



Director's Overview

Playing in the Rain...

By: D. Ross Camidge, MD, PhD

At its worst, a diagnosis of lung cancer can touch down like a tornado in someone's life. Plans are thrown around, relationships are in disarray, health is scattered. Things can seem completely out of control and, at



times, the whole experience can just feel terribly lonely. Add to that an ongoing pandemic, with hospitals stretched to the point of exhaustion, many healthcare professionals questioning their own life-choices and retiring or leaving to pursue other careers adding further chaos to patient's lives, and the future after that diagnosis can look overwhelmingly bleak.

Yet, as I gathered together the stories of patients and research breakthroughs lead by the UCHHealth and CU Medicine teams for this year's newsletter, I saw things differently. In the midst of the bad, we are often surrounded by so much good, we don't see it. Disasters give people the gift of being able to help others and the gift of letting others help them. Chaos can bring people together in wonderful, unimaginable ways. Despite the risk of tornadoes, people still find time to play in the rain.

After the last decade of research, we are almost 'used to' breakthroughs happening in patients with specific genetic changes in their lung cancers. Survival for years with advanced disease has become a commonplace occurrence for some. However, while such changes may most commonly happen in young patients who have never smoked, the danger is these 'trends' then turn into prejudices. As such, some of the delights of this newsletter are stories of patients thriving and gently pushing back against any stereotypes the world has created of who should or should not have a breakthrough on hand. Beyond our own advances in targeted therapy, the next wave of research is also moving beyond simple mutation testing and focusing on determining who will do better or worse with personalized therapy and why.

Help us to deliver the resources to keep CU at the cutting edge, through COVID times and beyond. If you are reading this and you or someone you know has a thoracic cancer - please support the LCCF and help change the world for the better. Our LCCF website includes an archive of all the past newsletters and details of where every dollar has gone.

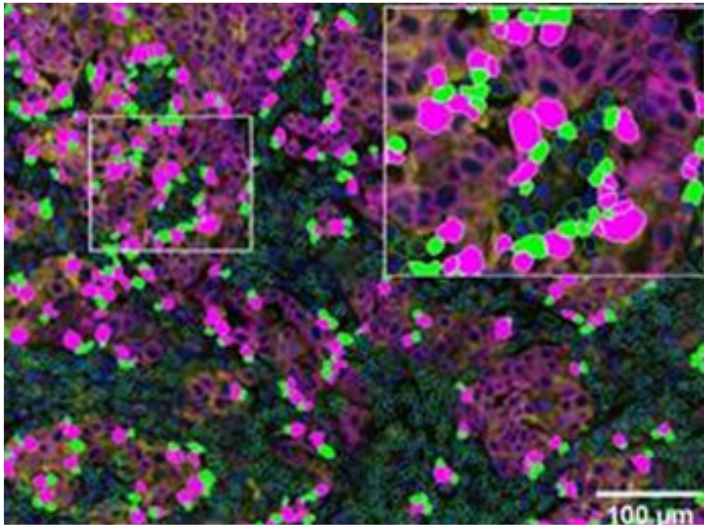
What will the future hold for those affected by thoracic cancers?

You.... Get.... To... Decide....

<https://medschool.cuanschutz.edu/lccf>

Dr. Erin Schenk leans into the innate immune system to fight lung cancer

By Rachel Sauer



Multispectral imaging reveals T cells (green) recognizing lung cancer cells (pink) in a patient's resected tumor.

One of the reasons why cancer continues developing and growing is not just because cancer cells exist, but because they can recruit help from the body's own blood vessels, stromal cells, and immune cells.

Fusion-driven non-small cell lung cancers (NSCLC) initially develop because of oncogenes, an altered form of a gene involved in normal cell growth. A common treatment for fusion-driven NSCLC are targeted therapies, also known as tyrosine kinase inhibitors (TKI) that block the effect of oncogenes, but tumors commonly become resistant and the cancers recur.

University of Colorado Cancer Center member Erin Schenk, MD, PhD, an assistant professor of medical oncology, is researching new ideas about why that resistance develops and how

these cancers could be treated by targeting innate immunity. She recently received a three-year LUNgevity Career Development Award, given by the LUNgevity Foundation to support critical lung cancer research.

"I'm really excited to have the support to keep working on these questions," Schenk says. "We're really working to understand how and why this resistance develops."

Schenk's research focuses on how innate immune cells interact with cancer cells. The innate immune system is the body's first line of defense against abnormal cells, and through her research Schenk has found that in many oncogene-driven lung cancers, innate immune cells interface with cancer cells.

"We're trying to understand how these innate immune cells interact with cancer cells," Schenk explains. "Basically, we're seeing that innate immune cells are sending care packages to cancer cells, releasing factors that are favorable to cancer cell growth."

When that interface between the two cells types happens, cancer cells are not as responsive to TKI therapies, she says. TKIs are the preferred first-line treatment for patients with most fusion-driven NSCLC because of their usual level of effectiveness and fewer side effects when compared to other treatments like chemotherapy. T cell-targeting immunotherapies, which are widely available in clinical practice, have not significantly helped patients with fusion-driven NSCLC. Schenk believes her findings suggest a different type of immunotherapy may benefit these patients.

"One of the first hurdles is conceptually helping people to understand that the immune system is important in these specific types of lung cancer," Schenk says. "Clinically, the immunotherapies we have do not work well for patients with fusion-driven NSCLC. In my laboratory, we're looking at a

new way of thinking about the immune system and fusion-driven NSCLC and hopefully identifying new targets for these patients.”

Through the support she received, Schenk’s laboratory is focused on combining therapies that deplete broad populations of innate immune cells with TKIs for fusion-driven NSCLC. These initial experiments will help establish the role of innate immune cells in TKI response. “There’s a huge diversity in these types of immune cells and we’re excited to tease out which is the key player so treatment approaches that are more specific to that cell type can be considered,” she says.

Working with tissue samples donated by patients with lung cancer, many of whom have received treatment at the CU Cancer Center, Schenk is working to identify not only the types of cells present, but also using bioinformatic approaches to study where the cells are positioned, and whether there is a significant interface between the cell membranes. In other words, whether the cancer cells and innate immune cells are “touching,” which suggests they may be actively communicating with one another.

Understanding how and where this communication is happening may lead to developing more targeted therapies to eliminate these pro-tumor innate immune cells. Ultimately, the hope is that by removing these innate immune cells, other components of the immune system have easier access to identify and eliminate the cancer cells.



Dr. Erin Schenk

“I think the benefit will be one, recognizing a new target in these patients to develop better therapeutics and two, working toward eliminating these innate immune cells that are helping the cancer and clearing the way for T cells to come in,” Schenk says. “If we can have either more tumor shrinkage with the first TKI treatment, or if we can find a way to reboot the TKI response that was lost by targeting innate immune cells, there’s a potential for patients to do better for longer.”



The CU Lung Cancer Team Virtual Run/Walk for LUNgevity at Wash Park Fall 2021 (in the future the plan is there will be a Denver in-person event with half proceeds going to LCCF)

“We Want to Give People the Opportunity to Grow Older”

By Rachel Sauer



At her lowest point, after hearing there wasn't much more that medicine or science could do for her, Connie Walters asked her best friend and ex-husband, Abel, to stay with her overnight. She wasn't sure she would wake up and she didn't want to die alone.

A part of her was ashamed she had lung cancer and embarrassed to admit her diagnosis to anyone because “a lot of times people want to say something negative or ask what you did to get it. If you smoked, there's this sense that you deserve it.

“I smoked for 40 years and even though I quit the day I got diagnosed, there were times I'd think I brought this on myself. People would say, ‘Don't be like Connie’ and that made me feel really ashamed.”

After three rounds of chemotherapy beginning in June 2012, she'd reached a point of resignation. She was coming close to accepting what felt like the inevitable end of her life after hearing there was nothing more that doctors could do for her.

However, in one final attempt to help, her previous oncologist referred her to the University of Colorado Cancer Center and Ross Camidge, MD, PhD, a professor of medical oncology and CU Cancer Center member.

Camidge and the multidisciplinary team that accepted Walters as a patient decided to perform another biopsy to get a bigger sample of the dominant mass in her right lung. Markers of specific mutations or other genetic changes driving some lung cancers have transitioned the care of advanced lung cancer in recent years. However, most of these tend to occur among those who get lung cancer and have never smoked.

Testing on Walters' previous biopsy had not shown any of these specific markers, but the sample they tested had been very small. “We wondered if something had been missed, so we thought it was worth another look,” Camidge says. Results from the new biopsy showed that Walters' cancer was ALK positive. Her cancer cells had acquired a break in the anaplastic lymphoma kinase gene. She had not been born with it, but this new change in some of her cells would turn out to be the ring leader of her particular cancer.

ALK positivity is rare in lung cancer in general – it is barely seen in one of every 20 cases – but it is even more rare to find it in someone with a significant smoking history.

“When ALK was first discovered in the late 2000s, some big cancer centers advocated to only test for it in people with lung cancer who had never smoked. We ignored that approach from the start,” Camidge explains. “It’s important that we treat every patient without judgment. With Connie we did not want to judge a book by its cover, we just said let’s give her the benefit of the doubt. The fact that she tested positive for the ALK change is one of the reasons why we shouldn’t let prejudices interfere with who we do tests on.”

For a long time, Walters didn’t have time to slow down and think about how it was getting harder and harder to catch her breath. For decades she was the lady at Denver International Airport who wore a variety of hats, from working in accounts for the companies that operated the airport’s restaurants and bars, to repairing cash registers and leading training in customer service.

