Calorie restriction research: key to stopping cancer?

Rozalyn Anderson, PhD and her colleagues think they know the key to aging well: caloric restriction (CR), or eating around 20-25 percent fewer calories each day without giving up vital nutrients.

Decades of studies of lab animals and more recent clinical studies in humans shows CR leads to a reduction in cancer, heart disease and many other aging-related diseases. Animals on CR also live longer.

The problem is, it is not very practical. “Very few people would tolerate caloric restriction,” says Anderson, an associate professor of geriatrics in the UW School of Medicine and Public Health and a member of the UW Carbone Cancer Center. “Instead, I study long-lived animals on CR to try to understand how they resist developing aging-associated disease. The argument is that if we can harness those pathways that are responding to nutrition, we can use that as targets for pharmacological interventions.”

Recently, Anderson and her research group at the VA Hospital have refocused their research on cancer. In mouse models of cancer, mice on the CR protocol develop fewer spontaneous cancers. And, when researchers implant tumors, growth is slower in mice on CR.

“So we’ve got these really amazing anti-cancer effects of CR and no one really knows why that is,” Anderson says. “These tumors fail to thrive in the CR animals – CR somehow creates a non-permissive environment for tumor growth, and I think that’s a really interesting avenue of research.”

Anderson and her group’s current hypothesis is that CR both alters cell metabolism in a way that is both detrimental to cancer cell growth and puts the brakes on growth signals in the animal. To understand what is happening with CR at each level – from individual cells to the whole animal – her research group uses mouse and non-human primate models, and cultures animal cells in the lab.

“We take an observation in mice, let’s say, and then we can test it in cell culture through drugs or genetic manipulations to try to break down what is changing with those cellular pathways, and can we identify a mechanism to tweak?” Anderson says. “And then we go back and say, “Well, is this observation also true in the monkeys? Is there evidence for our observation playing a role in CR?’ So we ping-pong between the models to keep mechanisms in focus with potential for translation.”

Through continued research, Anderson and her group hope to better understand the ‘why’ behind CR’s health benefits. She said they have identified and begun testing drugs that appear to function as CR mimics in the lab, though they are not yet ready for human trials.

Anderson is also working with UW Carbone urologist Dr. Tracy Downs (pictured left) on a project to identify metabolism-related blood markers to improve outcomes for African American men with prostate cancer. To read more, please visit uwhealth.org/restrictingcancer
Dealing with a new diagnosis, facing life after divorce or separation, experiencing loss of ability or health and grieving the death of a loved one are among many stressors that can make emotions more pronounced and life more challenging. It is important to recognize these emotions, making space for yourself in the midst of the transition from a dreary winter to life-giving spring.

As the seasons change and as time passes you may feel the need to keep the same routine or you may not feel like participating in familiar activities. Regardless of what you decide, be sure to be gentle with yourself in this season, allowing time to feel the emotions that are true to you and making a conscious effort to participate in the events that serve you well.

It is important to be intentional with your time, energy, and emotional, mental, and spiritual resources. These are some things that people have found to be helpful when grieving:

- Visit a familiar or meaningful place
- Partake in known traditions
- Make new traditions
- Reflect quietly
- Eat familiar and comforting foods
- Write in a journal or write letters to your loved ones
- Say a prayer or have a prayer service for/with your loved ones
- Care for yourself by relaxing and being with friends and family
- Exercise, get a massage or find another activity to lessen stress for your mind, body, and spirit

Some things that are meaningful or important at the beginning of your journey with grief may change as time passes. Similarly, you may find that new activities or traditions become a part of your routine with the passing of time. When keeping your best interest at heart whatever decisions you make will be the right ones.

There may be others around you who are also experiencing grief and they may or may not have similar ways of coping. Everyone deals with grief and loss differently and that is okay. Talking may be hard at first and you might not know what to say, but it is important that you are communicating with your loved ones during this time, letting them know how you are doing and allowing them to help when you need them by your side.

As we leave the darkness and cold of winter it is my hope that you are surrounded by people and activities that are good for you, bringing new life, peace, and healing to you wherever you are in your journey.
In 2018 alone, there were 266,120 new cases of breast cancer. This number is too astounding to sit idly by,” says Mary Hetrick, content manager at Saris, a bicycling accessory company in Madison.

Saris is just one example of the many companies, local and afar, that choose to give to cancer research at the UW Carbone Cancer Center through cause marketing – where a product or promotion is used to raise awareness as well as funds. In Saris’s case, they began producing special pink editions of their popular Bones on-car bike racks and donating five dollars to UW Carbone for every rack sold.

