Cutting-edge Cancer Research

Patients share their clinical trials experiences

COMPREHENSIVE CANCER CENTER UNIVERSITY OF MICHIGAN HEALTH SYSTEM





On the cover:

Nancy Van Dyke is midway through a clinical trial and back to baking with her grandkids.



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Research Round-Un

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| 1971: | National Cancer Act greatly increases research |
|-------|---|
| 1986: | World Health Organization sets guidelines on pa |
| 2000: | Chief of surgery at the NCI says 50% of cancer of |
| 2003: | Scientists decode the entire human genome, pa |
| 2007: | NCI reports the number of cancer survivors incr |
| 2012: | The number of cancer survivors in the U.S. reac |
| 2015: | Cancer moonshot initiative invests \$1 billion in r |

Visit mCancer.org/thrive for a link to a detailed timeline of specific advances in cancer since the late 1800s.

cancer cells.

1500 E. Medical Center Dr., Ann Arbor, MI 48109-5944. If you do not wish to receive future issues of Thrive, please call Beth Johnson at 734-764-8311. Theodore S. Lawrence, M.D., Ph.D, director Scott Wood, chief administrative officer Nicole Fawcett, manager of cancer communications Beth Johnson, editor and senior writer Shelley Zalewski, contributing writer Karen Moeller, art director, MOEdesign Chas Moeller, project management, MOEdesign Edda Pacifico, photographer, Edda Photography

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For more information about the stories in Thrive or any other cancer-related information, please call the Cancer AnswerLine at 800-865-1125.

STATE OF THE NATION: Cancer Update

Moonshot is the term for launching a spaceship to the moon, but it's also used to describe big-picture, breakthrough, right-on-target efforts to get something done: like curing cancer. Vice President Joe Biden is leading the U.S. moonshot initiative to cure cancer with a boost of research funding to advance our understanding of the disease, develop new treatments and end cancer as we know it.

Research dollars from our government have historically played a big role in finding new ways to treat this ever-changing, very complicated illness. Biden's moonshot won't simplify cancer, but it is a push in the right direction.

"There has never been a more exciting time in cancer research," says Ted Lawrence, M.D., Ph.D., director of the University of Michigan Comprehensive Cancer Center. "New discoveries in the laboratory are coming fast, and there are tremendous opportunities to turn those discoveries into new treatments."

An increased commitment by our government for cancer research is much needed after cuts were made several years ago. Here's a look at where we've been

funding and is considered the start of the "war on cancer"

ain medication to provide relief to 90% of patients

diagnoses can be cured using surgery, radiation and/or chemotherapy

aving the way for understanding genetic defects that cause cancer

reased by 19% since 2001

hes nearly 14 million, an all-time high

new cancer research funding

Over the years, more precise radiation, smaller and less invasive surgeries and adding chemotherapy into treatment plans stand out as big advances in cancer care. Cure rates are higher and patients experience fewer side effects.

Which way is the moonshot? Keep an eye out for research news in these areas:

Precision medicine brings more targeted therapies to patients as physicians better understand how each person's genes interact with cancer cells.

Advances in **immunotherapy** mean we're finding ways to boost the body's ability to kill

Robotic surgery makes operations even more precise.

Cancer vaccines will become routine in cancer prevention.

And, more and more research data is being collected and shared by the cancer

community in order to make advancements faster. The U.S. moonshot includes large databases containing information on cancer.

Make Yourself Comfortable

Addressing symptoms of cancer treatment to feel better



Susan Urba, M.D.



To make an appointment at the Symptom Management and Supportive Care Clinic, call **877-907-0859**.



Cancer patients see a wide range of caregivers, from oncologists to surgeons, radiologists to anesthesiologists. Each plays a role in the treatment process to help patients have the best quality of life possible.

So which person on your care team is the one to talk to about tingling pain in your feet? What about nausea? Or maybe you're so full of anxiety at night that you can't sleep. Who is the best caregiver to go to for that?

