Melanoma research: more than skin deep

Melanoma medical oncologist Mark Albertini, MD, thinks we are in a “true age of enlightenment” when it comes to treating skin cancer, especially with immunotherapy-based treatments.

“I’ve been doing this about a quarter of a century, so unfortunately I’ve lived through the dark ages where we had painfully few treatments for advanced melanoma,” Albertini said. “And then, with the advent of primarily laboratory-based understandings of targeted therapies, and perhaps more importantly with identifying ways to unleash immune cell attacks against the cancer, we’re now seeing responses in up to 50 percent of patients.”

Not content to stop at 50 percent, Albertini and other melanoma researchers at the UW Carbone Cancer Center are studying ways to improve response and survival rates even more.

Albertini’s research group takes the immunotherapy approach to studying melanoma. Immunotherapies have been incredibly successful in some patients, but other patients have shown no response. Now, in work funded by a UW Carbone pilot grant and philanthropy group Ann’s Hope, Albertini is isolating patient’s immune cells that were activated in response to the cancer, and using them to look for markers that will help him and other clinicians predict who is going to respond to immunotherapy.

“These studies have no direct benefit for these individual patients, but they will go a long way in helping us figure out what’s working and what’s not in the treatments, and if there are any signatures we can identify to tell who in fact is going to go on to get a good response or not,” Albertini said.

Dermatology professor Nihal Ahmad, PhD, and his research group look at the biology of melanoma and are identifying more features that can be targeted specifically with drugs. His lab identified one such target: the pro-cancer protein PLK-1 that is highly expressed in many melanomas. Perhaps most promising, a PLK-1-targeting drug is already in clinical trials for other cancers.

“Current combinations of targeted therapies work initially, but resistance almost always develops,” Ahmad said. Albertini and Ahmad direct their current research with the goal of translating it into the clinic, to both increase survival rates and decrease the need for non-specific – and less effective – chemotherapies.

“We used to use chemotherapy a fair amount to treat melanoma without very positive outcomes,” Albertini said. “But now, with these laboratory-based understandings, survival rates are increasing, and it’s been a while since I’ve written a chemotherapy prescription for melanoma.”
Q: What is CAR T-cell therapy?
A: Chimeric Antigen Receptor T-cell (CAR T) therapy is highly innovative immunotherapy for cancer. A patient’s white blood cells (immune system cells) are removed from the bloodstream through a process called apheresis. The T cells (specific immune system cells) are then separated out and engineered in the laboratory to be able to specifically bind to a target on the cancer cell surface. These cells are “expanded” in the laboratory and then given back to the patient. They are then able to find, bind and kill the cancer cells. These CAR T-cells are able to survive in the patient for a while and continue to keep a check against the cancer.

Q: Which patients are eligible for CAR T-cell therapy?
A: In October 2017, the Food and Drug Administration (FDA) approved Yescarta (axicabtagene ciloleucel), a CAR T therapy (aimed at CD19, which is found on the surface of most B cell lymphomas) for adult patients with certain types of large B cell lymphoma who have not responded to or who have relapsed after at least two other kinds of treatment. This CAR T-cell is manufactured by Kite Pharma, Inc. In May 2018, the FDA approved Kymriah (tisagenlecleucel), a similar type of CAR T-cell from a company called Novartis, for the same patient population. Studies with both CAR T products have proven to be effective in patients with large B cell lymphoma, with approximately 40 percent of patients attaining a long-standing remission. Kymriah is also FDA approved for children and young adults with B-cell acute lymphoblastic leukemia that is refractory or in second or later relapse. In addition to having the disease type specified by the FDA approval, patients also need to be carefully evaluated to make sure they are otherwise healthy and fit enough to undergo CAR T therapy.

Q: What are the potential risks of CAR T-cell therapy?
A: Treatment with CAR T-cells can cause severe side effects in about 10 to 20 percent of patients. The most severe is cytokine release syndrome (CRS), that is the body’s inflammatory response caused by the immune system cells going to work. This can involve fever, instability of heart rate and blood pressure, and requirement for oxygen support. Neurologic changes can also be seen. These can be life-threatening complications however, there are effective treatments as long as patients are under close monitoring and receive rapid treatment. Other side effects also include low blood counts and a weakened immune system.

Q: Will CAR T-cell therapy be available for other types of cancers?
A: UW will be participating in clinical trials to study CAR T therapy in other types of blood cancers in the near future. We are already offering the FDA approved therapies and will hopefully be able to offer CAR T therapy to patients with other types of lymphoma, leukemias and myeloma very soon.

Dr. Kenkre is an Assistant Professor of Medicine within the Division of Hematology/Oncology at the UW School of Medicine and Public Health. She specializes in the care of lymphoma patients, with focused clinical and research efforts in stem cell transplant and cellular therapies.
Have you ever wondered how a doctor decides which chemotherapy drugs to give to a cancer patient? Mark Burkard, MD, PhD, has an answer:

“There’s usually a list of drugs that have worked for that type of cancer in the past and the doctor chooses the one that is likely most effective and safest for the patient,” said Burkard, a medical oncologist and researcher at the UW Carbone Cancer Center. “Often, patients will get multiple drugs from that list, one after another, until the doctor finds one that works.”