She was raising a son and a daughter – Brandon and Autumn, both now adults – and setting up her own cash register repair business while being on 24-hour call for repairs at the airport. She was one of just a few women in Colorado who repaired cash registers. It was busy and high-stress, but she enjoyed the work and the financial independence it allowed her and her family.

Through the first months of 2012, though, she noticed it was getting more and more difficult to walk the airport’s long hallways and concourses. It got to the point that she was having to pause every so often and pant for air, so she scheduled an appointment with her doctor.

She tried not to think about it, but in the back of her mind was a constant reminder that her sister, Debbie, had died at age 47 of lung cancer that migrated to her bones and brain, and that her mother was also battling cancer. Walters had always been a positive thinker, so she tried to keep her mind from going to negative places.

But the first biopsy revealed the news she didn’t want: She had lung cancer. “I was in shock, despite my family history,” she said. “My whole world kind of stopped. I forgot about the airport, I forgot about fixing registers, I forgot about accounting and data input, my phone ringing non-stop. I gave notice at work because I knew I had to focus on me and on getting better, but part of me thought my life was over.”

Between June 2012 and July 2013, she had three rounds of chemotherapy that exhausted her, made her gain a lot of weight, and left her feeling bruised and broken. She felt miles away from the woman who had done every workout with Richard Simmons during her 2003 Caribbean cruise vacation with her mother.

She ended up feeling as though the physical and emotional toll has been for nothing, because the chemotherapy couldn’t kill all the cancer. Her previous oncologist, who also treated her mother, had taken Walters’ treatment as far as he could, but he gave her Camidge’s card as one of the last things he could do to help her.

When you first meet Connie, what you notice right away is that she’s the most positive person,” Camidge says. “One of the things I really like about working with people with cancer is when they’re first diagnosed, the relationship is more one-way, more about what we’re going to do for them. But

over time there's a shift in that and it becomes more two-way. I get an enormous amount out of interacting with Connie. She makes my day better, she makes all my staff happy, she gives as much to us as we have to her."

The ALK positive marker in Walters' cancer had only been described in lung cancer a few years previously. Fortunately, the CU team had been involved in the trials that lead to the first targeted drugs for treating this subtype of the disease. Because of that involvement, testing for ALK positivity had been part of the Cancer Center's routine practice for its patients since 2009. Walters started on Crizotinib pills, the first licensed ALK inhibitor, which had only been approved by the Food and Drug Administration in 2011.

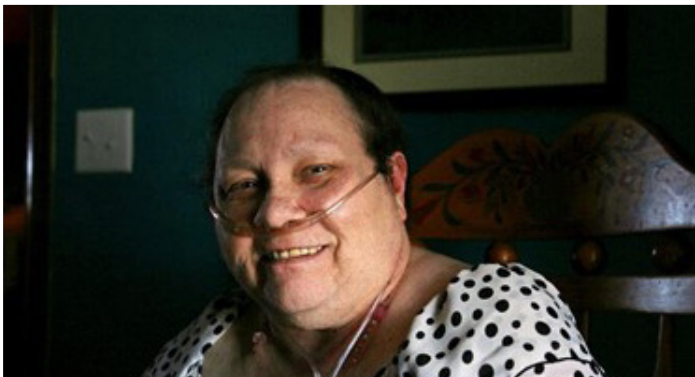
"I knew that this was kind of a 'magic pill,' but they might have hesitated to give it to me because they thought I was on death's door," Connie recalls. "I tried my best not to be on death's door, I tried to sit up straight and have some energy, but I was so sick.

"Dr. Camidge knew I was very ill, but he gave me this pill anyway – they call it a miracle pill – and it brings people back to life that are dying of lung cancer. It brought me back to life and I was like, 'Oh, my God, I'm alive again, I can function again.' I was so happy and so thankful to Dr. Camidge for that."

A few years later, however, one of the problems with Crizotinib emerged: It couldn't stop the cancer from getting into Walters' brain. Even though the rest of her body was responding beautifully to the drug, she developed about 10 sites in her brain that required focused radiation in June 2015. Three months later she joined a clinical trial for another, now-approved ALK inhibitor drug called Lorlatinib and has taken it ever since with occasional adjustments to the dose.

"There's always a reason to be happy"

"The ideal goals of treatment for lung cancer are to achieve perfect control of cancer and perfect quality of life," Camidge says. "It doesn't matter whether we achieve it or not, that's what we're aiming for. So it's not always 'no pain, no gain.' Our approach is to understand both you and your cancer. If we are controlling it, our job is also to manage all the other health issues in your life so you can be a friend and a mother and a companion. We want to give people the opportunity to grow older."



Connie Walters at home in Aurora, Colorado

Walters, now 62, laughs that she's gained years she thought she wouldn't have, and with them the various maladies of growing older. She developed diabetes and is working to manage it, as well as other conditions that have limited her mobility if not her positive attitude.

"Each day is a gift," she says. "I have Autumn and my (6-year-old) grandson here with me, and Abel comes every day. I feel blessed that I have my home and I get to be with the people I love. There was a point when I thought I wouldn't get any of this, when they told me it was hopeless, but I'm still here and there's always a reason to be happy."

A New Treatment for Brain Metastases from Small-Cell Lung Cancer

By Greg Glasgow



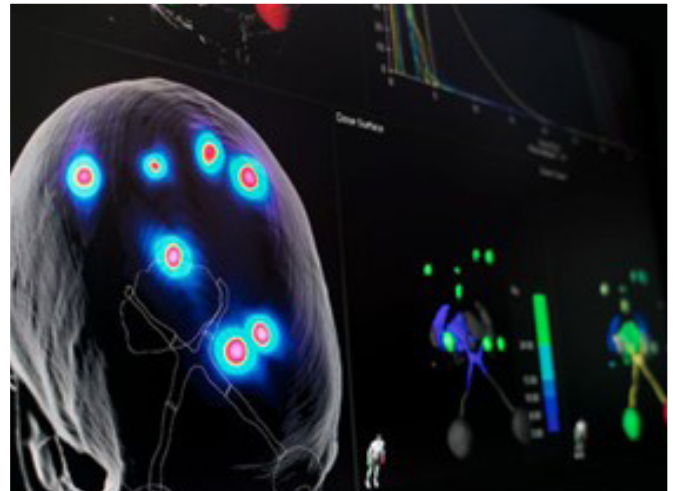
A new phase 3 randomized clinical trial overseen by CU Cancer Center member Chad Rusthoven, MD, and Vinai Gondi, MD, from Northwestern University, is testing whether a new treatment approach could result in improved

outcomes for patients with small cell lung cancer (SCLC) that has spread to the brain.

Funded by the National Cancer Institute and carried out at clinics around the country — including the CU Cancer Center — the clinical trial (NRG-CC009) will compare the effects of two different types of radiation treatment on brain metastases related to SCLC, one called hippocampal-avoidance whole brain radiation therapy (WBRT) and the other called stereotactic radiosurgery (SRS).

“Historically, brain metastases related to SCLC have been treated with WBRT,” Rusthoven explains. “WBRT treats the brain metastases you can see, as well any microscopic disease that may not be visible yet. WBRT is a well-established treatment strategy for controlling brain metastases, but it can also have side effects related to cognitive function and quality of life for some patients.”

The new treatment strategy for SCLC brain metastases that Rusthoven and Gondi are studying in this trial is SRS, a more focused type of radiation that aims to treat the individual brain metastases with as little dose to the surrounding normal brain structures as possible. SRS is most often delivered as a one-time treatment, as opposed to a common 10-treatment cycle for WBRT. In previous clinical trials that have not included SCLC patients, SRS alone has been associated with similar survival outcomes and fewer side effects related to cognitive function and quality of life when compared to treatment strategies incorporating WBRT.



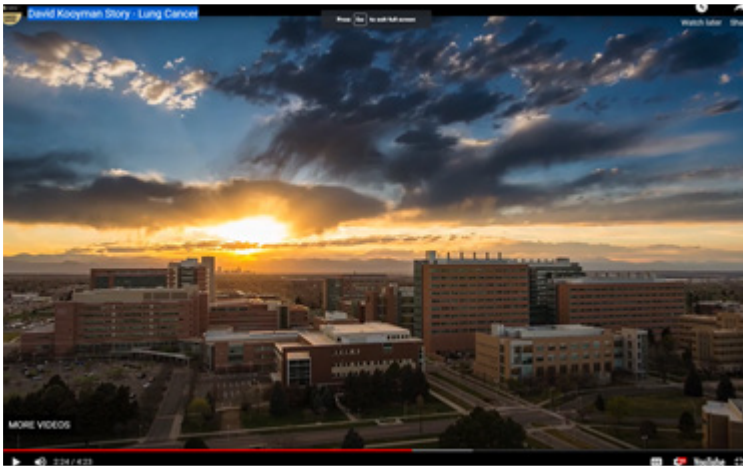
Stereotactic radiosurgery (SRS) for the brain



Dr. Chad Rusthoven

“There have been a number of randomized phase 3 trials comparing SRS to treatment strategies involving WBRT for brain metastases in other settings excluding SCLC patients,” Rusthoven says. “These trials have tended to show similar overall survival and better tolerability with SRS alone.”

Traveling to CU Cancer Center for a Lung Cancer Clinical Trial - A conversation between David and Joleene Kooyman and Dr Tejas Patil



David: "I am 71 years old, from Logan, Utah. I am married to my wife Joleene. We have eight children and 23 grandchildren."

Joleene: "The whole cancer journey has been very emotional, it has pulled us closer as a couple."