“Since we manufacture here in Madison, we’re able to make changes to our products quickly. In the case of our best-selling Bones rack, we were already making the rack in fun colors such as blue or yellow,” Hetrick said. “The idea came about to make cause-conscious colors, including pink for breast cancer research, so we began partnering with the UW Carbone Cancer Center in 2007.”

The current total: over $30,000 donated to the Breast Cancer Research Fund at UW Carbone in just over ten years.

The pink racks cost the same to consumers as any other color, so Hetrick says it is a fun, colorful way for their customers to show support for breast cancer patients, survivors and research without having to pay extra. For Hetrick, the pink rack and what it represents holds a special place in her heart, as her mother is a breast cancer survivor.

With the pink Bones cause marketing program going strong and the racks continuing to be popular with consumers, Saris will continue their partnership with UW Carbone for as long as they’re able.

“Saris is proud to partner with the go-to cancer resource in Wisconsin, and to help support the UW Carbone Cancer Center’s important and life-changing work,” Hetrick says.
A person’s genome, the sequence of their DNA, tells a story of personal traits, ancestry and health. Similarly, the genes that are expressed in cells reveal how they function, give key insights for cancer research, and are becoming an instructive tool in the clinic as well. Traditional sequencing methods combine the genetic information of thousands or even millions of cells. But what if the important sequences are the proverbial needle in a haystack?

A complimentary technique, called single cell genomics, allows researchers to glean genetic information one cell at a time. This in-depth look can reveal new insights into complicated diseases, like cancer, where a single mutated cell can give rise to disease.

In 2016, the UW Biotechnology Center purchased its first instrument capable of performing single cell genomics analyses. This technology has opened numerous research capabilities for labs associated with the UW Carbone Cancer Center and is having an impact in many areas.

Emery Bresnick, PhD, professor of cell and regenerative biology at UW-Madison and co-leader of the UW Carbone Cancer Center program on Genetics and Epigenetic Mechanisms (GEM) and senior scientist Kirby Johnson, PhD, are among those who conducted initial experiments at UW with this technology. Bresnick studies a class of proteins called the GATA family and how mutations in the DNA that code for these proteins give rise to blood cancers. One of these mutations involves only a single site in the DNA, but this minor change can have major implications.

“This mutation is necessary for acute myeloid leukemia to develop, but it’s not sufficient to do so,” Bresnick said. “So, what makes it sufficient?”

To answer that question, one of the researchers in his lab, Alexandra (Ali) Soukup, PhD, generated a mouse model with that single human mutation.

“The mouse embryos developed normally to adulthood. But Ali discovered when you stress the blood system of the animals, they die at a much higher rate because they lack the ability to efficiently regenerate the blood system,” Bresnick said, adding that under normal conditions, this mutation is “silent” and has no consequences.

Bresnick believes that studying this mutation can answer questions of how leukemia develops in humans.

“If a person has this gene mutation, our feeling is that with the right stressor, there’s only one cell that goes awry, for example, becoming hyperproliferative and not responding to normal constraints.”

With the single cell genomics instrument and their mouse models, Bresnick and Soukup will test that hypothesis. The information they learn will deepen understanding of leukemia and could identify new therapeutic targets.

“Let’s say you’re looking at population of 500 cells and five were triggered. In a population analysis, you’d never see the change,” Bresnick said. “Sometimes the discovery is made in a large population, but then to be able to understand it with biological sophistication, you have to know what’s happening at the single cell level.”
Hearing the words “you have cancer” from your doctor can be a difficult experience. All of our physicians at the UW Carbone Cancer Center know how hard it can be for patients – and they know how important it is for each patient to receive the treatment that makes the most sense for him or her. UW Carbone physicians recommend asking the following five questions at your first visit.

“These questions help improve your relationship with your doctor, and they improve your ability as a patient to know what is right for you,” says hematologist Chris Fletcher, MD. “Importantly, patients are certainly not limited to these five questions, and we encourage you to write down questions in between visits as they come up and to bring them to your next appointment.”

1. What kind of cancer do I have? Where is the cancer? Has it spread?
2. Can my cancer be treated? What are my treatment options?
3. What can I expect during treatment?
4. How much time do I have to think about my options or get a second opinion?
5. What local resources are there to help me cope with my diagnosis?

To read Fletcher’s detailed take on these five questions, or to download a worksheet to take to your appointment, please visit uwhealth.org/fivequestions
Like many single 27-year-olds, Megan Parkin has an idea of who she does and does not want to date.

