Ovarian cancer accounts for 3% of cancers among women, but it causes more deaths than any other cancer of the female reproductive system. Mary Crowley has been active in studying the genes responsible for familial ovarian cancer. Research is beginning to yield clues about how these genes normally work and how disrupting their action can lead to cancer. To maximize efforts, Mary Crowley has joined forces with community gynecologic oncologists to provide more options to women. Dr. Bruce Fine, Gynecologic Oncologist, feels new treatments are desperately needed since little progress has been made since the approval of Taxol-carboplatin in 1994.

Dr. Allen Munoz, Gynecologic Oncologist says “the unfortunate difficulty with ovarian cancer is catching it early because women experience very subtle changes, and when the symptoms do occur in women, it’s already in advanced stage. We do also know that ovarian cancer patients respond to chemotherapy. The unfortunate thing about ovarian cancer, though, is that in the advanced stage its recurrence rate is quite high.”

“We now have the opportunity with ovarian cancer to help sort out and identify relevant signals that are related to ovarian cancer growth and bring more and more of the targeted therapies into our program, and the technology to measure the relevant genes,” says immunotherapies,” says Dr. Nemunaitis. To view a recent ovarian cancer documentary, produced by Mary Crowley, use the following link: http://youtu.be/xvD9hdzpLm0. Listed below are three of the 11 ovarian clinical trials currently available at Mary Crowley:

**MC# 15-37:** Phase I trial evaluating BAX69 in refractory Ovarian Cancer patients with malignant ascites, requiring at least 2 paracentesis in a 30 day period. BAX69 is a fully humanized monoclonal antibody targeting anti-macrophage migration inhibitory factor (MIF). MIF acts as an upstream regulator of the inflammatory cascade; influencing adaptive and innate immunity. Scheduled to open March/April 2016.

**MC# 16-03:** Phase Ib trial evaluating DPX-Survivac in combination with Epacadostat in Ovarian, Fallopian and Peritoneal Cancer following the first relapse. DPX-Survivac is an immunotherapeutic vaccine that targets survivin, a member of the inhibitor of apoptosis protein family, to initiate apoptosis. Epacadostat is an inhibitor of the enzyme IDO1, which, when inhibited, prevents the catabolism of tryptophan and may restore antitumor cell-mediated immune responses. Scheduled to open April 2016.

**MC# 15-01:** Phase III trial evaluating Vigil™, in...
Dr. John Nemunaitis, Mary Crowley Executive Medical Director. "With next generation gene sequencing, investigators can identify the generating power of the cancer cell or the molecular signal. We are then able to match those power generators in the cancer, so to speak, with the therapy that can potentially destroy it - that patient with a particular signal defect can go onto the trial with that therapy, designed to destroy that signal defect. It involves both molecular and treatment naïve, stage III/IV Ovarian Cancer patients. The Vigil™ vaccine is an autologous tumor vaccine composed of irradiated tumor cells that have been Transfected with the Vigil™ plasmid, designed to suppress TGFß1 & TGFß2 proteins and simultaneously express rhGMCSF protein. Eligible patients for this trial will have been scheduled for a standard of care tumor debulking surgery, following diagnosis.

**UPDATES**

**MARY CROWLEY GENOMIC BIOINFORMATICS LECTURE SERIES**

Keeping abreast of evolving genomic knowledge is not only challenging but a necessity for cancer research clinicians. Clinical researchers must manage and navigate today’s patients through a genomic maze, analyzing how each investigational agent impacts cancer. To capitalize on this growing genomic-bioinformatic field, Mary Crowley has initiated a lecture series for the staff and community oncologists/surgeons. The first Lecture was conducted by Dr. Neil Senzer, Mary Crowley Scientific Director, on March 3rd entitled Target the Target. The presentation focused on the three types of driver genes:

1. Oncogenes that activate and allow the maintenance of cancer activity
2. Tumor Suppressor Genes that block cancer activity
3. Stability Genes that affect the cell's ability to repair damage and mutations that lead to cancer growth

Says Dr. Senzer, “An important gene in the cancer process is NEDD8. If we can break down cancer cells and knock out NEDD8, it will destabilize MDM2, which increases p53, which leads to programmed tumor death, or apoptosis. Using wild-type p53 to kill its own cancer is an extremely effective way to make progress against the spread of cancer mutations."

