University of Colorado Hospital FOUNDATION

University of Colorado Foundation

University of Colorado Cancer Center

2014 Director's Overview: Everything is an Experiment

D. Ross Camidge, MD, PhD

After the first half of my medical school studies and before going on to a hospital to complete my full medical training, I took a four year detour to get a PhD in molecular biology. After the rote-learning of textbook medicine (this was before the days of being able to google everything, so over generations physicians have been selected out to have rather good memories), I recall being initially frustrated by the uncertainties of science. Every hypothesis was built on other hypotheses. Every seemingly solid building block, was made up from the results of experiments that were each susceptible to criticism. Every data point had some strengths and some weaknesses. I recall a friend, who was a historian, asking me one day if I was making progress in my experiments. 'I don't know,' I told him.

'How can you not know?' he puzzled. Science from the outside often seems so much more concrete than other aspects of real life (probably particularly compared to the task of divining the intentions and meaning of whatever medieval individuals my friend had been studying at the time). However, by the end of my PhD, I understood science better. Not because I had found some undeniable truth, hidden beneath the rubble of my lab benchwork. Instead, I simply learned that the key to science lay in understanding and being comfortable with different degrees of uncertainty. Some 'facts' have so much supporting data that they are almost completely solid – you can reliably build a house, or a road (or a career) out of them. But others are more flimsy, they are not fully shored up yet. Maybe they are enough to lay out an initial architectural plan or map out a new journey for future research, but you have to have your wits about you, as they could suddenly collapse and you have to be ready to move on in other directions at a moment's notice.

Trying to become comfortable with uncertainty, recognizing that every new day, every new approach, new challenge or interaction with every new individual is, in some senses, an experiment that we don't always know the results of straight away, is something that scientists, physicians and all those affected by serious diseases like cancer, may have in common, albeit in very different ways. Uncertainty can be unsettling, of course. On its worst days, as a cancer patient (or someone caring for a cancer patient), it feels like walking across a mine-field, where sometimes the encouragement of friends and family is the only thing that can get you though. On other days, when anyone starts a new treatment, you can have the same mixture of trepidation and anticipation that you get whenever you set out on a new adventure.

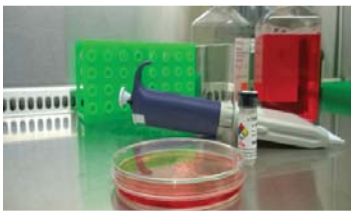


Photo by Anh Le, Doebele Lab

In this year's Lung Cancer Colorado Fund newsletter, you will see that we are all in lots of different experiments together. My colleagues have started to screen for lung cancers in some high risk individuals, to try and increase the cure rate from this disease by catching it early, but we need people to screen. We've identified yet more molecularly defined subpopulations of advanced lung cancer that may respond to specific targeted therapies, but we need patients to test and to treat. For at least one of these approaches, we are really trying to change the way that clinical trials are run, by using the internet to expand the trial specific tumor testing to anyone who needs it in the USA, but with government grants funding barely 5% of new ideas, we need ongoing philanthropic support to carry forward these advances. On campus, we have now created an outstanding multidisciplinary clinic offering newly diagnosed patients the opportunity to see a surgeon, a radiation oncologist and a medical oncologist all in the same visit to come to a tailored treatment plan for each individual as quickly as possible, but we need people to know we are here. Anything you can do to get the word out, and increase our support continues to be tremendously appreciated.

In this newsletter, you will also see stories of patients. Many of them have done well, and you will see how they and their friends and families have dealt with their own 'experimental experiences' finding new meaning in whatever their 'new normal' has become. But this year, as part of another experiment, you will also see some other stories. Stories about what happens when the battle with cancer comes to end, and how those left behind have coped. With the increased support from the Lung Cancer Colorado Fund (our annual intake continues to rise and we have had several five figure gifts this year), we are continuing

2014 Director's Overview continued

to make progress, but we also have to recognize that we are still dealing with a very deadly disease. As a true community of scientists, physicians, carers and patients we need to be able to both celebrate our successes, while at the same time honor all those who have helped us get there, even if they themselves have moved on. Please read these pages, share this newsletter and know, that as fellow participants in so many of life's different experiments, we are all in this together. http://uch.thankyou4caring.org/lungcancercolorado

University of Colorado Hospital Now Offering Lung Cancer Screening

Jackie Brinkman

Just in time for Lung Cancer Awareness Month, University of Colorado Hospital is now offering a lung cancer screening program designed to catch cancerous tumors as early as possible and potentially save patients' lives. If lung cancer is detected early, the number of cures can be increased.

Screening is open to patients referred by their physicians who meet the following criteria:

•Current or former smokers who quit < 15 years ago

•Between the ages of 55 and 74

•Smoking history of at least 30 pack-years (this means 1 pack a day for 30 years, 2 packs a day for 15 years, etc.)

•No personal history of lung cancer

•Medicare recently announced plans to start covering the screening for eligible patients, and many private insurance plans already pay for lung cancer screening.

The recommended screening test for lung cancer is low-dose computed tomography (also called a low-dose CT scan). In this test, an X-ray machine scans the body and uses low doses of radiation to make detailed pictures of the lungs, often enabling detection of tumors before someone experiences symptoms. The test is not recommended for everyone, however, and it has risks as well as benefits.

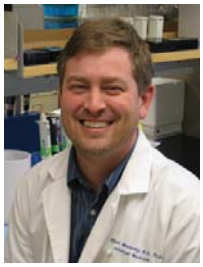
"I believe our lung cancer screening program will save lives," says Dr. Peter Sachs, associate professor of radiology and chief of thoracic imaging, University of Colorado Hospital. "Studies have clearly shown that individuals at high risk for lung cancer should receive this low-dose CT scan every year because it can help catch lung cancer in the earliest stages. That's important, because the survival rate for early stage lung cancer, when it hasn't spread around the body, is much higher than for later stages of the disease."

The National Cancer Institute's Lung Cancer Screening Trial established that lung cancer mortality in specific high-risk groups could be reduced by these annual screenings.

"These screenings also often find non-cancerous nodules in patients' lungs that should be monitored over time," said Dr. Stephen Malkoski, MD, PhD, associate professor, Pulmonary Sciences & Critical Care, University of Colorado Cancer Center. "For that reason, we have integrated our lung cancer screening program into our Lung Nodule Clinic. We're able to track those nodules from year to year and will quickly discover any changes. This is good news for patients because cancerous tumors can be treated quickly without unnecessary procedures to remove non-cancerous lung nodules."

For patients without insurance coverage, University of Colorado Hospital offers a self-pay discounted rate of $301. Screenings are available for any patient who meets the criteria for a heavy smoker with a physician referral. For more information please call 855-586-4824 or 720-557-7171 for an appointment.

Peter Sachs, MD
Chief of Thoracic Imaging



Steve Malkoski, MD PhD,
Associate Professor of Pulmonology

A right upper lung nodule (bottom left in image) possibly representing an early lung cancer, as might be detected on lung cancer screening CT scan.

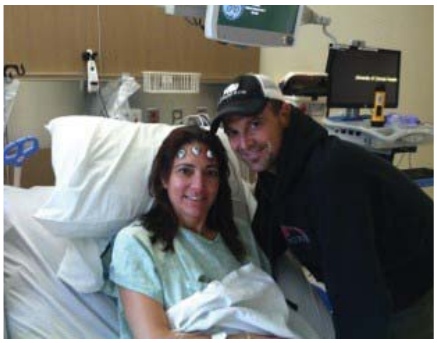
Susan's Story: Breathless in Colorado

Susan Nunn (with Stefani Bender-Prybylski, RN)

I was diagnosed in August of 2012 at the age of 41. Because of a persistent cough and a decrease in my stamina running, my primary care doctor did a chest x-ray leading to a CT and found several masses in my lung. My primary care doctor was concerned but said the chances of me actually having lung cancer at my age and with my lifestyle, were slim to none. Unfortunately, as it turned out, I fell into the slim category.

I was referred to another hospital for a biopsy. After a ton of research I had convinced myself that I had a fungal lung condition common in Arizona, called valley fever. I spent a great deal of my childhood there and, while my husband, Tyson, and I were terrified by any diagnosis, we felt we could handle this.

The day of the lung biopsy arrived. The doctors there were also hopeful that it was valley fever.



Me and Tyson after my brain surgery

The result of the biopsy was horrible news. I had stage IV lung cancer. Tyson said this was probably the very worst day of his life. I was still naïve and thought, whatever it meant, we would fight. It couldn't be that bad. At this time, we still did not know I had an ALK rearrangement. One week later, we heard the ALK results, which meant a more "positive" prognosis. Our doctor at the time still did not know much about ALK positive lung cancer other than that a new drug called crizotinib existed.

I knew we needed a second opinion, but wasn't sure where to get that. So, I googled "ALK positive lung cancer" and, like magic, found University of Colorado right here in Denver. I called the next day.

We met with the new doctor, terrified and ready to hear the bad news. But he was different. He gave us hope. He gave us options. He was optimistic, but realistic at the same time. The numbers and stats were the same, but his knowledge and optimism helped us start to move forward and move out of the deep dark place we had been hanging out in.

We realized it was time to talk to our children. It was the hardest thing I have ever done. We kept it simple, but they knew the word cancer and that it was scary and potentially deadly. There were a lot of tears from all of us. It was beyond awful. Tyson and I had no idea what we were doing or if we were handling any of this in the right way. It wasn't fair that our children had to have these worries. How could we protect them? We decided to put them on a need to know basis, one day at a time. We notified family, friends, and the children's school. Our "village" rose to the challenge, ready to fight with us. People came out of the woodwork. Friends and loved ones from near and far, past and present were willing to help us with whatever we needed. The love and support we received from the beginning to this day has been beyond words. We are never treated differently, just embraced and lifted up. It was overwhelming at first, but we could not have survived without this support.

