One of the few silver linings in the past decade has been the advances in understanding the mechanics of cancer and the consequent changes in therapy. Naming but a few: timely, low-cost gene sequencing; the introduction of patient-centric trials; a more rapid and efficient FDA approval process; front-line immunotherapy; and the approval of the first immune-enhanced, oncolytic virus. All of these and more will continue to develop. So from where do I think the next generation of life-promoting changes will come for patients with cancer diagnoses?

Firstly, from a change in our conceptual approach. Despite progress made, basic research and clinical applications continue to be based on reductionist thinking. This involves breaking down “cancer” into its component parts and then studying the behavior of these parts. However, “cancer” is not a thing; it is a process, a complex adaptive system, and therefore would best be approached by systemic thinking. In other words, evaluating the connections and flows between its functional components both temporally (the evolution of mutations) and spatially (between cancer and both local surrounding tissues and distant metastatic sites).

Secondly, from the development of computational multiscalar algorithms. Gene sequencing suggests what changes in control and information pathways have been involved in the development of the cancer, but only by understanding the interactions between the gene changes, the coded template mRNA and the proteins produced along with their effects on each other, can we even begin to understand cancer’s complexity and the multiple targets needed to destroy it.

Thirdly, from the introduction of liquid biopsies. To allow for maximum benefit from computational multiscalar algorithms, we need to sample cancers not only at diagnosis but serially in order to initially choose the best therapy, to rapidly assess its effectiveness, and to understand the mechanisms of resistance so that we can rationally defend against them. Serial blood sampling is easy and safe, whereas multiple surgical biopsies are difficult, potentially painful, and could produce complications.

Fourthly, from the clinical application of gene editing technologies. Although existing technologies, for example, Zinc Finger Nucleases (ZFN) and Transcription Activator Like Effectors Nucleases (TALEN) have shown some promise, they are cumbersome and can evoke off-target side effects leading to adverse side effects for patients. A new and exciting technology, Clustered Regionally Interspaced Short Palindromic Repeats (CRISPR), appears to be easy to construct, efficient, capable of deleting cancer-associated mutated genes, and adding cancer suppressing genes, and more and more allowing for prevention of unwanted off-target side effects.

So, to paraphrase the author Chuck Palahniuk, when will the future switch from being a promise to being a reality? We at Mary Crowley Cancer Research are trying to make it so!

- Nei Senzer MD, Mary Crowley Scientific Director
DALLAS COWBOYS BIRTHDAY SURPRISE FOR MICHELE

Some Mary Crowley patients travel great distances to access one-of-a-kind clinical trials. When Dallas Cowboys’ Executive VP Charlotte Jones Anderson heard about Michele Baron being in Dallas to receive a cancer vaccine on her 14th birthday, she and her dad Jerry Jones decided to make it special. The Baron family traveled from Germany to Dallas in December because they found the best option for Michele’s cancer in a clinical trial at Mary Crowley, which is not available anywhere else in the world. Michele received an autographed Tony Romo jersey and a Jerry Jones-signed Cowboys hat from the famous father-daughter Cowboys’ owners, who wanted to give Michele a Texas-sized Happy Birthday. Pictured (Ellen Deerman), VP Philanthropic Development with Andrea, Michele, Ada and Randi.

NEW MOLECULAR THERAPY COORDINATOR

Rachel received B.A. in Health Sciences from the University of South Florida and minioned in Public Health before moving to Dallas in 2013. Rachel worked at Mary Crowley as a Data Coordinator for one year before taking on her new role as Molecular Therapy Coordinator for the Molecular Patient Registry, which tracks the molecular profiles of Mary Crowley patients. Rachel works with patients to secure their consent, transcribes pathology reports into the database, and runs reports for Mary Crowley researchers. In her spare time, Rachel leads a small group of 6th grade girls that she trained to analyze alternative molecular mechanisms to approach the cancer target.

If a new investigational targeted agent has less effectiveness for a patient, the expert investigators at Mary Crowley are trained to analyze alternative molecular mechanisms to approach the cancer target.