The next Go To Meeting lecture titled: Metabolome - Is It a Cancer Target? will be held on Thursday, April 14th, from 3:00 to 4:00 PM. For reservation information, please contact Tasha Bolden at 972-566-3000.

**DOCTORS FIND 'CRYSTAL BALL FOR CHILDHOOD CANCER' IN GENE STUDY**

RESEARCHERS HAVE ISOLATED GENES THAT COULD HELP PREDICT WHETHER CHILDREN WILL DEVELOP CANCER.

**ASK NEIL SENZER, MD**

Since his article Predicting Next Pivotal Cancer Advances appeared in our last newsletter, readers have responded with additional questions for Dr. Neil Senzer, Mary Crowley's Scientific Director.

**Q: Do gene signals within a growing cancer change in response to chemotherapy or a targeted therapy? How can that be managed?**

**A:** Yes, there are several types of changes that occur: First, spontaneous changes result from the normal process of cell division and redistribution of DNA, with occasional structural errors, between the two daughter cells. Second, changes result from the same cancer being in two different environments, such as when lung cancer spreads to the liver and is subject to different surrounding growth factors. Finally, not exactly changes, but small percentages of originally resistant tumor cells remain after the majority of sensitive tumor cells are destroyed by therapy. Researchers attempt to prevent #3 by using a combination chemo/targeted therapy, or combination chemo or targeted therapy with immunotherapy. When liquid biopsy becomes clinically available and more sensitive, repeated analyses will have the potential to identify resistant mutations leading to an early change in therapy.

**Q: Do you think the technology behind liquid biopsies will ultimately become sensitive or effective in identifying all cancer indications? If not, which indications do you envision would be most reliable?**

**A:** Eventually the combination of liquid biopsy detecting both circulating DNA and circulating tumor cells containing tumor DNA, RNA and protein will detect almost all tumor types.

If you have additional questions for Dr. Senzer, please send to pbrown@marycrowley.org.
In a paper published in the New England Journal of Medicine on November 18th, 2015, Dr. James Downing and his colleagues at St. Jude Children's Hospital report that there are a surprising number of genes that can predispose children to developing cancer, before they take their first breath. Such mutations in the cells they inherit from their mothers and fathers, called germ line mutations, can contribute to cancer even in families where there isn't a strong family history of tumors. About 8.5% of the people with childhood cancers showed germ line genetic mutations, or genetic changes that they inherited from their parents and put them at higher risk of getting tumors. Source: TIME.com

MEET PHYLLIS YOUNT, ONCOLOGY SOCIAL WORKER A veteran with over 30 years in the field, Phyllis Yount brings a wealth of experience to Mary Crowley's clinic staff. "I chose social work because of the opportunity to make a difference for patients and their families when they are at their most vulnerable," says Phyllis, who specializes in interfacing with newly-diagnosed patients. Her goal is to supplement Mary Crowley's services by focusing on patient education and support groups for patients as well as caregivers. "Mary Crowley is a place of HOPE for cancer patients.”

Originally from Houston, Phyllis and her husband Steve enjoy traveling in France and have served in Malawi, Africa on a short-term mission trip. Among her many hobbies, she enjoys cooking and gardening.

PHILANTHROPY

A MILLION THANKS! Allen W. Newberry, longtime supporter of Mary Crowley's genetic research, successfully nominated Mary Crowley to receive a $10,000 grant from the Million Dollar Round Table (MDRT) Foundation. This grant has been designated for the Innovative Clinical Trial Program that matches patients with the clinical trials that are specific to their individual molecular profiles.

Newberry is a 45-year member of MDRT, an international, independent association of nearly 36,000 of the world’s best life insurance and financial services professionals from over 80 countries. MDRT members demonstrate exceptional product knowledge, strict ethical conduct and outstanding client service. MDRT membership is recognized internationally as the standard of sales excellence in the life insurance and financial services business.

"WHEELERS FOR HOPE" SPIN SUCCESS!

Mary Crowley Wheelers for HOPE participated in Wheel to Survive Dallas, an indoor cycling fundraiser hosted by Be the Difference Foundation. Thirteen Mary Crowley staff members and friends raised $3,726 in the team's inaugural year. Be the Difference Foundation supports ovarian cancer research and programs for patients; in 2015, they gifted $150,000 toward Mary Crowley’s ovarian cancer targeted molecular therapy program. Pictured Above: Members of 'Mary Crowley Wheelers for HOPE.’
Since 1959, the MDRT Foundation, the philanthropic arm of the MDRT, has awarded more than $30 million in life-changing grants to charitable organizations worldwide.

