



Transforming Cancer Care in Our Lifetime

Mary Crowley Cancer Research is pleased to announce the appointment of Ashley E. Ross, MD, PhD, as Executive Medical Director. He comes to Dallas from Johns Hopkins Medical Institute where he was Associate Professor in the Departments of Urology and Oncology at Johns Hopkins School of Medicine, Director of Johns Hopkins Urology Prostate Cancer Program and Chief Medical Advisor at Genome Dx Biosciences. While at Hopkins, he also earned his Doctorate in Biochemistry and Molecular Biology. Dr. Ross has received numerous awards and authored over 130 peer-reviewed publications. He characterized Mary Crowley as being one of the best-positioned centers in the country to capitalize on personalized or precision medicine for cancer patients.

On June 11, 2018, friends and supporters gathered to meet Dr. Ross and hear his vision. Here is an excerpt from his remarks:

"We are at a transformational time in medical oncology. We have an increased availability and understanding of molecular biology, genetics and genomics that drive disease, and we have an increased ability to harness the immune system and utilize it. That has led to logarithmic increase in the number of novel investigational therapies we have for our patients. In fact, therapies that were approved just a few years ago are now becoming first line for metastatic cancer.

The direction now is to utilize the tools of molecular biology and immune-oncology to rapidly advance discovery and impact the care of cancer patients within their lifetime. I believe Mary Crowley may be one of the best-positioned centers in the country to lead this initiative. Why do I think that?

- Mary Crowley is **singularly focused** – we perform clinical trials in humans to help determine how to accelerate this discovery forward to the mass population.
- Mary Crowley is a **well-established center** – we are very adept at running clinical trials, and running many trials at the same time.
- Mary Crowley emphasizes a **partnership with the patient's primary oncologist**

Though there is a strong foundation, to reach its full potential, Mary Crowley will need to focus on three areas:

Awareness: Mary Crowley is a gem – a huge resource for DFW! The breadth of investigational molecular therapies that we offer patients has widely expanded and will continue to expand. We want to raise awareness among medical oncologists and within our patient community.

Accessibility: We want to ensure that access to Mary Crowley is seamless for the patient and their provider and focus on bringing in more patients earlier in their treatment course so that we can help them understand their tumor uniqueness and all of their potential options.

Advancing Scientific Discovery: Mary Crowley needs to continue being proactive in defining the direction of medical science. We need to rapidly capture molecular data and help determine the potential predictors of response. We also need to expand our network of clinical advisors to ensure that we bring in the best trials – the ones our communities really need.

Mary Crowley Cancer Research is an inspiring and exciting place, and I am humbled to be part of pursuing and developing new therapies for our patients."

Earlier and Expanded Use of Checkpoint Inhibitors to Treat Malignancies

by Ashley E. Ross, M.D., PhD
Executive Medical Director

In a process called "immune surveillance", the immune system attacks and eliminates cancer cells. To overcome immune surveillance, cancers create immune-suppressive environment, learn to hide unique epitopes, and upregulate checkpoint pathways such as the PD-1/PD-L1 pathway. Drugs inhibiting checkpoints boost immune surveillance and allow for long-lasting, adaptable anti-cancer responses.

Checkpoint inhibitors have revitalized and repositioned the role of immune-based cancer therapy. Mary Crowley Cancer Research has played an active role in developing these therapies, completing 6 trials with these agents of which 3 have become FDA approved and available for patients worldwide. Many questions remain ...**What predicts response? When should therapy be given? Can immunotherapy be combined with chemotherapy?** Recent clinical research sheds light on these issues.

The mutagenicity of tumors can create new tumor antigens that can be recognized as non-self. Tumors highly prone to mutation (those with mismatch repair (MMR) deficiencies or microsatellite instability (MSI)) respond well to immunotherapy regardless to tumor type. MSI-high and MMR deficient tumors comprise a small subset of metastatic tumors and some MSI-low tumors can still carry a high tumor mutational burden (TMB). The wide availability of tumor DNA sequencing provides an assessment of TMB. A recent clinical trial in non-small cell lung cancer found that patients with higher TMB (at least 10 mutations per megabase, comprising >40% of these patients) had an exaggerated response to first line immunotherapy.