I truly thought I was going to be the University's star patient and would be on crizotinib longer than anyone, but life had other plans. After a few months, I progressed. I went through chemotherapy, radiation therapy and ultimately neuro surgery for new metastatic disease that had spread to my brain and which, literally, crippled me, causing me to have to learn to do everyday functions like write and walk again. At this point, I was recommended for a clinical trial of a new ALK inhibitor drug and since starting in July of 2013, it has been amazing. The cancer is under control, I worked hard to recover from my neurosurgery. Now I feel like I have my life back and have even been able to return to my love of running and recently back to work again (even that I love, as it keeps my brain active in a different way).

This past Mother's Day we planned an event up the infamous Manitou Incline in Colorado Springs. We planned this with family and friends to celebrate my one year anniversary post brain surgery. It was a celebration of life and health. It was not a fundraiser, but we made t-shirts for the event to help spread the word and try and "advertise" how, like Chris Draft says, we were trying to "change the face of lung cancer". We had an amazing turn out, despite the rain and snow. With all that support and being out there with nature, it was just a perfect day.

Show of support doing the Manitou Incline after I learned to walk again

Tyson and I are now trying to turn

our focus towards helping Lung Cancer Research instead of merely surviving as a result of it. We know, in order to further research, we need to get my story and other stories out there. We need to help educate people about this disease. There are thousands of charities and thousands of ways to ask people to donate for a cause. Tyson and I are just scratching the surface in this department. How do you get others to believe in YOUR cause?? Lung Cancer is a tough one. It does not naturally draw in supporters, as we all know. Tyson decided to start by using something he loved, something that requires massive amounts of lung function.

Tyson and the Leadville 100 belt

You see Tyson is an ultra-runner. I like running but Tyson is in his own league. He wanted to use this talent to help, so he signed up for the infamous Leadville Trail 100, a 100 mile run at altitude, and did it in my honor. He sent out an email to family and friends and to raise money for the Lung Cancer Colorado Fund. He asked for sponsorship per minute. Over 600 runners started the race, only 357 finished. Tyson finished the 100 miles in 24:00 hours flat. Imagine that, running for an entire day. Only 88 runners finished under 25 hours to earn the coveted GOLD belt buckle. It's so impressive, I wish he could wear it everywhere, but imagine the metal detectors at the airport picking up that thing! We have no idea how much money we raised from his event as the money went direct to the LCCF. We know we need to do a lot more as we plan to be in this for the long run.

Dr. Oton Taking On Major Position at Eli Lilly

In late 2014, Dr Ana Belon Oton is moving on to take up a key leadership position in the Oncology Development Division of the Eli Lilly pharmaceutical company. Dr Oton has been a great member of the lung cancer program's clinical and clinical research teams during the seven years she has spent at the University of Colorado and Denver Health Hospitals. Her patients have already been offered follow up with other members of the medical oncology team and the program is actively looking for additional Medical Oncology Faculty to recruit. We are very excited for Dr Oton's potential to help lung cancer patients through this role and wish her the best in her new career path.

LCCF Seed Grant Research Progress Updates

Since the beginning of the LCCF, the idea of supporting research has been paramount. The University of Colorado is one of the best known places for lung cancer research and making and implementing new discoveries is the main way that change will happen for the better in lung cancer. To get large grants capable of supporting the development and implementation of new ideas you first have to convince someone you are on the right path – i.e. you need preliminary data. That's where the LCCF support of the seed grants within the CU Lung Cancer Specialized Program of Research Excellence (SPORE) fits in. The SPORE is a National Cancer Institute Funded Project that builds basic infrastructure to help support collaborative and translational research at a given institution for working on a specific disease. Or, to put it another way, the SPORE, at least at CU, represents a group of interested physicians and scientists incentivized to focus their research on lung cancer. The SPORE investigators have already established the means to solicit, review and award seed grants of several 10s of thousands of dollars each to get new scientific ideas off the ground. Each year we have given money to the SPORE to initially fund part of ongoing projects, but since 2013 onwards we have been able to support all of a seed grant chosen by the SPORE. Here we provide an update on where some of that money has been used to date.

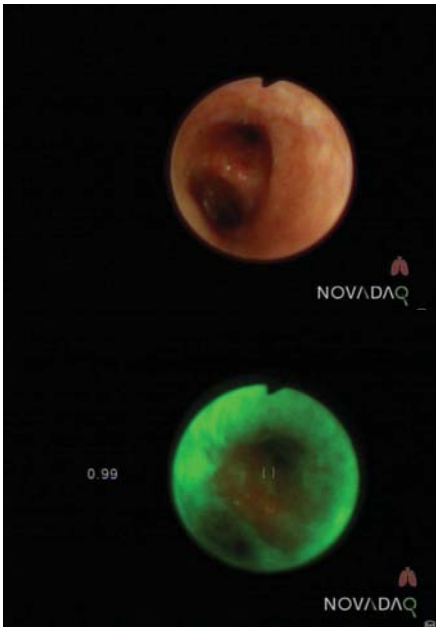
Timeline:

April 2011 - LCCF created

Fall 2012 - $20,000 donated to SPORE. These funds were split to assist two ongoing projects. Drs. vanBokhoven ($10,000 for multiplex mutation analysis of banked tumor specimens) and Miller ($10,000 for analyzing copy number of different genes in tumor bank of airway epithelium from smokers and non-smokers), both of which were designed to improve opportunities for these resources to act as better tools for research projects. The mutational analysis project was profiled by Dr Lynn Heasley in the 2012 newsletter. Dr Miller's project is profiled below:

"The airways of smokers frequently contain abnormal groups of cells that appear under a microscope to have partially progressed to squamous cell lung cancer. These are termed premalignant lesions and the SPORE in Lung Cancer has studied them using bronchoscopy. Fortunately, the large majority of these lesions do not progress to lung cancer, but rather revert to more normal appearance. We have recently found that current or ex-smokers who have several such lesions that do not revert to normal are at significantly higher risk for developing squamous cell lung cancer. Our study goal has been to better understand the genetic alterations in these lesions so that they can be more easily identified and in order to discover methods to treat them and prevent the development of lung cancer. We have studied the genetic changes in these lesions using a variety of molecular techniques that allow the detection of

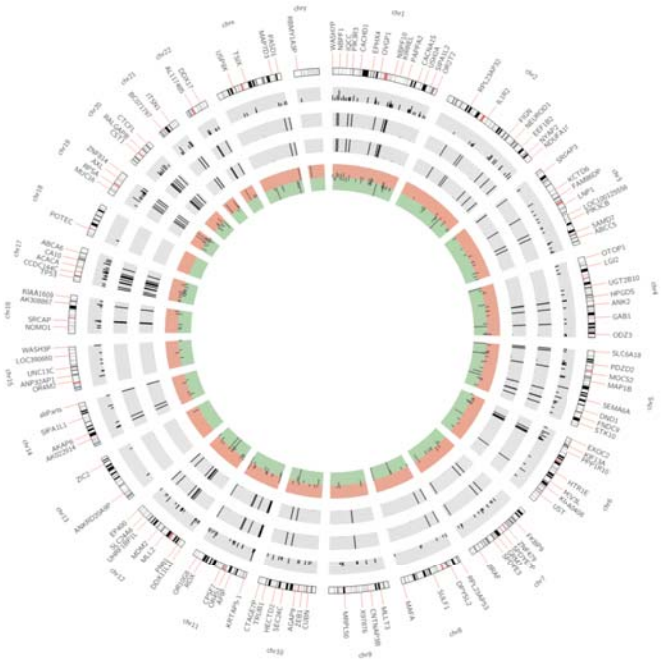
gene deletions, gene amplifications and other mutations. We have also developed a technique to grow these cells in culture and found that at least in some cases, they retain the genetic abnormalities found in the airway lesions. In one early case, a number of mutations that are common in full blown squamous cell lung cancer have been found in both the airway lesion and the cultured cells. At least one of the mutations causes a change in a growth factor receptor that can be inhibited by an available drug. We are very excited about these discoveries supported by the seed grant, because they may lead to a new approach to testing drugs to prevent lung cancer in high risk patients."



Bronchoscopic images of an advanced airway lesion. The white light image (top) shows a reddened area where the airway divides that might not be remarked on, but the autofluorescence image (in green, below) shows the contrast between normal airway cells, which are green, and advanced premalignant cells, which are brownish-red. Molecular analysis of the premalignant lesion revealed mutations in the p53 tumor suppressor, the growth factor receptor for fibroblast growth factor, and several members of the Notch family, important in development. Our research goal is to use this information to develop means to specifically inhibit these lesions and prevent lung cancer from developing.

Fall 2013 - $30,000 donated to SPORE for LCCF Seed Grant. Awarded to Subhajyoti De, PhD. "Detecting novel regulatory driver mutations in non-small cell lung cancer." Dr De was profiled in our 2013 newsletter. While we already know some key mutations can drive different lung cancers, Dr De's project attempts to find different kinds of genes – regulatory genes – that act by altering expression levels of proteins that can drive the cancer cell, even if the proteins themselves are technically normal. This year he reports the following progress on his seed grant project:

"We have now performed a large-scale analysis, analyzing 499 lung adenocarcinoma and 496 squamous cell carcinoma, combining data for somatic mutations, gene expression, reference functional genomic annotation, and conservation data to identify the potential regulatory mutations that are associated with altered expression of the candidate gene and also have evidence for perturbation of regulatory motifs. We are also extending it to other cancer types. We have, so far, identified 121 recurrent potential regulatory mutations. One of them, is associated with altered expression of a common tumor suppressor gene and may influence cell death and cell cycle arrest in response to toxic stimuli. Further experimental validation and functional genomics analysis of the identified regulatory mutation is currently ongoing. A manuscript is also in preparation for publication and will be submitted as soon as we receive the experimental validation. It remains to be tested whether small cell lung cancer and other cancers also harbor similar regulatory mutations. We are planning to submit for an NCI R01 and an ACS research scholar grant, using the findings as preliminary data."



