“Personalized” oncology, defined as the delivery of rationally based singlet or combinatorial therapeutics targeting a patient’s tumor-specific rewired pathway dysfunctional operational sites, has rapidly become the current paradigm of cancer treatment. Despite consensus on this strategy, tactical implementation remains limited in scope. The most appropriate methodology of target identification, including sequential parallel qualitative and quantitative retrieval of “omics” strata (i.e., genomics, epigenomics, transcriptomics, proteomics and metabolomics), data interrogation, and systems analysis has yet to be identified. However, the exigencies of patient care require the application of best available resources.

Retrospective analysis utilizing “next generation sequencing (NGS)” was done on cancer tissue harvested from 14 patients prior to receiving MLN8237, a novel Aurora Kinase A inhibitor. The responding patients (n=4) were characterized by stable disease ≥6 months and prolonged time of progression (≥1.3 fold prior treatment). Differential patterns of nodal connectivity in protein-protein interaction networks (consequent to determined genomic alterations) emerged from the comparison between responder and non-responder groups. The responding patient population showed high connectivity within MYC related genes including regulators of the Wnt/beta-catenin pathway. On the other hand, the non-responding patients showed high connectivity centered on the TP53/RBL1 axis. Matching “targeted therapy to target” is a sine qua non for maximizing effective therapy in appropriate patients and NGS mapping may further our understanding of the relationships between molecular biological pathways and targeted therapy response. While awaiting further progress in systems analysis across “omic” levels (genomic-transcriptomic-proteomic), research involving of NGS sequence mapping to interrogate patient response to therapy in order to help elucidate molecular therapeutic predictors is justified based on the urgent needs of patient care.

Matching targeted therapy to target, including multiple target enumeration based on pathway crosstalk and feedback, is a complicated process that requires further discovery. However, while our multistrata “omic” toolbox continues to expand its capabilities, patients are in need of care. Although only a first step, the application of NGS to target assessment has now become patient-ready and can supplement existing tools to provide further increments in treatment outcome.


“One patient was guided to this trial three years ago through molecular testing. He is still on the trial and without disease.”
- John Nemunaitis, MD
What is a checkpoint inhibitor?

Immune checkpoint inhibitors are drugs – often made of antibodies – that unleash an immune system attack on cancer cells. They’ve scored some impressive successes in recent years, particularly in some patients with metastatic melanoma or Hodgkin’s lymphoma, and are showing promise in clinical trials involving patients with other types of cancer.

Checkpoint inhibitors seek to overcome one of cancer’s main defenses against an immune system attack. Immune system T cells patrol the body constantly for signs of disease or infection. When they encounter another cell, they probe certain proteins on its surface, which serve as insignia of the cell’s identity. If the proteins indicate the cell is normal and healthy, the T cells leave it alone. If the proteins suggest the cell is infected or cancerous, the T cells will lead an attack against it. Once T cells initiate an attack, the immune system increases a series of additional molecules to prevent the attack from damaging normal tissues in the body. These molecules are known as immune checkpoints.

Tumor cells often wear proteins that reveal the cells’ cancerous nature. But they sometimes commit what amounts to identity theft, arraying themselves in proteins of normal cells. Recent research has shown that cancer cells often utilize immune checkpoint molecules to suppress and evade an immune system attack. T cells, deceived by these normal-looking proteins, may allow the tumor cell to go unmolested.

Checkpoint inhibitors block these normal proteins on cancer cells, or the proteins on T cells that respond to them. The result is to remove the blinders that prevented T cells from recognizing the cells as cancerous and leading an immune system assault on them. Source: blog.dana-farber.org

Ask a Mary Crowley Investigator

Q: Dr. Strauss, there have been a number of recent FDA approved drugs for melanoma, so how would you compare Mary Crowley’s current melanoma trials to those of the approved drugs?

A: Five new drugs have received approval by the FDA in the past four years for the treatment of advanced melanoma (Ipilimumab, Vemurafenib, Trametinib, Pembrolizumab, and Nivolumab). These new treatments apply discoveries about DNA mutations in melanomas and discoveries about the control of the immune system. The new drugs extend survival for patients with advanced melanoma and have produced some cures. However, there is no question that the results are still not enough for the needs of many of our patients.

Mary Crowley Cancer Research can be proud that these studies at the Center contributed to the development and approval of several of these drugs.

Currently, Mary Crowley has five studies open for treatment of patients with melanoma. There are separate studies for those with what is known as locally advanced melanoma (still possibly removable with surgery) and for those with melanoma that has metastasized. These studies are testing new immunotherapy techniques added to the newly-approved drugs.

Immunotherapy treatments will have the best chance to help if used as early as possible. I think that even with the availability of newly-approved drugs, it is best for a patient to consider the option of being in a study. Because of these recent advances, patients and medical and surgical oncologists have every reason to look to a research study of immunotherapy for melanoma as the first line of treatment.
17th ANNUAL MARINE INDUSTRY CHARITY GOLF & SOFTBALL TOURNAMENT

For the third year in a row, our friends at AEP River Operations have selected Mary Crowley as the beneficiary of their 17th Annual Charity Golf and Softball Tournament. Held in Kirkwood, MO, on August 15-16, 2015, the event raised $45,000! Over the past three years, AEP River Operations employees and associates have worked hard to contribute over $112,000, making a tremendous difference for Mary Crowley’s cancer patients. AEP is based in St. Louis, MO and boasts a fleet of 3000 boats nationwide; in 2014, they moved 69 million tons of cargo for their clients. Thank you, AEP River Ops! Pictured Above Left to Right: Donna Caviecy, Dan Rosskoph, Heather Tomko, Natalie Mundell, Sarah Looper of AEP River Operations, Pat Brown of Mary Crowley Cancer Research Center, Linda Cassens, and Rick Tidwell of AEP River Operations.

