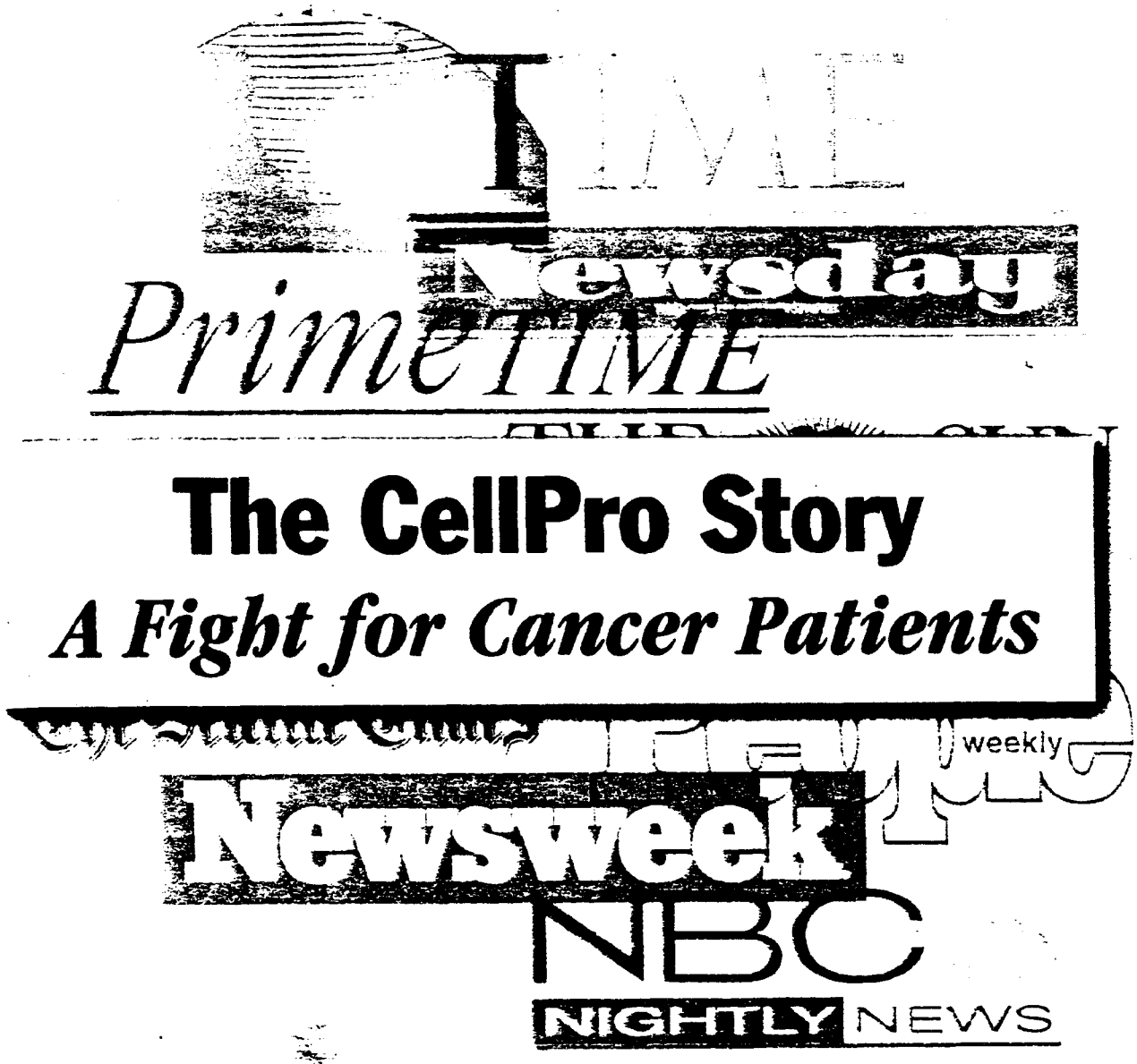
TIME
Newsday
PrimeTIME
The CellPro Story
A Fight for Cancer Patients
weekly
Newsweek
NBC
NIGHTLY NEWS
FINANCIAL TIMES
Seattle Post-Intelligencer
TODAY

CellPro, Incorporated
22215 26th Avenue SE
Bothell, Washington 98021
(206) 485-7644
(206) 485-4787 Fax

Dear Friend,

In the last few weeks, dozens of national news organizations —newspapers, magazines and television programs— have helped tell the story of CellPro's fight to keep a promising new therapy on the market and available to victims of breast cancer, leukemia, multiple myeloma and other deadly cancers.

Many stories have focused on my own battle with non-Hodgkin's lymphoma and treatment with the then-experimental CEPRATE®SC System. The story seems to have struck a responsive chord in thousands of cancer patients, their friends and families, who contacted CellPro to ask about the CEPRATE®SC System and the patent fight that threatens to force it from the market. Key members of the United States Senate and House of Representatives, as well leaders of cancer research organizations and support groups have lent their support as well.

We cannot begin to express our gratitude to all of them. That we have come this far against bigger and much better financed adversaries is a tribute in significant measure to their support and encouragement.

Unfortunately, our fight is not over. The patent dispute has already spanned two trials, and there is the prospect of a lengthy appeal. At the same time, CellPro's petition to the US Department of Health and Human Services / National Institutes of Health for a government-granted license to the technology behind the CEPRATE®SC System is now being considered by NIH Director Dr. Harold Varmus. A decision could be made as soon as early August.

The NIH will consider public opinion on this important public health issue. You can help ensure that this promising new device remains available to cancer patients and that important clinical research continues uninterrupted with the CEPRATE®SC System. We think the attached summary of articles from publications as diverse as *PEOPLE* and the journal *SCIENCE* tell a compelling story. Consider them, and then please, call your congressman or senator or the National Institutes of Health and let them know what you think. Dr. Harold Varmus, the Director of the National Institutes of Health, can be reached at (301) 496-2433. And as always, thank you for your time, for your support and for your encouragement.

Sincerely Yours,

Rick Murdock

Richard D. Murdock
President and Chief Executive Officer
CellPro, Inc.

What doctors have said about CEPRATE®SC System *

"It is my strong opinion that compelling public interests demand the continued, and legally unfettered, availability of the CellPro device for both experimental and fully-approved therapeutic applications."

Cesar O. Freytes, M.D.
Director of Bone Marrow Transplant Program — Associate Professor of Medicine/Hematology
University of Texas Health Science Center, San Antonio, TX

"If for any reason the CellPro TCD device were to become unavailable, this study would need to be shut down. If that were to happen, children would die."

Andrew M. Yeager, M.D.
Professor and Director — Bone Marrow Transplant/Leukemia Program
Department of Medicine, Emory School of Medicine, Atlanta, GA

"I strongly believe that if the CellPro device were for any reason to become unavailable for my use, my research pursuits would suffer a serious setback and the interests of my patients would be compromised – fatally, in some cases."

Richard Burt, M.D.
Director of Allogeneic Bone Marrow Transplant
Northwestern Memorial Hospital, Chicago, IL

"I believe that there is an unquestionable benefit to be derived from keeping the CellPro device (as the only FDA-approved device) on the market as its availability would spur new and novel treatment procedures."

Charles Hesdorffer, M.D.
Director, Bone Marrow Transplant Program
College of Physicians and Surgeons of Columbia University, New York, NY

"Removal of the CEPRATE®SC device would severely limit treatment of cancer patients using high dose chemotherapy."

Kenneth Anderson, M.D.
Physician, Department of Medicine, Division of Medical Oncology,
Dana Farber Cancer Institute, Boston, MA

* Excerpted from declarations submitted to the U.S. Department of Health and Human Services in connection with the CellPro petition for "march-in" rights.

Key members of the United States Senate and House of Representatives, as well leaders of cancer research organizations and support groups, have backed CellPro's fight to keep its promising new therapy on the market and available to victims of breast cancer, leukemia, multiple myeloma and other deadly diseases.

United States Senate

WASHINGTON, D.C. 20510

May 16, 1997

The Honorable Donna E. Shalala
Secretary
Department of Health and Human Services
200 Independence Avenue, SW
Washington, D.C. 20201

Dear Madam Secretary:

We are writing to you on behalf of breast cancer victims, leukemia patients, multiple myeloma patients and the many others across our states and the nation who suffer from cancer. It is our understanding that a pivotal new tool in the fight against these diseases, and breast cancer in particular, may soon face removal from the marketplace. It is also our understanding that this product is the only one of its type to be approved by the Food and Drug Administration (FDA). Our purpose in writing to you is to enlist your help in ensuring that these victims and others who do currently or could potentially benefit from this technology have uninterrupted access to it as part of their medical options.

The device in question is the CEPRATE®SC System, used in purifying the bone marrow transplantation (BMT) process, and thus enabling safe and more effective use of this vital form of cancer treatment.

We are not concerned with the patent dispute that is driving the legal action which now threatens the treatment of American cancer victims. But, unless a suitable, FDA approved alternative is widely accessible, we find it unacceptable that this product's availability could somehow be curtailed.

Under the provision of the Bayh-Dole Act of 1980, the Department of Health and Human Services (HHS) was given certain override authorities when circumstances such as these arise. Specifically, in cases where research, funded by the federal government results in patents, the government retains "march-in" authority to require licenses to be issued under reasonable terms when there is a "compelling public interest."

Please take this letter as an expression of our view that access for cancer patients to the latest in approved medical devices certainly qualifies as "compelling."

It is our understanding that an alternative product is a long way off from receiving FDA approval. If this is indeed the case, it would be a horrible injustice to American cancer victims and their families if their access to the CEPRATE®SC System was denied for a non-medical reason.

Under Bayh-Dole, you have the power to take immediate action to ensure that this product remains available without delays or extensions. By doing so, we can save lives, extend the years and improve the quality of life for our constituents.

At the very least, we would hope that you would use the power of your office to take advantage of any and all means available to bring together all parties so that this essential device is allowed to remain available to every cancer victim who needs it. It is unfortunate that we find ourselves at this terrible impasse, but saving lives must always remain our top priority and number one concern.

We look forward to working with you on this most important issue. Please keep us apprised of any developments -- it is of critical importance to cancer patients all across our great land.

Thank you for your time in this undertaking. It is very much appreciated.

Sincerely,

Patty Murray

Slade Gorton

Wendell H. Ford

Alfonse M. D'Amato

Daniel K. Inouye

Sam Brownback

Russell D. Feingold

Mitch McConnell

Ron Wyden

Gordon Smith

Pat Roberts

Christopher Bond

injunction in the absence of a comparable FDA-approved alternative would work a terrible hardship on cancer patients whose therapy now--or in the immediate future might--depend on the system.

We hope you will consider this as you evaluate the CellPro petition.

Thank you.

Sincerely,

Diane Blum, ACSW
Executive Director

National Office
1180 Avenue of the Americas
New York, NY 10036-8402
Tel: (212) 221-3300
Fax: (212) 719-0263
E-Mail: info@cancercare.org
Web Site: http://www.cancercare.org

Cancer Care Counseling Line
1-800-813-HOPE (4673)

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Norwalk, CT 06851-5703
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Long Island
20 Crossways Park North
Woodbury, NY 11797-2007
(516) 364-8130

New Jersey
241 Millburn Avenue
Millburn, NJ 07041-1718
(201) 379-7500

Cancer Care, Inc.

March 19, 1997

The Honorable Donna E. Shalala
Secretary
Department of Health and Human Services
200 Independence Avenue S.W.
Washington, DC 20201

RE: CellPro March in Petition

Dear Secretary Shalala:

On behalf of the 50,000 cancer patients who we serve each year, we respectfully request that the Department carefully consider the above referenced petition in light of its immediate implications for thousands of cancer patients in the United States.

As you may know, the petition arises out of a patent dispute currently before the United States District Court in Delaware. In 1995, CellPro, Inc. obtained a jury verdict in its favor in a patent dispute related to an antibody used in CellPro's CEPRATE® SC Stem Cell Concentration System. Instead of entering the verdict, the judge in the case granted a new trial resulting in a determination earlier this week that CellPro must pay damages to the plaintiffs, Baxter HealthCare, Becton Dickinson and Johns Hopkins University. CellPro has said it will appeal the Court's decision. Notwithstanding that there is no comparable FDA - approved alternative to the CellPro system, the plaintiffs have said they will ask the Court to prohibit the sale of the system and its components throughout the duration of the appeal, something which could take years.

To date, the CEPRATE® SC System has been used on over 5,000 patients around the world. In approving it for use in the United States, the FDA found that the system eliminates many of the side effects associated with standard bone marrow transplantation. As a result, the CEPRATE System makes the process of bone marrow transplantation safer and available to a much broader range of patients who could potentially benefit from the therapy.

Without in any way attempting to evaluate or prejudice the merits of the appeal, and irrespective of its effects on the company, we believe that an

Congress of the United States

Washington, DC 20515

May 27, 1997

The Honorable Donna E. Shalala
Secretary
Department of Health and Human Services
200 Independence Avenue SW
Washington DC 20201

Dear Secretary Shalala:

We are writing to you on behalf of breast cancer victims, leukemia patients, multiple myeloma patients and the many others across our states and the nation who suffer from cancer. It is our understanding that a pivotal new tool in the fight against these diseases, and breast cancer in particular, may soon face removal from the marketplace. It is also our understanding that this product is the only one of its type to be approved by the Food and Drug Administration (FDA). Our purpose in writing to you is to enlist your help in ensuring that these victims and others who do currently or could potentially benefit from this technology have uninterrupted access to it as part of their medical options.

The device in question is the CEPRATE®SC System, used in purifying the bone marrow transplantation (BMT) process, and thus enabling safer and more effective use of this vital form of cancer treatment.

We are not concerned with the patent dispute that is driving the legal action which now threatens the treatment of American cancer victims. But, unless a suitable FDA approved alternative is widely accessible, we find it unacceptable that this product's availability could somehow be curtailed.

Under the provisions of the Bayh-Dole Act of 1980, the Department of Health and Human Services (HHS) was given certain override authorities when circumstances such as these arise. Specifically, in cases where federally funded research results in patents, the government retains "march-in" authority to require licenses to be issued under reasonable terms "to alleviate health or safety needs."

Please take this letter as an expression of our view that access for cancer patients to the latest in approved medical devices certainly qualifies as a compelling "health or safety need."