The use of the data contained in the Molecular Patient Registry and correlative response data enable the Mary Crowley team to coordinate focused development with FDA and the sponsor to a specific target population for product approval opportunity.

This tool box of molecular patient data also demonstrates how many patients have similar mutations. The top 10 seen among Mary Crowley patients are: TP53, KRAS, APC, PIK3CA, CDKN2A, CDKN2B, PTEN, MYC, CDK4, and BRAF.

* A form of molecular medicine that utilizes therapies to target or block growth of cancer cells by interfering with specific molecules needed for the growth of cancer cells.

MARY CROWLEY RESEARCH VP TO ADDRESS ACRP

Nadine Nemunaitis, Vice President of Research Operations at Mary Crowley, has been invited to speak at the Association of Clinical Research Professionals (ACRP) 2016 Meeting & Expo in Atlanta on Tuesday, April 19. She will present “Standardizing Principle Investigator Delegation Records: An Alternative Approach for Sites,” with co-presenter Certified Principal Investigator and Medical Director, Dorian Williams of West Virginia University School of Medicine. Of the 232 abstracts she has presented to ACRP, this is the 89th to be accepted for presentation. Nemunaitis directs the development, implementation and oversight of Research Operations, and she provides regulatory expertise to Mary Crowley’s Research Operations and Central Institutional Review Board (IRB). ACRP’s Meeting & Expo supports the professional growth and development of individuals conducting clinical trials through educator, exchange, and peer-to-peer engagement.

MOLECULAR PATIENT REGISTRY, MARY CROWLEY TOOL BOX

Currently, the Food and Drug Administration (FDA) has approved over 30 targeted therapies for cancer. However, with increasing knowledge of complex genetic changes in cancer, more targeted investigational agents are still needed to support new findings. Since 2012, Mary Crowley has conducted molecular testing on the majority of its patients and has preserved their data in a Molecular Patient Registry to support the Target the Program®, which will bring new cancer options to patients. This molecular data base serves several purposes for Mary Crowley Investigators:

Correlating and aligning existing patients with the most appropriate available targeted clinical trials

Providing a prospective view of new cancer signals and for dialogue with potential new drug developers.

HOW IT WORKS:

• Patients in the database (without a prior matched target trial available) may be contacted when a new clinical trial is opened that matches their molecular defects.

• A new investigational targeted agent has less effectiveness for a patient, the expert investigators at Mary Crowley are trained to analyze alternative molecular mechanisms to approach the cancer target.

• The use of the data contained in the Molecular Patient Registry and correlative response data enable the Mary Crowley team to coordinate focused development with FDA and the sponsor to a specific target population for product approval opportunity.

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NATIONAL CANCER INSTITUTE

NCI-MATCH TRIAL

NCI-Molecular Analysis for Therapy Choice (NCI-MATCH) is a clinical trial that analyzes patients’ tumors to determine whether they contain genetic abnormalities for which a targeted drug exists that is (“actionable mutations”) and assigns treatment based on the abnormality. NCI-MATCH seeks to determine whether treating cancers according to their molecular abnormalities will show evidence of effectiveness. The trial was opened for enrollment in August 2015 with ten arms. Each arm will enroll adults 18 years of age and older with advanced solid tumors and lymphomas that are no longer responding to standard therapy and have begun to grow. Source: www.cancer.gov

SPEDDING UP CANCER RESEARCH

Pat Brown, VP of Strategic Development, and Ellen Deerman, VP Philanthropic Development, joined US Army, Texas Tech, and University of Texas at Austin for the 2015 Texas Motor Speedway Tree Lighting Ceremony to receive $46,438 from Speedway Children’s Charities-Texas Chapter (SCC-TX) on behalf of Mary Crowley’s Ewing’s Sarcoma Program. The gift was made possible by SCC-TX’s annual “Silver Dollar at the Ranch” fundraising event. Sheri Hale, 2015 “Silver Dollar at the Ranch” Event Chair, and Scott Murray, SCC-TX President, presented the check at the annual tree lighting and grant ceremony. SCC-TX was created to assist nonprofit organizations in improving the lives of children in North Texas; they have awarded $10M in grants since 1997. “Silver Dollar at the Ranch” has raised $57,438 for Mary Crowley since 2012.