The easy answer, says Susan Urba, M.D., is someone on your primary oncology team.

Cancer and its treatment comes with symptoms and side effects. Most patients experience them at one point, some minor and others intolerable. Every caregiver at the Cancer Center—from front-line staff at check in to nurses taking your vital signs to the technician giving your chemotherapy—is concerned about how you're feeling and can get you to the right person for help.

Symptoms and side effects often need added care and attention. We sat down with Urba, who directs the Cancer Center's Symptom Management and Supportive Care Program. She discusses the variety of issues patients might face and what resources are available.

What are some examples of symptoms and side effects that patients need help with?

One of the most common symptoms we see is pain. It might be neuropathic pain, burning in the hands and feet, that often results from chemo. Some pain comes from the cancer itself. There are numerous types of pain medicines to get the best treatment. There are nerve blocks and physical interventions for their pain. We have an anesthesia pain doctor come to our clinic six times per month. We also partner with a Physical Medicine and Rehabilitation physician who visits our clinic twice a week to develop programs for patients who may benefit from physical modalities to help their pain.

Another common issue patients need help with is nausea. Though patients take anti-nausea medication with chemotherapy, some still struggle. We take it a step further by adding other medications and approaches to help control that symptom. Dietitians in our clinic help counsel patients on what to eat or not to eat during periods of nausea or diarrhea.

What about the importance of emotional support?

Cancer comes with psychological struggles. People might need help dealing with stress or issues of faith. We frequently call our chaplain to offer spiritual support. We have a clinical social worker who offers psychological support, practical assistance, meditation, visualization and relaxation techniques. We interact with the art therapist and music therapist. These support services are available to all patients.

For patients struggling with serious psychological issues like depression, the PsychOncology Program has psychiatric health providers who specialize in treating patients with cancer.

Why offer a separate clinic for symptom management?

We want to support patients in many ways. Sometimes, depending on their situation with cancer, patients may have several doctors, like a radiologist, an oncologist and surgeon. It can be confusing who is steering the ship. We try to help advocate for good communication between the patient and his or her many health providers.

Our clinic is a part of the cancer care team that can provide an extra layer of support and intervention to improve the patient's quality of life. Any clinician on your care team can refer you here for an appointment. You can also self-refer. Generally speaking, we see patients for what we call high-burden symptoms. Often we can begin to help manage them within a week to 10 days.

What is an appointment like at the Symptom Management and Supportive Care Clinic?

We want to make each patient feel like an individual in our large system. Our appointments are often longer than standard clinics because we know it takes time to manage some of these difficult symptoms. We have tried to make the clinic's environment as relaxing and comforting as possible, and coordinate with as many teams as possible to get them the support they need.

We always try to coordinate visits when the patient is here for another appointment. The patient can get numerous services in one visit that are harder to orchestrate separately. If someone comes from a distance for treatment, we aim to coordinate appointments around that.

A patient will either see a nurse practitioner or me, the physician, so we can assess what's going on. Then we'll coordinate with whatever other services are needed. It could be a nutritionist, pain management specialist, a social worker or psychiatric health provider.

Is this palliative care? Is it only for patients near the end of life?

Palliative care, broadly, means trying to provide relief of suffering. Patients might need help managing symptoms at all stages of their disease, starting from the time of diagnosis and at various points throughout their care. Yes, we treat end-of-life patients. They are an important sub-set of the patients in our clinic.

We are a supportive care team for all patients at the Cancer Center.

FORUM | Make Yourself Comfortable

Types of caregivers you'll find in the Symptom Management and Supportive Care Program:

Anesthesiologist

Art therapist

Chaplain

Clinical social worker

Dietitian

Medical assistant

Medical oncologist

Music therapist

Nurse practitioner

Pharmacist

Physical Medicine and Rehabilitation physician

Scheduler

Quality of Care and Life

A clinical trial gives one patient the best of both

Mike Sanders wants you to know: participating in a clinical trial does not rule your life. Nor does it mean your doctors only care about whether the medication is working or not.