David: "In November of 2017, I had pneumonia. I went to my doctor and they corrected the pneumonia, but I was left with a cough. I came back and had pneumonia again in November of 2018. I went to my physician and also an ENT, they were con-

cerned about the cough and had tried a number of things over the previous year. Finally, in December of 2019, I went to a local hospital and had a CT scan and he was concerned about dark spots at the bottom of the right lung."

Dr. Patil: "David and I connected through a colleague of mine, Dr. Puri, at Salt Lake City who works at the University of Utah Huntsman Cancer Center. She had taken care of this patient and in the process of managing his lung cancer she had identified a very unique gene fusion called an NRG1 fusion. They had tried a variety of different treatment methods, including chemotherapy with immunotherapy, and a novel clinical trial, and unfortunately, when she reached out to me, David had not responded to either of these therapies."

David: "They moved the cancer to stage IV because the CT scan showed it had moved to my left lung. Which moved it to stage IV and then the concern came about what is going to happen now because of being in the blood and of course cancer grows and who knows where it goes."

Dr. Patil: "We were fortunate to be opening a clinical trial here at the University of Colorado that took a novel approach at dealing with what had been a tricky gene fusion to deal with in lung cancer."

Joleene: "From the first time we came to the University of Colorado Cancer Center we felt like we were important, that this drug trial was an important thing, that it was a choice that we made. We felt like it was definitely worth the effort to get here. We had an opportunity to have it in Salt Lake and we decided nope. We needed a teaching university, we needed a research university where there are multiple eyes looking at his reports, looking at his records, looking at the lab tests, looking at everything at every angle."

Dr. Patil: "I would say that the University of Colorado has an infrastructure that allows clinical trials that are conducted here to be successful."

David: "We did preliminary labs in the first part of December and started our clinical trial in the middle of December."

Joleene: "The overall experience here has been fantastic. Just everyone here is so positive and it makes our experience a lot better."

David: "Tomorrow we will complete our 17 infusions, for 17 straight weeks, where we fly over every Monday, get our infusion on Tuesday, we fly back Tuesday night.

Dr. Patil: "David has done remarkably well on this therapy. We are now almost 8 months in with persistent control."

David: "This is my doctor, this is him. The best of the best. If I could take the people who have taken care of us here at the University of Colorado, I would tell them thank you for being who you are. Thank you for making your expertise available to someone like me."



Dr. Tejas Patil and David Kooyman



Lung Cancer Survivors watching the Denver Broncos as part of the Lung Cancer Super Bowl Challenge



Lung Cancer Survivor Melissa Turner (left) and her friend, Kathy, at the Estes Park Women's Monument

LCCF Distributions 2021

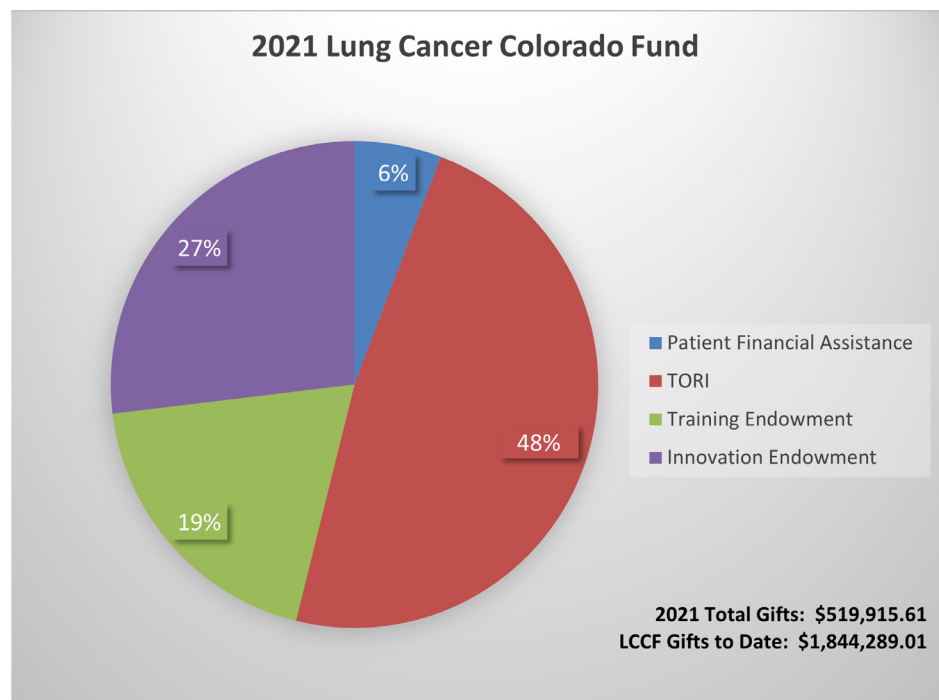
By D. Ross Camidge, MD, PhD

By November 2021, when the LCCF committee met to review the distribution of the funds raised for the LCCF in the year, the annual amount raised from the last meeting in 2020 was \$519,915.61.

- No specific infrastructure projects were identified for support.
- We agreed to give \$30,000 to support patient welfare through our social work department.
- We agreed to give \$250,000 to fund research pilot projects across the full range of research fields within the CU Thoracic Oncology Research Initiative (TORI).
- We agreed to give \$100,000 to our first permanent quasi-endowment (to help support the salary of trainees in any aspect of the program in the future). We hope that a single donor/group will take over the additional funding required to complete this permanent Fellowship fund. The current total is \$597,298.06 and we are looking for someone to add at least 1M to have the Fellowship named by them if they so wish. Contact ross.camidge@cuanschutz.edu if interested.
- Finally, we continued to crowd-source our new Thoracic Oncology Program Support 'Innovation Fund' with \$139,915.61, with the same goal re a single donor/group taking it over to complete the fund. The current total is \$386,673.49 and we are looking for someone to add at least 1M to have this fund named by them if they so wish. Contact ross.camidge@cuanschutz.edu if interested.

LCCF overview:

- Since its inception in May 2011, the total direct donations to the LCCF has reached \$1,844,289.01. Listing the total down to one cent may seem silly, but it is not. It many senses it embodies the funds' founding principle - everyone working together, in no matter how large or small a way, will change the world for the better.
- However, the value of the LCCF can also be measured indirectly. Quasi-endowments and other large funds are invested to earn interest until their dollars are needed. The environment of the LCCF also encourages philanthropy through other avenues. The LCCF's transparency and its commitment to help support all aspects of the program has led to multiple other donations separate from the general LCCF. These include endowed professorships for retaining and recruiting the best faculty, project specific funds focused on this or that subtype of a disease, and general program development funds.
- Sometimes, major donor's names are attached to specific projects, sometimes they are not. It is entirely up to the donor.

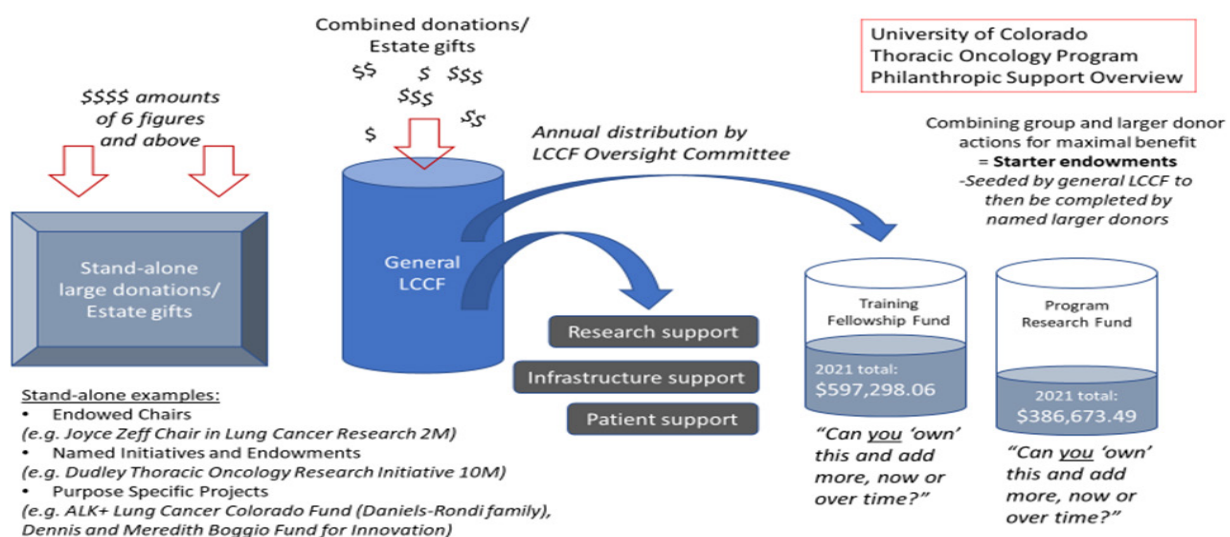


- Quasi-endowments, current monies, endowments and all that jazz:

Perhaps you had a windfall that you want to put to good use. Perhaps you want to plan to include support of the LCCF in your will. Perhaps you want to stagger your donations over a few years – 200,000 a year for five years is a million dollars.

Figure 1 shows five stacks of square blocks, each stack containing four blocks. The stacks are colored white, yellow, red, green, and black, corresponding to the five colors of the blocks used in the experiment. The blocks are arranged in a 2x2 grid, with the white stack on the left, followed by yellow, red, green, and black on the right.

The LCCF has had a vision to prime the pump on several quasi-endowments in the hope that each fund, addressing a specific need of the program will then be completed with at least \$1M by a larger donor/group who would also be able to name the fund, if they so wish. Please speak to your MD or ross.camidge@cuanschutz.edu if you are interested in these or other opportunities.