“I used to be looking for the sexiest man alive, even if they didn’t have the qualities I was looking for. I dated a lot of the wrong guys,” Parkin says. “Now, I’d say it’s the complete opposite. I still want to have a handsome partner but I want to make sure they are strong enough in our relationship.”

Chalk it up to good old-fashioned growing up, but Parkin’s change in attitude also has a lot to do with her health: in June 2017, she found a lump in her breast. Within weeks, she was diagnosed with breast cancer and had a lumpectomy. After rounds of chemotherapy and radiation, she later learned she tested positive for the BRCA2 gene that predisposes women to early-onset breast cancer. Nearly two years later, Parkin considers herself cancer free (she likes to think of herself as being cancer free the day of her surgery) and she is living life as fully as possible – including having hopes of finding a partner and father to the children she wants to have. But being a cancer survivor is very much a part of who she is now, and she knows it affects how she forms new relationships.

“In my old life, I was crazy and happy, like I couldn’t have any gaps in time where I wasn’t doing something. Now, crazy to me is being calm. I’m calm and I’m happy,” Parkin says. “I can’t take back the fact that I had cancer – I wouldn’t want to, because I wouldn’t be me without it – and if I’m really finding a man with the qualities that I want now, he’ll be receptive and supportive of that fact.”

According to Kirsten Norslien, program director at Gilda’s Club Madison, dating as a cancer survivor is not entirely different from dating in general: the best new relationships start when partners are happy with themselves. Still, there are unique concerns for survivors related to dating, regardless of age, gender or sexual orientation.

“I think for survivors, the question comes up a lot: when do I tell this person that I’m a survivor? How do I
explain my scars? How can I handle my fatigue without feeling like a party pooper?” Norslien says. “And there’s often the assumption that once you’re done with treatment you should be fine, but that’s not true. Many survivors are concerned about recurrence, and the lingering impact of the disease and treatment can be ongoing for a long time.”

And that is not to even mention concerns with sexual health and fertility.

“Sexuality, your ability to be intimate, all can be impacted by treatment, and having that conversation is hard even in the best of circumstances,” Norslien says. “Fertility can also be impacted by treatment, and then you have to work with those effects. And again, when do you bring that up?”

Part of Norslien’s role at Gilda’s Club is to facilitate support groups and social activities for patients and survivors. People in the support groups tend to have mixed diagnoses and mixed ages, which she says works surprisingly well to help people form intergenerational friendships and seek advice from survivors in different stages in their lives.

“At our support groups, discussions of dating and intimate relationships are absolutely allowed!” Norslien says. “As are discussions about any relationships. I think sometimes people get so focused on what is going on with their cancer that they sometimes forget to focus on how cancer has impacted all their relationships.”

For her part, Parkin could not agree more. Whether it is looking for a new romantic partner or navigating old friendships, she learned that cancer can impact any relationship.

“I feel like cancer will really make or break relationships, between you and a man, you and friends, you and family, it doesn’t matter,” Parkin says. “I am very protective of who I let around me now, because I am very focused on being happy, healthy and peaceful.”

“Sexuality, your ability to be intimate, all can be impacted by treatment, and having that conversation is hard even in the best of circumstances.”

— Kirsten Norslien

RESOURCES FOR CANCER SURVIVORS

Gilda’s Club
gildasclubmadison.org

UW Health support groups
uwhealth.org/support

UW Health Women’s Integrative Sexual Health program (WISH)
uwhealth.org/wish

UW Health Men’s Health Clinic
uwhealth.org/menshealth

First Descents
firstdescents.org

Please note: Gilda’s hosts a number of support groups as well as an annual Midwest Young Adult Cancer Conference, scheduled for Saturday, April 27, 2019.
ADVANCES

If you have moved, are receiving duplicate copies or do not wish to receive this publication in the future, please contact:
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WINNER WINNER, CHICKEN DINNER

Andy North, one of UW Carbone’s biggest fans, teamed up with our Emerging Leadership Board (ELB) to host the 6th Annual Trivia Night at the Sylvee. Friendly competition coupled with fun prizes resulted in more than $36,000 raised! The ELB, a dedicated group of young professionals, has raised more than $400,000 for UW Carbone since its inception in 2011.

TO LEARN MORE ABOUT THE ELB, BECOME INVOLVED OR ATTEND ONE OF THEIR EVENTS VISIT FACEBOOK.COM/ELBUWCARBONE

To learn more about the 2019 Andy North and Friends initiative or attend one of their upcoming events, visit ANDYNORTHANDFRIENDS.COM