Sanders is not what most people envision when they think of a stage 4 cancer patient. Just 32 at the time of his sarcoma diagnosis in 2014, he and his wife Elizabeth were preparing to move from their hometown of Grand Rapids for a new job.

Sanders bumped his leg against equipment at the gym but the injury was disproportionately painful. As a childhood cancer survivor, he knew about his increased risk of developing adult cancer in the long bones of his body. After injuring the leg a second time, he went straight from a biopsy to the Grand Rapids hospital for surgery.

Sarcoma is a rare form of cancer of the tissue that connects and supports the body, such as muscles, nerves and tendons. It often starts in an arm or leg, but can form in the torso, head, neck or anywhere in the body. Sanders' cancer had metastasized to his lungs.

The Sanders' cancelled their move in order to stay close to family and his current doctors. He also travelled to the University of Michigan Comprehensive Cancer Center, where he met Rashmi Chugh, M.D., at the Comprehensive Sarcoma Clinic.

"When I first met Mike, his tumor had already grown despite aggressive standard treatments in Grand Rapids," Chugh says. "There are relatively few effective standard treatments for sarcoma, and it often affects patients who are young, otherwise healthy and in the prime of their lives."

Joining a clinical trial was not a guarantee of positive results, but Sanders decided to try after qualifying for an immunotherapy study. Immunotherapy is a growing area of cancer research and treatment that works the opposite of chemotherapy. Instead of attacking cancer cells, it boosts the body's ability to fight cancer.

"There are many forms of immunotherapy under study. Because of promising results in melanoma and lung cancer, as well as generally tolerable side effects, there is a lot of hope and excitement surrounding immunotherapy in all types of cancer," Chugh says.

"The most difficult part during my initial treatment was the negative side effects. I was exhausted and had neuropathy. I became more depleted from advancement of the disease. We wanted to preserve some sort of quality of life balance during the time I have," Sanders says. TURE | Quality of Care and Life

—Mike Sand

"They couldn't make promises it will make a positive change. I was willing to make a personal sacrifice with the understanding you might help others if not yourself."

Visit **mC**ancor or **/**

Visit **mCancer.org/thrive** for more information on immunotherapy and other advances in cancer treatment.



"I had renewed hope because of the physical improvements and mental boost. The side effects of my current treatment are very minimal compared with before. My physician seems very enthusiastic," Sanders says.

After several months on the trial, Sanders' cancer responded positively to the drugs. His scans show significant reduction in the size of some of his tumors. Others appear to have stopped growing and died.

"Even though the standard treatments can work in some patients, they weren't helpful for Mike. With the immunotherapy, Mike had dramatic shrinkage in his cancer with minimal side effects. We are still trying to figure out why immunotherapies work in some patients and not others," Chugh says.

More than six months after starting the clinical trial, most of Sanders' disease remains controlled by the immunotherapy, but some of the areas are slightly enlarging. Sanders is pleased with the positive results and with the improvement in how he feels overall. He is back to basketball and working out.

He and Elizabeth will travel from Grand Rapids to Ann Arbor for cycles of infusion treatment until the clinical trial concludes. Every eight weeks, he receives a CT scan of his chest to check the nodes on his lungs and an MRI on the leg of the original tumor site. He will have options to continue taking the medication after the trial if it continues to work.

"My trial has shown you can have really positive results for yourself and a possible legacy for other people," Sanders says. "It is not an exhaustive process and doesn't take up all my time. You're not abandoned just to see the effects of the medication. My care team wants to see me successful, happy and healthy."







Mike and Elizabeth Sanders reminisce about his time on the U-M campus as a student.



The Sanders' try to end each infusion appointment with lunch in Ann Arbor.