K

Fall 2014 - $30,000 donated to SPORE for LCCF Seed Grant. Awarded to Kurt Davies, PhD. "MER as a mechanism of resistance to EGFR, ALK and ROS1 targeted therapies."

Dr. Davies received his PhD from the Department of Pharmacology at the University of Colorado Anschutz Medical Campus. He then went on to a post-doctoral fellowship at Array BioPharma, during which he examined the effects of CHK1 kinase inhibition in pre-clinical cancer models. He returned to the University of Colorado for a second post-doctoral fellowship and researched ROS1 gene fusions in non-small cell lung cancer. His current research focuses on establishing TAM receptor tyrosine kinases as therapeutic targets in lung cancer. Dr Davies' new project is outlined below:

"Targeted therapies for patients bearing lung tumors positive for activating EGFR mutations, ALK rearrangements, or ROS1 rearrangements are more efficacious than standard chemotherapies and are associated with more tolerable side effects. However, the drugs never cure the patients due to intrinsic resistance and acquired resistance to therapy. Therefore, there is an urgent need to develop novel therapeutic strategies that enhance the ability of these aforementioned drugs to kill tumor cells so that intrinsic resistance is overcome and acquired resistance is delayed

Continued...

Continued from Page 5

or prevented. One possible way to achieve this is by identifying targetable proteins that promote tumor cell survival upon inhibition of the EGFR, ALK or ROS1 kinases. Drugs that inhibit these proteins can then be included in combination therapy strategies. Dr. Kurt Davies hypothesizes that MER, a receptor tyrosine kinase overexpressed in many different cancers, may represent such a resistance mechanism. In the LCCF-supported study, Dr. Davies will determine if MER cooperates with oncogenic EGFR, ALK and ROS1 in NSCLC cells to co-activate signaling pathways driving neoplastic growth and whether MER activity can partially maintain cell survival and proliferation in the setting of targeted therapies. The findings from this study have the potential to establish MER as a viable target for combination therapy strategies and thus potentially improve the treatment of NSCLC patients who are currently managed with single drugs."

Kurt Davies, PhD

Thoracic Oncology Multidisciplinary Clinic

John Mitchell, MD and Kristen Petrelli, NP

The Thoracic Oncology Multidisciplinary Clinic is designed to offer newly diagnosed patients a one-stop, comprehensive evaluation of their disease. The goal of this clinic is to provide patients with a thorough assessment of their disease and the best options for treating it, with input from multiple specialists.

Thoracic malignancies are often challenging, and may require multiple treatment modalities to provide optimal outcomes. In a traditional medical system, appointments can drag out over weeks or months as patients visit the many specialists who need to be consulted. At our clinic, patients are seen by a team of specialists over a day-long period, with the goal of having a treatment plan by the end of the visit.

Within the University of Colorado Cancer Center, the Multidisciplinary Clinic brings together a team of experts (surgeons, oncologists, radiation oncologists, pathologists, radiologists, nutritionists, smoking cessation specialists and social work) focused on an individual's disease and the factors impacting treatment. The joint discussions and unified treatment plans save precious time and patient anxiety that had been spent on phone calls between specialists and multiple patient appointments.

Navigating the healthcare system can be difficult and overwhelming for patients, particularly following discovery of malignant disease. In order to make this process easier, a Nurse Navigator is available to assist patients in scheduling appointments, answering questions, listening to concerns and coordinating the different services involved beginning with the initial visit through completion of the treatment plan. Since the start of the Thoracic Oncology Multidisciplinary Clinic, patient feedback has been extremely positive. Patients have verbalized relief at having their questions addressed and a treatment plan proposed in one visit, and are pleased with the visible collaboration between specialists involved with their care.

Patients or loved ones who have interest in having expertise and care provided through the University of Colorado's Thoracic Oncology Multidisciplinary Clinic may contact Kristen Petrelli, Nurse Practitioner, at (720) 848-8027 or toll-free 855-LUNG-UCH.

Hyperlink: http://www.youtube.com/watch?v=2oVx-X2kUZc

Thoracic Oncology Multidisciplinary Conference

Major Publication: Crizotinib Effective in Phase 1 Trial Against ROS1 Lung Cancer

Garth Sundem

The New England Journal of Medicine is one of the most prestigious medical journals in the world. This year the journal reported positive results of a phase 1 clinical trial of the drug crizotinib against the subset of lung cancer marked by rearrangement of the gene ROS1. In this multi-center study of 50 patients with advanced non-small cell lung cancer testing positive for ROS1 gene rearrangement, the response rate was 72 percent, with 3 complete responses and 33 partial responses. Median progression-free survival – the time it takes for the disease to resume its growth after being slowed by treatment – is estimated at 19.2 months with exactly half of patients remaining on observation for disease progression that has not yet occurred.

Over 200,000 people in the United States are diagnosed with lung cancer annually and advanced stage lung cancer has a 5-year survival rate of only about 2 percent. ROS1 rearrangements are found in approximately 1 percent of lung cancer patients, the majority of whom have never smoked.

"This is a major advance for the clinical treatment of lung cancer," says Robert C. Doebele, MD, PhD, investigator at the University of Colorado Cancer Center, associate professor of Medical Oncology at the CU School of Medicine, and one of the study authors. Doebele was involved primarily in the characterization of ROS1 gene rearrangements. Additional CU Cancer Center researchers involved in the project include Marileila Varella-Garcia, PhD, who developed a test for the ROS1 rearrangement in patient tumor samples, and Ross Camidge, MD, PhD, who was involved in the clinical testing of crizotinib against both ALK-positive and now ROS1-positive lung cancers.

In fact, current results follow similar activity seen earlier for the drug against lung cancers marked by rearrangement of the gene ALK. Crizotinib earned FDA approval for treatment of ALK-positive lung cancer in 2011. Both ALK and ROS1 are proteins in the family of tyrosine kinases that normally control the behavior of cells; in the case of these rearrangements, the altered genes continuously signal cells to improperly grow, spread and survive, making the cells act cancerous.

As in the case of ALK-positive lung cancer, in which the gene ALK improperly fuses with the nearby gene EML4, in this newly studied subtype of lung cancer, the gene ROS1 fuses with a nearby partner. Tumor samples studied in the current study showed 5 known gene partners for ROS1 fusion and 2 new partners. The most commonly rearrangement was of ROS1 with the gene CD74, but no matter the ROS1 partner, all rearrangements were equally susceptible to treatment with crizotinib.

"This is ongoing work in which the primary goal of this phase one study was to characterize the safety of the drug. Not only was the safety profile promising, but we saw anti-cancer activity that makes us extremely optimistic for future trials," Doebele says.

In fact, and though it will need to be confirmed by future trials, crizotinib may have an even more durable action against ROS1-positive lung cancer than it does against ALK-positive lung cancer, the disease for which the drug was initially developed and approved. Specifically, median progression free survival for crizotinib against ROS1-positive lung cancer is just more than double the progression free survival for the drug against ALK-positive lung cancer.

Robert C. Doebele, MD, PhD, Associate Professor of Medical Oncology

Janet Freeman-Daily: A ROS1 patient blogs her way to raising funds for LCCF

Hello to my friends at University of Colorado Cancer Center.

My first "professional" blog for CURE Today online magazine is up! Once I've posted all sections of that story, I will be writing original content for the magazine.

I will be donating all proceeds from my CURE Today blogs to the Lung Cancer Colorado Fund at University of Colorado. I get paid by the number of views the site receives (250 unique visits = $25), so if you have a minute, please click on the link below and check it out. If you're comfortable with the idea, please forward this to others so they can click too.

From a cough to metastatic lung cancer

(http://www.curetoday.com/community/janet-freeman-daily/2014/11/from-a-cough-to-metastatic-lung-cancer)

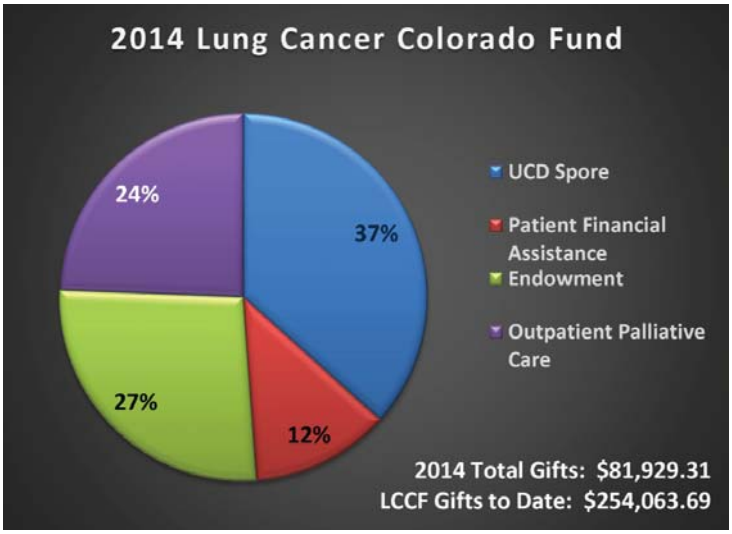
Thanks! Janet

(Also, check out Janet's awesome TED-X style talk at the Stanford Medicine Conference that forms the basis for her initial blog through the link below)

http://m.youtube.com/watch?v=YvC-7h0sR5U

Income and Expenditures

Lung Cancer Colorado Fund



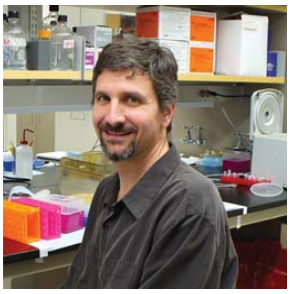
LCCF Expenditures: New Directions

From our start in May 2011, in total by August 2014 we had raised $254,063.69 ($252,213.69 entered through the UCH version and $1850 entered through the new 'mirror image' CU version of the LCCF (established Jan 2014), which now maximizes the options for getting matching funds by offering both 'hospital' and 'higher educational' status for donations). At the time of the 2014 distribution, the sum from the last distribution (Nov 2013 through August 11th 2014) was $81,929.31. This year we funded another seed grant for research ($30,000), continued our patient support through the social work department ($10,000) but, in addition, did two new things.