Kathy Griffin's Lung Cancer Diagnosis: What Nonsmokers Need to Know

By Greg Glasgow



Comedian Kathy Griffin, 60, shared the news with the world via Twitter: She was about to undergo surgery for stage I lung cancer.

"Yes, I have lung cancer even though I've never smoked!" she wrote in the post. "The doctors are very optimistic as it is stage one and contained to my left lung. Hopefully no chemo or radiation after this and I should have normal function with my breathing. I should be up and running around as usual in a month or less."

CU Cancer Center member Robert Meguid, MD, MPH, associate professor of cardiothoracic surgery at the University of Colorado School of Medicine, says cases like Griffin's are somewhat rare, but that lung cancer among nonsmokers — defined as people who have smoked fewer than 100 cigarettes in their lifetime — still makes up around 20% of all lung cancer.

At the CU School of Medicine, Meguid and fellow CU Cancer Center member John Mitchell, MD, chief of general thoracic surgery, perform around 200 minimally invasive lung cancer operations per year using a surgical robot.

We sat down with Meguid to talk more about Griffin's case and what other patients should know about lung cancer.

Q: Griffin was fortunate that her cancer was caught at an early stage during a routine screening for an unrelated condition. Are there any symptoms of early-stage lung cancer, particularly in nonsmokers?

A: There are symptoms in some patients — typically it's a cough that doesn't get better over time or go away, or, very rarely, coughing up blood. It's frustrating, though, because low-stage lung cancer, in smokers and nonsmokers, usually has few or no symptoms. We rely on the detection of early-stage lung cancer through screening protocols that are specifically for someone who has a smoking history. It's such a low incidence in never-smokers in general that we don't have a protocol for screening them. Lung cancer is typically identified in never smokers incidentally on a chest X-ray or CT scan in the ER because of a car accident or for some other reason.

Q: Do you know what causes lung cancer in never-smokers?

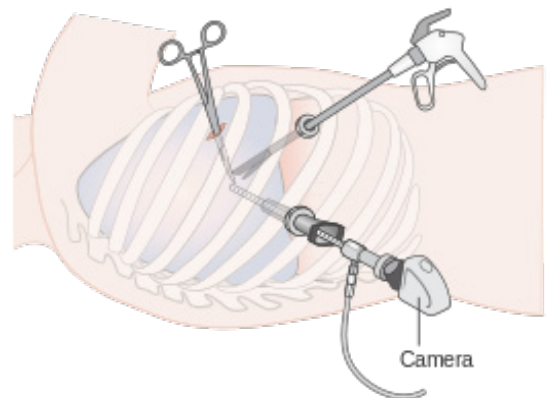
A: In never-smokers we query if there is a family history of lung cancer. Do they have exposure to environmental risks for lung cancer? These include secondhand smoke, but also radon exposure and environmental exposures, such as chemicals, diesel fumes, and asbestos. But most commonly we aren't able to identify a distinct cause of lung cancer in never-smokers in the way we do in smokers.

Q: Griffin mentioned in an interview that she had a needle biopsy after doctors saw a mass on her lung in a scan. Is that the typical test for lung cancer?

A: Yes. We like to confirm the suspicion of lung cancer with a tissue biopsy and also obtain tissue to do additional testing on the tumor to not only determine what type of tumor it is, but to determine if there's a genetic mutation which makes it treatable with different types of chemotherapy, immunotherapy, or targeted therapy agents. Many lung cancer patients who are never-smokers have a mutation in the cancer cells which makes it amenable to treatment with a targeted therapy agent or an immunotherapy agent. Those are nontraditional chemotherapies that are typically a pill taken at home. The data on outcomes for those patients treated with targeted therapy or immunotherapy, either alone or in conjunction with traditional chemotherapy, show an improvement in survival. So that's really good news for never-smokers with lung cancer.

Q: Griffin had surgery for her stage I lung cancer — she described it as “having half of my lung surgically removed.” Is that a better or worse option than the targeted therapy given to people with the specific genetic mutation?

A: Most people who are detected early don't need chemotherapy or radiation therapy. Typically, surgical resection of the area of the lung with the nodule, plus the lymph nodes around it, is the standard of care for management. That gives us the best chance of removing the tumor and minimizing the likelihood of recurrence. From her description, Kathy Griffin probably had a lobectomy. Typically in low-stage lung cancer, when we're treating it with surgery, we treat it with either a lobectomy, which is taking out one of the five lobes of the lung, or if it's small enough and appropriately located, with a segmentectomy, which is less than a lobe of the lung but it's still an anatomic unit of the lung. The aim of the lobectomy or segmentectomy is to not only take out the tumor, plus an area of normal tissue around it, but to be able to check lymph nodes adjacent to the tumor to make sure it hasn't spread to those.



Q: What is the recovery like for that surgery? Does it result in reduced lung function?

A: Typically, with a minimally invasive lung cancer resection, the recovery is a two- to five-day hospital stay. Then it takes a couple of weeks until patients are off of pain medication, and a total of six weeks from surgery until they are back to baseline. It reduces the lung function typically by somewhere between 5% and 25% of the total lung function, depending on which lobe or lung segment is removed.



Dr. Rob Meguid

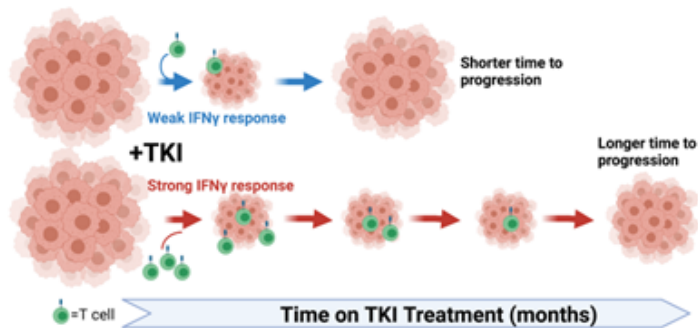
Q: Are there any specific programs at CU Cancer Center's clinical partner UCHealth University of Colorado Hospital to help patients who have lung cancer or need to get screened for it?

A: We have the Pulmonary Nodule Clinic at UCHealth, where pulmonologists provide diagnosis and treatment for lung nodules, and the UCHealth Lung Cancer Clinic/Thoracic Multidisciplinary Clinic provides multidisciplinary care for patients diagnosed with lung cancer at any stage.

The good and bad of targeted therapy

By Lynn Heasley

Basic scientists working in the lab and clinicians working in the lung cancer clinic have revealed clues as to why some anti-cancer drugs stop working.



Hypothesis: Strong induction of an IFN γ response in TKI-treated EGFR mutant lung cancers is associated with longer duration of therapeutic response. Treatment of patients bearing EGFR mutant lung cancers with specific tyrosine kinase inhibitors (TKIs) induces prompt tumor shrinkage. Within tumors where the TKI induces a strong IFN γ response, chemokine stimulate transient infiltration of T cells which provides additional anti-tumor activity and thus, longer time to progression. By contrast, induction of a weak IFN γ response results in low recruitment of T cells and more rapid tumor progression due to repeat selection and outgrowth of TKI resistant tumor cell clones.

Tyrosine kinase inhibitors (TKIs) are pills that can target lung cancers driven by specific molecular changes in the tumor. Although the treatment can be very effective, some near-dormant disease remains and may act as safe-space – a nursery- from which drug-resistant forms of the cancer will later emerge.

Why some people develop more or less of this dormant disease has been a mystery. Dr Lynn Heasley, PhD looked at what happened to laboratory models of lung cancer, driven by an EGFR mutation, when an anti-EGFR TKI (osimerti-

nib) was added. Together with his clinical colleagues he also looked at tumor samples taken from patients before and after two weeks of the drug. Osimertinib stimulated changes in many different genes in the cells in the lab and in the tumors in patients. Some of the genes turned on in some of the patients were associated with stimulating the patients' immune response (called an interferon activation signature) and seemed to be associated with better outcomes on the drug.

“Normally, we think these targeted drugs act independently of the immune system, but that may not be true,” said Heasley. “Maybe the people who are getting the best outcomes have a team approach to treating the cancer in their bodies.”

The goal of the team, working as part of the University of Colorado's Thoracic Oncology Research Initiative, is to extend these observations. If they are confirmed the next step will be to try and pull apart why some people's cancers react in this way, while others don't.



Lynn Heasley, PhD



The CU Lung Cancer Nurses and Pharmacist dressed as different Oreo varieties for Halloween (Katie, in the middle, is holding 'double stuff' because she's pregnant!)

Hockey Fights Cancer has one goal: Lifting spirits

By Kati Blocker



Derek Babb with his personalized Hockey Fights Cancer jersey personally signed by his favorite all-time player, Joe Sakic.

Derek Babb with his personalized Hockey Fights Cancer jersey personally signed by his favorite all-time player, Joe Sakic.

Derek Babb remembers it clearly, the game in 1999, when he sat beside his buddy who had bomb diggity seats – the best he'd ever had – for a Colorado Avalanche game. Then, to top it off, a handful of Denver Broncos players arrived to celebrate their recent Super Bowl Championship.

Babb could not believe his luck and he cherishes the memory as one of his all-time best sports experiences. Until something even better happened this summer.

The day didn't start out that great. In fact, it hadn't been a very good few months. Babb, with his Avs-themed mask covering his nose and mouth, made his way into the UCHHealth Cancer Care and Hematology Clinic in Loveland. He sat down to start yet another round of immunotherapy. As he settled in, his oncologist, Dr. Douglas Kemme, whom Babb had been working with since he was first diagnosed with stage 4 lung cancer in May, appeared from around the corner with a long stick in his hand.