SPRING 2016

A typical day of infusion treatment for Sanders:

- Arrives at Cancer Center at 9 a.m.
- Gets blood drawn
- Visits physician or physician assistant to review blood results and discuss how he's feeling
- Heads to the infusion clinic at 10:30 a.m.
- Nurses double-check his weight, height, allergies and port
- Receives 90-minute infusion treatment
- Heads to campus with Elizabeth to enjoy lunch and a walk around 1 p.m.

Find the Target, Take Aim Dne patient tries a clinical trial after gene sequencing reveals proteins feeding her cancer



Tancy Van Dyke was so healthy she had never taken an antacid. She **V** rarely saw a doctor. At 64 and recently retired, the long-time employee • of Oakridge High School in Muskegon had just started to settle into a retirement lifestyle with plans to travel with her husband Joe and spend time with their adult children and grandchildren.

A gastrointestinal attack in June 2015 led to a surprise trip to her local hospital and within a half hour, doctors suspected the problem was more than gallstones. She was diagnosed with cancer—they weren't clear of the original location—that had metastasized to her liver and chest.

Van Dyke visited doctors in Muskegon and traveled to the University of Michigan Comprehensive Cancer Center to discuss treatment options. Eventually she was diagnosed with bile duct cancer, cholangiocarcinoma. These ducts drain bile from the liver to the small intestine. She tried chemotherapy close to home with no positive results.

ANOTHER PATH TO PURSUE

At the U-M Comprehensive Cancer Center, Van Dyke opted to have her genes sequenced to identify all types of genetic mutations that could play a role in her cancer. The findings are used to help direct therapies that might work best for patients with advanced cancer.

This area of research, known as precision medicine, is growing rapidly. Two genes were identified that came together abnormally in her cancer which likely contributes to its growth.

Researchers had seen success stopping the growth of other cancers in instances where a genetic change was present by using new treatments targeted against the effects of that change. But Van Dyke's tumors were in the liver. She was screened to see whether her illness qualified her to participate in a clinical trial: it did not, a huge disappointment.

"Studies have very specific qualifications to ensure the safety of patients participating," says Rashmi Chugh, M.D., VanDyke's Cancer Center oncologist. "These requirements are particularly stringent in phase I studies when we are learning about new agents that haven't been used in people before. As the studies get further along and we understand the side effects better, there is sometimes increasing flexibility in understanding which patients can safely participate."



with her grandchildr<u>en is a</u> family tradition.

COVER | Find the Target, Take Aim



Nancy and Joe Van Dyke plan to travel in their retirement and spend time with family.



Visit mCancer.org for more information on gene sequencing for patients with advanced cancer.

says.

The process began with a visit to the Cancer Center for tests, including an eye exam, EKG, CAT scans and blood work. Documentation is essential in a clinical trial. These are baseline tests for comparison.

Van Dyke's treatment is in pill form. She does not know whether she is being given the trial drug or a placebo. Her care team carefully performs the required tests and measurements as outlined in the study protocol. For example, on day 1 and day 8 of a cycle, she'll get an EKG within so many minutes of taking her pills.

IS IT WORKING?

do right now, I got my miracle." continue taking them. and looks forward to seeing them.

UPDATE:

Four days later, the situation changed and Van Dyke received approval to join the trial as the first patient with abnormal liver tests due to tumors to try the treatment.

LIFE AS A TRIAL PARTICIPANT

"My doctors explained to me that the trial might not help me at all, but my participation would help their research. I thought, what do I have to lose," Van Dyke

At the time of our interview, Van Dyke needs to finish the third round before her care team measures changes to her disease. Despite not knowing, she is hopeful. "I feel healthy," she says. "I am no longer exhausted from chemo or need to take naps during the day. If I can live the rest of my life—no matter how long it is—feeling like I

If her scans show the drugs are working against her cancer, she will be able to

Also, she feels well cared for by her U-M care team. She describes them as "her girls"

"Clinical research is in incredible team effort," says Chugh. "This includes the faces our patients see in clinic such as nurses, research coordinators, research extenders,



physicians, the research infusion team and more. There is also a whole army of faces that patients don't see who are equally important and dedicated to each patient and their clinical research experience. Everyone involved has the same ultimate goal of finding a new strategy to help our patients."

