A cancer patient tells her story, as an unprecedented array of researchers across campus is developing the latest prospects for surviving the disease.

All For One

STORY BY JOHN BEAHLER

ANNE WELLER IS LUCKY. A ROUTINE mammogram found the small tumor growing in her breast before it had time to spread. She and her doctors know that now, but after her first surgery in January they weren't as sure. That's because breast cancer can invade other organs if it isn't caught early enough. As a precaution, surgeons routinely remove lymph nodes under the arm, the spot where breast cancer is most likely to spread.

Removing those nodes gives cancer patients a safety margin, but it also can cause severe problems—burning pain, numbness, swelling and chronic infections. Many women need physical therapy after the surgery to restore loss of motion. "My cancer was caught early and was very small, so the chances of it being in the lymph nodes were slight," Weller says. "I just couldn't see any sense in taking all of the nodes." Determined to make sound decisions about her own treatment, she went to work learning all she could about her disease. "I wanted to know what my options were," says Weller, a development officer for the University of Missouri-Rolla. "I wanted to know the why. I wanted to know all the statistics of what my chances of recurrence were going to be. What my long-term survivability would be. I needed more information than my surgeon was willing or prepared to give me, so I sought out a different level of care."

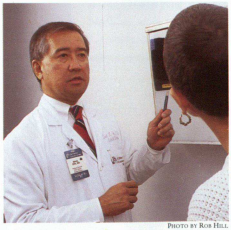

PHOTO BY ROB HILL

As medical director of MU's Ellis Fischel Cancer Center, David Ota offers patients life-saving experimental treatments for cancer.

Her Internet research led her to a national study under way at select cancer centers around the country. The study is evaluating an experimental treatment called sentinel node biopsy. With this technique, surgeons use a dye or a radioactive marker to identify a primary lymph node that drains the breast cancer. They remove only that node, or just a few others, and put the tissue through a battery of lab tests searching for the tiniest evidence of tumor cells. Early study results suggest that if the sentinel node is free of disease there's an overwhelming likelihood that breast cancer has not spread to other lymph nodes. If the test is positive, it gives doctors more information about treating individual cases with additional surgery or with radiation and drugs.

Weller made another important discovery on the Internet. MU's Ellis Fischel Cancer Center, 90 miles up Highway 63 in Columbia, is one of just a few dozen hospitals involved in the sentinel node study. A family friend put her in touch with cancer surgeon David Ota, who is medical director of Ellis Fischel.

The next day she was sitting in Ota's office as he described the new technique and enrolled her in the study. Since then, Weller has had the sentinel node surgery followed by radiation therapy and is taking part in two additional research studies.

Thousands of Missourians have discovered that same high level of care ever since Ellis Fischel first opened its doors in 1940. Back then, the state-run hospital treated cancer patients who were too poor to pay for medical care.

One in three Americans will develop cancer during their lifetime. Specialists like Ota are optimistic about the prospects for curing cancer one day. "We're making important strides," Ota says. "Cure rates are going up. There are better screening and early detection programs. We're developing more effective

PHOTO BY STEVE MORSE

After she discovered she had breast cancer, Rolla, Mo., resident Anne Weller also discovered that MU's Ellis Fischel Cancer Center offered her treatment options that weren't available elsewhere in the state.

treatments. The pipeline is full of new drugs that will come out in the next few years. But we still need better tools."

That's why MU is taking the next big step to elevate its cancer research and treatment program. Mizzou has launched an initiative that will build Ellis Fischel and the University into a comprehensive cancer center, as designated by the National Cancer Institute. Scientists and doctors all over campus are joining the effort, but it's a big job.

The National Cancer Institute has awarded this prestigious ranking to only 34 institutions around the country that demonstrate excellence in both basic cancer research and in clinical treatment. There are no comprehensive cancer centers in Missouri or in the surrounding states of Iowa, Arkansas or Kansas.

"The comprehensive cancer center designation puts an institution in a class with very few others," says Daniel Winship, MU's vice chancellor for health affairs. "It really is the highest level of achievement that can be recognized in the whole area of cancer research, education and care."

But the designation carries more than prestige, Winship explains. "You have a leg up on your ability to have grant proposals accepted, on your ability to be included in cancer protocol studies throughout the nation. You're in a position to participate in ways that you never were before." It also will help MU recruit the country's finest cancer doctors and researchers.