Kemme had an Av's hockey stick that had been autographed by numerous players.

"Wow," Babb said as he looked over the signatures.

Babb's roommate, Chris Blackburn was there for the magic moment.

"His face!" Blackburn said, "And then when he got to hold it, that was good, but when he confirmed that he got to keep it — he was better than a kid at Christmas."

Bomb diggity.

This spring, during the first wave of the pandemic, Babb didn't feel well but the thought that it could be COVID-19 — made Babb hesitant to go to the hospital. News of the worldwide novel coronavirus was scary, even in his home town of Loveland, Colorado. Babb had heard of people going to the hospital with COVID-19, and not coming out. He did not want to be that person. So he waited.



Derek and Dr. Douglas Kemme after Kemme gave him the Colorado Avalanche-signed hockey stick during one of Derek's session of immunotherapy for small cell lung cancer.

Months passed. The number of people infected with COVID-19 had soared, and then fallen, and Babb still felt horrible. He had trouble breathing.

"I kept telling him to see a doctor," Blackburn said. "Finally, I said, 'Listen here, if you're not ready by 3, I'm taking you, or I'm calling an ambulance.'"

Babb got ready and they went to the emergency room at UCHealth Medical Center of the Rockies. Babb got a COVID-19 test immediately, but it would take a few days for the results to come back. In the meantime, doctors ordered a few more tests, which showed Babb's lung full of fluid. Babb spent the next six days in the hospital while a chest tube drained the liquid, at which time he also had an X-ray of his lungs.

It wasn't COVID-19 but something potentially worse: lung cancer.

At his first appointment with Kemme shortly after his diagnosis, Babb wore a mask sporting the logo of the Colorado Avalanche. He'd received it from a fellow Av's enthusiast and coworker. It's the only mask he likes to wear. He also had on an Avalanche jersey and hat, part of his huge sports collection in his "man cave" at home.

Kemme knew that UCHealth is the official health partner of the Colorado Avalanche. To enhance patients' experience and to help them feel better, players and mascots from Colorado sports teams often visit patients to inspire hope for those experiencing tough challenges.

"When our patients receive a special recognition or gift from their heroes, the smile is from ear to ear," Kemme said. "They follow the teams and players and to be part of their world makes their world a bit more manageable."

So Kemme sought out the hockey stick for Babb. Any little boost, he thought, would be needed for the battle ahead.

The tumor in Babb's chest was large: 15 cm. It occupied the whole right side of his lung and interfered with his lung function.

"It's a very special type of lung cancer called small cell, which is different from all non-small cell types," Kemme said. "When it is limited to just one half of the chest like with Derek, there is maybe a 20-30% chance of a 5-year cure. It's not the best, but there is a fighting chance. And this young kid has the most positive attitude."

At one point, Kemme told Babb that he may have only 6-9 months to live.

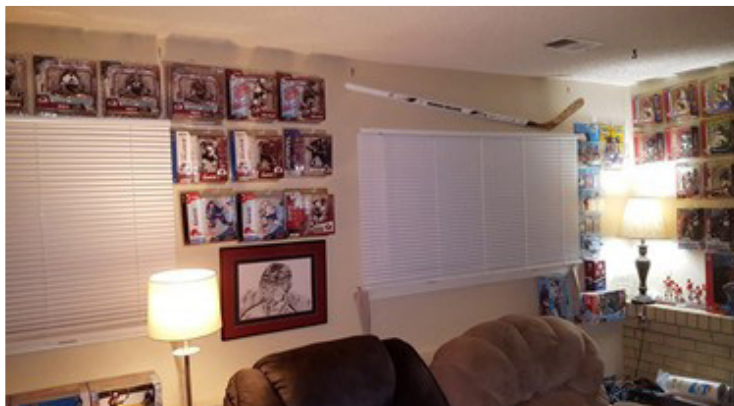
Babb admitted that the diagnosis was devastating, but he immediately wanted to beat it. He leans on family and friends, including Blackburn, for support, and they've helped him to hold onto that optimism.

"You've got to stay positive," Blackburn said. "When we first found out, another coworker was over that night, and she got home and Googled (small-cell lung cancer). Then I Googled it. I told Derek we have to figure out how to think positive about it and not about all the bad stuff I had just read.

Then I told him, 'Please don't ever Google it.'"

Babb has always had a positive outlook on life — a trait his friends and family admire — and cancer wasn't going to change that.

"You keep positive and positive things happen to you. As dark as it can be, you stay positive and do the right thing, things will turn around for you," Babb said. "It is what it is, and I'm making the best out of the days I have remaining."



The 'man cave' of Derek Babb, who is getting immunotherapy for small cell lung cancer, holds all his sports memorabilia including a signed Avs hockey stick he recently got from his oncologist.

Babb started treatment right away, with four cycles of a combination of chemotherapy and immunotherapy. It shrunk the tumor to 8 cm and his lung started functioning properly again.

Providing immunotherapy for small cell lung cancer alongside chemotherapy is a newer treatment tool, Kemme explained. Chemotherapy kills the fast-growing cancerous cells with chemicals. Immunotherapy works on the cancer in a different fashion by altering the immune system to recognize cancer, allowing the body to fight it directly.

Immunotherapy does have some side effects, but nothing compared to chemotherapy, Kemme said. Those side effects don't compound as treatment continues, so it can be used alongside chemotherapy and radiation to make those treatments more effective.

After chemo, Babb had radiation therapy. He will continue immunotherapy for the next year and in mid-December, he will have a CT scan to see if the radiation has helped.

"Even with a big and scary tumor, there is still hope that he will have a long-term response," Kemme said.

Babb is hopeful. He feels better now, physically and mentally. He recently marked six months since his diagnosis, and is on his way to living longer than the 6-9 months that Dr. Kemme had warned about.

"I promised him I'd beat those odds," Babb said. "It's been six months, and I feel I'll pass that prognosis."

Inspired by Babb's story and his love for their team, the Colorado Avalanche, with help from UCHHealth, orchestrated one more surprise for Babb. Under the impression that he would be doing an interview with Altitude Sports' Kyle Keefe, Babb joined the sports anchor via a virtual call. But Keefe had a few more surprises for Babb.

"I expected to talk with Kyle and was super excited to talk to him," Babb said. "But then the other guys joined — that was unbelievable. It just made my day. It was just fantastic."

"It's humbling," Babb said. "It's just been unbelievable what everyone has done at UCHHealth for me, primary with my outcome, but also all this other stuff. This was a bucket list-type of experience."

GOAL Consortium Facilitates Group Purchases and Knowledge Sharing for Academic Pathology Testing Labs

By Valerie Gleaton



When Dara Aisner, MD, PhD, an associate professor in the Department of Pathology at the University of Colorado School of Medicine, was approached by a colleague at another university about splitting the cost of a bulk purchase of new clinical testing products, she initially declined. Al-

though it would be a valuable resource — and might even save her lab money in the long-term — the short-term cost was prohibitive.

But it got her and her colleague thinking: What if not just one or two but several academic labs could go in together on such purchases? Out of that idea was born the Genomics Organization for Academic Laboratories (GOAL).

Aisner, a CU Cancer Center member, is the medical director of the Colorado Molecular Correlates Laboratory, a state-of-the-art molecular testing facility on the CU Anschutz Medical Campus. “We basically produce the results that are the basis for personalized cancer therapies,” Aisner explains. “What this involves is taking a patient’s tumor samples and evaluating the DNA in those tumor cells to determine what types of genetic alterations they have that might impact the choice of therapy.”

Clinical molecular testing is performed at dozens of academic centers across the country, but it’s also done by large commercial laboratories. And as a result, Aisner says it’s getting more difficult for academic labs to compete financially.

“So, every academic center has to take a look at what they’re doing and ask if they want to continue doing this testing in-house or if they should start sending it out to commercial labs,” Aisner says.

There are a host of benefits that a local lab brings for patients. One is that in-house pathologists like Aisner are able to connect directly with the clinicians who are working with patients. She’s also able to work with extremely small samples that larger labs typically reject.

“The other big argument for keeping testing local is that the data we generate stays within our own system,” Aisner adds. “When you start sending samples out, you no longer have control of the data. And increasingly, being able to connect the data on what a patient’s tumor genomics look like to the therapy they received and how they did with that therapy is incredibly valuable.”

The downside, of course, is that there are often substantial costs for medical centers to run these in-house labs.

“Because we’re not big venture capital-backed organizations, we’re always stretched to stay at the forefront,” Aisner says.

That's why partnering with other academic labs to share and reduce costs by taking advantage of bulk discounts had such a strong appeal.

"When you recognize the squeeze that's being put on academic labs, coming together seems to offer a lot of benefits," Aisner says.

After their initial conversation about potentially splitting the cost of a reagent set, Aisner and her colleague, Jeremy Segal, MD, PhD, the director of the Division of Molecular and Cytogenetic Pathology at the University of Chicago, began discussing the possibility of approaching more academic labs.

"Because neither of us felt like we could drum up the initial capital, we put feelers out to a number of other organizations to see if, instead of having two organizations come together to make a purchase, we could get five," Segal says. "We were both surprised and astonished when more than five said they wanted to join us. In fact, we got 15!"

Once they had 17 labs on board (including their own), Aisner and Segal found a company that was willing to partner with the group by manufacturing and divvying up the reagents and then shipping them to all of the different labs.



DNA Sequencing

According to Aisner and Segal, what started off as a fairly straightforward group purchase order has since grown into a community with a set of overlapping missions.