For Van Dyke, she sees the future of health care in her care team.

"They are a group of 20- and 30-something young women with access to the best technology and health information available. When I come up the hill and see the hospital with the big M, I think, Thank you god, for the people in there, the care I've gotten. I feel so blessed." 🚦

9 weeks into treatment, Van Dyke learned her cancer is shrinking. While not every patient on a clinical study experiences benefit from treatment, she and her care team are glad to see a positive impact when standard therapy was ineffective.



e and

A patient story of helping, healing and leaving a legacy

Thristine Knight's family has always joked she was born with a needle in her hand. She began sewing at age 5 and has continued crafting her entire life. Now 65, she has been loyal to quilting since her 30's. Like many wives and mothers with full-time jobs, her hobby came second to her busy life.

That changed in fall 2013. While on a business trip, she noticed a difference in a mole on her back. She was proactive and called a dermatologist at home in Jackson, Mich.

"I was able to have it removed and didn't worry much about it," she says. "Then the nurse called a few days later and said the news was not good and I needed to notify my family."

Knight had melanoma, the most serious of skin cancers that develops in the cells that produce skin pigment. After visiting the University of Michigan Comprehensive Cancer Center for a larger excision, she learned her cancer had spread.

What Knight wanted was hope, but the diagnosis of stage 4 melanoma left her with limited treatment options for a cancer that often does not respond well to chemotherapy or other current therapies.

"That week, I was a basket case," Knight says. "I reverted back to my faith. I had heard that people with stage 4 melanoma, your chances of being around very long are pretty slim."

Knight found the hope she was looking for at her first appointment with Christopher Lao, M.D., at the Multidisciplinary Melanoma Clinic on Christmas Eve 2013. He believed Knight might be a good fit for an immunotherapy clinical trial.

Immunotherapy is a growing area of cancer research and treatment that uses the body's immune system to fight or kill cancer cells.

"The breakthroughs in cancer immunotherapy have surpassed anything we have had to date. When it works, it can control the disease for years and possibly forever," Lao says. "We have worked hard to bring the best therapies to U-M and I met Chris at the right time. It was a perfect fit and I'm thrilled she agreed to participate."

Baseline tests before she could begin in the trial included MRI, biopsy and CT scans. Her first day as a trial participant involved having blood



drawn, a visit with Lao, and a variety of tests. Her trial was double blind, meaning she did not know which drugs she was receiving, or in what combination.

"I never had any reservations about the clinical trial," Knight says. "I felt it was my only option because of the type of cancer I had. Some people feel like guinea pigs, but for me it wasn't about that. For me, the disease is much worse than any side effects I might have from the medication."

Knight's cancer had spread to her chest, abdomen and lymph nodes under her arm. A bone in her back was also affected. After six cycles of infusion treatments over a period of five months, her scans became free of cancer. Her side effects were minimal, including some fatigue and itching.

"My bone was very responsive to treatment and has completely healed. I do not have cancer now. I still don't know which combination of drugs I received. I won't know unless my cancer comes back."

During her cancer experience, Knight's outlook on life changed. She decided she should find time to have fun every day and enjoy each day to the fullest. With clear scans since April 2015, she goes to her home quilting studio every day for at least an hour. On weekends, she'll spend the whole day sewing and laughing with friends.

"It makes you feel so hopeful to understand how many people are being helped by cancer research. Because of this research and my participation, people might be able to live longer. I

feel really honored to be part of a solution," she says. Knight continues to work at Eaton, her employer of 38 years. She has created a quilt for everyone in her family. She also shares her craft and teaches quilting. She visited the Michigan State Capitol with Lao to share her experiences on the clinical trial.