Since the start of the LCCF we have been keeping a little each year behind to start to build for medium term projects. Working with University of Colorado Foundation we have now created the first LCCF Educational Endowed Fellowship Fund. An endowment is a long term investment that generates income from the interest on a sizable capital sum allowing projects to continue to be funded for much longer periods. Technically, to allow maximal flexibility we created a 'quasi-endowment' which reinvests the interest to help grow the capital sum and also would allow funds to be taken from both the capital principle and from interest as needed. In 2014, we kick started this fund with $87,437.96 ($21,929.31 from 2014 plus the prior 'hold back' amounts). Our goal is to get to 500,000 dollars, to generate sufficient income from the interest to make a reasonable contribution to the salary of an outstanding clinical or basic science research trainee in the future. Should an individual donor donate at least 75% of this, they would gain permanent naming rights for the fund and the trainees. This combination of using both 'crowd sourcing' and major donations to achieve these larger projects is part of the vision for change in the LCCF. There are many other endowment size projects we really want to get off the ground, so if your passion is to make a major difference please speak to your doctor or contact Ross Camidge (ross.camidge@ucdenver.edu) the Director of the LCCF, directly.

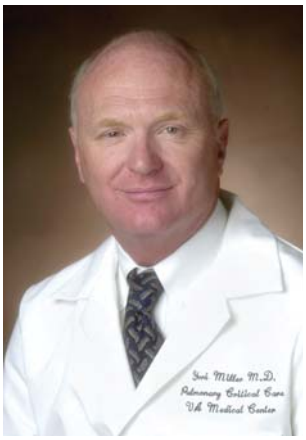
We have also started another new project to keep a little aside for this year. Although palliative care in the community is well established, UCH still doesn't have an outpatient palliative care program that could integrate with the ongoing care in the cancer clinics. This year we kept $20,000 aside to help get this new initiative off the ground.

New LCCF Board Members



James Degregori, PhD– Dr. DeGregori is a Professor in the Department of Biochemistry and Molecular Genetics at the University of Colorado and the Associate Director for Basic Science in the University of Colorado Cancer Center. He received his undergraduate degree in microbiology from the University of Texas and his PhD in biology from MIT. He has been on faculty at University of Colorado since 1997. Studies in the DeGregori lab are geared towards the development of novel therapeutic strategies to treat non-small cell lung cancers. The lab performs genome-wide screens using novel genetic methods to identify genes whose inhibition will synergize with current targeted therapeutics to eliminate lung cancer cells. Their screens have identified a number of genes that synergistically inhibit NSCLC cells, in combination with clinically used targeted inhibitors, and these genes have been validated as therapeutic targets by using both pharmacological and genetic approaches. These studies could lead to discovery of adjuvants to current therapies that will more effectively treat or possibly even cure these devastating cancers.

York E. Miller, MD – Dr. Miller is a pulmonary physician with a primary clinical base at the Denver Veterans Affairs Medical Center. He is the co-Leader of the University of Colorado Cancer Center Lung, Head and Neck Cancer Program, co-Principal Investigator of the Specialized Program of Research Excellence in Lung Cancer and the Thomas L. Petty Endowed Professor of Pulmonary Research. His research is focused on the early detection of lung cancer through CT scanning and bronchoscopy as well as the development of agents to prevent the development of lung cancer. Dr. Miller is a member of a collaborative team, including Drs. Robert Keith, Mark Geraci and others, which is evaluating the effect of inhaled iloprost on premalignant airway lesions. If an effective agent to prevent lung cancer can be developed, large number of former smokers could potentially benefit.



Michael J. Weyant, MD – Dr. Weyant is an Associate Professor of Surgery in the University of Colorado Denver School of Medicine. He received an undergraduate degree in biology from Syracuse University, and graduated from the Mount Sinai School of Medicine in New York. He completed a residency in general surgery at the New York-Presbyterian Hospital and Weill Medical College of Cornell University, before continuing his training in New York, entering a fellowship in thoracic surgery at Memorial Sloan-Kettering Cancer Center. Dr. Weyant joined the University of Colorado medical school faculty in 2005. Dr. Weyant's clinical interests include areas of minimally invasive thoracic surgery pertaining to lung, esophageal, and mediastinal tumors. Dr. Weyant also actively performs research in several areas including early detection of lung cancer and the molecular biology of lung and esophageal cancer. He is an invited specialist in thoracic surgical oncology for several national and international societies including the society of thoracic surgeons, American Association of Thoracic Surgery, and the International Association for the Study of Lung Cancer.

Paul A. Bunn, Jr, MD earns 2014 "Giants of Cancer Care" award

Erika Matich

University of Colorado Cancer Center investigator Paul A. Bunn, Jr, MD, has been named one of the 2014 "Giants of Cancer Care" by OncLive, the official home of Oncology & Biotech News, OncologyLive, Urologists in Cancer Care, Oncology Nursing News, Oncology Business Management and Contemporary Oncology.

Bunn is one of 16 luminaries nationwide selected by oncology industry peers for remarkable achievements in research and/or clinical practice. The Giants of Cancer Care awards recognize and celebrate individuals who have achieved landmark success within the field of oncology.

Bunn's research interests focus on novel therapies for lung cancer. He has published more than 300 articles in peer-reviewed journals, over 122 reviews and editorials, and 90 book chapters on lung cancer. His studies have set standards for the treatment of lung cancer, have identified issues of natural history and have identified biomarkers of prognosis and therapy selection. Bunn has been the principal investigator on numerous national and local therapeutic trials and is also the principal investigator for the SPORE grant in lung cancer that is designed to conduct translational research in lung cancer.

Giants are chosen by an exclusive advisory board of 29 oncology educators, clinicians and researchers. Advisory Board members have dedicated their valuable time to the program, providing guidance to OncLive as it further develops the program and, most importantly, selects the oncologists who will be named Giants.

In evaluating criteria for selection to the inaugural class of Giants, the Advisory Board considered individuals who have made a significant contribution to patient care, clinical trials or translational research. One Giant will be named the Pioneer, an oncologist that has amassed a large body of work and have already accomplished their most notable contributions to oncology.

OncLive Chairman and CEO Mike Hennessy said, "It is our distinct privilege to honor these unsung medical heroes. It is our mission to continue recognizing the leaders in the oncology field for their remarkable achievements in research and clinical practice."

The 2014 Giants of Cancer Care were announced and honored at an invitation-only reception Friday, May 30, in Chicago.

Lung Cancer Awareness Video Gains 5000 Views in 18 Hours

Kim Ringen, a veterinary oncologist, diagnosed herself with advanced lung cancer after finding a lymphnode above her own collarbone one day. Recently, she made a lung cancer awareness video and through facebook achieved almost 5,000 views in the first 18 hours. Kim is an awe-inspiring person and we are proud to share her awareness raising video with you.

http://youtu.be/KSaOlEkGCjU

THE "WORLD CONFERENCE ON LUNG CANCER" IS COMING TO DENVER, COLORADO!

Under the auspices of the International Association for the Study of Lung Cancer (IASLC) Denver will be hosting the next World Conference on Lung Cancer, September 6-9, 2015 at the Denver Convention Center. Nearly 10.000 from all over the world participants are expected to attend the conference. Participants will include all disciplines dealing with lung cancer care, including nurses and patient advocates. The program will include scientific programs and educational tracks for doctors of all specialties, and (new for this conference) specific tracks for health care personnel in community practices, for nurses and for patient advocates.

In conjunction with the conference there will also be several awareness events, such as a 'Lung Fun Run' on Sunday, September 6 where celebrities, doctors/nurses, patients and their families will be invited to participate and run/walk together. This particular event is arranged in collaboration with the Addario Lung Cancer Foundation. Special gifts are planned for all participants!

The local committee for the 'World Conference', which includes experts from the University of Colorado and the National Jewish Health, has diligently worked over the last year to prepare what should be the largest success in the IASLC's 40 year history, and we welcome all health care personnel dealing with lung cancer, patients and their families to take part in this historical event.

For further information, please see www, iaslc.org or contact pia.hirsch @ iaslc.org

University of Colorado's Online Screening for Rare Lung Cancer Subtypes Opens Door to New Kind of Clinical Trial

Garth Sundem

In the previous few years, several breakthrough treatments have become available for key subtypes of lung cancer. Patients who may benefit from these treatments can be pre-identified by looking for defined genetic abnormalities in their cancer. For example, patients whose lung cancer is driven by rearrangement of the gene ALK derive significant benefit from the drug crizotinib, which targets this abnormality. Many ongoing clinical trials are now attempting to replicate this success by matching different drugs with specific subtypes of the disease based on the presence of such "predictive biomarkers." However, testing these new drugs in clinical trials requires finding and enrolling patients with what may be very rare molecular subtypes of a disease – one of the challenges is discovering enough needles in enough haystacks to prove the effectiveness of each biomarker-drug pairing.