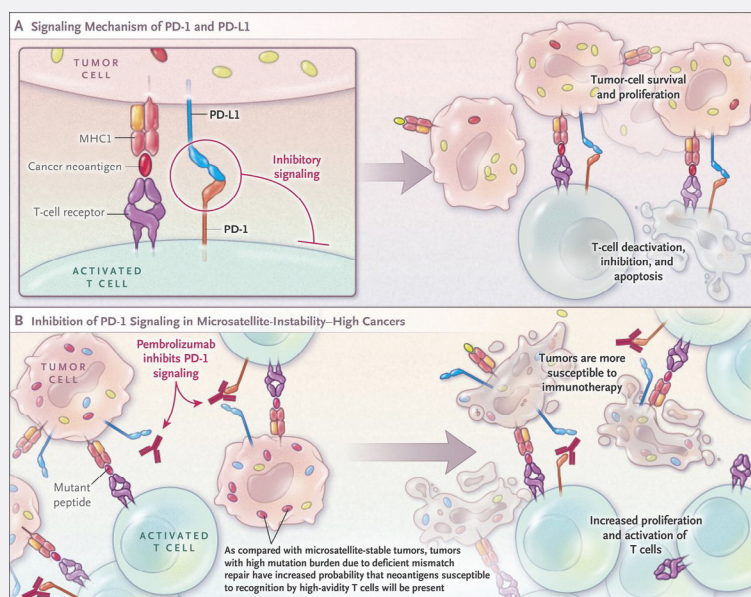
Studies also indicate that moving immunotherapy earlier in treatment is beneficial. In one study of resectable lung cancer, neo-adjuvant (before surgery) exposure to PD-1 inhibition elicited dramatic pathological responses in roughly half of the patients and allowed for the formation of memory T cells. In another larger study of locally advanced melanoma, adjuvant (after

surgery) checkpoint blockade significantly delayed the time to tumor progression.

An important consideration is whether immunotherapy added to chemotherapy (which may hinder the immune system) can be effective. In a large trial, PD-1 checkpoint inhibition combined with chemotherapy in non small cell lung cancer was superior to chemotherapy alone, almost doubling patient survival.

Manipulating the immune system is key to cancer therapy. Earlier exposure to immunotherapy is beneficial and understanding a patient's tumor genetics is critical.

Combination therapies are feasible, efficacious, and may render tumors that currently are not thought to be immunogenic, responsive to therapy. To help determine which immunotherapies and combinations may be most promising, Mary Crowley is currently conducting approximately 20 separate trials using immune targeted agents, two-thirds of which combine novel agents with checkpoint blockade.



Leмеры, Keegan, and Pazdur. *New England Journal of Medicine* 2017; 377:15.

Drug-Drug Interaction Studies for Oral Medications

by Robert Nunan, MS, PharmD, BCOP
Investigational Drug Repository Manager



One of the important steps in the development of oral investigational agents is the completion of a Drug-Drug Interaction (DDI) study. DDI studies are another expertise offered at Mary Crowley Cancer Research. The location of our pharmacy directly adjacent to the patient area proves particularly advantageous during these types of studies.

DDI studies are necessary to obtain information on **what the investigational agent does to the patient** when administered as well as **what the body does to the agent**. These end points are commonly referred to as **pharmacokinetics (PK)** and **pharmacodynamics (PD)**.

PK studies deal with how the agent is absorbed, distributed, metabolized and excreted from the body versus PD studies which deal with the mechanism of the agent.

Usually the drugs tested against the study agent either induce (e.g. speed up the liver's metabolism) or inhibit (stop) drugs from being metabolized. The majority of drugs are eliminated by the liver. Within the liver are many different pathways (called the cytochrome P-450 system) by which drugs are broken down and eliminated. Sponsors perform these DDI studies to see how their drug potentially interacts with medications and food once it is approved for commercial use. Foods that can affect the liver include grapefruit and grapefruit juice, Seville oranges, star fruit, and caffeine (e.g. coffee, soft drinks, etc.), as well as over-the-counter medication and herbal products. All of these can either induce or inhibit the enzymes with the liver and affect how much drug is actual available within the body.

This information becomes part of the packet insert, which helps physicians know how to prescribe these new oral drugs as well as to how to manage the use of them with other oral medications the patients may be taking.

Thank You, Marlane Miller!

On Friday, May 11, 2018, staff members gathered to meet Marlane Miller, cancer survivor, author and longtime supporter of Mary Crowley Cancer Research. Ms. Miller first learned about the organization through her next door neighbor and friend Pat Brown, former COO of Mary Crowley.

Ms. Miller toured the Clinic and shared remarks with staff members. "When I recently received funds from the sale of family property, the first thing of thought of was you... You are the healers. You are the people who make dreams come true... You are the leading edge of science and care, and I salute you with this small donation. I honor the hours, the care, the love you put into your work... You change lives, heal families and touch hearts." Staff members were visibly moved by her kind words.

Ms. Miller then presented a generous gift of \$150,000 to support innovative clinical trials.