"Originally the plan was to buy these reagents and then all go our separate ways, but we've come to understand that there's a lot more that we can do together as an academic community and a lot more benefit for the individual labs if we can leverage some of these things jointly," she says. Some of these benefits include the creation of real-time communication platforms that allow people in the labs to ask each other questions, as well as sharing protocols.

"Sometimes you spend a lot of time troubleshooting something in your lab, but now you can also ping a question out to the group and maybe save yourself a lot of effort. Because there are a lot of people who know a lot about this topic who are coming together," Segal says.

Seeing the benefits, Aisner and Segal wanted to try and expand their reach to even more institutions, but — like that initial group purchase order — they knew they couldn't do it on their own. "The process of getting those first 17 sites to talk to each other made us realize that there was a lot more that we can and should do to facilitate this very niche space of molecular testing in the academic setting," Aisner says. "We also recognized that to do that effectively, we were going to need a separate, independent organization."

This led to the formation of the Genomic Organization for Academic Laboratories (GOAL), an independent organization designed to facilitate collaboration between all of the academic labs, which

have since grown from those initial 17 sites to 28. The organization has incorporated and is in the process of establishing its nonprofit status.

In addition to the communications platform and, of course, group purchase orders for lab supplies, GOAL currently hosts a monthly virtual “coffee shop” where members can drop in and ask for help or advice from their peers. Aisner and Segal say they’re also working on a concordance study to send tumor samples to different labs within the organization to show the consistency the

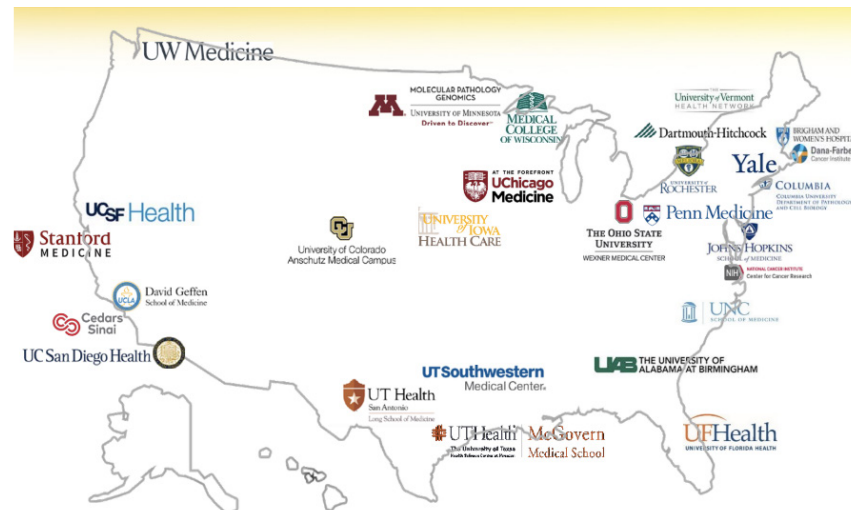
communally developed approach achieves.

Aisner says the organization also hopes to stand up funded, multi-institutional studies in the future, as well as data-sharing networks where labs can share anonymized data in order to help each other with the process of issuing reports for patients. Simultaneously, the organization has successfully garnered sponsorship from several pharmaceutical companies to help drive its mission.

Aisner and Segal stress that the consortium isn't just a



Dara Aisner, MD PhD



The 28 members of GOAL

boon to labs — it's also a way to keep improving patient care.

“By being part of this network that is lowering barriers to bring in cutting-edge molecular testing, we’re able to offer our patients the most advanced and scientifically sound clinical testing,” Segal says. “And by lowering costs across the board for all of our sites, we can potentially decrease the financial burden on both the patient and the hospital system.” Both Aisner and Segal say that the consortium is an energizing step forward, and Aisner noted that “the sky is the limit for what direction we could take this, and we’re excited to see how it evolves.”



Lung Cancer Survivor Agnes Stogicza – after a 2500-foot elevation bike ride in Romania, with her dog Laska, and one lung.

'Miracle' drug stopped working, but lung cancer patient lives on

By Todd Neff

For Gail Sadler, who has quadrupled her expected survival time, clinical trial picked up where standard therapy left off.

Last time UCHHealth Today wrote about Gail Sadler, the headline read, "She was given two years to live with lung cancer, max. That was four years ago."

That was nearly four years ago.

To review: When diagnosed in December 2013 with stage 4 non-small cell lung cancer, Sadler, then 52, was given six months to two years to live. She went on chemotherapy (cisplatin first, then docetaxel) to address tumors in her left lung, left hip, right femur, vertebra, sternum, and throat. Chemotherapy helped until about a year after diagnosis. Then in December 2014, nivolumab (trade name Opdivo) was approved by the U.S. Food and Drug Administration.

Cancer spreads in part by chemically hiding itself from an immune system that would otherwise attack the malignant cells. Immunotherapies such as Opdivo work by poking holes in that chemical cloak so the immune system can take the fight to cancer and keep the disease in check. It doesn't always work, but for Sadler, Opdivo was a revelation: The cancer disappeared, and she experienced no side effects.

But all the while her cancer was trying on countless molecular disguises. Ultimately it evolved into one that fooled even her Opdivo-enhanced immune system. In March 2020, shortly after Sadler moved from Littleton to Castle Pines and the COVID-19 pandemic hit, a tumor appeared on a lymph node on her neck. The woman who was perhaps one of the world's longest-term Opdivo "customers" had relapsed. The FDA had approved Opdivo based on a clinical trial that found the drug to extend survival by about three months; Sadler had received 86 Opdivo infusions over more than five years.

What next for a stage 4 lung cancer patient?

Ten rounds of radiation therapy led by UCHHealth and University of Colorado School of Medicine radiation oncologist Dr. Brain Kavanaugh eradicated the neck tumor. The question, though, was how to keep the rest of her cancer under control now that Opdivo was no longer doing its job. Not long ago, Sadler's story would be coming to an end. But the last few years have brought a revolution to lung cancer treatment, and these

life-extending innovations show no signs of slowing down.



Gail Sadler on the tarmac outside Modern Aviation where she works at Centennial Airport. Sadler was given max two years to live – more than seven years ago. Photo by Cyrus McCrimmon for UCHHealth.



Sadler prepares to undergo radiation therapy for a lymph-node tumor in March 2020. She was at that point the longest-surviving patient on Bristol Myers Squibb's immunotherapy drug Opdivo. Photo courtesy of Gail Sadler.

Opdivo was the first new immunotherapy-based lung cancer drug when it was approved in late 2014. In the six-plus years since, multiple other immunotherapy drugs and targeted therapies have joined it in the lung cancer armamentarium – most recently at the end of May. Many of these drugs target the mutations of specific genes known to drive individual variants of non-small cell lung cancer – eight mutations now have a specific drug licensed for them. Dr. Ross Camidge, who leads lung cancer research at the CU School of Medicine and sees patients at UCHHealth University of Colorado Hospital on the Anschutz Medical Campus, says those mutations account for more than half all non-small cell lung cancers (88% of lung cancers are NSCLCs, he adds). He expects the number of targeted genes to grow, he says. “Not that we have an answer for everybody yet, but we are pulling bricks out of the wall one by one,” Camidge said.

The fruits of pharmaceutical progress are plain to see, he says.

“Last week in clinic, I had two patients who have been stage 4 for 10 years,” Camidge said. “We are creating long-term lung cancer. It used to be that you were either cured or had a short amount of time left.”

What’s interesting about Sadler’s case, Camidge says, is that she’s done so well despite her cancer not being attributable to a single mutated gene. She’s far from alone in having what he called a “committee” of cancer drivers. None of these remarkable new drugs, typically prescribed for people with specific mutations Sadler doesn’t have, were designed to help her. Opdivo isn’t gene-specific, and that it worked so well remains a mystery Camidge and colleagues in Colorado and around the world are still working to understand.

“Her immunotherapy can be given to almost anybody. It works amazingly well in 20% of people, but we don’t know who those 20% of people are,” Camidge said.

The issue isn’t the 20% of patients for whom Opdivo or other broad-based therapies mysteriously work; it’s the 80% for whom they don’t. They lose time as their cancer spreads. That uncertainty also hinders the scientific community’s ability to develop and prescribe drugs for subsets of patients whose lung cancers, like Sadler’s, probably have roots in multiple genetic and other factors. A year ago, Sadler and her UCHHealth care team faced exactly this problem. Opdivo had failed and the roots of her cancer remained unexposed. What could they do for her?



Sadler has done well despite her cancer not being attributable to a single mutated gene. Photo by Cyrus McCrimmon for UCHealth.

Lung cancer patients seek clinical trials

Sadler has for years received the vast majority of her medical care at UCHealth Lone Tree Medical Center – it's close to home, which is no small matter given the roughly 100 appointments a year a late-stage cancer patient can expect. Dr. Regina Brown, and, more recently, Dr. Jose Pacheco, who also sees patients at the UCHealth Lung Cancer clinic – Anschutz Medical Campus, saw that clinical trials of promising cancer-drug candidates would be the path forward for Sadler. About 40% of UCHealth lung-cancer patients are on clinical trials, the highest percentage of any U.S. lung cancer center, according to Camidge.

"When immunotherapy stops working after it has clearly worked before, that's likely a different issue than when it doesn't work in the first place, said Camidge. "The behavior of the cancer tells you something about its underlying biology. It tips its hand a little,"

Pacheco and the lung cancer care team settled upon a clinical trial featuring a combination of two approved drugs: ramucirumab (trade name Cyramza) and pembrolizumab (trade name Keytruda). Keytruda works much like Opdivo; Cyramza would help Ketruda reestablish immune control. Sadler would take them through infusions every three weeks at UCHealth Lone Tree Medical Center. Pacheco, who is leading the trial's implementation across the UCHealth network in Colorado, was particularly familiar with the potential of the combination.