It is our understanding that an alternative product is a long way off from receiving FDA approval. If this is indeed the case, it would be a horrible injustice to American cancer victims and their families if their access to the CEPRATE®SC System were denied for a non-medical reason.

We look forward to working with you on this most important issue. Please keep us appraised of any developments — it is of critical importance to cancer patients all across our great land.

Thank you for your time in this undertaking, it is very much appreciated.

Sincerely,

Rick White
Member of Congress

John Conyers
Member of Congress

Jennifer Dunn
Member of Congress

Jim McDermott
Member of Congress

Pete Stark
Member of Congress

Jon Fox
Member of Congress

Sander Levin
Member of Congress

David Price
Member of Congress

Dan Burton
Member of Congress

George Nethercutt
Member of Congress

Elizabeth Furse
Member of Congress

Eva Clayton
Member of Congress

Edolphus Towns
Member of Congress

Danny Davis
Member of Congress

Major Owens
Member of Congress

Ron Dellums
Member of Congress

Martin Frost
Member of Congress

Eddie Johnson
Member of Congress

Bart Gordon
Member of Congress

Vern Ehlers
Member of Congress

Sherrod Brown
Member of Congress

James Clyburn
Member of Congress

Jack Metcalf
Member of Congress

Brad Sherman
Member of Congress

National news organizations reported extensively on CellPro CEO Rick Murdock's own battle with non-Hodgkin's lymphoma and his treatment with the then-experimental CEPRATE®SC System. Rick's story struck a responsive chord with thousands of cancer patients, their friends and families, who contacted CellPro to ask about the CEPRATE®SC System and the patent fight that threatens to force it from the market.

THE WALL STREET JOURNAL

Thursday, May 1, 1997

CEO Owes His Life to His Company's Technology

By Bill Richards
Staff Reporter of The Wall Street Journal

Rick Murdock is betting his life on an unproved product made by his biotech company. It's possible that neither the man nor the company will survive.

A year ago, Mr. Murdock, chief executive officer of CellPro Inc., discovered he had advanced mantle cell lymphoma, a rare form of cancer that oncologists regarded as a near-certain death sentence. "There is no

MEDICINE

cure we know of," says Oliver Press, a lymphoma specialist at the University of Washington Medical Center in Seattle and one of Mr. Murdock's doctors. The life expectancy of someone diagnosed with the disease is about 30 months.

The most unusual aspect of Mr. Murdock's case was the one-in-a-million happenstance that CellPro was working on a radical new approach to treating certain cancers, including lymphomas. The procedure involves purging cancer cells from a patient's blood, then reinfusing healthy stem cells—the basic blood-making cells in human bone marrow—into the patient after blasting him or her with radiation and chemotherapy.

The problem: CellPro's therapy was months, if not years, away from human trials. But with time running out and few options, Mr. Murdock chose to become his company's human guinea pig.

Today, Mr. Murdock, who is 50 years old, is believed to be cancer-free. While a long-term prognosis is premature, his condition has become Exhibit No. 1 in the fight for his company's survival. The stem-cell part of the procedure used in his recovery, cleared last December by the Food and Drug Administration, is central to a patent-infringement lawsuit brought against CellPro by Baxter International Inc. in federal district court in Delaware in 1995. CellPro, appealing a jury verdict last month awarding Baxter damages of $2.3 million, says any ruling that it must stop selling the procedure would put it out of business.

The procedure hadn't been tested outside the laboratory in CellPro's Bothell, Wash., headquarters when Mr. Murdock broke the news of his illness to Joseph Tarnowski, CellPro's chief technical officer, and told him he wanted to try it himself. "Rick," Mr. Tarnowski blurted, "we're not ready."

CellPro did have a cell-separation process on the European market, but the company's researchers hadn't had much success with using the process to purge tumor cells. "Some days it worked, some days it didn't," Mr. Tarnowski recalls. Mr. Murdock said he understood, but there was no time. "Do what you can," he said.

"Rick needs a favor," Mr. Tarnowski told Nicole Provost, the head of CellPro's purging-research team. How soon, Mr. Tarnowski asked, could they have a lymphoma purge ready to try?

Nine months, Ms. Provost estimated.

Mr. Murdock's cancer was too advanced to wait that long. "We need it in eight weeks," Mr. Tarnowski said.

Suddenly, CellPro's research became "the Rick Project." Each afternoon, when the day's fresh blood supply arrived, Ms. Provost's lab got first choice for experiments. Her three researchers stayed late into the night, monitoring the eight-hour-long test purges.

But the purges weren't working. Test runs produced plenty of healthy stem cells, but tumor cells remained. Ms. Provost and Mr. Tarnowski held off telling Mr. Murdock.

Hu Kruslo

'People dread turning 50 and getting old,' Rick Murdock said on the eve of his 50th birthday. 'All I can think is, I made it.'

Early in May, Ms. Provost gathered her team in the tiny coffee room across the hall from the purging lab. "Guys," she pleaded, "give me input." The little group huddled around a table for two hours, throwing out ideas. They finally decided to try reversing the process, stripping the tumor cells first, then gathering the stem cells—in effect, starting over.

Ms. Provost's team broke through in late May. Some of the lymphoma purges showed almost no detectable levels of tumor cells. At the urging of Mr. Murdock's doctors, the FDA granted a "compassionate use exemption" for CellPro to test its purge on its CEO.

In early June, Ms. Provost sent two of her technicians to Seattle's Fred Hutchinson Cancer Research Center, a pioneer in bone-marrow transplants. Scott Rowley, the center's transplant chief, apologized for the mess—his lab was in the midst of moving—but he didn't want to wait. "It looked like a bomb had hit the place," Ms. Provost recalls.

On June 17, with a special drug in his system to boost his stem-cell production, Mr. Murdock entered the cancer center's fifth-floor outpatient transplant room. A technician hooked him up to an apheresis machine (apheresis, in Greek, means "take away"). In three hours, the machine processes 12 liters of blood, distilling out a rich pink broth of plasma and concentrated cells. The process was run three times, producing three small pouches of the broth. Each pouch contained billions of stem cells and more billions of lymphoma tumor cells; they were sent to Dr. Rowley's

CellPro Treatment Helps CEO

Continued From Page B1

lab downstairs for cell separation. Mr. Murdock would live or die, depending on which set of cells made it back into his body.

Dr. Rowley's team ran the first bag through CellPro's separation machine. The pink plasma drained slowly down a tall, clear, plastic column filled with tiny beads that looked like BBs. The tumor cells, invisible, were genetically programmed to stick to the beads, like Velcro. The purged plasma then went through a second column where the stem cells were separated in similar fashion.

A second pouch would be used if the first was unsuitable, but the third pouch was frozen, unpurged, as a backup; Dr. Rowley needed some cells – even contaminated cells – to put back into Mr. Murdock after the radiation and chemotherapy or he would have no immune system and quickly die.

As it turned out, batch one was still contaminated. Some tumor cells had made it past the first column, and the chemical reagent that was supposed to block them from going any further hadn't been strong enough. Ms. Provost, waiting nearby with three CellPro researchers, got the bad news by phone. "What do we do now?" she asked her crew. They debated, then reached a consensus: boost the concentration of the reagent fivefold.

Early the next morning, the remaining unfrozen pouch began dripping into the cell-separation machine in Dr. Rowley's lab. The technicians stared at the reddish liquid filtering down the first column. It took about 40 minutes for the plasma to flow through both columns. A laser printer whirred out the analysis. Dr. Rowley looked at the readout and picked up the phone. "The pouch is swarming with healthy stem cells," he told Dr. Press. There was no evidence of any tumor cells at all.

Mr. Murdock was elated. He had cleared the first hurdle. And the company's purging procedure had worked, at least in a one-patient test. But there was still a big obstacle to be cleared – the radiation and chemotherapy treatments. Nearly 5% of bone-marrow transplant patients die during this stage, mostly from infection when their body's immune system is immobilized.

On Aug. 2, Mr. Murdock entered room 6318 at the University of Washington Medical Center. A technician wheeled in "Big Bertha," a radioactive isotope lined with 6 inches of lead. Because his mantle cell lymphoma was so treatment-resistant, Mr. Murdock was getting an extra-heavy radiation dose. He cracked a joke about glow-in-the-dark underwear. The technician smiled thinly and blocked off the door.

After 12 days of radiation, Mr. Murdock began a regimen of chemotherapy, designed to kill any tumor cells left in his bone marrow. The treatments were brutal. The patient's mucous glands, ravaged by the drugs, stopped functioning and his mouth became an open sore. Full of morphine, he barely noticed as the doctors pumped the little bag of stem cells into the catheter in his chest.

Twice his nose started to bleed. More ominous, a fever began building. With no immune system to fight back, that could be lethal. His doctors experimented with one antibiotic after another, desperately trying to slow down the fever until the infused stem cells took hold.

As his fever climbed to 104, Mr. Murdock, stared in a drugged haze at a picture that his wife, Patricia, had hung on the wall. It was an angry abstract, slashed with dark colors. But in it, Mr. Murdock thought he could see beach scenes, then a space fantasy, then Bill and Hillary Clinton at a garden party.

On the morning of day 10, Dr. Press checked Mr. Murdock's white-cell count and spotted a flicker of activity. The stem cells had begun growing; his immune system was kicking in. Almost immediately, the fever dropped and Mr. Murdock's white-cell count started to climb.

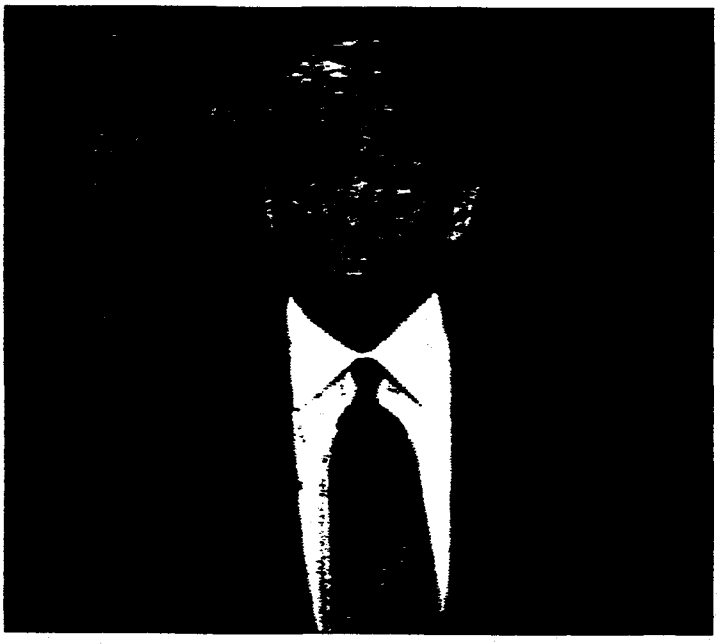
By day 12, the fever was gone. Mr. Murdock hadn't eaten in more than three weeks, and his weight had fallen from 170 pounds to 158 pounds. But the sores in his mouth were healing, and he wanted to go home. Dr. Press, amazed at the speed of his rebound, offered a deal: If Mr. Murdock could hold down 1,000 calories, he could leave. Mr. Murdock forced down some applesauce and a pair of high-calorie drinks; the next day, he went home.

His recovery remains startling. By last Christmas, he could do 50 pushups and was working a full schedule. Last month, on the eve of his 50th birthday, Mr. Murdock and his wife sat in their living room. Dr. Press had just finished testing his blood and found no sign of tumor cells. "People dread turning 50 and getting old," Mr. Murdock said. "I don't. I'm going to be 50 and all I can think is, I made it."

Sooner or later just about everyone who hears about Rick Murdock's cancer uses the same word – irony. "You've got a guy who's head of a company working in that field, and lo and behold he contracts a disease that requires and desires that technology," says Richard Miller, a Stanford University oncologist and another of Mr. Murdock's doctors. "It doesn't get any more ironic than that."

This week, Mr. Murdock is lobbying federal officials in Washington, asking them to use a long-ignored law that permits the government to "march in" and grant CellPro a license for its process on the ground it is required "to alleviate health or safety needs." To date, the company says, some 5,000 people have been treated with its procedure.

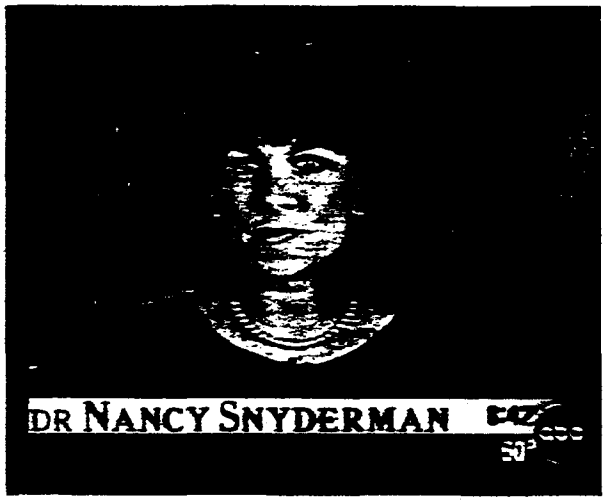
Mr. Murdock's recovery won't be deemed permanent by his doctors for at least three years. Dr. Rowley, the Hutchinson transplant chief, calls Mr. Murdock's case "a work in progress." Mr. Murdock concurs. His personal story, while riveting, is not the crux of his company's case, he says. "In this equation," he adds, "my survival only equals one."

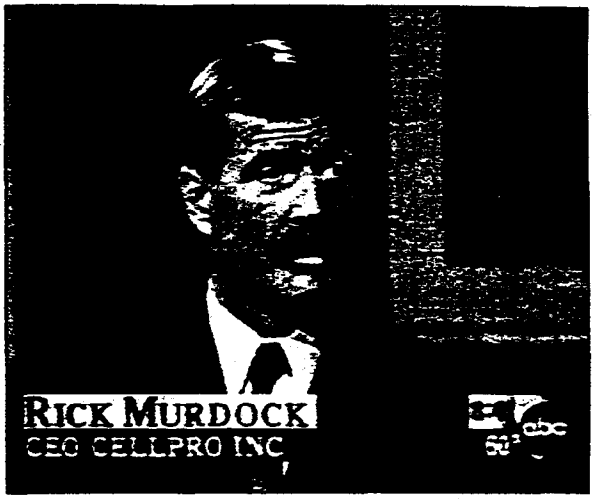


"How many victims of cancer, or their families, have thought, if I could just order up a cure?"