Pictured: Deborah Montonen, VP and Chief Development Officer; Pat Brown, former COO; Marlane Miller; Dr. James Strauss, Clinical Research Director and Physician Investigator; Donna German; Robert Nunan, Investigational Drug Repository Manager

Marquis Energy Grant: \$10K

Mary Crowley Cancer Research salutes Marquis Energy and the family of Stephanie & Jason Marquis of Hennepin, IL, for their generous support of Big HOPE 1, the big pink barge. Marquis Energy produces high-octane ethanol, animal feed and corn oil, and Big HOPE 1 transports their products. Recently the big pink barge docked with Marquis Energy's fleet.



Pictured: Marquis Energy Chief Operations Officer Jason Marquis, wife Stephanie, their two children and Marquis Energy employees in front of Big Hope 1, the pink barge that raises awareness and funds for cancer research.

The company donated \$10,000 to Mary Crowley Cancer Research, said Danielle Anderson, Director of Public Relations and Political Affairs for Marquis Energy. "This is an especially important time for us having this barge, as cancer touches many of our families' lives, but especially our Chief Operations Officer, Jason Marquis, whose daughter is beating leukemia." Marquis' daughter is 3 years old and cancer-free right now, Anderson confirmed.

Inspired by numerous employees and families impacted by cancer, Ceres Barge Line of East Saint Louis, MO, launched Big HOPE 1 in 2012, promising to contribute a percentage of the net earnings from the barge to fund cancer research. The barge and related fundraising efforts hosted by Ceres and others have generated more than \$861,000 for innovative clinical trials at Mary Crowley Cancer Research.

Laps for Lung Cancer

On Saturday, May 19th, Mary Crowley team members participated in and sponsored a booth at the Bonnie J. Addario Lung Cancer Foundation Dallas 2018 "Your Next Step is the Cure" 5K Fun Run at the Continental Bridge in Trinity Groves. Each step takes you closer to the cure!



Pictured: Mark Bushong, Volunteer; Deborah Montonen, VP and Chief Development Officer; Britney Nuckolls, Oncology Research Liaison and Jenna Armour, Digital Marketing Manager.

Introducing Deborah Montonen, CFRE Vice President and Chief Development Officer



Mary Crowley is delighted to welcome Deborah Montonen, CFRE, as Vice President and Chief Development Officer. Deborah is responsible for development, marketing, fundraising, and donor relations.

Deborah has spent almost four decades in the philanthropy arena, working for local and international nonprofit organizations and private foundations. She started her career in Dallas as executive director of The Philip R. Jonsson Foundation. Deborah has also worked for organizations such as the Dean Learning Center, Visiting Nurses Association in Washington, D.C., CARE International, The Irving School's Foundation, KERA, Klyde Warren Park and Junior Achievement of Dallas. Deborah has also been active with the Junior League of Dallas and London and the Association of Fundraising Professionals, where she has held numerous leadership positions over the years. Deborah was named Outstanding Fundraising Executive by the organization in 2011 for her dedication to fundraising and mentoring new philanthropy professionals, a passion that she continues today.

Deborah received a Bachelor of Science from Texas Tech University in Lubbock, TX and did graduate studies at Southern Methodist University in Dallas, TX.

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Mary Crowley depends on donors like you.
 Your gift directly impacts cancer patients in need
 of innovative clinical trials.

Give today at www.marycrowley.org



Patient Story: Denis Schwanke

It was on Friday the 13th of December 2013 that Denis Schwanke learned about his cancer. Prior to this date he had noticed blood in his urine, and a biopsy confirmed a diagnosis of bladder cancer. He underwent seven months of chemotherapy under the care of his community oncologist before having his bladder and prostate surgically removed in August 2014. He was later referred to Mary Crowley in 2015 with evidence of cancer spreading to his spleen and lymph nodes surrounding his lungs. Denis enrolled on a Phase I targeted immune therapy clinical trial for five months that resulted in a 61% decrease of his tumors! Three years later, in June 2018, he continues to have stable disease.

Denis always enjoyed his trade as a carpenter in Arizona before retiring and moving to Prosper, TX, to be near his brother and nephew. A man of few words but with a dry sense of humor, he enjoys sports, particularly watching his nephew play baseball. Perhaps the love of his life is Mimo, his Maltese poodle, in addition to the staff at Mary Crowley. He could not say enough nice things about the care he received at Mary Crowley, noting his appreciation for the outstanding staff. He continues to drop by Mary Crowley for hugs which are abundantly given!



4/6/18
 I want to thank you all
 for allowing me to take
 part in this study you
 were all very professional
 and very supportive to me
 Thanks to this study Dr.
 Steven Pentecost says my
 latest scans show no signs
 of cancer & I've been
 free of meds for 2 1/2 years.

God bless
 each of you!
 Denis Schwanke

We will beat cancer!