This process can be tedious, time-consuming and cause unnecessary side effects in patients.

Burkard is conducting a clinical trial to find better ways to predict which drugs will work best for patients. Funding for this work has come from Garding Against Cancer, which is led by UW Men’s basketball coach, Greg Gard and his wife, Michelle.

His clinical trial looks at a common chemotherapy drug, Taxol, which is used to treat hundreds of patients across Wisconsin each day for many types of cancer. Taxol works by interfering with the cell division process that cancer cells use to replicate. When one cancer cell grows and divides into two cells, Taxol treatment reduces the chances that those new cells will have the correct amount of DNA that they need to survive.

“However, Taxol only works in half of the patients, and we can’t predict which ones it will work in,” Burkard said. The clinical trial is seeking to identify a marker that can predict a benefit from Taxol.

Burkard also stressed how important it is to have funding from philanthropic organizations such as Garding Against Cancer, as opposed to industry funding to conduct studies like this one.

“Taxol is a generic FDA-approved drug that’s already widely used, so no pharmaceutical companies have a vested interest in this study since there would be no return on their investment,” Burkard said. “But this research is critically important for our patients, and philanthropic funding is what makes it possible.”
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Sometimes cancer development is not just about a cell having mutations in its DNA, but about when and how those mutations change the cell’s behavior. UW Carbone Cancer Center member Peter Lewis, PhD, studies how these behavioral changes can lead to cells becoming cancer – and how clinicians and researchers can take advantage of these changes to more effectively target cancers.

In one aspect of his research, Lewis focuses on how genes are turned on and off during embryonic development, and how misregulation in those genes can lead to some childhood cancers.

“In most adult cancers, tumors likely arise from the accumulation of mutations to tumor-suppressing and promoting genes over many years, and in the right context those mutations can lead to cancers,” Lewis said. “But of course children don’t have decades to accumulate mutations, so how do children get tumors early?”

Lewis and his research group at the Wisconsin Institute for Discovery study how mutations in DNA-organizing histone proteins lead to cancer development. For example, in one type of pediatric brain cancer, 85 percent of all tumors have one histone mutation in common. Lewis and his colleagues have shown that, if present at the right time in development, this histone mutation prevents proper gene regulation and causes the stem cells to remain “stuck” in stem cell form, promoting cancer formation. However, if they introduce the mutation into other cells, cancer does not form.

“Most of us get past this window and develop normally, but the children who get these cancers seem to acquire the histone mutation in these specific cell types and in the right developmental window,” Lewis said. “And there are other types of mutations that only work in other specific types of cancer. We don’t know why some cells are exquisitely sensitive to the mutations at specific times, but we do know it’s not a unique problem.”

Lewis’s work has implications not only in pediatric brain cancers, but also in other childhood cancers, in comparing adult to pediatric cancers and in better understanding early human development.

In related research, Lewis and his group look at mutations not in the histones themselves, but in the proteins that deposit histones in DNA to ensure the DNA is organized correctly. When that process goes awry, it can turn on pro-cancer genes – but it may also kick on an immune response mechanism. To learn more about how Lewis’s histone research can be applied to improving cancer immunotherapy, see uwhealth.org/histone.
Cancer does test the strength and quality of relationships – both with partners/spouses as well as friends. The only certainty about relationships is change. When cancer comes into our lives it forces us to ride a roller coaster along with love, fear, sacrifice, loss and hope. Cancer will force you to look at yourself and others in a way you never had to do before.

**Be Realistic**
You are not a super hero nor involved with one although you may both be amazed at the amount of courage that is found.

**Be Flexible**
This is the time to redefine relationship and roles because you won’t have a choice.

**Research shows good relationships are based on the ability to renegotiate the “rules” spoken or unspoken in the relationship.**

**Communicate, Communicate, Communicate**
Relationships, if they count, are never easy. If you don’t let one another in, the relationship loses power when it needs more energy.

**Be Aware of the Beauty of the Person Beside You and Take It In**
Recognize the strengths of the other and try to be kind about their deficits. Do the same for yourself. Try to remain true to yourself and allow the other to do the same.

**Seek Support**
Be smart, ask for assistance whether that be a good talk with a friend or relationship counseling.
Resilience and Fortitude: Claudia’s Pancreatic Cancer Journey

Claudia McCormick hopes to someday be the world’s longest living pancreatic-cancer survivor. She’s got the battle scars to prove it. Two rounds of abdominal surgery left her with an incision she proudly describes as “a map of Route 66.”

The Beloit woman also wants to use her hard-won wisdom to inspire others faced with the diagnosis of pancreatic cancer.