– Tom Brokaw
NBC Nightly News

abc



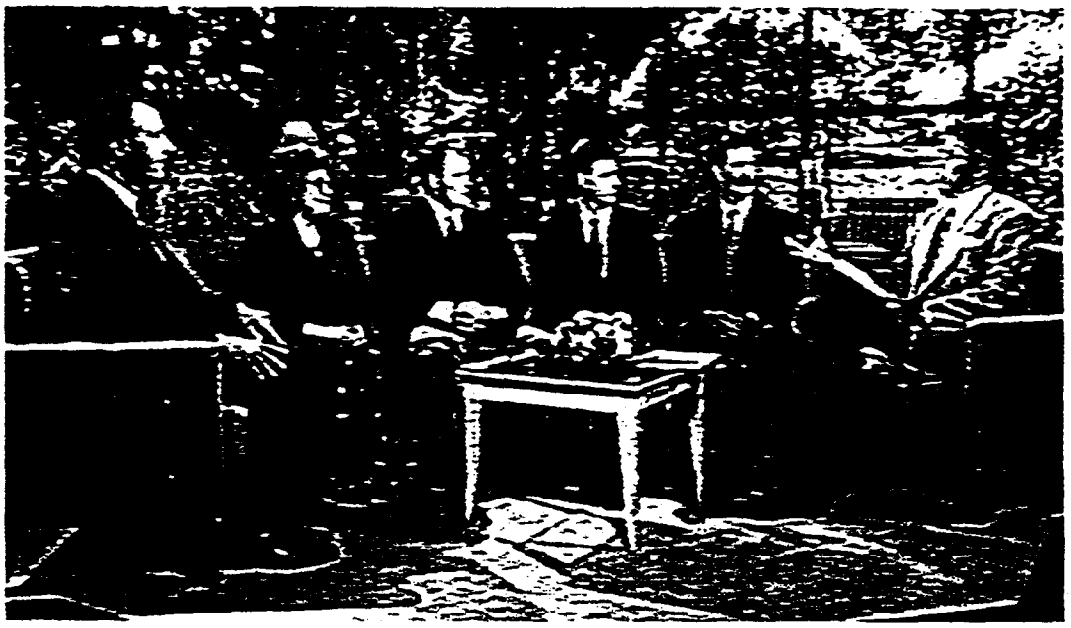


"These kinds of fights between companies make doctors and patients very nervous. . . the reality is the technology is a huge step forward. And when doctors and patients get caught in the middle, I think it makes those of us in the medical community quite uneasy.

"This is a huge step forward and doctors around the country and in Canada, and at various medical centers attest to the fact that they like this technique, they like what CellPro has come up with.

"There's no doubt in my mind that this technology is saving lives and will continue to save lives."

– Dr. Nancy Snyderman
ABC News Medical Correspondent
Practicing Surgeon and Pediatrician



"I think this story illustrates so many of the fundamental advances that have been made – understanding that cancer is a genetic disease, understanding the role that the immune system plays in it."

– Patrick Boregan, M.D.
Memorial Sloan-Kettering Cancer Center

PrimeTIME

abc

"As Dr. Nancy Snyderman reports, the extraordinary efforts to save one patient may eventually help thousands of people every year."

– Sam Donaldson
PrimeTIME LIVE

"The bottom line is it makes transplantation available to a group of patients who do not have matched donors available, and would otherwise have fatal or incurable illnesses."

– Dr. Stan Calderwood
Hospital for Sick Children
Toronto, Canada

U.S. SENATOR

Al D'Amato

NEW YORK

NEWS RELEASE • NEWS RELEASE • NEWS RELEASE • NEWS RELEASE • NEWS RELEASE

FOR IMMEDIATE RELEASE:
Friday, May 2, 1997

CONTACT: Chris Staszack 212-736-3865
Lisette McSoud 202-224-6498

D'AMATO URGES SUCCESSFUL CANCER TREATMENT STAY ON MARKET

Legal Dispute Threatens Availability of Device Which Has Aided Thousands

NEW YORK – U.S. Senator Alfonse M. D'Amato (R-NY) today announced that he and three other Senators are writing Health and Human Services Secretary (HHS) Donna Shalala urging her to take immediate action to prevent a successful cancer treatment device from being removed from the market while its manufacturer is involved in a patent dispute with another company.

"We can't sacrifice the health of women to the profits of companies. This device has benefitted thousands of people, including more than 2,000 breast cancer patients nationwide," said D'Amato, who was joined by Dr. Charles S. Hesdorffer, Director of the Bone Marrow Transplant Unit at Columbia University Hospital. "Cancer patients should not be forced to put their treatments or their hopes on hold while the legal process runs its course."

The device, the CEPRATE SC System, eliminates many of the serious, and potentially fatal side effects associated with bone marrow transplants, a vital form of cancer treatment. The device's manufacturer, Cell Pro of Washington State, is involved in a patent dispute in Delaware Federal District Court with Baxter Health Care. In the meantime, Baxter has asked the court to prohibit the sale of the CEPRATE device throughout the entire period of the pending court case, which could take years.

According to D'Amato, because the research behind this device was funded by the federal government, the Health and Human Services Secretary has certain powers that can be used to resolve this matter until the court case is settled. Under the "march-in" provisions of the U.S. patent law, Secretary Shalala has the authority to take over the patent for a product whenever life-saving treatment is in jeopardy of being withheld from the public.

"Access for cancer patients to the latest in approved medical devices certainly qualifies as a life-saving treatment," D'Amato said. "FDA approval of an alternative device could be years away, and given the tremendous benefits of this technology to cancer victims, we need action now."

Bone marrow transplants provide critically ill cancer patients with the ability to fight cancer using their own immune systems. The CEPRATE device is utilized in a procedure which involves purging cancer cells from a patient's blood, then reinfusing healthy cells back into the patient. This procedure "scrubs" the infected blood from the patient's blood supply and allows the human body to begin the disease-fighting process.

Joining Senator D'Amato in the letter to Secretary Shalala were Senators Slade Gorton (R-WA), Patty Murray (D-WA), and Wendell Ford (D-KY).

# # #

United States Senate • Washington, D.C. 20510 • (202) 224-6542

Regional Offices: New York (212) 947-7390 • Albany (518) 472-4343 • Syracuse (315) 423-5471 • Rochester (716) 263-5866 • Buffalo (716) 846-4111

CBS

"Certainly this device should not be withheld from the public. That is the great danger we face today . . .

"I believe, if the time permitted, virtually every Senator and every Member of Congress would ask Secretary (Shalala) to step into what could become a matter of life and death."

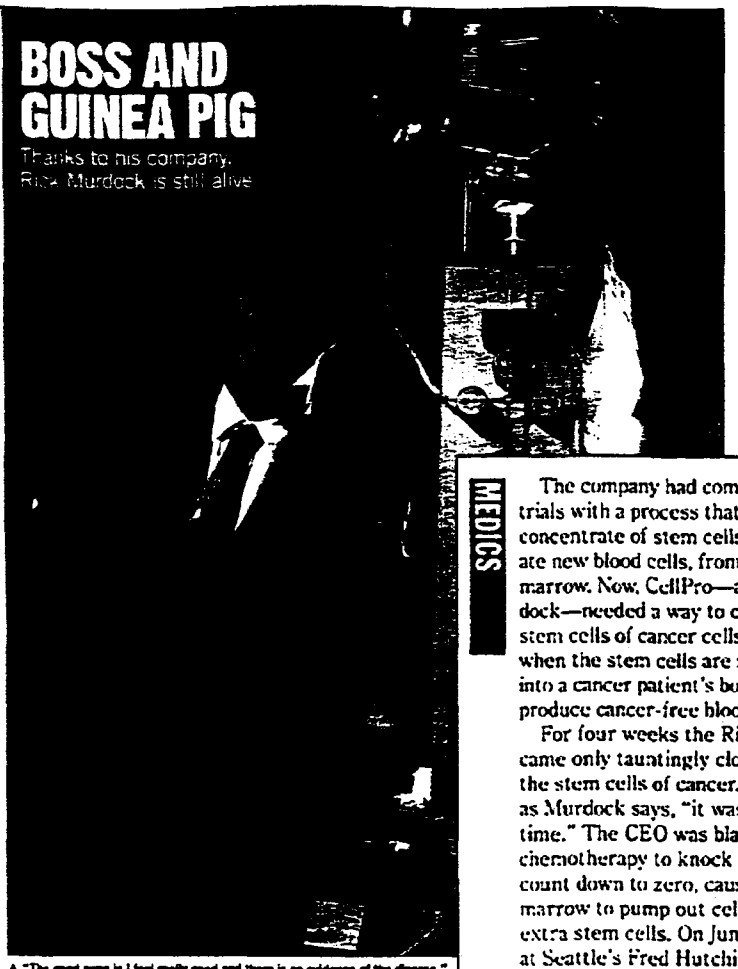
– Alfonse M. D'Amato
United States Senator

People weekly

MEDICS

BOSS AND GUINEA PIG

Thanks to his company, Rick Murdock is still alive



▲ "The good news is I feel really good and there is no evidence of the disease," says Murdock (with CellPro's cell-separation device).

MEDICS

The company had completed clinical trials with a process that produces a concentrate of stem cells, which create new blood cells, from blood or bone marrow. Now, CellPro—and Murdock—needed a way to cleanse the stem cells of cancer cells, so that when the stem cells are reintroduced into a cancer patient's body they can produce cancer-free blood.

For four weeks the Rick Project came only tauntingly close to purging the stem cells of cancer. But by now, as Murdock says, "it was almost show time." The CEO was blasted with chemotherapy to knock his blood count down to zero, causing his bone marrow to pump out cells, including extra stem cells. On June 17, doctors at Seattle's Fred Hutchinson Cancer Research Center extracted three small bags of stem cell broth contaminated with tumor cells.

Then came the crucial procedure to purge them. The broth was run through a column filled with tiny beads: the stem cells were supposed to stick to the beads, while the tumor cells passed through.

But cancer cells in the first bag also made it through. "That was panic time for Nicole and her team," says Murdock. Believing a chemical reagent had been too weak, the researchers made a command decision to strengthen it fivefold for the second bag. Success! Not a single tumor cell could be detected in the broth.

On July 26, Murdock re-entered the University of Washington Medical Center, where he began intense radiation treatments. For 12 days he lived alone in a lead-lined room, taking his vital signs and giving himself injections. "It was not a pleasant experience," he says. "After the third day I stopped eating. Food tasted terrible."

On Aug. 12, following more chemotherapy to kill any remaining cancer in his body, doctors transplanted Murdock's cleansed stem cells back into him. For 10 days his fever rose steadily, peaking at 104. Finally his white blood cell count flickered upward, and the fever began to recede. The stem cells were growing; Murdock's immune system was making a comeback. He had pulled through.

Three weeks after Murdock got out of the hospital, a bone marrow biopsy confirmed that he was indeed free of cancer. This liberating news at once sent him on foot to a local creek to see salmon on spawning runs. He painted the deck of the family's brick and cedar house in suburban Woodinville. On Nov. 1 he was back working full-time at CellPro. "I needed to get back in the groove," he says. "We were in a *big legal battle.*"

The latest battle, to add a final irony, is over the cell-separation device that saved his life. CellPro will appeal a court decision this past March in Wilmington, Del., that the tiny company infringed on a patent owned by Baxter International, a giant pharmaceutical firm. But Murdock almost welcomes the legal skirmish. "It's too early to know if I am fully recovered," he says, "but the worst thing for me would be to sit around and contemplate whether I am going to relapse. I would rather be in the firefight."

• WILLIAM PLUMMER
• GIOVANNA BRITT *in Seattle*

MEDICS

< The most traumatic thing about chemotherapy, says Murdock (in the hospital), was "losing my hair."

The boss had a cancer with no known cure

TANNED AND FIT, RICK MURDOCK, CEO of a small Seattle-area biotech company, radiates health as he strides down the hall of the University of Washington Medical Center, shaking hands with doctors and nurses who greet him as if he were a returning war hero—which in a way he is. But Murdock is disquieted. "It's a strange feeling I get every time I walk in the front door of UW," he says. "There's a smell that takes me back: 'Oh, God, here I go again. It's starting over.' "

A little more than a year ago, Murdock, 50, discovered that he had an advanced case of mantle cell lymphoma, a rare form of cancer with no known cure. Doctors gave him 30 months to live. Murdock, however, had a weapon not available to others with the disease. At that very moment, his medical device company, CellPro, happened to be experimenting with a radical new approach to treating lymphomas.

If any cancer patient can be said to be lucky, Rick Murdock was lucky, except for one potentially fatal flaw: CellPro's system, based on a means of purging lymphoma cells from blood, was still nine months away from completion, and Murdock needed it in two months. "You've got to be kidding," said project head Nicole Provost of the new timetable. Incredulity gave way to urgency mixed with irony. "We've got this guinea pig," Provost recalls thinking, "and he's my *boss*."

Murdock had first noticed a swollen lymph node in his neck while shaving one morning in December 1995. Three days later he found a second lump, in his groin. "I knew this was serious," he says, "and I needed to do something about it."

Testing positive for non-Hodgkin's lymphoma, he immediately started chemotherapy, lost his hair (he had a wig made), then, more alarmingly, his mustache. "Every time I would look in the mirror, I would scare myself to death," he says. But during four months of chemotherapy, Murdock never missed a day of work. He even went East with his wife, Patricia, 50, and his son Ben, 19—the Murdocks have another son, Jamie, 21—to look at prospective colleges.

Then, in April, after he had weathered three sieges of chemotherapy, Murdock got a wrenching e-mail from Dr. Oliver Press, his lymphoma specialist at the University of Washington. A second biopsy had revealed the deadly mantle cell type of lymphoma. "All of a sudden," Murdock says, "we went from something we thought was fairly treatable to a particularly virulent form of the disease that is not very treatable by standard therapy."

When a fourth cycle of chemotherapy proved ineffectual, Murdock pinned his hopes on the still-experimental CellPro lymphoma purging system. The Rick Project team abruptly shifted into a 60-hour workweek. "I think the group felt we were responsible for Rick's life," says team member Sharon Adams.