The University of Colorado Cancer Center is now taking a novel approach to this problem, reaching out via the internet to expand the pool of patients potentially eligible for just such a biomarker-preselected clinical trial. After completing the interactive online screening questions, eligible patients with advanced lung cancer will be consented via the phone to permit a pre-existing biopsy sample of their lung cancer tissue to be shipped to the CU Cancer Center for trial-specific molecular testing. The testing is designed to identify patients who may have lung cancers driven by alterations in the gene FGFR1. Patients whose tumors turn out to be FGFR1-positive and meet the other trial screening criteria will then be offered treatment for their cancer within a clinical trial at CU Cancer Center using the experimental FGFR1 inhibitor drug ponatinib. Ponatinib is already licensed for treating certain blood cancers, but work by CU scientists in laboratory models suggest it may also be a potent agent in some specific molecular subtypes of lung cancer driven by, among other things, changes in the FGFR1 gene.

"FGFR1 has already been explored by the pharmaceutical industry, with rather limited success, but those approaches

University of Colorado's Online Screening for Rare Lung Cancer Subtypes Opens Door to New Kind of Clinical Trial

continued from page 11

used a very different way of looking to see if FGFR1 was driving the lung cancer," says Ross Camidge, MD, PhD, director of the thoracic oncology clinical program at the CU Cancer Center and the trial's principal investigator. "Based on some really innovative work coming out of our own Specialized Program of Excellence in Lung Cancer, the tests we are employing in this trial seem to define a completely separate subtype of lung cancer – one that has really not been explored before. Now the challenge is in finding enough people whose cancers are positive for our biomarkers to prove whether the markers will predict for clinical benefit from ponatinib."

Having built the infrastructure to allow nationwide molecular prescreening for the trial, Camidge's team plans to also use internet awareness to speed accrual into their trial.

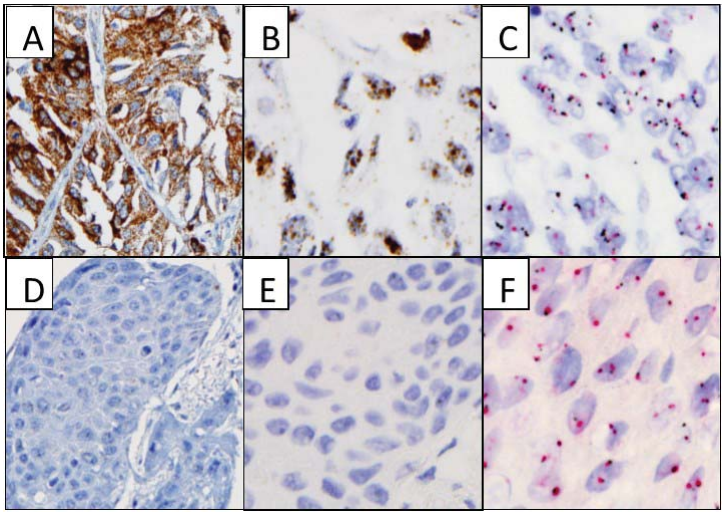
"We know that the vast majority of the U.S. population now routinely uses the internet to find out about medical conditions, so we thought we'd get Dr. Google to help us out," says Camidge. "Several very high profile internet resources for lung cancer patients, including the Bonnie J. Addario Lung Cancer Foundation (BJALCF - http://www.lungcancerfoundation.org) and the Global Resource for Advancing Cancer Education (GRACE - http://cancergrace.org) have helped us craft this trial and we are very grateful for their commitment to increase awareness about the opportunity it presents for lung cancer patients who might benefit from the molecular prescreening."

Indeed, Dr Jack West, the CEO of GRACE, co-wrote a position paper (http://www.ncbi.nlm.nih.gov/pubmed/22334010) with Camidge in the Journal of Thoracic Oncology in 2012 titled "Have Mutation, Will Travel" to highlight the pressing need to transform the way clinical trials are conducted in the new era of molecular diversity.

"While Big Pharma sometimes spends millions of dollars to open biomarker-selected trials at hundreds of different locations to find enough patients, the kind of innovative approaches that are homegrown in university settings will never have the resource to do that," said Dr West. "Regardless of whether the FGFR1-ponatinib pairing works or not, what the Colorado team is trying to do could really change the future of clinical cancer research for the better. Patients are increasingly becoming empowered about their own cancer care. Anything we at GRACE can do to get the word out about the Colorado approach will be a very good thing."

Bonnie Addario, chair and founder of the BJALCF and a ten-year lung cancer survivor herself, is similarly enthusiastic. "If we are going to change the survival rates for lung cancer, we have to stop treating everyone the same. We have to do things differently, and if Dr. Camidge's approach can bring a little bit of Colorado's expertise into easy reach of anyone with a computer, then this is a new way of accelerating the process and much more convenient for the patient. We will do all we can to assist in getting patients involved in this exciting new approach," Addario says.

Over the next 3-5 years the Colorado team plans to screen up to 700 lung cancer patients and optimize the biomarker signatures for predicting benefit from ponatinib over time, tweaking the criteria as they go along based on the emerging results in each group of treated patients.



Fibroblast Growth Factor Receptor 1 testing in resected lung cancer specimens. A, B and C show positive protein, message and gene copy number expression, respectively. D, E and F show negative samples for the same tests.

"Clinical research is very expensive and sources of support for this kind of clinical research, as for everything else, are rather limited," says Camidge. However, Camidge's novel approach has already allowed him to secure several hundreds of thousands of dollars in support from sponsors including the manufacturer of ponatinib, Ariad, from the CU Cancer Center and from the CU Lung Cancer Specialized Program of Excellence in Lung Cancer.

"However, if this trial takes off, that's probably only about half of what we'll need. That's why we've taken to the internet to crowd-source trial accrual through the Consano philanthropy website. It's amazing — the internet is giving us new opportunities at every turn. I am very optimistic; although we are having to do this on a very limited budget, I know from experience that we can produce major breakthroughs even from a small study if the approach is right," Camidge says.

University of Colorado's Online Screening for Rare Lung Cancer Subtypes Opens Door to New Kind of Clinical Trial

continued from page 12

Please visit the trial enrollment website (http://www.ucdenver.edu/academics/colleges/medicalschool/centers/cancercenter/CancerCare/lung-cancer-ponatinib-trial/Pages/Home.aspx) and the study description at ClinicalTrials.gov (*https://clinicaltrials.gov/ct2/show/NCT01935336?term=ponatinib+camidge&rank=1*) to learn more about the study. As the goal of this study is to find as many advanced stage lung cancer patients who might benefit from this trial as possible, Dr. Camidge and his team would be very grateful if you would consider sharing this information via your own social media outlets.

Purrfectly Gigi

By Reagan Hudgens

In the spring of 2013 my mom, Dorothy Hudgens, was diagnosed with lung cancer. The diagnosis stunned us. Mom was a very active person with a healthy lifestyle. We thought that being a never smoker meant never getting lung cancer. She was a retired teacher, entrepreneur and real estate agent. At the time she was enjoying retirement with my dad, playing bridge, volunteering and actively engaging in life.

As mom started treatment, I started planning a Gigi calendar for my parents. Gigi is a spirited tabby that came to my parents' home as a foster kitten and never left. She has a unique willingness to accessorize that began when she occasionally modeled baby hats mom was knitting for the hospital. Mom and I thought perhaps others would enjoy Gigi's special beauty and we could raise funds for lung cancer research with her pictures. Purrfectly Gigi was born.

Gigi – with hat, pearls and snaggle tooth

Mom loved cats and loved using Gigi pictures to create something upbeat…something that might make people smile. We created a calendar and cards. Our goal was to produce fun items, with each purchase benefiting lung cancer research. We wanted to support this cause without screaming cancer. We also wanted to communicate that anyone can get lung cancer, that funding for research is badly needed and small gestures are important. Mom chose to donate proceeds to the Lung Cancer Colorado Fund after a patient consultation with Dr. Camidge and learning about advances being made at University of Colorado.

Back row: Mom (Dorothy) and Dad (Ron)

Front row: Peach and Gigi

During this time my dad was also diagnosed with cancer. We found working on this small project provided a positive focus for a challenging situation. The project proved to be both comforting and uplifting.

Sadly my mom passed away in 2014. She maintained her sense of dignity, her wit and her joy for life throughout her illness. She got a kick out of Gigi's photos, loved the Gigi project and felt positive about supporting research. Every calendar and card sold boosted her spirits and made her feel we could make a difference. We continue Purrfectly Gigi in her honor (www.purrfectlygigi.com).

Team Draft - A Survivor at Every Stadium 2014

Chris Draft

In November 2012, Team Draft celebrated Lung Cancer Awareness Month by launching its inaugural Survivor at Every Stadium initiative on CNN during a nationally-televised prime time special focusing on the disease and a National Campaign to Change the Face of Lung Cancer. The initiative proved to be an immediate and overwhelming success. By the time this first "national celebration of survivorship" concluded at the Pro Bowl in Hawaii, lung cancer survivors representing 30 different cancer centers and nearly every NFL team had participated. In its second year, the Survivor at Every Stadium initiative expanded to create a Survivor Series by branching out beyond the NFL to include the NHL and NBA, among others. The Survivor at Every Stadium initiative also grew by adding the NFL's International Series in London, specially designated lung cancer awareness games here at home—including the Monday Night Football game between the Green Bay Packers and the Chicago Bears—and a national media tour, which resulted in more 35 national and local media placements, reaching more than 13 million people.

