

SOLVING THE CANCER PUZZLE

Even the healthiest people get sick. But scientists are making new discoveries about risk and targeting the disease with amazing precision. Could the war on cancer be winnable?

BY KATHERINE HOBSON

When Ann Malik started feeling ill in spring 2014, she was in peak health. A cofounder of the gear company FuelBelt, Malik, then 39, loved to run near her home in Barrington, Rhode Island, ate lots of fresh produce and had never taken a puff of a cigarette. But for months she'd experienced mental fog, fatigue and a 10-pound weight loss. Doctors thought the problem was chronic fatigue syndrome or pneumonia until tests yielded shocking news: She had stage IV lung cancer.

There was one ray of hope: new, effective drugs Malik could take—if her tumor tested positive for one of three key genetic mutations. When the test for a mutation called ROS1 came back positive, even Malik's doctor "cried with relief," she recalls. She started the drug Xalkori, which, along with chemotherapy, has stopped the disease in its tracks.

Malik is benefiting from precision medicine, which uses genetic and molecular info to match a treatment to a tumor, like finding the right key for a lock. Drugs based on this approach are helping a growing number of cancer cases, says Richard L. Schilsky, M.D., chief medical officer of the American Society of Clinical Oncology. This year, the White House even announced a \$215 million Precision Medicine Initiative. Here's how precision is changing cancer as we know it.



Understand your odds

WHEN IT COMES TO PLAYING THE GENETIC HAND WE'RE DEALT, KNOWLEDGE REALLY IS POWER.

Everyone's talking about "the cancer gene," but did you know that all cancer is caused by genetic mutations? A mix of lifestyle and environmental factors—what you eat, whether you smoke, the air you breathe—are responsible for many harmful changes to DNA, causing cells to grow out of control. Inheriting a gene from a parent plays a role in probably 10 to 15 percent of cases, says Mary Daly, M.D., chairwoman of the department of clinical genetics at Fox Chase Cancer Center in Philadelphia, though researchers are looking into even more genetic links. The rest, at this point, is probably chance (Ann Malik's doctors blame her cancer on "bad luck"). So what do you need to know to better understand your risk?

Start with your family history. "This is the time to talk to your mom about her mom," says Elizabeth Swisher, M.D., professor of ob/gyn at

HEALTH HERO ANNE WOJCICKI

Cofounder and CEO of 23andMe, a personal genetic information company

HER BREAKTHROUGH

23andMe, one of the first at-home gene-testing kits, set a model for a giant global database that can be used to study disease.

WHY IT MATTERS

The company, which has sold more than 1 million kits, is looking to partner with researchers seeking genetic links to disease, as well as with drug developers. "As we identify more genes that fuel breast or skin cancer, say, we can point pharmaceutical companies in the right direction," Wojcicki says.

the University of Washington School of Medicine and coleader of Stand Up to Cancer's Ovarian Cancer Dream Team. Talk to your dad, too; paternal history is just as important, even for cancers that affect only women. Strong family history (two or more close relatives with cancer) is currently the most reliable predictor of risk. A genetic counselor can help you make the call about whether to be tested.

Know what to expect from the test. If you do opt to get gene-tested, don't think of it as a crystal ball for every type of cancer. The test your doctor would order typically looks for mutations in a few genes—mainly linked to breast, ovarian and gastrointestinal cancers. But there's a movement afoot to make testing more widely available with affordable online kits. Color Genomics offers a \$249 test that analyzes 19 genes linked to breast and ovarian cancers and can assign you necessary genetic counseling to review the results.

Genes aren't necessarily destiny. Some inherited mutations, like BRCA1 and BRCA2, can raise a person's lifetime breast cancer risk to as much as 65 percent and ovarian cancer risk up to 39 percent. Other genetic mutations carry a moderate risk of 20 to 40 percent, says Nadine Tung, M.D., director of the cancer risk and prevention program at Beth Israel Deaconess Medical Center in Boston. That's scary but still far from inevitable: Other factors will affect whether a person ultimately develops cancer, like the position of the gene mutation, the influence of other genes and the lifestyle factors you already know about.

Not everyone will go the Angelina Jolie route. Different risk profiles may present different choices. Meredith Swinney, 33, tested positive for BRCA2 in 2010, several years after her mother died of ovarian cancer. "I wasn't ready to have all those parts of me removed," says the Philadelphia-based academic program coordinator; her doctor worked out a plan of semiannual breast MRIs and mammograms, and she plans to undergo ovarian surgery at 35. Some women with the BRCA mutations have options, based on age and genetic risk, says Sue Friedman, executive director of FORCE, a nonprofit focused on hereditary breast and ovarian cancers.