TIME

MEDICINE

HUMAN GUINEA PIG: CellPro's Murdock is feeling much better, thanks to a contraption that separates blood from cancer cells

By His Own Device

A biotech lab races to perfect a new treatment for cancer just in time to save its dying CEO

By ELAINE LAFFERTY

IT'S NOT THAT THE LAB FOLKS AT TINY CellPro, Inc. are uninterested in saving lives. It's just that like most biotech researchers, they prefer to toil far away from the gritty reality of illness and human suffering. So when the CEO of their Bothell, Wash., company announced a year ago that he had developed a deadly lymphatic cancer and that his slim chance for survival might rest on their lab results, it was more than they'd bargained for. They already knew their company was fighting for survival, locked in a legal battle over patents with a competitor. Now they were also supposed to save their boss?

Rick Murdock says he did not mean to put pressure on his employees, but his life hung in the balance. At 49, the deceptively tanned and fit executive had just received the kind of diagnosis that is a hypochondriac's nightmare: a rare case of advanced mantle-cell lymphoma. Doctors told him the average life expectancy for the disease was 30 months, and indeed, his initial round of conventional chemotherapy was unsuccessful. But in a coincidence that was both ironic and edifying, CellPro scientists were experimenting with a new way to boost the success rate of the very operation recommended for this type of cancer: a bone-marrow transplant.

In one form of this procedure, doctors remove from the patient's bone marrow a supply of stem cells—the body's blood-making factories—and put them aside for safekeeping. Then they use powerful doses of radiation and chemotherapy to destroy all the cancer cells in the blood—in the process, destroying the healthy blood cells as well. Finally, they try to rebuild the blood supply from scratch by reinfusing the patient with the original stem cells.

Invariably, however, some cancer cells slip in with the stem cells. CellPro was working on a procedure that would reliably separate cancer cells from stem cells. If those cancer cells could be completely purged from the blood, the cancer might not recur. The problem was that CellPro's experiments were still in their infancy. Said Nicole Provost, leader of the purging team: "I told them we needed about nine months. They told me we had eight weeks. Our first reaction was, 'Oh, man.' I mean, this was Rick's life!"

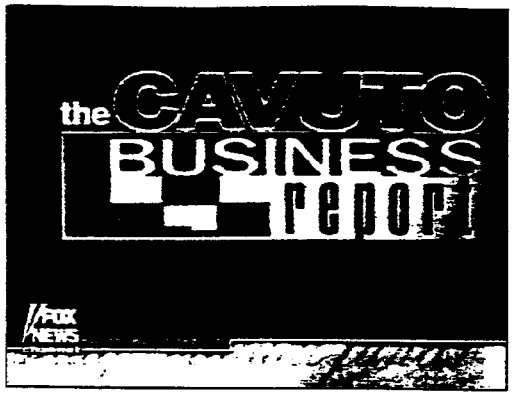
Thus began what Provost and her three-member team called "the Rick project." Their lives now dictated by pagers and cell phones, they took turns in the lab, almost round the clock, running tests over and over. First the stem cells were collected in an elaborate maze of plastic tubing, then they were purged of cancer cells—a confetti of malignant cells sticking to columns of coated beads like flies to flypaper. Unfortunately, the purging process wasn't eliminating all the cancer cells. The experiment seemed to be failing. Then, in a last-minute brainstorm, Provost's team decided to reverse the order: purge the cancer first, then collect the stem cells.

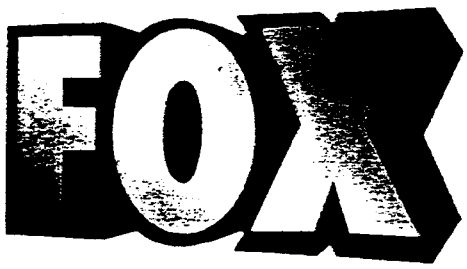
"It worked," said Joe Tarnowski, CellPro senior V.P. "Doing the separations later gave us a second level of purging." With a "compassionate use" waiver from the FDA, the procedure was ready for testing. "Rick was the guinea pig," says Tarnowski.

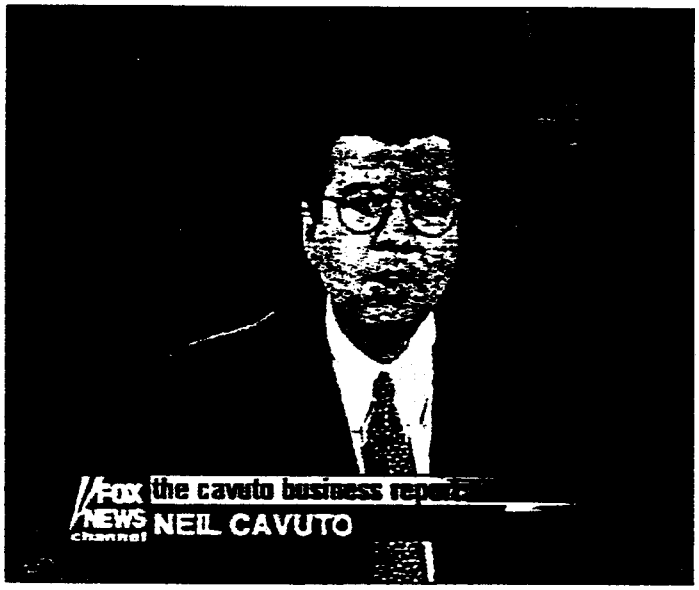
On June 17, 1996, with Murdock set up on the fifth floor of the Fred Hutchinson Cancer Center in Seattle, the trial began. About four hours later, the patient went home, a catheter in his chest, to await the verdict. Tarnowski called that night to tell him that the purging had finally worked. Then began some two months of grueling radiation, chemotherapy and the new, improved bone-marrow transplant.

Almost a year later, Murdock shows no signs of cancer. He is back home, sailing with his sons and watching the salmon swim in a creek a mile from his house. He is too savvy to declare himself cured—that determination could take three years—but he is ready for battle, both to save his company and to get the new device into doctors' hands. CellPro lost the latest round in its patent fight with competitors in federal court in April, and in a month a judge could issue a ruling preventing CellPro from selling its product to new customers. "This is personal now," said Murdock. "I'm not just a CEO. I'm a patient. It would be a crime against humanity if a business dispute kept us from getting this procedure to other patients."

Others agree. Dr. Kent Holland, director of the Hemapheresis Center of the bone-marrow-transplant program at Emory University School of Medicine, is already using the CellPro procedure on young leukemia patients. "I don't have any other device that works as well to offer these people," he says. Another supporter is former Senator Birch Bayh, who co-authored the 1980 Bayh-Dole Act, which gives the government the power to seize a patent in the name of public health or safety and issue a license. Bayh says the CellPro case perfectly illustrates the law's intent: to get new treatments to the people who need them. It may not work, since the law has never been invoked, but neither had anyone ever undergone Murdock's treatment before. And so far the prognosis is good. ■







"Rarely does one's life work make the difference between life and death. But for Rick Murdock it did. After being diagnosed with a rare case of lymphatic cancer it was his own biotechnology company, CellPro, that came up with the procedure that ultimately looked like it saved his life. And one year later, Mr. Murdock is alive and well."

– Neil Cavuto
Fox News

Seattle Post-Intelligencer

April 23, 1997

PHIL H. WEBBER/P-I

In the past year, Rick Murdock, CEO of CellPro Inc., has battled for his life against cancer and for the survival of his Bothell-based biotechnology company, which is locked in a fierce patent dispute.

CellPro chief fights for life on two fronts

Murdock beats cancer to face patent challenge

By CAROL SMITH
P-I REPORTER

When Rick Murdock, CEO of Bothell-based CellPro Inc., first noticed the lump on his neck, he never imagined his own company's researchers would rally and perhaps save his life.

He never imagined, either, that he would be fighting two life-and-death battles in the space of a year – one for himself, and one for his company. Or that the battle for his company's survival would invoke a little-known provision of a federal act designed to ensure that technology discovered with federal dollars gets to patients – patients like him.

Murdock first noticed the lump on a business trip in January 1996. He had it checked immediately.

"Around here we're pretty sensitized to the issue of cancer," he said.

CellPro is in the business of developing new therapeutics for the treatment of cancer. Its first product, a stem cell separation system used to purify and concentrate the cells used in bone-marrow transplants, received approval in December for use in treating breast cancer, lymphoma and multiple myeloma.

Still, even Murdock was not prepared for the irony of the findings of his lymph node biopsy.

Murdock had a relatively rare form of non-Hodgkins lymphoma called mantle cell lymphoma, which does not respond well to standard chemotherapy. According to his physicians, his best shot at a cure was to have a bone-marrow transplant.

What Murdock knew that his physicians didn't, however, was that his company was in the early stages of developing an improved stem cell purification system that, in theory at least, could enhance the likelihood of a successful transplant.

Stem cells, which are mostly found in bone marrow, are the progenitors of all blood and immune system cells. Without stem cells, patients die. But various forms of cancer treatment, such as high doses of chemotherapy, kill stem cells. By doing stem cell transplants, which are a type of bone-marrow transplant, doctors are able to reconstitute a new immune system in the patient after treatment for a disease.

The company's newest system was designed to remove tumor cells from the patient's stem cells before the purified stem cells are put back in the patient. Removing the tumor cells reduces the chance of a recurrence of the cancer.

"It was not ready for prime time," said Murdock. But in an unspoken swell of support for their leader, the company's 160 employees focused on bringing the new system to the stage where Murdock could use it.

Murdock applied for "compassionate use" status from the Food and Drug Administration and became the first patient treated with the experimental system.

But in yet another ironic twist, Murdock is once again engaged in a battle for survival – only this time it's

See CELLPRO, Page B8

CellPro: Murdock isn't giving up

From Page B5

for his company.

The technology that may have saved Murdock's life may not be enough to save the company, which is locked in a fierce patent dispute with industry giants Baxter International Inc. and Becton Dickinson and Co. over an antibody originally patented by Johns Hopkins University.

Like a cancer that appeared in remission, a patent battle CellPro thought it had won has roared back in amplified form. To avoid going under, the company has taken the unprecedented step of asking the federal government to "march in" under provisions of the 1980 Bayh-Dole Act and essentially repossess the patent, issuing a license to CellPro to keep the treatment available to patients.

It's a move that industry, research organizations and patient advocacy groups are watching intently. If the government exercises its march-in rights, it could have wide-ranging implications for future licensing arrangements in the biotech industry.

"Seventeen years into the Bayh-Dole Act, and the government has never once exercised its (march-in) rights," said John DesRosier, director of industry relations for the University of Washington School of Medicine. If it does, it would be "fairly significant" to the research community on both the corporate and institutional sides.

The Bayh-Dole Act, co-sponsored by Sen. Birch Bayh of Indiana and Sen. Bob Dole of Kansas, was conceived as an incentive for companies to commercialized government research. Before it was enacted, fewer than 250 patents were issued to universities each year, and those could only be granted to outside companies on a non-exclusive basis.

"The government would fund all this research, make discoveries, but often they just stayed on the shelf," said Tom Connaughton, a partner in the law firm of Bayh, Connaughton & Malone in Washington, D.C. "No company was willing to invest (in technology) if everyone could have it."

Bayh-Dole, which allowed universities to own patents on government-sponsored research and to assign exclusive licensing rights to private companies, changed that. The Bayh-Dole Act has been largely credited with spawning the biotech revolution.

Embedded in the act, however, is a provision allowing the government to step in if a licensee is not taking steps to commercialize a technology fast enough, or if there is a compelling public interest, Connaughton said. Basically, the march-in provision was designed to keep companies from sitting on the technology, and to ensure that life-saving technology gets to the public in a reasonable time period.

At issue in the CellPro dispute is whether CellPro, which already has an approved device being used to treat patients, can be forced off the market by Baxter, which does not yet have a comparable product approved in the United States. Even though CellPro never believed the Johns Hopkins patents were valid, it did have discussions as far back as 1992 about sublicensing the technology from Baxter to avoid a parent dispute.

The two companies are fighting over a market currently estimated at about $60 million a year, but possibly worth a great deal more, depending on new applications. The two parties could never agree on terms, however. In addition to a 16 percent royalty for a non-exclusive license and an upfront payment, Baxter wanted exclusive distribution rights to CellPro's system in Europe and Japan, and non-exclusive distribution rights in the United States, Canada and Mexico, Murdock said. "Baxter wanted to take our company," he added.

According to industry observers, the CellPro case is the type of situation that the march-in rights were designed to address. If CellPro is successful in getting a government-issued license to the technology, this would potentially give other biotech companies leverage in their fight to keep licensing rates at "commercially reasonable" levels.

Research institutions fear a more insidious effect, however. If the march-in rights are invoked, such a move would change the way companies look at institutional licenses, said Catherine Hennings, director of technology transfer for the Fred Hutchinson Cancer Research Center. Companies may be less likely to license those technologies and commit the money to develop them if they fear the government can march in and take away their exclusive rights, she said. "This would really set quite a precedent."

The CellPro patent battle is a classic David and Goliath tale, only this time "Goliath got to pick up, dust himself off and start swinging again," said Tom Kiley, a San Francisco area patent attorney and one of the founders of CellPro. "At that point, David had no stones left."

The CellPro patent battle dates back to 1991, when Johns Hopkins received four patents for a monoclonal antibody that binds to the surface of stem cells. CellPro uses a similar antibody developed independently by Fred Hutchinson in its stem cell separation column.

In 1992, CellPro filed suit over the validity of the Johns Hopkins patents, claiming they didn't extend to the Fred Hutchinson antibody, and in August 1995 the company won a unanimous jury verdict stating the Johns Hopkins patents were invalid.

In a stunning reversal, however, the judge in the case refused to enter the verdicts, instead ordering a new trial on the basis that he had made a mistake in instructing the jury about the patent claims.

Earlier this month, Baxter, Becton Dickinson and Johns Hopkins won a $2.3 million judgment against CellPro. Baxter is now asking the court for triple damages as well as $7 million in court costs and an injunction to stop the sale of CellPro's product.

The court found that CellPro "willfully infringed" on the patents, said Deborah Spak, spokeswoman for Baxter in Wilmington, Del. "It's not appropriate for them to continue to reap the benefit."

A hearing on the injunction is scheduled for April 30 in U.S. District Court in Delaware.

The injunction is to be phased in to "assure a smooth transition to a licensed technology," Spak said. Baxter currently does not have a comparable product on the market in the United States, although last month it submitted a system it uses in Europe for U.S. approval.

Even if Baxter's system gets the go-ahead, approval is still more than two years away, based on FDA approval records for medical devices, which take an average of 27 months.