SOUTH TEXAS CANCER RESEARCH

Young Texans Against Cancer (YTAC)-Dallas was founded in 2008 by young people who have personally battled cancer or witnessed loved ones struggling with the disease. YTAC-Dallas members, ages 22-45, raise funds and awareness among their peer-group through a multitude of events. YTAC-Dallas selected Mary Crowley to receive $70,000 for their targeted therapy clinical trial for children with Ewing’s Sarcoma. Pictured: YTAC-Dallas Co-Presidents Allison Edwin (left) and Ashley O’Nalley (right), Ellen Deerman (center), VP of Philanthropic Development at Mary Crowley.

YTAC PUTS THE FUN IN FUNDING CANCER RESEARCH

Young Texans Against Cancer (YTAC)-Dallas was founded in 2008 by young people who have personally battled cancer or witnessed loved ones struggling with the disease. YTAC-Dallas members, ages 22-45, raise funds and awareness among their peer-group through a multitude of events. YTAC-Dallas selected Mary Crowley to receive $70,000 for their targeted therapy clinical trial for children with Ewing’s Sarcoma. Pictured: YTAC-Dallas Co-Presidents Allison Edwin (left) and Ashley O’Nalley (right), Ellen Deerman (center), VP of Philanthropic Development at Mary Crowley.

THE DIFFERENCE MAKING A DIFFERENCE

The Foundation was formed by four ovarian cancer survivors and co-founders, Rachel Desplancke, Shannon Cagnina, Dr. Charles Ritter, and Michele Baron, to share the same passion: to Be the Difference and end the fight against ovarian cancer. Says Julie Shrel, Co-Founder, President and Survivor: “We are excited about the research and discoveries occurring at Mary Crowley and have great hope that our support, along with the other funding for this study, will be a catalyst in finding better treatments or a cure for ovarian cancer.” Mary Crowley has conducted nine clinical trials for ovarian cancer since 2012, with an additional trial in development that targets MIF macrophage migration inhibition factor. With this grant, Mary Crowley will expedite the targeted molecular therapy program specifically designed for ovarian cancer. By opening new and more clinical trial options for patients in 2016, the Foundation has brought our vision one BIG step forward in ovarian cancer research.

Ovarian cancer is the most lethal gynecological cancer affecting 1 in 70 women. Today more than 70% of ovarian cancer patients will die of their disease. When ovarian cancer is detected and treated early, the five year survival rate is greater than 92%.

Pictured Above From BTDF: Gary Gardner - Board Member; Jil Bach - Co-Founder and Survivor; Lynn Lentscher - Co-Founder and Survivor; Julie Shrel - Chair; Ellen Nemunaitis, Sheryl Nonack - BTDF Board Member; Ellen Deerman - VP of Philanthropic Development at Mary Crowley, and Jon Mize - Director of Work to Win

THANK YOU, ALLISON’S HOPE!

“Allison’s HOPE-1 MILLION AND COUNTING Foundation (Allison’s HOPE) traveled to Dallas to present a $57,438 check to Shannon Cagnina, COO, Jeanne Jones, VP of Clinical Operations, and Pat Brown, VP of Strategic Development. This is one of many donations from Allison’s HOPE, based in Edwardsville, Illinois. They have raised over $1M for Mary Crowley since 2004 through their annual Golf Outing, the Hauling Hope transport fleet, HOPE Gala and other community events. Allison’s HOPE was established to honor Allison Cassen’s dying wish to raise money for cancer research. Years later her father Allen Cassen was also diagnosed with cancer and was a patient at Mary Crowley. Thanks to the generosity of family and friends, Allison’s HOPE is on their way toward raising another $1M to advance new treatments for cancer patients. Thank you, Allison’s HOPE!”