Your test could help someone else. Doctors might find an atypical gene variation, but not be sure of what it means, says Dr. Daly. Registries like PROMPT allow people who've been tested to contribute their genetic data so researchers can provide better risk estimates in the future.





Live smart, live long

AN APPLE A DAY IS A GOOD START. HERE'S WHAT ELSE YOU NEED TO KNOW ABOUT CANCER PREVENTION AND SCREENING.

How can I reduce my risk? Don't smoke, avoid UV rays, eat lots of fruit and veggies, and exercise regularly. "If people did everything we know about preventing cancer, ideally, we could eliminate half of cancer incidence and prevent half of deaths," says Carolyn Aldigé,

president and founder of the Prevent Cancer Foundation. Tobacco—recently implicated in nearly half of all deaths across a dozen types of cancer—and obesity are the biggest risk factors. A 2011 study of more than 100,000 women also found that even three to six drinks

a week was associated with a 15 percent additional risk for breast cancer.

I already do those things. What else?

If you're under 26, talk to your doctor about an HPV vaccine. It protects against the most dangerous types of the virus, which can cause cancer beyond just the cervix, says Aimée Kreimer, Ph.D., an investigator at the National Cancer Institute.

What about environmental causes?

According to the American Cancer Society, roughly 6 percent of cancer deaths are attributable to environmental pollutants and exposure to carcinogens on the job. There are red flags from animal studies on parabens (used as preservatives in cosmetics and medications), but no direct links to cancer in humans. It's hard to study someone's lifetime exposure to thousands of chemicals, notes Julia Brody, Ph.D., executive director of the Silent Spring Institute. (Still, the President's Cancer Panel has said that the true chemical influence has been "grossly underestimated.")

Could I be missing cancer warning signs?

You have to check it to detect it. Even if you've been vaccinated against HPV, get screened for cervical cancer. If you're between 21 and 29, the American Cancer Society recommends a Pap smear every three years. Women 30 and over should have a Pap plus an HPV test every five years (though a Pap alone every three years is fine, says the ACS). As for skin cancer, the American Academy of Dermatology advises self-exams and physician skin checks (talk to your dermatologist).

SMART MAMMOGRAMS

Breast cancer screening can be a super confusing—and controversial—topic. Read this for a dose of perspective.

YOU'VE HEARD

You don't need to start getting mammograms until you're 50.

YOU SHOULD KNOW

The U.S. Preventive Services Task Force now recommends that women in their 40s who aren't high-risk confer with their physicians. While regular scans between 40 and 49 do save lives, they can also lead to false positives or unnecessary surgeries for cancer that wouldn't have become life-threatening. Others argue that catching cancer earlier might mean the difference between having chemo or not. Says oncologist Marisa Weiss, M.D., president of BreastCancer.org, "My advice is still to start getting annual mammograms at age 40."

YOU'VE HEARD

Dense breasts mean you're more likely to get cancer.

YOU SHOULD KNOW

Finding cancer in dense breasts, which are packed with connective and glandular tissue, can be "like trying to find a polar bear in a blizzard," says Dr. Weiss. So physicians may also screen with ultrasound and MRI. Forty-five percent of women between 40 and 74 have dense breasts but not all of them get cancer, says Karla Kerlikowske, M.D. She led a recent study that looked at degree of density, family history, age and ethnicity to pinpoint risk. Of the women with dense breasts, only 24 percent were at high risk for a missed cancer.



Breakthroughs that could save your life...

OR YOUR MOM'S. OR FRIEND'S. ONE IN THREE WOMEN WILL SOMEDAY GET CANCER—AND THESE DISCOVERIES COULD MAKE A DIFFERENCE.

Most cancer is still treated with surgery, chemotherapy and radiation. While these often do the job, doctors can't always predict who will respond. And because chemo and radiation kill healthy cells, too, they can have debilitating side effects. But as scientists decode the DNA of tumors, they're able to target cancer more precisely. Here's the scoop on the latest treatments.

They take aim at the source of cancer. The new drugs are directed at specific genetic glitches that “drive” a person's cancer. (It's more of a laser-guided missile than an atomic bomb.) This allows doctors to target mutations in tumors rather

than just in the organ of origin (breast or lung, for example). Bonus: These treatments often have fewer side effects.

Cancer can be something you live with. Although the drugs can produce quick, dramatic responses, they aren't necessarily cures. That's because the cancer, wily and adaptable, may eventually find another way to grow, and a new drug will have to be deployed, explains James Gulley, M.D., director of the National Cancer Institute's Medical Oncology Service. Still, these drugs can be used to hold off cancer for months, even years. When it comes to someone you love, any extra time matters.