Sadler has responded to the drug without side effects as of late May – more than a year into treatment. She has been working since March 2020 as a customer-service lead at Modern Aviation, which serves private-jet clients from Centennial Airport. Despite Sadler possessing a smile as wide as an aircraft's wings and a personality and energy level seemingly fueled by some hidden turbine, she was pleasantly surprised by the job offer.

"Not everyone will hire someone with stage 4 lung cancer," she said. "They took a chance on me."

She insists on scheduling her infusions and other medical appointments on Fridays, one of her days off, so that she misses a minimal amount of time at work. She tips her hat to UCHealth for being able to work around her schedule.

There have been setbacks along the way. Most recently, on May 11 Sadler had three holes drilled into a femur that had probably fractured because prior radiation treatments had weakened it.



Sadler with friend and Modern Aviation colleague Janet Gallagher. Gallagher and others at Modern Aviation "went out on a limb" when they hired her a year ago; Sadler says. "Not everyone will hire someone with stage 4 lung cancer." Photo by Cyrus McCrimmon for UCHealth.

But for years now, she has lived her life. She loves her job. She has cherished time with her daughter Shannon and granddaughter Ava; she experienced the wedding of son Cameron; and she was in San Diego 10 days after the femur surgery to join her daughter Alex, recently engaged, for some wedding-dress shopping. The wedding is scheduled for October 2022, and Sadler plans on being there.

“Nobody’s getting out alive – I mean, what the hell,” Sadler said. “But my fear of dying right now is like zero.”

Should the current trial’s drugs stop working, she’s confident that Pacheco will find her another option, she says.

“I’m in the best possible hands. I’ve always felt that way,” she said. “These people care. They dig in. They’re with you in this fight. You never feel like you’re a one-woman army.”

Those who know Sadler would argue that she’s a one-woman battalion at least.

Certain is this: Whatever happens next, she’ll be up for the challenge.

Jamie Studts works to reduce stigma blocking use of lung cancer screening

By Garth Sundem

It didn’t take long for Jamie Studts, PhD, to notice a big difference between Kentucky, where he worked for 13 years in the Department of Behavioral Science at the University of Kentucky College of Medicine, and Colorado, where he was recently appointed Co-Leader of the CU Cancer Center Cancer Prevention & Control Program: “After my recruitment, I was on a visit to search for a house and I went to a bar with some family who live in the area. Outside there were 100 people and not one of them was smoking. There were maybe two or three people vaping, but nobody was smoking. That’s pretty different in Kentucky,” he says.



For Studts, it was more than just an interesting observation. With training in clinical psychology and a history of research in behavioral factors that influence the use of lung cancer screening, Studts is a leading expert in the psychosocial aspects of tobacco use and lung cancer. Now his challenge is to help patients, doctors, policy makers, and health systems navigate a paradigm shift in the way we prevent, diagnose, and treat the disease. One of these challenges is to help Colorado and the rest of the country get up to speed with the nationwide implementation of lung cancer screening. The United States Preventative Service Task Force recommends

lung cancer screening for people 55-80 years old who have a 30 pack-year history of smoking (each pack-year is 20 cigarettes smoked every day for a year). However, a National Cancer Institute study found that only 5.9 percent of people in this high-risk group actually received the recommended screening. At CU Cancer Center, Studts will be working with ongoing projects by researchers including Cathy Bradley, PhD, and Russel Glasgow, PhD, to understand the barriers that keep high-risk individuals from completing this recommended screening. One of these factors is stigma.

“We have lung cancer screening – what’s slowing down our efforts to make it available to everyone who could benefit? Part of the answer is stigma,” Studts says. For example, one of his studies found that nearly half the participants did not let their spouses know they had gone for lung cancer screening.

“If a woman who is eligible for mammography tells a friend she decided against it, the stigma is the opposite – the friend will talk her into it. With lung cancer screening, that’s not the case. People still feel like they need to hide their lung cancer risk and status,” Studts says. Interestingly, Studts sees the problem of lung cancer stigma through the lens of having grown up in a family with a strong anti-smoking bias.

“Of my four grandparents, three lived past 96 and one didn’t make it to 55. Guess who was the tobacco user?” he says. When his grandfather passed away early from cardiovascular disease, Studts’s grandmother became a passionate anti-smoking advocate. “My grandmother got remarried to an American Legion guy,” he says. “It was a heavy tobacco-using community, smoke filled room after smoke filled room. But whenever someone sat smoking next to her, she would take out a battery powered fan and blow it back at them. That’s how I grew up thinking about smoking. But growing up with this attitude forced me to become aware of and deal with my own biases. Now I see that lung cancer stigma kills – it keeps people from getting the screening and treatment they need.” Instead of blaming smokers, Studts sees this common cause of lung cancer as a societal challenge. “Society blames the individual when society also endorsed smoking at high rates.

Part of the problem is we don’t approach individuals at risk or diagnosed with the same empathy, compassion and support that we do individuals diagnosed with breast, prostate, pancreas, and other cancers. Society rallies around other cancer patients to say we value you, you’re special. But you want to shut down a conversation, mention lung cancer,” he says.

Studts saw an expression of this stigma in an elementary school anti-smoking program. “They had kids make drawings of individuals who use tobacco – you should have seen the way children depict them. We train them very early to think about ‘smokers’ in this light. I understand that we want to teach kids about the dangers of smoking, but aren’t there better ways to do this with compassion and empathy?”

Studts also explores lung cancer survivorship care, with the goal of developing tools to increase quality of life in these long-term and former patients. It’s a new line of research, in large part because until recently very few people survived the disease long enough to worry about quality of life. “Individuals diagnosed have not had a good prognosis – they’re diagnosed at a late stage and treatments haven’t been especially successful. However, innovations in care from prevention to end of life care have changed the landscape for lung cancer. It’s infused a new optimism and hope that we’re trying to leverage to overcome the fatalism and stigma that have been associated with lung cancer diagnosis.”

These innovations were an important factor in Studts's decision to leave his work in Kentucky for his position at CU Cancer Center.

"Colorado has an embarrassment of riches when it comes to research in lung cancer. Folks here have been on the pioneering edge of lung oncology care, from the center's founder, Paul Bunn, to work in targeted treatments for lung cancer by people like Bob Doebele, Ross Camidge, and the research of York Miller, Evelyn Borrayo, Bob Keith and so many others. It's a great place for me scientifically with the landscape of lung cancer in Colorado allowing us to test some of our ideas developed in Kentucky, especially in reaching Colorado's wide-open spaces that still experience high smoking and high rates of lung cancer."

That idea points to another direction in Studts work, namely in reaching underserved populations in communities beyond the immediate reach of National Cancer Institute-designated cancer centers. "We want to layer on behavioral science and community-based approaches on top of the excellent work being done here on the population health side to make sure the innovations being developed here benefit all Coloradans. It's not easy to make sure these things are available in the community," Studts says. "We can lead in developing new strategies only as long as we develop things that can't only be done here."

Lung cancer used to be a nearly uniformly fatal disease, relegated to the shadows of cancer care by the feeling that patients were to blame for their own condition. Now, new lung cancer treatments are helping patients live longer, better lives and we are understanding the condition's causes more from the perspective of culture and addiction than as a personal failing. Since its founding, CU Cancer Center has been at the forefront of lung cancer research and care. Now with the recent recruitment of Jamie Studts, the center will continue to push the boundaries of understanding of the behavioral, cultural, societal, and individual factors that allow lung cancer patients and survivors live longer, better lives.



Jamie Studts, PhD

The LCCF Main Page URL is: <https://medschool.cuanschutz.edu/lccf>

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Estate Planning Special Edition

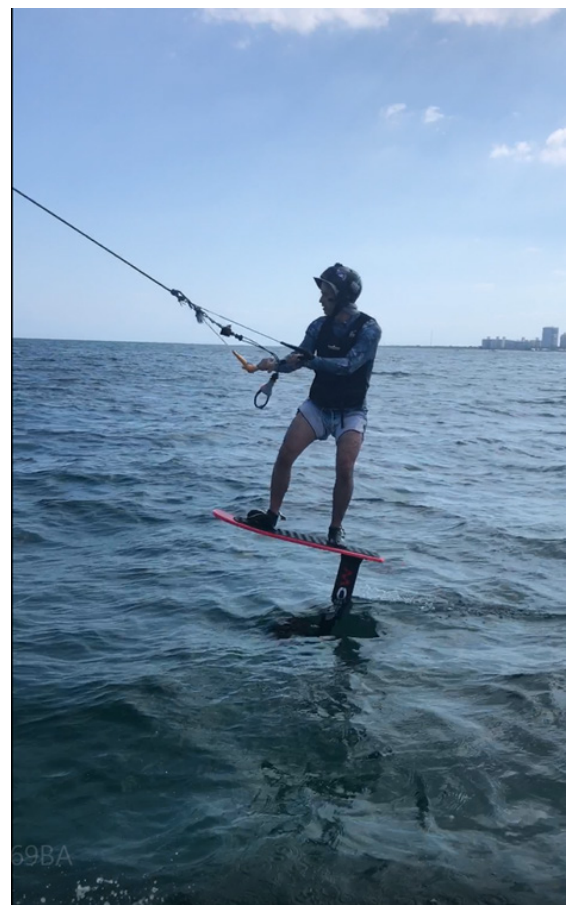
Colorado C-stories: Images of life after a cancer diagnosis.