Michael Moore (middle), stage IV lung cancer survivor, with his two brothers at the CU Buffs game courtesy of Team Draft

Through this growing initiative, lung cancer survivors and lung cancer doctors from local cancer centers and their guests attend one of the local NFL or College team's home games during the months of October and November.

Our goals are to create a unique experience for participating survivors and to raise awareness on a local and national level by using each game and each survivor's story to weave a broader narrative about the state of lung cancer and the hope that now exists for those battling the disease. This year, in Colorado we were thrilled, as before, to have so many survivors to offer this opportunity to. Enjoy the photos!

Chris Draft
Founder, President, and CEO
Chris Draft Family Foundation
www.teamdraft.org

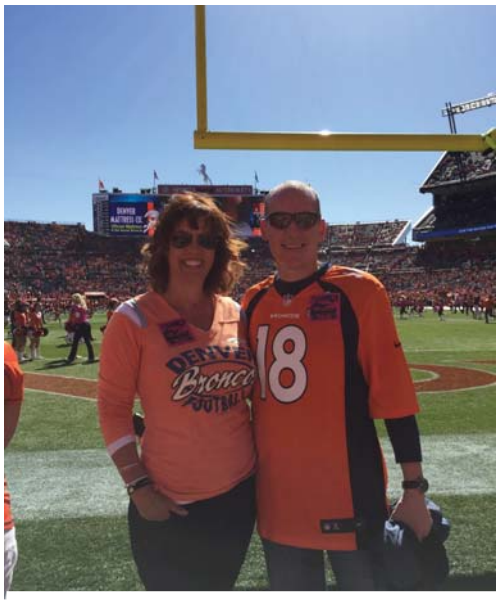
What is Team Draft?

Team Draft is an initiative of the Chris Draft Family Foundation created by nationally recognized health advocate and former NFL linebacker, Chris Draft and his late wife, Keasha during Keasha's year-long battle with lung cancer. Their hope was that Keasha's valiant fight to dance, smile and live would give hope, comfort and inspiration to the patients, caregivers and healthcare providers who are battling the disease every day.

While attending Clemson University, Keasha was a member of the Rally Cat's dance squad before graduating with a degree in Electrical Engineering. After graduation, Keasha worked as an engineer while dancing for the NBA's Charlotte Hornets before working in the pharmaceutical industry. She was an energetic, vibrant young woman who had never smoked when she was diagnosed with Stage IV Lung Cancer in December 2010. At the time, her only "symptom" was a slight shortness of breath a few days earlier. Despite

the diagnosis and knowing the long odds they faced, Keasha and Chris decided to fight back. On November 27, 2011, standing side-by-side, they launched Team Draft at their wedding. One month later, Keasha lost her courageous fight and died at the age of 38.

Andy Bonnett (left), Stage IV NSCLC survivor, and friends at the Arizona State game courtesy of Team Draft



Jonathan Wilmot, stage IV lung cancer survivor, and his wife enjoying the Broncos end zone courtesy of Team Draft

Can Exercise Actually be a Form of Anti-Cancer Treatment? ...You Bet It Is!

Tom Purcell, MD, MBA

Cancer treatment has evolved into a complex sequence of surgery, radiation and chemotherapy. Often neglected are supportive care oncology programs such as nutrition, psychological assistance, fertility issues, prehabilitation and rehabilitation and cancer exercise. It has been shown that patients who have at least moderate or vigorous exercise have lower recurrence rates for several cancers, including breast and colon cancer. Evidence for primary, secondary and quality of life improvements continue to develop with exercise being a key component of improving each of these areas. Treating cancer patients as 'athletes' by developing specific programs for cancer nutrition, exercise and other areas of supportive care oncology to supplement traditional treatments is now evolving. Issues such as understanding a patient's metabolic function, mitochondrial efficiency and lactate clearance are topics of future cancer exercise research.

Balancing lifestyle and genomics research for cancer prevention has been a major focus of clinical research. The "big four" modifiable risk factors for patients include tobacco use, diet, obesity and lack of exercise. Only 25% of adults in the United States meet the recommended requirements for exercise. 58% of adults are sedentary and do not participate in any exercise. The Cooper Institute has shown that as patients' age, the lack of cardio-respiratory fitness can be a key predictor of a higher death rate in both the 70-79 year age group and in patients over 80 years old. Unfortunately, oncology providers do not recommend exercise as frequently as you would think. In a Mayo clinic survey, less than 50% of oncology patients have discussed exercise with their oncologist. When exercise came up as a topic, there was just 'general encouragement to be active' and not a specific prescription of how exercise should be approached.

Tom Purcell, MD MBA, Associate Professor of Medical Oncology

A key question is "Why would exercise actually help in the management of cancer?" Research has shown that exercise decreases insulin production and high circulating levels of insulin have been linked to the development of certain cancers. Exercise also lowers levels of biologically available sex hormones which have some effect in diseases such as breast, ovarian and endometrial cancer. Physical activity also decreases colon transit time which could decrease colonic exposures to carcinogens within the stool and people who are physically active may an increased intake of non-steroidal

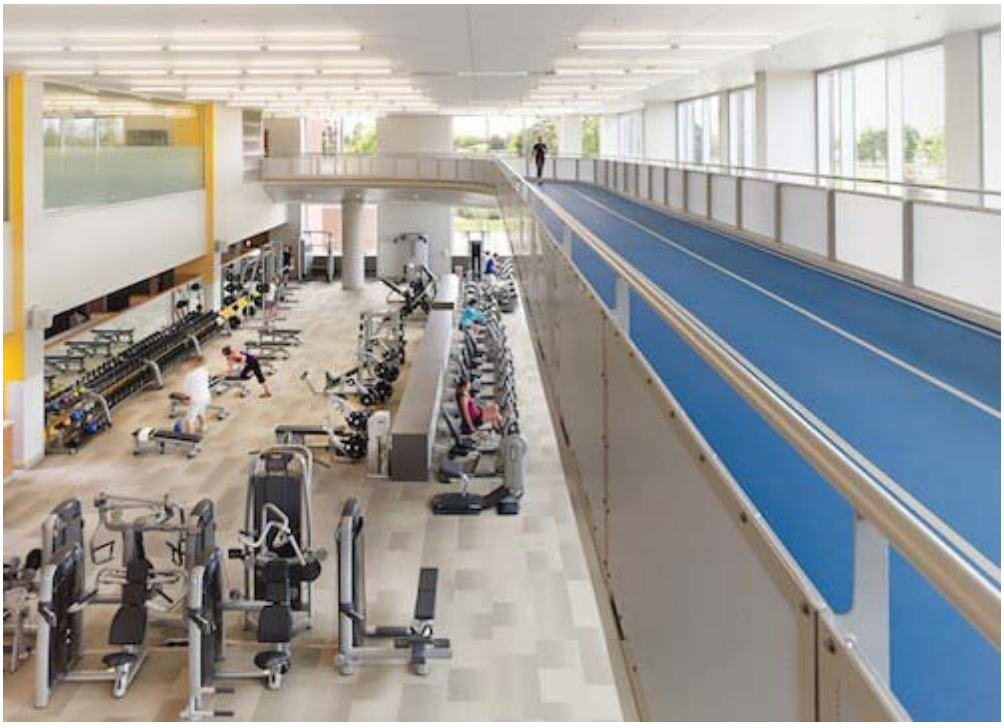
anti-inflammatory drugs like aspirin or ibuprofen, which are associated with decreased colon cancer risk. There is also the possibility that mitochondrial function, mitochondrial density in skeletal muscle and the ability to clear lactic acid could have something to do with the overall success of oncology treatment.

What is the actual evidence for reduced cancer risks you may ask? In 2013 in the Journal of Clinical Oncology, the Cooper Institute published results of 17,049 men who were enrolled in the study with a median age of 50 and were followed over the next 20 years. Of the 17,049 men, 2,885 men were diagnosed with prostate, lung or colorectal cancer. The hypothesis for the study was that people with lower fitness were at more risk for developing cancer later in life. Men who had high cardio-respiratory function, measured by a treadmill test, had a 68% less chance of developing lung cancer and a 38% less chance of developing colorectal cancer. Interestingly, there was no effect on the incidence of prostate cancer. The Cooper Clinic, in a previous study, has shown that patients with high cardio-vascular fitness have a lower risk of death from all causes in comparison to other patients with similar risk factors such as hypertension, Chronic Obstructive Pulmonary Disease, diabetes, smoking, BMI greater than 30 or hypercholesterolemia.

Routine physical activity is also associated with a 20-30% relative risk reduction in the incidence of breast cancer in comparison to inactive women. There is also significant evidence for secondary prevention which originated from the Nurses' Health Study. In the Nurses' Health Study, women with potentially curable breast cancer who exercised either moderately or vigorously had a 30-40% reduction in breast cancer recurrence in comparison to those who did not exercise. Exercise has also been associated with numerous areas of improvement of quality of life in cancer patients, particularly with relation to treatment-related side effects. This includes improvement in confidence, body image, decreases in stress and improvement of sleep, improved effectiveness of the immune system, decreasing fatigue, improvement in physical and psychological function as well as improvements in connective tissue integrity and improved carbohydrate, fat and protein metabolism.