Your immune system's a powerful tool.

You may have heard of immunotherapy—it's an emerging treatment that “releases the brakes” on the immune system so it can attack cancer in the body. About 15 to 25 percent of patients in studies are responding, says Dr. Gulley, offering hope for those like Stefanie Joho. At 22, the former Gawker staffer was diagnosed with colon cancer. After two surgeries and two regimens of chemo, she still had an inoperable tumor in her abdomen. Joho joined a clinical trial for the immunotherapy drug Keytruda and started to feel better almost immediately. A year later, her tumor has shrunk and her status is stable.

Treatment is getting more accessible.

About 20 percent of patients are eligible for targeted therapy, says Keith Flaherty, M.D., director of clinical research at Massachusetts General Hospital Cancer Center. That number jumps to 40 percent at major medical centers—and will only grow as more research is done.

CANCER GETS PERSONAL

PRECISION MEDICINE HELPED ME BEAT CANCER

Kimberly Jessop, 38, had melanoma that wasn't responding to treatment—so she took a risk on an experimental drug.

In December 2010, my husband pointed out a small cyst on my back. I thought it was nothing but saw a dermatologist anyway. A biopsy turned up stage IV melanoma. I was dumbfounded. With a cancer like this, traditional treatments don't do much. At Vanderbilt University Medical Center in Nashville, I was lucky enough to qualify for an immunotherapy treatment called Interleukin-2. I was hospitalized for a week at a time for treatment. After 26 infusions, I felt half-dead. My scans showed that some of my tumors had shrunk—but some had grown. I needed to get on a drug that caused all my tumors to respond. Soon after, doctors started me on a clinical trial of a different immunotherapy—a PD-1 inhibitor. I'd drive three hours to Vanderbilt and then drive back, continuing to work and take care of my family (my kids were 2 and 5 at the time). Things seemed to be going well, but I had to



wait eight weeks until my first scan to be sure. When my doctor called me on my drive home and told me that my tumors were getting smaller, I screamed with joy! Hearing that gave me more hope for the treatment, because it had been hard spending many precious hours away from my family.

I did have a couple of setbacks, including being diagnosed with chronic myeloid leukemia. By that point, my husband and I were less fazed by bad news. Cancer taught me that until everyone tells you there are no options, there are options. I now take a targeted-therapy drug twice a day, and that's kept my leukemia stable. Since February 2013, I've been in remission for both. I don't have symptoms or side effects, and I feel so lucky.

HEALTH HERO

ELANA SIMON

*Cancer researcher,
Harvard sophomore*

HER BREAKTHROUGH

Simon was diagnosed at 12 with a rare liver cancer. At 16, with the help of her biophysicist father and his lab team at Rockefeller University, Simon recruited fellow patients via YouTube to send in tumor samples. "If someone were going to work on this, it had to be people who were affected by it," she says. The team sequenced normal and malignant liver tissue, discovering the genetic mutation that likely caused Simon's cancer.

WHY IT MATTERS

Simon's finding may likely lead to new targeted treatments. Earlier this year, she introduced the president at the launch of the White House's Precision Medicine Initiative.

GET THE BEST TREATMENT

IF YOU HEAR THE WORD **CANCER**, IT'S IMPORTANT NOT TO PANIC, SAY EXPERTS. INSTEAD, TAKE THESE STEPS TO BECOME A SAVVY HEALTH ADVOCATE.

1

ASK ADVICE

Women who develop breast, colon or lung cancer at an uncommonly young age should usually get more than one opinion, says Richard Wender, M.D., chief cancer control officer with the American Cancer Society. Look for oncologists who specialize in your cancer.

2

SEEK OPTIONS

Chemotherapy and radiation may not be the best treatment plan for your specific case—don't assume you'll need them. Find out from your physician if any of the newer treatments apply to you. This may involve asking if you need genetic testing for specific mutations.

3

FIND A TRIAL

Look for clinical trials or large open studies of experimental drugs that are not yet available on the market. Ask your doctor if any are being conducted in your area, or at a nearby cancer center, that you might be eligible for. (Cancer.org also has a clinical trials matching service.)

4

LOOK AHEAD

Picture your postcancer future. Talk about what you want life to look like after treatment. "Twenty years ago, surviving was the only goal," says Lillie Shockney, R.N., associate professor at Johns Hopkins University School of Medicine. "That shouldn't be the case anymore."



SHAZAM THIS PAGE FOR ANSWERS TO YOUR BIGGEST CANCER QUESTIONS, INSPIRING SURVIVOR STORIES AND MORE.