SAINTS FOR A CURE

The First Baptist Academy school in Dallas paid tribute to Julia Shoemake, one of their Lower School principals on October 9th, 2015. The occasion was to recognize their own who have been diagnosed, currently fighting or who have survived breast cancer. “This year, First Baptist Academy sold “Saints for a Cure” t-shirts to raise money for breast cancer research in honor of Julia Shoemake. We are thrilled to announce that God has blessed us beyond our wildest dreams. With his power, we raised $1346.15”, says Shawn Weiss of First Baptist Academy. The proceeds were donated to Mary Crowley Cancer Research and designated for breast cancer research. Thank you ‘Saints’ for marching with us toward a cure! Pictured Left to Right: Julia Shoemake, Terri Coleman, Stacy Cinatl, and Suzanne Brooks.

RUTLEDGE FOUNDATION SURPRISES DR. MAURIZIO GHISOLI WITH AWARD

The Rutledge Foundation held its annual luncheon benefitting Mary Crowley’s Ewing’s Sarcoma Pediatric Cancer Research on Thursday, October 8, 2015. Rutledge family members and trustees recognized Mary Crowley Principle Investigator Dr. Maurizio Ghisoli, certified Pediatric Hematologist/Oncologist, with an award for his successful efforts to accelerate the development of a new targeted investigational therapy for Ewing’s Sarcoma. “His passion has been not only to provide outstanding care for his pediatric and young adult cancer patients, but also to create opportunities to bring less toxic and curative treatments to his patients”, said Laura Rutledge. Pictured Above: Dr. Maurizio Ghisoli and Laura Rutledge.

NORTH TEXAS GIVING DAY-COMUNITIES FOUNDATION OF TEXAS GRANT

Thank you for your donations on North Texas Giving Day! For the 7th year in a row, Communities Foundation of Texas (CFT) hosted “North Texas Giving Day,” the nation’s largest online giving event that provides support for DFW-area nonprofits. We are pleased to announce that Mary Crowley raised $16,815! In addition, Mary Crowley’s Nurse Navigation Program received a special grant of $20,000 from CFT discretionary funds. Mary Crowley is proud to partner with CFT to improve the lives of cancer patients by facilitating access to innovative clinical trials, extending survival, and moving one step closer to a cure.

DON’T MISS THESE UPCOMING EVENTS

UNDY 5000: November 14, 2015 – Join the Mary Crowley Crawlers for our 7th year of participation in the Colon Cancer Alliance’s UNDY 5000 Run and Walk for Colon Cancer! Mary Crowley is a Community Health Partner with the Colon Cancer Alliance and is honored to help them further their mission of providing hope and support to colorectal cancer patients and their families. For more information, go to www.marycrowley.org. Pictured Above: The Mary Crowley Crawlers Team 2014

CRYSTAL CHARITY BALL: Saturday, December 5, 2015 - Mary Crowley Cancer Research Centers has been selected as a beneficiary of $500,000 from the 63rd Annual Crystal Charity Ball. This funding will help drive research development for pediatrics to the forefront and initially to Ewing’s Sarcoma patients who have exhausted all other treatment modalities. For more information on our Ewing’s Sarcoma research, visit www.marycrowley.org. For more information on the Crystal Charity Ball, go to www.crystalcharityball.org.
Laura was just 37 years old when she noticed a small lump in her breast. She mentioned it to her physician during one of her annual exams, and they both concluded that it was most likely fibroid tissue. Since she was not yet 40 years old, she was not getting annual mammograms and if she chose to have one it would be an out-of-pocket expense. Soon after that time, she noticed a lump under her right arm, and then her physician sent her immediately to get a mammogram followed by a biopsy. In May, 2013, Laura was diagnosed with triple negative breast cancer, which is a type of cancer that does not respond well to approved treatments. Her scan report also showed that the cancer had metastasized to a tiny area on her spine.

Laura underwent the routine chemotherapy and a double mastectomy. After surgery, they saw a few more positive cancer cells, so she had another round of chemotherapy and radiation. While Laura was undergoing her treatment, her mother was diagnosed with breast cancer and began her own treatment schedule. Laura completed her treatment in May 2014, followed by reconstruction surgery in August 2014. Laura is an interior designer and while she continued working through her treatment regimen, she was now ready to get back to a normal routine. But, in March 2015, Laura had a PET scan and the PET scan revealed the cancer spread to her lungs, adrenal gland and lymph nodes. Not only was this bad enough, but the timing could not have been worse. She and her mother had planned a trip to London with her family and received stereotactic radiation when she returned. After a 6-week washout period, Laura started the clinical trial at Mary Crowley. This innovative clinical trial is a checkpoint immunotherapy that is designed to block a key cancer growth pathway. She is grateful for the opportunity to try something new and less toxic than her past chemotherapy.

“I am so thankful to be able to participate in this clinical study at Mary Crowley. It is a true blessing to have access to a cutting edge treatment that is close to my home. The staff at Mary Crowley has been so kind and encouraging to me and my family.”

- Patient, Laura Pulis