Unfortunately, for greater than 70% of the United States population, there is an inability or unwillingness to meet the minimum physical activity guidelines as established by the American College of Sports Medicine. At the University of Colorado we have now launched an exercise and wellness program for all cancer patients treated at the Anschutz Cancer Pavilion. This program, called "Fit2BWell" focuses on exercise with a designated one on one cancer exercise specialist to coach and safely instruct each participant at the Anschutz Health and Wellness Center on campus. There is a comprehensive wellness report providing insight into physical and metabolic fitness, diet and nutrition, sleep and stress and quality of life. Numerous research metrics are tracked both before and after the program and are reviewed with each participant.

If you have any questions or wish to pursue the Fit2BWell program, please contact Dr. Tom Purcell at tom.purcell@ucdenver.edu.



The state-of-the-art new Anschutz Health and Wellness Center

Putting your lungs to work: Singing the National Anthem at the Cubs game

Ginger Tam, a stage IV lung cancer survivor, who flies from Chicago to receive treatment in a clinical trial of a new EGFR inhibitor at the University of Colorado was asked to sing the national anthem at a Cubs baseball game to raise awareness about lung cancer. Watch this stunning video and feel the hairs stand up on the back of your neck. What a voice!

https://www.youtube.com/watch?v=JxVA_QC9QLU

Ginger Tam singing the National Anthem at Cubs Game

I think the treatment is working: Matt has not left the dance floor in 3 hours

Mandie Hiznay

Lung cancer is one sneaky disease. It creeps up on you and taps you on the back without warning, especially if you are a healthy 24 year old never smoker. Matt Hiznay (my son) developed a cough during a summer internship after he had completed his first year of medical school. Being an allergy patient, he thought it was a seasonal flair up. Little could anyone guess that one month later (August 26, 2011), he would receive a diagnosis of Stage IV lung cancer. A week after that, Hiznay found himself in the ICU of the Cleveland Clinic, on a ventilator, with tubes draining the fluid from around his heart and both lungs. According to Matt, "the hill got really steep really fast." But if one word personifies my son, that word would be HOPE. That is something Matt has never lost, despite the often grim statistics that go along with his diagnosis.

Although something terrible happened to Matt on August 26th, something very good happened as well. The FDA approved a new lung cancer drug (Xalkori) for people with a specific type of genetic mutation that affects about 4% of lung cancer patients. After testing positive for the anaplastic lymphoma kinase (ALK) mutation, the drug was overnighted to Matt's bedside in the ICU on September 10th. Within a week, all tubes were removed and he was transferred out of the ICU. He walked out of the hospital one week later, and on November 10, 2011, his CT scans showed no evidence of his cancer. If this were a fairy tale, the story would end here with the prince living happily ever after. But as is said in the first line of this story, lung cancer is one sneaky disease.

In May of 2012, after making preparations to return to medical school, the lung cancer found a way to become resistant to the Xalkori. While doing extensive research on the disease, one name that appeared often was a doctor at the University of Colorado. With the help of his Cleveland Clinic oncologist, Matt and I soon found our way to Colorado. There, doctors were working on a clinical trial for a new drug named LDK378. He entered the trial, and several weeks later had a dramatic response. Realizing that medical school was no longer an option, Matt entered a Molecular Medicine PhD program to study the very basis of the disease he was battling. Another very important event happened that summer – he got engaged to his college sweetheart Ally Stojkoska.

The LDK378, which eventually gained FDA approval, worked for five months until the cancer became resistant again. Our University of Colorado and Cleveland Clinic doctors consulted, and, based on Colorado research, it was decided Matt would go on a specific chemotherapy regimen beginning in November of 2012. After 6 treatments of 3 drugs, Matt had a complete therapeutic response to the medication and began maintenance chemo every three weeks. With the cancer in check, at least for the time being, Matt and his fiancé began to make plans for their June 14, 2014 wedding. His mantra: "Never give up hope. Believe in God, believe in medicine, and believe in yourself."

Ally and Matt tie the knot

Fast forward to April 2014 –an uninvited guest would try to ruin the wedding. The sneaky lung cancer was back. With a collaborative effort between the medical team at CCF and CU, it was decided Matt would add in radiation treatments. Never one to give up hope, Matt was determined that the cancer would not interfere with one second of his wedding day. Hiznay had his 26th (of 32) radiation

treatments the Thursday morning before his wedding, and took the rest of the weekend off from treatment. He and his bride enjoyed every minute of their wedding day. Guests included his CU doctor and our oncology team from CCF.

In August, following more collaboration between Cleveland and Colorado, and again based on some research conducted in Colorado, Matt opted to rechallenge the cancer with Xalkori. Latest scans show he is responding to treatment. He was able to enjoy himself while dancing at another friend's wedding in October (when I sent the email to his doctor that is the title of this article). Throughout it all, he has remained on schedule in his PhD program, and is now in his third year. He speaks often to educate others about lung cancer and the importance of raising funds for research. His bride graduated from pharmacy school and is doing a residency at St. John Medical Center. The newlyweds live in Cleveland.

Matt is now 'starring' in a series of videos arranged by the Bonnie Addario Lung Cancer Foundation designed to give faces to those with lung cancer who are doing well. Check out the final cut of Matt's story in the Bonnie Addario Lung Cancer Foundation here:

https://www.youtube.com/watch?v=DhQqE-MDqEE

It has been rumored that when the 2015 edition of Webster's dictionary is released, a picture of Matt Hiznay will appear next to the definition of the word HOPE.

I think the treatment is working: Matt (in the middle) has not left the dance floor in 3 hours

Responses with crizotinib in MET-amplified lung cancer show new targetable form of disease

Erika Matich

A study presented at the American Society of Clinical Oncology (ASCO) Annual Meeting 2014 reports the results of a first-in-human, phase 1 dose escalation trial of crizotinib (XALKORI) in 14 patients with advanced, MET-amplified non-small cell lung cancer (NCT00585195).

In 2011, the drug crizotinib earned accelerated approval by the US FDA to target the subset of advanced non-small cell lung cancers caused by rearrangements of the anaplastic lymphoma kinase (ALK) gene, and subsequently was granted regular approval in 2013. The drug also has shown dramatic responses in patients whose lung cancers harbored a different molecular abnormality, namely ROS1 gene rearrangements. Previously unreported phase 1 clinical trial results now show that crizotinib may have a third important molecular target. In advanced non-small cell lung cancer patients with intermediate and high amplifications of the MET gene, crizotinib produced either disease stabilization or tumor response. Sixty-seven percent of patients with high MET amplification showed prolonged response to the drug, which lasted from approximately 6 months to nearly 2.5 years.

"Though more patients are needed to really pin down the exact MET criteria that will predict benefit from MET inhibition, we're hopeful this line of research will define yet another key molecular subtype of lung cancer sensitive to a targeted drug," says Ross Camidge, MD, PhD, director of the thoracic oncology clinical program at the University of Colorado Cancer Center and the study's lead author.

Crizotinib showed early activity against MET-dependent cells in preclinical laboratory studies, and the phase I clinical trial design included plans for treatment of cancer patients preselected for evidence of MET activation once the recommended dose was determined.

Matching the drug to MET amplifications required testing for this genetic abnormality in patient tumors, something that hasn't been part of standard lung cancer screening in most clinical centers. Working at the CU Cancer Center, Marileila Garcia, PhD, was able to rapidly deploy an assay for MET for the trial based on fluorescent in situ hybridization (FISH).

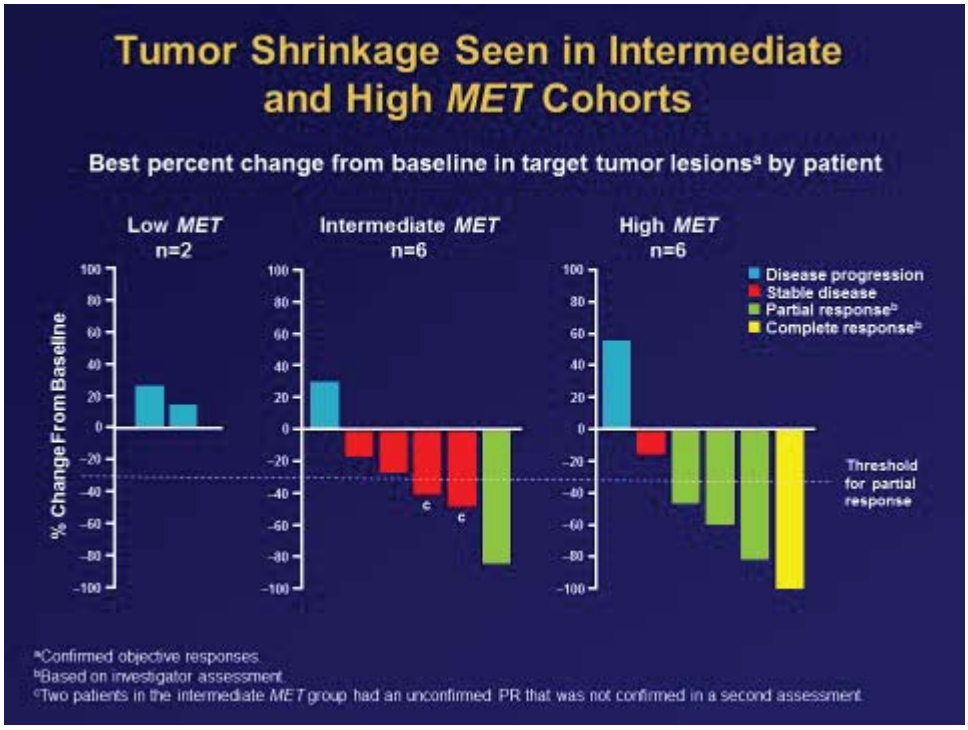
Garcia's previous work, also shown for the first time in this presentation, gives insight into the frequency of MET amplification in lung cancer. Consistent with other reports, Garcia found some degree of MET amplification present in 7.4 percent of 800 consecutive samples of non-small cell lung cancer tested at the Colorado Molecular Correlates Lab from 2009 to 2012. However, the level of MET amplification in these samples was not uniform. Low MET amplification (MET/CEP7 ratio of ≥1.8–≤2.2) was present in 3.8 percent, intermediate amplification (MET/CEP7 ratio of >2.2–<5.0) was present in 3 percent, and high amplification (MET/CEP7 ratio of >2.2–<5.0) was present in 0.8 percent.