BUILDING HOPE

Dr. Charles Ritter, Co-Founder, President and Survivor: “This is one of those times that we get to build HOPE. It’s a wonderful day to be at Mary Crowley and have great hope that our support, along with the other funding for this study, will be a catalyst in finding better treatments or a cure for ovarian cancer.” Mary Crowley has conducted nine clinical trials for ovarian cancer since 2012, with an additional trial in development that targets MIF macrophage migration inhibition factor. With this grant, Mary Crowley will expedite the targeted molecular therapy program specifically designed for ovarian cancer. By opening new and more clinical trial options for patients in 2016, the Foundation has brought our vision one BIG step forward in ovarian cancer research.

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Be the Difference Foundation (BTDF) and Mary Crowley are pedaling toward HOPE in the fight against ovarian cancer. BTDF’s annual cycling event “Wheel to Survive Dallas” is an inspirational fundraiser that promotes awareness of ovarian cancer symptoms, funds programs for women battling the disease, and provides research funds for a cure. Cyclists of all levels participate as teams or individuals. The event will feature uplifting stories from survivors and their families. Proceeds will benefit Mary Crowley’s targeted molecular therapy program specifically designed for ovarian cancer. Join us!

**WHEEL TO SURVIVE DALLAS DETAILS:**

**WHEN:** Saturday, February 28th 9 AM - 3 PM  
**WHERE:** Jewish Community Center of Dallas  
7900 Northaven Road  

**HOW:** Register as a team or individual at www.wheeltosurvive.org  

Wheel to Survive events are also taking place in Austin, Lubbock, El Paso, Houston, and San Francisco, CA.

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**STRUT: FASHION SHOW**

The Dallas Chapter of Young Texans Against Cancer (YTAC) has raised funds for beneficiaries through a variety of creative platforms, and the March 3rd event will certainly be a “show stopper.” The first annual YTAC fashion show - STRUT (Striving to Resolve, Unite, and Triumph) - will highlight cancer survivors and champions as models, including a Mary Crowley patient! These women will “strut” down the runway and take a stand against cancer. Participants will be pampered, styled, and accessorized by Front Door Fashion. The evening will include a VIP reception, silent auction, and refreshments. Don’t miss this fun event!

**WHEN:** Thursday, March 3, 2016 | VIP 6-7 PM  
General Admission 7-10 PM  
**WHERE:** Front Door Fashion  
2251 Vantage St. #400, Dallas  

**WHY:** Supporting cancer survivors and organizations  

**HOW:** Purchase tickets at dallas.ytac.org  

**ADDITIONAL UPCOMING YTAC EVENTS INCLUDE:**

- YTAC Chili Cookoff | Saturday, April 2nd  
1-4 PM at the Foundry Bar  

- Young Texans RACE Against Cancer | Saturday, May 14th  
8 AM at Trinity Groves  

- BubblyQ | Thursday, October 13th  
7-10 PM at Fearing’s at The Ritz - Carlton, Dallas  

For additional information, please visit dallas.ytac.org  

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MARY CROWLEY IS BENEFICIARY OF 2016 SILVER DOLLAR AT THE RANCH EVENT

SILVER DOLLAR AT THE RANCH

Saturday, May 14th

6:30 PM TO MIDNIGHT

XO RANCH
AUBREY, TX

TICKET PRICES START AT $150
INCLUDES: DINNER, OPEN BAR, DANCING & CONCERT

ENTERTAINMENT BY FAN FAVORITE NEAL MCCOY

APPEARANCES BY LOCAL AND NATIONAL CELEBRITIES INCLUDING
PAM MINICH, HONORARY CHAIRPERSON

LIVE AND SILENT AUCTIONS

MIDWAY GAMES THAT GIVE THE STATE FAIR OF TEXAS A RUN FOR THEIR MONEY

ROUNDING UP A CURE FOR PEDIATRIC CANCER RESEARCH

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VISIT SILVERDOLLARATTHERANCH.COM OR CALL 817.215.8421

MARY CROWLEY CANCER RESEARCH
HOPE LIVES HERE.

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www.speedwaycharities.org

a Wish with Wings