Receiving the news of any cancer diagnosis can be devastating. Patients may feel like their lives are coming to an end, that they will not be able accomplish many goals they had. Yet time and again the human spirit (with a little advanced medical care) prevails and people remember to be the people they were before they became patients – not just living with a cancer diagnosis but thriving. At CU, we see patients from all over the country and the world. Here are a selection of the CU's finest showing that life remains about living, even, or perhaps especially, after a cancer diagnosis.

Send your pictures and a line or two to ross.camidge@cuanschutz.edu and each newsletter going forward we'll aim to show others what 'hope' really looks like. Look for more images scattered throughout this newsletter.



Lung Cancer Survivor Heidi Onda, co-founder of the White Ribbon Project, shows off her handiwork at Sky Ridge Hospital



Lung Cancer Survivor Ricardo Salgado learning to foil surf in Florida.

Estate Planning

Consider including the Lung Cancer Colorado Fund in your estate plans – It makes a huge difference and is not that complicated. Please review the Special Estate Planning LCCF Newsletter Edition ('Ben and Ellen's Adventures in Estate Planning') available in the clinic rooms or on-line at: <https://medschool.cuanschutz.edu/lccf> or call The Office of Advancement at CU on 303-724-8227.

Five+ Year Cancer Survivors' party – Updates

COVID challenges all of us to not give up, but to find new ways to celebrate

In 2018, for the first time, the CU Thoracic Oncology Program made a decision to invite all those who were at least 5 years out from their initial diagnosis of a thoracic cancer to come and celebrate. Partly, it was to have an excuse to eat birthday cake. However, it was mostly to photograph the group and to be able to show to those earlier in their diagnosis that hope had a face and that that face could look like any one of us. The second celebration took place in the Fall of 2019 and then, in 2020 and 2021, COVID got in the way. Behind the scenes we continue to work on the means to bring this important celebration back.



Where is LCCF-funded research going?

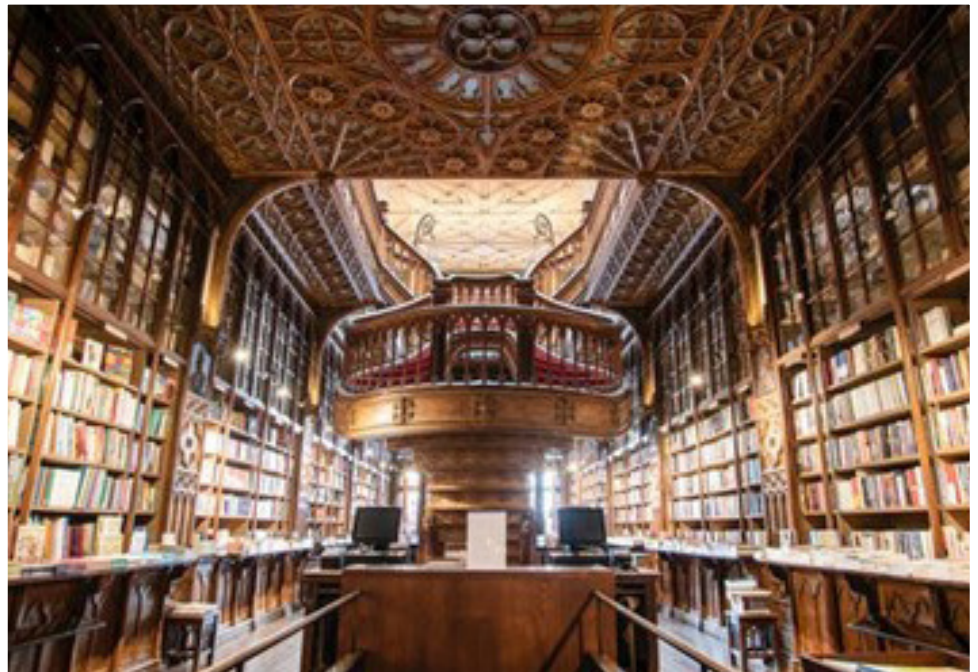
By Raphael Nemenoff, PhD and James DeGregori, PhD

TORI stands for the Thoracic Oncology Research Initiative and is the collective term for the organization and infrastructure to facilitate the full range of research going on in lung cancer and other thoracic cancers at CU. During the past year, TORI has focused on using funds provided by the Cancer Center and the LCCF to support projects to strengthen the whole lung cancer research program from laboratory science to tobacco control. An Executive Committee encompassing faculty specializing in all aspects of lung cancer research meets monthly to evaluate progress on projects and identify new research directions. Some of the initiatives that TORI has recently supported include:

1. Develop a comprehensive clinical data base and enhance collection of specimens from lung cancer patients – (Drs Patil and Schenk) This database allows for retrospective and prospective capture of key clinical patient details so blood and tumor specimens analyzed in future and ongoing studies have complete, associated clinical data.

In addition, the initiative has and continues to catalyze the development of novel patient-derived lung cancer cell lines for basic and translational research – growing versions of a patient's cancer in the lab to study in more detail.

2. Development of novel laboratory mouse models representing oncogene-driven lung cancers – (Drs Nemenoff and Heasley) Just as humans have very different kinds of lung cancer, if the models in mice do not reflect the same heterogeneity their relevance is far less. The project has already successfully engineered mouse lung cancer that mimic EGFR mutant, KRAS mutant, ALK and RET-rearranged lung cancers.



3. Biospecimen collection from subjects enrolled in the IMPRINT-Lung (Randomized Phase II Trial of Immunotherapy with Pembrolizumab for the Prevention of Lung Cancer) trial – (Drs Merrick, Ghoush, Keith, Schenk and Miller) Just as treatment of lung cancer is important, so is preventing it. Some people have early 'pre-cancerous' changes present in their airways, and this trial aims to see if giving immunotherapy lessens the chances that such high-risk individuals will go on to develop lung cancers in the future.

4. Biostatistical support of TORI research – (Dr Gao) A breakthrough is not a breakthrough

unless you can prove the results are true. To do that you need statistics. TORI support of the program's statisticians allows this service to be applied as needed to ongoing lung cancer trials as well as preclinical research studies.

In addition, TORI supported 3 'pilot' grants, designed to open up new areas for research:

1. Targeting TRKB in lung-to-brain metastases (Diana Cittelly PhD, Ross Camidge, MD, PhD). These studies are focusing on developing preclinical models of lung cancer which spread to the brain in mice to enable future experimental therapeutics investigations. The hope is that by identifying some signaling pathways leading to lung cancers growing in the brain, which could be blocked by drugs, trials designed to prevent this spread in patients in the future may be supported.



2. Expansion of Lung Cancer Screening, focusing on the scope and distribution of screening in Colorado (Jamie Studts, PhD). Colorado is a large state with both rural and urban areas, together with inequities in access to health care by location, race, sex and education. Among smokers, lung cancer screening, allowing cancer to be caught while they are still curable by surgery or radiation, can save lives, yet the uptake remains low in many key populations. TORI is facilitating the expansion of programs to extend the effectiveness of screening in Colorado.

3. CyTOF analysis of peripheral blood lymphocytes from lung cancer patients prior to and during treatment (Erin Schenk MD, PhD, Eric Clambey PhD, Raphael Nemenoff PhD, Lynn Heasley PhD). CyTOF stands for Cytometry Time of Flight. What this really means is that key molecules may be analyzed from normal blood and tissue cells and from cancer cells using a tool called mass spectrometry. A mass spectrometer vaporizes samples, and then separates out the component molecules as they fly from one end of the analyzer to the other by size and electrical charge. This allows the unique signature of each to be identified and the location of the molecules in the original specimen to be deduced. This specific project uses this technique to look at rapid changes in immune cells in the blood of lung cancer patients at the start of chemotherapy, immunotherapy and targeted therapy. Already, clues as to why some people may do better than others, despite everything else seeming to be the same, have been derived. The next steps will be to confirm these findings and then explore why the differences occur and whether they could be manipulated to help improve patients' outcomes in the future.



Raphe Nemenoff, PhD



James DeGregori, PhD

New faces and other changes

Simran K Randhawa, MD **Assistant Professor** **Section of General Thoracic Surgery**

During my formative years, I watched my grandparents succumb to cancer, which stimulated my ardor for medicine and oncology. Very early on in my surgical training, I got involved with lung cancer care both clinically as well as through research. Through my research on lung cancer screening, I was able to appreciate the magnitude of the disease and the barriers that exist to the screening program in the community setting. This not only enhanced my interest in the field, but it is also immensely satisfying to know I can work towards a change. Becoming a thoracic surgeon here at UC Health has allowed me to get closer to fulfilling my ambition of bridging the gap between laboratory research and clinical practice, while participating in something that I enjoy and love with zeal.



Charity Holien, RN **Lung Nurse Navigator**

My first experience in cancer was losing my grandmother to breast cancer when I was 10 years old. At that time, I had no idea how it would shape my life or career. I graduated nursing school at Minnesota State University-Mankato in 1998. When I moved to the Washington DC area shortly after college the only nursing position for a new graduate was in oncology. I thought, I am not sure I want to take on this type of nursing since I saw what cancer did to my family with losing my grandmother. Well here I am, 20-some years later and I am still working in oncology. I have been working as a clinic nurse in the lung cancer clinic since 2015. Even though our program was amazing, I felt like we could do more to make the transition for new patients smoother by providing information upfront, coordinating tests/appointments to expedite care, and decrease anxiety of them coming to discuss treatment options. The summer of 2020 I started developing a new role of the nurse navigator for the lung cancer clinic. It has been a welcomed challenge and a new way to share my knowledge with patients. When I am not working I enjoy hiking, kayaking, traveling and off-roading in my Jeep Wrangler.





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2021/2022

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