That's 27 months during which patients will not have access to the technology, Murdock said. There were about 25,000 bone-marrow transplants performed last year, a number that has been increasing at a rate of about 30 percent a year.

"This action will affect, without question, whole layers of patient care and will set back the field," said Dr. Kent Holland, director of the Hemapheresis Center of the bone-marrow transplant program at Emory University School of Medicine, in a statement regarding the proposed terms of the injunction. Emory, along with five other sites, including Fred Hutchinson, are involved in using the product to treat children with leukemia for whom other treatment options have been exhausted.

An injunction could also end the approximately 60 clinical trials currently under way to test the system for applications in other diseases, including AIDS, multiple sclerosis, arthritis and lupus.

"If this product goes down, then we go down as a company," said Joann Reiter, CellPro's director of corporate development. "And the follow-up products go down as well. We need this lead product to give us the momentum. We're counting on that to give us the revenues to keep moving forward."

So far, it has cost $75 million to get the product to market, not including court costs. The company, which was founded in 1989, had sales of $6.8 million in 1996 and has about $55 million in cash left. Its stock closed yesterday at $5 a share, down from a recent high of $20 a share.

But Murdock isn't giving up. Once the final judgment is entered, CellPro plans to appeal. It is also busy working on a Plan B, eliminating the disputed antibody from its product altogether. A redesigned product could still be years from market, however, because it will require new clinical trials and a new approval process.

Still, CellPro has already proved it can meet impossible deadlines.

"After Rick found out (he had cancer), we ramped up one of the development projects to a high-pitch level," Reiter said. Murdock continued to work through four rounds of chemotherapy. His hair fell out and his energy flagged, but his optimism and his sense of style didn't.

A stylish dresser, he wore fedoras and worked until the new system was ready to go.

He received his transplant at the University of Washington, and his outlook is good. The system he tested is now poised to begin clinical trials to determine whether it should be approved for use in a wide patient population.

For Murdock, however, the answer is already in. Today, eight months later, he looks fit and relaxed in an impeccably tailored pin-striped suit, his trim mustache turned up just slightly at the corners. His doctors tell him he is cancer-free.

"I just turned 50," he allows in a moment of introspection. "I thought, 'Wow, I made it.'"

He hopes to say the same for CellPro.

The Seattle Times

May 9,1997

TERESA TAMURA / SEATTLE TIMES

Pro chief *Rick Murdock explains the Ceprate SC system. Development of the system — which removes 'er cells from blood-producing stem cells — was speeded up after Murdock was diagnosed with cancer.*

CellPro's "project": Rid cancer in 8 weeks

Isolating tumor cells cures its own chief

BY KEITH ERVIN
Seattle Times Eastside business reporter

Nicole Provost could scarcely believe what her boss was asking her.

Could the biochemist's research team develop a new technique for removing cancer cells from blood-producing stem cells in eight weeks? he wondered.

"My heart just sank. My head was swimming. I just thought, 'How are we going to do this?' "

CellPro's technical director, Joe Tarnowski, was asking her to do a job that normally would take nine to 12 months. But there was a special reason for the urgency: The Bothell company's president and chief executive officer, Rick Murdock, had just been diagnosed with mantle-cell lymphoma, a disease that kills most of its patients within three years.

Thus was born what Provost's research team dubbed "the Rick Project" — a crash research effort aimed at boosting the odds that Murdock would emerge cancer-free from a stem-cell transplant.

The researchers found a way to separate tumor cells from blood-producing stem cells. And, just three months after Murdock lay near death on a bed in the University of Washington Hospital, he was back at work full-time — with no detectable cancer in his blood.

"I think I feel better than I did before. That's no guarantee that I won't relapse," says the 50-year-old president.

His illness and apparent recovery has drawn national attention to CellPro and a patent-rights battle it is waging with health-care giant Baxter

PLEASE SEE **CellPro** ON D 2

CellPro cures its own chief from lymphoma

CELLPRO
CONTINUED FROM D 1

International.

Four U.S. senators – Alfonse D'Amato, R-N.Y.; Wendell Ford, D-Ky.; Slade Gorton, R-Wash.; and Patty Murray, D-Wash. – last week asked their 96 colleagues to join them in a plea to Health and Human Services Secretary Donna Shalala to grant CellPro a patent license pending resolution of the legal dispute. A similiar letter is circulating in the House.

A federal court jury in March found that CellPro's flagship product infringed on a Johns Hopkins University patent licensed to Becton Dickinson and sublicensed to Baxter International. Baxter, which wants federal approval of a competing product, is seeking heavy financial penalties against CellPro and a phase-out of sales of its Ceprate SC system.

Ceprate SC, which isolates stem cells, was used to treat Murdock last summer along with a secondary process developed by Provost's research team.

Before Murdock's cancer was diagnosed as mantle cell, CellPro researchers were working on two "purging devices" to remove cancer cells from stem cells – one for breast cancer, the other for lymphoma. The lymphoma project "wasn't going anywhere fast," Provost recalls.

She called together the three purging-device developers: Kirsten Stray, Sharon Adams and Stan Corpuz. "I don't want to lay this big heavy thing on you and say Rick's life is in your hands," Provost said, "but can you get something together for him in this short amount of time?"

For the next eight weeks, the Rick Project got first dibs on the donated blood samples that came into CellPro's Canyon Creek headquarters almost every weekday. They worked into the night testing different antibodies, chemical reagents and mechanical processes.

Nothing succeeded in separating tumor cells from stem cells until they reversed the process they used to purge breast-cancer cells. Instead of isolating stem cells and then removing tumor cells, they removed the tumor cells first. The technique worked.

Murdock called someone he knew at the Food and Drug Administration and asked for "compassionate-use" permission to use the untested procedure. The FDA approved the request.

Provost's team omitted a number of experimental steps that would be followed under ordinary circumstances. They were ready for the next step: to draw blood from Murdock and prepare a batch of cancer-free stem cells for transplantation. The idea was to set aside stem cells that could be injected back into Murdock's bloodstream after he underwent high-dose radiation and chemotherapy.

In June, Murdock went into the Fred Hutchinson Cancer Research Center, where blood was drawn for the upcoming transplant. Provost and her team were attending a seminar in Bellevue's Meydenbauer Center when she was paged by her boss, Tarnowski.

The new cell-depletion technique failed to remove all the tumor cells from Murdock's blood as it had in the laboratory. The lab research had been done with tumor cells different from Murdock's. The researchers huddled and came up with an idea: they would use five times as much of a chemical reagent. They prepared the chemical that night. The next morning, Murdock's next bag of blood was processed. It worked. They had isolated a bag of cancer-free stem cells.

"It's kind of like these Star Wars things," says a grateful Murdock. "You have one shot at the Death Star. The results were spectacular. We took the tumor-cell level below detectable levels, with plenty of stem cells ready for transplant."

Then came the bleakest time for Murdock. For 12 days, he was subjected to such high doses of radiation that no one could enter his room at the University Hospital. The bag of healthy stem cells was injected into him and he was given an experimental radioactive isotope designed to mop up any cancer remaining in the spleen and lymph nodes.

Murdock languished in a morphine-induced haze. Gradually, however, the stem-cell transplant rejuvenated his immune system. The fever went down, and the pain became manageable without morphine.

Fewer than three months after the transplant, Murdock went back to work part-time. A month after that – far sooner than doctors recommended – he was at his desk full-time.

"The company needed leadership," explains Murdock, 50.

This summer, CellPro plans to begin clinical trials with an improved version of the tumor-cell depletion process used on Murdock – "assuming Baxter doesn't put us out of business," he says.

Baxter International executives say they only want the royalties to which they're legally entitled. In a recent letter, Baxter chief Vernon Loucks offered Murdock any assistance his company could give for his lymphoma. Loucks also wrote that Baxter would not deny treatment to any cancer patient.

CellPro, helped by national news stories about Murdock's cancer treatment, has worked to cultivate an image as a life-saving David facing down a ruthless, corporate Goliath.

Or, to borrow Murdock's Star Wars image, his small teams of researchers are more like the rebels' fast-moving X-wing fighters speeding across the Empire's lumbering Death Star.

The CellPro rebels, Murdock says, developed their first commercial product "at light speed." The Rick Project, fortunately for him, moved even faster.

Other news organizations looked closely at the research being done with the CEPRATE®SC System to treat AIDS, multiple sclerosis, lupus, sickle cell anemia and a host of other diseases.

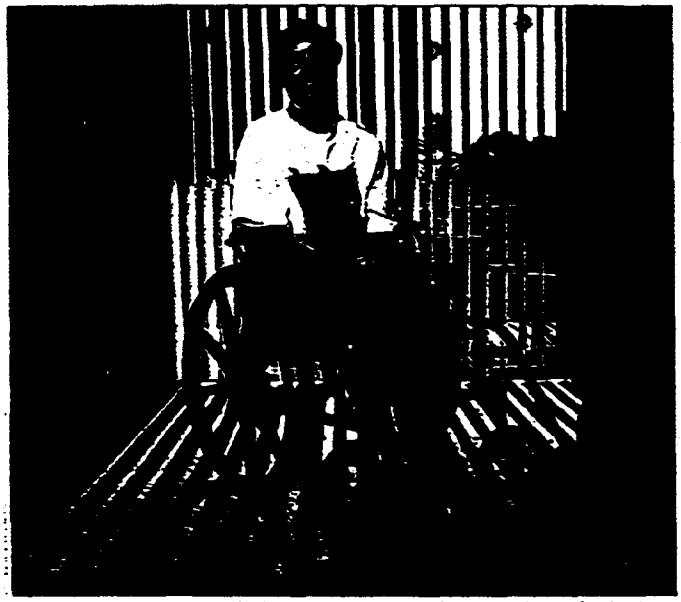
Newsweek

BUSINESS

HEALTH CARE

A Deadly Serious Fight

Lives may be at stake in this biotech battle



Tully: *Incapacitated until she had a bone-marrow transplant using disputed technology*

BY MICHAEL MEYER AND TARA WEINGARTEN

NANCY TULLY WAS AN ATTRACTIVE, outgoing young woman who worked as an X-ray technician by day and studied for her college degree by night. Then she was diagnosed with multiple sclerosis. As the disease took its course, she found herself confined to a wheelchair, scarcely able to speak. Three months ago, severely incapacitated, Tully traveled to Northwestern University in Chicago for a bone-marrow transplant using an experimental new technology. Today at 34, she is back at home in Florida, swimming daily and guardedly hopeful that she is on the path to recovery.

Others like her may not be so fortunate. The reason has little to do with medicine but rather with a nasty corporate fight. On one side is CellPro Inc., a small Seattle biotech company that has given some 3,000 desperately ill patients like Tully a second chance at life. On the other is Baxter International, a giant pharmaceutical company that has accused its tiny rival of infringing on one of its patents. It wants CellPro to yank the therapy off the market or hand over its profits on the treatment. But doing so would bankrupt the company, according to CellPro's executives, stranding thousands of potential patients. That's because only CellPro makes the product—and Baxter itself is at least a year from receiving regulatory approval for its own.

The stakes in the controversy are huge. Some 25,000 patients receive bone-marrow transplants each year for diseases ranging from AIDS to lymphoma to breast cancer. And that number is growing by 30 percent annually, as doctors learn more about how diseases can be treated with aggressive transplant therapy. CellPro's product uses a unique technology to remove cancerous cells and to specifically select healthy, immune-building cells from bone marrow extracted from a patient. The marrow is re-implanted following radiation and chemotherapy. The process may reduce the risk of recurrence and moderate the often severe side effects of such therapy. "If this technology passes all the tests," says biotech analyst Rich van den Broek at Hambrecht & Quist, "it could become a $100 million business in a very short time."

CellPro won approval of its treatment for certain types of cancer from the Food and Drug Administration last December. Clinical trials for using the technology to treat other diseases are underway at scores of medical centers in the United States and Europe. Emory University, for example, is using it to try to save children dying of leukemia; other researchers believe it could help bring cures for lupus and, as in Tully's case, multiple sclerosis. Dr. Kent Holland at Emory calls it "one of the biggest breakthroughs in transplant therapy in the last decade." Four U.S. senators and the president of the American Cancer Society recently encouraged Secretary Donna Shalala of the Department of Health and Human Services to force Baxter to extend a license to CellPro in the public interest.

It's unclear which company is in the right. Earlier this spring, a federal judge ruled that CellPro had knowingly used technology patented by Johns Hopkins University and licensed by Baxter. (Many medical researchers, on the other hand, disagree with the court's verdict—as did the jury in the case, which the judge overruled.) Baxter also accuses CellPro of using "scare tactics" to try to steal the drug company's rights to the treatment. "CellPro is saying this technology won't be available to cancer patients, and that's not true," says John Osth, president of Baxter's immunotherapy division. "We're not asking for their product to be taken off the market until ours can replace it."

That would be cold comfort for CellPro, especially if it's forced to yield a big chunk of its sales revenues to Baxter. What's more, CellPro executives argue that allowing their products to remain on the market only until Baxter comes up with its own is really just a clever way for the drug company to cash in on CellPro's clinical trials without incurring any costs. Clearly, both sides are playing a savvy game of pharmaceutical hardball here, and the outcome is anyone's guess. "We'll prevail on appeal," promises CellPro president Rick Murdock, whose commitment to CellPro's product is nothing less than messianic. And small wonder. Diagnosed a year ago with a rare type of lymphoma and given less than two years to live, Murdock became CellPro's first human test case. That he today appears to be cancer-free is a testament to the human dimension of what otherwise would be just another business squabble. ■

The Seattle Times

THURSDAY, APRIL 17, 1997

Patent litigation threatens cell-therapy progress

RON WURZER / SEATTLE TIMES

Litigation threatens *cancer and other research supported by CellPro products. Here Julie Nolan works on filling columns of bead gel at the biotech company's Bothell facility.*

Trials depend on CellPro product

BY KEITH ERVIN
Seattle Times Eastside business reporter

Nearly three years ago, physicians at the Emory University School of Medicine in Atlanta began testing a new therapy in a last-ditch effort to save the lives of children suffering from acute leukemia.

Most of the children died, either from complications from the stem-cell transplant or from a recurrence of leukemia. Four of them are alive and well, apparently cancer-free.

Now, after enrolling more children for a follow-up study using an improved method for removing incompatible donor cells, researchers are worried that a legal dispute between competing rival biotechnology firms could stop the research.