"Cancer therapy across the board continues to improve and immunotherapy happens to be one that can work in a variety of different cancers. We still have a long way to go to improve what we do so that eventually there is an effective treatment for everyone," Lao says.



FEATURE | Hope and Heirlooms





Visit mCancer.org/thrive for more information on cancer research and clinical trials looking for participants.

"Quilts are heirlooms when created for someone and carried down through the family."

-Christine Knight

"The dedication and commitment of patients to participating in clinical trials is what drives the improvement in cancer care."

-Christopher Lao, M.D.

Support Services in All Shapes and Sizes

very patient copes with cancer diagnosis and Ltreatment differently. The Cancer Center's Patient and Family Support Services Program meets all types of challenges. Patients can use our services and complementary therapies to take an active role in their treatment. This includes resources offered by the PsychOncology Clinic, Social Work and Spiritual Care staff. Additional creative therapies like art, music and guided imagery use tranquil activities to tap into the healing power of self-expression, which has been shown to lessen the emotional toll and side effects of cancer treatment.

"Our teams have worked with thousands of cancer patients and their care teams," says Donna Murphy, L.M.S.W., director of the Patient Family Support Services Program and co-director of the Cancer Center's PsychOncology Program. "Although no two patients are alike, one thing we notice is that patients tend to tackle physical symptoms first. Struggling with emotional issues often comes later. We strive to meet each patient's priorities at the moment, whatever and whenever that might be."



"The swelling in my legs makes it difficult to get around." have no appetite." **"I'm nauseous."**

"I'm taking the pain meds my doctor has prescribed, but I'm experiencing quite a bit of pain."

"I can't sleep."

"Stress about my bills and worries about my insurance coverage are getting to me." "My prognosis is good, but my son is anxious about my cancer returning. He's having trouble sleeping and at school."

> "My doctor is encouraged by my progress, but I feel sad and scared all the time. I can't snap out of it."

"It's been years since I've prayed or worshipped. I'm not sure what I believe anymore; *I have a lot of questions.*"

| PROGRAM | WHAT IT IS / HOW IT HELPS |
|-----------------------------------|--|
| Art Therapy | Art classes provide an outlet for th to boost self-awareness and build management and stress reduction |
| Guided Imagery | One-on-one sessions with a social relaxation and healing. Helpful in re like pain and nausea. |
| Families Facing Cancer Program | Counseling and activities focused and cope with cancer-related issue |
| Music Therapy | Visits from a therapist who uses m emotions. Helpful in reducing pain, |
| Financial Counselor | One-on-one meetings to provide a insurance issues. Helpful in overco |
| PsychOncology Clinic | Counselors use tools like talk thera patients address depression and a sleep or concentration. |
| Social Work | Trained professionals problem-sol to address practical issues causing |
| Spiritual Care | Chaplains lend support to patients profound questions or need spiritu |

COPING | Support Services in all Shapes and Sizes

'Because you never know when concerns will arise, we make our services available to any patient who has received treatment at the Cancer Center within the last two years," says Murphy.

| | HOW TO CONNECT |
|---|---|
| oughts and feelings when words fail, positive coping skills. Helpful in pain 1. | Call 734-232-2215 to self-refer. |
| worker to use the imagination for educing stress, anxiety and side effects | Call 734-232-2215 to self-refer. |
| on helping patients' children understand es. | Call 877-907-0859 to learn more. |
| usic to help express a full range of , managing stress and improving sleep. | Call 734-232-2215 to self-refer. |
| ssistance with medical billing and oming financial worries. | Call 877-326-9155 Monday – Friday, 8 a.m. – 5 p.m. |
| apy, medication and education to help anxiety, which can disrupt mood, appetite, | Ask your doctor for a referral for a clinic appointment. |
| ve and connect patients with resources g distraction or concern. | Call 734-232-2215 to self-refer. |
| of any faith who are struggling with life's al or religious connection. | Call 734-232-2215 or ask staff to page the on-call chaplain. |
| | |

