of advancing cancer research for people in the future.

Finally, in some cases we can offer research therapies to patients earlier in the process, alongside traditional standard therapies... Those are the conversations that get me most excited!

What do you enjoy doing in your free time?

I love travel -- I've been to every state in the US except Maine. I like creative endeavors: photography, painting, and writing children's poetry. I was an undergraduate English major, so I read a lot. I love any book that, long after you've closed the back cover, resonates with you and causes you to think about life differently.

New Volunteer Program at Mary Crowley Cancer Research



Mary Crowley Cancer Research is seeking volunteers to assist with patient relations and other clinic duties.

- Must be 18 years or older
- Candidates may be cancer survivors or family members, students in need of patient-related volunteer hours, retired individuals or community volunteers interested in helping cancer patients
- Must be able to commit four hours per month for a preferred six month minimum
- Must complete wellness test, background screening and orientation

Join us in Building HOPE though Volunteering!

For more information on volunteering, contact Phyllis Yount at pyount@marycrowley.org

Staff Spotlight: Britney Nuckolls, Oncology Research Liaison

Mary Crowley Cancer Research offers an extensive number of solid tumor clinical trials involving the latest technologies in gene, targeted and immune therapies. Many trials include combination therapy with approved standard of care drugs, like Nivolumab.

How do oncologists learn about clinical trials for their cancer patients?

Although it is very easy for patients to refer themselves for an appointment at Mary Crowley Cancer Research, many patients are referred by their primary oncologists. To make sure referring physicians are fully informed about Mary Crowley's innovative clinical trials, Britney Nuckolls, Oncology Research Liaison, works to collaborate with and educate physicians about the new and exciting clinical trials conducted at Mary Crowley. Britney provides updated information to oncologists so they, in turn, can provide the best treatment options for their patients.

After working several years in the private medical sector, Britney transitioned her career towards research in 2015, as she loves learning about the advanced technologies used to treat cancer patients. Originally from Orlando, Florida, Britney earned her Bachelor of Science degree from the University of Central Florida. In her spare time, she enjoys traveling to new countries, mountain biking, and spending time with her husband and puppy.



To refer a patient or receive information about innovative clinical trials, contact Britney Nuckolls at bnuckolls@marycrowley.org



Pushing HOPE in Oklahoma!

Mary Crowley Community Partner Big Hope 1 made a stop in Catoosa, OK, on January 9, where the barge's signature bright pink paint made a big impact. Mary Crowley COO Donna German, Ceres Barge Officer Mark Fletcher, and others spoke before a crowd of supporters and local press, spreading awareness about Mary Crowley's innovative clinical trials for cancer patients and remembering friends and loved ones in the barge industry who lost their fight against cancer. Mary Crowley is grateful to Big Hope 1 for their support over the years. Keep an eye out for news about their annual Pushing Hope golf tournament coming up in August!



Pictured: Donna German, COO at Mary Crowley Cancer Research; family members of people in the barge industry who have passed away from cancer; Mark Fletcher and Vince Schu of Ceres Barge Line, and Mike Eckart from Sherwin Williams, which donated the paint for the pink barge!



Wheel to Survive 2018

Mary Crowley Wheelers for HOPE pedaled in support of ovarian cancer patients at Wheel to Survive Dallas 2018. This inspirational fundraiser hosted by Be the Difference Foundation promotes awareness of ovarian cancer symptoms, funds programs for women battling the disease and provides research funds for a cure. This marks the third year that Mary Crowley physicians and staff have enthusiastically committed to raising funds and riding in the event.

Recently, Be the Difference Foundation presented Mary Crowley with a generous gift of \$80,500 for ovarian cancer clinical trials. Mary Crowley is grateful for our partnership to "be the difference" in the fight against ovarian cancer.

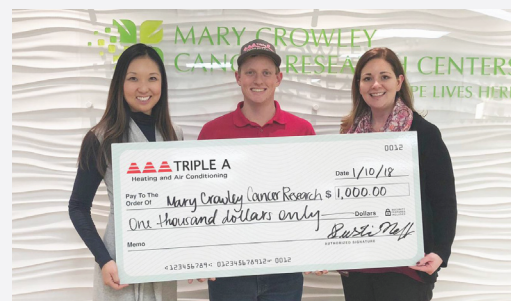
Pictured: Minal Barve, MD; Donna German; Alli Deluca; Jenna Armour; James Strauss, MD

On Air with All Things EPIC

Mary Crowley Cancer Research participated in the All Things EPIC radio show on February 16. COO Donna German, Development Coordinator Eunice Kuo, and VP of Clinical Operations Jeanne Jones chatted with former Cowboys player Tyler Clutts, Sean Heatley, and Kristen Untch about the history of Mary Crowley, what we do for cancer patients, and where the future of cancer medicine is headed. Watch online on the Mary Crowley Facebook page or listen on the All Things EPIC Soundcloud website!



Pictured: Donna German, Eunice Kuo, Tyler Clutts, Sean Heatley, Kristen Untch, Jeanne Jones



Pictured: Eunice Kuo, Dustin Neff, Jennifer Sala

Thank You Triple A Air Conditioning

Our wonderful friends at Triple A Air Conditioning Flower Mound presented Mary Crowley with a \$1,000 donation from their October campaign, "Tune Up for Tatas," to raise awareness in the fight against breast cancer. Thank you to Triple A for their generous donation and to Mary Crowley VP of Compliance Jennifer Sala for making the connection!

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Patient Story: Osvaldo DeLima

Osvaldo DeLima, his wife Silvana and their two daughters relocated to the United States from Brazil in 2003. Mr. DeLima's job required travel that was easier to manage from North Texas, and the family quickly learned to love their new home.

Osvaldo had always enjoyed excellent health and was disciplined with diet and exercise. In March 2016, he experienced abdominal pain that he thought was a pulled muscle. The physician diagnosed him with pancreatitis, which the family refers to as "blessed pancreatitis" because it led to an earlier detection of pancreatic cancer. Doctors removed a 4.5 cm tumor, and Osvaldo underwent chemotherapy and radiation from April until December 2016.

In July 2017, scans revealed that the cancer had spread to his lungs. **Acknowledging there were very few options for patients with Stage IV pancreatic cancer, his oncologist recommended two options: another chemotherapy that might give him 4-5 more months of life -- or a clinical trial.** Osvaldo and Silvana contacted several major cancer research centers including one close to home – Mary Crowley Cancer Research.

Osvaldo realized he had little to lose by trying a therapy that might prolong his life. In August 2017 he enrolled on a combination clinical trial. Osvaldo said "At Mary Crowley I felt HOPE... The staff is so

friendly and pleasant, and we always feel welcome." After the first cycle, scans showed that Osvaldo's cancer was stable. After the second cycle, the tumors had shrunk by 6%. After the third cycle, scans revealed a 23% reduction – a remarkable response for advanced pancreatic cancer. **Currently he is participating on a phase II study of combined targeted therapy plus gemcitabine and nab-paclitaxel.** The DeLimas are grateful for the progress, and they find it rewarding to know that data from his trial will help future patients.

Silvana asserts that Osvaldo's positive attitude has been a tremendous asset to his cancer journey. Osvaldo says, "It's important to look at cancer in a holistic fashion... physicians, the right treatment plan, good nutrition and exercise, faith and family support and an understanding employer are important to your success... I believe that things happen for a reason. It helps to believe in a higher power who is guiding you toward a good purpose." Osvaldo continues to work, and he enjoys spending time with his family and friends. Both Osvaldo and Silvana agree "Esperanca mora aqui. Hope lives here."