The litigation is also taking a heavy toll on CellPro, the 8-year-old Bothell company that produces the system – one used to separate blood-producing stem cells from other cells, including tumor cells.

CellPro's Ceprate SC Stem Cell Concentration System was approved by the Food and Drug Administration in December for use in bone-marrow transplants for breast cancer, lymphoma and other cancers. It is also under study in hospitals around the country for treatment of cancers and immune-system disorders such as multiple sclerosis.

The system uses an antibody patented by Johns Hopkins University to isolate stem cells.

A federal court jury in Wilmington, Del., last month found that CellPro had willfully infringed on two Johns Hopkins patents. The jury ordered the Bothell firm to pay $2.3 million in damages to Johns Hopkins and its licensees, health-care giants Becton Dickinson and Baxter International. CellPro stock, once trading for more than $30 per share, closed at $5.75 yesterday.

A number of cancer researchers are worried that clinical trials will be halted if CellPro is prevented from providing free antibodies. Switching research from the CellPro product to the competing Baxter product would delay research for at least a year, according to research administrators at Emory and Northwestern universities.

CellPro, claiming the Johns Hopkins patent is invalid, plans to appeal the ruling. The company has also asked the U.S. Department of Health

PLEASE SEE *CellPro* ON D 4

Patent litigation threatens CellPro-backed clinical trials

CellPro

CONTINUED FROM D 1

and Human Services for permission to continue selling the product, based on a compelling public interest and the fact that the research at Johns Hopkins was supported with federal dollars.

The future of CellPro and continued research using its products are further clouded by motions pending in U.S. District Court for additional damages and for restrictions on sales: Johns Hopkins, Becton Dickinson and Baxter have asked for treble damages of $6.9 million, legal costs of $7 million, and a phase-out of sales.

The phase-out plan would require that CellPro pay royalties of at least $2,000 for each use of its product and cease providing any products free.

Deborah Spak, spokeswoman for Baxter International, said the phased injunction was proposed as a way of ensuring that patients' needs are met until Baxter's own stem-cell separator receives FDA approval.

"We would have been well within our legal rights to ask for a permanent injunction immediately," Spak said. "We want to make sure there's a smooth transition to a technology that's licensed under the patents. At the same time it's not fair for CellPro to reap financial reward from continued infringement of those two patents."

But CellPro President Richard Murdock accused Baxter and its partners of a public-relations ploy, saying they "know full well" that his company can't afford to sell its product while paying the proposed damages and royalties. Murdock claims the Baxter-proposed injunction would stop clinical trials now underway.

Among those studies is a joint effort by six hospitals, including the Fred Hutchinson Cancer Research Center, using CellPro's Ceprate SC and Ceprate TCD systems to treat children for whom no other treatment is available. The TCD system is intended to remove donors' immune-system cells that can cause complications after peripheral blood stem-cell transplants.

"It's unfortunate that these sorts of things in corporate America can threaten therapeutic clinical trials and potentially life-saving therapies," said Dr. Andrew Yeager, director of Emory University's bone-marrow transplant programs.

During an earlier study using only Ceprate SC, four of 16 children with childhood leukemia recovered from the disease after stem-cell transplants at Emory. The new study is intended to improve survival rates by removing incompatible immune-system cells from the stem cells of "mismatched" donors.

Also concerned about possible effects of the litigation is Dr. Richard Burt, director of allogeneic bone-marrow transplants at Northwestern University outside Chicago. He said Ceprate SC has reduced cancer patients' hospital stays after transplants from four weeks to 11 days.

Burt also reports "encouraging results" in using the antibody to treat patients suffering from potentially fatal forms of multiple sclerosis, lupus and rheumatoid arthritis. But more studies are needed, he said.

Biotech stock analysts say CellPro is blessed with enough cash reserves to continue battling. For investors who own CellPro stock, "I would recommend that they keep holding it," said Ragen MacKenzie analyst Andrew Heyward. "But we're not buying or selling it."

AP Associated Press

Cancer Patients in Patent Fight

By LAURAN NEERGAARD
Associated Press Writer
Monday, May 5, 1997 5:56 pm EDT

WASHINGTON (AP) -- Desperate cancer patients including children with leukemia are caught in the middle in a fight between a drug giant and a biotechnology company over a patent for better bone-marrow transplants.

Doctors for one side say the court fight could kill patients by yanking the therapy off the market. The other company accuses those doctors of scare tactics. Now, some U.S. senators and patient advocates are pushing the government to intervene, in a complex battle that illustrates how business and medicine often intertwine.

The case ``could be precedent-setting,'' said Washington patent attorney Kate Murashige. ``It's a pretty extreme case, where you've got a real public interest here in people's health.''

CellPro Inc.'s Ceprate system won Food and Drug Administration approval in December as the first device to purify the cells vital for a bone-marrow transplant to succeed. Purification significantly cuts the severe side effects that cancer victims suffer when their bone-marrow cells are reinfused after chemotherapy, the FDA said.

In addition, 60 clinical trials nationwide are testing other life-saving uses. They include an Emory University attempt to save children dying of leukemia who cannot find matching bone marrow. Another trial involves ``purging'' cancer that lurks in transplant cells, an experiment that CellPro's own president believes saved him from otherwise untreatable lymphoma.

The problem: A federal judge this spring ruled that CellPro used technology it knew was patented by Johns Hopkins University and licensed to Baxter International.

Now Baxter has asked for an injunction on Ceprate sales. But CellPro says that would put it out of business -- and consequently take a life-saving product off the market.

``We won't be able to offer treatment to any of these children'' if that happens, said Emory's Dr. Kent Holland. In a small pilot trial, he found the experimental treatment saved about 40 percent of certain leukemic children ``who have no other therapy that they could even attempt to undergo.''

A furious Baxter accuses CellPro of unfairly scaring vulnerable patients. Attorney Donald Ware argues Baxter would allow limited Ceprate sales,

with fair compensation, and continued experimental access to Ceprate until Baxter's own cancer treatment wins FDA approval. That could be two years away.

"I'm offended and hurt by the implication that I would be part of anything that would hurt a patient," said Dr. Curt Civin, the Johns Hopkins pediatric oncologist who patented the technology.

Nevertheless, CellPro has taken the unprecedented step of asking the federal government to allow Ceprate sales to continue under an obscure law that essentially could repossess the patent.

Lawmakers including Sen. Alfonse D'Amato, R-N.Y., and the American Cancer Society are lobbying Donna Shalala, the Health and Human Services secretary, to take that step.

It's a case that illustrates how medicine is business -- because lucrative patent laws, not some charitable instinct, provide the incentive to create treatments, explained Paul Root Wolpe of the University of Pennsylvania's Center for Bioethics.

CellPro is "not the poor innocent company who got shafted," he said. "Everybody in business knows you don't use a patented product without a license. As so often is the unfortunate result, the people who end up suffering are the patients."

At issue is purifying stem cells, the progenitors of blood and immune cells found in bone marrow and certain types of blood.

Patients typically freeze bone marrow before high-dose chemotherapy, and then get back the thawed cells, but remaining traces of toxic preservatives can cause serious side effects.

CellPro's therapy uses a monoclonal antibody, a "cellular bloodhound" that latches onto the stem cells -- the only cells the body really needs -- and, with a magnetized machine, pulls the thimble-full of life-saving cells from a liter of marrow. The result is safer treatment.

But Hopkins' Civin discovered the first stem cell antibody in 1981, winning a patent to the entire class of cell hunters, including the one CellPro later used. Yet CellPro rejected as too expensive a Baxter offer for a patent sublicense in 1991, fighting the patent as too broad.

Baxter counters that CellPro should have simply spent its estimated $10 million in attorneys' fees on a patent license.

CellPro President Rick Murdock argues the court action could end exciting Ceprate experiments. Emory's Holland, for example, is creating matching stem cells for leukemic children who can't find a matching bone-marrow donor.

And Murdock used Ceprate to purge from his own stem cells traces of cancer that had leaked into his bloodstream before his chemotherapy. He is in remission a year later.

"We're going to prevail when it gets to the appeals court," Murdock predicted. "But if they take us off the market in the meantime, we won't survive."

Newsday
THE LONG ISLAND NEWSPAPER
June 4, 1997

One Step Closer To New Odds

Some breast cancer patients on Long Island may owe a debt to Carmen Imbo.

Carmen Vella Imbo grew up both in Astoria, Queens, and, in the summertime, in her family's summer cottage in Mastic Beach, where at 15 she met the boy next door, Ralph Imbo. Now, 28 years later, Carmen and Ralph and their two children, Alexandra, 14, and Jonathan, 12, live in Port Jefferson Station. Carmen's mother, Anna Vella, lives in Bayside. Carmen's sister, Mary Ann Bechhofer, lives in Shirley; and her mother-in-law, Connie, who will watch the Imbo children during Carmen's stem cell, bone marrow transplant, still lives in Mastic Beach.

Ed Lowe

Carmen Imbo was diagnosed with breast cancer three years ago, at the age of 40.

"When I was 38," she said, "I went for a screening mammogram. It was read as negative, and I was told to come back in two years. Luckily, eight months later, I went to reach for a twenty-pound box of laundry detergent in my garage, and it fell on me. I lost my grip, and the box hit me in the right breast, causing an inflammation. When the inflammation didn't clear up, I went for a second mammogram, and they told me to see a surgeon immediately, because there was a problem. When the surgeon looked at that mammogram and compared it to the previous one, what he saw was on the previous one, too. It was just missed. I often think to myself that something or someone saved my life by pushing this soap onto me. I had a lumpectomy. I had chemotherapy and radiation. I had a 94 percent chance of beating it.

"I was fine up until January of this year," she said. "I found a tiny lump at the base of my neck, very tender to the touch. To make a long story short, they found that the cancer had metastasized. After that, I went to see my oncologist, who started me on chemotherapy again in preparation for a stem cell transplant, which he said I should have. I happen to work for a doctor, and I happened to read an article about the purging of blood of tumor cells through a machine developed by a company in Seattle and used at Johns Hopkins in Baltimore. I asked the head of the transplant team at Stony Brook about it, Dr. Jonathan Harrison, and he said he had asked about this machine for Stony Brook, but that not enough studies had been done to prove that the machine increases your odds. *Sloan-Kettering doesn't even have it.* But common sense said to me that in any case, you don't go through all this just to put back into your system blood carrying tumor cells, not if you can avoid it."

Imbo felt so strongly about the technology — coincidentally widely publicized last month in news stories about a David-Goliath battle between CellPro, the Seattle-based manufacturer of the blood filtration technology, and Baxter International, a giant pharmaceutical company that claims CellPro has infringed on one of its patents — that she seriously considered the consequences of going to Baltimore for her bone marrow transplant. "It might mean selling our house, if my health insurance doesn't cover it," she said last week. "At the very least, it would mean being away from my entire family for the month that I would have to stay down there."

CellPro's product, called an apheresis machine, filters cancerous cells and specifically selects healthy, immune-building cells from bone marrow extracted from a patient. Only CellPro manufactures the machine, but Baxter has claimed in court that the process includes technology on which Baxter holds a patent. However, Baxter does not have the technology in production and won't for some time. Team leader

Please see LOWE on Page A49

Persistence of One May Help Many With Cancer

LOWE from Page A8

Harrison and Imbo's oncologist, Dr. Stanley Ostrow, agreed that Imbo's "common sense" argument made, well, common sense, but both said that research has not proved the procedure of significant value. "The very fact that nobody in the Northeast is routinely using it tells you a lot," said Harrison. "If its value was so clear-cut, believe me, a lot of people would be using it routinely. The issue here I think is that we're dealing with modifications in technology which may or may not make a difference, when it's the treatment — the transplant, itself — that is the key, not the possible modifications in the treatment, or the techniques, depending on the center you go to."

Understandably zealous, and convinced that her doctors privately agreed with her but had to use cautionary language publicly to spare University Medical Center at Stony Brook any implied criticism, Imbo contacted breast cancer research advocate Lorraine Pace of West Islip, hoping she could start a foundation to donate the technology to the medical center in time for her own surgery about a month from now. Last week, during a breast cancer news conference at Stony Brook involving actor Alec Baldwin and his mother, Carol, a breast cancer survivor, Pace asked assembled hospital executives whether they would accept the CellPro technology if a foundation suddenly raised the money to buy it. They said yes.

On Friday, Imbo called CellPro to ask how much money she would have to raise, and could such a foundation buy the machine. CellPro never had received a call from a patient before, and said that because of their huge legal entanglements they now may be enjoined from selling it to anybody. (Four U.S. senators, including Alfonse D'Amato (R-N.Y.), and the president of the American Cancer Society recently petitioned Secretary of Health and Human Services Donna Shalala to force Baxter to extend a license to CellPro in the public interest.)

Anyway, one of CellPro's marketing executives next spoke with company CEO Rick Murdock, who in world-class irony last year became the technology's first, human test case, when stem cell purging by his own product evidently cleared his system of a rare form of advanced, mantle-cell lymphoma.

On hearing Imbo's story, Murdock told company officials to give Stony Brook the device.

SCIENCE
6 JUNE 1997
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Varmus to Rule in Fight Over Cell-Sorting Technology

When a scrappy biotech company near Seattle called CellPro Inc. lost a patent fight to Johns Hopkins University in March, it lashed out with an emotional counterattack. Aided by a high-priced publicity firm—Burson-Marsteller of New York—it began spreading a heart-tugging tale of distress. Its message: A cell-sorting device made by CellPro, which had helped save the life of the company's own CEO, Rick Murdock, and could be used to help thousands of other cancer patients, is being suppressed by its competitors, Becton Dickinson and Co. and Baxter Healthcare Corp. The two companies have licensed rights to the technology from Hopkins, which holds patents on the cell-sorting concept. To protect the public, CellPro argues, Secretary of Health and Human Services Donna Shalala should take control of the disputed patents and give CellPro a reduced-cost license to exploit them.

Shalala received CellPro's formal appeal in May amid a well-orchestrated blast of publicity and a swarm of letters from Congress favoring CellPro (see sidebar, p. 1490). She promptly handed it to Harold Varmus, director of the National Institutes of Health (NIH). It landed on Varmus's lap because NIH funded the basic science behind the device, which is used to collect stem cells from patients who are undergoing cell-killing cancer therapy. The cells are saved and returned to the patients to rebuild their blood and immune systems.