Ellen Dearman, VP Development, said, "We are thankful for Allen's advocacy on behalf of Mary Crowley's patients, and we are grateful for the continued partnership with MDRT Foundation."

Pictured above: Shannon Cagnina, COO; Dr. John Nemunaitis, Executive Medical Director of Mary Crowley; Allen Newberry; and Ellen Dearman, Mary Crowley VP of Development.

PATIENT STRUTS WITH YTAC Jill Blase, Mary Crowley patient and breast cancer survivor, worked the runway at YTAC's inaugural STRUT (Striving To Resolve, Unite and Triumph) Fashion Show, hosted at Front Door Fashion in Dallas. Blase and women representing YTAC's 2016 beneficiaries "strutted" to the applause of YTAC's members and friends. Said Blase: 'I can't thank you enough for letting me be a part of this event, representing Mary Crowley. Getting to know the other women in the fashion show was heartwarming. Their stories of survival are inspiring. And of course, all of the fun and pampering in getting ready for the fashion show. It was a fun bonding time... Every moment was fabulous!"


UPCOMING EVENTS:

Gold Ribbon Games: Sunday, April 10th - Gold Ribbon Games is a co-ed, high-school-age-and-up kickball tournament that raises funds in a community-building, fun and memorable way. Teams compete for prizes awarded for kickball skills and for top fundraising honors. Participants come from all over DFW to participate and raise awareness and funds for sarcoma research. Sarcoma is a young adult cancer that has the lowest of survival rates. Hosted by the Rutledge Foundation, the tournament will take place at The Benbrook Baseball & Softball Park in Ft. Worth, Texas. To register, please go to www.rutledgefoundation.org

Silver Dollar at the Ranch: Saturday, May 14th - The event of the year, Silver Dollar at the Ranch, hosted by Speedway Children's Charities-Texas, promises an exciting evening under the stars filled with games, exceptional Texas cuisine, silent and live auctions and live entertainment from prominent country western artist Neal McCoy! Proceeds will go to Mary Crowley, allowing for a new genetically targeted clinical trial for Ewing's Sarcoma occurring in children. Additionally, proceeds will benefit a Wish with Wings, an organization granting wishes to children with a terminal illness. This "party in the pasture" takes place at XO Ranch in Aubrey, Texas. Tickets are $150 per person! For more information, visit www.silverdollarattheranch.com

Jill Blase: HOPE for a "Fruitful" Future!

She had reconstructive surgery in January 2013 and was given a good report. In June 2014, however, Jill's two-year checkup revealed four small lesions in her lungs and lymph node. Since the cancer had originated from the breast, it was classified as metastatic triple negative breast cancer; patients with this type of cancer are usually told they have 18 months to live. Jill briefly enrolled in a clinical trial
In May 2012, Jill had just quit working and was looking forward to raising her two young children. She and her husband Chris had just purchased a plot of land in Rockwall, Texas, which they developed into a blueberry farm and pumpkin patch – the Blase Family Farm.

In June 2012, Jill found a lump in her breast and scheduled an appointment with her doctor. Knowing Jill’s family history of cancer, the doctor requested a 3D mammogram. Jill knew immediately from the technician’s expression that the results were not good, and the doctor later confirmed that Jill had triple negative breast cancer. Jill underwent a double mastectomy and chemotherapy.

That was not successful; she then began researching on her own and learned about immunotherapy. At Jill’s request, her oncologist found a trial at Mary Crowley Cancer Research. In May 2015, Jill enrolled in a combination PD-L1 immunotherapy clinical trial, and her disease has been stable for over nine months! In December 2015, Jill passed her 18th month since being diagnosed with metastatic triple negative breast cancer.

“I am incredibly grateful to have the opportunity to be a part of Mary Crowley’s immunotherapy clinical trial. The doctors, PAs, and nurses are extraordinary. The kindness and caring they show patients is heartwarming. I am thankful to experience no side effects and I feel great. I have hope for my future every day, thanks to this treatment.” - Jill Blase

The Blase Family Farm continues to be a popular destination. Jill and Chris welcome visitors! Go to www.blasefamilyfarm.com for more information.