BE HEALTHFUL

The Wonder Bug: Probiotics

BY NANCY BURKE, R.D., DANIELLE KARSIES, M.S., R.D. AND MELISSA SHANNON-HAGEN, R.D., C.S.O. UNIVERSITY OF MICHIGAN COMPREHENSIVE CANCER CENTER SYMPTOM MANAGEMENT AND SUPPORTIVE CARE PROGRAM

Whether you're a healthy person looking to reduce cancer risk or a patient in treatment experiencing diarrhea, probiotics could be your wonder bug.



These friendly bacteria help ferment, decompose and digest the food we eat. They keep disease-causing bacteria in check and play a role in immune health. Some probiotics are bacteria while others are yeast. Their benefits vary.

For example, yeast strains such as Saccharomyces boulardii are recommended for antibiotic-induced diarrhea. VSL#3 helps with irritable bowel syndrome or diarrhea from pelvic radiation.

GOOD SOURCES OF PROBIOTICS:

Yogurt, by law, contains at least two strains of probiotics: Lactobacillus bulgaricus and Streptococcus thermophilus. Always check the label and be sure "live and active cultures" is listed.

Kefir is a yogurt-like drink that contains even more probiotics.

Excellent news for those with lactose intolerance: probiotics help you digest lactose sugar during fermentation so most people can tolerate yogurt and kefir. If not, there are non-dairy probiotics:

- unpasteurized sauerkraut
- kimchi, seasoned and fermented Korean vegetables
- fermented soybean, including tempeh, miso and natto
- kefir made from coconut water or milk

WHAT ABOUT A PILL?

A lack of federal regulation of supplements and the effects of heat, processing and age on probiotic counts make foods the best choice. However, probiotic supplements can be a viable option. Look for supplements that contain multiple strains, including *lactobacillus* rhamnous and saccharomyces boulardii, and at least 3-4 billion probiotic count.

A WORD OF CAUTION

For most people, the potential benefits of probiotics far outweigh any risk.

An exception: if you are immunocompromised from certain chemotherapies or post-organ transplant, high doses of probiotics may not be recommended. Ask your physician.



Probiotics may decrease:

- radiation-induced diarrhea when given at the start of radiation
- ✓ diarrhea during treatment
- ✓ post-treatment intestinal complications

Nearly a third of all cancers have mutations in the RAS family of genes, including KRAS. In pancreatic cancer, a particularly aggressive and difficult-to-treat disease, almost every tumor is driven by KRAS mutations. But KRAS has been thought to be "undruggable" - researchers cannot identify an effective therapy against it.

Now, researchers at the University of Michigan Comprehensive Cancer Center have dug deeper and exposed a key interaction that may contribute to why mutations in KRAS lead to cancer.

"We came at this from a different angle," says study author Arul Chinnaiyan, M.D., Ph.D., director of the Michigan Center for Translational Pathology. "Knowing how critical KRAS is in cancer development, we looked for important protein interactions that we might try to disrupt. We picked up on an interactor called AGO2. It was a very robust interaction."

AGO2 plays a role in silencing genes and processing microRNA – so it impacts many genes. The researchers found AGO2 interacted with both mutated and normal KRAS. The link appeared in all 12 of the cell lines tested.

Studies in cell lines and mouse models showed that AGO2 enhanced the cancer-causing ability of KRAS. The higher the level of AGO2, the more cancerous activity, the researchers found. At the same time, KRAS inhibits AGO2's ability to process microRNA. This impacts the downstream oncogenes and tumor suppressor genes controlled by microRNA.

The finding suggests potential to explore interrupting the KRAS-AGO2 interaction as a possible therapy. Additional research is needed.

