

Hope for a Rare Disease Through TCGA

My perspective as a caregiver, patient advocate and physician

December 4, 2017 By Sara Selig

Being diagnosed with a rare and aggressive form of [cancer](#) can instill feelings of fear, isolation, and desperation. I see this clinically working with patients, and, unfortunately, I have felt this first hand when my husband, Gregg, was diagnosed with uveal [melanoma](#) (UM) in 2006. When Gregg's cancer spread to his liver one year later, we felt intensified fear, isolation and hopelessness. At the time Gregg was [diagnosed](#), we found very little support for patients and [caregivers](#), and even less support for research in this area.

Establishing Patient and Scientific Communities Through CURE OM

Our challenging circumstances drove us to advocate for Gregg, and, ultimately, for the entire UM community. We worked to help provide additional resources for patients and family members, increase communication between the patient and provider communities, and facilitate research into UM. We set to work very quickly—we were in the fight of our lives and working against the clock.

Gregg and I founded the CURE OM (Community United for Research and Education of [Ocular Melanoma](#)) initiative with the Melanoma Research Foundation (MRF) to unite, educate and support UM patients, and to galvanize the UM scientific community. By helping to build collaboration and coordination within the UM scientific community, as well as provide direct support for research, we were able to combat our feelings of hopelessness because the scientific advances we saw unfolding offered hope for Gregg and for the entire UM community.

Establishing a Scientific Community Through TCGA

I attentively watch for scientific advances and initiatives happening both inside and outside of the UM field. I began this effort first as a dedicated partner and caregiver to Gregg, and now continue it as part of my work with CURE OM.

Thus, when I first learned of [The Cancer Genome Atlas](#) (TCGA) initiative of the National Institutes of Health ([NIH](#)) in 2011, I was intrigued and hopeful that TCGA discoveries might have some indirect relevance to UM. The work of TCGA is extremely important and likely to uncover molecular

underpinnings of cancer that will translate into innovative and effective treatments for multiple cancer type—even rare cancers like UM.

When the TCGA effort was expanded to include rare cancers, I saw this as a huge opportunity to include UM and bring critical resources to this under-resourced disease. At a leading melanoma meeting in the summer of 2012, Jeffrey Gershenwald, MD, professor of surgery and cancer biology at the University of Texas MD Anderson Cancer Center, suggested CURE OM advocate for the inclusion of UM into TCGA. As the lead for our group, I connected with then-TCGA Director Kenna Shaw, PhD, and we formed an amazing partnership.

The CURE OM initiative helped acquire more than 50 patient samples for TCGA's UM study, a direct result of our close collaboration with Dr. Shaw and TCGA as well as our connections with an extended network of dedicated and collaborative researchers and medical providers in the field, for whom I am extremely grateful. In a nutshell, I am humbled and honored to be a part of the massive team effort undertaken for this study.

Setting a New Course for UM Diagnosis and Treatment

The [results of the TCGA UM study](#), published in the journal Cancer Cell on August 14, 2017, represent a tremendous opportunity for the UM community that will accelerate research in this area exponentially. From 80 samples of primary UM, the study identified four distinct molecular profiles, each with distinct clinical outcomes, requiring unique patient management strategies and potential areas of treatment to investigate.

While alterations in the [gene](#) BAP1 were previously known to be associated with poor outcome, this study helps us understand the gene's molecular partners—potential targets for preventing [metastasis](#), the clinical fate that Gregg unfortunately suffered. “Distinctly different cellular signaling pathways were identified within different subsets of BAP1-altered samples, and these pathways present potentially discrete targets,” explains corresponding author Scott E. Woodman MD, PhD, a physician-scientist at the University of Texas MD Anderson Cancer Center.

The study also offers improved methods for predicting metastasis with more granularity. According to Dr. Woodman, “beyond BAP1, there are complex [chromosome](#) alterations, epigenetic changes, and altered [gene expression](#) levels that may allow us to better predict metastasis, potentially influencing how we implement [surveillance](#), prioritize patients for [clinical trials](#), and affect a host of other personal choices for patients.” Needless to say, a better understanding of metastasis is crucial for a patient, potentially making years of difference in expected survival.

There is no [FDA](#)-approved treatment for UM once the cancer metastasizes. This study brings hope to change this by charting the potential treatments worth investigating for each subtype of UM. DDR-modulating agents, anti-hypoxia drugs, direct or indirect anti-MYC therapeutics are among the potential UM drugs that are currently being investigated in clinical trials for other diseases. The researchers also suggest that certain metastatic UM patients may benefit only from a specific subset of immune checkpoint inhibitors.

Enduring and Persevering for Other Families

I take comfort in knowing that the inclusion of UM in TCGA has been a critical step toward the development of effective treatments. The comprehensive data that has been generated by TCGA's network and their integrative analysis have been made freely available and will be widely used by the cancer research community. I see this as not only a critical opportunity and path forward for the UM community, but as a resource for other rare disease communities and the broader cancer community. With data from TCGA, what we learn about drivers for UM may inform and help “unlock” not only UM, but the molecular components of additional cancers as well.

We are grateful to be partnered with TCGA and appreciate all the work that goes into this cutting edge and innovative work. I am grateful to Dr. Shaw for her strong vision of, and commitment to, patient-centered research. We are also grateful to all the patients who allowed their tissue to be used for research purposes. Working together, we know we will improve outcomes for generations to come. Although the cure will come too late for Gregg, who died in January 2012, I am confident it will come in time to save many lives and prevent families from enduring the challenges Gregg and I, as well as many other families, have endured.

I'd like to end with Gregg's words—these are closing words from Gregg's talk addressing researchers and clinicians at the first international UM scientific meeting we planned and I think this captures our collective vision as well as our gratitude for the amazing collaboration of dedicated researchers in the field:

“You have more than risen to the occasion to help me, my family and countless others fighting uveal melanoma—now I ask that you think about yourselves just as we think about you—not divided by institution, by beliefs, by treatment expertise—but, moving forward from today, please see yourself as a TEAM—believe in each other as a TEAM, create a vision as a TEAM—we are so much stronger as a TEAM.

“Thank you so very much for your passionate dedication to uveal melanoma—we hope our collective team work eventually helps increase our understanding of this disease, leading to improved treatments and lives saved.”

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