RICH FRISHMAN

Lifesaver? CellPro CEO Rick Murdock with disputed machine used in his own treatment.

CellPro is appealing to Shalala under the Bayh-Dole Act, a 1980 law designed to encourage academic scientists to patent and exploit their federally funded discoveries. The law says the government retains the right to march in and redistribute patents in rare circumstances—if the patent holder fails to develop an invention "within a reasonable time," or if the government must "alleviate health or safety needs which are not reasonably satisfied." No company has persuaded the government to do this before.

A great deal rides on Varmus's review. At this writing, a Delaware court is weighing what penalty to impose on CellPro for infringing Hopkins's patents. And CellPro claims that if it is not rescued, the court may force it to stop distributing its device to new customers, denying patients lifesaving treatment. Hopkins and its partners are trying to persuade the court to adopt an order that would, among other things, require CellPro to share about 50% of sales revenue.

Hopkins, arguing that no patients will be deprived of therapy, says the fight is really about property—whether one clever group of researchers can grab another's work. "It's scary," says Hopkins spokesperson Gary Stephenson, "to think that popular pressure might overturn our legal rights." Frank Adkinson, vice dean of research at Hopkins's medical school, says that if the government marches in to break the patent agreements, biotech companies may be scared off from investing in university projects in the future. "What's at stake here is much broader than just Hopkins's interests," says Adkinson. The CellPro appeal, he argues, puts at risk "all inventions derived from government-sponsored research."

The NIH-funded research that spawned this brawl took place in the early 1980s in the laboratory of Hopkins oncologist Curt Civin. No one disputes that Civin was the first to identify a human antibody (My-10) that binds to a surface protein on primitive cells in blood and bone marrow (now called CD34 cells). Civin's discovery, published in 1984, suggested a way to isolate large quantities of elusive stem cells, prized for their ability to generate all other types of blood cells and replenish the immune system.

After publishing his findings, Civin and Hopkins sought broad patents on the My-10 antibody and methods of using it to isolate precursor cells. They won four patents, issued from 1987 to 1992. And Hopkins licensed the commercial rights to Becton Dickinson and Co. and, in subsidiary agreements, to Baxter and two other companies.

Scientists at the Fred Hutchinson Cancer Research Center in Seattle, meanwhile, began to look for ways to exploit Civin's discovery. One group found an antibody, called 12.8, that recognizes a different element, or epitope, of the same My-10 antigen on CD34 cells. The new find proved very useful because—unlike My-10, which links only to human cells—12.8 also links to baboon CD34 cells. This makes 12.8 valuable for animal experiments, essential to pave the way to human clinical trials, which, in turn, are essential for winning marketing approval from the Food and Drug Administration (FDA) for a new medical device.

A Hutchinson researcher, Ronald Berenson, obtained licenses from Hutchinson to the 12.8 monoclonal antibody system, which Hutchinson had not patented, and, in 1989,

The Madison Avenue Treatment

The Wall Street Journal may have been the first national publication to add a touch of human drama this spring to a fight over patents on a blood-processing technique (see main text). In a 1 May report headlined, "CEO Owes His Life to His Company's Technology," the *Journal* described how Rick Murdock, the chief executive of CellPro Inc., in Bothell, Washington, was threatened by a rare and usually fatal cancer (mantle cell lymphoma). Murdock volunteered to be a "guinea pig" in 1996 for treatment with CellPro's own machine. Physicians at the Fred Hutchinson Cancer Research Center in Seattle used the device to concentrate stem cells from Murdock's blood and rebuild his immune system after radiation and chemotherapy.

Murdock improved. But the *Journal* noted that Murdock's company might not survive because it has been sued by Johns Hopkins University for infringing the university's patents, and might be barred from selling its blood-processing machine. Shortly afterward, similar reports appeared in *Time*, *Newsweek*, and on the television show *Prime Time Live*.

Almost at the same time, members of Congress began sending appeals to their colleagues and to Donna Shalala, Secretary of the Department of Health and Human Services, urging HHS to grant CellPro a waiver from the patent laws. Representative Rick White (R–WA), whose district is home to CellPro, along with 24 other House members and 12 senators, pleaded for CellPro. The American Cancer Society also lobbied Shalala to help CellPro "on behalf of hundreds of thousands of cancer patients and their families." But two members of Congress, Senator Barbara Mikulski (D–MD) and Representative John Porter (R–IL), representing the home states of Hopkins and its business partner, Baxter Healthcare Corp., wrote to Shalala asking her not to intervene.

"The media have just been pummeling us," grumbles Johns Hopkins medical school spokesperson Gary Stephenson, crediting a "phenomenal job" by CellPro's publicity agency in New York, Burson-Marsteller. Even John Osth, president of the Baxter division that licensed the Hopkins patents, marvels that his adversary's public relations has been "very, very good." When CellPro's director of corporate relations, Joann Reiter, was asked how reporters learned of Murdock's cancer, she said: "We told them. We said, 'We think this would be a great story: What do you think?' "

Baxter, meanwhile, is taking a leaf out of its competitor's notebook. It has retained the Madison Avenue firm of Manning Selvage & Lee to flog its own message—that Shalala should not intervene in this patent fight. –E.M.

By His Own Device

A biotech lab races to perfect a new treatment for cancer just in time to save its dying CEO

CEO Owes His Life to His Company's Technology

A Deadly Serious Fight

Lives may be at stake in this biotech battle

Media blitz. CellPro has generated widespread publicity about the treatment of its CEO.

joined with others to form CellPro. In 1991, CellPro received advice from its attorneys that the company did not have to honor the Hopkins patents. CellPro has subsequently argued that Civin's discovery was too obvious to deserve a patent, and that, in any case, patents based on My-10 do not cover a product based on Hutchinson's 12.8 antibody.

The Hopkins group didn't see it that way, however. After several attempts to negotiate shared rights to CD34 technology failed, Hopkins, Baxter, and Becton Dickinson sued CellPro in 1994 for infringing the Civin patents.

When CellPro's legal defenses were put to trial in Delaware's federal district court beginning in 1995, the jury ruled in favor of CellPro on every point. However, after deliberating for nearly a year, Judge Roderick McKelvie threw out the jury's verdict, saying he had made an error in instructing the jury. In 1996 McKelvie ordered a new trial, asking the jury to determine one thing: Did CellPro act willfully in infringing the patents? In March 1997 the new jury ruled that CellPro had indeed acted willfully. CellPro intends to appeal, but it isn't just waiting for the court to act.

Even before the verdict, CellPro began marshaling its political and legal forces to petition Shalala and Varmus. To present its case, CellPro hired the co-author of the Bayh-Dole Act, former Senator Birch Bayh (D–IN) and Washington, D.C., attorney and former White House counsel Lloyd Cutler. In briefs recently submitted to Shalala and NIH, they claim that Hopkins and its partners "essentially sat on the sidelines" while CellPro developed a workable CD34 cell processing device. They note that CellPro submitted a premarketing application to FDA in 1993 and won approval in December 1996. Baxter, which obtained its license in 1990, submitted its FDA application in February 1997. It cannot be certain if, or when, its machine will be approved for sale.

CellPro's lawyers pulled out all the stops in describing what may happen if the government does not intervene. "Thousands of victims of the most acute forms of metastatic breast cancer ... would be forced to undergo less optimal treatment with unnecessary suffering, and, in some cases, death," they write. And they warn that children with leukemia "will surely die" unless they are allowed to use CellPro's machine to purge aggressive T cells from imperfectly matched donor material. Hopkins dismisses these arguments, contending that Baxter's cell-concentrating device works as well as, or better than, CellPro's and has been marketed in Europe since 1995. Baxter executive John Osth claims that scores of his machines have already been approved for experimental use in U.S. clinics.

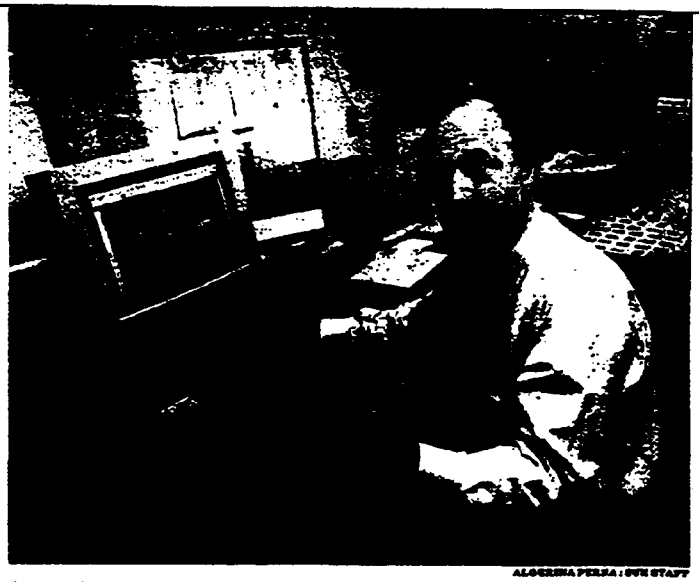
Several bone marrow transplantation experts who spoke to *Science* confirmed that both the Baxter and CellPro devices work well and are available in clinics. But Malcolm Brenner of St. Jude Children's Research Hospital in Memphis, Tennessee, says the main advantage of the CellPro machine is not its technical capabilities but the fact that the CellPro device has an FDA license. This means that any clinician can simply buy one and use it, while one must get Baxter's permission and apply for an FDA experimental-use permit to use the Baxter machine. "It certainly makes our life easier" if a machine is already approved, Brenner says.

One remarkable element in this fight is that most of the clinics that are buying the CellPro machine aren't using it for the procedure for which it was approved: autologous bone marrow transplantation. The procedure is "not done much," says Brenner, who notes that the machines are being used primarily for stem-cell collection from peripheral blood for experimental therapies—"off-label uses" not approved by the FDA. Although such uses are legal, advertising them is not. Indeed, FDA reprimanded CellPro in January 1997 for sending out a "false and misleading" Christmas card that, in FDA's view, promoted CellPro's device for use in parent-to-child peripheral blood transplants.

In serving as arbiter, NIH has set a goal of deciding within 60 days (possibly in early August) whether the evidence of a public health crisis is strong enough to warrant action. NIH may call for public hearings, providing a basis for a final decision on whether or not the government should take control of the Hopkins patents.

–Eliot Marshall

THE SUN



ALGERINA PEREZ : SUN STAFF

Researcher: *Dr. Curt I. Civin, chief of pediatric oncology at Johns Hopkins Hospital, found a way to flag "good cells" and extract them from blood or bone marrow.*

Patients, patents, profits tangled in technology suit

Hopkins scientist's cancer-fighting find is at the center of dispute

By M. William Salganik
SUN STAFF

Sitting in Room 212 at the Johns Hopkins Oncology Center are two machines — apparently normal hospital lab equipment. Unremarkable as they seem, they are at the center of a battle with literal life-or-death consequences.

It is a battle over cancer patients, arcane patent laws and the right to claim a multimillion-dollar market.

Both machines sort cells. They can paw through blood or bone marrow to pluck out "good" cells and discard cancerous or other unwanted cells. The process can improve the chances of cancer patients who receive blood or bone marrow transplants.

One machine — still in the approval process — is made by medical device giant Baxter Healthcare, under license from Hopkins. The other — on the market since December — is made by biotech start-up CellPro. According to a federal court ruling in April, CellPro violated Hopkins' patents. After a $20 million legal battle, the court said, in effect, CellPro had stolen Hopkins' research.

Now, Hopkins and Baxter want the court to order CellPro to turn over any profits it makes from its machine to them. If that happens, CellPro says, the only approved machine would be taken off the market — denying treatment to thousands of cancer patients and cutting short promising research.

"If we lose money on every sale, we go out of business, and the patients don't get treated," says Joann Reiter, CellPro's director of investor relations. [*See Machines, 12A*]

TERESA TANGEA : SPECIAL TO THE SUN

The Ceprate: *CellPro CEO Richard Murdock with the machine developed by his company — and used to fight his own cancer.*

article continues on next page.

Hopkins scientist's cancer-fighting find is at center of suit

Hopkins and Baxter contend that they have no intention of stymieing research or denying treatment to anyone. The CellPro device can be used until the Baxter machine receives full approval, which could come by the end of the year, they say.

"CellPro's continuing campaign to glorify its theft of Hopkins' intellectual property in the name of patient care misrepresents the facts and threatens to undermine long-term investment in new medical technologies," they said in a filing Monday with the federal government.

CellPro is "scaring a lot of people," says Dr. Curt I. Civin, the Hopkins scientist who made the discoveries the machine evolved from. "We're getting calls from frightened patients and their families. This sure looks to me like ... a calculated business strategy."

CellPro is still fighting in court, arguing over the order to be issued in the patent case and preparing an appeal. Beyond that, it is taking the highly unusual step of asking the federal government to step in under a never-before-exercised provision of law and grant it a license to keep marketing its machine in the public interest.

To get the government's attention, CellPro is mounting an unabashed lobbying and public relations campaign. "Political pressure certainly plays a part here," says Richard Murdock, CellPro's chief executive officer. "That's a lot of the reason we've been trying to tell everybody the story — because of the importance of this issue."

Murdock himself has a compelling story to tell. A year ago, he developed mantle-cell lymphoma — a rare form of cancer. His doctors told him that there was no treatment, that he had less than three years to live. His own lab staff worked day and night on "the Rick Project," scrambling to find a way to use CellPro's machine in a way it hadn't been used before, to purge cancer cells. It worked; he is cancer free.

Over the past few weeks, the tale has been covered in the *Wall Street Journal* ("CEO Owes Life to His Company's Technology"), *Time* ("A biotech lab races to perfect a new treatment for cancer just in time to save its dying CEO"), *Newsweek* ("Lives may be at stake in this biotech battle"), and the television show "Prime Time Live."

In a memo to Hopkins trustees, Dr. William R. Brody, president, and Dr. Edward D. Miller Jr., dean of the medical school, wrote: "What CellPro could not win in court, it has sought to win in a public relations campaign."

ALGERINA PERNA: SUN STAFF

Together: *In the oncology department at Johns Hopkins Hospital, CellPro's machine (left) and Baxter Healthcare's, sit adjacent. The equipment is the subject of a patent suit.*

At stake is access to a vast market — large enough that each side says it has spent more than $50 million developing its machine.