"This is not a nearterm solution. It is a basic science discoverv that has potential to be translated. It's exciting to consider that KRAS may not be the undruggable target we thought it is," Chinnaiyan says.



RESEARCH ROUND-UP

FOOD PRESERVATIVE KILLS **CANCER CELLS, SUPERBUGS**

Nisin, a naturally occurring food preservative that grows on dairy products, delivers a one-two punch to two of medicine's most lethal maladies: cancer and deadly, antibiotic-resistant bacteria.

A new University of Michigan study found that feeding rats a "nisin milkshake" killed 70-80 percent of head and neck tumor cells after nine weeks and extended survival, says Yvonne Kapila, DDS, Ph.D., a professor at the University of Michigan School of Dentistry.

Kapila has studied nisin in cancerous tumors and as an antimicrobial to combat diseases of the mouth. In this study, after nine weeks of nisin treatment, tumors were comparable to tumors at three weeks.

Kapila's group has published positive results with less potent nisin, but the highly purified nisin ZP used in the present study nearly doubled its effectiveness.

Nisin, a colorless, tasteless powder, is typically added to food at the rate of .25 to 37.5 mg/kg. Many foods contain nisin, but nowhere near the 800 mg/kg needed to kill cancer cells.

Several products available to consumers also contain nisin—creams and pharmaceuticals to fight infection and mastitis, and a sanitizer in lactating cows. While promising, the results are small and in mice only, so it's too early to say if nisin will act the same

way in humans, Kapila says. She does not advise patients to take nisin at this time.

The next step for Kapila's lab will be to test nisin in a clinic setting.





Cancer Treatment 101

Cancer can be treated with many types of therapy. I like to think of it as CREST.



Shawna Kraft, Pharm.D. Have a question for the pharmacist? Email us at *ThriveMagazine@ med.umich.edu*.

Chemotherapy attacks cancer by affecting how it grows, causing the cells to die. Chemotherapy is not specific to cancer cells so can affect our normal cells, especially those that grow quickly (hair, skin, mouth, bone marrow). This is why many chemotherapies cause hair loss, skin issues and mouth sores, and also can decrease our infection-fighting cells, platelets and hemoglobin.

Radiation is the use of high-energy x-rays to kill cancer cells. Side effects vary depending where on your body you receive treatment. They can include diarrhea, fatigue, nausea and skin irritation. Another form of radiation treatment involves placing radioactive sources in or next to a tumor (brachytherapy).

Endocrine or hormonal therapies decrease or stop production of estrogen, progesterone, testosterone or cortisol levels in the body, usually to fight breast, prostate or adrenal cancers. These medications prevent the normal hormones in our bodies from helping cancer grow. Side effects include hot flashes or joint pain.

Surgery is used to remove tumors and surrounding tissue, to reduce the size of tumors or to relieve symptoms caused by a tumor. It can range from small incisions to major procedures with varying side effects.

Targeted therapy makes up a range of cancer medications that treat cancer by precisely identifying and attacking genes or proteins causing cancer growth. Side effects are often less severe than chemotherapy because the drugs have less impact on normal cells. Types of targeted therapy might include:

Immunotherapy stimulates the immune system to attack cancer.

Small molecule inhibitors usually target a specific mutation that helps cancer grow.

Biologic agents range from affecting the immune system to targeting specific cancer cells. An example cetuximab, an antibody that targets cancer cells driven by the epidermal growth factor receptor.

Just a Phone Call Away

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mCancer.org/thrive

- A detailed timeline of advances in cancer since the late 1800s
- Information on clinical trials looking for participants
- A link to information on MiOncoseq and gene sequencing for patients with advanced cancer
- Past Thrive articles about our Patient and Family Support Services
- Details on how to find our Symptom Management and Supportive Care Clinic
- More information on the future of cancer research, such as immunotherapy and precision medicine