Achieving that designation will require Mizzou to invest millions of dollars in people and in bricks-and-mortar infrastructure. That investment, though, will yield huge returns in public and private financing and in improved cancer care. In the process, MU will be training a new cadre of cancer professionals to treat patients around the state and the country.

Every comprehensive cancer center must have a major cancer research focus, not just a researcher here and there. "You need a critical mass of people who are carrying out research in a variety of areas," Winship says. MU must also demonstrate an institutional commitment, substantial interdisciplinary collaboration and outreach efforts around the area.

"All of these things we have," Winship says. "We can point and say we have all of those pieces, but every one of them needs to be enlarged, expanded and refined, and developed further in order to get us over this threshold." Currently, the University is looking to a number of sources for funding, including state and federal grants and private donations. Cancer research will become one of the priorities of the campus mission enhancement program.

The costs will be great, but so will the benefits, when the latest research at MU and other universities becomes available to doctors who are treating cancer patients. A key component of the comprehensive cancer center designation is what's called "translational research," or, as Ota describes it, "mouse-to-man research" in which knowledge gained in the laboratory is put to use at a patient's bedside.

A number of important resources help MU make unique contributions to cancer research. Radiation is one of the most important tools to treat the disease, and Mizzou's Research Reactor is the most powerful reactor at any university in the country. The reactor produces radioactive isotopes used in new medicines to target and kill cancer cells. It's the only reactor in the country to produce an isotope of a rare element called samarium, which a team of MU researchers used to invent a new drug called Quadramet.

The drug is almost a miracle for thousands of people who suffer the crushing pain of bone cancer. After one injection some patients live relatively pain-free for as long as a year.

Scientists at Mizzou have been responsible for developing other drugs like Quadramet which, because they contain radioactive isotopes, are known as radiopharmaceuticals. Another drug under development uses microscopic ceramic spheres to carry cancer-killing radiation that attacks tumors in the liver. MU's reactor is one of the few able to produce radioactive isotopes that decay very quickly. That's crucial for the drug to do its work on cancer cells and then leave the body before it damages healthy tissue.

When it comes to basic life sciences research that helps unlock the mysteries of cancer, MU is in a good position as one of a handful of universities that are home to both a medical school and a college of veterinary medicine. Strong basic research programs exist across campus in genetics, medical informatics, cell biology and nutrition, among others. Ellis Fischel Cancer Center is the cornerstone of the entire enterprise. Cancer specialists there are involved in more than a hundred experimental treatments, and that number will grow if it becomes a comprehensive cancer center.

Jeffrey Bloss is one of a handful of doctors around the country testing a novel new therapy that shows remarkable promise for treating ovarian cancer. Right now, ovarian cancer is one of the most difficult to treat. The tumor responds well to initial surgery and chemotherapy, but the cancer often reappears within a year and kills nearly half the women who at first appeared to be cured. Bloss, director and associate professor of gynecologic oncology, is taking on the problem with a new drug called Ovarex. Unlike traditional chemotherapy, this drug doesn't kill tumor cells with poison; rather it helps the immune system fight off the invader.

As scientists learn more and more about tumors, they can turn that knowledge into a weapon. "For years there were three ways that you could address a cancer," Bloss says. "You could poison it with a drug, you could kill it with energy—radiation or a laser beam—or you could cut it out with surgery. Now, we've taken it one step further and we're asking 'Well, what caused it? What can we do to the actual mechanism of the cell to make it revert back to normal?' Because cancer isn't something you inhale—it's one of your cells that's gone haywire, and we want to get it back on track."

One of the ways scientists like Bloss can get those cancerous cells back on track is through a basic understanding of how healthy cells function. For instance, they know that nearly every cell in the body contains a tumor suppressor gene called P53. It's something like a cell policeman. The gene helps cells grow normally, do the work they're supposed to do and then die of old age. This tumor suppressor gene also patrols the cell looking for growth abnormalities, such as cancer-causing mutations. When it finds them, the normal P53 gene causes a cell to commit suicide.

Some cancers, particularly ovarian cancer, are caused by defects in these cellular policemen. "The gene gets damaged, so those cells in the ovary without that gene grow uncontrolled," Bloss says. "They no longer function normally and they don't ever die, they just keep growing and growing. That's the definition of cancer—uncontrolled growth that just won't stop."