Murdock says the potential market can be estimated by taking the number of cancer-related transplants in the United States (about 25,000 a year) and Europe (about 22,000) and multiplying by $4,325, the cost of the CellPro materials per patient. That's about $200 million a year — and Murdock says the number of transplants is growing by 20 percent to 30 percent a year.

John A. Osth, president of Baxter's immunotherapy division, says that the market will be "over the next three to five years, on a global basis, at least $100 million," but that as new uses for the technology are developed, "you pick a number at that point."

Hope in an antibody

The story began nearly two decades ago when Civin, then a young Hopkins researcher, now chief of pediatric oncology, discovered that stem cells — the immature cells that grow into blood and immune system cells — have a chemical called CD34 on their surface. He developed a protein, an antibody, that would bind with CD34.

"The antibody puts a flag on stem cells," Civin says. "And we can turn that flag into a hook."

Doctors use such a "hook" to isolate stem cells for transplants in cancer patients. Transplanting stem cells exclusively avoids two dangers: a potentially fatal rejection if a donor's blood or marrow containing mature immune system cells is used; or the reinsertion of stray cancer cells if the patient's blood or marrow, removed prior to chemotherapy or radiation, is used.

"I think this is a breakthrough technology — not just applicable to cancer," says Dr. Hillard Lazarus, who runs the bone marrow transplant program at the Ireland Cancer Center of Case Western Reserve University in Cleveland.

Researchers believe the technology can also be applied to autoimmune diseases, such as lupus or multiple sclerosis, in which the body attacks itself.

Many researchers, however, are taking a wait-and-see approach, says Dr. Barry Meisenberg, deputy director of the Greenebaum Cancer Center at the University of Maryland Medical Center.

"There's no proof that this is important for the long-term prognosis," says Meisenberg, until recently director of the bone marrow transplant program at the Scripps Clinic in California. While lab studies are encouraging, he says, the new device has no track record to show whether patients are better off five or 10 years later.

And stem cells cannot help some types of cancer. Still, he says, given what is known, "If I were having treatment, I would grant one of these devices used."

Patent for protection

In 1984, three years after Civin developed his technology to hook the stem cells, Hopkins obtained four patents covering his discoveries and negotiated a license agreement with Becton, Dickinson & Co., which sued Baxter and Becton in federal court in Washington state in 1992, seeking to have the patents declared invalid. "We tried to keep Hopkins out of it," Murdock says. "Hopkins is one of our biggest customers." (Both the CellPro and Baxter machines are used.) Interest when the holder of a patent based on government-funded research fails to develop an invention quickly enough. CellPro initiated the march-in argument with NIH because the agency provided grants to Civin

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Patent for protection

In 1984, three years after Civin developed his technology to hook the stem cells, Hopkins obtained four patents covering his discoveries and negotiated a license agreement with Becton, Dickinson & Co., a large medical supply company that, among other lines of business, sells antibodies.

Becton kept the research and diagnostic rights to the Hopkins patents, but sublicensed the therapeutic rights to Baxter in 1990.

Although slower than some other universities to get into technology licensing, Hopkins now aggressively seeks patents on research done in its labs and expects its revenue from them to grow. Howard Califano, who runs the technology licensing office for the medical school, says his department has about 150 active licensing agreements, generating from $3 million to $4 million a year in royalties.

Of that, about a third goes to the faculty inventor, about a third to the lab where the research took place, and the remaining third is divided among the department, the school (such as medicine or engineering) and the university as a whole.

Civin says patents remove the potential conflict between publishing in academic journals — giving new research a wide public audience — and keeping discoveries secret so someone else won't commercialize it.

Califano says royalties on Civin's cell-selection technology have been about $100,000 a year, but he expects the figure to rise substantially when the Baxter device, now sold in Europe, is approved in the United States. A 3 percent royalty — Hopkins' typical royalty rate for medical devices is 3 percent to 5 percent of sales — on $200 million in sales is $6 million.

Baxter says it offered a sublicense to CellPro in 1992. Two other companies bought sublicenses for $750,000 and 8 percent of sales, according to a filing by Baxter and Hopkins with NIH. CellPro, the filing says, offered $500,000 up front and a royalty rate that worked out to 3.2 percent. The deal died.

CellPro tells a different story.

Murdock, its CEO, says Baxter offered a license but with unacceptable terms: "They wanted worldwide rights to our product." He says, "They offered us a license one time, then took [the offer] back." CellPro, he says, made other efforts to negotiate a license, and "each time we talked to them, the price went up."

Reiter, the investor relations director, says CellPro didn't believe it needed a license, but tried to get one "to avoid a five-year patent battle."

"It was a completely different technology, or we certainly thought it was," says Reiter.

But a five-year patent battle — so far — is what has resulted.

CellPro, based in suburban Seattle, sued Baxter and Becton in federal court in Washington state in 1992, seeking to have the patents declared invalid. "We tried to keep Hopkins out of it," Murdock says. "Hopkins is one of our biggest customers." (Both the CellPro and Baxter machines are used at Hopkins.) But the court ruled that Hopkins, as patent holder, was a necessary party, so the case could not proceed.

Hopkins, Baxter and Becton sued CellPro in 1994 in federal court in Delaware. (Both CellPro and Baxter are incorporated there.) In 1995, a jury found for CellPro. But the judge threw out the verdict, ruling that it was contrary to the evidence, and ordered a new trial.

In March, the judge ruled that the Hopkins patents were valid and that CellPro had infringed upon them. Frederick G. Savage, Hopkins' associate general counsel, says the ruling made it clear that the Hopkins patents covered not just the specific antibody Civin had constructed, but any antibody that attaches to CD34.

"The only way anybody knows how to get stem cells out is with a CD34 antibody," he says, "so adding that component into their machine makes it an infringing use."

The jury in the second trial was left to decide only whether CellPro had violated the patents intentionally and what damages should be. The answers: yes, the violation was "willful"; and $2.3 million.

CellPro says it has spent about $10 million on the legal battle. Savage says his side has spent about $9 million. Under the licensing agreement, he says, Baxter and Becton have been paying all the out-of-pocket legal costs.

An uncertain future

Now, the judge must decide what happens to CellPro and its machines.

Hopkins and Baxter ask that any profits from sales of CellPro's treatment materials — which they say is a minimum of $2,000 on the $4,325 product — go to them. (The machines are essentially provided free, but hospitals pay for the antibodies and disposable parts needed for each treatment.)

If CellPro is made to pay $2,000, "for every patient we treat, we lose money," Murdock says. "It would be more responsible to our shareholders to close our doors."

CellPro's doors are not about to close. Hopkins and Baxter argue in their NIH filings: "Since 1989 ... CellPro has been able to raise over $160 million from venture capitalists and in two public offerings. As of the end of 1996, it had $60 million in cash, the fruit of its unlawful infringement of Hopkins' patents. CellPro's cries of poverty are disingenuous."

CellPro wants the government to exercise "march-in rights" under the Bayh-Dole Act, something the government has never done in the nearly two decades since the law was passed. It allows government to "march in" in the public interest when the holder of a patent based on government-funded research fails to develop an invention quickly enough. CellPro initiated the march-in argument with NIH because the agency provided grants to Civin.

In its filing, CellPro asks for a license for its Ceprate machine. "There is a major health need," CellPro wrote, "that can only be satisfied by the Ceprate system."

Hopkins and Baxter reply that they expect Baxter's machine to be approved for use within the year.

CellPro counters that the approval process is more likely to take three years, and Baxter has no assurance that its machine will be approved at all.

Although long and expensive, the court fight is "a garden-variety case," says Stephen A. Bent, a specialist in intellectual property law who chairs the biotechnology practice at the Washington firm Foley and Lardner.

What is unusual, he continues, is "to have a technology with such immediate patient impact" in dispute, and CellPro's highly public effort to push the government to step in and order Hopkins to give it a license. He can recall only one other public push for such government action, involving an AIDS treatment, and there the impetus came from AIDS patients, not from a competing business.

Meanwhile, users of the CellPro device are concerned. Dr. Richard Burt, director of marrow transplants at Northwestern University, says he went through a complicated process to get federal permission for research using Ceprate to treat multiple sclerosis, lupus and rheumatoid arthritis. "For me to make a switch from CellPro to Baxter would shut me down a year because of the bureaucracy and the paperwork. Everything would come to a stop in what's helping patients and advancing medicine."

Patients seeking stem cell transplants "are desperate people — many of them fighting for their lives," says Diane Blum, executive director of Cancer Care, a support organization for cancer patients. "We don't want to see the [CellPro] product taken off the market, unless another product could replace it immediately."

"Our biggest concern comes down to the patient and access to a system that's proven beneficial," says Kerrie Wilson, vice president for advocacy and government operations for the American Cancer Society, which has written to Donna E. Shalala, secretary of Health and Human Services, asking for "careful consideration" of CellPro's march-in petition.

"We're not weighing in on the merits of the patent infringement case," says Wilson. "We just don't want the rights of the patient to be lost in this fight over patents and money and who owns what."

Separating good cells from bad

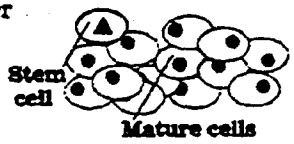
The problem:

Cancer patients are often treated with radiation or chemotherapy to knock out the cancer. The treatment can also weaken the immune system, which defends the body against diseases, making the patient vulnerable to infections and other disorders. Doctors often remove some blood or bone marrow before the cancer treatment, then put it back in the patient's body to restart the immune system. The blood or marrow, however, may contain cancer cells. In addition, blood or marrow from a donor contains immune system cells that may start to fight the body of the recipient.

The solution:

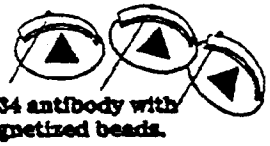
Dr. Curt I. Civin, a Johns Hopkins oncologist, developed a method for isolating rare stem cells – immature cells that can grow into healthy blood or immune system cells – for transplant. Below are simplified diagrams showing Baxter Healthcare technology as well as the technology employed in CellPro's machine.

Stem cells are rare – there's only one per 10,000 to 100,000 marrow cells and even rarer in blood



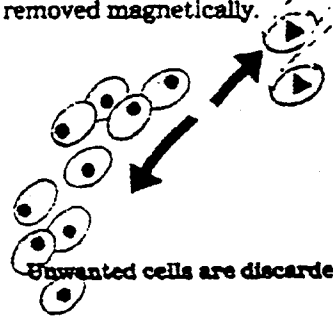
Baxter's technology

1 An antibody designed by Civin and containing a tiny magnetic bead – less than one-twentieth the width of a human hair – binds to a chemical on the surface of the stem cells. That chemical, called CD34, is not present in most mature cells or cancer cells.



CD34 antibody with magnetized beads.

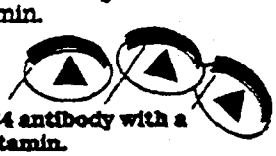
2 The stem cells, with the beads attached, are removed magnetically.



Unwanted cells are discarded.

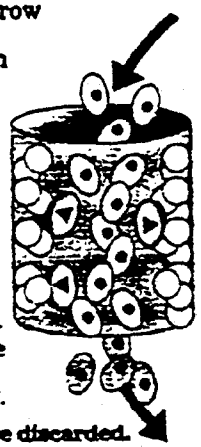
CellPro's technology

1 CellPro uses a different antibody to bind to the CD34 on stem cells and attaches instead of a magnetic bead, a B vitamin.



CD34 antibody with a B vitamin.

2 Blood or marrow is then run through a column lined with beads coated with a protein from egg whites. The B-vitamin on the stem cells sticks to the egg protein while the unwanted cells are discarded into a bag. The remaining stem cells are then collected into another bag.



Unwanted cells are discarded.

CHARLES HAZARD : SUN STAFF

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TECHNOLOGY

Bad blood over patent

A small US biotechnology company is fighting to keep a cancer treatment on the market as it opposes a large medical equipment company and a prominent university over a patent.

The skirmish pits CellPro, based in Bothell, Washington against Johns Hopkins University and Baxter International. The dispute concerns a CellPro treatment, based on research carried out at the Fred Hutchinson Cancer Center in Seattle, which allegedly infringes a patent held by Johns Hopkins University.

CellPro's treatment, Ceprate, is used in bone marrow transplants connected with cancer treatment. It collects healthy stem cells, the progenitors of blood and immune cells. The cells are reintroduced to patients after their chemotherapy.

More than 5,000 patients have received Ceprate, including children with intractable leukaemia – with some encouraging results.

CellPro portrays itself as an advocate for desperately ill cancer patients and the target of a ploy by Baxter to remove the only competitor to its own stem cell system, called Isolex. Baxter and Johns Hopkins say CellPro is unnecessarily scaring patients by saying a court order will shut down its clinical trials and drive it out of business.

In an unprecedented move, CellPro has asked the government to keep Ceprate on the market under the Bayh-Dole Act, which allows the government to repossess a patent to address a public health need. The company has the support of the American Cancer Society and congressmen, who have asked the government to intervene.

Patent lawyer Cal Griffith, of Jones, Day Reavis & Pogue, based in Cleveland, thinks CellPro has a chance. "The petition with the government is a nice first step. It raises the profile and publicity of this case, and puts the most pressure on," he said.

At issue are the special antibodies used to ferret out stem cells. A Johns Hopkins researcher discovered how to isolate and purify the cells and Hopkins received patents on the technology. Hopkins gave an exclusive licence to Becton Dickinson, which sublicensed Baxter.

Ceprate was approved in Europe in July 1996, six months after Baxter's Isolex came on the market. In the US Ceprate received government marketing approval last December, and Baxter expects to win approval for Isolex by the end of the year.

Richard Murdock, CellPro's chief executive, said the company "has always been willing to pay a reasonable royalty to avoid litigation," but Baxter kept on changing the terms of the agreement. Baxter said CellPro refused to accept a licence on three occasions on the same terms accepted by two other biotechnology companies. "If we were trying to clear the market of competitors, we certainly would not have licensed out the technology," said Baxter.

In March a federal judge ruled that CellPro wilfully infringed the Hopkins patent. An injunction may follow within the month. In the meantime, Baxter and Johns Hopkins have asked the federal court to permit CellPro to continue selling its device until an alternative is approved, and complete all its government-approved clinical trials. They want CellPro to pay them about $2,000 for each Ceprate system it sells.

Murdock said these conditions would put CellPro out of business. "We certainly will file an appeal. There is a lot to do here to save this company."

Marjorie Shaffer