From: [redacted]
To: jeevacation@gmail.com
Subject: fyi
Date: Tue, 25 Jan 2011 14:38:26 +0000

The Wall Street Journal

- BUSINESS
- JANUARY 25, 2011

Novel Effort To Fight Cancer With Cancer Cells

By RON WINSLOW

In an audacious twist on the concept of fighting fire with fire, scientists have developed a provocative strategy of fighting cancer with cancer.

Researchers at the Rogosin Institute are taking tumor cells from mice, encapsulating them in beads made from a seaweed-derived sugar called agarose, and implanting them in the abdomen of cancer patients. There, cells in the beads secrete proteins researchers believe could signal a patient's cancer to stop growing, shrink or even die.

So far, at least 30 patients have been treated with the cancer beads in an initial human study, and a phase two or intermediate-stage trial has been launched—with the approval of the U.S. Food and Drug Administration—to test the technique in patients with advanced colon, pancreatic and prostate cancers.

It's too early to know whether or how well the beads work in people, but in studies involving laboratory mice as well as dogs and cats stricken with cancer, the treatment substantially reduced the size of tumors. In some cases animals lived significantly longer than expected, according to two articles being published Tuesday in the peer-reviewed journal Cancer Research.

A Bead on Cancer

In a novel treatment currently under study, scientists are testing whether cancer cells implanted into patients can signal the patients' tumors to stop growing, shrink or even die.

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"This is a completely novel way of thinking about cancer biology," says Howard L. Parnes, a researcher in the division of cancer prevention at the National Cancer Institute who is familiar with the work but wasn't involved with it. "We talk about thinking outside the box. It's hard to think of a better example."

In animal and human studies so far, researchers led by Barry Smith, director of the Rogosin Institute, an independent treatment and research center affiliated with Weill Cornell Medical College and New York Presbyterian Hospital, have yet to

find evidence that putting mouse tumors into humans or other species causes any harm or serious side effects. Moreover, when they put human cancer cells in the beads and implanted them in mice, they saw the mouse cancer recede.

"They demonstrate a remarkable proof of principle that tumor cells from one animal can be manipulated to produce factors that can inhibit the growth of cancers in other animals," Dr. Parnes says. "This suggests that these cancer inhibitory factors have been conserved over millions of years of evolution."

Supporting this research is neither a big drug company nor a biotechnology startup. In a highly unusual set-up, Metromedia Co., the privately held broadcast and telecommunications company run by billionaire John Kluge until his death in September, is financially backing it.

The company's Metromedia Biosciences unit has put $50 million into the cancer project and intends to funnel the bulk of any revenue from the treatment should it reach the market into Mr. Kluge's charitable foundation.

The company is now developing a way to manufacture the beads on a large scale, says Stuart Subotnick, president of Metromedia and chief executive of the biosciences business.

Cancer is often described as a process of uncontrolled growth, but even tumor cells reach a point where when they're surrounded by enough similar cells, growth regulators kick in and instruct them to stop proliferating. The new strategy is based in part on that premise.

Dr. Smith and his colleagues believe the proteins secreted by the encapsulated tumor cells trick the patient's actual tumor cells into sensing similar cells are nearby.

The beads initially contain about 150,000 mouse kidney cancers mixed with agarose and wrapped with a layer of agarose that creates a shell. They are incubated in a culture where within days, 99% of the tumor cells die, Dr. Smith says. Those that remain have characteristics of cancer stem cells. They recolonize the beads within a few weeks.

"They reach a stable state in which there is cell division and cell death," Dr. Smith says. They are producing inhibitory factors that regulate their growth.

In the human studies, the beads, about the size of a pea, are implanted in the abdominal cavity. The number is determined by body weight, but typically involves 550 and 750 beads per treatment. The hypothesis is that in the body, the inhibitory factors are secreted by the beads, picked up by the bloodstream and detected by tumor cells outside the bead. Researchers believe the treatment effect begins to wane after about four months; retreatment is possible.

In the research being published Tuesday, Dr. Smith and his colleagues reported that in mice implanted with tumors, treatment with the cancer beads resulted 30 days later in tumors that were 30% to 60% smaller than tumors in untreated mice.

Among 54 dogs and cats, whose cancers occurred naturally, treatment with the beads was associated with longer-than-expected survival and in some cases, near-eradication of tumors. There wasn't a control group in the treatments involving dogs and cats, pets that had failed conventional treatment and whose owners agreed to try the experimental technique.

In one group of 11 dogs with prostate cancer that were treated with the beads, the median survival from diagnosis was 177 days, or nearly six months, compared to an expected survival of less than 50 days. One of the dogs lived for more than two years. A cat with breast cancer who received four treatments with the beads lived eight years after the initial diagnosis before dying of the disease.

"The lab data looks very compelling," says Daniel P. Petrylak, director of the prostate-cancer program at Columbia University Medical Center. He wasn't involved in the basic research and says he was initially skeptical of the approach. Now he plans to enroll prostate cancer patients in the phase-two study. "The real question is whether this is going to translate into patients," he says.

Dr. Smith says research so far indicates more than 700 different proteins or small proteins called peptides are secreted by the beads, including 25 to 30 that are known to have anti-tumor effects.

Among those are factors that turn up processes that promote cell death and reduce a cell's ability to induce formation of blood vessels needed to survive, Dr. Smith says.

Cancer researchers increasingly use a cocktail of chemotherapy and other so-called targeted therapies to disrupt the redundant systems many tumors have that enable them to evade or bounce back from the initial treatments.

"What we think we're doing is inhibiting the tumor's ability to do its normal thing from several different directions," Dr. Smith says.

Researchers hope data from the 30-patient early stage study will be presented later this year.

Write to Ron Winslow at [redacted]