“I want to help other people and let them know to get a second opinion,” she says. “I would be dead right now if I hadn’t followed my instinct.”

Dr. Sharon Weber, her surgeon at the University of Wisconsin Carbone Cancer Center, says that McCormick’s story inspires hope. “Claudia’s story is one that all of us want to be able to tell more — she is an amazing woman with resilience and fortitude, who agreed to all of our recommended aggressive treatments for pancreas cancer, and because of this, she has beaten the odds,” says Weber. “She has an incredible multidisciplinary team of doctors helping her through this, but the victory is all hers.”

McCormick’s journey began in the fall of 2016, when she noticed some vague early symptoms. She felt tired; her skin was itchy and slightly yellow. Her doctor wasn’t sure what was wrong; that’s when McCormick’s survival instinct kicked in the first time.

“I asked her to check my liver enzymes and I didn’t even know what liver enzymes were, she says. They came back high. A follow-up ultrasound and biopsy revealed a tumor about one and a half inches big in the head of her pancreas. The diagnosis was stage 1B adenoma carcinoma.

After three months of FOLFIRINOX, a combination of five chemotherapy drugs, in March 2017, a surgeon at a community hospital attempted to do a Whipple procedure to remove the head of the pancreas, the gallbladder, bile duct, and parts of the stomach and small intestine.

“If I’m not helping someone every day, then I am not doing enough,” says pancreatic cancer patient, Claudia McCormick pictured with Dr. Sharon Weber.
But when the surgeon opened her up, he decided he couldn’t safely operate. While McCormick was still unconscious, the surgeon gathered her family. McCormick heard the verdict herself, later.

“He said there was nothing he or anyone could do and that I had months to live,” she says. “He basically wrote me off.”

McCormick, a mother of two grown sons, and a grandmother of one, began putting her affairs in order. She got very depressed. But then she got mad.

“He’s not God, and not going to tell me when it’s time to go,” she says.

Family and friends rallied around her. Her partner, Al, who had lost a wife to colon cancer, became her “best angel,” cooking and caring for her. Her sisters and brother-in-law chipped in with support from afar, and lots of Internet research on her disease.

“I wanted to show them that their support was really meaningful,” she says. “Knowing how much they were doing for me, I couldn’t just give up and die.”

She asked her medical oncologist to look into clinical trials, and she began another round of oral chemotherapy along with external beam radiation.

Her younger sister found supplements that she believes helped her body heal, including high dose CBD oil, Frankincense oil, turkey tail mushroom, and a Chinese remedy called “bitter melon,” among others.

Finally, in late August 2017, she came to the UW Carbone Cancer Center, where Weber met with her to discuss her case. McCormick was impressed.

“She has this aura about her that is really serene, and these beautiful long fingers,” McCormick recalls. Weber was willing to attempt another Whipple procedure, although she told McCormick her odds of being able to complete the operation were only about 50-50.

So when McCormick woke up after surgery in November 2017, her first question was: “Did it happen?”

“When I heard yes, I started crying,” McCormick remembers.

The biopsy showed that the tumor had shrunk and had been completely removed. Since then, two scans have shown her clear of cancer. Her CA 19-9 number, which measures antigens in the blood released by tumor cells, fell from 535 at diagnosis to 35 after treatment to 13, well in the normal range, at her last check-up.

“Now I have a second chance at life, and I want to get out there and help other people,” she says. “I tell them: You have to fight. You also need a support system. I couldn’t do it alone and no one else can, either.”

She recommends the information and support available at the Pancreatic Cancer Action Network (PanCAN). Her brother-in-law found the site, and through it, she found Weber.

McCormick is getting involved in advocacy for more funding for pancreas cancer research and volunteers with UW’s Pancreas Cancer Task Force – made up of patients, community leaders, family members and caretakers dedicated to funding pancreas cancer research at UW’s Carbone Cancer Center.

Years ago, during her corporate career, she was inspired by motivational speaker Tony Robbins, and wanted to use that passion to help others.

“Since I have a second chance at life, I now have that chance to help others overcome the odds and beat this disease,” she says. “If I’m not helping someone every day, then I’m not doing enough. This, I feel absolutely passionate about. I can’t waste a day!”

“I want to help other people and let them know to get a second opinion. I would be dead right now if I hadn’t followed my instinct.”

— Claudia McCormick

Estimated New Cases in 2018 55,440

Estimated Deaths in 2018 44,330

PANCREATIC CANCER represents 3.2% of all NEW cancer cases in the U.S.
IN THE HABIT OF SUPPORTING WOMEN’S CANCER RESEARCH

Community members charged the field June 20 for Football 101 at Camp Randall in Madison, Wisconsin. Among them, those famous Badger Nuns with a habit of showing up at the stadium—this time supporting women’s cancer research at the event that raised more than $80,000 for UW Carbone, which included a $10,000 match from Coach Paul and Robin Chryst.

MORE EVENT PHOTOS AT: FACEBOOK.COM/UWCARBONE