A human hair dwarfs these microscopic ceramic spheres, which pack a precise one-two punch of radiopharmaceuticals for treating liver cancer.

At Ellis Fischel, Bloss and his colleagues are testing a new therapy to rein-

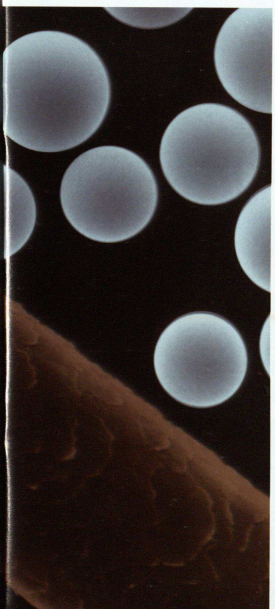

Photo courtesy of Delbert Day. Color added.

troduce the P53 gene into cancer patients. The gene is biochemically "glued" to a harmless virus, which carries this gene into cancer cells. "What we're doing is putting the genetic blueprint back into the cell," Bloss says. "What we've seen, both in the laboratory and now in humans as well, is that the cell reverts back to normal and the cancer goes away."

Experimental results have been dramatic, but he cautions that the therapy is too new to draw hard-and-fast conclusions. Although earlier studies show this gene therapy shrinks tumors in humans, Bloss says, "We're now in the process of learning how well it works and for how long. Will the patient stay cancer-free, or will the cancer come back when you quit giving the product?"

The explosion of knowledge about human genetics is another bright spot in the fight against cancer. Because all cancers involve some genetic abnormality, learning more about how genetic defects cause cancer could provide answers. As a pathologist at Ellis Fischel, Charles Caldwell has spent decades studying the impact of those genetic abnormalities in cancers. In recent years he's had important new tools at his disposal—high-speed computers that analyze data in a fraction of the time that it used to take.

This new field is called bioinformatics. One giant step is a new research technique called microarray technology, which allows researchers to compare tens of thousands of DNA sequences simultaneously. "It allows us to hunt across all the genes that exist in a person and identify abnormalities in a tumor virus vs. normal DNA," Caldwell says. That technology would let researchers determine who might be more susceptible to certain cancers and other diseases. It could help to determine what kinds of chemotherapy might work best on a tumor, or, it could help find a genetic switch to turn off tumors. Microarray technology might even answer questions about why the same type of tumor grows more rapidly in some people than in others.

Caldwell is another Ellis Fischel physician who has experienced the synergy that can exist between doctors and basic researchers around campus—the kind of synergy generated at a comprehensive cancer center. Caldwell has been working with computer engineers Jim Keller and Paul Gader to adapt "fuzzy logic" computer technology to cancer research. The U.S. military first developed fuzzy logic to search for hidden land mines or scan satellite photos looking for enemy tanks lurking behind trees. Caldwell is studying how to use the same technology to search for cancer cells hiding in human tissue samples.

A comprehensive cancer center at MU would be a catalyst for more of these research interactions. "We have people spread all over campus who have interests that right now aren't necessarily focused on cancer, but they might," Caldwell says. "Right now they're looking at cell biology or gene control or something else, but they're starting to think along the lines of evolving their research toward cancer.

"You know, computer engineers are good programmers, but they don't know what problems need to be solved in cancer. The cancer people know the problems they have, but they don't know what tools are available to apply to those problems. If you bring these people together, they sort of click."

That synergy is evident among scientists in disciplines that span the campus. As MU builds its programs toward a nationally recognized comprehensive cancer center, research produced in university laboratories can go to work helping more cancer patients like Anne Weller with innovative treatments.

And Weller's experience had an impact on her co-workers. "It encouraged some of the younger women in my office to get their annual mammogram. It's kind of a tough way to be a role model, but I can't stress that enough. You need to go for those exams, along with self-examination and routine medical care."

The care Weller received at Ellis Fischel made all the difference in her treatment. "At Ellis Fischel, everyone you deal with is very sensitive to why you're being treated there," Weller says. "It's a time in your life when you're facing your mortality. You're asking yourself, 'Am I going to have a future? What am I going to do for my children?' So many things are passing through your mind.

"Until you need them, I guess the ordinary person doesn't think too much about the services that are covered at a cancer center," Weller says. "It really does make a difference to be able to go to a place where all they do is treat cancer."