In the phase 1 clinical trial, while disease in the 2 patients with low MET amplification did not appear to benefit from the drug, 1 of 6 patients with intermediate MET amplification achieved a partial response with 4 of the 6 having more minor responses (stable disease), and in the high MET amplified group 1 of 6 achieved a complete response, 3 of 6 achieved a partial response and 1 of the 6 had a minor response (stable disease). Overall objective response rates in the low, intermediate and high MET amplified cohorts were 0, 17 and 67%, respectively.

"We've been through a similar experience with ALK-positive lung cancers – patients whose cancers depend on a specific molecular abnormality can see significant benefit when we remove the cancer's access to the driving abnormality," Camidge says. "However, unlike classical activating mutations or gene rearrangements, MET is likely to be a more challenging biomarker because it is not simply black or white – not simply off or on – but rather it is a continuous variable. Although the dataset is still pretty small, there is a strong suggestion that a definable cut-point in MET amplification exists which could really delineate who will or will not benefit from this drug. Screening for MET amplification and treating these patients in clinical trials is the only way we will be able to discover this important threshold."

The implications of crizotinib used to target MET amplifications may go beyond non-small cell lung cancer. The gene is activated in many different ways in many different cancers, and patients with MET-amplified cancers continue to enroll in the crizotinib phase I study.

"With these targeted therapies, it can look at first like a drug may only be useful to a small percentage of patients with the targeted genetic abnormality. But then you start to see the same abnormality across cancer types and the drug that looked like it might have been useful in, say, 3 percent of lung cancer patients, turns out to have a use in x-percent of all these other cancer types as well. It's a new paradigm: we're working to pick off these molecular aberrations one by one," Camidge says.



Waterfall plot (each bar represents the size of tumors in an individual) showing the influence of MET amplification levels on sensitivity to a MET inhibitor.

The First Year. . .

Barb Cassou

I became a Lung Cancer widow on September 10th, 2013, less than two months after my 50th birthday. My husband Bob was diagnosed in March of 2008 and fought for five and a half years to spend as much time as possible with me, our daughter Nicole, age 18 at the time of his death, and my step-children, his twins, Christine and Alex, ages 33.

When someone you love has fought and suffered for such a long time you say out loud, "it was a blessing" when they pass. It is so difficult to watch your spouse go through surgeries, multiple rounds of chemo, radiation and oral drug therapies, with all of their debilitating side effects, and then finally hospice, and not feel a sense of peace when they are gone. However, I have learned that the peace or blessing I have spoken of has been shattered time and time again as I navigate my new life without my partner of 25 years, and without my only child's father.

Thanksgiving 2013

The house was full of laughter and lots of conversation today. That was intentional. Nicole, my DU Freshman swimmer invited two of her International teammates to our home for the weekend, and I had one of my closest friends' and her family join us for dinner. I knew the first major holiday would be difficult; however, we were successful in our efforts to avoid grieving all day by filling the house with people and activity. When it was time to eat, I took the head of the table, the place where Bob always sat, and I could not hold back my tears any longer. I missed his booming voice, his laughter, his urging me to hurry up and sit before the food got cold. My girlfriend Stephanie led us in the Lord's Prayer, and we toasted to friendship. I dried my eyes and diverted my attention, watching the two young adults who had never participated in an American Thanksgiving devour my traditional food.

I thought the toughest part of the day had passed, but tonight, now that everyone is gone, the kitchen is clean and the college kids are asleep, I feel devastatingly alone. I am exhausted and in our king size bed, by myself, and have been trying to pray. I have so much to be thankful for, don't I? I should give thanks for all the good things in my life, but I cannot. I cannot be thankful today, and I simply cannot pray. Why God? Why Bob? Why me? Why my innocent Nicole? I cannot pray. . .

Hawkeye Invitational – University of Iowa, December 2013

Arriving at the same hotel as the DU Swim Team just past 7 p.m., I am excited as it is Nicole's first big collegiate meet. I am hoping to see her before the team's curfew, and I am hungry, so I text her and ask if she can meet me at the hotel restaurant. Elated to get a response right back, she has already eaten but can come and keep me company. My "little" 5'10" girl's face lights up when she starts telling me about the University of Iowa pool and the competition that starts tomorrow. "Great facility and big D1 teams with amazing swimmers!" I am so happy for her, for a fleeting moment, until her tears begin to flow. "Dad would have loved it here Mom. He would have loved seeing me race at this level of competition, at this beautiful pool. He would have been so proud of me!" How

Nicole and Barb Cassou at El Pomar Natatorium, University of Denver. The DU Swim Team has been a great support to Nicole since the loss of her Father to Lung Cancer September of her Freshman year.

do I keep it together and tell her that he is here and will always be part of every success in her life. Well I try and the words are there but I cannot compose myself. I am so sad and so angry that we are without him, that we are alone. I so want to be a pillar of strength and not have her remember these conversations with me sobbing, red-eyed, tears running down my face. But I have come to learn that is an unrealistic expectation for me. Times like these my tears are just under the surface and without a warning I fall from calm and composed to an emotional wreck. I hate attending meets by myself. I am the only freshman single parent. Ever since she was six Bob and I have been poolside together, losing our voices together, bickering about her technique together. And now, I am alone, filled with pain, unable to share the elation of her victories, and parent the agony of her defeats, without my partner, without her father.

Nicole's Septum/Tonsil Surgery – July 2014

After too many sinus infections her freshman year, and at the convincing of Nicole's ENT doctor, we are in Pre-Op at Littleton Hospital. The scene is all too familiar for both of us after sitting bedside pre-op with Bob prior to two lung surgeries, one brain surgery to remove lung cancer tumors and multiple diagnostic procedures. My husband was great in these settings with my daughter; sticking his tongue out at her to try and make her laugh so she would not worry about him. He would squeeze my hand

tightly when he would see my eyes welling up with tears, fear in my heart about the surgery and what else it may reveal in regard to his disease.

Nicole listens intently as the anesthesiologist and doctor ask questions and inform her as to exactly what will be happening in the next hour. I am holding her hand tightly, and trying to be discreet about wiping my tears from my cheeks with my other hand. My daughter has never had anesthesia and I am feeling very alone as the only parent in the pre-op area with my child. Every other bay has two people. We are both really missing Bob and uncomfortable in this all too familiar sterile environment without him. As they take her to surgery, I find the closest bathroom and come completely unglued, the tears will not stop and I cannot catch my breath. I am not supposed to have to carry the burden of events like these alone. It's too much, too stressful, no one to talk to make the time pass while she's out. . .

Seventy-five minutes later, they inform me in the waiting room that Nicole is out of surgery and doing well. They will take me back to see her in recovery when she is more awake. When that time comes, I cannot wait to see my girl! As I turn the corner and our eyes meet, I burst out laughing, there she is sticking her tongue out at me, just like her Daddy.

Bob was a Division 1 collegiate basketball player, active his whole life, and a highly successful businessman. He had never smoked, so when he was diagnosed with lung cancer in 2008 after a routine executive health screen it came as a complete shock. He had his initial surgery, thinking it was an early stage cancer, but unfortunately the cancer had already spread to the lining of his lungs. With a diagnosis of Stage 4 we immediately sought a second opinion, and quickly assessed that the University of Colorado was our choice to fight his disease. For five and a half years, the University of Colorado team was our team! They successfully tracked mutations driving Bob's cancer, using drugs, surgery and radiation to try and keep one step ahead of the disease.

When Bob passed, his doctor asked me to keep a journal of how I was coping (or sometimes not coping) with our new life, to try and help others in the future. I did not know what I was taking on when I agreed to write and share excerpts of my life. Bob and I helped set up the Lung Cancer Colorado Fund, as making a difference was important to us. This journal exercise was healing and a tool I will continue to use to help manage my grief. However, through the process I learned that it was extremely hard to find something positive to say. You cannot sugar-coat how difficult it is to navigate through life without your lover, your partner in parenting, and your best friend. After a year without Bob, if I had to counsel someone else when they are the one left behind I'd simply say, take one day at time, do not run from or bury your feelings, but do try and surround yourself with caring friends and family that will help you on your journey to the new normal.

Please start or continue to support The Lung Cancer Colorado Fund – among the LCCF's purposes are to fund creative research so those afflicted by lung cancer can be diagnosed earlier, and live longer, and more comfortable lives with those they love. . .

First Holiday without her Dad, Nicole had two International Students and Teammates from the DU Swim Team, Johanna is from Germany and Tim from Australia.

University of Colorado Hospital
FOUNDATION

Mail Stop F-485
Leprino Building
12401 E. 17th Ave.
Aurora, CO 80045

University of Colorado Hospital
FOUNDATION

University of Colorado Cancer Center

If you would like to add additional names to our newsletter distribution list, or if you wish to opt-out of receiving this newsletter, please contact Shana Spears at 720-848-5455 or shana.spears@ucdenver.edu

To contribute:

Lung Cancer Colorado Fund
University of Colorado Hospital Foundation
Mail Stop F485
12401 East 17th Avenue
Aurora, CO 80045

or online at: https://uch.thankyou4caring.org/

then choose Lung Cancer Colorado Fund from Drop down box, enter your donation amount, donation type and complete the general information requested.